ANTIBODY MOLECULES TO APRIL AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application Nos. 63/043,558, filed June 24, 2020; 63/091,002, filed October 13, 2020; 63/136,950, filed January 13, 2021; and 63/195,527, filed June 1, 2021. The contents of the aforementioned applications are hereby incorporated by reference in their entirety.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on June 17, 2021, is named P2029-7037WO_SL.txt and is 259,172 bytes in size.

BACKGROUND

IgA nephropathy is one of the most prevalent, chronic glomerular diseases worldwide. Conservative epidemiological estimates cite a global incidence of approximately 5-50 cases/million (children) and 10-40 cases /million (adults). This incidence of disease presents a regional bias with a higher prevalence in Asia and the Americas, with a particularly higher disease burden in Japan and regions of China. Biopsy confirmed cases of IgA nephropathy in Japan are projected at approximately 350,000. In the US, this projection is approximately 100,000—as such, it is the most frequently diagnosed 1° glomerular disease in adults. While a relatively indolent disease, IgA nephropathy leads to end stage renal disease (ESRD), *i.e.,* renal failure in 20-50% of patients within a 20-30 year span. These numbers are likely grossly underreported given the need to confirm the disease by kidney biopsy, a protocol that is variably practiced in various clinical settings. The disease has a complex pathogenesis with genetic, epidemiological, and potentially environmental components to disease etiology, pathology, and progression. It likewise has a variable clinical presentation ranging from asymptomatic to end-stage renal failure (ESRD). IgA nephropathy is caused by the deposition of IgA, typically in the form of immune complexes in the mesangium of the kidney. There are currently no disease-specific treatments to address primary disease or progression.

There is a need for developing new approaches for treating, preventing and diagnosing IgA nephropathy and other disorders that share similar disease mechanisms.

SUMMARY

Accordingly, in certain aspects, this disclosure provides a method for treating a disorder, the method comprising administering to a subject in need thereof an anti-APRIL antibody molecule described herein, wherein the antibody molecule is administered at a dose that reduces, or is likely to reduce, the level of aberrantly glycosylated IgA (a-g IgA), e.g. aberrantly glycosylated IgA1 (a-g IgA1), by at least 40% in the subject, thereby treating the disorder. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the level of a-g IgA is reduced by at least 40% about 4 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 8 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 12 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 16 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months. In an embodiment, the level of a-g IgA is reduced by at least 50%. In an embodiment, the level of a-g IgA is reduced by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the disorder is an APRIL-associated disorder. In an embodiment, the disorder is associated with an aberrant level of total IgA. In an embodiment, the disorder is a disorder associated with a-g IgA (e.g., a-g IgA1).

In an embodiment, the disorder is IgA nephropathy (IgAN). In an embodiment, the IgAN is a familial IgAN. In an embodiment, the IgA is an adult IgAN. In an embodiment, the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

In an embodiment, the disorder is a chronic kidney disease (CKD) or a disorder associated with CKD. In an embodiment, the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

In an embodiment, the disorder is Henoch-Schonlein purpura (HSP). In an embodiment, the disorder is cutaneous vasculitis or IgA vasculitis. In an embodiment, the disorder is IgA dermatitis, e.g., IgA bullous dermatosis. In an embodiment, the disorder is Waldenström macroglobulinemia (WM). In an embodiment, the disorder is lupus nephritis.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g

IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy. In an embodiment, the method further comprises determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the level of a-g IgA is determined in a sample from the subject. In an embodiment, the method described herein further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM and/or IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the anti-APRIL antibody molecule.

In an embodiment, administration of the anti-APRIL antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the anti-APRIL antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the anti-APRIL antibody molecule.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the anti-APRIL antibody molecule.

In an aspect, the disclosure features a method of treating a disorder, the method comprising administering to a subject in need thereof an anti-APRIL antibody molecule, wherein the administration reduces the level of a-g IgA (e.g., a-g IgA1) by at least 40% in the subject, thereby treating the disorder. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the level of a-g IgA is reduced by at least 40% about 4 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 8 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 12 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 16 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months. In an embodiment, the level of a-g IgA is reduced by at least 50%. In an embodiment, the level of a-g IgA is reduced by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the disorder is an APRIL-associated disorder. In an embodiment, the disorder is associated with an aberrant level of total IgA. In an embodiment, the disorder is a disorder associated with a-g IgA (e.g., a-g IgA1).

In an embodiment, the disorder is IgA nephropathy (IgAN). In an embodiment, the IgAN is a familial IgAN. In an embodiment, the IgA is an adult IgAN. In an embodiment, the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

In an embodiment, the disorder is a chronic kidney disease (CKD) or a disorder associated with CKD. In an embodiment, the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

In an embodiment, the disorder is Henoch-Schonlein purpura (HSP). In an embodiment, the disorder is cutaneous vasculitis or IgA vasculitis. In an embodiment, the disorder is IgA dermatitis, e.g., IgA bullous dermatosis. In an embodiment, the disorder is Waldenström macroglobulinemia (WM). In an embodiment, the disorder is lupus nephritis.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy. In an embodiment, the method described herein further comprises determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the level of a-g IgA is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject.

In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM and/or IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the anti-APRIL antibody molecule.

In an embodiment, administration of the anti-APRIL antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the anti-APRIL antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the anti-APRIL antibody molecule.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the anti-APRIL antibody molecule.

In yet another aspect, the disclosure features a method of treating a disorder, the method comprising administering to a subject in need thereof an anti-APRIL antibody molecule, wherein the antibody molecule is administered at a dosage (e.g., dose and frequency) that reduces, or is likely to reduce, the level of a-g IgA (e.g., a-g IgA1) by at least 40% in the subject, thereby treating the disorder. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the level of a-g IgA is reduced by at least 40% about 4 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 8 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is

reduced by at least 40% about 12 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 16 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months. In an embodiment, the level of a-g IgA is reduced by at least 50%. In an embodiment, the level of a-g IgA is reduced by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the disorder is an APRIL-associated disorder. In an embodiment, the disorder is associated with an aberrant level of total IgA. In an embodiment, the disorder is a disorder associated with a-g IgA (e.g., a-g IgA1).

In an embodiment, the disorder is IgA nephropathy (IgAN). In an embodiment, the IgAN is a familial IgAN. In an embodiment, the IgA is an adult IgAN. In an embodiment, the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

In an embodiment, the disorder is a chronic kidney disease (CKD) or a disorder associated with CKD. In an embodiment, the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

In an embodiment, the disorder is Henoch-Schonlein purpura (HSP). In an embodiment, the disorder is cutaneous vasculitis or IgA vasculitis. In an embodiment, the disorder is IgA dermatitis, e.g., IgA bullous dermatosis. In an embodiment, the disorder is Waldenström macroglobulinemia (WM). In an embodiment, the disorder is lupus nephritis.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy. In an embodiment, the method further comprises determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the level of a-g IgA is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM and/or IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the anti-APRIL antibody molecule.

In an embodiment, administration of the anti-APRIL antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the anti-APRIL antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the anti-APRIL antibody molecule.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of

tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the anti-APRIL antibody molecule.

In another aspect, the disclosure features a method of treating a disorder, the method comprising selecting a dose or dosage (e.g., dose and frequency) for an anti-APRIL antibody molecule, wherein administration of the antibody molecule at the dose or dosage reduces, or is likely to reduce, the level of a-g IgA (e.g., a-g IgA1) by at least 40% in a subject in need thereof; and administering the antibody molecule to the subject at the selected dose or dosage, thereby treating the disorder. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 4 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 8 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 12 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 16 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 50%. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the disorder is an APRIL-associated disorder. In an embodiment, the disorder is associated with an aberrant level of total IgA. In an embodiment, the disorder is a disorder associated with a-g IgA (e.g., a-g IgA1).

In an embodiment, the disorder is IgA nephropathy (IgAN). In an embodiment, the IgAN is a familial IgAN. In an embodiment, the IgA is an adult IgAN. In an embodiment, the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

In an embodiment, the disorder is a chronic kidney disease (CKD) or a disorder associated with CKD. In an embodiment, the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

In an embodiment, the disorder is Henoch-Schonlein purpura (HSP). In an embodiment, the disorder is cutaneous vasculitis or IgA vasculitis. In an embodiment, the disorder is IgA dermatitis, e.g., IgA bullous dermatosis. In an embodiment, the disorder is Waldenström macroglobulinemia (WM). In an embodiment, the disorder is lupus nephritis.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy. In an embodiment, the method further comprises determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the level of a-g IgA is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM and/or IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the anti-APRIL antibody molecule.

In an embodiment, administration of the anti-APRIL antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the anti-APRIL antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the anti-APRIL antibody molecule.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the anti-APRIL antibody molecule.

In an aspect, the disclosure features a method of treating a disorder, the method comprising responsive to a determination that administration of an anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA (e.g., a-g IgA1) by at least 40% in a subject in need thereof, administering to the subject an anti-APRIL antibody molecule, thereby treating the disorder. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 4 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 8 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 12 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 16 weeks after the antibody molecule is

administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 50%. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the disorder is an APRIL-associated disorder. In an embodiment, the disorder is associated with an aberrant level of total IgA. In an embodiment, the disorder is a disorder associated with a-g IgA (e.g., a-g IgA1).

In an embodiment, the disorder is IgA nephropathy (IgAN). In an embodiment, the IgAN is a familial IgAN. In an embodiment, the IgA is an adult IgAN. In an embodiment, the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

In an embodiment, the disorder is a chronic kidney disease (CKD) or a disorder associated with CKD. In an embodiment, the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

In an embodiment, the disorder is Henoch-Schonlein purpura (HSP). In an embodiment, the disorder is cutaneous vasculitis or IgA vasculitis. In an embodiment, the disorder is IgA dermatitis, e.g., IgA bullous dermatosis. In an embodiment, the disorder is Waldenström macroglobulinemia (WM). In an embodiment, the disorder is lupus nephritis.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy. In an embodiment, the method further comprises determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the level of a-g IgA is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM and/or IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the anti-APRIL antibody molecule.

In an embodiment, administration of the anti-APRIL antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the anti-APRIL antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the anti-APRIL antibody molecule.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of

tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the anti-APRIL antibody molecule.

In another aspect, the disclosure features a method of treating a disorder, the method comprising determining whether administration of an anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA (e.g., a-g IgA1) by at least 40% in a subject in need thereof, if the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, administration of the antibody molecule is initiated, continued, or maintained. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, administration of the antibody molecule is terminated, discontinued, or altered. In an embodiment, if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, a different therapeutic agent or modality is administered.

In an embodiment, the level of a-g IgA is reduced by at least 40% about 4 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 8 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 12 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 16 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months. In an embodiment, the level of a-g IgA is reduced by at least 50%. In an embodiment, the level of a-g IgA is reduced by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the disorder is an APRIL-associated disorder. In an embodiment, the disorder is associated with an aberrant level of total IgA. In an embodiment, the disorder is a disorder associated with a-g IgA (e.g., a-g IgA1).

In an embodiment, the disorder is IgA nephropathy (IgAN). In an embodiment, the IgAN is a familial IgAN. In an embodiment, the IgA is an adult IgAN. In an embodiment, the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

In an embodiment, the disorder is a chronic kidney disease (CKD) or a disorder associated with CKD. In an embodiment, the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

In an embodiment, the disorder is Henoch-Schonlein purpura (HSP). In an embodiment, the disorder is cutaneous vasculitis or IgA vasculitis. In an embodiment, the disorder is IgA dermatitis, e.g., IgA bullous dermatosis. In an embodiment, the disorder is Waldenström macroglobulinemia (WM). In an embodiment, the disorder is lupus nephritis.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy. In an embodiment, the method further comprises determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the level of a-g IgA is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM and/or IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the anti-APRIL antibody molecule.

In an embodiment, administration of the anti-APRIL antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the anti-APRIL antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the anti-APRIL antibody molecule.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the anti-APRIL antibody molecule.

In yet another aspect, the disclosure features a method of treating a disorder, the method comprising determining whether administration of an anti-APRIL antibody molecule at a dose or dosage reduces, or is likely to reduce, the level of a-g IgA1 (e.g., a-g IgA1) by at least 40% in a subject in need thereof, if the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% at the dose or dosage, administration of the antibody molecule at the dose or dosage is initiated, continued, or maintained. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40% at the dose or dosage, administration of the antibody molecule at the dose or dosage is terminated, discontinued, or altered.

In an embodiment, the level of a-g IgA is reduced by at least 40% about 4 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 8 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is

reduced by at least 40% about 12 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 16 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months. In an embodiment, the level of a-g IgA is reduced by at least 50%. In an embodiment, the level of a-g IgA is reduced by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the disorder is an APRIL-associated disorder. In an embodiment, the disorder is associated with an aberrant level of total IgA. In an embodiment, the disorder is a disorder associated with a-g IgA (e.g., a-g IgA1).

In an embodiment, the disorder is IgA nephropathy (IgAN). In an embodiment, the IgAN is a familial IgAN. In an embodiment, the IgA is an adult IgAN. In an embodiment, the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

In an embodiment, the disorder is a chronic kidney disease (CKD) or a disorder associated with CKD. In an embodiment, the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

In an embodiment, the disorder is Henoch-Schonlein purpura (HSP). In an embodiment, the disorder is cutaneous vasculitis or IgA vasculitis. In an embodiment, the disorder is IgA dermatitis, e.g., IgA bullous dermatosis. In an embodiment, the disorder is Waldenström macroglobulinemia (WM). In an embodiment, the disorder is lupus nephritis.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy. In an embodiment, the method further comprises determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the level of a-g IgA is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM and/or IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the anti-APRIL antibody molecule.

In an embodiment, administration of the anti-APRIL antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the anti-APRIL antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the anti-APRIL antibody molecule.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of

tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the anti-APRIL antibody molecule.

In an aspect, the disclosure features a method of treating a disorder, the method comprising determining whether administration of a therapeutic agent or modality other than an anti-APRIL antibody molecule described herein reduces, or is likely to reduce, the level of a-g IgA by at least 40% in a subject in need thereof, if the therapeutic agent or modality does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, administering an anti-APRIL antibody molecule described herein to the subject. In an embodiment, the antibody molecule is administered at a dose or dosage that reduces, or is likely to reduce, the level of a-g IgA by at least 40% in the subject. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the therapeutic agent or modality reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 4 weeks after the antibody molecule is administered. In an embodiment, the therapeutic agent or modality reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 8 weeks after the antibody molecule is administered. In an embodiment, the therapeutic agent or modality reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 12 weeks after the antibody molecule is administered. In an embodiment, the therapeutic agent or modality reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 16 weeks after the antibody molecule is administered. In an embodiment, the therapeutic agent or modality reduces, or is likely to reduce, the level of a-g IgA by at least 40% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months. In an embodiment, the therapeutic agent or modality reduces, or is likely to reduce, the level of a-g IgA by at least 50%. In an embodiment, the therapeutic agent or modality reduces, or is likely to reduce, the level of a-g IgA by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the therapeutic agent or modality is administered as a single dose. In an embodiment, the therapeutic agent or modality is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the disorder is associated with an aberrant level of total IgA. In an embodiment, the disorder is a disorder associated with a-g IgA (e.g., a-g IgA1).

In an embodiment, the disorder is IgA nephropathy (IgAN). In an embodiment, the IgAN is a familial IgAN. In an embodiment, the IgA is an adult IgAN. In an embodiment, the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

In an embodiment, the disorder is a chronic kidney disease (CKD) or a disorder associated with CKD. In an embodiment, the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

In an embodiment, the disorder is Henoch-Schonlein purpura (HSP). In an embodiment, the disorder is cutaneous vasculitis or IgA vasculitis. In an embodiment, the disorder is IgA dermatitis, e.g., IgA bullous dermatosis. In an embodiment, the disorder is Waldenström macroglobulinemia (WM). In an embodiment, the disorder is lupus nephritis.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy. In an embodiment, the method further comprises determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the level of a-g IgA is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM and/or IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the anti-APRIL antibody molecule.

In an embodiment, administration of the anti-APRIL antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the anti-APRIL antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the anti-APRIL antibody molecule.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the anti-APRIL antibody molecule.

In another aspect the disclosure features a method of reducing the level of a-g IgA (e.g., a-g IgA1) in subject, the method comprising administering an anti-APRIL antibody molecule to a subject in a need thereof, e.g., at a dose or dosage that reduces, or is likely to reduce, the level of a-g IgA by at least 40% in the subject, thereby reducing the level of a-g IgA. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the level of a-g IgA is reduced by at least 40% about 4 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 8 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 12 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% about 16 weeks after the antibody molecule is administered. In an embodiment, the level of a-g IgA is reduced by at least 40% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months. In an embodiment, the level of a-g IgA is reduced by at least 50%. In an embodiment, the level of a-g IgA is

reduced by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy. In an embodiment, the method further comprises determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

In an embodiment, the subject has or is identified as having an APRIL-associated disorder. In an embodiment, the subject has or is identified as having a disorder associated with an aberrant level of total IgA. In an embodiment, the subject has or is identified as having a disorder associated with a-g IgA (e.g., a-g IgA1).

In an embodiment, the subject has or is identified as having an IgA nephropathy (IgAN). In an embodiment, the IgAN is a familial IgAN. In an embodiment, the IgA is an adult IgAN. In an embodiment, the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

In an embodiment, the subject has or is identified as having a chronic kidney disease (CKD) or a disorder associated with CKD. In an embodiment, the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

In an embodiment, the subject has or is identified as having a Henoch-Schonlein purpura (HSP). In an embodiment, the subject has or is identified as having a cutaneous vasculitis or IgA vasculitis. In an embodiment, the subject has or is identified as having an IgA dermatitis, e.g., IgA bullous dermatosis. In an embodiment, the subject has or is identified as having a Waldenström macroglobulinemia (WM). In an embodiment, the subject has or is identified as having a lupus nephritis.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305,

2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the level of a-g IgA is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM and/or IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the anti-APRIL antibody molecule.

In an embodiment, administration of the anti-APRIL antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the anti-APRIL antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the anti-APRIL antibody molecule.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the anti-APRIL antibody molecule.

In yet another aspect, the disclosure features a method of selecting an anti-APRIL antibody molecule for treating a disorder, the method comprising determining whether administration of the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA (e.g., a-g IgA1) by at least 40% in a subject in need thereof, thereby selecting the anti-APRIL antibody molecule. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 4 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 8 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 12 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 16 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 50%. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal

subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy. In an embodiment, the method further comprises determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

In an embodiment, the subject has or is identified as having an APRIL-associated disorder. In an embodiment, the subject has or is identified as having a disorder associated with an aberrant level of total IgA. In an embodiment, the subject has or is identified as having a disorder associated with a-g IgA (e.g., a-g IgA1).

In an embodiment, the subject has or is identified as having an IgA nephropathy (IgAN). In an embodiment, the IgAN is a familial IgAN. In an embodiment, the IgA is an adult IgAN. In an embodiment, the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

In an embodiment, the subject has or is identified as having a chronic kidney disease (CKD) or a disorder associated with CKD. In an embodiment, the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

In an embodiment, the subject has or is identified as having a Henoch-Schonlein purpura (HSP). In an embodiment, the subject has or is identified as having a cutaneous vasculitis or IgA vasculitis. In an embodiment, the subject has or is identified as having a IgA dermatitis, e.g., IgA bullous dermatosis. In an embodiment, the subject has or is identified as having a Waldenström macroglobulinemia (WM). In an embodiment, the subject has or is identified as having a lupus nephritis.

In an embodiment, the level of a-g IgA is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM and/or IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent

with, or after administration of the anti-APRIL antibody molecule.

In an embodiment, administration of the anti-APRIL antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the anti-APRIL antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the anti-APRIL antibody molecule.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the anti-APRIL antibody molecule.

In another aspect, the disclosure features a method of selecting a dose or dosage (e.g., dose and frequency) for an anti-APRIL antibody molecule for treating a disorder, the method comprising determining whether administration of the anti-APRIL antibody molecule at a dose or dosage reduces, or is likely to reduce, the level of a-g IgA (e.g., a-g IgA1) by at least 40% in a subject in need thereof, thereby selecting the dose or dosage. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 4 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 8 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody

molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 12 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 16 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 50%. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy. In an embodiment, the method further comprises determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

In an embodiment, the subject has or is identified as having an APRIL-associated disorder. In an embodiment, the subject has or is identified as having a disorder associated with an aberrant level of total IgA. In an embodiment, the subject has or is identified as having a disorder associated with a-g IgA (e.g., a-g IgA1).

In an embodiment, the subject has or is identified as having an IgA nephropathy (IgAN). In an embodiment, the IgAN is a familial IgAN. In an embodiment, the IgA is an adult IgAN. In an embodiment, the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

In an embodiment, the subject has or is identified as having a chronic kidney disease (CKD) or a disorder associated with CKD. In an embodiment, the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

In an embodiment, the subject has or is identified as having a Henoch-Schonlein purpura (HSP). In an embodiment, the subject has or is identified as having a cutaneous vasculitis or IgA vasculitis. In an embodiment, the subject has or is identified as having a IgA dermatitis, e.g., IgA bullous dermatosis. In an embodiment, the subject has or is identified as having a Waldenström macroglobulinemia (WM). In an embodiment, the subject has or is identified as having a lupus nephritis.

In an embodiment, the level of a-g IgA is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM and/or IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the anti-APRIL antibody molecule.

In an embodiment, administration of the anti-APRIL antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the anti-APRIL antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the anti-APRIL antibody molecule.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the anti-APRIL antibody molecule.

In another aspect, the disclosure features a method of selecting a subject for treating a disorder, the method comprising determining whether administration of an anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA (e.g., a-g IgA1) by at least 40% in a subject in need thereof,

thereby selecting the subject. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 4 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 8 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 12 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% about 16 weeks after the antibody molecule is administered. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 50%. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has

received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy. In an embodiment, the method further comprises determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

In an embodiment, the subject has or is identified as having an APRIL-associated disorder. In an embodiment, the subject has or is identified as having a disorder associated with an aberrant level of total IgA. In an embodiment, the subject has or is identified as having a disorder associated with a-g IgA (e.g., a-g IgA1).

In an embodiment, the subject has or is identified as having an IgA nephropathy (IgAN). In an embodiment, the IgAN is a familial IgAN. In an embodiment, the IgA is an adult IgAN. In an embodiment, the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

In an embodiment, the subject has or is identified as having a chronic kidney disease (CKD) or a disorder associated with CKD. In an embodiment, the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

In an embodiment, the subject has or is identified as having a Henoch-Schonlein purpura (HSP). In an embodiment, the subject has or is identified as having a cutaneous vasculitis or IgA vasculitis. In an embodiment, the subject has or is identified as having an IgA dermatitis, e.g., IgA bullous dermatosis. In an embodiment, the subject has or is identified as having a Waldenström macroglobulinemia (WM). In an embodiment, the subject has or is identified as having a lupus nephritis.

In an embodiment, the level of a-g IgA is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM and/or IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the anti-APRIL antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the anti-APRIL antibody molecule.

In an embodiment, administration of the anti-APRIL antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more

than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the anti-APRIL antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the anti-APRIL antibody molecule.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the anti-APRIL antibody molecule.

In another aspect, the disclosure features a method of treating IgA nephropathy, the method comprising administering to a subject in need thereof an effective amount of an anti-APRIL antibody molecule (e.g., an anti-APRIL antibody molecule described herein), wherein the subject has received, or is going to receive, a vaccine (e.g., a vaccine described herein) within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks of administration of the anti-APRIL antibody molecule, thereby treating IgA nephropathy.

In an embodiment, the method further comprising administering the vaccine to the subject before, concurrently with, or after administration of the anti-APRIL antibody molecule.

In another aspect, the disclosure features a method of vaccinating a subject, the method comprising administering to the subject an effective amount of a vaccine (e.g., a vaccine described herein), wherein the subject has received, or is going to receive, an anti-APRIL antibody molecule (e.g., an anti-APRIL antibody molecule described herein) within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks of administration of the vaccine, thereby vaccinating the subject.

In an embodiment, the method further comprising administering the anti-APRIL antibody molecule to the subject before, concurrent with, or after administration of the vaccine.

In yet another aspect, the disclosure features a method of treating a disorder, the method comprising administering an anti-APRIL antibody molecule to a subject in a need thereof, e.g., at a dose or dosage that reduces, or is likely to reduce, the level of IgM by at least a predetermined percentage in the subject, thereby treating the disorder.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2,

HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of IgM by at least 20%, 25%, 30%, 35%, 40%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of IgM that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of IgM in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder.

In an embodiment, the disorder is associated an aberrant level of IgM. In an embodiment, the disorder is a chronic kidney disease (CKD) or kidney injury. In an embodiment, the disorder is a fibrosis. In an embodiment, the disorder is an IgM mediated neuropathy, e.g., anti-MAG neuropathy or a neuropathy associated with anti-GM1. In an embodiment, the disorder is systemic lupus erythematosus (SLE). In an embodiment, the administration does not reduce, or does not substantially reduce, the level of IgG in the subject. In an embodiment, the administration reduces the level of IgG by no more than a predetermined percentage in the subject. In an embodiment, the administration reduces the level of IgG by at least a predetermined percentage in the subject.

In an embodiment, the level of IgM is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of IgM in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgM in the sample. In an embodiment, the method further comprising determining the level of IgA (e.g., total IgA and/or a-g IgA) and/or IgG in the sample. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the antibody molecule.

In an embodiment, administration of the antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after the antibody molecule is administered.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after the antibody molecule is administered.

In another aspect, the disclosure features a method of reducing the level of IgM in a subject, the method comprising administering an anti-APRIL antibody molecule to a subject in a need thereof, e.g., at a dose or dosage that reduces, or is likely to reduce, the level of IgM by at least a predetermined percentage in the subject, thereby reducing the level of IgM.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-

1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of IgM by at least 20%, 25%, 30%, 35%, 40%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of IgM that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of IgM in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder.

In an embodiment, the disorder is associated an aberrant level of IgM. In an embodiment, the disorder is a chronic kidney disease (CKD) or kidney injury. In an embodiment, the disorder is a fibrosis. In an embodiment, the disorder is an IgM mediated neuropathy, e.g., anti-MAG neuropathy or a neuropathy associated with anti-GM1. In an embodiment, the disorder is systemic lupus erythematosus (SLE). In an embodiment, the administration does not reduce, or does not substantially reduce, the level of IgG in the subject. In an embodiment, the administration reduces the level of IgG by no more than a predetermined percentage in the subject. In an embodiment, the administration reduces the level of IgG by at least a predetermined percentage in the subject.

In an embodiment, the level of IgM is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of IgM in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgM in the sample. In an embodiment, the method further comprising determining the level of IgA (e.g., total IgA and/or a-g IgA) and/or IgG in the sample. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after

administration of the antibody molecule.

In an embodiment, administration of the antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after the antibody molecule is administered.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after the antibody molecule is administered.

In another aspect, the disclosure features a method of treating a disorder, the method comprising administering an anti-APRIL antibody molecule to a subject in a need thereof, e.g., at a dose or dosage that reduces, or is likely to reduce, the levels of IgA and IgM by at least predetermined percentages in the subject, thereby treating the disorder.

In an embodiment, the level of IgA comprises, or is, the level of total IgA and/or a-g IgA. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the administration does not reduce or does not substantially reduce, the level of IgG in the subject. In an embodiment, the administration reduces the level of IgG by no more than a predetermined percentage in the subject. In an embodiment, the administration reduces the level of IgG by at least a predetermined percentage in the subject.

In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of total IgA by at least 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of IgM by at least 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of IgA (e.g., total and/or a-g IgA) by at least 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% and the level of IgM by at least 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of IgM that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgM in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder.

In an embodiment, the disorder is an APRIL-associated disorder. In an embodiment, the disorder is associated an aberrant level of IgA (e.g., total IgA and/or a-g IgA) and/or IgM, e.g., a disorder described herein. In an embodiment, the disorder is systemic lupus erythematosus (SLE). In an embodiment, the administration does not reduce, or does not substantially reduce, the level of IgG in the subject. In an embodiment, the administration reduces the level of IgG by no more than a predetermined percentage in the subject. In an embodiment, the administration reduces the level of IgG by at least a predetermined percentage in the subject. In an embodiment, the level of IgA and/or IgM (and optionally IgG) is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further

comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM in the sample. In an embodiment, the method further comprising determining the level of IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the antibody molecule.

In an embodiment, administration of the antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after the antibody molecule is administered.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after the antibody molecule is administered.

In yet another aspect, the disclosure features a method of reducing the levels of IgA and IgM in subject, the method comprising administering an anti-APRIL antibody molecule to a subject in a need thereof, e.g., at a dose or dosage that reduces, or is likely to reduce, the levels of IgA and IgM by at least predetermined percentages in the subject, thereby reducing the levels of IgA and IgM.

In an embodiment, the level of IgA comprises, or is, the level of total IgA and/or a-g IgA. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-

0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the administration does not reduce or does not substantially reduce, the level of IgG in the subject. In an embodiment, the administration reduces the level of IgG by no more than a predetermined percentage in the subject. In an embodiment, the administration reduces the level of IgG by at least a predetermined percentage in the subject.

In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 20%, 25%, 30%, 35%, 40%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce the level of total IgA by at least 20%, 25%, 30%, 35%, 40%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of IgM by at least 20%, 25%, 30%, 35%, 40%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of IgA (e.g., total and/or a-g IgA) by at least 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% and the level of IgM by at least 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of IgM that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgM in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or

modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder.

In an embodiment, the disorder is an APRIL-associated disorder. In an embodiment, the disorder is associated an aberrant level of IgA (e.g., total IgA and/or a-g IgA) and/or IgM, e.g., a disorder described herein. In an embodiment, the disorder is systemic lupus erythematosus (SLE). In an embodiment, the administration does not reduce, or does not substantially reduce, the level of IgG in the subject. In an embodiment, the administration reduces the level of IgG by no more than a predetermined percentage in the subject. In an embodiment, the administration reduces the level of IgG by at least a predetermined percentage in the subject. In an embodiment, the level of IgA and/or IgM (and optionally IgG) is determined in a sample from the subject. In an embodiment, the method further comprises determining the level of a-g IgA in a sample from the subject. In an embodiment, the method further comprises determining the level of total IgA in the sample. In an embodiment, the method further comprising determining the level of IgM in the sample. In an embodiment, the method further comprising determining the level of IgG in the sample. In an embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the antibody molecule.

In an embodiment, administration of the antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after the antibody molecule is administered.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4,

5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after the antibody molecule is administered.

In another aspect, the disclosure features a method of treating a disorder, the method comprising administering to a subject in need thereof an effective amount of an anti-APRIL antibody molecule, wherein the disorder is:

(a) an advanced chronic kidney disease (CKD) (e.g., with an eGFR equal to or greater than about 30 or 45);

(b) a post -transplant IgAN;

(c) a pediatric IgAN;

(d) Henoch-Schonlein purpura (HSP) or cutaneous vasculitis;

(e) IgAN with crescentic glomerulonephritis (GN);

(f) IgA vasculitis;

(g) IgA dermatitis;

(h) IgM mediated neuropathy (anti-MAG or anti-GM1);

(i) Waldenström macroglobulinemia (WM); or

(j) lupus nephritis.

In an embodiment, the anti-APRIL antibody molecule is an anti-APRIL antibody molecule described herein. In an embodiment, the anti-APRIL antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the anti-APRIL antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the administration reduces, or is likely to reduce, the IgA in the subject. In an embodiment, the administration reduces, or is likely to reduce, the IgM in the subject. In an embodiment, the level of IgA comprises, or is, the level of total IgA and/or a-g IgA. In an embodiment, the level of a-g IgA comprises, or is, the level of a-g IgA1.

In an embodiment, the administration does not reduce or does not substantially reduce, the level of IgG in the subject. In an embodiment, the administration reduces the level of IgG by no more than a predetermined percentage in the subject. In an embodiment, the administration reduces the level of IgG by at least a predetermined percentage in the subject.

In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 20%, 25%, 30%, 35%, 40%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce the level of total IgA by at least 20%, 25%, 30%, 35%, 40%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of IgM by at least 20%, 25%, 30%, 35%, 40%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the anti-APRIL antibody molecule reduces, or is likely to reduce, the level of IgA (e.g., total and/or a-g IgA) by at least 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% and the level of IgM by at least 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., over a predetermined period. In an embodiment, the antibody molecule is administered as a single dose. In an embodiment, the antibody molecule is administered as a repeated dose. In an embodiment, the antibody molecule is administered subcutaneously. In an embodiment, the antibody molecule is administered intravenously.

In an embodiment, the subject is a human. In an embodiment, the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has, or is identified as having, a level of IgM that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgM in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject. In an embodiment, the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder. In an embodiment, the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder.

In an embodiment, the disorder is an advanced chronic kidney disease (CKD) (e.g., with an eGFR equal to or greater than about 30 or 45). In an embodiment, the disorder is a post -transplant IgAN. In an embodiment, the disorder is a pediatric IgAN. In an embodiment, the disorder is Henoch-Schonlein purpura (HSP) or cutaneous vasculitis. In an embodiment, the disorder is IgAN with crescentic glomerulonephritis (GN). In an embodiment, the disorder is IgA vasculitis. In an embodiment, the disorder is IgA dermatitis. In an embodiment, the disorder is IgM mediated neuropathy (anti-MAG or anti-GM1). In an embodiment, the disorder is Waldenström macroglobulinemia (WM). In an embodiment, the disorder is lupus nephritis.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

In an embodiment, the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule. In an embodiment, the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule. In an embodiment, the subject receives the vaccine before, concurrent with, or after administration of the antibody molecule.

In an embodiment, administration of the antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%. In an embodiment, administration of the antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine. In an embodiment, the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after the antibody molecule is administered.

In an embodiment, the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®). In an embodiment, the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after the antibody molecule is administered.

In another aspect, the disclosure features a method of treating a disorder associated with an autoantigen, the method comprising administering to a subject in need thereof an effective amount of a therapeutic agent or modality, wherein the administration reduces, or is likely to reduce, the level of autoantigen by at least a predetermined percentage in the subject.

In an embodiment, the subject is a human. In an embodiment, the subject has or is identified as having an APRIL-associated disorder.

In an embodiment, the level of the autoantigen is determined in a sample from the subject. embodiment, the method further comprises obtaining a sample from the subject. In an embodiment, the sample is a blood or serum sample.

In an embodiment, the method further comprises administering a second therapeutic agent or modality to the subject. In an embodiment, the second therapeutic agent or modality is a small molecule. In an embodiment, the second therapeutic agent or modality is an antibody molecule.

Enumerated Embodiments

1. A method of treating a disorder, comprising:

administering to a subject in need thereof an anti-APRIL antibody molecule described herein,

wherein the antibody molecule is administered at a dose that reduces, or is likely to reduce, the level of aberrantly glycosylated IgA (a-g IgA) by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject,

thereby treating the disorder.

2. A method of treating a disorder, comprising:

administering to a subject in need thereof an anti-APRIL antibody molecule described herein,

wherein the administration reduces the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject,

thereby treating the disorder.

3. A method of treating a disorder, comprising:

administering to a subject in need thereof an anti-APRIL antibody molecule described herein,

wherein the antibody molecule is administered at a dosage (e.g., dose and frequency) that reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject,

thereby treating the disorder.

4. A method of treating a disorder, comprising:

selecting a dose or dosage (e.g., dose and frequency) for an anti-APRIL antibody molecule described herein, wherein administration of the antibody molecule at the dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof; and

administering the antibody molecule to the subject at the selected dose or dosage,

thereby treating the disorder.

5. A method of treating a disorder, comprising:

responsive to a determination that administration of an anti-APRIL antibody molecule described herein reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof, administering to the subject an anti-APRIL antibody molecule,

thereby treating the disorder.

6. A method of treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule described herein reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof,

if the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, administration of the antibody molecule is initiated, continued, or maintained,

optionally wherein if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, administration of the antibody molecule is terminated, discontinued, or altered, and/or a different therapeutic agent or modality is administered.

7. A method of treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule described herein at a dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof,

if the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% at the dose or dosage, administration of the antibody molecule at the dose or dosage is initiated, continued, or maintained,

optionally wherein if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40% at the dose or dosage, administration of the antibody molecule at the dose or dosage is terminated, discontinued, or altered.

8. A method of treating a disorder, comprising:

determining whether administration of a therapeutic agent or modality other than an anti-APRIL antibody molecule described herein reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof,

if the therapeutic agent or modality does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, administering an anti-APRIL antibody molecule described herein to the subject.

9. A method of reducing the level of a-g IgA in subject, comprising:

administering an anti-APRIL antibody molecule described herein to a subject in a need thereof,

e.g., at a dose or dosage that reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject,

thereby reducing the level of a-g IgA.

10. A method of selecting an anti-APRIL antibody molecule for treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule described herein reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof,

thereby selecting the anti-APRIL antibody molecule.

11. A method of selecting a dose or dosage (e.g., dose and frequency) for an anti-APRIL antibody molecule for treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule described herein at a dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof,

thereby selecting the dose or dosage.

12. A method of selecting a subject for treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule described herein reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof,

thereby selecting the subject,

optionally wherein if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, administration of the antibody molecule is terminated, discontinued, or altered, or a different therapeutic agent or modality is administered.

13. The method of any of embodiments 1-12, wherein the a-g IgA comprises or is a-g IgA1.

14. The method of any of embodiments 1-13, wherein the level of a-g IgA is reduced by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months.

15. The method of any of embodiments 1-14, wherein the level of a-g IgA is reduced by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) about 4 weeks after the antibody molecule is administered.

16. The method of any of embodiments 1-15, wherein the level of a-g IgA is reduced by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) about 8 weeks after the antibody molecule is administered.

17. The method of any of embodiments 1-16, wherein the level of a-g IgA is reduced by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) about 12 weeks after the antibody molecule is administered.

18. The method of any of embodiments 1-17, wherein the level of a-g IgA is reduced by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) about 16 weeks after the antibody molecule is administered.

19. The method of any of embodiments 1-18, wherein the level of a-g IgA is reduced by at least 50%.

20. The method of any of embodiments 1-19, wherein the level of a-g IgA is reduced by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%.

21. The method of any of embodiments 1-20, wherein the antibody molecule is administered as a single dose.

22. The method of any of embodiments 1-20, wherein the antibody molecule is administered as a repeated dose.

23. The method of any of embodiments 1-22, wherein the antibody molecule is administered subcutaneously.

24. The method of any of embodiments 1-22, wherein the antibody molecule is administered intravenously.

25. The method of any of embodiments 1-24, wherein the disorder is an APRIL-associated disorder.

26. The method of any of embodiments 1-25, wherein the disorder is associated with an aberrant level of total IgA.

27. The method of any of embodiments 1-26, wherein the disorder is a disorder associated with a-g IgA.

28. The method of any of embodiments 1-27, wherein the disorder is IgA nephropathy (IgAN).

29. The method of embodiment 28, wherein the IgAN is a familial IgAN.

30. The method of embodiment 28, wherein the IgAN is an adult IgAN.

31. The method of embodiment 28, wherein the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

32. The method of any of embodiments 1-27, wherein the disorder is a chronic kidney disease (CKD) or a disorder associated with CKD.

33. The method of embodiment 32, wherein the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

34. The method of any of embodiments 1-27, wherein the disorder is Henoch-Schonlein purpura (HSP).

35. The method of any of embodiments 1-27, wherein the disorder is cutaneous vasculitis or IgA vasculitis.

36. The method of any of embodiments 1-27, wherein the disorder is IgA dermatitis, e.g., IgA bullous dermatosis.

37. The method of any of embodiments 1-27, wherein the disorder is Waldenström

macroglobulinemia (WM).

38. The method of any of embodiments 1-27, wherein the disorder is lupus nephritis.

39. The method of any of embodiments 1-38, wherein the subject is a human.

40. The method of any of embodiments 1-39, wherein the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject.

41. The method of any of embodiments 1-40, wherein the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject.

42. The method of any of embodiments 1-41, wherein the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder.

43. The method of any of embodiments 1-41, wherein the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder.

44. The method of any of embodiments 1-43, wherein the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule.

45. The method of any of embodiments 1-43, wherein the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule.

46. The method of embodiment 44 or 45, wherein the subject receives the vaccine before, concurrent with, or after administration of the antibody molecule.

47. The method of any of embodiments 44-46, wherein administration of the antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%.

48. The method of any of embodiments 44-47, wherein administration of the antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine.

49. The method of any of embodiments 44-48, wherein the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the antibody molecule.

50. The method of any of embodiments 44-49, wherein the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®).

51. The method of embodiment 50, wherein the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the antibody molecule.

52. The method of any of embodiments 1-51, wherein the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

53. The method of any of embodiments 1-52, further comprising determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

54. The method of any of embodiments 1-53, wherein the antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

55. The method of any of embodiments 1-54, wherein the antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

56. The method of any of embodiments 1-55, wherein the level of a-g IgA is determined in a sample from the subject.

57. The method of any of embodiments 1-56, further comprising determining the level of a-g IgA in a sample from the subject.

58. The method of any of embodiments 1-57, further comprising determining the level of total IgA in the sample.

59. The method of any of embodiments 1-58, further comprising determining the level of IgM and/or IgG in the sample.

60. The method of any of embodiments 1-59, further comprising obtaining a sample from the subject.

61. The method of embodiment 60, wherein the sample is a blood or serum sample.

62. The method of any of embodiments 1-61, further comprising administering a second therapeutic agent or modality to the subject.

63. The method of embodiment 62, wherein the second therapeutic agent or modality is a small molecule.

64. The method of embodiment 62, wherein the second therapeutic agent or modality is an antibody molecule.

65. A method of treating IgA nephropathy, comprising:

administering to a subject in need thereof an effective amount of an anti-APRIL antibody molecule (e.g., an anti-APRIL antibody molecule described herein),

wherein the subject has received, or is going to receive, a vaccine (e.g., a vaccine described herein) within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks of administration of the antibody molecule,

thereby treating IgA nephropathy.

66. The method of embodiment 65, further comprising administering the vaccine to the subject before, concurrent with, or after administration of the antibody molecule.

67. A method of vaccinating a subject, comprising:

administering to the subject an effective amount of a vaccine (e.g., a vaccine described herein),

wherein the subject has received, or is going to receive, an anti-APRIL antibody molecule (e.g., an anti-APRIL antibody molecule described herein) within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks of administration of the vaccine,

thereby vaccinating the subject.

68. The method of embodiment 67, further comprising administering the antibody molecule to the subject before, concurrent with, or after administration of the vaccine.

69. The method of any of embodiments 44-68, wherein the vaccine is administered intramuscularly.

70. A composition for use in treating IgA nephropathy in a subject, wherein the composition comprises an anti-APRIL antibody molecule (e.g., an anti-APRIL antibody molecule described herein) at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

wherein the subject has received, or is going to receive, a vaccine (e.g., a vaccine described herein) within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks of administration of the antibody molecule.

71. The composition for use of embodiment 70, further wherein the subject has been administered the vaccine before, concurrent with, or after administration of the antibody molecule.

72. A composition for use in vaccinating a subject, the composition comprising an effective amount of a vaccine (e.g., a vaccine described herein),

wherein the subject has received, or is going to receive, an anti-APRIL antibody molecule (e.g., an anti-APRIL antibody molecule described herein) within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks of administration of the vaccine, wherein the subject received, or is going to receive, the anti-APRIL antibody molecule at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12

mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg.

73. The composition for use of embodiment 72, wherein the subject is administered the antibody molecule before, concurrent with, or after administration of the vaccine.

74. A composition for use in treating a disorder in a subject, the composition comprising:

an anti-APRIL antibody molecule described herein at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

wherein the dosage reduces, or is likely to reduce, the level of aberrantly glycosylated IgA (a-g IgA) by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject.

75. A composition for use in treating a disorder in a subject, the composition comprising an anti-APRIL antibody molecule described herein at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

wherein the dosage reduces the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject.

76. A composition for use in treating a disorder in a subject, the composition comprising an anti-APRIL antibody molecule described herein at a dosage (e.g., dose and frequency) that reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject,

wherein the dosage is about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg.

77. A composition for use in treating a disorder in a subject, the composition comprising an anti-APRIL antibody molecule described herein to the subject at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

wherein the composition is formulated administered if administration of a therapeutic agent or modality other than an anti-APRIL antibody molecule described herein reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject.

78. A composition for use in reducing the level of a-g IgA in a subject, the composition comprising an anti-APRIL antibody molecule described herein to a subject in a need thereof at a dose or dosage that reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject,

wherein the dose or dosage is about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg.

79. A method of treating IgA nephropathy, comprising:

administering to a subject in need thereof an anti-APRIL antibody molecule (e.g., an anti-APRIL antibody molecule described herein) at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

wherein the subject has received, or is going to receive, a vaccine (e.g., a vaccine described herein) within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks of administration of the antibody molecule,

thereby treating IgA nephropathy.

80. The method of embodiment 79, further comprising administering the vaccine to the subject before, concurrent with, or after administration of the antibody molecule.

81. A method of vaccinating a subject, comprising:

administering to the subject an effective amount of a vaccine (e.g., a vaccine described herein),

wherein the subject has received, or is going to receive, an anti-APRIL antibody molecule (e.g., an anti-APRIL antibody molecule described herein) within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks of administration of the vaccine, wherein the subject received, or is going to receive, the anti-APRIL antibody molecule at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

thereby vaccinating the subject.

82. The method of embodiment 81, further comprising administering the antibody molecule to the subject before, concurrent with, or after administration of the vaccine.

83. A method of treating a disorder, comprising:

administering to a subject in need thereof an anti-APRIL antibody molecule described herein,

wherein the antibody molecule is administered at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6

mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

wherein the dosage administered to the subject reduces, or is likely to reduce, the level of aberrantly glycosylated IgA (a-g IgA) by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject,

thereby treating the disorder.

84. A method of treating a disorder, comprising:

administering to a subject in need thereof an anti-APRIL antibody molecule described herein at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

wherein the administration reduces the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject,

thereby treating the disorder.

85. A method of treating a disorder, comprising:

administering to a subject in need thereof an anti-APRIL antibody molecule described herein,

wherein the antibody molecule is administered at a dosage (e.g., dose and frequency) that reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject, and

wherein the dosage is about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

thereby treating the disorder.

86. A method of treating a disorder, comprising:

selecting a dose or dosage (e.g., dose and frequency) for an anti-APRIL antibody molecule described herein,

wherein the dose or dosage is about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

wherein administration of the antibody molecule at the dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof; and

administering the antibody molecule to the subject at the selected dose or dosage,

thereby treating the disorder.

87. A method of treating a disorder, comprising:

responsive to a determination that administration of an anti-APRIL antibody molecule described herein reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof, administering to the subject an anti-APRIL antibody molecule at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

thereby treating the disorder.

88. A method of treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule described herein reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof,

if the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, administration of the antibody molecule at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg is initiated, continued, or maintained,

optionally wherein if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, administration of the antibody molecule is terminated, discontinued, or altered, and/or a different therapeutic agent or modality is administered.

89. A method of treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule described herein at a dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof,

if the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40% at the dose or dosage, administration of the antibody molecule at the dose or dosage is initiated, continued, or maintained,

wherein the dose or dosage is about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

optionally wherein if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40% at the dose or dosage, administration of the antibody molecule at the dose or

dosage is terminated, discontinued, or altered.

90. A method of treating a disorder, comprising:

determining whether administration of a therapeutic agent or modality other than an anti-APRIL antibody molecule described herein reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof,

if the therapeutic agent or modality does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, administering an anti-APRIL antibody molecule described herein to the subject at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg.

91. A method of reducing the level of a-g IgA in subject, comprising:

administering an anti-APRIL antibody molecule described herein to a subject in a need thereof at a dose or dosage that reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in the subject,

wherein the dose or dosage is about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

thereby reducing the level of a-g IgA.

92. A method of selecting an anti-APRIL antibody molecule for treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule described herein at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof,

thereby selecting the anti-APRIL antibody molecule.

93. A method of selecting a dose or dosage (e.g., dose and frequency) for an anti-APRIL antibody molecule for treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule described herein at a dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof,

wherein the dose or dosage is about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

thereby selecting the dose or dosage.

94. A method of selecting a subject for treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule described herein at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg reduces, or is likely to reduce, the level of a-g IgA by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) in a subject in need thereof,

thereby selecting the subject,

optionally wherein if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, administration of the antibody molecule is terminated, discontinued, or altered, or a different therapeutic agent or modality is administered.

95. The method of any of embodiments 79-94, wherein the a-g IgA comprises or is a-g IgA1.

96. The method of any of embodiments 79-95, wherein the level of a-g IgA is reduced by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, or three months.

97. The method of any of embodiments 79-96, wherein the level of a-g IgA is reduced by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) about 4 weeks after the antibody molecule is administered.

98. The method of any of embodiments 79-97, wherein the level of a-g IgA is reduced by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) about 8 weeks after the antibody molecule is administered.

99. The method of any of embodiments 79-98, wherein the level of a-g IgA is reduced by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) about 12 weeks after the antibody molecule is administered.

100. The method of any of embodiments 79-99, wherein the level of a-g IgA is reduced by at least 40% (e.g., by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%) about 16 weeks after the antibody molecule is administered.

101. The method of any of embodiments 79-100, wherein the level of a-g IgA is reduced by at least 50%.

102. The method of any of embodiments 79-101, wherein the level of a-g IgA is reduced by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%.

103. The method of any of embodiments 79-102, wherein the antibody molecule is administered as a single dose, e.g., in a period of at least 1, 2, 3, 4, 5, 6, 7, 8, 9. 10, 11, 12, 13, 14, 15, 16, 17, or 18 months.

104. The method of any of embodiments 79-102, wherein the antibody molecule is administered as a repeated dose.

105. The method of any of embodiments 79-104, wherein the antibody molecule is administered subcutaneously.

106. The method of any of embodiments 79-104, wherein the antibody molecule is administered intravenously.

107. The method of any of embodiments 79-106, wherein the disorder is an APRIL-associated disorder.

108. The method of any of embodiments 79-107, wherein the disorder is associated with an aberrant level of total IgA.

109. The method of any of embodiments 79-108, wherein the disorder is a disorder associated with a-g IgA.

110. The method of any of embodiments 79-109, wherein the disorder is IgA nephropathy (IgAN).

111. The method of embodiment 110, wherein the IgAN is a familial IgAN.

112. The method of embodiment 110, wherein the IgAN is an adult IgAN.

113. The method of embodiment 110, wherein the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

114. The method of any of embodiments 79-108, wherein the disorder is a chronic kidney disease (CKD) or a disorder associated with CKD.

115. The method of embodiment 114, wherein the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

116. The method of any of embodiments 79-108, wherein the disorder is Henoch-Schonlein purpura (HSP).

117. The method of any of embodiments 79-108, wherein the disorder is cutaneous vasculitis or IgA vasculitis.

118. The method of any of embodiments 79-108, wherein the disorder is IgA dermatitis, e.g., IgA bullous dermatosis.

119. The method of any of embodiments 79-108, wherein the disorder is Waldenström macroglobulinemia (WM).

120. The method of any of embodiments 79-108, wherein the disorder is lupus nephritis.

121. The method of any of embodiments 79-120, wherein the subject is a human.

122. The method of any of embodiments 79-121, wherein the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject.

123. The method of any of embodiments 79-122, wherein the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject.

124. The method of any of embodiments 79-123, wherein the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder.

125. The method of any of embodiments 79-123, wherein the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder.

126. The method of any of embodiments 79-125, wherein the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule.

127. The method of any of embodiments 79-125, wherein the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule.

128. The method of embodiment 126 or 127, wherein the subject receives the vaccine before, concurrent with, or after administration of the antibody molecule.

129. The method of any of embodiments 126-128, wherein administration of the antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%.

130. The method of any of embodiments 126-129, wherein administration of the antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine.

131. The method of any of embodiments 126-130, wherein the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the antibody molecule.

132. The method of any of embodiments 126-131, wherein the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®).

133. The method of embodiment 132, wherein the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the antibody molecule.

134. The method of any of embodiments 79-133, wherein the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

135. The method of any of embodiments 79-134, further comprising determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

136. The method of any of embodiments 79-135, wherein the antibody molecule comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

137. The method of any of embodiments 79-136, wherein the antibody molecule comprises the VH and VL of any of antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

138. The method of any of embodiments 79-137, wherein the level of a-g IgA is determined in a sample from the subject.

139. The method of any of embodiments 79-138, further comprising determining the level of a-g IgA in a sample from the subject.

140. The method of any of embodiments 79-139, further comprising determining the level of total

IgA in the sample.

141. The method of any of embodiments 79-140, further comprising determining the level of IgM and/or IgG in the sample.

142. The method of any of embodiments 79-141, further comprising obtaining a sample from the subject.

143. The method of embodiment 142, wherein the sample is a blood or serum sample.

144. The method of any of embodiments 79-143, further comprising administering a second therapeutic agent or modality to the subject.

145. The method of embodiment 144, wherein the second therapeutic agent or modality is a small molecule.

146. The method of embodiment 144, wherein the second therapeutic agent or modality is an antibody molecule.

147. The method or composition for use of any of the preceding embodiments, wherein the subject is administered the anti-APRIL antibody molecule at a concentration of about 100, 150, 175, 180, 190, 200, 210, 220, 225, 230, 240, 250, or 300 mg/mL.

148. The method or composition for use of any of the preceding embodiments, wherein the subject is administered the anti-APRIL antibody molecule at a concentration of about 200 mg/mL.

149. The method or composition for use of any of the preceding embodiments, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dosage of about 200, 250, 300, 450, 400, 450, 500, 550, 600, 650, 700, 750, or 800 mg.

150. The method or composition for use of any of the preceding embodiments, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dosage of about 200 mg (e.g., at a volume of about 1 mL).

151. The method or composition for use of any of the preceding embodiments, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dosage of about 400 mg (e.g., at a total volume of about 2 mL, e.g., as two administrations of 1 mL volumes or as one administration of a 2 mL volume).

152. The method or composition for use of any of the preceding embodiments, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dosage of at least 200 mg.

153. The method or composition for use of any of the preceding embodiments, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dosage of 800 mg or less.

154. The method or composition for use of any of the preceding embodiments, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dosage of about 600 mg (e.g., at a total volume of about 3 mL, e.g., as one administration of a 2 mL volume and one administration of a 1 mL volume).

155. The method or composition for use of any of the preceding embodiments, wherein the subject is administered a single dose of the anti-APRIL antibody molecule.

156. The method or composition for use of any of the preceding embodiments, wherein the subject is administered one or more additional dosages of the anti-APRIL antibody molecules (e.g., 24 hours, 48 hours, 72 hours, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 1 month, 2 months, 3 months, 4 months, 5 months, or 6 months after the first administration).

157. The method or composition for use of any of the preceding embodiments, wherein the subject is administered the anti-APRIL antibody molecule subcutaneously.

158. The method or composition for use of any of the preceding embodiments, wherein the subject is administered the anti-APRIL antibody molecule intravenously.

159. The method or composition for use of any of the preceding embodiments, wherein the anti-APRIL antibody molecule is administered as a liquid.

160. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-

APRIL antibody molecule, for use in a method of treating a disorder in a human subject,

wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

wherein the administration reduces the level of aberrantly glycosylated IgA (a-g IgA) by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy.

161. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-APRIL antibody molecule, for use in a method of reducing the level of a-g IgA in a human subject,

wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

wherein the administration reduces the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence

of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the subject has, or is at risk of having, a disorder, e.g., IgA nephropathy.

162. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-APRIL antibody molecule, for use in a method of treating a disorder in a human subject,

wherein the method comprises selecting a dose or dosage for the antibody molecule;

wherein administration of the antibody molecule at the selected dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

optionally wherein the disorder is IgA nephropathy.

163. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-

APRIL antibody molecule, for use in a method of treating a disorder in a human subject,

wherein the method comprises responsive to a determination that administration of the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject, administering to the subject the antibody molecule at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy.

164. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-APRIL antibody molecule, for use in a method of treating a disorder in a human subject,

wherein the method comprises determining whether administration of an anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject,

if the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%, administration of the antibody molecule at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg is initiated, continued, or maintained; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions

(LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

optionally wherein the disorder is IgA nephropathy,

optionally wherein if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%, administration of the antibody molecule is terminated, discontinued, or altered, and/or a different therapeutic agent or modality is administered.

165. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-APRIL antibody molecule, for use in a method of treating a disorder in a human subject,

wherein the method comprises determining whether administration of a therapeutic agent or modality other than the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in a subject in need thereof,

if the therapeutic agent or modality does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%, administering the antibody molecule to the subject at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an

HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy.

166. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-APRIL antibody molecule, for use in a method of treating a disorder in a human subject,

wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

wherein the subject has received, or is going to receive, a vaccine within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks of administration of the antibody molecule, optionally wherein the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®),

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

optionally wherein administration of the antibody molecule at the selected dose or dosage reduces,

or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject.

167. A method of treating a disorder, comprising:

administering an anti-APRIL antibody molecule to a human subject in need thereof at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

wherein the administration reduces the level of aberrantly glycosylated IgA (a-g IgA) by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject; and

wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

optionally wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

thereby treating the disorder.

168. A method of reducing the level of a-g IgA, comprising:

administering an anti-APRIL antibody molecule to a human subject in need thereof,

wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

wherein the administration reduces the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and

a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the subject has, or is at risk of having, a disorder, e.g., IgA nephropathy,

thereby reducing the level of a-g IgA.

169. A method of treating a disorder, comprising:

selecting a dose or dosage for an anti-APRIL antibody molecule;

wherein administration of the antibody molecule at the selected dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

optionally wherein the subject has, or is at risk of having, IgA nephropathy,

thereby threating the disorder.

170. A method of treating a disorder, comprising:

responsive to a determination that administration of the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject, administering to a human subject in need thereof an anti-APRIL antibody molecule at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

thereby treating the disorder.

171. A method of treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject,

if the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%, administration of the antibody

molecule at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg is initiated, continued, or maintained; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

optionally wherein if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%, administration of the antibody molecule is terminated, discontinued, or altered, and/or a different therapeutic agent or modality is administered,

optionally wherein the disorder is IgA nephropathy,

thereby treating the disorder.

172. A method of treating a disorder, comprising:

determining whether administration of a therapeutic agent or modality other than an anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in a subject in need thereof,

if the therapeutic agent or modality does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%, administering the antibody molecule to a human subject at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH)

comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

thereby treating the disorder.

173. A method of treating a disorder, comprising:

administering an anti-APRIL antibody molecule to a human subject in need thereof at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

wherein the subject has received, or is going to receive, a vaccine within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks of administration of the antibody molecule, optionally wherein the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®),

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino

acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

optionally wherein administration of the antibody molecule at the selected dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject,

thereby treating the disorder.

174. A method of selecting an anti-APRIL antibody molecule for treating a disorder, comprising:

determining whether administration of the antibody molecule at a dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in a human subject in need thereof,

wherein the dose is about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

thereby selecting the antibody molecule.

175. A method of selecting a dose or dosage for an anti-APRIL antibody molecule for treating a disorder, comprising:

determining whether administration of the antibody molecule at a dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in a human subject in need thereof,

optionally wherein the dose is about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

thereby selecting the dose or dosage.

176. A method of selecting a human subject for treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject,

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence

of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

thereby selecting the subject,

177. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-176, wherein the a-g IgA comprises or is a-g IgA1.

178. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-177, wherein the level of a-g IgA is reduced by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, three, four, five, six, seven, eight, nine, ten, eleven, or twelve months.

179. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-178, wherein the level of a-g IgA is reduced by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% about 4 weeks after the antibody molecule is administered.

180. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-179, wherein the level of a-g IgA is reduced by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% about 8 weeks after the antibody molecule is administered.

181. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-180, wherein the level of a-g IgA is reduced by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% about 12 weeks after the antibody molecule is administered.

182. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-181, wherein the level of a-g IgA is reduced by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% about 16 weeks after the antibody molecule is administered.

183. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-182, wherein the level of a-g IgA is reduced by at least 50%.

184. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-183, wherein the level of a-g IgA is reduced by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%.

185. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-184, e.g., in a period of at least 1, 2, 3, 4, 5, 6, 7, 8, 9. 10, 11, 12, 13, 14, 15, 16, 17, or 18 months.

186. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-185, wherein the antibody molecule is administered as a repeated dose, e.g., in a period of at least 3, 6, 9. 12, 15, 18, 24, 30, or 36 months, optionally wherein the subject is administered one or more additional dosages of the anti-APRIL antibody molecules (e.g., 24 hours, 48 hours, 72 hours, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 1 month, 2 months, 3 months, 4 months, 5 months, or 6 months after the first administration).

187. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-186, wherein the antibody molecule is administered subcutaneously.

188. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-186, wherein the antibody molecule is administered intravenously.

189. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-188, wherein the disorder an APRIL-associated disorder.

190. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-189, wherein the disorder is associated with an aberrant level of total IgA.

191. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-190, wherein the disorder is a disorder associated with a-g IgA.

192. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-191, wherein the disorder is IgA nephropathy (IgAN).

193. The antibody molecule, pharmaceutical composition, method for use of embodiment 192, wherein the IgAN is a familial IgAN.

194. The antibody molecule, pharmaceutical composition, method for use of embodiment 192, wherein the IgAN is an adult IgAN.

195. The antibody molecule, pharmaceutical composition, method for use of embodiment 192, wherein the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

196. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-191, wherein the disorder is a chronic kidney disease (CKD) or a disorder associated with CKD.

197. The antibody molecule, pharmaceutical composition, method for use of embodiment 196, wherein the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

198. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-191, wherein the disorder is Henoch-Schonlein purpura (HSP).

199. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-191, wherein the disorder is cutaneous vasculitis or IgA vasculitis.

200. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-191, wherein the disorder is IgA dermatitis, e.g., IgA bullous dermatosis.

201. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-191, wherein the disorder is Waldenström macroglobulinemia (WM).

202. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-191, wherein the disorder is lupus nephritis.

203. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-202, wherein the subject is a human patient.

204. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-203, wherein the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject.

205. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-204, wherein the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject.

206. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-205, wherein the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder.

207. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-206, wherein the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder.

208. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-207, wherein the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule.

209. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-208, wherein the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule.

210. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 208 or 209, wherein the subject receives the vaccine before, concurrent with, or after administration of the antibody molecule.

211. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-210, wherein administration of the antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%,

30%, 35%, 40%, 45%, or 50%.

212. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-211, wherein administration of the antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine.

213. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-212, wherein the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the antibody molecule.

214. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-213, wherein the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®).

215. The antibody molecule, pharmaceutical composition, method for use of embodiment 214, wherein the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the antibody molecule.

216. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-215, wherein the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

217. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-216, further comprising determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

218. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-217, wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence

of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

219. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-218, wherein the antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 296, and a VL comprising the amino acid sequence of SEQ ID NO: 286,

optionally wherein the antibody molecule is an IgG2.

220. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-219, wherein the level of a-g IgA is determined in a sample from the subject.

221. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-220, further comprising determining the level of a-g IgA in a sample from the subject.

222. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-221, further comprising determining the level of total IgA in the sample.

223. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-222, further comprising determining the level of IgM and/or IgG in the sample.

224. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-223, further comprising obtaining a sample from the subject.

225. The antibody molecule, pharmaceutical composition, method for use of embodiment 224, wherein the sample is a blood or serum sample.

226. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-225, further comprising administering a second therapeutic agent or modality to the subject.

227. The antibody molecule, pharmaceutical composition, method for use of embodiment 226, wherein the second therapeutic agent or modality is a small molecule.

228. The antibody molecule, pharmaceutical composition, method for use of embodiment 227, wherein the second therapeutic agent or modality is an antibody molecule.

229. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-228, wherein the subject is administered the anti-APRIL antibody molecule at a concentration of about 100, 150, 175, 180, 190, 200, 210, 220, 225, 230, 240, 250, or 300 mg/mL.

230. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-229, wherein the subject is administered the anti-APRIL antibody molecule at a concentration of about 200 mg/mL.

231. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-230, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dose of about 200, 250, 300, 450, 400, 450, 500, 550, 600, 650, 700, 750, or 800 mg.

232. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-231, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dose of about 200 mg (e.g., at a volume of about 1 mL).

233. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-232, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dose of about 400 mg (e.g., at a total volume of about 2 mL, e.g., as two administrations of 1 mL volumes or as one administration of a 2 mL volume).

234. The antibody molecule, pharmaceutical composition, method for use of any of embodiments 160-233, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dose of about 600 mg (e.g., at a total volume of about 3 mL, e.g., as one administration of a 2 mL volume and one administration of a 1 mL volume).

235. The antibody molecule, pharmaceutical composition for use, or method of any of the preceding embodiments, wherein the subject is administered the anti-APRIL antibody molecule at a fixed

dosage of at least 200 mg.

236. The antibody molecule, pharmaceutical composition for use, or method of any of the preceding embodiments, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dosage of 800 mg or less.

237. The antibody molecule, pharmaceutical composition for use, or method of any of the preceding embodiments, wherein the anti-APRIL antibody molecule is administered as a liquid composition.

The disclosure contemplates all combinations of any one or more of the foregoing aspects and/or embodiments, as well as combinations with any one or more of the embodiments set forth in the detailed description and examples.

Other features, objects, and advantages of the compositions and methods herein will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 depicts the mean percent change (± standard deviation) from baseline of aberrantly glycosylated immunoglobulin concentration over time by the indicated treatments (pooled placebo, antibody 2419-1406 at 0.5 mg/kg, antibody 2419-1406 at 2.0 mg/kg, antibody 2419-1406 at 6.0 mg/kg, antibody 2419-1406 at 12.0 mg/kg, placebo + vaccine, and antibody 2419-1406 at 6.0 mg/kg + vaccine) for all patients of any ethnicity (pharmacodynamic population).

FIG. 2 is a series of graphs showing mean percentage change from baseline in aberrantly glycosylated immunoglobulin A (a-g-IgA1; left panel) and immunoglobulin A (IgA; right panel), by treatment.

FIG. 3 is a graph showing tetanus immunoglobulin G (IgG) titer levels in the safety population.

FIG. 4 is a graph showing diphtheria immunoglobulin G (IgG) titer levels in the safety population.

FIG. 5 is a series of graphs showing IgA suppression by mAb 2419-1406 in healthy volunteers. Results are shown for subcutaneous (SC) administration (left panel) and for intravenous (IV) administration (right panel), as indicated.

DETAILED DESCRIPTION

Disclosed herein are antibody molecules that bind to APRIL, *e.g.*, human APRIL, mouse APRIL, or both, with high affinity and specificity. Advantageously, several of the antibody molecules describe herein have improved ability to reduce (*e.g.,* inhibit, block, or neutralize) one or more biological activities of APRIL. Nucleic acid molecules encoding the antibody molecules, expression vectors, host cells, compositions (*e.g.*, pharmaceutical compositions), kits, and methods for making the antibody molecules, are also provided. The antibody molecules and pharmaceutical compositions disclosed herein can be used (alone or in combination with other agents or therapeutic modalities) to treat, prevent and/or diagnose disorders and conditions, *e.g.*, disorders and conditions associated with APRIL, *e.g.,* IgA nephropathy (IgAN) or disorders associated with IgAN (e.g., an advanced chronic kidney disease (CKD), post-transplant IgAN, pediatric IgAN, Henoch-Schonlein purpura (HSP) or cutaneous vasculitis, IgAN with crescentic glomerulonephritis (GN)), IgA vasculitis, IgA dermatitis (e.g., IgA dermatitis herpetiformis, IgA bullous dermatosis), IgM mediated neuropathy (e.g., anti-MAG peripheral neuropathy or IgM mediated neuropathy associated with anti-GM1 antibodies), Waldenstrom's macroglobulinemia (WM, also known as Waldenström macroglobulinemia), or lupus nephritis).

IgA nephropathy is one of the most prevalent, chronic glomerular diseases, with a global incidence of approximately 5-50 cases/million (children) and 10-40 cases/million (adults). While typically a relatively indolent disease, IgAN can progress to end-stage renal disease (e.g., kidney failure in 20%-50% of patients within 20 to 30 years). IgA nephropathy patients with minor urine abnormalities, normal blood pressure and normal glomerular filtration rate (GFR) typically need periodic monitoring. For those with more advanced disease, the therapeutic options can include nonspecific treatment to reduce blood pressure and proteinuria by RAS blockade, as well as other general measures, such as lipid lowering, dietary restriction of sodium, smoking cessation and avoidance of NSAIDs and other nephrotoxins.

Without wishing to be bound by theory, it is believed that in some embodiments, the etiology of IgA nephropathy represents a two-hit phenomenon, wherein the first hit occurs in response to a mucosal infection, as production of polymeric IgA1, containing an aberrantly galactosylated hinge region (aberrantly glycosylated IgA1 or a-g IgA1), presents as an autoantigen; and the second hit is the subsequent induction of autoantibodies that results in immune complex formation. These circulating immune complexes are then deposited in the kidney, where complement activation occurs, resulting in promotion of inflammatory pathways, mesangial hyperproliferation, glomerular damage, proteinuria, and progression of kidney disease leading to end-stage renal disease. Without wishing to be bound by theory, it is believed that in some embodiments, reduction of the autoantigen and/or autoantibody, and removal of the resulting immune complexes, and/or mitigation of complement activation can have a beneficial effect on progression of IgA nephropathy and other related diseases and disorders (e.g., an advanced chronic

kidney disease (CKD), post-transplant IgAN, pediatric IgAN, Henoch-Schonlein purpura (HSP) or cutaneous vasculitis, IgAN with crescentic glomerulonephritis (GN), IgA vasculitis, IgA dermatitis (e.g., IgA dermatitis herpetiformis, IgA bullous dermatosis), IgM mediated neuropathy (e.g., anti-MAG peripheral neuropathy or IgM mediated neuropathy associated with anti-GM1 antibodies), Waldenstrom's Macroglobulinemia (WM), or lupus nephritis).

Without wishing to be bound by theory, it is believed that in some embodiments, the aberrant biosynthesis of polymeric IgA and antigenic a-g IgA1 is correlated to both disease pathogenesis and progression. In an embodiment, the serum levels of a-g IgA1 are correlated as a heritable trait with substantial heritability in a significant number of adult and pediatric familial IgA nephropathy cases. In an embodiment, a-g IgA1 plays a role in disease pathogenesis, which can be determined, e.g., by *ex vivo* analysis of peripheral blood mononuclear cells (PBMCs) derived from patients. For example, a-g IgA1 can be secreted in immortalized B cells from IgA nephropathy patients and IgA1 production from patient lymphocytes can be correlated to serum levels of a-g IgA1. As another example, immune complexes derived in part from IgA1-producing cells that were then reconstituted *in vitro* using sera from IgA nephropathy patients can be pathogenic in mice following passive transfer. Without wishing to be bound by theory, it is believed that in some embodiments, serum levels of a-g IgA1 can be predictive of disease outcomes and provide diagnostic utility as a biomarker for clinical evaluation of disease progression, treatment, and also stratification of patient populations. For example, a targeted reduction in IgA can be therapeutically advantageous and can effectively reduce immune deposits and kidney damage. In an embodiment, treatment with an antibody molecule described herein results in clinically relevant reduction of autoantigen levels, e.g., a-g IgA levels.

Without wishing to be bound by theory, it is believed that in some embodiments, the anti-APRIL antibody molecules described herein (e.g., single doses up to 12.0 mg/kg) are safe and well tolerated in healthy adults. In an embodiment, a single dose of the anti-APRIL antibody molecule can suppress free serum APRIL to the lower level of quantification. In an embodiment, serum a-g IgA1 decreases in parallel with total serum IgA and recovers in a dose-dependent manner following detection of free APRIL in serum.

Without wishing to be bound by theory, it is believed that in some embodiments, the anti-APRIL antibody molecules described herein do not interfere with subjects' ability to mount an antigen-specific serum IgG or IgA boost response to vaccination (e.g., tetanus and diphtheria toxoid vaccination), indicating that qualitative T-cell dependent antibody responses are preserved during APRIL suppression.

Definitions

As used herein, the articles "a" and "an" refer to one or to more than one (*e.g.,* to at least one) of the grammatical object of the article.

The term "or" is used herein to mean, and is used interchangeably with, the term "and/or", unless context clearly indicates otherwise.

"About" and "approximately" shall generally mean an acceptable degree of error for the quantity measured given the nature or precision of the measurements. Exemplary degrees of error are within 20 percent (%), typically, within 10%, and more typically, within 5% of a given value or range of values.

The compositions and methods disclosed herein encompass polypeptides and nucleic acids having the sequences specified, or sequences substantially identical or similar thereto, *e.g.,* sequences at least 85%, 90%, 95% identical or higher to the sequence specified.

In the context of an amino acid sequence, the term "substantially identical" is used herein to refer to a first amino acid that contains a sufficient or minimum number of amino acid residues that are i) identical to, or ii) conservative substitutions of aligned amino acid residues in a second amino acid sequence such that the first and second amino acid sequences can have a common structural domain and/or common functional activity. For example, amino acid sequences that contain a common structural domain having at least about 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, *e.g.,* a sequence provided herein.

In the context of nucleotide sequence, the term "substantially identical" is used herein to refer to a first nucleic acid sequence that contains a sufficient or minimum number of nucleotides that are identical to aligned nucleotides in a second nucleic acid sequence such that the first and second nucleotide sequences encode a polypeptide having common functional activity, or encode a common structural polypeptide domain or a common functional polypeptide activity. For example, nucleotide sequences having at least about 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, *e.g.,* a sequence provided herein.

The term "functional variant" refers polypeptides that have a substantially identical amino acid sequence to the naturally-occurring sequence, or are encoded by a substantially identical nucleotide sequence, and are capable of having one or more activities of the naturally-occurring sequence.

Calculations of homology or sequence identity between sequences (the terms are used interchangeably herein) are performed as follows.

To determine the percent identity of two amino acid sequences, or of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (*e.g.,* gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). In a typical embodiment, the length of a

reference sequence aligned for comparison purposes is at least 30%, *e.g.,* at least 40%, 50%, 60%, *e.g.,* at least 70%, 80%, 90%, 100% of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position.

The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In some embodiments, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch ((1970) *J. Mol. Biol.* 48:444-453) algorithm which has been incorporated into the GAP program in the GCG software package (available at gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In certain embodiments, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. One suitable set of parameters (and the one that should be used unless otherwise specified) are a Blossum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

The percent identity between two amino acid or nucleotide sequences can be determined using the algorithm of E. Meyers and W. Miller ((1989) CABIOS, 4:11-17) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

The nucleic acid and protein sequences described herein can be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to a nucleic acid as described herein. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to protein molecules described herein. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, (1997) *Nucleic Acids Res.* 25:3389-3402. When utilizing BLAST and gapped BLAST programs, the default parameters of the respective programs (*e.g.,* XBLAST and NBLAST) can be used. See ncbi.nlm.nih.gov.

As used herein, the term "hybridizes under low stringency, medium stringency, high stringency, or very high stringency conditions" describes conditions for hybridization and washing. Guidance for performing hybridization reactions can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6, which is incorporated by reference. Aqueous and nonaqueous methods are described in that reference and either can be used. Specific hybridization conditions referred to herein are as follows: 1) low stringency hybridization conditions in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by two washes in 0.2X SSC, 0.1% SDS at least at 50°C (the temperature of the washes can be increased to 55°C for low stringency conditions); 2) medium stringency hybridization conditions in 6X SSC at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 60°C; 3) high stringency hybridization conditions in 6X SSC at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 65°C; and preferably 4) very high stringency hybridization conditions are 0.5M sodium phosphate, 7% SDS at 65°C, followed by one or more washes at 0.2X SSC, 1% SDS at 65°C. Very high stringency conditions 4) are suitable conditions and the ones that should be used unless otherwise specified.

It is understood that the molecules described herein may have additional conservative or non-essential amino acid substitutions, which do not have a substantial effect on their functions.

The term "amino acid" is intended to embrace all molecules, whether natural or synthetic, which include both an amino functionality and an acid functionality and capable of being included in a polymer of naturally-occurring amino acids. Exemplary amino acids include naturally-occurring amino acids; analogs, derivatives and congeners thereof; amino acid analogs having variant side chains; and all stereoisomers of any of any of the foregoing. As used herein the term "amino acid" includes both the D- or L- optical isomers and peptidomimetics.

A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.,* lysine, arginine, histidine), acidic side chains (*e.g.,* aspartic acid, glutamic acid), uncharged polar side chains (*e.g.,* glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.,* alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.,* threonine, valine, isoleucine) and aromatic side chains (*e.g.,* tyrosine, phenylalanine, tryptophan, histidine).

The terms "polypeptide," "peptide" and "protein" (if single chain) are used interchangeably herein to refer to polymers of amino acids of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified; for example, disulfide bond formation, glycosylation,

lipidation, acetylation, phosphorylation, or any other manipulation, such as conjugation with a labeling component. The polypeptide can be isolated from natural sources, can be a produced by recombinant techniques from a eukaryotic or prokaryotic host, or can be a product of synthetic procedures.

The terms "nucleic acid," "nucleic acid sequence," "nucleotide sequence," or "polynucleotide sequence," and "polynucleotide" are used interchangeably. They refer to a polymeric form of nucleotides of any length, either deoxyribonucleotides or ribonucleotides, or analogs thereof. The polynucleotide may be either single-stranded or double-stranded, and if single-stranded may be the coding strand or non-coding (antisense) strand. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. The nucleic acid may be a recombinant polynucleotide, or a polynucleotide of genomic, cDNA, semisynthetic, or synthetic origin which either does not occur in nature or is linked to another polynucleotide in a non-natural arrangement.

The term "isolated," as used herein, refers to material that is removed from its original or native environment (*e.g.,* the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or polypeptide, separated by human intervention from some or all of the co-existing materials in the natural system, is isolated. Such polynucleotides could be part of a vector and/or such polynucleotides or polypeptides could be part of a composition, and still be isolated in that such vector or composition is not part of the environment in which it is found in nature.

As used herein, the term "treat," *e.g.,* IgA nephropathy, means that a subject (*e.g.,* a human) who has a disorder, *e.g.,* IgA nephropathy, and/or experiences a symptom of a disorder, *e.g.,* IgA nephropathy, will, in an embodiment, suffer less a severe symptom and/or recover faster when an antibody molecule is administered than if the antibody molecule were never administered. In an embodiment, when IgA nephropathy is treated, a kidney biopsy will show less or no IgA deposits, *e.g.,* in the form of immune complexes in the mesangium of the kidney, after effective treatment for IgA nephropathy. For example, a diagnostic assay using immunofluorescence or electron microscopy will detect less no IgA deposits in a biological sample of a subject after administration of an antibody molecule described herein for the effective treatment of IgA nephropathy. Other assays, urine tests, blood tests, iothalamate clearance tests, or kidney imaging (*e.g.,* ultrasound, X-rays, or cystoscopy), can also be used to monitor treatment in a patient, or to detect the presence, *e.g.,* decreased presence (or absence), of a symptom of IgA nephropathy, after treatment of IgA nephropathy in the subject. Treatment can, *e.g.,* partially or completely, alleviate, ameliorate, relieve, inhibit, or reduce the severity of, and/or reduce incidence, and optionally, delay onset of, one or more manifestations of the effects or symptoms, features, and/or causes

of a disorder, *e.g.,* IgA nephropathy. In an embodiment, treatment is of a subject who does not exhibit certain signs of a disorder, *e.g.,* IgA nephropathy, and/or of a subject who exhibits only early signs of a disorder, *e.g.,* nephropathy. In an embodiment, treatment is of a subject who exhibits one or more established signs of a disorder, *e.g.,* IgA nephropathy. In an embodiment, treatment is of a subject diagnosed as suffering from a disorder, *e.g.,* IgA nephropathy.

As used herein, the term "prevent," a disorder, *e.g.,* IgA nephropathy, means that a subject (*e.g.,* a human) is less likely to have the disorder, *e.g.,* IgA nephropathy, if the subject receives the antibody molecule.

Various aspects of the compositions and methods herein are described in further detail below. Additional definitions are set out throughout the specification.

APRIL

APRIL (A PRoliferation Inducing Ligand), also known as CD256, TNF- and APOL-related Leukocyte Expressed Ligand 2 (TALL-2), or TNF-related Death Ligand 1 (TRDL-1), is a TNF family cytokine encoded by the Tumor Necrosis Factor Ligand Superfamily Member 13 (*TNFSF13*) gene (also known as *APRIL, TALL2, or ZTNF2*). APRIL plays a role in a number of biological processes such as signal transduction, regulation of cell proliferation, and IgA class switching (Hahne *et al. (1998) J. Exp. Med.* 188:1185-1190 (1998); Castigli *et al. Proc. Natl. Acad. Sci. U.S.A.* 101:3903-3908 (2004)).

APRIL is both functionally and structurally related to BAFF (B Cell Activating Factor F13B) also known as BLyS (B lymphocyte stimulator). Both cytokines are involved in regulating keys aspects of innate and adaptive immune functions. Both APRIL and BAFF bind the lymphocyte receptors TACI (transmembrane activator and CAML interactor) and BCMA (B cell maturation antigen). APRIL and BAFF appear to heterologously interact with each other through protein-protein interactions. While both APRIL and BAFF share biochemical (receptor binding), immunological and even some structural overlap (*e.g.,* as it relates to the three-dimensional topology of their respective receptor binding domains), the two cytokines, nevertheless, are both structurally and functionally distinct. APRIL binds to biologically relevant heparan sulfate (present in the extracellular matrices of cells as heparan sulfate proteoglycans); BAFF does not. This interaction plays a critical biological function with respect to promoting the oligomerization state of APRIL in concert with its localized interaction with TACI, which likewise requires HSPGS for full activity. Unlike BAFF which acts as a potent activator of B cells inclusive of both proliferation and differentiation, APRIL would appear to function more particularly with respect to the modulation of B cell phenotype, *e.g.,* as it relates to IgA production and the differentiation/survival of IgA positive plasma cells. As such, a targeted disruption in APRIL-receptor signaling is expected to have less perturbative effects on B cell homeostasis and overall immune function in comparison to other

immune related therapeutics that target BAFF (*e.g.,* belimumab) or anti CD20 therapies (*e.g.,* rituximab) that largely target pre and early B cells. APRIL has also been shown to be expressed at high levels on other myeloid related cells and lymphoid tissues, as well as hematological cancers (*e.g.,* myeloma, chronic lymphocytic leukemia (CLL)) and solid tumors (*e.g.,* colon, thyroid, and breast).

Exemplary amino acid and nucleotide sequences of human APRIL are described, *e.g.,* in Hahne *et al. J. Exp. Med.* 188:1185-1190 (1998); Shu *et al. J. Leukoc. Biol.* 65:680-683 (1999); Kelly *et al. Cancer Res.* 60:1021-1027(2000); and Pradet-Balade *et al. EMBO J.* 21:5711-5720 (2002).

The amino acid sequence of human APRIL (isoform alpha, also referred to as the "canonical" sequence (SEQ ID NO: 85)) is provided as follows.

>huAPRIL
MPASSPFLLAPKGPPGNMGGPVREPALSVALWLSWGAALGAVACAMALLTQQTELQSLRREVSRLQGTGG
PSQNGEGYPWQSLPEQSSDALEAWENGERSRKRRAVLTQKQKKQHSVLHLVPINATSKDDSDVTEVMWQP
ALRRGRGLQAQGYGVRIQDAGVYLLYSQVLFQDVTFTMGQVVSREGQGRQETLFRCIRSMPSHPDRAYNS
CYSAGVFHLHQGDILSVIIPRARAKLNLSPHGTFLGFVKL

There are several isoforms of human APRIL produced by alternative splicing.

Isoform beta has the following amino acid sequence (SEQ ID NO: 86):

>sp|O75888-2|TNF13_HUMAN Isoform Beta of Tumor necrosis factor ligand
superfamily member 13 OS=Homo sapiens GN=TNFSF13
MPASSPFLLAPKGPPGNMGGPVREPALSVALWLSWGAALGAVACAMALLTQQTELQSLRREVSRLQGTGG
PSQNGEGYPWQSLPEQSSDALEAWENGERSRKRRAVLTQKQKNDSDVTEVMWQPALRRGRGLQAQGYGVR
IQDAGVYLLYSQVLFQDVTFTMGQVVSREGQGRQETLFRCIRSMPSHPDRAYNSCYSAGVFHLHQGDILS
VIIPRARAKLNLSPHGTFLGFVKL

The sequence of isoform beta differs from the canonical sequence as follows: amino acids 113-129 of SEQ ID NO: 85: KQHSVLHLVPINATSKD → N

Isoform gamma has the following amino acid sequence (SEQ ID NO: 87):

>sp|O75888-3|TNF13_HUMAN Isoform Gamma of Tumor necrosis factor ligand
superfamily member 13 OS=Homo sapiens GN=TNFSF13
MPASSPFLLAPKGPPGNMGGPVREPALSVALWLSWGAALGAVACAMALLTQQTELQSLRREVSRLQGTGG
PSQNGEGYPWQSLPEQSSDALEAWENGERSRKRRAVLTQKQKKQHSVLHLVPINATSKDDSDVTEVMWQP
ALRRGRGLQAQGYGVRIQDAGVYLLYSQVLFQDVTFTMGQVVSREGQGRQETLFRCIRSMPSHPDRAYNS
CYSAGVFHLHQGDILSVIIPRARAKLNLSPHGTFLGL

The sequence of isoform gamma differs from the canonical sequence as follows: amino acids 247-249: Missing.

Isoform 4 has the following amino acid sequence (SEQ ID NO: 88):

>sp|O75888-4|TNF13_HUMAN Isoform 4 of Tumor necrosis factor ligand
superfamily member 13 OS=Homo sapiens GN=TNFSF13
MPASSPFLLAPKGPPGNMGGPVREPALSVALWLSWGAALGAVACAMALLTQQTELQSLRREVSRLQGTGG
PSQNGEGYPWQSLPEQHSVLHLVPINATSKDDSDVTEVMWQPALRRGRGLQAQGYGVRIQDAGVYLLYSQ
VLFQDVTFTMGQVVSREGQGRQETLFRCIRSMPSHPDRAYNSCYSAGVFHLHQGDILSVIIPRARAKLNL
SPHGTFLGFVKL

The sequence of isoform 4 differs from the canonical sequence as follows: amino acids 86-113: Missing.

Isoform TWE-PRIL has the following amino acid sequence (SEQ ID NO: 89):

```
>sp|O43508-2|TNF12_HUMAN Isoform TWE-PRIL of Tumor necrosis factor
ligand superfamily member 12 OS=Homo sapiens GN=TNFSF12
MAARRSQRRRGRRGEPGTALLVPLALGLGLALACLGLLLAVVSLGSRASLSAQEPAQEELVAEEDQDPSE
LNPQTEESQDPAPFLNRLVRPRRSAPKGRKTRARRAIAAHYEVHPRPGQDGAQAGVDGTVSGWEEARINS
SSPLRYNRQIGEFIVTRAGLYYLYCQSSDALEAWENGERSRKRRAVLTQKQKKQHSVLHLVPINATSKDD
SDVTEVMWQPALRRGRGLQAQGYGVRIQDAGVYLLYSQVLFQDVTFTMGQVVSREGQGRQETLFRCIRSM
PSHPDRAYNSCYSAGVFHLHQGDILSVIIPRARAKLNLSPHGTFLGFVKL
```

Isoform 5 has the following amino acid sequence (SEQ ID NO: 90):

```
>sp|O75888-5|TNF13_HUMAN Isoform 5 of Tumor necrosis factor ligand
superfamily member 13 OS=Homo sapiens GN=TNFSF13
MGGPVREPALSVALWLSWGAALGAVACAMALLTQQTELQSLRREVSRLQGTGGPSQNGEGYPWQSLPEQH
SVLHLVPINATSKDDSDVTEVMWQPALRRGRGLQAQGYGVRIQDAGVYLLYSQVLFQDVTFTMGQVVSRE
GQGRQETLFRCIRSMPSHPDRAYNSCYSAGVFHLHQGDILSVIIPRARAKLNLSPHGTFLGFVKL
```

The sequence of isoform 5 differs from the canonical sequence as follows: amino acids 1-17: Missing; amino acids 87-114: Missing.

Other variant and alternative sequences of human APRIL are described, *e.g.,* in The MGC Project Team, *Genome Res.* 14:2121-2127 (2004); Ota *et al. Nat. Genet.* 36:40-45 (2004); and Kelly *et al. Cancer Res.* 60:1021-1027 (2000).

As used herein, when an anti-APRIL antibody molecule binds, or substantially binds, to human APRIL, it binds, or substantially binds, to one or more isoforms of human APRIL, *e.g.,* one or more isoforms of human APRIL described herein. In an embodiment, the antibody molecule binds or substantially binds to human APRIL having the amino acid sequence of SEQ ID NO: 85.

Exemplary amino acid and nucleotide sequences of mouse APRIL are described, *e.g.,* in Yu *et al.* Nat. Immunol. 1:252-256 (2000); Carninci *et al.* Science 309:1559-1563 (2005); The MGC Project Team, Genome Res. 14:2121-2127 (2004); and Bossen *et al.* J. Biol Chem. 281: 13964-13971 (2006).

The amino acid sequence of mouse APRIL isoform 1 (SEQ ID NO: 91) is provided as follows.

```
>muAPRIL
MPASSPGHMGGSVREPALSVALWLSWGAVLGAVTCAVALLIQQTELQSLRREVSRLQRSGGPSQKQGERP
WQSLWEQSPDVLEAWKDGAKSRRRRAVLTQKHKKKHSVLHLVPVNITSKADSDVTEVMWQPVLRRGRGLE
AQGDIVRVWDTGIYLLYSQVLFHDVTFTMGQVVSREGQGRRETLFRCIRSMPSDPDRAYNSCYSAGVFHL
HQGDIITVKIPRANAKLSLSPHGTFLGFVKL
```

The amino acid sequence of mouse APRIL isoform 2 (SEQ ID NO: 92) is provided as follows.

MPASSPGHMGGSVREPALSVALWLSWGAVLGAVTCAVALLIQQTELQSLRREVSRLQRSGGPSQKQGERP
WQSLWEQSPDVLEAWKDGAKSRRRRAVLTQKHKKKHSVLHLVPVNITSKDSDVTEVMWQPVLRRGRGLEA
QGDIVRVWDTGIYLLYSQVLFHDVTFTMGQVVSREGQGRRETLFRCIRSMPSDPDRAYNSCYSAGVFHLH
QGDIITVKIPRANAKLSLSPHGTFLGFVKL

As used herein, when an anti-APRIL antibody molecule binds, or substantially binds, to mouse APRIL, it binds, or substantially binds, to one or more isoforms of mouse APRIL, *e.g.,* one or more isoforms of mouse APRIL described herein. In an embodiment, the antibody molecule binds or substantially binds to mouse APRIL having the amino acid sequence of SEQ ID NO: 91, SEQ ID NO: 92, or both.

As used herein, when an anti-APRIL antibody molecule does not bind, or does not substantially bind, to mouse APRIL, it does not bind, or does not substantially bind, to one or more isoforms of mouse APRIL, *e.g.,* one or more isoforms of mouse APRIL described herein. In an embodiment, the antibody molecule does not bind, or does not substantially bind, to mouse APRIL having the amino acid sequence of SEQ ID NO: 91 or 92. In a typical embodiment, the antibody molecule does not bind, or does not substantially bind, to mouse APRIL having the amino acid sequence of SEQ ID NO: 91 and mouse APRIL having the amino acid sequence of SEQ ID NO: 92.

Sequence alignment of exemplary human and mouse APRIL proteins (SEQ ID NOS: 85 and 91, respectively) is shown in FIG. 13 of International Application Publication No. WO2017/091683, the contents of which are incorporated herein by reference in its entirety.

Epitope

The antibody molecule described herein can bind to an epitope on APRIL (*e.g.,* human APRIL, mouse APRIL, or both). For example, an epitope bound by an antibody molecule described herein can include one or more epitope contact points described herein.

In an embodiment, the antibody molecule contacts (*e.g.,* binds, or substantially binds, to) one or more residues, or one or more regions, as described in any of **Tables 3-4 or 6**, or Table 8 or any of FIGS. 14, 22, 23A-23B, 24A-24B, 25A-25B, or 38A-38B of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all) of the amino acid residues shown in **Table 3**. In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) all of the amino acid residues shown in **Table 3**. For example, the antibody molecules described herein can contact the amino acid residues shown in **Table 3** in a manner that includes binding across two APRIL monomers (*e.g.,* as depicted positionally in **Table 3** as A vs. B). While not wishing to be bound by theory, it is believed that in an embodiment, at least some of the amino

acid residues shown in **Table 3** contribute to high affinity interactions between APRIL and the CDR2 domain of TACI. In an embodiment, contacting one or more of the amino acid residues in **Table 3** with an antibody molecule described herein inhibits, or substantially inhibits, binding of APRIL to TACI.

Exemplary human APRIL amino acid residues that can bind to the anti-APRIL antibody molecules described herein are shown in **Table 3**. A structural representation of this epitope (*e.g.*, defined both spatially and conformationally) is depicted in FIG. 14 of International Application Publication No. WO2017/091683.

Table 3. Exemplary Human APRIL Amino Acid Residues that Bind to Anti-APRIL Antibodies (amino acid numbering based on SEQ ID NO: 85)

Monomer	Amino Acid Position	Amino Acid
A	130	Asp
A	131	Ser
A	132	Asp
A	174	Val
A	175	Thr
A	176	Phe
A	177	Thr
A	178	Met
A	179	Gly
A	180	Gln
A	181	Val
A	192	Thr
A	195	Arg
A	196	Cys
A	197	Ile
A	200	Met
A	201	Pro
A	202	Ser
A	208	Tyr
A	230	Pro
A	231	Arg
A	232	Ala
A	241	His
B	170	Leu
B	205	Asp
B	206	Arg

In another embodiment, the antibody molecule contacts (*e.g.*, binds or substantially binds to) one or more (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, or all) of the amino acid residues shown in **Table 4**. In another

embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) all of the amino acid residues shown in **Table 4**. In an embodiment, the antibody molecule binds, or substantially binds to, the C-D loop (*e.g.,* the loop connecting β-sheets C and D), the G-H loop (*e.g.,* the loop connecting β-sheets G and H), or both, on APRIL.

A structural (spatial) representation of this epitope (sometimes referred herein as "core region") is depicted in FIG. 15 of International Application Publication No. WO2017/091683, which shows each APRIL protein molecule contains two packed antiparallel eight-stranded β-sheets (A to G), one inner and one outer, in a β-jelly roll topology. These B sheets are connected by loops that also define (based on secondary structure definitions) a desired epitope. While not wishing to be bound by theory, it is believed that as these positions/structures define a subset of key interactions with APRIL and the CRD2 domain of TACI, optimal inhibition of APRIL binding to TACI by such an antibody would be achieved.

Table 4. Exemplary Human APRIL Amino Acid Residues that Bind to Anti-APRIL Antibodies (amino acid numbering based on SEQ ID NO: 85)

Amino Acid Position	Amino Acid
174	Val
175	Thr
176	Phe
177	Thr
178	Met
179	Gly
180	Gln
181	Val
230	Pro
231	Arg
232	Ala

In another embodiment, the antibody molecule does not bind to one, two, or all of Asp129, Arg233, or HIS203, on human APRIL (*e.g.,* SEQ ID NO: 85). For example, one or more mutations at these positions, *e.g.,* Asp129Ala, Arg233Asn, His203Asp, or any combination thereof, would not reduce, or substantially reduce, the binding affinity of the antibody molecule to human APRIL, or the inhibitory effect of the antibody molecule on a human APRIL activity (*e.g.,* neutralization of APRIL binding to TACI).

In yet another embodiment, the antibody molecule binds, or substantially binds, to one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) residues of human APRIL (*e.g.,* SEQ ID NO: 85) from positions 105-114 and/or one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) residues of mouse APRIL (*e.g.,* SEQ ID NO: 91) from positions 96-105.

In another embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all) of the amino acid residues shown in **Table 7**. In another embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) all of the amino acid residues shown in **Table 7**.

Table 7. Exemplary Human APRIL Amino Acid Residues that Bind to Anti-APRIL Antibodies (amino acid numbering based on SEQ ID NO: 85)

Amino Acid Position	Amino Acid
132	Asp
170	Leu
175	Thr
176	Phe
177	Thr
178	Met
181	Val
192	Thr
195	Arg
197	Ile
205	Asp
206	Arg
208	Tyr
228	Iso
230	Pro
231	Arg
232	Ala
241	His

In an embodiment, the antibody molecule, *e.g.,* an anti-APRIL antibody molecule having one, two, three, four, five or six CDRs of any of monoclonal antibodies 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1210, 2419-1305, 2419-1306, 2419-1310, or 2419-1406, binds to one or more amino acids described in **Table 7**. In another embodiment, the antibody molecule, *e.g.,* a human-specific, anti-APRIL antibody molecule, *e.g.,* having one, two, three, four, five or six CDRs of any of monoclonal antibodies 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, binds to mouse APRIL when one or more (*e.g.,* 2, 3, 4 or all) following positions within mouse APRIL (mouse APRIL numbering applies) are mutated, *e.g.,* to the following: A120D, N224R, H163Q, K219I, or R181Q. In yet another embodiment, the antibody molecule, *e.g.,* a human-specific, anti-APRIL antibody molecule, *e.g.,* having one, two, three, four, five or six CDRs of

any of monoclonal antibodies 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, binds to mouse APRIL when the lysine at position 219 (mouse APRIL numbering applies) is mutated, *e.g.,* to an isoleucine (*i.e.,* K219I).

In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, or all) of the amino acid residues of human APRIL shown in Table 6 of International Application Publication No. WO2017/091683. In an embodiment, the antibody molecule is an antibody molecule described herein, *e.g.,* monoclonal antibody 2218, 2419, 2621, 2622, 3125, 3327, 3525, 3530, 4035, 3934, 3833, 3631, 3732, 4338, 4540, or 4237.

In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) of the amino acid residues of human APRIL chosen from D132, V174, F176, V181, Q190, R195, R206, Y208, I228, or N237. In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, 4, 5, or all) of the amino acid residues of human APRIL chosen from V174, F176, Q190, R195, R206, or Y208. In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, or all) of the amino acid residues of human APRIL chosen from F176, V181, Q190, or I228. In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, or all) of the amino acid residues of human APRIL chosen from V174, R206, or Y208.

In an embodiment, the antibody molecule does not contact (*e.g.,* does not bind or does not substantially bind to) at least one (*e.g.,* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20) of the amino acid residues of human APRIL shown in Table 6 of International Application Publication No. WO2017/091683. In an embodiment, the antibody molecule is an antibody molecule described herein, *e.g.,* monoclonal antibody 2218, 2419, 2621, 2622, 3125, 3327, 3525, 3530, 4035, 3934, 3833, 3631, 3732, 4338, 4540, or 4237.

In an embodiment, the antibody molecule does not contact (*e.g.,* does not bind or does not substantially bind to) one or more (*e.g.,* 2, 3, 4, 5, 6, or all) of the amino acid residues of human APRIL chosen from F176, V181, Q190, S226, I228, Y208, or N237. In an embodiment, the antibody molecule does not contact (*e.g.,* does not bind or does not substantially bind to) one or more (*e.g.,* 2, 3, or all) of the amino acid residues of human APRIL chosen from V181, S226, I228, or N237. In an embodiment, the antibody molecule does not contact (*e.g.,* does not bind or does not substantially bind to) one or both of the amino acid residues of human APRIL chosen from Y208 or N237. In an embodiment, the antibody

molecule does not contact (*e.g.,* does not bind or does not substantially bind to) one or more (*e.g.,* 2, 3, or all) of the amino acid residues of human APRIL chosen from F176, V181, Q190, or N237.

In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, 4, 5, or all) of the amino acid residues of human APRIL chosen from V174, F176, Q190, R195, R206, or Y208; and does not contact (*e.g.,* does not bind or does not substantially bind to) one or more (*e.g.,* 2, 3, or all) of the amino acid residues of human APRIL chosen from V181, S226, I228, or N237. In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or both of the amino acid residues of human APRIL chosen from V174 or R206; and does not contact (*e.g.,* does not bind or does not substantially bind to) one or both of the amino acid residues of human APRIL chosen from V181 or N237 (and optionally S226). In an embodiment, the antibody molecule comprises one or more (*e.g.*, two or three) heavy chain CDRs, one or more (*e.g.*, two or three) light chain CDRs, or both of monoclonal antibody 4035. In an embodiment, the antibody molecule comprises a heavy chain region, a light chain variable region, or both, of monoclonal antibody 4035. In an embodiment, monoclonal antibody 4035 is a humanized antibody molecule.

In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, or all) of the amino acid residues of human APRIL chosen from F176, V181, Q190, or I228; and does not contact (*e.g.,* does not bind or does not substantially bind to) one or both of the amino acid residues of human APRIL chosen from Y208 or N237. In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) amino acid residue I228 of human APRIL; and does not contact (*e.g.,* does not bind or does not substantially bind to) one or both of the amino acid residues of human APRIL chosen from Y208 or N237. In an embodiment, the antibody molecule comprises one or more (*e.g.*, two or three) heavy chain CDRs, one or more (*e.g.*, two or three) light chain CDRs, or both of monoclonal antibody 2419. In an embodiment, the antibody molecule comprises a heavy chain region, a light chain variable region, or both, of monoclonal antibody 2419. In an embodiment, monoclonal antibody 2419 is a humanized antibody molecule.

In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, or all) of the amino acid residues of human APRIL chosen from V174, R206, or Y208; and does not contact (*e.g.,* does not bind or does not substantially bind to) one or more (*e.g.,* 2, 3, or all) of the amino acid residues of human APRIL chosen from F176, V181, Q190, or N237. In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or both of the amino acid residues of human APRIL chosen from V174 or R206; and does not contact (*e.g.,* does not bind or does not substantially bind to) one or more (*e.g.,* 2, 3, or all) of the amino acid residues of human APRIL chosen from F176, V181, Q190, or N237. In an embodiment, the antibody molecule comprises one or more (*e.g.*, two or three) heavy chain CDRs, one or more (*e.g.*, two or three) light chain CDRs, or both of

monoclonal antibody 3833. In an embodiment, the antibody molecule comprises a heavy chain region, a light chain variable region, or both, of monoclonal antibody 3833. In an embodiment, monoclonal antibody 3833 is a humanized antibody molecule.

In an embodiment, the epitope overlaps with a CRD2 receptor binding site. In an embodiment, the epitope is non-linear epitope, *e.g.,* that spans across a monomer interface. In an embodiment, the epitope is in a region associated with both TACI and BCMA receptor blocking.

In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or all) of the amino acid residues of human APRIL chosen from V133, V181, E185, Q187, G188, R189, Q190, E191, T192, R195, H218, L219, H220, S226, I228, P230 (located in monomer A). In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) of the amino acid residues of human APRIL chosen from V121, I123, Q139, P140, A141, L142, N237, S239, P240, or H241 (located in monomer B). In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all) of the amino acid residues of human APRIL chosen from V133, V181, E185, Q187, G188, R189, Q190, E191, T192, R195, H218, L219, H220, S226, I228, P230 (located in monomer A); V121, I123, Q139, P140, A141, L142, N237, S239, P240, or H241 (located in monomer B).

In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, or all) of the amino acid residues of human APRIL chosen from V181, Q190, T192, and I228 (located in monomer A). In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or both of the amino acid residues of human APRIL chosen from A141 or H241 (located in monomer B). In an embodiment, the antibody molecule contacts (*e.g.,* binds or substantially binds to) one or more (*e.g.,* 2, 3, 4, 5, or all) of the amino acid residues of human APRIL chosen from V181, Q190, T192, and I228 (located in monomer A); A141 or H241 (located in monomer B).

In an embodiment, the antibody molecule comprises one or more (*e.g.*, two or three) heavy chain CDRs, one or more (*e.g.*, two or three) light chain CDRs, or both of monoclonal antibody 2419. In an embodiment, the antibody molecule comprises a heavy chain region, a light chain variable region, or both, of monoclonal antibody 2419. In an embodiment, monoclonal antibody 2419 is a humanized antibody molecule.

In an embodiment, the epitope comprise one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all) of the amino acid residues of human APRIL chosen from V133, V181, E185, Q187, G188, R189, Q190, E191, T192, R195, H218, L219, H220, S226, I228, P230

(located in monomer A); V121, I123, Q139, P140, A141, L142, N237, S239, P240, or H241 (located in monomer B). In an embodiment, the epitope comprises one or more (*e.g.,* 2, 3, 4, 5, or all) of the amino acid residues of human APRIL chosen from V181, Q190, T192, and I228 (located in monomer A); A141 or H241 (located in monomer B).

In an embodiment, a structural representation of this epitope is depicted in FIG. 38B of International Application Publication No. WO2017/091683. In an embodiment, the epitope comprises one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all) of the amino acid residues shown in Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule contacts (*e.g.*, binds, or substantially binds, to) all of the amino acid residues shown in any of **Tables 3-4 or 7**, or Table 8 of International Application Publication No. WO2017/091683. In an embodiment, the epitope comprises, or consists of, all of the amino acid residues shown in any of **Tables 3-4 or 7**, or Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule has one or more of the following properties described herein, *e.g.,* one or more (*e.g.,* two, three or all) of: (i) binds, or substantially binds, to human APRIL; (ii) binds, or substantially binds, to mouse APRIL; (iii) inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both); or (iv) inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both). In an embodiment, the antibody molecule binds, or substantially binds, to mouse APRIL. In another embodiment, the antibody molecule does not bind, or binds with low affinity, to mouse APRIL.

Antibody Molecules

Disclosed herein are antibody molecules that bind to APRIL, *e.g.,* an APRIL molecule described herein.

As used herein, the term "antibody molecule" refers to a protein, *e.g.*, an immunoglobulin chain or a fragment thereof, comprising at least one immunoglobulin variable domain sequence. The term "antibody molecule" includes, for example, full-length, mature antibodies and antigen-binding fragments of an antibody. For example, an antibody molecule can include a heavy (H) chain variable domain sequence (abbreviated herein as VH), and a light (L) chain variable domain sequence (abbreviated herein as VL). In another example, an antibody molecule includes two heavy (H) chain variable domain sequences and two light (L) chain variable domain sequence, thereby forming two antigen binding sites, such as Fab, Fab', F(ab')2, Fc, Fd, Fd', Fv, single chain antibodies (scFv for example), single variable

domain antibodies, diabodies (Dab) (bivalent and bispecific), and chimeric (*e.g.,* humanized) antibodies, which may be produced by the modification of whole antibodies or those synthesized *de novo* using recombinant DNA technologies. These functional antibody fragments retain the ability to selectively bind with their respective antigen or receptor. Antibodies and antibody fragments can be from any class of antibodies including, but not limited to, IgG, IgA, IgM, IgD, and IgE, and from any subclass (*e.g.,* IgG1, IgG2, IgG3, and IgG4) of antibodies. The antibody molecules can be monoclonal or polyclonal. The antibody molecule can also be a human, humanized, CDR-grafted, or *in vitro* generated antibody. The antibody molecule can have a heavy chain constant region chosen from, *e.g.,* IgG1, IgG2, IgG3, or IgG4. The antibody molecule can also have a light chain chosen from, *e.g.,* kappa or lambda. The term "immunoglobulin" (Ig) is used interchangeably with the term "antibody" herein.

Examples of antigen-binding fragments include: (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; (ii) a F(ab')2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a diabody (dAb) fragment, which consists of a VH domain; (vi) a camelid or camelized variable domain; (vii) a single chain Fv (scFv), see *e.g.*, Bird *et al.* (1988) *Science* 242:423-426; and Huston *et al.* (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883); (viii) a single domain antibody. These antibody fragments may be obtained using any suitable method, including several conventional techniques known to those with skill in the art, and the fragments can be screened for utility in the same manner as are intact antibodies.

The term "antibody" includes intact molecules as well as functional fragments thereof. Constant regions of the antibodies can be altered, *e.g.,* mutated, to modify the properties of the antibody (*e.g.,* to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function).

The antibody molecule can be a single chain antibody. A single-chain antibody (scFv) may be engineered (*see*, for example, Colcher, D. *et al.* (1999) *Ann N Y Acad Sci* 880:263-80; and Reiter, Y. (1996) *Clin Cancer Res* 2:245-52). The single chain antibody can be dimerized or multimerized to generate multivalent antibodies having specificities for different epitopes of the same target protein.

The antibody molecules disclosed herein can also be single domain antibodies. Single domain antibodies can include antibodies whose complementary determining regions are part of a single domain polypeptide. Examples include, but are not limited to, heavy chain antibodies, antibodies naturally devoid of light chains, single domain antibodies derived from conventional 4-chain antibodies, engineered antibodies and single domain scaffolds other than those derived from antibodies. Single domain antibodies may be any of the art, or any future single domain antibodies. Single domain antibodies may

be derived from any species including, but not limited to mouse, human, camel, llama, fish, shark, goat, rabbit, and bovine. According to some aspects, a single domain antibody is a naturally occurring single domain antibody known as heavy chain antibody devoid of light chains. Such single domain antibodies are disclosed in WO 94/04678, for example. For clarity reasons, this variable domain derived from a heavy chain antibody naturally devoid of light chain is known herein as a VHH or nanobody to distinguish it from the conventional VH of four chain immunoglobulins. Such a VHH molecule can be derived from antibodies raised in *Camelidae* species, for example in camel, llama, dromedary, alpaca and guanaco. Other species besides *Camelidae* may produce heavy chain antibodies naturally devoid of light chain; such VHHs are also contemplated.

The VH and VL regions can be subdivided into regions of hypervariability, termed "complementarity determining regions" (CDR), interspersed with regions that are more conserved, termed "framework regions" (FR or FW). The terms "complementarity determining region," and "CDR," as used herein refer to the sequences of amino acids within antibody variable regions which confer antigen specificity and binding affinity. As used herein, the terms "framework," "FW" and "FR" are used interchangeably.

The extent of the framework region and CDRs has been precisely defined by a number of methods (*see*, Kabat, E. A., *et al.* (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; Chothia, C. *et al.* (1987) *J. Mol. Biol.* 196:901-917; and the AbM definition used by Oxford Molecular's AbM antibody modeling software. *See*, generally, *e.g.,* Protein Sequence and Structure Analysis of Antibody Variable Domains. In: Antibody Engineering Lab Manual (Ed.: Duebel, S. and Kontermann, R., Springer-Verlag, Heidelberg). In an embodiment, the following definitions are used: AbM definition of CDR1 of the heavy chain variable domain and Kabat definitions for the other CDRs. In an embodiment, Kabat definitions are used for all CDRs. In addition, embodiments described with respect to Kabat or AbM CDRs may also be implemented using Chothia hypervariable loops. Each VH and VL typically includes three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4.

As used herein, an "immunoglobulin variable domain sequence" refers to an amino acid sequence which can form the structure of an immunoglobulin variable domain. For example, the sequence may include all or part of the amino acid sequence of a naturally-occurring variable domain. For example, the sequence may or may not include one, two, or more N- or C-terminal amino acids, or may include other alterations that are compatible with formation of the protein structure.

The term "antigen-binding region" refers to the part of an antibody molecule that comprises determinants that form an interface that binds to an antigen, *e.g.*, APRIL, or an epitope thereof. With

respect to proteins (or protein mimetics), the antigen-binding region typically includes one or more loops (of at least, *e.g.,* four amino acids or amino acid mimics) that form an interface that binds to the antigen, *e.g.*, APRIL. Typically, the antigen-binding region of an antibody molecule includes at least one or two CDRs and/or hypervariable loops, or more typically at least three, four, five or six CDRs and/or hypervariable loops.

The terms "compete" or "cross-compete" are used interchangeably herein to refer to the ability of an antibody molecule to interfere with binding of an anti-APRIL antibody molecule, *e.g.,* an anti-APRIL antibody molecule provided herein, to a target, *e.g.,* APRIL. The interference with binding can be direct or indirect (*e.g.,* through an allosteric modulation of the antibody molecule or the target). The extent to which an antibody molecule is able to interfere with the binding of another antibody molecule to the target, and therefore whether it can be said to compete, can be determined using a competition binding assay, for example, a FACS assay, an ELISA or BIACORE assay. In an embodiment, a competition binding assay is a quantitative competition assay. In an embodiment, a first anti-APRIL antibody molecule is said to compete for binding to the target with a second anti-APRIL antibody molecule when the binding of the first antibody molecule to the target is reduced by 10% or more, *e.g.,* 20% or more, 30% or more, 40% or more, 50% or more, 55% or more, 60% or more, 65% or more, 70% or more, 75% or more, 80% or more, 85% or more, 90% or more, 95% or more, 98% or more, 99% or more in a competition binding assay (*e.g.,* a competition assay described herein).

The terms "monoclonal antibody" or "monoclonal antibody composition" as used herein refer to a preparation of antibody molecules of single molecular composition. A monoclonal antibody composition displays a single binding specificity and affinity for a particular epitope. A monoclonal antibody can be made by hybridoma technology or by methods that do not use hybridoma technology (*e.g.,* recombinant methods).

An "effectively human" protein is a protein that does not evoke a neutralizing antibody response, *e.g.,* the human anti-murine antibody (HAMA) response. HAMA can be problematic in a number of circumstances, *e.g.,* if the antibody molecule is administered repeatedly, *e.g.,* in treatment of a chronic or recurrent disease condition. A HAMA response can make repeated antibody administration potentially ineffective because of an increased antibody clearance from the serum (*see*, *e.g.,* Saleh *et al.*, *Cancer Immunol. Immunother.*, 32:180-190 (1990)) and also because of potential allergic reactions (see, *e.g.,* LoBuglio *et al.*, *Hybridoma*, 5:5117-5123 (1986)).

The antibody molecule can be a polyclonal or a monoclonal antibody. In some embodiments, the antibody can be recombinantly produced, *e.g.,* produced by any suitable phage display or combinatorial methods.

Various phage display and combinatorial methods for generating antibodies are known in the art (as described in, *e.g.,* Ladner *et al.* U.S. Patent No. 5,223,409; Kang *et al.* International Publication No. WO 92/18619; Dower *et al.* International Publication No. WO 91/17271; Winter *et al.* International Publication WO 92/20791; Markland *et al.* International Publication No. WO 92/15679; Breitling *et al.* International Publication WO 93/01288; McCafferty *et al.* International Publication No. WO 92/01047; Garrard *et al.* International Publication No. WO 92/09690; Ladner *et al.* International Publication No. WO 90/02809; Fuchs *et al.* (1991) *Bio/Technology* 9:1370-1372; Hay *et al.* (1992) *Hum Antibod Hybridomas* 3:81-85; Huse *et al.* (1989) *Science* 246:1275-1281; Griffths *et al.* (1993) *EMBO J* 12:725-734; Hawkins *et al.* (1992) *J Mol Biol* 226:889-896; Clackson *et al.* (1991) *Nature* 352:624-628; Gram *et al.* (1992) *PNAS* 89:3576-3580; Garrad *et al.* (1991) *Bio/Technology* 9:1373-1377; Hoogenboom *et al.* (1991) *Nuc Acid Res* 19:4133-4137; and Barbas *et al.* (1991) *PNAS* 88:7978-7982, the contents of all of which are incorporated by reference herein).

In an embodiment, the antibody molecule is a fully human antibody (*e.g.,* an antibody made in a mouse which has been genetically engineered to produce an antibody from a human immunoglobulin sequence), or a non-human antibody, *e.g.,* a rodent (mouse or rat), goat, primate (*e.g.,* monkey), camel antibody. In an embodiment, the non-human antibody is a rodent (mouse or rat antibody). Methods of producing rodent antibodies are known in the art.

Human monoclonal antibodies can be generated using transgenic mice carrying the human immunoglobulin genes rather than the mouse system. Splenocytes from these transgenic mice immunized with the antigen of interest are used to produce hybridomas that secrete human mAbs with specific affinities for epitopes from a human protein (*see e.g.*, Wood *et al.* International Application WO 91/00906, Kucherlapati *et al.* PCT publication WO 91/10741; Lonberg *et al.* International Application WO 92/03918; Kay et al. International Application 92/03917; Lonberg, N. *et al.* 1994 *Nature* 368:856-859; Green, L.L. et al. 1994 *Nature Genet.* 7:13-21; Morrison, S.L. *et al.* 1994 *Proc. Natl. Acad. Sci. USA* 81:6851-6855; Bruggeman *et al.* 1993 *Year Immunol* 7:33-40; Tuaillon *et al.* 1993 *PNAS* 90:3720-3724; Bruggeman *et al.* 1991 *Eur J Immunol* 21:1323-1326).

An antibody can be one in which the variable region, or a portion thereof, *e.g.*, the CDRs, are generated in a non-human organism, *e.g.*, a rat or mouse. Chimeric, CDR-grafted, and humanized antibodies are within the invention. Antibodies generated in a non-human organism, *e.g.*, a rat or mouse, and then modified, *e.g.*, in the variable framework or constant region, to decrease antigenicity in a human are within the invention.

Chimeric antibodies can be produced by any suitable recombinant DNA technique. Several are known in the art (*see* Robinson *et al.*, International Patent Application Publication No. WO1987/002671; Akira, *et al.,* European Patent Application Publication No. 184,187; Taniguchi, M., European Patent

Application Publication No. 171,496; Morrison *et al.*, European Patent Application Publication No. 173,494; Neuberger *et al.*, International Patent Application Publication No. WO 86/01533; Cabilly *et al.* U.S. Patent No. 4,816,567; Cabilly *et al.*, European Patent Application Publication No. 125,023; Better *et al.* (1988 *Science* 240:1041-1043); Liu *et al.* (1987) *PNAS* 84:3439-3443; Liu *et al.*, 1987, *J. Immunol.* 139:3521-3526; Sun *et al.* (1987) *PNAS* 84:214-218; Nishimura *et al.*, 1987, *Canc. Res.* 47:999-1005; Wood *et al.* (1985) *Nature* 314:446-449; and Shaw *et al.*, 1988, *J. Natl Cancer Inst.* 80:1553-1559).

A humanized or CDR-grafted antibody will have at least one or two but generally all three recipient CDRs (of heavy and or light immunoglobulin chains) replaced with a donor CDR. The antibody may be replaced with at least a portion of a non-human CDR or only some of the CDRs may be replaced with non-human CDRs. It is only necessary to replace the number of CDRs required for binding of the humanized antibody to lipopolysaccharide. In an embodiment, the donor will be a rodent antibody, *e.g.,* a rat or mouse antibody, and the recipient will be a human framework or a human consensus framework. Typically, the immunoglobulin providing the CDRs is called the "donor" and the immunoglobulin providing the framework is called the "acceptor." In some embodiments, the donor immunoglobulin is a non-human (*e.g.,* rodent). The acceptor framework is typically a naturally-occurring (*e.g.,* a human) framework or a consensus framework, or a sequence about 85% or higher, *e.g.,* 90%, 95%, 99% or higher identical thereto.

As used herein, the term "consensus sequence" refers to the sequence formed from the most frequently occurring amino acids (or nucleotides) in a family of related sequences (See *e.g.*, Winnaker, From Genes to Clones (Verlagsgesellschaft, Weinheim, Germany 1987). In a family of proteins, each position in the consensus sequence is occupied by the amino acid occurring most frequently at that position in the family. If two amino acids occur equally frequently, either can be included in the consensus sequence. A "consensus framework" refers to the framework region in the consensus immunoglobulin sequence.

An antibody can be humanized by any suitable method, and several such methods known in the art (*see e.g.,* Morrison, S. L., 1985, *Science* 229:1202-1207, by Oi *et al.*, 1986, *BioTechniques* 4:214, and by Queen *et al.* US 5,585,089, US 5,693,761 and US 5,693,762, the contents of all of which are hereby incorporated by reference).

Humanized or CDR-grafted antibodies can be produced by CDR-grafting or CDR substitution, wherein one, two, or all CDRs of an immunoglobulin chain can be replaced. *See e.g.*, U.S. Patent 5,225,539; Jones *et al.* 1986 *Nature* 321:552-525; Verhoeyan *et al.* 1988 *Science* 239:1534; Beidler *et al.* 1988 *J. Immunol.* 141:4053-4060; Winter US 5,225,539, the contents of all of which are hereby expressly incorporated by reference. Winter describes a CDR-grafting method which may be used to prepare humanized antibodies (UK Patent Application GB 2188638A, filed on March 26, 1987; Winter US 5,225,539), the contents of which is expressly incorporated by reference.

Also provided are humanized antibodies in which specific amino acids have been substituted, deleted or added. Criteria for selecting amino acids from the donor are described in, *e.g.,* US 5,585,089, *e.g.,* columns 12-16 of US 5,585,089, the contents of which are hereby incorporated by reference. Other techniques for humanizing antibodies are described in Padlan *et al.* EP 519596 A1, published on December 23, 1992.

In an embodiment, the antibody molecule has a heavy chain constant region chosen from, *e.g.,* the heavy chain constant regions of IgG1, IgG2 (*e.g.,* IgG2a), IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE; particularly, chosen from, *e.g.,* the (*e.g.,* human) heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4. In another embodiment, the antibody molecule has a light chain constant region chosen from, *e.g.,* the (*e.g.,* human) light chain constant regions of kappa or lambda. The constant region can be altered, *e.g.,* mutated, to modify the properties of the antibody molecule (*e.g.,* to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, and/or complement function). In an embodiment, the antibody molecule has effector function and can fix complement. In another embodiment, the antibody molecule does not recruit effector cells or fix complement. In certain embodiments, the antibody molecule has reduced or no ability to bind an Fc receptor. For example, it may be an isotype or subtype, fragment or other mutant, which does not support binding to an Fc receptor, *e.g.,* it has a mutagenized or deleted Fc receptor binding region.

In an embodiment, a constant region of the antibody molecule is altered. Methods for altering an antibody constant region are known in the art. Antibody molecules s with altered function, *e.g.* altered affinity for an effector ligand, such as FcR on a cell, or the C1 component of complement can be produced by replacing at least one amino acid residue in the constant portion of the antibody with a different residue (see *e.g.,* EP 388,151 A1, U.S. Pat. No. 5,624,821 and U.S. Pat. No. 5,648,260, the contents of all of which are hereby incorporated by reference). Amino acid mutations which stabilize antibody structure, such as S228P (EU nomenclature, S241P in Kabat nomenclature) in human IgG4 are also contemplated. Similar type of alterations could be described which if applied to the murine, or other species immunoglobulin would reduce or eliminate these functions.

In an embodiment, the antibody molecule comprises an Fc region that comprise one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more) of mutations or combinations of mutations described in **Table 6**.

Table 6. Exemplary Fc mutations

Name	Mutation (according to EU numbering)
FcMut001	I253M
FcMut002	L309H_D312A_N315D
FcMut003	L309N

FcMut004	M252E_S254R
FcMut005	M252E_S254R_R255Y
FcMut006	S254H
FcMut007	S254M
FcMut008	T256D_T307R
FcMut009	T256L_N286I_T307I
FcMut010	T256I_N286I_T307I
FcMut011	K248S_D376Q
FcMut012	K248S_D376N
FcMut013	D376Q_E380A
FcMut014	D376N_E380A
FcMut015	D376Q_M428L
FcMut016	K248S_A378I
FcMut017	L314K
FcMut018	T250Q_M428L
FcMut019	M428L_N434A
FcMut020	N434A
FcMut021	T307A_E380A_N434A
FcMut022	M252W
FcMut023	V308F
FcMut024	V308F_N434Y
FcMut026	T256D_T307R_D376N
FcMut027	L309R_D312E
FcMut028	L309R_Q311P_D312E
FcMut029	K246N_P247A
FcMut030	K246N_P247A_D376N
FcMut031	T256E_T307R
FcMut032	T256R_T307D
FcMut033	T256R_T307E
FcMut034	Q311P
FcMut035	D376Q
FcMut036	L234A_L235A
FcMut037	L235V_G236A
FcMut038	L234P_L235P
FcMut039	L235P
FcMut040	P329G
FcMut041	P329E
FcMut042	E233K
FcMut043	T256D_N286D_A287S_T307R
FcMut044	T256D_P257L_T307R
FcMut045	T256D_T307R_Q311V
FcMut046	P247D_T256D_T307R
FcMut047	P247D_N286D_A287S_Q311V
FcMut048	P257M_V308N
FcMut049	V279I_Q311L_N315T
FcMut050	M428L_N434S
FcMut051	N434S
FcMut052	H433G_N434P
FcMut053	V259I_V308F_M428L

FcMut067	T256D_N286D_T307R
FcMut068	T256D_N286E_T307R
FcMut069	T256D_N286Q_T307R
FcMut070	T256D_P257T_T307R
FcMut071	T256D_P257V_T307R
FcMut072	T256D_T307R_Q311I
FcMut073	T256D_T307R_Q311L
FcMut074	T256D_T307R_Q311M
FcMut075	T256D_P257L_N286D_T307R_Q311V
FcMut076	T256D_T307R_M428L
FcMut077	M428L
FcMut078	M252Y_S254T_T256Q
FcMut079	M252Y_S254T_T256E_K288E
FcMut080	T256K_K288E
FcMut081	T256D_E258T
FcMut082	E283Q_H285E
FcMut083	R344D_D401R
FcMut084	K248E_E380K
FcMut085	K248E_E380R
FcMut086	K246H
FcMut087	K248H
FcMut088	T250I
FcMut089	T250V
FcMut090	L251F
FcMut091	L251M
FcMut093	P257V
FcMut094	N276D
FcMut095	H285N
FcMut096	H285D
FcMut097	K288H
FcMut098	K288Q
FcMut099	K288E
FcMut100	T307E
FcMut101	T307Q
FcMut102	V308P
FcMut103	V308I
FcMut104	V308L
FcMut105	L309H
FcMut106	L309M
FcMut107	Q311H
FcMut108	L314F
FcMut109	Y319H
FcMut110	I336T
FcMut111	P343D
FcMut112	P343V
FcMut113	E345Q
FcMut114	P346V
FcMut115	P374T
FcMut116	D376N

FcMut117	A378S
FcMut118	A431T
FcMut119	A431P
FcMut120	A431G
FcMut121	L432V
FcMut122	L432I
FcMut123	L432Q
FcMut124	N434T
FcMut125	H435N
FcMut126	Y436H
FcMut127	K439Q
FcMut128	T256D
FcMut129	T307R
FcMut130	A378T
FcMut131	A378D
FcMut132	A378H
FcMut133	A378Y
FcMut134	A378V
FcMut135	D376R
FcMut136	D376F
FcMut137	D376W
FcMut138	L314H
FcMut139	L432E_T437Q
FcMut140	D376Q_A378T
FcMut141	D376Q_I377M_A378T
FcMut142	P244Q_D376Q
FcMut143	P247T_A378T
FcMut144	P247N_A378T
FcMut145	T256D_T307R_L309T
FcMut146	A339T_S375E_F404Y
FcMut147	L235V_G236A_T256D_T307R
FcMut148	L235V_G236A_D376Q_M428L
FcMut149	L314N
FcMut150	N315D
FcMut151	A378T
FcMut152	T437Q
FcMut153	L432E
FcMut154	Y436R
FcMut155	L314M
FcMut156	L234A_L235A_T256D_T307R_Q311V
FcMut157	L234A_L235A_T256D_P257V_T307R
FcMut158	L234A_L235A_T256D_P257L_N286D_T307R_Q311V
FcMut159	L235V_G236A_T256D_T307R_Q311V
FcMut160	L235V_G236A_T256D_P257V_T307R
FcMut161	L235V_G236A_T256D_P257L_N286D_T307R_Q311V
FcMut162	S267T_A327N_A330M
FcMut163	S267T_A327N
FcMut164	L235V_G236A_S267T_A327N_A330M
FcMut165	L235V_G236A_S267T_A327N

FcMut166	M252Y_S254T
FcMut167	T256E
FcMut168	G236A_I332E
FcMut169	S239D_I332E
FcMut170	G236A_S239D_I332E
FcMut171	T256D_N286D_T307R_Q311V
FcMut172	T256D_E258T_T307R
FcMut173	T256D_E258T_T307R_Q311V
FcMut174	T256D_P257V_E258T_T307R
FcMut175	T256D_P257L_E258T_N286D_T307R_Q311V
FcMut176	T256D_E258T_N286D_T307R_Q311V
FcMut177	A378V_M428L
FcMut178	A378V_M428I
FcMut179	A378V_M428V
FcMut180	T256D_N286D
FcMut181	T256D_A378V
FcMut182	T256D_Q311V
FcMut183	T256D_Q311V_A378V
FcMut184	T256D_T307R_A378V
FcMut185	T256D_N286D_T307R_A378V
FcMut186	T256D_T307R_Q311V_A378V
FcMut187	H285D_A378V
FcMut188	H285D_Q311V
FcMut189	T256D_H285D
FcMut190	T256D_H285D_Q311V
FcMut191	T256D_H285D_T307R
FcMut192	T256D_H285D_T307R_A378V
FcMut193	H285D_L314M_A378V
FcMut194	T256D_E258T_H285D_Q311H
FcMut195	T256D_E258T_H285D
FcMut196	H285D_N315D
FcMut197	H285N_T307Q_N315D
FcMut198	H285D_L432E_T437Q
FcMut199	T256D_E258T_N315D
FcMut200	P257V_H285N
FcMut201	H285N_L432F
FcMut202	H285N_T437I
FcMut203	T256D_E258T_L314M
FcMut204	T256D_E258T_T307Q
FcMut205	T256D_E258T_A378V
FcMut206	V308P_A378V
FcMut207	P257V_A378T
FcMut208	P257V_V308P_A378V
FcMut209	N315D_A378T
FcMut210	H285N_L314M
FcMut211	L314M_L432E_T437Q
FcMut212	T307Q_N315D
FcMut213	H285D_T307Q_A378V
FcMut214	L314M_N315D

FcMut215	T307Q_Q311V_A378V
FcMut216	H285D_Q311V_A378V
FcMut217	Q311V_N315D_A378V
FcMut218	T256D_E258T_Q311V
FcMut219	T256D_N315D_A378V
FcMut220	T256D_Q311V_N315D
FcMut221	T256D_T307Q_A378V
FcMut222	T256D_T307Q_Q311V
FcMut223	T256D_H285D_A378V
FcMut224	T256D_H285D_T307R_Q311V
FcMut225	T256D_H285D_N286D_T307R
FcMut226	T256D_H285D_N286D_T307R_Q311V
FcMut227	T256D_H285D_N286D_T307R_A378V
FcMut228	T256D_N286D_T307R_Q311V_A378V
FcMut229	T256D_H285D_T307R_Q311V_A378V
FcMut230	V308P_Q311V_A378V
FcMut231	T256D_V308P_A378V
FcMut232	T256D_V308P_Q311V
FcMut233	T256D_E258T_V308P
FcMut234	H285D_V308P_Q311V
FcMut242	E258T
FcMut243	N286D
FcMut244	Q311V
YTE	M252Y_S254T_T256E

In an embodiment, the Fc region comprises FcMut001. In an embodiment, the Fc region comprises FcMut002. In an embodiment, the Fc region comprises FcMut003. In an embodiment, the Fc region comprises FcMut004. In an embodiment, the Fc region comprises FcMut005. In an embodiment, the Fc region comprises FcMut006. In an embodiment, the Fc region comprises FcMut007. In an embodiment, the Fc region comprises FcMut008. In an embodiment, the Fc region comprises FcMut009. In an embodiment, the Fc region comprises FcMut010. In an embodiment, the Fc region comprises FcMut011. In an embodiment, the Fc region comprises FcMut012. In an embodiment, the Fc region comprises FcMut013. In an embodiment, the Fc region comprises FcMut014. In an embodiment, the Fc region comprises FcMut015. In an embodiment, the Fc region comprises FcMut016. In an embodiment, the Fc region comprises FcMut017. In an embodiment, the Fc region comprises FcMut018. In an embodiment, the Fc region comprises FcMut019. In an embodiment, the Fc region comprises FcMut020. In an embodiment, the Fc region comprises FcMut021. In an embodiment, the Fc region comprises FcMut022. In an embodiment, the Fc region comprises FcMut023. In an embodiment, the Fc region comprises FcMut024. In an embodiment, the Fc region comprises FcMut026. In an embodiment, the Fc region comprises FcMut027. In an embodiment, the Fc region comprises FcMut028. In an embodiment, the Fc region comprises FcMut029. In an embodiment, the Fc region comprises FcMut030. In an

embodiment, the Fc region comprises FcMut031. In an embodiment, the Fc region comprises FcMut032. In an embodiment, the Fc region comprises FcMut033. In an embodiment, the Fc region comprises FcMut034. In an embodiment, the Fc region comprises FcMut035. In an embodiment, the Fc region comprises FcMut036. In an embodiment, the Fc region comprises FcMut037. In an embodiment, the Fc region comprises FcMut038. In an embodiment, the Fc region comprises FcMut039. In an embodiment, the Fc region comprises FcMut040. In an embodiment, the Fc region comprises FcMut041. In an embodiment, the Fc region comprises FcMut042. In an embodiment, the Fc region comprises FcMut043. In an embodiment, the Fc region comprises FcMut044. In an embodiment, the Fc region comprises FcMut045. In an embodiment, the Fc region comprises FcMut046. In an embodiment, the Fc region comprises FcMut047. In an embodiment, the Fc region comprises FcMut048. In an embodiment, the Fc region comprises FcMut049. In an embodiment, the Fc region comprises FcMut050. In an embodiment, the Fc region comprises FcMut051. In an embodiment, the Fc region comprises FcMut052. In an embodiment, the Fc region comprises FcMut053. In an embodiment, the Fc region comprises FcMut067. In an embodiment, the Fc region comprises FcMut068. In an embodiment, the Fc region comprises FcMut069. In an embodiment, the Fc region comprises FcMut070. In an embodiment, the Fc region comprises FcMut071. In an embodiment, the Fc region comprises FcMut072. In an embodiment, the Fc region comprises FcMut073. In an embodiment, the Fc region comprises FcMut074. In an embodiment, the Fc region comprises FcMut075. In an embodiment, the Fc region comprises FcMut076. In an embodiment, the Fc region comprises FcMut077. In an embodiment, the Fc region comprises FcMut078. In an embodiment, the Fc region comprises FcMut079. In an embodiment, the Fc region comprises FcMut080. In an embodiment, the Fc region comprises FcMut081. In an embodiment, the Fc region comprises FcMut082. In an embodiment, the Fc region comprises FcMut083. In an embodiment, the Fc region comprises FcMut084. In an embodiment, the Fc region comprises FcMut085. In an embodiment, the Fc region comprises FcMut086. In an embodiment, the Fc region comprises FcMut087. In an embodiment, the Fc region comprises FcMut088. In an embodiment, the Fc region comprises FcMut089. In an embodiment, the Fc region comprises FcMut090. In an embodiment, the Fc region comprises FcMut091. In an embodiment, the Fc region comprises FcMut093. In an embodiment, the Fc region comprises FcMut094. In an embodiment, the Fc region comprises FcMut095. In an embodiment, the Fc region comprises FcMut096. In an embodiment, the Fc region comprises FcMut097. In an embodiment, the Fc region comprises FcMut098. In an embodiment, the Fc region comprises FcMut099. In an embodiment, the Fc region comprises FcMut100. In an embodiment, the Fc region comprises FcMut101. In an embodiment, the Fc region comprises FcMut102. In an embodiment, the Fc region comprises FcMut103. In an embodiment, the Fc region comprises FcMut104. In an embodiment, the Fc region comprises FcMut105. In an embodiment, the Fc region comprises FcMut106. In an embodiment, the Fc

region comprises FcMut107. In an embodiment, the Fc region comprises FcMut108. In an embodiment, the Fc region comprises FcMut109. In an embodiment, the Fc region comprises FcMut110. In an embodiment, the Fc region comprises FcMut111. In an embodiment, the Fc region comprises FcMut112. In an embodiment, the Fc region comprises FcMut113. In an embodiment, the Fc region comprises FcMut114. In an embodiment, the Fc region comprises FcMut115. In an embodiment, the Fc region comprises FcMut116. In an embodiment, the Fc region comprises FcMut117. In an embodiment, the Fc region comprises FcMut118. In an embodiment, the Fc region comprises FcMut119. In an embodiment, the Fc region comprises FcMut120. In an embodiment, the Fc region comprises FcMut121. In an embodiment, the Fc region comprises FcMut122. In an embodiment, the Fc region comprises FcMut123. In an embodiment, the Fc region comprises FcMut124. In an embodiment, the Fc region comprises FcMut125. In an embodiment, the Fc region comprises FcMut126. In an embodiment, the Fc region comprises FcMut127. In an embodiment, the Fc region comprises FcMut128. In an embodiment, the Fc region comprises FcMut129. In an embodiment, the Fc region comprises FcMut130. In an embodiment, the Fc region comprises FcMut131. In an embodiment, the Fc region comprises FcMut132. In an embodiment, the Fc region comprises FcMut133. In an embodiment, the Fc region comprises FcMut134. In an embodiment, the Fc region comprises FcMut135. In an embodiment, the Fc region comprises FcMut136. In an embodiment, the Fc region comprises FcMut137. In an embodiment, the Fc region comprises FcMut138. In an embodiment, the Fc region comprises FcMut139. In an embodiment, the Fc region comprises FcMut140. In an embodiment, the Fc region comprises FcMut141. In an embodiment, the Fc region comprises FcMut142. In an embodiment, the Fc region comprises FcMut143. In an embodiment, the Fc region comprises FcMut144. In an embodiment, the Fc region comprises FcMut145. In an embodiment, the Fc region comprises FcMut146. In an embodiment, the Fc region comprises FcMut147. In an embodiment, the Fc region comprises FcMut148. In an embodiment, the Fc region comprises FcMut149. In an embodiment, the Fc region comprises FcMut150. In an embodiment, the Fc region comprises FcMut151. In an embodiment, the Fc region comprises FcMut152. In an embodiment, the Fc region comprises FcMut153. In an embodiment, the Fc region comprises FcMut154. In an embodiment, the Fc region comprises FcMut155. In an embodiment, the Fc region comprises FcMut156. In an embodiment, the Fc region comprises FcMut157. In an embodiment, the Fc region comprises FcMut158. In an embodiment, the Fc region comprises FcMut159. In an embodiment, the Fc region comprises FcMut160. In an embodiment, the Fc region comprises FcMut161. In an embodiment, the Fc region comprises FcMut162. In an embodiment, the Fc region comprises FcMut163. In an embodiment, the Fc region comprises FcMut164. In an embodiment, the Fc region comprises FcMut165. In an embodiment, the Fc region comprises FcMut166. In an embodiment, the Fc region comprises FcMut167. In an embodiment, the Fc region comprises FcMut168. In an embodiment, the Fc region comprises

FcMut169. In an embodiment, the Fc region comprises FcMut170. In an embodiment, the Fc region comprises FcMut171. In an embodiment, the Fc region comprises FcMut172. In an embodiment, the Fc region comprises FcMut173. In an embodiment, the Fc region comprises FcMut174. In an embodiment, the Fc region comprises FcMut175. In an embodiment, the Fc region comprises FcMut176. In an embodiment, the Fc region comprises FcMut177. In an embodiment, the Fc region comprises FcMut178. In an embodiment, the Fc region comprises FcMut179. In an embodiment, the Fc region comprises FcMut180. In an embodiment, the Fc region comprises FcMut181. In an embodiment, the Fc region comprises FcMut182. In an embodiment, the Fc region comprises FcMut183. In an embodiment, the Fc region comprises FcMut184. In an embodiment, the Fc region comprises FcMut185. In an embodiment, the Fc region comprises FcMut186. In an embodiment, the Fc region comprises FcMut187. In an embodiment, the Fc region comprises FcMut188. In an embodiment, the Fc region comprises FcMut189. In an embodiment, the Fc region comprises FcMut190. In an embodiment, the Fc region comprises FcMut191. In an embodiment, the Fc region comprises FcMut192. In an embodiment, the Fc region comprises FcMut193. In an embodiment, the Fc region comprises FcMut194. In an embodiment, the Fc region comprises FcMut195. In an embodiment, the Fc region comprises FcMut196. In an embodiment, the Fc region comprises FcMut197. In an embodiment, the Fc region comprises FcMut198. In an embodiment, the Fc region comprises FcMut199. In an embodiment, the Fc region comprises FcMut200. In an embodiment, the Fc region comprises FcMut201. In an embodiment, the Fc region comprises FcMut202. In an embodiment, the Fc region comprises FcMut203. In an embodiment, the Fc region comprises FcMut204. In an embodiment, the Fc region comprises FcMut205. In an embodiment, the Fc region comprises FcMut206. In an embodiment, the Fc region comprises FcMut207. In an embodiment, the Fc region comprises FcMut208. In an embodiment, the Fc region comprises FcMut209. In an embodiment, the Fc region comprises FcMut210. In an embodiment, the Fc region comprises FcMut211. In an embodiment, the Fc region comprises FcMut212. In an embodiment, the Fc region comprises FcMut213. In an embodiment, the Fc region comprises FcMut214. In an embodiment, the Fc region comprises FcMut215. In an embodiment, the Fc region comprises FcMut216. In an embodiment, the Fc region comprises FcMut217. In an embodiment, the Fc region comprises FcMut218. In an embodiment, the Fc region comprises FcMut219. In an embodiment, the Fc region comprises FcMut220. In an embodiment, the Fc region comprises FcMut221. In an embodiment, the Fc region comprises FcMut222. In an embodiment, the Fc region comprises FcMut223. In an embodiment, the Fc region comprises FcMut224. In an embodiment, the Fc region comprises FcMut225. In an embodiment, the Fc region comprises FcMut226. In an embodiment, the Fc region comprises FcMut227. In an embodiment, the Fc region comprises FcMut228. In an embodiment, the Fc region comprises FcMut229. In an embodiment, the Fc region comprises FcMut230. In an embodiment, the Fc region comprises FcMut231. In an

embodiment, the Fc region comprises FcMut232. In an embodiment, the Fc region comprises FcMut233. In an embodiment, the Fc region comprises FcMut234. In an embodiment, the Fc region comprises FcMut242. In an embodiment, the Fc region comprises FcMut243. In an embodiment, the Fc region comprises FcMut244.

Other exemplary Fc mutations are described, *e.g.*, in International Application Publication No. WO2018/052556, US Patent Application Publication No. US2018/0037634, and Booth et al., MAbs. 2018; 10(7):1098-1110, the contents of which are incorporated by reference in their entirety.

In an embodiment, the Fc region is altered to extend half-life. For example, the Fc region can contain one or more of: FcMut183 (T256D-Q311V-A378V), FcMut197 (H285N-T307Q-N315D), FcMut213 (H285D-T307Q-A378V), FcMut215 (T307Q-Q311V-A378V), or FcMut228 (T256D-N286D-T307R-Q311V-A378V) (all according to EU numbering).

In an embodiment, the Fc region is altered to enhance ADCC. For example, the Fc region can contain one or more of: A330L-I332E-S239D, F243L-R292P-Y300L-V305I-P396L, or S298A-E333A-K334A. In an embodiment, afucosylation can be achieved by expression in a cell line such as CHO in which fucosyltransferase (FucT8) is knocked out.

In an embodiment, the Fc region is altered to enhance CDC. For example, the Fc region contains S267E-H268F-S324T.

In an embodiment, the Fc region is altered to enhance antibody-dependent cellular phagocytosis (ADCP). For example, the Fc region contains S239D-I332E-A330L.

In an embodiment, the only amino acids in the antibody molecule are canonical amino acids. In an embodiment, the antibody molecule comprises naturally-occurring amino acids; analogs, derivatives and congeners thereof; amino acid analogs having variant side chains; and/or all stereoisomers of any of any of the foregoing. The antibody molecule may comprise the D- or L- optical isomers of amino acids and peptidomimetics.

A polypeptide of an antibody molecule described herein may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The antibody molecule may also be modified; for example, by disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation, such as conjugation with a labeling component. The polypeptide can be isolated from natural sources, can be a produced by recombinant techniques from a eukaryotic or prokaryotic host, or can be a product of synthetic procedures.

The antibody molecule described herein can be used alone in unconjugated form, or can be bound to a substance, *e.g.,* a toxin or moiety (*e.g.,* a therapeutic drug; a compound emitting radiation; molecules of plant, fungal, or bacterial origin; or a biological protein (*e.g.,* a protein toxin) or particle (*e.g.,* a

recombinant viral particle, *e.g.,* via a viral coat protein). For example, the anti-APRIL antibody can be coupled to a radioactive isotope such as an α-, β-, or γ-emitter, or a β-and γ-emitter.

An antibody molecule can be derivatized or linked to another functional molecule (*e.g.,* another peptide or protein). As used herein, a "derivatized" antibody molecule is one that has been modified. Methods of derivatization include but are not limited to the addition of a fluorescent moiety, a radionucleotide, a toxin, an enzyme or an affinity ligand such as biotin. Accordingly, the antibody molecules are intended to include derivatized and otherwise modified forms of the antibodies described herein, including immunoadhesion molecules. For example, an antibody molecule can be functionally linked (by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other molecular entities, such as another antibody (*e.g.,* a bispecific antibody or a diabody), a detectable agent, a toxin, a pharmaceutical agent, and/or a protein or peptide that can mediate association of the antibody or antibody portion with another molecule (such as a streptavidin core region or a polyhistidine tag).

Some types of derivatized antibody molecule are produced by crosslinking two or more antibodies (of the same type or of different types, *e.g.,* to create bispecific antibodies). Suitable crosslinkers include those that are heterobifunctional, having two distinctly reactive groups separated by an appropriate spacer (*e.g.,* m-maleimidobenzoyl-N-hydroxysuccinimide ester) or homobifunctional (*e.g.,* disuccinimidyl suberate). Such linkers are available from Pierce Chemical Company, Rockford, Ill.

Useful detectable agents with which an anti-dengue antibody molecule may be derivatized (or labeled) to include fluorescent compounds, various enzymes, prosthetic groups, luminescent materials, bioluminescent materials, fluorescent emitting metal atoms, *e.g.,* europium (Eu), and other anthanides, and radioactive materials (described below). Exemplary fluorescent detectable agents include fluorescein, fluorescein isothiocyanate, rhodamine, 5dimethylamine-1-napthalenesulfonyl chloride, phycoerythrin and the like. An antibody may also be derivatized with detectable enzymes, such as alkaline phosphatase, horseradish peroxidase, β-galactosidase, acetylcholinesterase, glucose oxidase and the like. When an antibody is derivatized with a detectable enzyme, it is detected by adding additional reagents that the enzyme uses to produce a detectable reaction product. For example, when the detectable agent horseradish peroxidase is present, the addition of hydrogen peroxide and diaminobenzidine leads to a colored reaction product, which is detectable. An antibody molecule may also be derivatized with a prosthetic group (*e.g.,* streptavidin/biotin and avidin/biotin). For example, an antibody may be derivatized with biotin, and detected through indirect measurement of avidin or streptavidin binding. Examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; and examples of bioluminescent materials include luciferase, luciferin, and aequorin.

Labeled antibody molecules can be used, for example, diagnostically and/or experimentally in a number of contexts, including (i) to isolate a predetermined antigen by standard techniques, such as affinity chromatography or immunoprecipitation; (ii) to detect a predetermined antigen (*e.g.,* in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the protein; (iii) to monitor protein levels in tissue as part of a clinical testing procedure, *e.g.,* to determine the efficacy of a given treatment regimen.

An antibody molecule may be conjugated to another molecular entity, typically a label or a therapeutic (*e.g.*, antimicrobial (*e.g.*, antibacterial or bactericidal), immunomodulatory, immunostimularoty, cytotoxic, or cytostatic) agent or moiety. Radioactive isotopes can be used in diagnostic or therapeutic applications. Radioactive isotopes that can be coupled to the antibody molecules include, but are not limited to α-, β-, or γ-emitters, or β-and γ-emitters. Such radioactive isotopes include, but are not limited to iodine (^{131}I or ^{125}I), yttrium (^{90}Y), lutetium (^{177}Lu), actinium (^{225}Ac), praseodymium, astatine (^{211}At), rhenium (^{186}Re), bismuth (^{212}Bi or ^{213}Bi), indium (^{111}In), technetium (^{99} mTc), phosphorus (^{32}P), rhodium (^{188}Rh), sulfur (^{35}S) , carbon (^{14}C), tritium (^{3}H), chromium (^{51}Cr), chlorine (^{36}Cl), cobalt (^{57}Co or ^{58}Co), iron (^{59}Fe), selenium (^{75}Se), or gallium (^{67}Ga). Radioisotopes useful as therapeutic agents include yttrium (^{90}Y), lutetium (^{177}Lu), actinium (^{225}Ac), praseodymium, astatine (^{211}At), rhenium (^{186}Re), bismuth (^{212}Bi or ^{213}Bi), and rhodium (^{188}Rh). Radioisotopes useful as labels, *e.g.,* for use in diagnostics, include iodine (^{131}I or ^{125}I), indium (^{111}In), technetium (^{99}mTc), phosphorus (^{32}P), carbon (^{14}C), and tritium (^{3}H), or one or more of the therapeutic isotopes listed above.

The present disclosure provides radiolabeled antibody molecules and methods of labeling the same. In an embodiment, a method of labeling an antibody molecule is disclosed. The method includes contacting an antibody molecule, with a chelating agent, to thereby produce a conjugated antibody. The conjugated antibody is radiolabeled with a radioisotope, *e.g.,* ^{111}Indium, ^{90}Yttrium and ^{177}Lutetium, to thereby produce a labeled antibody molecule.

In some aspects, this disclosure provides a method of making an antibody molecule disclosed herein. The method includes: providing an antigen, *e.g.,* APRIL or a fragment thereof; obtaining an antibody molecule that specifically binds to the antigen; evaluating efficacy of the antibody molecule in modulating activity of the antigen and/or organism expressing the antigen, *e.g.,* APRIL. The method can further include administering the antibody molecule, including a derivative thereof (*e.g.,* a humanized antibody molecule) to a subject, *e.g.,* a human.

This disclosure provides an isolated nucleic acid molecule encoding the above antibody molecule, vectors and host cells thereof. The nucleic acid molecule includes, but is not limited to, RNA, genomic DNA and cDNA.

Amino acid and nucleotide sequences of exemplary antibody molecules are described in **Tables 1 and 2**, respectively. Amino acid sequences of additional exemplary humanized antibody molecules are described in **Table 5**.

5

Table 1. The amino acid sequences of the heavy chain variable region (VH) and light chain variable region (VL) of the exemplary anti-APRIL antibodies are provided as follows. CDRs, defined according to the Kabat system, are underlined and bold, while CDRs defined according to the Chothia system are italicized.

Antibody	Chain	Amino Acid Sequence	SEQ ID NO	Chothia CDR		SEQ ID NO	Kabat CDR		SEQ ID NO
2218	VH	DVQLQESGPGLVKPSQSLSLTCSVT*GYSIT**SGYYW**N*WIRQFPGNKLEWMG**YI*SYDGY*NNYNPSLKN*RISITRDTSKNQFFLKLNSVTTEDTATYYCAN***YYDYEDW YFGV***WGTGTTVTVSS	9	HCDR1	GYSITSGY	1	HCDR1	SGYYWN	7
				HCDR2	SYDGY	2	HCDR2	YISYDGYNNYNPSLKN	8
				HCDR3	YYDYEDWYFGV	3	HCDR3	YYDYEDWYFGV	3
	VL	DIVLTQSPASLAMSLGKRATISC***RASESVSIIGTN SIH***WYQQKPGQPPKLLIY***HASNLET***GVPARFSGSGSRTDFTLTIDPVEEDDVAIYYC***LQSRKIPYT***FGGGTKLEIK	10	LCDR1	RASESVSIIGTNSIH	4	LCDR1	RASESVSIIGTNSIH	4
				LCDR2	HASNLET	5	LCDR2	HASNLET	5
				LCDR3	LQSRKIPYT	6	LCDR3	LQSRKIPYT	6
2419	VH	QVQLQQSGAELVKPGASVRLSCEAS*GYTFT**DYTIH**WVKQRSGQGLEWIG**WIYPLRGSINYNEKFKD**KATLTADKSSSTVYLELGRLTSKDSAVYFCAR***HGAYYSN AFDY***WGQGTTLTVSS	19	HCDR1	GYTFTDY	11	HCDR1	DYTIH	17
				HCDR2	YPLRGS	12	HCDR2	WIYPLRGSINYNEKFKD	18
				HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	13
	VL	NIVMTQSPASLAVSLGQRATISC***RASESVDNDGIR FMH***WYQQKPGQPPKLLIY***RASNLES***GIPARFSGSGSRTDFTLTINPVETDDVATYYC***QQSNKDPYT***FGGGTKLELK	20	LCDR1	RASESVDNDGIRFMH	14	LCDR1	RASESVDNDGIRFMH	14
				LCDR2	RASNLES	15	LCDR2	RASNLES	15
				LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	16
2419-1305	VH	QVQLVQSGAEVKKPGASVKVSCKAS*GYTFT**DYTIH**WVRQATGQGLEWMG**WIYPLRGSINYAQKFQG**RVTMTANKSISTVYMELSSLRSEDTAVYFCAR***HGAYYSN AFDY***WGQGTLVTVSS	283	HCDR1	GYTFTDY	11	HCDR1	DYTIH	
				HCDR2	YPLRGS	12	HCDR2	WIYPLRGSINYAQKFQG	
				HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	
	VL	EIVMTQSPATLSVSPGERATLSC***RASESVDNDGIR FLH***WYQQKPGQAPRLLIY***RASNRET***GIPARFSGSGSGTEFTLTISSLQSEDFAVYYC***QQSNKDPYT***FGGGTKVEIK	284	LCDR1	RASESVDNDGIRFLH	280	LCDR1	RASESVDNDGIRFLH	
				LCDR2	RASNRET	281	LCDR2	RASNRET	
				LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	
2419-1306	VH	QVQLVQSGAEVKKPGASVKVSCKAS*GYTFT**DYTIH**WVRQATGQGLEWMG**WIYPLRGSINYAQKFQG**RVTMTANKSISTVYMELSSLRSEDTAVYFCAR***HGAYYSN AFDY***WGQGTLVTVSS	283	HCDR1	GYTFTDY	11	HCDR1	DYTIH	
				HCDR2	YPLRGS	12	HCDR2	WIYPLRGSINYAQKFQG	
				HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	
	VL	EIVMTQSPATLSVSPGERATLSC***RASESVDNDGIR FLH***WYQQKPGQAPRLLIY***RASTRAT***GIPARFSGSGSRTEFTLTISSLQSEDFAVYYC***QQSNKDPYT***FGGGTKVEIK	286	LCDR1	RASESVDNDGIRFLH	280	LCDR1	RASESVDNDGIRFLH	
				LCDR2	RASTRAT	285	LCDR2	RASTRAT	
				LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	
2419-1310	VH	QVQLVQSGAEVKKPGASVKVSCKAS*GYTFT**DYTIH**WVRQATGQGLEWMG**WIYPLRGSINYAQKFQG**RVTM	283	HCDR1	GYTFTDY	11	HCDR1	DYTIH	
				HCDR2	YPLRGS	12	HCDR2	WIYPLRGSINYAQKFQG	
				HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	

		TANKSISTVYMELSSLRSEDTAVYFCAR***HGAYYSN***							
	VL	DIVMTQSPDSLAVSLGERATINC***KSSQSVDNDGIR***	316	LCDR1	KSSQSVDNDGIRFLH	314	LCDR1	KSSQSVDNDGIRFLH	314
		FLHWYQQKPGQPPKLLIY***RASTRES***GVPDRFSGSG		LCDR2	RASTRES	315	LCDR2	RASTRES	315
		SGTDFTLTISSLQAEDVAVYYC***QQSNKDPYT***FGGG		LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	16
		TKVEIK							
2419-0806	VH	EVQLVQSGAEVKKPGESLKISCKAS***GYTFTDYTIH***	288	HCDR1	GYTFTDY	11	HCDR1	DYTIH	17
		WVRQMPGKGLEWMG***WIYPLRGSINYSPSFQG***QVTI		HCDR2	YPLRGS	12	HCDR2	WIYPLRGSINYSPSFQG	287
		SADKSISTVYLQWSSLKASDTAMYFCAR***HGAYYSN***		HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	13
		AFDYWGQGTLVTVSS							
	VL	EIVMTQSPATLSVSPGERATLSC***RASESVDNDGIR***	286	LCDR1	RASESVDNDGIRFLH	280	LCDR1	RASESVDNDGIRFLH	280
		FLHWYQQKPGQAPRLLIY***RASTRAT***GIPARFSGSG		LCDR2	RASTRAT	285	LCDR2	RASTRAT	285
		SRTEFTLTISSLQSEDFAVYYC***QQSNKDPYT***FGGG		LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	16
		TKVEIK							
2419-0205	VH	QVQLVQSGAEVKKPGSSVKVSCKAS***GYTFTDYTIH***	289	HCDR1	GYTFTDY	11	HCDR1	DYTIH	17
		WVRQAPGQGLEWMG***WIYPLRGSINYAQKFQG***RVTI		HCDR2	YPLRGS	12	HCDR2	WIYPLRGSINYAQKFQG	282
		TADKSTSTAYMELSSLRSEDTAVYFCAR***HGAYYSN***		HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	13
		AFDYWGQGTLVTVSS							
	VL	EIVMTQSPATLSVSPGERATLSC***RASESVDNDGIR***	284	LCDR1	RASESVDNDGIRFLH	280	LCDR1	RASESVDNDGIRFLH	280
		FLHWYQQKPGQAPRLLIY***RASNRET***GIPARFSGSG		LCDR2	RASNRET	281	LCDR2	RASNRET	281
		SGTEFTLTISSLQSEDFAVYYC***QQSNKDPYT***FGGG		LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	16
		TKVEIK							
2419-0406	VH	QVQLVQSGAEVKKPGSSVKVSCKAS***GYTFTDYTIH***	291	HCDR1	GYTFTDY	11	HCDR1	DYTIH	17
		WVRQAPGQGLEWMG***WIYPLRGSINYAEKFKG***RVTL		HCDR2	YPLRGS	12	HCDR2	WIYPLRGSINYAEKFKG	290
		TADKSTSTVYMELSSLRSEDTAVYFCAR***HGAYYSN***		HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	13
		AFDYWGQGTLVTVSS							
	VL	EIVMTQSPATLSVSPGERATLSC***RASESVDNDGIR***	286	LCDR1	RASESVDNDGIRFLH	280	LCDR1	RASESVDNDGIRFLH	
		FLHWYQQKPGQAPRLLIY***RASTRAT***GIPARFSGSG		LCDR2	RASTRAT	285	LCDR2	RASTRAT	
		SRTEFTLTISSLQSEDFAVYYC***QQSNKDPYT***FGGG		LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	
		TKVEIK							
2419-0605	VH	QVQLVQSGAEVKKPGASVKVSCKAS***GYTFTDYTIH***	317	HCDR1	GYTFTDY	11	HCDR1	DYTIH	
		WVRQAPGQGLEWMG***WIYPLRGSINYAQKFQG***RVTL		HCDR2	YPLRGS	12	HCDR2	WIYPLRGSINYAQKFQG	
		TADKSTSTVYMELSSLRSEDTAVYFCAR***HGAYYSN***		HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	
		AFDYWGQGTLVTVSS							
	VL	EIVMTQSPATLSVSPGERATLSC***RASESVDNDGIR***	284	LCDR1	RASESVDNDGIRFLH	280	LCDR1	RASESVDNDGIRFLH	
		FLHWYQQKPGQAPRLLIY***RASNRET***GIPARFSGSG		LCDR2	RASNRET	281	LCDR2	RASNRET	
		SGTEFTLTISSLQSEDFAVYYC***QQSNKDPYT***FGGG		LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	
		TKVEIK							
2419-0805	VH	EVQLVQSGAEVKKPGESLKISCKAS***GYTFTDYTIH***	288	HCDR1	GYTFTDY	11	HCDR1	DYTIH	
		WVRQMPGKGLEWMG***WIYPLRGSINYSPSFQG***QVTI		HCDR2	YPLRGS	12	HCDR2	WIYPLRGSINYSPSFQG	
		SADKSISTVYLQWSSLKASDTAMYFCAR***HGAYYSN***		HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	
		AFDYWGQGTLVTVSS							
	VL	EIVMTQSPATLSVSPGERATLSC***RASESVDNDGIR***	284	LCDR1	RASESVDNDGIRFLH	280	LCDR1	RASESVDNDGIRFLH	
		FLHWYQQKPGQAPRLLIY***RASNRET***GIPARFSGSG		LCDR2	RASNRET	281	LCDR2	RASNRET	

		SGTEFTLTISSLQSEDFAVYYC***QQSNKDPYT***FGGG TKVEIK		LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	16
2419-0105	VH	QVQLVQSGAEVKKPGASVKVSCKAS*GYTFT**DYTIH** WVRQAPGQGLEWMG**WI*YPLRGSI*NYAQKFQG**RVTM TADKSISTVYMELSRLRSDDTAVYYCAR***HGAYYSN*** ***AFDY***WGQGTLVTVSS	292	HCDR1	GYTFTDY	11	HCDR1	DYTIH	17
				HCDR2	YPLRGS	12	HCDR2	W*I*YPLRGSINYAQKFQG	282
				HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	13
	VL	EIVMTQSPATLSVSPGERATLSC***RASESVDNDGIR*** ***FLH***WYQQKPGQAPRLLIY***RASNRET***GIPARFSGSG SGTEFTLTISSLQSEDFAVYYC***QQSNKDPYT***FGGG TKVEIK	284	LCDR1	RASESVDNDGIRFLH	280	LCDR1	RASESVDNDGIRFLH	280
				LCDR2	RASNRET	281	LCDR2	RASNRET	281
				LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	16
2419-1204	VH	QVQLVQSGAEVKKPGASVKVSCKAS*GYTFT**DYTIH** WVRQATGQGLEWMG**WI*YPLRGSI*NYAQKFQG**RVTM TANKSSSTVYMELSSLRSEDTAVYFCAR***HGAYYSN*** ***AFDY***WGQGTLVTVSS	294	HCDR1	GYTFTDY	11	HCDR1	DYTIH	17
				HCDR2	YPLRGS	12	HCDR2	W*I*YPLRGSINYAQKFQG	282
				HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	13
	VL	EIVMTQSPATLSVSPGERATLSC***RASESVDNDGIR*** ***FLH***WYQQKPGQAPRLLIY***RASTLET***GIPARFSGSG SGTEFTLTISSLQSEDFAVYYC***QQSNKDPYT***FGGG TKVEIK	295	LCDR1	RASESVDNDGIRFLH	280	LCDR1	RASESVDNDGIRFLH	280
				LCDR2	RASTLET	293	LCDR2	RASTLET	293
				LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	16
2419-1205	VH	QVQLVQSGAEVKKPGASVKVSCKAS*GYTFT**DYTIH** WVRQATGQGLEWMG**WI*YPLRGSI*NYAQKFQG**RVTM TANKSSSTVYMELSSLRSEDTAVYFCAR***HGAYYSN*** ***AFDY***WGQGTLVTVSS	294	HCDR1	GYTFTDY	11	HCDR1	DYTIH	17
				HCDR2	YPLRGS	12	HCDR2	W*I*YPLRGSINYAQKFQG	282
				HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	13
	VL	EIVMTQSPATLSVSPGERATLSC***RASESVDNDGIR*** ***FLH***WYQQKPGQAPRLLIY***RASNRET***GIPARFSGSG SGTEFTLTISSLQSEDFAVYYC***QQSNKDPYT***FGGG TKVEIK	284	LCDR1	RASESVDNDGIRFLH	280	LCDR1	RASESVDNDGIRFLH	280
				LCDR2	RASNRET	281	LCDR2	RASNRET	281
				LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	16
2419-1210	VH	QVQLVQSGAEVKKPGASVKVSCKAS*GYTFT**DYTIH** WVRQATGQGLEWMG**WI*YPLRGSI*NYAQKFQG**RVTM TANKSSSTVYMELSSLRSEDTAVYFCAR***HGAYYSN*** ***AFDY***WGQGTLVTVSS	294	HCDR1	GYTFTDY	11	HCDR1	DYTIH	
				HCDR2	YPLRGS	12	HCDR2	W*I*YPLRGSINYAQKFQG	
				HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	
	VL	DIVMTQSPDSLAVSLGERATINC***KSSQSVDNDGIR*** ***FLH***WYQQKPGQPPKLLIY***RASTRES***GVPDRFSGSG SGTDFTLTISSLQAEDVAVYYC***QQSNKDPYT***FGGG TKVEIK	316	LCDR1	KSSQSVDNDGIRFLH	314	LCDR1	KSSQSVDNDGIRFLH	
				LCDR2	RASTRES	315	LCDR2	RASTRES	
				LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	
2419-1406	VH	QVQLVQSGAEVKKPGASVKVSCKAS*GYTFT**DYTIH** WVRQATGQGLEWMG**WI*YPLRGSI*NYAQKFQG**RVTM TADKSISTVYMELSSLRSEDTAVYFCAR***HGAYYSN*** ***AFDY***WGQGTLVTVSS	296	HCDR1	GYTFTDY	11	HCDR1	DYTIH	
				HCDR2	YPLRGS	12	HCDR2	W*I*YPLRGSINYAQKFQG	
				HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	
	VL	EIVMTQSPATLSVSPGERATLSC***RASESVDNDGIR*** ***FLH***WYQQKPGQAPRLLIY***RASTRAT***GIPARFSGSG SRTEFTLTISSLQSEDFAVYYC***QQSNKDPYT***FGGG TKVEIK	286	LCDR1	RASESVDNDGIRFLH	280	LCDR1	RASESVDNDGIRFLH	
				LCDR2	RASTRAT	285	LCDR2	RASTRAT	
				LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	
2419-0206	VH	QVQLVQSGAEVKKPGSSVKVSCKAS*GYTFT**DYTIH** WVRQAPGQGLEWMG**WI*YPLRGSI*NYAQKFQG**RVTI	289	HCDR1	GYTFTDY	11	HCDR1	DYTIH	
				HCDR2	YPLRGS	12	HCDR2	W*I*YPLRGSINYAQKFQG	

		TADKSTSTAYMELSSLRSEDTAVYFCAR***HGAYYSN***		HCDR3	HGAYYSNAFDY	13	HCDR3	HGAYYSNAFDY	13
		AFDYWGQGTLVTVSS							
	VL	EIVMTQSPATLSVSPGERATLSC***RASESVDNDGIR***	286	LCDR1	RASESVDNDGIRFLH	280	LCDR1	RASESVDNDGIRFLH	280
		FLHWYQQKPGQAPRLLIY***RASTRAT***GIPARFSGSG		LCDR2	RASTRAT	285	LCDR2	RASTRAT	285
		SRTEFTLTISSLQSEDFAVYYC***QQSNKDPYT***FGGG		LCDR3	QQSNKDPYT	16	LCDR3	QQSNKDPYT	16
		TKVEIK							
2621	VH	EVQLQQSGAELVRPGSSVKMSCKTS*GYTFT****SYGIN***	29	HCDR1	GYTFTSY	21	HCDR1	SXGIN	27
		WVKQRPGQGLEWIG***YIYIGNGYAEYNERFKG***KATL		HCDR2	YIGNGY	22	HCDR2	YIYIGNGYAEYNERFKG	28
		TSDTSSSTAYMQLSSLTSEDSAIYFCAL***YYPWFTY***		HCDR3	YYPWFTY	23	HCDR3	YYPWFTY	23
		WGQGTLVTVSA							
	VL	DIQMTQSPASLSASVGDSVTITC***RASENIYSYLA***W	30	LCDR1	RASENIYSYLA	24	LCDR1	RASENIYSYLA	24
		YQQKQGKSPQLLVY***NAKTLAE***GVPSRFSGSGSGTQ		LCDR2	NAKTLAE	25	LCDR2	NAKTLAE	25
		FSLKINSLQPEDFGNYYC***QHHYDTPFT***FGGGTKLE		LCDR3	QHHYDTPFT	26	LCDR3	QHHYDTPFT	26
		IK							
2922	VH	QVQLHQSGPELVKPGASVKLSCKTS*GYTFT****SYDVF***	39	HCDR1	GYTFTSY	21	HCDR1	SYDVF	37
		WVKQRPGQGLEWIG***WIYPRDSSTKYNEKFKG***KATL		HCDR2	YPRDSS	32	HCDR2	WIYPRDSSTKYNEKFKG	38
		TVDTSSSTAYMELHSLTSEDSAVYFCAK***EGYDYDK***		HCDR3	EGYDYDKRGFDY	33	HCDR3	EGYDYDKRGFDY	33
		RGFDYWGQGTTLTVSS							
	VL	DIVLTQSPASLAVSLGQRAIISC***KASQSVSFAGTN***	40	LCDR1	KASQSVSFAGTNLMH	34	LCDR1	KASQSVSFAGTNLMH	34
		LMHWYQQRPGQQPKLLIY***RASNLEP***GVPTRFSGSG		LCDR2	RASNLEP	35	LCDR2	RASNLEP	35
		SRTDFTLNIHPVEEDDAATYYC***QQSREYPWT***FGGG		LCDR3	QQSREYPWT	36	LCDR3	QQSREYPWT	36
		TKLEIK							
3125	VH	QVQLQQSGAELVRPGASVTLSCKAS*GYTFT****DYEMH***	49	HCDR1	GYTFTDY	11	HCDR1	DYEMH	47
		WVKQTPVHGLEWIG***AIDPETGGTAYNQRFKG***KAIL		HCDR2	DPETGG	42	HCDR2	AIDPETGGTAYNQRFKG	48
		TTDKSSITAYMELRSLTSEDSAVYYCTR***WNDGDY***W		HCDR3	WNDGDY	43	HCDR3	WNDGDY	43
		GQGTTLTVSS							
	VL	DVVMTQTPLSLSVTIGQPASISC***KSSQSLLYSNGK***TYLN	50	LCDR1	KSSQSLLYSNGKTYLN	44	LCDR1	KSSQSLLYSNGKTYLN	44
		TYLNWFQQRPGQSPKRLMY***QVSKLDP***GIPDRFSGS		LCDR2	QVSKLDP	45	LCDR2	QVSKLDP	45
		GSETDFTLKISRVEAEDLGLYYC***LQGTYYPYT***FGG		LCDR3	LQGTYYPYT	46	LCDR3	LQGTYYPYT	46
		GTKLEIK							
3327	VH	EVQLQQSGPELVKPGASVKMSCKAS*GYSFT****GYFMN***	59	HCDR1	GYSFTGY	51	HCDR1	GYFMN	51
		WVKQSHGKSLEWIG***RINPYNGDTFYNQKFKG***KATL		HCDR2	NPYNGD	52	HCDR2	RINPYNGDTFYNQKFKG	52
		TVDKSSSTAHMELRSLTSEDSALYYCAS***EGDGYYW***		HCDR3	EGDGYYWYFDV	53	HCDR3	EGDGYYWYFDV	53
		YFDVWGAGTTVTVSS							
	VL	DIVLTQSPASLAVSLGQRATISC***RASESVDNYGIS***	60	LCDR1	RASESVDNYGISFMN	54	LCDR1	RASESVDNYGISFMN	54
		FMNWFQQKPGQPPKLLIY***AASNQGS***GVPARFSGSG		LCDR2	AASNQGS	55	LCDR2	AASNQGS	55
		SGTDFSLNIHPMEEDDTAMYFC***QQSKEVPRT***FGGG		LCDR3	QQSKEVPRT	56	LCDR3	QQSKEVPRT	56
		TKLEIK							
3525	VH	QVQLQQSGAELVRPGASVKLSCKAS*GYTFT****DHEMH***	66	HCDR1	GYTFTDH	61	HCDR1	DHEMH	61
		WVRQTPVHGLEWIG***VIDPDTGDTTYNQKFKG***KATL		HCDR2	DPDTGD	62	HCDR2	VIDPDTGDTTYNQKFKG	62
		TADKSSSTAYMDLRSLTSEDSAVFYCTR***WTGGDY***W		HCDR3	WTGGDY	63	HCDR3	WTGGDY	63
		GHGTTLTVSS							
	VL	DVVMTQTPLSLSVTIGQPASISC***KSSQSLLYSNGK***TYLN	50	LCDR1	KSSQSLLYSNGKTYLN	44	LCDR1	KSSQSLLYSNGKTYLN	44
		TYLNWFQQRPGQSPKRLMY***QVSKLDP***GIPDRFSGS		LCDR2	QVSKLDP	45	LCDR2	QVSKLDP	45

		GSETDFTLKISRVEAEDLGLYYC***LQGTYYPYT***FGG GTKLEIK		LCDR3	LQGTYYPYT	46	LCDR3	LQGTYYPYT	46
3530	VH	QVQLQQSGAELVRPGASVKLSCKAS*GYTFT****DHEMH*** WVRQTPVHGLEWIG***VIDPDTGDTTYNQKFKG***KATL TADKSSSTAYMDLRSLTSEDSAVFYCTR***WTGGDY***W GHGTTLTVSS	66	HCDR1	GYTFTDH	61	HCDR1	DHEMH	64
				HCDR2	DPDTGD	62	HCDR2	VIDPDTGDTTYNQKFKG	65
				HCDR3	WTGGDY	63	HCDR3	WTGGDY	63
	VL	DAVMTQTPLSLSVTIGQPASISC***KSSQSLLYSDGK TYLN***WFQQRPGQSPKRLMY***QVSKLDP***GIPDRFSGS GSETDFTLKISRVEAEDLGVYYC***LQGTYYPYT***FGS GTKLEIK	70	LCDR1	KSSQSLLYSDGKTYLN	67	LCDR1	KSSQSLLYSDGKTYLN	67
				LCDR2	QVSKLDP	45	LCDR2	QVSKLDP	45
				LCDR3	LQGTYYPYT	46	LCDR3	LQGTYYPYT	46
4035	VH	QVQLKESGPGLVAPSQSLSITCTVS*GFSLT****IYDVH*** WVRQSPGKGLEWLG***VIWSDGSTDYNAAFIS***RLSIS KDNSKSQVFFKMNSLQADDTAIYYCAR***NWVDQAWF AY***WGQGTLVTVSA	101	HCDR1	GFSLTIY	93	HCDR1	IYDVH	99
				HCDR2	WSDGS	94	HCDR2	VIWSDGSTDYNAAFIS	100
				HCDR3	NWVDQAWFAY	95	HCDR3	NWVDQAWFAY	95
	VL	DIQMTQSPASLSASVGETITITC***RASKNIYSYLA***W YQQKQGKSPQLLVY***NAKTLPE***GVPSRFSGSGSGTQ FSLKINSLQPEDFGSYYC***QHHYGTPLT***FGAGTKLE LK	102	LCDR1	RASKNIYSYLA	96	LCDR1	RASKNIYSYLA	96
				LCDR2	NAKTLPE	97	LCDR2	NAKTLPE	97
				LCDR3	QHHYGTPLT	98	LCDR3	QHHYGTPLT	98
4035-062	VH	QVQLQESGPGLVKPSETLSLTCTVS*GFSLT****IYDVH*** WVRQPPGKGLEWIG***VIWSDGSTDYNPSLKS***RVTIS KDTSKNQVSLKLSSVTAADTAVYYCAR***NWVDQAWF AY***WGQGTLVTVSS	225	HCDR1	GFSLTIY	93	HCDR1	IYDVH	99
				HCDR2	WSDGS	94	HCDR2	VIWSDGSTDYNPSLKS	273
				HCDR3	NWVDQAWFAY	95	HCDR3	NWVDQAWFAY	95
	VL	DIQMTQSPSSLSASVGDRVTITC***RASKNIYSYLA***W YQQKPGKAPKLLVY***NAKTLPE***GVPSRFSGSGSGTD FTLTISSLQPEDFATYYC***QHHYGTPLT***FGQGTKLE IK	229	LCDR1	RASKNIYSYLA	96	LCDR1	RASKNIYSYLA	96
				LCDR2	NAKTLPE	97	LCDR2	NAKTLPE	97
				LCDR3	QHHYGTPLT	98	LCDR3	QHHYGTPLT	98
3934	VH	QVQLQQSGPELVKPGASVKLSCKAA*GYIFT****DYTIN*** WVKQSPGQGLEWIG***WIYPGSGNRKYNDKFKG***KATM TADKSSSTAYMQLSSLTSEDSAVYFCAR***ESNYVGY YAMDY***WGQGTSVTVSS	111	HCDR1	GYIFTDY	103	HCDR1	DYTIN	
				HCDR2	YPGSGN	104	HCDR2	WIYPGSGNRKYNDKFKG	
				HCDR3	ESNYVGYYAMDY	105	HCDR3	ESNYVGYYAMDY	
	VL	DVLMTQTPLSLPVSLGDQASISC***RSSQSVVNSNGN TYLE***WYLQKPGQSPNLLIY***KVSNRFS***GVPDRFSGS GSGTDFTLKISRVEAEDLGVYYC***FQGSHVPWT***FGG GTKLEIK	112	LCDR1	RSSQSVVNSNGNTYLE	106	LCDR1	RSSQSVVNSNGNTYLE	
				LCDR2	KVSNRFS	107	LCDR2	KVSNRFS	
				LCDR3	FQGSHVPWT	108	LCDR3	FQGSHVPWT	
3833	VH	QVQLQQSGAELVRPGTSVKMSCKAA*GYTFT****NYWIG*** WVKQRPGHGLEWIG***DIYPGGIGGGYTKYNEKFKG***K ATLTADTSSSTAYMQLGSLTSEDSAIYFCSR***SETG RAMDY***WGQGTSVTVSS	121	HCDR1	GYTFTNY	113	HCDR1	NYWIG	
				HCDR2	YPGGIGGGY	114	HCDR2	DIYPGGIGGGYTKYNEK FKG	
				HCDR3	SETGRAMDY	115	HCDR3	SETGRAMDY	
	VL	DIQMTQSPSSLSASLGGKVTITC***KASQDINKYIA***W YQHKPGKGPRLLIH***YTSTLKP***GIPSRFSGSGSGRD YSFSISDLEPEDIATYYC***LQYDNLNT***FGGGTKLEI K	122	LCDR1	KASQDINKYIA	116	LCDR1	KASQDINKYIA	
				LCDR2	YTSTLKP	117	LCDR2	YTSTLKP	
				LCDR3	LQYDNLNT	118	LCDR3	LQYDNLNT	
3631	VH	EIQLQQSGPELVKPGASVKVSCKAS*GYSFT****DYNIY*** WVKQSHGKSLEWIG***YIDPSNGGPGYNQKFRG***KATL	131	HCDR1	GYSFTDY	123	HCDR1	DYNIY	
				HCDR2	DPSNGG	124	HCDR2	YIDPSNGGPGYNQKFRG	

		TVDKSSSTAFLHLNSLTSEDSAVYYCAR***RDNYGSG*** ***TMDY***WGQGTSVTVSS		HCDR3	RDNYGSGTMDY	125	HCDR3	RDNYGSGTMDY	125
3732	VL	DIVMTQSQKFMSTSVGDRVSITC***KASQNVGTDVS***W YQQKPGKSPKPLIY***WASNRFT***GVPDRFIGSGSGTD FTLTISNVQSEDLADYFC***EQYSIYPLT***FGAGTKLE LK	132	LCDR1	KASQNVGTDVS	126	LCDR1	KASQNVGTDVS	126
				LCDR2	WASNRFT	127	LCDR2	WASNRFT	127
				LCDR3	EQYSIYPLT	128	LCDR3	EQYSIYPLT	128
	VH	EIQLQQSGPELVKPGASVKVSCKAS***GYSFTDDNMY*** WVKQSHGKSLEWIG***YIDPLNGGTGYNQKFKG***KATL TVDKSSSTAFLHLNSLTSEDSAVYYCAR***RDNYATG*** ***TMDY***WGQGTSVTVSS	140	HCDR1	GYSFTDD	133	HCDR1	DDNMY	138
				HCDR2	DPLNGG	134	HCDR2	YIDPLNGGTGYNQKFKG	139
				HCDR3	RDNYATGTMDY	135	HCDR3	RDNYATGTMDY	135
	VL	DIVMTQSQKFMSTSVGDRVSITC***KASKNVGTDVS***W YQQKPGKSPKPLIY***WASNRFT***GVPDRFTGSGSGTD FTLTINNVQSEDLADYFC***EQYSSYPLT***FGAGTKLE LK	141	LCDR1	KASKNVGTDVS	136	LCDR1	KASKNVGTDVS	136
				LCDR2	WASNRFT	127	LCDR2	WASNRFT	127
				LCDR3	EQYSSYPLT	137	LCDR3	EQYSSYPLT	137
4338	VH	EVQLQQSGPELVKPGASVKISCKAS***GYTFTDYNMD*** WVKQSHGKSLEWIG***NIYPINGYTGYNQRFKN***KATL TVDKSSSTAYMELHSLTSEDSAVYYCAR***DSNYVGW*** ***YFDV***WGAGTTVTVSS	151	HCDR1	GYTFTDY	11	HCDR1	DYNMD	149
				HCDR2	YPINGY	142	HCDR2	NIYPINGYTGYNQRFKN	150
				HCDR3	DSNYVGWYFDV	143	HCDR3	DSNYVGWYFDV	143
	VL	DVVMTQTPLSLPVSLGDQASISC***RSSQSLVHSNGN*** ***TYLH***WYLQKPGQSPKLLIY***KVSNRFS***GVPDRFSGS GSGTDFTFKISRVEAEDLGVYFC***SQSTHVPRT***FGG GTKLEIK	152	LCDR1	RSSQSLVHSNGNTYLH	144	LCDR1	RSSQSLVHSNGNTYLH	144
				LCDR2	KVSNRFS	107	LCDR2	KVSNRFS	107
				LCDR3	SQSTHVPRT	145	LCDR3	SQSTHVPRT	145
	VL	DIVLTQSPASLTVSLGQRATFSC***RASKSVSTSGYS*** ***YMH***WYQQKPGQPPKLLIY***FTSDLEP***GVPARFTGSG SGTDFTLNIHPVEEDAATYYC***QHSRELPYP***FGGG TKLEIK	153	LCDR1	RASKSVSTSGYSYMH	146	LCDR1	RASKSVSTSGYSYMH	146
				LCDR2	FTSDLEP	147	LCDR2	FTSDLEP	147
				LCDR3	QHSRELPYP	148	LCDR3	QHSRELPYP	148
4540	VH	QVQLQQSGPELVKPGASVKISCKAS***GYTFADYYIN*** WVKQRPGQGLEWIG***WIFPGSGSTYYNEKFKG***KATL TVDKSSSTAYMLLSSLTSEDSAVYFCAR***GDSGRAM*** ***DY***WGQGTSVTVSS	161	HCDR1	GYTFADY	154	HCDR1	DYYIN	
				HCDR2	FPGSGS	155	HCDR2	WIFPGSGSTYYNEKFKG	
				HCDR3	GDSGRAMDY	156	HCDR3	GDSGRAMDY	
	VL	DIQMTQSPSSLSASLGGKVTITC***KASQDINKYIA***W YQHKPGKGPRLLIH***YTSTLQS***GIPSRFSGSGSGRD YSFSISNLEPEDNATYYC***LQYDNLLT***FGAGTKLEL K	162	LCDR1	KASQDINKYIA	116	LCDR1	KASQDINKYIA	
				LCDR2	YTSTLQS	157	LCDR2	YTSTLQS	
				LCDR3	LQYDNLLT	158	LCDR3	LQYDNLLT	
4540-063	VH	QVQLVQSGAELKKPGASVKVSCKAS***GYTFADYYMN*** WVRQAPGQGLEWMG***WIFPGSGSTYYNQKFQG***RVTM TVDKSSSTAYMELSRLRSDDTAVYYCAR***GDSGRAM*** ***DY***WGQGTLVTVSS	258	HCDR1	GYTFADY	154	HCDR1	DYYMN	
				HCDR2	FPGSGS	155	HCDR2	WIFPGSGSTYYNQKFQG	
				HCDR3	GDSGRAMDY	156	HCDR3	GDSGRAMDY	
	VL	DIQMTQSPSSLSASVGDRVTITC***QASQDINKYLA***W YQHKPGKAPKLLIH***YTSTLET***GVPSRFSGSGSGTD FTFTISSLQPEDIATYYC***LQYDNLLT***FGGGTKVEI K	261	LCDR1	QASQDINKYLA	274	LCDR1	QASQDINKYLA	
				LCDR2	YTSTLET	275	LCDR2	YTSTLET	
				LCDR3	LQYDNLLT	158	LCDR3	LQYDNLLT	
4540-033	VH	QVQLVQSGAEVKKPGASVKVSCKAS***GYTFADYYIN*** WVRQAPGQGLEWMG***WIFPGSGSTYYAQKLQG***RVTM	256	HCDR1	GYTFADY	154	HCDR1	DYYIN	
				HCDR2	FPGSGS	155	HCDR2	WIFPGSGSTYYAQKLQG	

		TTDTSTSTAYMELRSLRSDDTAVYYCAR***GDSGRAM***		HCDR3	GDSGRAMDY	156	HCDR3	GDSGRAMDY	156
		DYWGQGTLVTVSS							
	VL	DIQMTQSPSSLSASVGDRVTITC***QASQDINKYLA***W	261	LCDR1	QASQDINKYLA	274	LCDR1	QASQDINKYLA	274
		YQHKPGKAPKLLIH***YTSTLET***GVPSRFSGSGSGTD		LCDR2	YTSTLET	275	LCDR2	YTSTLET	275
		FTFTISSLQPEDIATYYC***LQYDNLLT***FGGGTKVEI		LCDR3	LQYDNLLT	158	LCDR3	LQYDNLLT	158
		K							
4237	VH	QAHLKESGPGLVAPSQSLSITCTVS*GFSLT****DYDVH***	171	HCDR1	GFSLTDY	163	HCDR1	DYDVH	169
		WVRQSPGKGLEWLG***VIWNDGSTDYNTAFIS***RLTIS		HCDR2	WNDGS	164	HCDR2	VIWNDGSTDYNTAFIS	170
		KDNSKSQVFFKMNSLQADDTAIYYCAR***NWYGGYWF***		HCDR3	NWYGGYWFAY	165	HCDR3	NWYGGYWFAY	165
		AYWGQGTLVTVSA							
	VL	DIQMTQSPASLSASAGETVTITC***RSSENIYSYLA***W	172	LCDR1	RSSENIYSYLA	166	LCDR1	RSSENIYSYLA	166
		YQQKQGKSPQLLVY***NANALAE***GVPSRFSGSGSGTQ		LCDR2	NANALAE	167	LCDR2	NANALAE	167
		FSLKINSLQPEDFGSYYC***QHHYGTPFT***FGSGTKLE		LCDR3	QHHYGTPFT	168	LCDR3	QHHYGTPFT	168
		IK							
4439	VH	EIQLQQSGAELVKPGASVKISCKAS*DYSFT****GYNMN***	271	HCDR1	DYSFTGY	266	HCDR1	GYNMN	269
		WVMQSHGKSLEWIG***NIHPYYGGTSFNQKFMG***KATL		HCDR2	HPYYGG	267	HCDR2	NIHPYYGGTSFNQKFMG	270
		TADKSSSTAYMQLNSLTSEDSAVYYCAR***ERSNFHA***		HCDR3	ERSNFHALDY	268	HCDR3	ERSNFHALDY	268
		LDYWGQGTSVTVSS							
	VL	DIVLTQSPASLTVSLGQRATFSC***RASKSVSTSGYS***	272	LCDR1	RASKSVSTSGYSYMH	146	LCDR1	RASKSVSTSGYSYMH	146
		YMHWYQQKPGQPPKLLIY***FTSDLEP***GVPARFTGSG		LCDR2	FTSDLEP	147	LCDR2	FTSDLEP	147
		SGTDFTLNIHPVEEEDAATYYC***QHSRELPYP***FGGG		LCDR3	QHSRELPYP	148	LCDR3	QHSRELPYP	148
		TKLEIK							

Table 2. Nucleotide sequences of heavy chain variable regions (VHs) and light chain variable regions (VLs) of exemplary antibody molecules

Antibody	Chain	Nucleotide Sequence	SEQ ID NO
2218	VH	GATGTACAGCTTCAGGAGTCAGGACCTGGCCTCGTGAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTGTCACTGGC TACTCCATCACCAGTGGTTATTACTGGAACTGGATCCGGCAGTTTCCAGGAAACAAACTGGAATGGATGGGCTACATA AGCTACGATGGTTACAATAACTACAACCCATCTCTCAAAAATCGAATCTCCATCACTCGTGACACATCTAAGAACCAG TTTTTCCTGAAGTTGAATTCTGTGACTACTGAGGACACAGCCACATATTACTGTGCAAACTACTATGATTACGAAGAC TGGTACTTCGGTGTCTGGGGCACAGGGACCACGGTCACCGTCTCCTCA	71
	VL	GACATTGTGCTGACCCAATCTCCAGCTTCTTTGGCTATGTCTCTAGGGAAGAGGGCCACCATCTCCTGCAGAGCCAGC GAAAGTGTCAGTATTATTGGTACTAATTCAATACACTGGTACCAACAGAAACCAGGACAGCCACCCAAACTCCTCATC TATCATGCATCCAACCTAGAAACTGGAGTCCCTGCCAGGTTCAGTGGCAGTGGGTCTAGAACAGACTTCACCCTCACC ATTGATCCTGTGGAGGAAGATGATGTTGCAATCTATTACTGTCTGCAAAGTAGGAAGATTCCGTACACGTTCGGAGGG GGGACCAAGCTGGAAATAAAA	72
2419	VH	CAGGTCCAGCTGCAGCAGTCTGGAGCTGAGCTGGTGAAACCCGGGGCATCAGTGAGGCTGTCCTGCGAGGCTTCTGGC TACACCTTCACGGACTATACTATACACTGGGTAAAGCAGAGGTCTGGACAGGGTCTTGAGTGGATTGGATGGATTTAC CCTCTAAGAGGTAGTATAAACTACAATGAGAAATTCAAGGACAAGGCCACACTTGACTGCGGACAAATCCTCCAGCACA GTCTATTTGGAGCTTGGTAGATTGACATCTAAGGACTCTGCGGTCTATTTCTGTGCAAGACACGGAGCCTACTATAGT AACGCCTTTGACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCA	73
	VL	AACATTGTAATGACCCAATCTCCAGCTTCATTGGCTGTGTCTCTAGGTCAGAGGGCCACCATCTCCTGCAGAGCCAGC GAGAGTGTTGATAATGATGGCATTAGATTTATGCACTGGTACCAGCAGAAACCAGGACAGCCACCCAAACTCCTCATC TATCGTGCATCCAACCTAGAATCTGGGATCCCTGCCAGGTTCAGTGGCAGTGGGTCTAGGACAGACTTCACCCTCACT ATTAATCCTGTGGAGACTGATGATGTTGCAACCTATTACTGTCAGCAAAGTAATAAGGATCCGTACACGTTCGGAGGG GGGACCAAGCTGGAGCTGAAA	74
2419-1305	VH	CAAGTTCAGTTGGTGCAAAGCGGGGGCAGAAGTGAAGAAACCTGGTGCTTCTGTGAAAGTTTCCTGCAAGGCCAGCGGC TACACCTTTACTGATTACACAATACACTGGGTACGGCAGGCAACTGGGCAAGGATTGGAATGGGATGGGGTGGATATAC CCATTGCGAGGGTCTATAAACTACGCACAGAAATTTCAAGGTCGAGTAACAATGACAGCCAACAAATCAATAAGCACC GTTTATATGGAACTCTCATCTCTCAGGAGTGAGGATACCGCCGTGTATTTCTGCGCACGACACGGTGCATATTACTCA AACGCTTTCGACTATTGGGGCCAGGGCACCCTTGTGACTGTTAGTAGC	304
	VL	GAGATAGTAATGACTCAGTCTCCCGCTACACTTAGTGTAAGCCCAGGGGAGCGAGCAACCCTCAGTTGCAGAGCATCT GAGAGTGTTGATAATGATGGAATACGTTTTCTCCATTGGTATCAACAAAAACCAGGGCAGGCCCCCAGATTGCTGATC TACCGTGCTTCCAATCGCGAGACTGGCATTCCTGCACGTTTCAGCGGCAGCGGCTCCGGAACCGAGTTTACACTTACT ATTAGCTCACTCCAGTCTGAAGACTTCGCTGTGTATTACTGTCAGCAATCCAACAAGGACCCATACACTTTCGGAGGC GGCACTAAGGTTGAGATCAAA	305
2419-1306	VH	CAAGTTCAGTTGGTGCAAAGCGGGGGCAGAAGTGAAGAAACCTGGTGCTTCTGTGAAAGTTTCCTGCAAGGCCAGCGGC TACACCTTTACTGATTACACAATACACTGGGTACGGCAGGCAACTGGGCAAGGATTGGAATGGGATGGGGTGGATATAC CCATTGCGAGGGTCTATAAACTACGCACAGAAATTTCAAGGTCGAGTAACAATGACAGCCAACAAATCAATAAGCACC GTTTATATGGAACTCTCATCTCTCAGGAGTGAGGATACCGCCGTGTATTTCTGCGCACGACACGGTGCATATTACTCA AACGCTTTCGACTATTGGGGCCAGGGCACCCTTGTGACTGTTAGTAGC	304
	VL	GAGATAGTTATGACTCAGTCTCCCGCCACACTTTCAGTAAGTCCCGGTGAACGCGCCACCCTGTCCTGCCGTGCTTCC GAATCAGTGGATAAATGACGGCATTAGGTTTTTGCACTGGTACCAACAAAAGCCCGGACAGGCCCCCCGCCTGCTGATA	306

		TATCGTGCATCAACACGAGCAACAGGGATCCCCGCTCGATTTAGTGGATCCGGAAGCAGGACCGAATTTACACTTACC ATTTCCTCACTTCAGTCAGAAGATTTCGCCGTTACTACTGTCAGCAGTCAAATAAGGATCCTTACACATTTGGGGGC GGTACAAAAGTCGAGATCAAA	
2419-1310	VH	CAAGTTCAGTTGGTGCAAAGCGGGGCAGAAGTGAAGAAACCTGGTGCTTCTGTGAAAGTTTCCTGCAAGGCCAGCGGC TACACCTTTACTGATTACACAATACACTGGGTACGGCAGGCAACTGGGCAAGGATTGGAATGGATGGGGTGGATATAC CCATTGCGAGGGTCTATAAACTACGCACAGAAATTTCAAGGTCGAGTAACAATGACAGCCAACAAATCAATAAGCACC GTTTATATGGAACTCTCATCTCTCAGGAGTGAGGATACCGCCCGTGTATTTCTCGCCACGACACGGTGCATATTACTCA AACGCTTTCGACTATTGGGGCCAGGGCACCCTTGTGACTGTTAGTAGC	304
	VL	GACATTGTAATGACCCAGTCTCCCGATAGCCTCGCTGTCTCACTCGGAGAACGCGCAACCATCAACTGCAAGTCCTCC CAAAGCGTTGACAATGACGGCATTAGGTTTTTGCACTGGTACCAGCAGAAACCCGGTCAACCTCCTAAGTTGCTCATT TACCGAGCATCTACCCGCGAGTCAGGAGTACCTGATCGCTTTTCCGGTAGCGGTAGTGGAACAGATTTTACTCTGACC ATTAGTTCACTCCAGGCAGAAGATGTGGCTGTCTACTACTGCCAACAGTCAAATAAAGACCCTTATACCTTCGGTGGG GGTACCAAAGTAGAGATCAAA	318
2419-0806	VH	GAGGTCCAGTTGGTCCAGTCAGGAGCCGAAGTCAAGAAGCCTGGGGAAAGCCTGAAAATAAGTTGCAAAGCTAGTGGA TATACATTTACAGATTATACCATTCATTGGGTCCGGCAAATGCCAGGAAAAGGCTTGGAGTGGGTGGATTTAT CCCCTCCGAGGCTCAATAAATTATAGTCCTAGTTTTCAGGGGCAGGTAACTATTAGCGCTGATAAAAGTATTTCTACA GTTTATTTGCAGTGGAGTTCATTGAAGGCTAGTGACACCGCTATGTATTTCTGCGCTAGACATGGTGCATATTATTCA AATGCCTTCGACTATTGGGGCCAGGGCACCCTCGTCACTGTGAGTTCC	307
	VL	GAGATAGTTATGACTCAGTCTCCCGCCACACTTTCAGTAAGTCCCGGTGAACGCGCCACCCTGTCCTGCCGTGCTTCC GAATCAGTGGATAATGACGGCATTAGGTTTTTGCACTGGTACCAACAAAAGCCCGGACAGGCCCCCGCCTGCTGATA TATCGTGCATCAACACGAGCAACAGGGATCCCCGCTCGATTTAGTGGATCCGGAAGCAGGACCGAATTTACACTTACC ATTTCCTCACTTCAGTCAGAAGATTTCGCCGTTTACTACTGTCAGCAGTCAAATAAGGATCCTTACACATTTGGGGGC GGTACAAAAGTCGAGATCAAA	306
2419-0205	VH	CAGGTGCAACTTGTTCAGTCAGGGGCTGAAGTAAAGAAGCCAGGCTCATCAGTCAAGGTATCATGCAAAGCATCTGGC TATACATTTACAGATTACACCATTCACTGGGTGAGGCAAGCTCCCGGTCAAGGTCTCGAGTGGATGGGGTGGATATAC CCTCTCAGAGGCTCTATAAATTACGCTCAGAAATTTCAAGGGAGAGTTACAATTACTGCTGATAAAAGTACCAGCACT GCTTATATGGAGCTTTCCTCACTTCGTTCAGAGGACACCGCCGTTTACTATTTGTGCCCGGCATGGTGCCTATTATTCA AATGCCTTCGATTATTGGGGGCAGGGAACTTTGGTCACAGTTTCATCT	308
	VL	GAGATAGTAATGACTCAGTCTCCCGCTACACTTAGTGTAAGCCCAGGGGAGCGAGCAACCCTCAGTTGCAGAGCATCT GAGAGTGTTGATAATGATGGAATACGTTTTCTCCATTGGTATCAACAAAAACCAGGGCAGGCCCCCAGATTGCTGATC TACCGTGCTTCCAATCGCGAGACTGGCATTCCTGCACGTTTCAGCGGCAGCGGCTCCGGAACCGAGTTTACACTTACT ATTAGCTCACTCCAGTCTGAAGACTTCGCTGTGTATTACTGTCAGCAATCCAACAAGGACCCATACACTTTCGGAGGC GGCACTAAGGTTGAGATCAAA	305
2419-0406	VH	CAAGTTCAACTTGTCCAAAGTGGGGCTGAAGTTAAAAAACCTGGATCATCAGTCAAGGTTTCATGCAAAGCCAGCGGT TACACATTTACAGACTATACAATACATTGGGTTCGACAGGCTCCCGGGCAAGGGCTCGAATGGATGGGATGGATTTAT CCCCTCAGGGGCTCAATTAACTATGCTGAGAAATTTAAGGGTCGTGTAACACTCACCGCCGATAAATCCACCTCAACC GTATATATGGAGCTTTCTTCTCGCTCTGAAGATACCGCCGTCTATTTCTGCGCACGACACGGGGCATACTATTCT AATGCTTTTGACTACTGGGGACAAGGGACACTTGTGACCGTTAGTAGC	309
	VL	GAGATAGTTATGACTCAGTCTCCCGCCACACTTTCAGTAAGTCCCGGTGAACGCGCCACCCTGTCCTGCCGTGCTTCC GAATCAGTGGATAATGACGGCATTAGGTTTTTGCACTGGTACCAACAAAAGCCCGGACAGGCCCCCCGCCTGCTGATA	306

		TATCGTGCATCAACACGAGCAACAGGGATCCCCGCTCGATTTAGTGGATCCGGAAGCAGGACCGAATTTACACTTACC ATTTCCTCACTTCAGTCAGAAGATTTCGCCGTTACTACTGTCAGCAGTCAAATAAGGATCCTTACACATTTGGGGGC GGTACAAAAGTCGAGATCAAA	
2419-0605	VH	CAGGTGCAGTTGGTCCAGAGCGGGGCAGAGGTTAAGAAGCCTGGGGCCTCAGTAAAGGTATCCTGCAAGGCTTCTGGG TACACCTTCACAGATTACACTATTCATTGGGTGCGCCAAGCACCTGGTCAAGGCCTTGAATGGATGGGATGGATTTAC CCCTTGCGAGGGAGTATTAATTATGCACAGAAGTTCCAGGGAAGGGTTACTCTTACCGCCGACAAGTCCACATCAACC GTTTACATGGAGCTTTCCTCTCTCAGGTCCGAAGACACTGCTGTATATTTCTGCGCTCGGCATGGGGCTTATTACAGC AACGCCTTCGATTACTGGGGTCAGGGTACATTGGTCACAGTGTCCAGT	319
	VL	GAGATAGTAATGACTCAGTCTCCCGCTACACTTAGTGTAAGCCCAGGGAGCGAGCAACCCTCAGTTGCAGAGCATCT GAGAGTGTTGATAATGATGGAATACGTTTTCTCCATTGGTATCAACAAAAACCAGGGCAGGCCCCCAGATTGCTGATC TACCGTGCTTCCAATCGCGAGACTGGCATTCCTGCACGTTTCAGCGGCAGCGGCTCCGGAACCGAGTTTACACTTACT ATTAGCTCACTCCAGTCTGAAGACTTCGCTGTGTATTACTGTCAGCAATCCAACACAAGGACCCATACACTTTCGGAGGC GGCACTAAGGTTGAGATCAAA	305
2419-0805	VH	GAGGTCCAGTTGGTCCAGTCAGGAGCCGAAGTCAAGAAGCCTGGGGAAAGCCTGAAAATAAGTTGCAAAGCTAGTGGA TATACATTTACAGATTATACCATTCATTGGGTCCGGCAAATGCCAGGAAAAGGCTTGGAGTGGATGGGGTGGATTTAT CCCCTCCGAGGCTCAATAAATTATAGTCCTAGTTTTCAGGGGCAGGTAACTATTAGCGCTGATAAAAGTATTTCTACA GTTTATTTGCAGTGGAGTTCATTGAAGGCTAGTGACACCGCTATGTATTTCTGCGCTAGACATGGTGCATATTATTCA AATGCCTTCGACTATTGGGGCCAGGGCACCCTCGTCACTGTGAGTTCC	307
	VL	GAGATAGTAATGACTCAGTCTCCCGCTACACTTAGTGTAAGCCCAGGGGAGCGAGCAACCCTCAGTTGCAGAGCATCT GAGAGTGTTGATAATGATGGAATACGTTTTCTCCATTGGTATCAACAAAAACCAGGGCAGCCCCCCAGATTGCTGATC TACCGTGCTTCCAATCGCGAGACTGGCATTCCTGCACGTTTCAGCGGCAGCGGCTCCGGAACCGAGTTTACACTTACT ATTAGCTCACTCCAGTCTGAAGACTTCGCTGTGTATTACTGTCAGCAATCCAACACAAGGACCCATACACTTTCGGAGGC GGCACTAAGGTTGAGATCAAA	305
2419-0105	VH	CAAGTGCAGTTGGTCCAGAGTGGAGCAGAGGTGAAGAAGCCTGGTGCTTCCGTCAAGGTGAGTTGCAAGGCATCTGGT TATACTTTCACTGACTACACAATTCATTGGGTCAGGCAGGCCCCTGGACAGGGACTGGAATGGATGGGATGGATCTAT CCACTTAGAGGATCAATCAACTATGCTCAAAAGTTCCAGGGTCGTGTAACAATGACCGCAGACAAAAGTATCTCAACT GTATACATGGAATTGTCCCGATTGAGGAGCGACGACACAGCCGTATATTATTGTGCCAGGCACGGAGCCCTACTACAGT AATGCCTTCGACTACTGGGGCAGGGCACCCTTGTTACCGTGTCCAGC	310
	VL	GAGATAGTAATGACTCAGTCTCCCGCTACACTTAGTGTAAGCCCAGGGGAGCGAGCAACCCTCAGTTGCAGAGCATCT GAGAGTGTTGATAATGATGGAATACGTTTTCTCCATTGGTATCAACAAAAACCAGGGCAGGCCCCCCAGATTGCTGATC TACCGTGCTTCCAATCGCGAGACTGGCATTCCTGCACGTTTCAGCGGCAGCGGCTCCGGAACCGAGTTTACACTTACT ATTAGCTCACTCCAGTCTGAAGACTTCGCTGTGTATTACTGTCAGCAATCCAACACAAGGACCCATACACTTTCGGAGGC GGCACTAAGGTTGAGATCAAA	305
2419-1204	VH	CAAGTGCAGCTCGTTCAGTCTGGCGCAGAAGTGAAGAAGCCAGGAGCTTCCGTTAAAGTGTCCTGTAAAGCCTCTGGA TATACATTCACAGATTATACAATTCACTGGGTGAGACAAGCAACCGGTCAAGGTCTCGAATGGATGGGCTGGATATAC CCCCTCCGAGGTTCCATCAACTACGCTCAAAAATTCCAAGGACGAGTCACTATGACAGCAAACAAGAGTTCCTCCACT GTATATATGGAACTCTCTAGTTTGCGCTCTGAAGACACCGCCGTGTACTTCTGTGCCAGGCACGGCGCATACTATTCT AATGCATTTGACTATTGGGGCAGGGCACATTGGTAACAGTTAGTTCC	311
	VL	GAAATTGTAATGACCCAGAGCCCCGCCACCCTTAGTGTGTCCCCAGGCGAGAGGGCCACTCTTTCTTGCCGCGCAAGC GAATCCGTAGACAACGATGGTATAAGATTTTTGCATTGGTATCAGCAAAAGCCAGGCCAGGCACCCCGGCTTCTCATC	312

		TACAGAGCTAGCACCCTCGAAACTGGAATCCCCGCTCGTTTTTCAGGATCTGGTAGCGGAACAGAATTTACTTTGACA ATTAGTAGTTTGCAGTCAGAGGACTTTGCTGTCTATTATTGCCAGCAGTCTAATAAAGATCCATACACCTTCGGCGGA GGGACCAAAGTAGAGATTAAA	
2419-1210	VH	CAAGTGCAGCTCGTTCAGTCTGGCGCAGAAGTGAAGAAGCCAGGAGCTTCCGTTAAAGTGTCCTGTAAAGCCTCTGGA TATACATTCACAGATTATACAATTCACTGGGTGAGACAAGCAACCGGTCAAGGTCTCGAATGGATGGGCTGGATATAC CCCCTCCGAGGTTCCATCAACTACGCTCAAAAATTCCAAGGACGAGTCACTATGACAGCAAACAAGAGTTCCTCCACT GTATATATGGAACTCTCTAGTTTGCGCTCTGAAGACACCGCCGTGTACTTCTGTGCCAGGCACGGCGCATACTATTCT AATGCATTTGACTATTGGGGGCAGGGCACATTGGTAACAGTTAGTTCC
	VL	GACATTGTAATGACCCAGTCTCCCGATAGCCTCGCTGTCTCACTCGGAGAACGCGCAACCATCAACTGCAAGTCCTCC CAAAGCGTTGACAATGACGGCATTAGGTTTTTGCACTGGTACCAGCAGAAACCCGGTCAACCTCCTAAGTTGCTCATT TACCGAGCATCTACCCGCGAGTCAGGAGTACCTGATCGCTTTTCCGGTAGCGGTAGTGGAACAGATTTTACTCTGACC ATTAGTTCACTCCAGGCAGAAGATGTGGCTGTCTACTACTGCCAACAGTCAAATAAAGACCCTTATACCTTCGGTGGG GGTACCAAAGTAGAGATCAAA
2419-1406	VH	CAAGTTCAGTTGGTGCAAAGCGGGGCAGAAGTGAAGAAACCTGGTGCTTCTGTGAAAGTTTCCTGCAAGGCCAGCGGC TACACCTTTACTGATTACACAATACACTGGGTACGGCAGGCAACTGGGCAAGGATTGGAATGGATGGGGTGGATATAC CCATTGCGAGGGTCTATAAACTACGCACAGAAATTTCAAGGTCGAGTAACAATGACAGCCGACAAATCAATAAGCACC GTTTATATGGAACTCTCATCTCTCAGGAGTGAGGATACCGCCGTGTATTTCTGCGCACGACACGGTGCATATTACTCA AACGCTTTCGACTATTGGGGCCAGGGCACCCTTGTGACTGTTAGTAGC
	VL	GAGATAGTTATGACTCAGTCTCCCGCCACACTTTCAGTAAGTCCCGGTGAACGCGCCACCCTGTCCTGCCGTGCTTCC GAATCAGTGGATAATGACGGCATTAGGTTTTTGCACTGGTACCAACAAAAGCCCGGACAGGCCCCCGCCTGCTGATA TATCGTGCATCAACACGAGCAACAGGGATCCCCGCTCGATTTAGTGGATCCGGAAGCAGGACCGAATTTACACTTACC ATTTCCTCACTTCAGTCAGAAGATTTCGCCGTTTACTACTGTCAGCAGTCAAATAAGGATCCTTACACATTTGGGGGC GGTACAAAAGTCGAGATCAAA
2419-1205	VH	CAAGTGCAGCTCGTTCAGTCTGGCGCAGAAGTGAAGAAGCCAGGAGCTTCCGTTAAAGTGTCCTGTAAAGCCTCTGGA TATACATTCACAGATTATACAATTCACTGGGTGAGACAAGCAACCGGTCAAGGTCTCGAATGGATGGGCTGGATATAC CCCCTCCGAGGTTCCATCAACTACGCTCAAAAATTCCAAGGACGAGTCACTATGACAGCAAACAAGAGTTCCTCCACT GTATATATGGAACTCTCTAGTTTGCGCTCTGAAGACACCGCCGTGTACTTCTGTGCCAGGCACGGCGCATACTATTCT AATGCATTTGACTATTGGGGGCAGGGCACATTGGTAACAGTTAGTTCC
	VL	GAGATAGTAATGACTCAGTCTCCCGCTACACTTAGTGTAAGCCCAGGGGAGCGAGCAACCCTCAGTTGCAGAGCATCT GAGAGTGTTGATAATGATGGAATACGTTTTCTCCATTGGTATCAACAAAAACCAGGGCAGGCCCCCAGATTGCTGATC TACCGTGCTTCCAATCGCGAGACTGGCATTCCTGCACGTTTCAGCGGCAGCGGCTCCGGAACCGAGTTTACACTTACT ATTAGCTCACTCCAGTCTGAAGACTTCGCTGTGTATTACTGTCAGCAATCCAACACAAGGACCCATACACTTTCGGAGGC GGCACTAAGGTTGAGATCAAA
2419-0206	VH	CAGGTGCAACTTGTTCAGTCAGGGGCTGAAGTAAAGAAGCCAGGCTCATCAGTCAAGGTATCATGCAAAGCATCTGGC TATACATTTACAGATTACACCATTCACTGGGTGAGGCAAGCTCCCGGTCAAGGTCTCGAGTGGATGGGGTGGATATAC CCTCTCAGAGGCTCTATAAATTACGCTCAGAAATTTCAAGGGAGAGTTACAATTACTGCTGATAAAAGTACCAGCACT GCTTATATGGAGCTTTCCTCACTTCGTTCAGAGGACACCGCCGTTTACTTTTGTGCCCGGCATGGTGCCTATTATTCA AATGCCTTCGATTATTGGGGGCAGGGAACTTTGGTCACAGTTTCATCT
	VL	GAGATAGTTATGACTCAGTCTCCCGCCACACTTTCAGTAAGTCCCGGTGAACGCGCCACCCTGTCCTGCCGTGCTTCC GAATCAGTGGATAATGACGGCATTAGGTTTTTGCACTGGTACCAACAAAAGCCCGGACAGGCCCCCCGCCTGCTGATA	

		TATCGTGCATCAACACGAGCAACAGGGATCCCCGCTCGATTTAGTGGATCCGGAAGCAGGACCGAATTTACACTTACC ATTTCCTCACTTCAGTCAGAAGATTTCGCCGTTACTACTGTCAGCAGTCAAATAAGGATCCTTACACATTTGGGGGC GGTACAAAAGTCGAGATCAAA	
2621	VH	GAGGTCCAGCTTCAGCAGTCTGGAGCTGAGCTGGTGAGGCCTGGGTCCTCAGTGAAGATGTCCTGCAAGACTTCTGGA TATACTTTCACAAGCTACGGTATAAACTGGGTGAAGCAGAGGCCTGGACAGGGCCTGGAATTGGATTGGATATATTTAT ATTGGAAATGGTTATGCTGAGTACAATGAGAGGTTCAAGGGCAAGGCCACACTGACTTCAGACACATCCTCCAGCACA GCCTACATGCAGCTCAGCAGCCTGACATCTGAGGACTCTGCAATCTATTTCTGTGCACTATACTATCCCTGGTTTACT TACTGGGGCCAGGGGACTCTGGTCACTGTCTCTGCA	75
	VL	GACATCCAGATGACTCAGTCTCCAGCCTCCCTTTCTGCATCTGTGGGAGATTCTGTCACCATCACATGTCGAGCAAGT GAGAATATTTACAGTTATTTAGCATGGTATCAGCAGAAACAGGGAAAATCTCCTCAGCTCCTGGTCTATAATGCAAAA ACCTTAGCTGAAGGTGTGCCATCAAGGTTCAGTGGCAGTGGATCAGGCACACAGTTTTCTCTGAAGATCAACAGCCTG CAGCCTGAAGATTTTGGGAATTATTACTGTCAACATCATTATGATACTCCGTTCACGTTCGGAGGGGGGACCAAGCTG GAAATAAAA	76
2922	VH	CAGGTTCAGCTGCACCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGTTGTCCTGCAAGACTTCTGGC TACACCTTCACAAGCTACGATGTCTTCTGGGTGAAGCAGAGGCCTGGACAGGGACTTGAGTGGATTGGATGGATTTAT CCTAGAGATAGTAGTACTAAATACAATGAGAAGTTCAAGGGCAAGGCCACACTTGACTGTAGACACATCCTCCAGCACA GCATACATGGAGCTCCACAGCCTGACATCTGAGGACTCTGCGGTCTATTTCTGTGCAAAAGAGGGGTATGATTATGAC AAGAGGGGCTTTGACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCA	77
	VL	GACATTGTGCTGACCCAATCTCCAGCTTCTTTGGCTGTGTCTCTAGGGCAGAGGGCCATCATCTCCTGCAAGGCCAGC CAAAGTGTCAGTTTTGCTGGTACTAATTTAATGCACTGGTACCAACAGAGACCAGGGCAGCAACCCAAACTCCTCATC TATCGTGCATCCAACCTAGAACCTGGGGTTCCTACCAGGTTTAGTGGCAGTGGGTCTAGGACAGACTTCACCCTCAAT ATCCATCCTGTGGAGGAAGATGATGCTGCAACCTATTACTGTCAGCAAAGTAGGGAATATCCGTGGACGTTCGGTGGA GGCACCAAGCTGGAAATCAAA	78
3125	VH	CAGGTTCAACTGCAGCAGTCTGGGGCTGAGCTGGTGAGGCCTGGGGCTTCAGTGACGCTGTCCTGCAAGGCTTCGGGC TACACTTTTACTGACTATGAAATTGCACTGGGTGAAGCAGACACCTGTGCATGGCCTGGAATGGATTGGAGCTATTGAT CCTGAAACTGGTGGTACTGCCTACAATCAGAGGTTCAAGGGCAAGGCCATACTGACTACAGACAAATCCTCCATCACA GCCTACATGGAGCTCCGCAGCCTGACATCTGAGGACTCTGCCGTCTATTACTGTACAAGATGGAATGATGGCGACTAC TGGGGCCAAGGCACCACTCTCACAGTCTCCTCA	79
	VL	GATGTTGTGATGACCCAGACTCCACTGTCTTTGTCGGTTACCATTGGACAACCAGCCTCCATTTCTTGCAAGTCAAGT CAGAGCCTCTTATACAGTAATGGAAAGACATATTTGAATTGGTTTCAACAGAGGCCTGGCCAGTCTCCAAAGCGCCTA ATGTATCAGGTGTCCAAACTGGACCCTGGCATCCCTGACAGGTTCAGTGGCAGTGGATCAGAAACAGATTTTACACTT AAAATCAGCAGAGTGGAGGCTGAAGATTTGGGACTTTATTACTGCTTGCAAGGTACATATTATCCGTACACGTTCGGA GGGGGGACCAAGCTGGAAATAAAA	80
3327	VH	GAGGTCCAGCTGCAGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGATGTCCTGCAAGGCTTCTGGT TACTCCTTTACTGGCTACTTTATGAACTGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGTGGATTGGACGTATTAAT CCTTACAATGGTGATACTTTCTACAACCAGAAGTTCAAGGGCAAGGCCACACTTGACTGTAGACAAATCCTCTAGCACA GCCCACATGGAGCTCCGGAGCCTGACATCTGAGGACTCTGCACTCTATTATTGTGCAAGCGAAGGTGATGGTTACTAC TGGTACTTCGATGTCTGGGGCGCAGGGACCACGGTCACCGTCTCCTCA	81
	VL	GACATTGTGCTGACCCAATCTCCAGCTTCTTTGGCTGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCAGAGCCAGC GAAAGTGTTGATAATTATGGCATTAGTTTTATGAACTGGTTCCAACAGAAACCAGGACAGCCACCCAAACTCCTCATC	82

		TATGCTGCATCCAACCAAGGATCCGGGGTCCCTGCCAGGTTTAGTGGCAGTGGGTCTGGGACAGACTTCAGCCTCAAC ATCCATCCTATGGAGGAGGATGATACTGCAATGTATTTCTGTCAGCAAAGTAAGGAGGTTCCTCGGACGTTCGGTGGA GGCACCAAGCTGGAAATCAAA	
3525	VH	CAGGTTCAACTGCAGCAGTCTGGGGCTGAGGCCTGGGGCTTCAGTGAAGCTGTCCTGCAAGGCTTCGGGC TACACATTTACTGACCATGAAATTGCACTGGGTGAGACAGACACCTGTGCATGGCCTGGAATTGGATTGGAGTTATTGAT CCTGACACTGGTGATACTACCTACAATCAGAAATTCAAGGGCAAGGCCACACTGACTGCAGACAAATCCTCCAGCACA GCCTACATGGACCTCCGCAGCCTGACATCTGAGGACTCTGCCGTCTTTTACTGTACACGGTGGACTGGGGGGGACTAC TGGGGCCATGGCACCACTCTCACAGTCTCCTCA	83
	VL	GATGTTGTGATGACCCAGACTCCACTCTTTGTCGGTTACCATTGGACAACCAGCCTCCATTTCTTGCAAGTCAAGT CAGAGCCTCTTATACAGTAATGGAAAGACATATTTGAATTGGTTTCAACAGAGGCCTGGCCAGTCTCCAAAGCGCCTA ATGTATCAGGTGTCCAAACTGGACCCTGGCATCCCTGACAGGTTCAGTGGCAGTGGATCAGAAACAGATTTTACACTT AAAATCAGCAGAGTGGAGGCTGAAGATTTGGGACTTTATTACTGCTTGCAAGGTACATATTATCCGTACACGTTCGGA GGGGGGACCAAGCTGGAAATAAAA	80
3530	VH	CAGGTTCAACTGCAGCAGTCTGGGGCTGAGGCCTGGGGCTTCAGTGAAGCTGTCCTGCAAGGCTTCGGGC TACACATTTACTGACCATGAAATTGCACTGGGTGAGACAGACACCTGTGCATGGCCTGGAATTGGATTGGAGTTATTGAT CCTGACACTGGTGATACTACCTACAATCAGAAATTCAAGGGCAAGGCCACACTGACTGCAGACAAATCCTCCAGCACA GCCTACATGGACCTCCGCAGCCTGACATCTGAGGACTCTGCCGTCTTTTACTGTACACGGTGGACTGGGGGGGACTAC TGGGGCCATGGCACCACTCTCACAGTCTCCTCA	83
	VL	GATGCTGTGATGACCCAGACTCCACTCTTTGTCGGTTACCATTGGACAACCAGCCTCTATCTCTTGCAAGTCGAGT CAGAGCCTCTTATATAGTGATGGAAAGACATATTTGAATTGGTTCCAACAGAGGCCAGGCCAGTCTCCAAAGCGCCTA ATGTATCAGGTGTCCAAACTGGACCCTGGCATCCCTGACAGGTTCAGTGGCAGTGGATCAGAGACAGATTTTACACTT AAAATCAGCAGAGTGGAGGCTGAGGATTTGGGAGTTTATTACTGCTTGCAAGGTACATATTATCCGTATACGTTCGGA TCGGGGACCAAGCTGGAAATAAAA	84
4035	VH	CAGGTGCAGCTGAAGGAGTCAGGACCTGGCCTGGTGGCGCCCTCACAGAGCCTGTCCATCACCTGCACAGTCTCTGGT TTCTCATTAACCATCTATGATGTACACTGGGTTCGCCAGTCTCCAGGAAAGGGTCTGGAGTGGCTGGGAGTGATATGG AGTGATGGAAGCACAGACTATAATGCAGCTTTCATATCTAGACTGAGCATCAGCAAGGACAACTCCAAGAGCCAAGTT TTCTTTAAAATGAACAGTCTGCAAGCTGATGACACAGCCATATACTACTGTGCCAGAAATTGGGTCGACCAGGCCTGG TTTGCTTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCA	173
	VL	GACATCCAGATGACTCAGTCTCCAGCCTCCCTATCTGCATCTGTGGGAGAAACTATCACCATCACATGTCGAGCAAGT AAGAATATTTACAGTTATTTAGCATGGTATCAGCAGAAACAGGGAAAATCTCCTCAGCTCCTGGTCTATAATGCAAAA ACCTTACCAGAAGGTGTGCCATCAAGGTTCAGTGGCAGTGGATCAGGCACACAGTTTTCTCTGAAGATCAACAGCCTG CAGCCTGAAGATTTTGGGAGTTATTACTGTCAACATCATTATGGTACTCCGCTCACGTTCGGTGCTGGGACCAAGCTG GAGCTGAAA	174
4035-062	VH	CAGGTACAACTCCAGGAATCCGGGCCTGGGCTCGTCAAACCAAGCGAAACACTCTCTCACCTGCACCGTTTCTGGG TTTTCTCTTACTATCTATGACGTACATTGGGTAAGGCAACCACCCGGGAAGGGGCTGGAGTGGATCGGTGTAATCTGG TCAGATGGATCTACAGACTACAACCCATCCCTTAAAAGCAGGGTGACCATTTCTAAGGACACTTCCAAGAACCAAGTA TCCCTTAAATTGTCCTCTGTAACCGCAGCAGACACCGCAGTTTACTACTGCGCACGAAATTGGGTTGACCAAGCATGG TTTGCATATTGGGGACAGGGAACTCTTGTCACTGTGTCTTCA	299
	VL	GATATTCAAATGACCCAATCCCCCTCATCACTTTCAGCATCTGTCGGTGATCGGGTCACCATTACTTGCAGAGCCAGT AAGAATATCTACAGCTACCTGGCTTGGTATCAGCAAAAACCTGGTAAGGCCCCTAAACTTCTCGTTTACAATGCTAAG	300

		ACCCTTCCCGAGGGAGTTCCTTCCAGGTTTCCGGTAGCGGGAGTGGAACAGATTTCACCTTGACTATTTCTAGCTTG CAGCCCGAGGATTTCGCTACATACTACTGCCAGCATCACTATGGAACCCCCCCTGACCTTCGGTCAGGGAACCAAGCTC GAGATCAAA	
3934	VH	CAGGTCCAACTGCAGCAGTCTGGACCTGAGCTGGTGAAGCCTGGAGCTTCAGTGAAGCTGTCCTGCAAGGCTGCTGGC TACATCTTCACTGACTATACTATAAACTGGGTGAAGCAGAGTCCTGGACAGGGACTTGAGTGGATTGGATTTTAT CCTGGAAGTGGTAATCGTAAATACAATGACAAGTTCAAGGGCAAGGCCACACAATGACTGCAGACAAATCCTCCAGCACA GCCTACATGCAGCTCAGCAGCCTGACCTCTGAGGATTCTGCGGTCTATTTCTGTGCAAGAGAGTAACTACGTGGGG TACTATGCTATGGACTATTGGGGTCAAGGAACCTCAGTCACCGTCTCCTCA	175
	VL	GATGTTTTGATGACCCAAACTCCACTCTCCCTGCCTGTCAGTCTTGGAGATCAAGCCTCCATCTCTTGCAGATCTAGT CAGAGCGTTGTAAATAGTAATGGAAACACCTATTTAGAATGGTACCTGCAGAAACCAGGCCAGTCTCCAAATCTCCTG ATCTACAAAGTTTCCAATCGATTTTCTGGGGTCCCAGACAGGTTCAGTGGCAGTGGATCGGGGACAGATTTCACACTC AAGATCAGCAGAGTGGAGGCTGAGGATCTGGGAGTTTATTACTGTTTTCAAGGTTCACATGTTCCGTGGACGTTCGGT GGAGGCACCAAGCTGGAAATCAAA	176
3833	VH	CAGGTCCAGCTGCAGCAGTCTGGAGCTGAGCTGGTAAGGCCTGGGACTTCAGTGAAGATGTCCTGCAAGGCTGCTGGA TACACCTTCACAAACTACTGGATAGGTTGGGTAAAGCAGAGGCCTGGACATGGCCTTGAGTGGATTGGAGATATTTAC CCTGGAGGTATAGGAGGTGGTTATACTAAGTACAATGAGAAGTTCAAGGGCCAAGGCCACACTGACTGCAGACACATCC TCCAGCACAGCCTACATGCAGCTCGGCAGCCTGACATCTGAGGACTCTGCCATCTATTTCTGTTCAAGATCGGAAACT GGACGGGCTATGGACTACTGGGGTCAAGGAACCTCAGTCACCGTCTCCTCA	177
	VL	GACATCCAGATGACACAGTCTCCATCCTCACTGTCTGCATCTCTGGGAGGCAAAGTCACCATCACTTGCAAGGCAAGC CAAGACATTAATAAGTATATAGCTTGGTACCAACACAAGCCTGGAAAAGGTCCTAGGCTGCTCATACATTACACATCT ACATTAAAGCCAGGCATCCCATCAAGGTTCAGTGGAAGTGGGTCTGGGAGAGATTATTCCTTCAGCATCAGTGACCTG GAGCCTGAAGATATTGCAACTTATTATTGTCTACAGTATGATAATCTGAACACGTTCGGAGGGGGGACCAAGCTGGAA ATAAAA	178
3631	VH	GAGATCCAGCTGCAGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGGTGTCCTGCAAGGCTTCTGGT TATTCATTCACTGACTACAACATCTACTGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGTGGATTGGATATATTGAT CCTTCCAATGGTGGTCCTGGCTACAACCAGAAGTTCAGGGGCAAGGCCACATTGACTGTTGACAAGTCCTCCAGCACA GCCTTCCTGCATCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTACTGTGCAAGAAGGGACAACTACGGCTCG GGGACTATGGACTACTGGGGTCAAGGAACCTCAGTCACCGTCTCCTCA	179
	VL	GACATTGTGATGACCCAGTCTCAAAAATTCATGTCCACATCAGTAGGAGACAGGGTCAGCATCACCTGTAAGGCCAGT CAGAATGTGGGTACTGATGTATCCTGGTATCAACAGAAACCAGGGAAATCTCCTAAACCACTGATTTACTGGGCATCA AACCGGTTCACTGGAGTCCCTGATCGCTTCATAGGTAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAATGTG CAGTCTGAAGACTTGGCAGATTATTTCTGTGAGCAATATAGCATCTATCCGCTCACGTTCGGTGCTGGGACCAAGCTG GAGCTGAAA	180
3732	VH	GAGATCCAGCTGCAGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCGTCAGTGAAGGTATCCTGCAAGGCTTCTGGT TACTCATTCACTGACGACAACATGTACTGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGTGGATTGGATATATTGAT CCTCTCAATGGTGGTACTGGCTACAACCAGAAATTCAAGGGCAAGGCCACACTGACTGTTGACAAGTCCTCCAGCACA GCCTTCCTGCATCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTACTGTGCAAGAAGGGACAACTACGGCCAC GGGACTATGGACTACTGGGGTCAAGGAACCTCAGTCACCGTCTCCTCA	181
	VL	GACATTGTGATGACCCAGTCTCAAAAATTCATGTCCACATCAGTAGGAGACAGGGTCAGCATCACCTGCAAGGCCAGT AAGAATGTGGGTACTGATGTATCCTGGTATCAACAGAAACCAGGGAAATCTCCTAAACCACTGATTTACTGGGCATCA	182

		AACCGGTTCACTGGAGTCCCTGATCGCTTCACAGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAACAATGTG CAGTCTGAAGACTTGGCAGATTATTTCTGTGAGCAATATAGCAGCTATCCGCTCACGTTCGGTGCTGGGACCAAGCTG GAGCTGAAA	
4338	VH	GAGGTCCAGCTGCAGCAGTCTGGCCCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGGCTTCTGGA TACACATTCACTGACTACAACATGGACTGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGTGGATTGGAAATATTTAT CCTATCAATGGTTATACTGGCTACAACCAGAGGTTCAAGAACAAGGCCACATTGACTGTAGACAAGTCCTCCAGCACA GCCTACATGGAACTCCACAGCCTGACATCTGAGGACTCTGCGGTCTATTACTGCGCAAGAGATAGTAACTACGTTGGC TGGTACTTCGATGTCTGGGGCGCAGGGACCACGGTCACCGTCTCCTCA	183
	VL	GATGTTGTGATGACCCAAACTCCACTCTCCCTGCCTGTCAGTCTTGGAGATCAAGCCTCCATCTCTTGCAGATCTAGT CAGAGCCTTGTACACAGTAATGGAAACACCTATTTACATTGGTACCTGCAGAAGCCAGGCCAGTCTCCAAAGCTCCTG ATCTACAAAGTTTCCAACCGATTTTCTGGGGTCCCAGACAGGTTCAGTGGCAGTGGATCAGGGACAGATTTCACATTC AAGATCAGCAGAGTGGAGGCTGAGGATCTGGGAGTTTATTTCTGCTCTCAAAGTACACATGTTCCTCGGACGTTCGGT GGAGGCACCAAGCTGGAAATCAAA	184
	VL	GACATTGTGCTGACACAGTCTCCTGCTTCCTTAACTGTATCTCTGGGGCAGAGGGCCACCTTCTCATGCAGGGCCAGC AAAAGTGTCAGTACATCTGGCTATAGTTATATGCACTGGTACCAACAGAAACCAGGACAGCCACCCAAACTCCTCATC TATTTACATCCGACCTAGAACCTGGGGTCCCTGCCAGGTTCACTGGCAGTGGGTCTGGGACAGACTTCACCCTCAAC ATCCATCCTGTGGAGGAGGAGGATGCTGCAACCTATTACTGTCAGCACAGTAGGGAGCTTCCGTACCCCTTCGGAGGG GGGACCAAGTTGGAAATAAAA	185
4540	VH	caggtccagctacagcagtctggacctgagctggtgaagcctggggcttcagtgaagatatcctgcaaggcttctggc tacaccttcgctgactatataaactgggtgaagcagaggcctggacagggacttgagtggattggatgatttt cctggaagtggtagtacttactacaatgagaagttcaagggcaaggccacacttactgtagacaaatcctccagcaca gcctacatgttgctcagcagcctgacctctgaggactctgcggtctatttctgtgcaagaggggactccggtagggct atggactactggggtcaaggaacctcagtcaccgtctcctca	186
	VL	gacatccagatgacacagtctccatcctcactgtctgcatctctgggaggcaaagtcaccatcacttgcaagggcaagc caagacattaacaaatatatagcttggtaccaacaacaagcctggaaaaggtcctaggctgctcatacattacacatct acattacagtcaggcatcccatcaaggttcagtggaagtgggtctgggagagattatcctttcagcatcagcaacctg gagcctgaagataatgcaacttatattattgtctacagtatgataatcttctccacgttcggtgctgggaccaagctggag ctgaaa	187
4540-063	VH	CAAGTCCAGCTCGTACAGAGCGGGGCAGAGCTGAAGAAGCCTGGGGCCTCCGTCAAGGTCTCCTGTAAGGCTTCTGGT TACACATTTGCCGACTACTACATGAACTGGGTACGGCAAGCCCCAGGTCAAGGGCTGGAATGGGATGGATTTTT CCAGGGAGCGGCAGCACTTACTACAACCAGAAATTTCAAGGTCGTGTGACAATGACCGTGGATAAAAGCAGCTCTACA GCTTACATGGAGCTTTCCCGCTTGAGGTCCGATATACTGCCGTATATTATTGTGCCCGTGGTGACTCAGGTAGGGCC ATGGACTATTGGGGACAGGGCACCCTCGTGACCGTGTCCAGC	301
	VL	GATATCCAGATGACACAATCCCCTTCATCCTTGAGCGCATCAGTTGGCGACAGGGTCACCATAACTTGTCAGGCTAGT CAGGATATTAACAAGTACCTGGCTTGGTATCAACACAAGCCTGGAAAGGCCCCCAAATTGCTGATTCACTACACCTCT ACATTGGAAACTGGCGTACCCAGTCGCTTTCTGGGAGTGGAAGCGGAACTGATTTCACTTTCACTATATCCAGTCTT CAGCCAGAAGATATCGCAACTACTATTGTCTTCAGTATGATAACTTGCTTACTTTCGGAGGAGGGACCAAAGTTGAA ATCAAG	302
4540-033	VH	CAGGTGCAGTTGGTCCAATCCGGGGCTGAGGTGAAGAAGCCTGGGGCCTCTGTTAAAGTTAGTTGCAAGGCATCAGGC TACACCTTCGCTGACTACTACATCAACTGGGTTAGACAGGCCCCCGGGCAGGGGTTGGAGTGGATGGGTTGGATTTTT	303

		CCAGGATCAGGTTCAACATATTACGCACAAAAACTGCAAGGTAGAGTAACCATGACAACTGATACTAGCACCTCCACA GCCTATATGGAACTCCGCTCTCTCAGGAGTGACGATACAGCCGTTATTACTGCGCCCGTGGGGATTCAGGCCGTGCA ATGGATTACTGGGGTCAAGGGACCCTCGTGACCGTAAGTTCA	
4237	VL	GATATCCAGATGACACAATCCCCTTCATCCTTGAGCGCATCAGTTGGCGACAGGGTCACCATAACTTGTCAGGCTAGT CAGGATATTAACAAGTACCTGGCTTGGTATCAACACAAGCCTGGAAAGGCCCCCAAATTGCTGATTCACTACACCTCT ACATTGGAAACTGGCGTACCCAGTCGCTTTTCTGGGAGTGGAAGCGGAACTGATTTCACTTTCACTATATCCAGTCTT CAGCCAGAAGATATCGCAACTTACTATTGTCTTCAGTATGATAACTTGCTTACTTTCGGAGGAGGGACCAAAGTTGAA ATCAAG	302
	VH	CAGGCGCACCTGAAGGAGTCAGGACCTGGCCTGGTGGCGCCCTCACAGAGCCTGTCCATCACCTGCACAGTCTCTGGT TTCTCATTAACCGACTATGATGTACACTGGGTTCGCCAGTCTCCAGGAAAGGGTCTGGAGTGGCTGGGAGTGATATGG AATGATGGAAGCACAGACTATAATACAGCTTTCATATCTAGACTGACCATCAGCAAGGACAACTCCAAGAGCCAAGTT TTCTTTAAAATGAACAGTCTGCAAGCTGATGACACAGCCATATACTACTGTGCCAGAAATTGGTATGGTGGCTACTGG TTTGCTTACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCA	188
	VL	GACATCCAGATGACTCAGTCTCCAGCCTCCCTATCTGCATCTGCGGGAGAAACTGTCACCATCACATGTCGATCAAGT GAGAATATTTACAGTTATTTAGCATGGTATCAGCAGAAACAGGGAAAATCTCCTCAGCTCCTAGTCTATAATGCAAAT GCCTTAGCAGAAGGTGTGCCATCGAGGTTCAGTGGCAGTGGATCAGTCACACAGTTTTCTCTGAAGATCAACAGCCTG CAGCCTGAAGATTTTGGGAGTTATTACTGTCAACATCATTATGGTACTCCATTCACGTTCGGCTCGGGGACAAAGTTG GAAATAAAA	189
4439	VH	GAGATCCAGCTGCAGCAGTCTGGAGCTGAACTGGTGAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGGCTTCTGAT TACTCATTCACTGGCTACAACATGAACTGGGTGATGCAGAGCCATGGAAAGAGCCTTGAGTGGATTGGAAATATTCAT CCTTACTATGGTGGTACTAGCTTCAATCAGAAGTTCATGGGCAAGGCCACACTTGACTGCAGACAAATCTTCCAGCACA GCCTACATGCAGCTCAACAGCCTGACATCTGAAGACTCTGCAGTCTATTACTGTGCAAGAGAGAAGTAACTTCCAT GCTCTGGACTACTGGGGTCAGGGAACCTCAGTCACCGTCTCCTCA	297
	VL	GACATTGTGCTGACACAGTCTCCTGCTTCCTTAACTGTATCTCTGGGGCAGAGGGCCACCTTCTCATGCAGGGCCAGC AAAAGTGTCAGTACATCTGGCTATAGTTATATGCACTGGTACCAACAGAAACCAGGACAGCCACCCAAACTCCTCATC TATTTTACATCCGACCTAGAACCTGGGGTCCCTGCCAGGTTCACTGGCAGTGGGTCTGGGACAGACTTCACCCTCAAC ATCCATCCTGTGGAGGAGGATGCTGCAACCTATTACTGTCAGCACAGTAGGGAGCTTCCGTACCCCTTCGGAGGG GGGACCAAGTTGGAAATAAAA	298

Table 5. The Amino Acid Sequences of the Heavy Chain Variable Region (VH) and Light Chain Variable Region (VL) of the Exemplary Humanized Anti-APRIL Antibodies Are Provided As Follows.

Antibody Chain	Amino Acid Sequence	SEQ ID NO
>Hu_2218_VH01	QVQLQESGPGLVKPSQTLSLTCTVSGYSITSGYYWNWIRQHPGKGLEWIGYISYDGYNNYNPSLKNRVTISVDTSKNQF SLKLSSVTAADTAVYYCARYYDYEDWYFGVWGQGTMVTVSS	190
>Hu_2218_VH02	QVQLQESGPGLVKPSQTLSLTCTVSGYSITSGYYWSWIRQHPGKGLEWIGYISYDGYTYYNPSLKSRVTISVDTSKNQF SLKLSSVTAADTAVYYCARYYDYEDWYFGVWGQGTMVTVSS	191
>Hu_2218_VH03	QVQLQESGPGLVKPSQTLSLTCTVSGYSITSGYYWNWIRQHPGKGLEWIGYISYDGYNNYNPSLKSRVTISRDTSKNQF SLKLSSVTAADTAVYYCARYYDYEDWYFGVWGQGTMVTVSS	192
>Hu_2218_VH04	QVQLQQWGAGLLKPSETLSLTCAVYGYSITSGYYWNWIRQPPGKGLEWIGYISYDGYNNYNPSLKNRVTISVDTSKNQF SLKLSSVTAADTAVYYCANYYDYEDWYFGVWGQGTTVTVSS	193
>Hu_2218_VH05	QVQLQQWGAGLVKPSETLSLTCAVYGYSITSGYYWNWIRQPPGKGLEWIGYISYDGYNNYNPSLKNRVTISRDTSKNQF SLKLSSVTAADTAVYYCANYYDYEDWYFGVWGQGTTVTVSS	194
>Hu_2218_VH06	QVQLQESGPGLVKPSETLSLTCTVSGYSITSGYYWNWIRQPPGKGLEWIGYISYDGYNNYNPSLKNRVTISVDTSKNQF SLKLSSVTAADTAVYYCANYYDYEDWYFGVWGQGTTVTVSS	195
>Hu_2218_VH07	QVQLQESGPGLVKPSETLSLTCTVSGYSITSGYYWNWIRQPPGKGLEWIGYISYDGYNNYNPSLKNRVTISRDTSKNQF SLKLSSVTAADTAVYYCANYYDYEDWYFGVWGQGTTVTVSS	196
>Hu_2218_VH08	QVQLQESGPGLMKPSETLSLTCSVSGYSITSGYYWSWIRKPPGKGLEYIGYVSYDGSTYYNPSLKSRVTISVDTSKNRF SLKLNSVTAADTAVYYCANYYDYEDWYFGYWGQGILVTVSS	197
>Hu_2218_VH09	QVQLQESGPGLMKPSETLSLTCSVSGYSITSGYYWNWIRKPPGKGLEWIGYISYDGYNNYNPSLKSRVTISRDTSKNRF SLKLNSVTAADTAVYYCANYYDYEDWYFGVWGQGILVTVSS	198
>Hu_2218_VH10	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSGYYWNWIRQAPGKGLEWVASISYDGYNNYNPSVKGRITISRDDSKNTF YLQMNSLRAEDTAVYYCANYYDYEDWYFGVWGQGTLVTVSS	199
>Hu_2218_VH11	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSGYYWNWIRQAPGKGLEWVAYISYDGYNNYNPSVKGRITISRDTSKNTF YLQMNSLRAEDTAVYYCANYYDYEDWYFGVWGQGTLVTVSS	200
>Hu_2218_VH12	QVQLVESGGGVVQPGRSLRLSCAASGYSITSGYYWNWVRQAPGKGLEWVAYISYDGYNNYNPSVKGRFTISRDNSKNTL YLQMNSLRAEDTAVYYCANYYDYEDWYFGVWGQGTMVTVSS	201
>Hu_2218_VL01	EIVLTQSPATLSLSPGERATLSCRASESVSIIGTNSIHWYQQKPGQAPRLLIYHASNLETGIPARFSGSGPGTDFTLTI SSLEPEDFAVYYCLQSRKIPYTFGQGTKLEIK	202
>Hu_2218_VL02	DIVLTQSPASLAVSPGQRATITCRASESVSIIGTNSIHWYQQKPGQPPKLLIYHASNLETGVPARFSGSGSGTDFTLTI NPVEANDTANYYCLQSRKIPYTFGGGTKLEIK	203
>Hu_2218_VL03	EIVMTQSPATLSVSPGERATLSCRASESVSIIGTNSLHWYQQKPGQAPRLLIYHASQSISGIPARFSGSGSGTEFTLTI SSLQSEDFAVYYCQQSRKIPYTFGGGTKVEIK	204
>Hu_2218_VL04	EIVMTQSPATLSVSPGERATLSCRASESVSIIGTNSIHWYQQKPGQAPRLLIYHASNLETGIPARFSGSGSRTEFTLTI SSLQSEDFAVYYCLQSRKIPYTFGGGTKVEIK	205
>Hu_2218_VL05	DIQLTQSPSSLSASVGDRVTITCRASESVSIIGTNSMNWYQQKPGKAPKLLIYHASYLESGVPSRFSGSGSGTDFTLTI SSLQPEDFATYYCLQSRKIPYTFGQGTKVEIK	206

>Hu_2218_VL06	DIQLTQSPSSLSASVGDRVTITCRASESVSIIGTNSMHWYQQKPGKAPKLLIYHASNLESGVPSRFSGSGSRTDFTLTI SSLQPEDFATYYCLQSRKIPYTFGQGTKVEIK	207
>Hu_2218_VL07	DIQMTQSPSSLSASVGDRVTITCRASESVSIIGTNSMHWYQQKPGKAPKLLIYHASNLESGVPSRFSGSGSGTDFTFTI SSLQPEDIATYYCLQSRKIPYTFGQGTKVEIK	208
>Hu_2419_VH01	QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYTIHWVRQAPGQGLEWMGWIYPLRGSINYNEKFKDRVTSTRDTSISTA YMELSRLRSDDTVVYYCARHGAYYSNAFDYWGQGTLVTVSS	209
>Hu_2419_VH02	QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYYMHWVRQAPGQGLEWMGRIYPLRGSTNYAQKFQGRVTSTRDTSISTA YMELSRLRSDDTVVYYCARHGAYYSNAFDYWGQGTLVTVSS	210
>Hu_2419_VH03	QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYTIHWVRQAPGQGLEWMGWIYPLRGSINYNEKFKDRVTMTADTSSSTA YMELSRLRSDDTVVYYCARHGAYYSNAFDYWGQGTLVTVSS	211
>Hu_2419_VH04	QVQLVQSGAEVKKPGASVKVSCEASGYTFTDYTIHWVRQAPGKGLEWMGWIYPLRGSINYNEKFKDRVTMTADTSTDTA YMELSSLRSKDTAVYYCARHGAYYSNAFDYWGQGTLVTVSS	212
>Hu_2419_VH05	QVQLVQSGAEVVKPGASVKLSCKASGYTFTDYTMYWVKQAPGQGLEWIGEIYPLRGSINFNEKFKSKATLTVDKSASTA YMELSSLRSEDTAVYYCARHGAYYSNAFDYWGQGTLVTVSS	213
>Hu_2419_VH06	QVQLVQSGAEVVKPGASVKLSCKASGYTFTDYTMHWVKQAPGQGLEWIGEIYPLRGSINFNEKFKSKATLTVDKSASTA YMELSSLRSEDTAVYYCARHGAYYSNAFDYWGQGTLVTVSS	214
>Hu_2419_VL01	EIVLTQSPATLSLSPGERATLSCRASESVDNDGIRFMHWYQQKPGQAPRLLIYRASNLESGIPARFSGSGPGTDFTLTI SSLEPEDFAVYYCQQSNKDPYTFGQGTKLEIK	215
>Hu_2419_VL02	EIVLTQSPATLSLSPGERATLSCRASESVDNDGIRFMHWYQQKPGQAPRLLIYRASNLESGIPARFSGSGPGTDFTLTI SSLEPEDVAVYYCQQSNKDPYTFGQGTKLEIK	216
>Hu_2419_VL03	DIVMTQSPASLAVSLGERATINCRASESVDNDGIRFMHWYQQKPGQPPKLLIYRASNLESGVPDRFSGSGSRTDFTLTI SSLQAEDVAVYYCQQSNKDPYTFGGGTKVEIK	217
>Hu_2419_VL04	DIVMTQSPASLAVSLGERATINCRASESVDNDGIRFMHWYQQKPGQPPKLLIYRASNLESGVPDRFSGSGSRTDFTLTI NSLQAEDVAVYYCQQSNKDPYTFGGGTKVELK	218
>Hu_2419_VL05	DIVLTQSPATLSVSPGERATISCRASESVDNDGIRFMHWYQQKPGQPPKLLIYRASNLESGVPARFSGSGSRTDFTLTI SSVEPEDFATYYCQHSWEIPPTFGGGTKLEIK	219
>hu_4035_VH01	QVQLVESGGGVVQPGRSLRLSCAASGFSLTIYDVHWVRQAPGKGLEWVAVIWSDGSTDYNAAFISRFTISRDNSKNTLY LQMNSLRAEDTAVYYCARNWVDQAWFAYWGQGTLVTVSS	220
>hu_4035_VH02	QVQLVESGGGVVQPGRSLRLSCAASGFSLTIYDVHWVRQAPGKGLEWVGVIWSDGSTDYNAAFISRFTISKDNSKNTLY LQMNSLRAEDTAVYYCARNWVDQAWFAYWGQGTLVTVSS	221
>hu_4035_VH03	QVQLVESGGGVVQPGRSLRLSCAASGFSLTIYDVHWVRQAPGKGLEWVAVIWSDGSTDYADSVKGRFTISKDNSKNTLY LQMNSLRAEDTAVYYCARNWVDQAWFAYWGQGTLVTVSS	222
>hu_4035_VH04	QVQLVESGGGVVQPGRSLRLSCAVSGFSLTIYDVHWVRQAPGKGLEWVGVIWSDGSTDYADSVKGRFTISKDNSKNTVY LQMNSLRAEDTAVYYCARNWVDQAWFAYWGQGTLVTVSS	223
>hu_4035_VH05	QVQLQESGPGLVKPSETLSLTCTVSGFSLTIYDVHWIRQPPGKGLEWIGVIWSDGSTDYNAAFISRVTISVDTSKNQFS LKLSSVTAADTAVYYCARNWVDQAWFAYWGQGTLVTVSS	224
>hu_4035_VH06	QVQLQESGPGLVKPSETLSLTCTVSGFSLTIYDVHWVRQPPGKGLEWIGVIWSDGSTDYNPSLKSRVTISKDTSKNQVS LKLSSVTAADTAVYYCARNWVDQAWFAYWGQGTLVTVSS	225
>hu_4035_VH07	QVQLQESGPGLMKPSETLSLTCSVSGDSITIYDWHWIRQPPGKGLEWIGVVWSDGSTDYNPSLKSRVTISVDTSKNRFS LKLSSVTAADTAVYYCARNWVDQAWFAYWGQGTLVTVSS	226

>hu_4035_VH07	QVQLQESGPGLVKPSETLSLTCTVSGFSLTIYDVHWIRQPPGKGLEWIGVIWSDGSTDYNPSLKSRVTISKDNSKNQFS LKLSSVTAADTAVYYCARNWVDQAWFAYWGQGTLVTVSS	227
>hu_4035_VH09	QVQLQESGPGLVKPSETLSLTCTVSGFSLTIYDVHWIRQPPGKGLEWIGVIWSDGSTDYNPSLKSRVTISKDTSKNQVS LKLSSVTAADTAVYYCARNWVDQAWFAYWGQGTLVTVSS	262
>hu_4035_VH10	QVQLQESGPGLVKPSETLSLTCTVSGGSITTIYDWHWVRQPPGKGLEWIGVIWSDGSTDYNPSLKSRVTISKDTSKNQFS LKLSSVTAADTAVYYCARNWVDQAWFAYWGQGTLVTVSS	263
>hu_4035_VH11	QVQLQESGPGLVKPSETLSLTCTVSGGSITTIYDWHWVRQPPGKGLEWIGVIWSDGSTDYNPSLKSRVTISVDTSKNQFS LKLSSVTAADTAVYYCARNWVDQAWFAYWGQGTLVTVSS	264
>hu_4035_VH12	QVQLQESGPGLVKPSETLSLTCTVSGGSITTIYDWHWIRQPPGKGLEWIGVIWSDGSTDYNPSLKSRVTISVDTSKNQFS LKLSSVTAADTAVYYCARNWVDQAWFAYWGQGTLVTVSS	265
>hu_4035_VL01	DIQMTQSPSSLSASVGDRVTITCRASKNIYSYLAWYQQKPGKAPKLLIYNAKTLPEGVPSRFSGSGSGTDFTLTISSLQ PEDFATYYCQHHYGTPLTFGQGTKLEIK	228
>hu_4035_VL02	DIQMTQSPSSLSASVGDRVTITCRASKNIYSYLAWYQQKPGKAPKLLVYNAKTLPEGVPSRFSGSGSGTDFTLTISSLQ PEDFATYYCQHHYGTPLTFGQGTKLEIK	229
>hu_4035_VL03	EIVLTQSPATLSLSPGERATLSCRASKNIYSYLAWYQQKPGQAPRLLIYNAKTRATGIPARFSGSGSGTDFTLTISSLE PEDFAVYYCQHHYGTPLTFGQGTKLEIK	230
>hu_4035_VL04	EIVLTQSPATLSLSPGERATLSCRASKNIYSYLAWYQQKPGQAPRLLVYNAKTLPEGIPARFSGSGSGTDFTLTISSLE PEDFAVYYCQHHYGTPLTFGQGTKLEIK	231
>hu_4035_VL05	EIVMTQSPATLSVSPGERATLSCRASKNIYSYLAWYQQKPGQAPRLLIYNAKTRATGIPARFSGSGSGTEFTLTISSLQ SEDFAVYYCQHHYGTPLTFGGGTKVEIK	232
>hu_4035_VL06	DIQLTQSPSFLSASVGDRVTITCRASKNIYSYLAWYQQKPGKAPKLLIYNAKSLQSGVPSRFSGSGSGTEFTLTISSLQ PEDFATYYCQHHYGTPLTFGGGTKLEIK	233
>hu_4035_VL07	DIQLTQSPSFLSASVGDRVTITCRASKNIYSYLAWYQQKPGKAPKLLIYNAKSLQSGVPSRFSGSGSGTEFTLTISSLQ PEDFATYYCQHHYGTPLTFGGGTKLEIK	234
>hu_4237_VH01	QLQLQESGSGLVKPSQTLSLTCAVSGFSLTDYDVHWVRQPPGKGLEWIGVIWNDGSTDYNPSLISRVTISKDNSKNQVS LKLSSVTAADTAVYYCARNWYGGYWFAYWGQGTLVTVSS	235
>hu_4237_VH02	QLQLQESGSGLVKPSQTLSLTCAVSGGSITDYDWHWVRQPPGKGLEWIGVIWNDGSTDYNPSLISRVTISVDNSKNQFS LKLSSVTAADTAVYYCARNWYGGYWFAYWGQGTLVTVSS	236
>hu_4237_VH03	QVQLVESGGGVVQPGRSLRLSCAASGFSFTDYDMHWVRQAPGKGLEWVAVIWNDGSTDYATSVIGRFTISRDNSKNTLY LQMNSLRAEDTAVYYCARNWYGGYWFAYWGQGTLVTVSS	237
>hu_4237_VH04	QVQLVESGGGVVQPGRSLRLSCAASGFSFTDYDMHWVRQAPGKGLEWVGVIWNDGSTDYATSVIGRFTISRDNSKNTLY LQMNSLRAEDTAVYYCARNWYGGYWFAYWGQGTLVTVSS	238
>hu_4237_VH05	QVQLQESGPGLMKPSETLSLTCSVSGGSITDYDWHWIRQPPGKGLEWIGVVWNDGSTDYNPSLKSRVTISVDTSKNRFS LKLNSVTAADTAVYYCARNWYGGYWFAYWGQGILVTVSS	239
>hu_4237_VH06	QVTLKESGPALVKPTQTLTLTCTFSGFSLTDYDVHWIRQPPGKALEWLAVIWNDGSTDYSPSLKSRLTITKDTSKNQVV LTMTNMDPVDTATYYCARNWYGGYWFAYWGQGTLVTVSS	240
>hu_4237_VL01	DIQMTQSPSSLSASVGDRVTITCRSSENIYSYLAWYQQKPGKAPKLLVYNANALAEGVPSRFSGSGSVTDFTLTISSLQ PEDFATYYCQHHYGTPFTFGQGTKLEIK	241
>hu_4237_VL02	DIQMTQSPSTLSASVGDRVTITCRSSENIYSYLAWYQQKPGKAPKLLVYNANALAEGVPSRFSGSGSVTEFTLTISSLQ PDDFATYYCQHHYGTPFTFGQGTKLEIK	242

>hu_4237_VL03	EIVMTQSPATLSVSPGERATLSCRASENIYSYLAWYQQKPGQAPRLLIYNANASAEGIPARFSGSGSGTEFTLTISSLQ SEDFAVYYCQQHYGTPFTFGGGTKVEIK	243
>hu_4237_VL04	DIQMTQSPSSLSASVGDRVTITCRASENIYSYLAWYQQKPGKAPKLLLYNANRLESGVPSRFSGSGSGTDFTLTISSLQ PEDFASYYCQHHYGTPFTFGSGTKLEIK	244
>hu_4237_VL05	DIQMTQSPSSLSASVGDRVTITCRASENIYSYLAWYQQKPGKAPKLLLYNANRLESGVPSRFSGSGSGTDYTLTISSLQ PEDFASYYCQHHYGTPFTFGSGTKLEIK	245
>hu_3833_VH01	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYWIGWVRQAPGQGLEWMGDIYPGGIGGGYTKYNEKFKGRVTMTADTST STAYMELRSLRSDDTAVYYCSRSETGRAMDYWGQGTLVTVSS	246
>hu_3833_VH02	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYWIGWVRQAPGQGLEWMGDIYPGGIGGGYTKYAQKLQGRVTMTADTST STAYMELRSLRSDDTAVYYCSRSETGRAMDYWGQGTLVTVSS	247
>hu_3833_VH03	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYWIGWVRQAPGQGLEWMGDIYPGGIGGGYTKYAQKFQGRVTMTADTST STAYMELSSLRSEDTAVYYCSRSETGRAMDYWGQGTLVTVSS	248
>hu_3833_VH04	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYWIGWVRQAPGQGLEWMGDIYPGGIGGGYTKYNEKFKGRVTMTADTST STAYMELSSLRSEDTAVYFCSRSETGRAMDYWGQGTLVTVSS	249
>hu_3833_VH05	QVQLVQSGAELKRPGASVKVSCKASGYTFTNYWMGWVKQAPGQGLEWMGDIYPGGIGGGYTNYAQKFKGKATMTADTSS STAYMQLSRLRSEDTAVYYCSRSETGRAMDYWGQGTLVTVSS	250
>hu_3833_VL01	DIQMTQSPSSLSASVGDRVTITCQASQDINKYLAWYQQKPGKAPKLLIHYTSTLKPGVPSRFSGSGSGTDFTFTISSLQ PEDIATYYCLQYDNLNTFGGGTKLEIK	251
>hu_3833_VL02	DIQMTQSPSSLSASVGDRVTITCKASQDINKYIAWYQQKPGKAPKLLIHYTSTLKPGVPSRFSGSGSGRDYTFTISSLQ PEDIATYYCLQYDNLNTFGGGTKLEIK	252
>hu_3833_VL03	DIQMTQSPSSLSASVGDRVTITCQASQDINKYLAWYQQKPGKAPKLLIYYTSTLETGVPSRFSGSGSGTDFTFSISSLQ PEDIATYYCLQYDNLNTFGGGTKLEIK	253
>hu_4540_VH01	QVQLVQSGAEVKKPGASVKVSCKASGYTFADYYINWVRQAPGKGLEWMGWIFPGSGSTYYNEKFKGRVTMTVDKSTSTA YMELSSLRSEDTAVYFCARGDSGRAMDYWGQGTLVTVSS	254
>hu_4540_VH02	QVQLVQSGAEVKKPGASVKVSCKASGYTFADYYMNWVRQAPGQGLEWMGWIFPGSGSTYYAEKFKGRVTSTRDTSISTA YMELSRLRSDDTVVYYCARGDSGRAMDYWGQGTLVTVSS	255
>hu_4540_VH03	QVQLVQSGAEVKKPGASVKVSCKASGYTFADYYINWVRQAPGQGLEWMGWIFPGSGSTYYAQKLQGRVTMTTDTSTSTA YMELRSLRSDDTAVYYCARGDSGRAMDYWGQGTLVTVSS	256
>hu_4540_VH04	QVQLVQSGAEVKKPGASVKVSCKASGYTFADYYINWVRQAPGQGLEWMGWIFPGSGSTYYAQKLQGRVTMTVDKSSSTA YMELRSLRSDDTAVYYCARGDSGRAMDYWGQGTLVTVSS	257
>hu_4540_VH05	QVQLVQSGAELKKPGASVKVSCKASGYTFADYYMNWVRQAPGQGLEWMGWIFPGSGSTYYNQKFQGRVTMTVDKSSSTA YMELSRLRSDDTAVYYCARGDSGRAMDYWGQGTLVTVSS	258
>hu_4540_VL01	DIQMTQSPSSLSASVGDRVTITCKASQDINKYIAWYQQKPGKAPKLLIHYTSTLQSGVPSRFSGSGSGTDFTFTISSLQ PEDIATYYCLQYDNLLTFGQGTKLEIK	259
>hu_4540_VL02	DIQMTQSPSSLSASVGDRVTITCKASQDINKYIAWYQHKPGKAPKLLIHYTSTLQSGVPSRFSGSGSGRDYTFTISSLQ PEDIATYYCLQYDNLLTFGQGTKLEIK	260
>hu_4540_VL03	DIQMTQSPSSLSASVGDRVTITCQASQDINKYLAWYQHKPGKAPKLLIHYTSTLETGVPSRFSGSGSGTDFTFTISSLQ PEDIATYYCLQYDNLLTFGGGTKVEIK	261

In an embodiment, the antibody molecule comprises one, two, or three CDRs of the VH region of an antibody molecule described herein, *e.g.,* in **Table 1 or 5** (*e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, 4439, or 4237), using the Kabat or Chothia definitions of CDRs. In an embodiment, the antibody molecule comprises one, two, or three CDRs of the VL region of an antibody molecule described herein, *e.g.,* in **Table 1 or 5** (*e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, 4439, or 4237), using the Kabat or Chothia definitions of CDRs. In an embodiment, the antibody molecule comprises one or more (*e.g.*, two or three) CDRs of the VH region and/or one or more (*e.g.*, two or three) CDRs of the VL region of an antibody molecule described herein, *e.g.,* in **Table 1 or 5** (*e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, 4439, or 4237), using the Kabat or Chothia definitions of CDRs.

In an embodiment, the antibody molecule comprises one, two, or three VH CDRs described in **Table 1 or 5**. In an embodiment, the antibody molecule comprises one, two, or three VL CDRs described in **Table 1 or 5**. In an embodiment, the antibody molecule comprises one or more (*e.g.*, two or three) VH CDRs and/or one or more (*e.g.*, two or three) VL CDRs described in **Table 1 or 5**.

In an embodiment, the antibody molecule comprises one, two, three, or four frameworks of the VH region of an antibody molecule described in **Table 1 or 5** (*e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, 4439, or 4237). In an embodiment, the antibody molecule comprises one, two, three, or four frameworks of the VL region of an antibody molecule described in **Table 1 or 5** (*e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, 4439, or 4237). In an embodiment, the antibody molecule comprises one or more (*e.g.*, two, three, or four) frameworks of the

VH region and/or one or more (*e.g.*, two, three, or four) frameworks of the VL region of an antibody molecule described in **Table 1 or 5** (*e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237).

In an embodiment, the antibody molecule comprises a heavy chain variable region of an antibody molecule described herein, *e.g.,* in **Table 1 or 5** (*e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237). In an embodiment, the antibody molecule comprises a light chain variable region of an antibody molecule described herein, *e.g.,* in **Table 1 or 5** (*e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237). In an embodiment, the antibody molecule comprises a heavy chain variable region and a light chain variable region of an antibody molecule described herein, *e.g.,* in **Table 1 or 5** (*e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237).

In an embodiment, the antibody molecule comprises a heavy chain variable region having an amino acid sequence described in **Table 1 or 5**, or an amino acid sequence substantially identical thereof. In an embodiment, the antibody molecule comprises a light chain variable region having an amino acid sequence described in **Table 1 or 5**, or an amino acid sequence substantially identical thereof. In an embodiment, the antibody molecule comprises a heavy chain variable region having an amino acid sequence described in **Table 1 or 5** (or an amino acid sequence substantially identical thereof) and a light chain variable region having an amino acid sequences described in **Table 1 or 5** (or an amino acid sequence substantially identical thereof).

In an embodiment, the antibody molecule comprises a heavy chain variable region encoded by a nucleotide sequence described in **Table 2**, or a nucleotide sequence substantially identical thereof. In an embodiment, the antibody molecule comprises a light chain variable region encoded by a nucleotide sequence described in **Table 2**, or a nucleotide sequence substantially identical thereof. In an embodiment, the antibody molecule comprises a heavy chain variable region encoded by a nucleotide sequence described in **Table 2** (or a nucleotide sequence substantially identical thereof) and a light chain

variable region encoded by a nucleotide sequence described in **Table 2** (or a nucleotide sequence substantially identical thereof).

In an embodiment, the antibody molecule further comprises a heavy chain constant region. In an embodiment, the heavy chain constant region is an IgG1 constant region, *e.g.,* any of SEQ ID NOS: 320-322, or a functional portion thereof. In another embodiment, the heavy chain constant region is an IgG2 constant region, *e.g.,* any of SEQ ID NOS: 323-326, or a functional portion thereof. In an embodiment, the antibody molecule further comprises a light chain constant region. In an embodiment, the antibody molecule further comprises a heavy chain constant region and a light chain constant region. In an embodiment, the antibody molecule comprises a heavy chain constant region, a light chain constant region, and heavy and light chain variable regions of an antibody molecule described in **Table 1 or 5**. In certain embodiments, the antibody molecule comprises a heavy chain constant region, a light chain constant region, and variable regions that comprise one, two, three, four, five, or six CDRs of an antibody molecule described in **Table 1 or 5**.

Exemplary heavy chain constant regions are described below.

Exemplary IgG1 constant regions

>IGHG1*01
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTV
PSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP (SEQ ID NO: 320)

>IGHG1*03
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT
VPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTP
EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
LPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP (SEQ ID NO: 321)

>IGHG1*04
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT
VPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTP
EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKA
LPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPV
LDSDGSFFLYSKLTVDKSRWQQGNIFSCSVMHEALHNHYTQKSLSLSP (SEQ ID NO: 322)

Exemplary IgG2 constant regions

>IGHG2*01
STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTV
PSSNFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCV
VVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPI

EKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDG
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP (SEQ ID NO: 323)

>IGHG2*02
STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTV
TSSNFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCV
VVDVSHEDPEVQFNWYVDGMEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPI
EKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDG
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP (SEQ ID NO: 324)

>IGHG2*04
STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTV
PSSSLGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCV
VVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPI
EKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDG
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP (SEQ ID NO: 325)

>IGHG2*06
STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTV
PSSNFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCV
VVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPI
EKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDISVEWESNGQPENNYKTTPPMLDSDG
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP (SEQ ID NO: 326)

In an embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 12; or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 13, or

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of SEQ ID NO: 280; an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the SEQ ID NO: 285; or

an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 16.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12; and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13, and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of the LCDR1 of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285; or an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

In an embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 282; or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 13, or

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the SEQ ID NO: 285; or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 16.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282; and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13, and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285; or an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 296. In an embodiment, the antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 286. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 296 and a VL comprising the amino acid sequence of SEQ ID NO: 286.

In an embodiment, the antibody molecule comprises a VH encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 313. In an embodiment, the antibody molecule comprises a VL encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 306. In an embodiment, the antibody molecule comprises a VH encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 313 and a VL encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 306.

In an embodiment, the antibody molecule further comprises a heavy constant region of IgG2, *e.g.,* any of SEQ ID NOS: 323-326.

In an embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 12; or an HCDR3 comprising an amino

acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 13, or

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of SEQ ID NO: 280; an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the SEQ ID NO: 285; or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 16.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12; and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13, and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of the LCDR1 of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285; or an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

In an embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 282; or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 13, or

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain

variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the SEQ ID NO: 285; or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 16.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282; and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13, and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285; or an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 289. In an embodiment, the antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 286. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 289 and a VL comprising the amino acid sequence of SEQ ID NO: 286.

In an embodiment, the antibody molecule comprises a VH encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 308. In an embodiment, the antibody molecule comprises a VL encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 305. In an embodiment, the antibody molecule comprises a VH encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 308 and a VL encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 306.

In an embodiment, the antibody molecule further comprises a heavy constant region of IgG2, *e.g.,* any of SEQ ID NOS: 323-326.

In an embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 12; or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 13, or

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of SEQ ID NO: 280; an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the SEQ ID NO: 281; or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 16.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12; and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13, and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of the LCDR1 of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 281; or an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

In an embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid

sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 282; or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 13, or

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the SEQ ID NO: 281; or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 16.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282; and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13, and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 281; or an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 289. In an embodiment, the antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 284. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 289 and a VL comprising the amino acid sequence of SEQ ID NO: 284.

In an embodiment, the antibody molecule comprises a VH encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 308. In an embodiment, the antibody molecule comprises a VL encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 305. In an embodiment,

the antibody molecule comprises a VH encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 308 and a VL encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 305.

In an embodiment, the antibody molecule further comprises a heavy constant region of IgG2, *e.g.*, any of SEQ ID NOS: 323-326.

In an embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 93; an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 94; or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 95, or

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of SEQ ID NO: 96; an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the SEQ ID NO: 97; or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 98.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprising the amino acid sequence of SEQ ID NO: 93; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 94; and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 95, and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of the LCDR1 of SEQ ID NO:

96; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 97; or an LCDR3 comprising the amino acid sequence of SEQ ID NO: 98.

In an embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 99; an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 273; or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 95, or

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 96; an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the SEQ ID NO: 97; or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of SEQ ID NO: 98.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprising the amino acid sequence of SEQ ID NO: 99; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 273; and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 95, and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of SEQ ID NO: 96; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 97; or an LCDR3 comprising the amino acid sequence of SEQ ID NO: 98.

In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 225. In an embodiment, the antibody molecule comprises a VL comprising the amino acid

sequence of SEQ ID NO: 229. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 225 and a VL comprising the amino acid sequence of SEQ ID NO: 229.

In an embodiment, the antibody molecule comprises a VH encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 299. In an embodiment, the antibody molecule comprises a VL encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 300. In an embodiment, the antibody molecule comprises a VH encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 299 and a VL encoded by a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 300.

In an embodiment, the antibody molecule further comprises a heavy chain constant region of IgG1, *e.g.,* any of SEQ ID NOS: 320-322.

In an embodiment, the antibody molecule described herein has one or more (*e.g.,* 2, 3, 4, 5, or all) of the following properties: (a) is a humanized antibody molecule; (b) binds to human APRIL at an EC_{50} of 60 pM or less, as determined by ELISA; (c) inhibits binding of human APRIL to TACI, *e.g., in vitro*, at an IC_{50} of 0.5 nM or less; (d) inhibits binding of human APRIL to BCMI, *e.g., in vitro*, at an IC_{50} of 0.6 nM or less; (e) is an IgG2κ; or (f) has an Fc region engineered to reduce complement activation. In an embodiment, the antibody molecule comprises one or more (*e.g.,* 2, 3, 4, 5, or all) CDRs, one or both of heavy chain variable region or light chain variable regions, or one or both of heavy chain or light chain, of any of antibody molecules 2419-1406, 2419-0205, or 2419-0206. In an embodiment, the antibody molecule is suitable for use in treating a disorder in kidney, *e.g.,* IgA nephropathy. In another embodiment, the antibody molecule is suitable for use in treating a caner, *e.g.,* a multiple myeloma.

In an embodiment, the antibody molecule described herein has one or more (*e.g.,* 2, 3, 4, 5, or all) of the following properties: (a) is a humanized antibody molecule; (b) binds to human APRIL at an EC_{50} of 50 pM or less, as determined by ELISA; (c) inhibits binding of human APRIL to TACI, *e.g., in vitro*, at an IC_{50} of 0.3 nM or less; (d) inhibits binding of human APRIL to BCMA, *e.g., in vitro*, at an IC_{50} of 0.2 nM or less; (e) is an IgG1κ; or (f) has higher BCMA neutralization activity, *e.g.,* has an IC_{50} of 0.1 nM or less. In an embodiment, the antibody molecule comprises one or more (*e.g.,* 2, 3, 4, 5, or all) CDRs, one or both of heavy chain variable region or light chain variable regions, or one or both of heavy chain or light chain, of antibody molecule 4035-062. In an embodiment, the antibody molecule is suitable for use in treating a cancer or an autoimmune disorder.

The antibody molecules described herein can have several advantageous properties. For example, the antibody molecules can be used to effectively treat, prevent or diagnose a disorder associated with APRIL, *e.g.,* a disorder described herein, *e.g.,* IgA nephropathy.

In an embodiment, the antibody molecule is capable of binding, or substantially binding, to human APRIL and mouse APRIL. In an embodiment, the antibody molecule is capable of binding, or substantially binding, to human APRIL, but is not capable of binding, or substantially binding to mouse APRIL. In an embodiment, the antibody molecule binds to APRIL with high affinity, *e.g.,* with a dissociation constant (K_D) of less than about 100 nM, typically about 10 nM, and more typically, about 10-0.001 nM, about 10-0.01 nM, about 10-0.01 nM, about 5-0.01 nM, about 3-0.05 nM, about 1-0.1 nM, or stronger, *e.g.,* less than about 80, 70, 60, 50, 40, 30, 20, 10, 8, 6, 4, 3, 2, 1, 0.5, 0.2, 0.1, 0.05, 0.01, 0.005, or 0.001 nM. In an embodiment, the antibody molecule binds to APRIL with a K_{off} slower than 1×10^{-4}, 5×10^{-5}, or 1×10^{-5} s^{-1}. In an embodiment, the antibody molecule binds to APRIL with a K_{on} faster than 1×10^{4}, 5×10^{4}, 1×10^{5}, or 5×10^{5} $M^{-1}s^{-1}$.

In an embodiment, the antibody molecule is capable of inhibiting, or substantially inhibiting, binding of human APRIL to TACI. In an embodiment, the antibody molecule is capable of inhibiting, or substantially inhibiting, binding of human APRIL to TACI. In an embodiment, the antibody molecule is capable of inhibiting, or substantially inhibiting, binding of human APRIL to BCMA. In an embodiment, the antibody molecule is capable of inhibiting, or substantially inhibiting, binding of human APRIL to TACI and BCMA. In an embodiment, the antibody molecule is capable of inhibiting, or substantially inhibiting, binding of human APRIL to TACI, but is not capable of inhibiting, or substantially inhibiting, binding of human APRIL to BCMA. In an embodiment, the antibody molecule is capable of inhibiting, or substantially inhibiting, binding of human APRIL to BCMA, but is not capable of inhibiting, or substantially inhibiting, binding of human APRIL to TACI.

In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI by 50% or more, *e.g.,* 60% or more, 70% or more, 80% or more, 85% or more, 90% or more, 95% or more, 96% or more, 97% or more, 98% or more, 99% or more, or 100%, as determined by a method described herein (*e.g.,* normalized to the no antibody control).

In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA by 30% or more, *e.g.,* 40% or more, 50% or more, 60% or more, 70% or more, 80% or more, 85% or more, 90% or more, 95% or more, 96% or more, 97% or more, 98% or more, 99% or more, or 100%, as determined by a method described herein (*e.g.,* normalized to the no antibody control).

In an embodiment, the antibody molecule does not substantially inhibit binding of human APRIL to human BCMA, *e.g.,* inhibits binding of human APRIL to human BCMA by less than 10%, as determined by a method described herein (*e.g.,* normalized to the no antibody control).

In an embodiment, the antibody molecule binds to a linear or conformational epitope on APRIL. In an embodiment, the antibody molecule binds to an epitope conserved between human APRIL and mouse APRIL. In an embodiment, the antibody molecule binds to an epitope described herein. In an embodiment, the antibody molecule binds, or substantially binds, to the same, similar, or overlapping epitope on APRIL, as a second antibody molecule (*e.g.,* a monoclonal antibody described in **Table 1 or 5**). In an embodiment, the antibody molecule competes with a second antibody molecule (*e.g.,* a monoclonal antibody described in **Table 1 or 5**) for binding to APRIL.

In an embodiment, the antibody molecule binds, or substantially binds, one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, residues within a region of APRIL as defined in **Table 3**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all of the human APRIL residues from **Table 3**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from **Table 3**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises APRIL residues from two monomers, *e.g.,* one or more residues from monomer A and monomer B as shown in **Table 3**.

In an embodiment, the antibody molecule binds, or substantially binds, one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or more, residues within a region of APRIL as defined in **Table 4**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or all of the human APRIL residues from **Table 4**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from **Table 4**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises one or more APRIL residues from the C-D loop (*e.g.,* the loop connecting β-sheets C and D), the G-H loop (*e.g.,* the loop connecting β-sheets G and H), or both.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) residues of human APRIL from positions 105-114 and/or one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) residues of mouse APRIL from positions 96-105.

In an embodiment, the antibody molecule binds, or substantially binds, one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or more, residues within a region of APRIL as defined in **Table 7**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all of the human APRIL residues from **Table 7**. In an embodiment, the antibody molecule binds, or substantially binds, to an

epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from **Table 7**.

In an embodiment, the antibody molecule binds, or substantially binds, one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, residues within a region of APRIL as defined in Table 8 of International Application Publication No. WO2017/091683. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the epitope is a conformational epitope.

In an embodiment, the antibody molecule does not bind, or does not substantially bind, to one, two or all of Asp129, Arg233, or His203 of human APRIL.

In an embodiment, binding of the antibody molecule to APRIL (*e.g.,* human APRIL) inhibits, or substantially inhibits, the binding of the CRD2 domain of TACI (*e.g.,* human TACI) to APRIL (*e.g.,* human APRIL). In another embodiment, binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all of the APRIL residues from **Table 3**. In yet another embodiment, binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or all of the human APRIL residues from **Table 4**. In still another embodiment, binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all of the human APRIL residues from **Table 7**. In still another embodiment, binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683.

Exemplary Anti-APRIL Antibody Molecules

This disclosure provides, at least in part, antibody molecules that bind to APRIL, *e.g.*, human and/or mouse APRIL, and that comprise one or more functional and structural properties disclosed herein. In an embodiment, the antibody molecule binds to and/or reduces (*e.g.,* inhibits, blocks or neutralizes) one or more activities of APRIL. In an embodiment, the antibody molecule binds to a region in APRIL that

interacts with TACI (*e.g.,* the CRD2 domain of TACI). In an embodiment, the antibody molecule binds to one or more residues within a region of human APRIL as defined in any of **Tables 3-4 or 7**, or Table 8 of International Application Publication No. WO2017/091683. While not wishing to be bound by theory, it is believed that in an embodiment, improved or optimal inhibition of APRIL activities can be achieved, by targeting certain region(s) on APRIL (*e.g.,* the region(s) associated with the interactions between APRIL and the CDR2 domain of TACI). In an embodiment, the antibody molecule is selected from **Table 1 or 5**, or competes for binding to APRIL with an antibody molecule selected from **Table 1 or 5**. In an embodiment, the antibody molecule binds to the same or overlapping epitope as the epitope recognized by an antibody molecule selected from **Table 1 or 5**. In an embodiment, the antibody molecule comprises one or more heavy chain variable regions and/or one or more light chain variable regions described in **Table 1 or 5**. In an embodiment, the antibody molecule comprises one or more heavy chain CDRs and/or one or more light chain CDRs described in **Table 1 or 5**. In an embodiment, nucleic acid molecules encoding the antibody molecules, expression vectors, host cells, compositions (*e.g.*, pharmaceutical compositions), kits, containers, and methods for making the antibody molecules, are also provided. The antibody molecules disclosed herein can be used (alone or in combination with other agents or therapeutic modalities) to treat, prevent and/or diagnose disorders associated with APRIL, such as IgA nephropathy.

In an embodiment, the antibody molecule has one or more (*e.g.,* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, or 23) of the following properties:

a) Binds to human APRIL with high affinity, *e.g.,* with a dissociation constant (K_D) of less than about 100 nM, typically about 10 nM, and more typically, about 10-0.001 nM, about 10-0.01 nM, about 5-0.01 nM, about 3-0.05 nM, about 1-0.1 nM, or stronger, *e.g.,* less than about 80, 70, 60, 50, 40, 30, 20, 10, 8, 6, 4, 3, 2, 1, 0.5, 0.2, 0.1, 0.05, 0.01, 0.005, or 0.001 nM,

b) Binds to mouse APRIL with high affinity, *e.g.,* with a dissociation constant (K_D) of less than about 100 nM, typically about 10 nM, and more typically, about 10-0.001 nM, about 10-0.01 nM, about 5-0.01 nM, about 3-0.05 nM, about 1-0.1 nM, or stronger, *e.g.,* less than about 80, 70, 60, 50, 40, 30, 20, 10, 8, 6, 4, 3, 2, 1, 0.5, 0.2, 0.1, 0.05, 0.01, 0.005, or 0.001 nM,

c) Does not bind to mouse APRIL, or binds mouse APRIL with low affinity, *e.g.,* with a dissociation constant (K_D) of greater than about 500 nM, *e.g.,* greater than about 1000 nM,

d) Does not bind, or binds with low affinity, *e.g.,* with a dissociation constant (K_D) of greater than about 500 nM, *e.g.,* greater than about 1000 nM, to one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, or more) cytokines from the TNF superfamily (TNFSF) other than APRIL (*e.g.,* TNFα, CD40

(TNFSF4), FasL (TNFSF6), TRAIL (TNFSF10), RANKL (TNFSF11), Tweak (TNFSF12), BAFF (TNFSF13B), or LIGHT (TNFSF14)),

e) Binds to one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all) residues within a region of APRIL as defined in **Table 3**, or binds specifically to an epitope on APRIL, *e.g.,* an epitope comprising one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all) residues described in **Table 3**,

f) Binds to one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or all) residues within a region of APRIL as defined in **Table 4**, or binds specifically to an epitope on APRIL, *e.g.,* an epitope comprising one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or all) residues described in **Table 4**,

g) Binds to one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all) residues within a region of APRIL as defined in **Table 7**, or binds specifically to an epitope on APRIL, *e.g.,* an epitope comprising one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all) residues described in **Table 7**,

h) Binds to one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all) residues within a region of APRIL as defined in **Table 8** of International Application Publication No. WO2017/091683, or binds specifically to an epitope on APRIL, *e.g.,* an epitope comprising one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all) residues described in **Table 8** of International Application Publication No. WO2017/091683,

i) Binds specifically to an epitope on APRIL, *e.g.,* the same, similar, or overlapping epitope as the epitope recognized by a monoclonal antibody described in **Table 1 or 5**, *e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237,

j) Reduces (*e.g.,* inhibits, blocks, or neutralizes) one or more biological activities of APRIL (*e.g.*, human APRIL, mouse APRIL, or both), *in vitro*, *ex vivo*, or *in vivo*,

k) Reduces (*e.g.,* inhibits, blocks, or neutralizes) binding of human APRIL to TACI, *e.g.,* at an IC_{50} of about 50 nM or less, typically about 0.01-50 nM, 0.1-25 nM, 0.1-10 nM, 0.5-5 nM, or 1-5 nM, *e.g.,* less than about 40, 30, 20, 10, 5, 1, 0.5, 0.2, 0.1, 0.05, or 0.01 nM, *e.g.,* as determined by a method described herein,

l) Reduces (*e.g.,* inhibits, blocks, or neutralizes) binding of mouse APRIL to TACI, *e.g.,* at an IC_{50} of about 100 nM or less, typically about 0.01-75 nM, 0.1-50 nM, 0.1-25 nM, 0.1-10 nM,

0.5-5 nM, or 1-5 nM, *e.g.,* less than about 80, 60, 40, 20, 10, 5, 1, 0.5, 0.2, 0.1, 0.05, or 0.01 nM, *e.g.,* as determined by a method described herein,

m) Reduces (*e.g.,* inhibits, blocks, or neutralizes) binding of human APRIL to BMCA, *e.g.,* at an IC_{50} of about 50 nM or less, typically about 0.01-50 nM, 0.1-25 nM, 0.1-10 nM, 0.5-5 nM, or 1-5 nM, *e.g.,* less than about 40, 30, 20, 10, 5, 1, 0.5, 0.2, 0.1, 0.05, or 0.01 nM, *e.g.,* as determined by a method described herein,

n) Reduces (*e.g.,* inhibits, blocks, or neutralizes) binding of mouse APRIL to BMCA, *e.g.,* at an IC_{50} of about 200 nM or less, typically about 0.01-200 nM, 0.1-150 nM, 0.1-100 nM, 0.1-50 nM, 0.1-25 nM, 0.1-10 nM, 0.5-5 nM, or 1-5 nM, *e.g.,* less than about 150, 100, 50, 40, 30, 20, 10, 5, 1, 0.5, 0.2, 0.1, 0.05, or 0.01 nM, *e.g.,* as determined by a method described herein,

o) Shows the same or similar binding affinity or specificity, or both, as a monoclonal antibody described in **Table 1 or 5**, *e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237,

p) Shows the same or similar binding affinity or specificity, or both, as an antibody molecule comprising a heavy chain variable region and/or light chain variable region described in **Table 1 or 5**, *e.g.,* a heavy chain variable region and/or light chain variable region of any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237,

q) Shows the same or similar binding affinity or specificity, or both, as an antibody molecule comprising one or more (*e.g.*, two or three) heavy chain CDRs and/or one or more (*e.g.*, two or three) light chain CDRs described in **Table 1 or 5**, *e.g.*, one or more (*e.g.*, two or three) heavy chain CDRs and/or one or more (two or three) light chain CDRs of any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237,

r) Shows the same or similar binding affinity or specificity, or both, as an antibody molecule comprising an amino acid sequence shown in **Table 1 or 5**,

s) Shows the same or similar binding affinity or specificity, or both, as an antibody molecule comprising an amino acid sequence encoded by a nucleotide sequence shown in **Table 2**,

t) Inhibits, *e.g.,* competitively inhibits, the binding of a second antibody molecule to human APRIL, mouse APRIL, or both, wherein the second antibody molecule is an antibody molecule chosen from **Table 1 or 5**, *e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237,

u) Competes for binding with a second antibody molecule to human APRIL, mouse APRIL, or both, wherein the second antibody molecule is a monoclonal antibody chosen from **Table 1 or 5**, *e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237,

v) Has one or more biological properties of a monoclonal antibody chosen from **Table 1 or 5**, *e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237,

w) Has one or more structural properties of a monoclonal antibody chosen from **Table 1 or 5**, *e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237, or

x) Has one or more pharmacokinetic properties of a monoclonal antibody chosen from **Table 1 or 5**, *e.g.,* any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the anti-APRIL antibody molecule:

(i) binds, or substantially binds, to human APRIL;

(ii) binds, or substantially binds, to mouse APRIL;

(iii) inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both); and

(iv) inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both).

In an embodiment, the antibody molecule is a synthetic antibody molecule. In an embodiment, the antibody molecule is an isolated antibody molecule.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule binds, or substantially binds, to mouse APRIL at an EC_{50} of 100 nM or less, *e.g.,* 80 nM or less, 60 nM or less, 40 nM or less, 20 nM or less, 10 nM or less, 9 nM or less 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 100 nM, *e.g.,* between 0.001 nM and 50 nM, between 0.01 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM or between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both), at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both), *e.g.,* at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule is an IgG antibody molecule, *e.g.,* comprising a heavy chain constant region of IgG, *e.g.,* chosen from IgG1, IgG2 (*e.g.,* IgG2a), IgG3, or IgG4, *e.g.,* IgG2 or IgG4. In an embodiment, the antibody molecule is an IgG1 antibody molecule, *e.g.,* having an IgG1 constant region described herein. In another embodiment, the antibody molecule is an IgG2 antibody molecule *e.g.,* having an IgG2 constant region described herein. In an embodiment, the antibody molecule comprises a light chain constant region of kappa or lambda light chain.

In an embodiment, the antibody molecule comprises an Fc region. In an embodiment, the Fc region comprises one or more mutations located at the interface between the CH2 and CH3 domains (*e.g.,* to increase the binding affinity to neonatal receptor FcRn and/or the half-life of the antibody molecule). In an embodiment, the Fc region comprises one or more mutations, *e.g.,* one or more (*e.g.,* 2, 3, 4, 5, 6 or all) mutations chosen from T250Q, M252Y, S254T, T256E, M428L, H433K, N434F, or any combination thereof, of IgG1. In an embodiment, the Fc region comprises one or more mutations at positions 233-236 or 322 of human IgG1 or IgG2, or one or more substitutions at positions 327, 330 or 331 of human IgG4 (*e.g.,* to reduce complement-dependent cytotoxicity (CDC)). In an embodiment, the Fc region comprises one or more (*e.g.,* 2, 3, 4, 5, 6, 7 or all) mutations chosen from E233P, L234V, L235A, G236, K322A, A327G, A330S, P331S, or any combination thereof.

In an embodiment, the antibody molecule is a humanized antibody molecule, *e.g.,* comprising one or more framework regions derived from human framework germline sequence. In an embodiment, the antibody molecule comprises a heavy chain variable region (VH) described in **Table 1 or 5**. In an embodiment, the antibody molecule comprises a light chain variable region (VL) described in **Table 1 or 5**. In an embodiment, the antibody molecule comprises a heavy chain variable region (VH) and a light chain variable region (VL) described in **Table 1 or 5**. In an embodiment, the antibody molecule comprises one, two, or three CDRs of a heavy chain variable region (VH) described in **Table 1 or 5.** In an embodiment, the antibody molecule comprises one, two, or three CDRs of a light chain variable region (VL) described in **Table 1 or 5.** In an embodiment, the antibody molecule comprises one, two, or three

CDRs of a heavy chain variable region (VH) described in **Table 1 or 5**, and one, two, or three CDRs of a light chain variable region (VL) described in **Table 1 or 5.** In an embodiment, the antibody molecule comprises two heavy chain variable regions and two light chain variable regions. In an embodiment, the antibody molecule is a Fab, F(ab')2, Fv, Fd, or a single chain Fv fragment (scFv).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 61); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 62); or (ii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 61); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 62); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 61); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 62); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 64); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 65); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid

residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 64); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 65); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 64); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 65); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 66). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 70).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 66); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 70). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 66); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 70).

In an embodiment the antibody molecule is monoclonal antibody 3530. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3530.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 61); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 62); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following:

(i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 61); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 62); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises: (i) a VH comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprises the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 61); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 62); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63), and (ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining

regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 64); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 65); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 64); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 65); or an HCDR3 comprising an amino acid

sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprises the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 64); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 65); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3525 (*e.g.*, SEQ ID NO: 66). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3525 (*e.g.*, SEQ ID NO: 50).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3525 (*e.g.*, SEQ ID NO: 66); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3525 (*e.g.*, SEQ ID NO: 50). In an embodiment, the antibody molecule

comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3525 (*e.g.*, SEQ ID NO: 66); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3525 (*e.g.*, SEQ ID NO: 50).

In an embodiment the antibody molecule is monoclonal antibody 3525. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3525.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 113); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 114); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 118).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 113); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence

of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 114); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 118).

In an embodiment, the antibody molecule comprises: (i) a VH comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprises the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 113); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 114); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115), and (ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 118).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 119); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 120); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more

than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 118).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 119); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 120); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 118).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprises the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 119); an

HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 120); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 118).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3833 (*e.g.*, SEQ ID NO: 121). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3833 (*e.g.*, SEQ ID NO: 122).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3833 (*e.g.*, SEQ ID NO: 121); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3833 (*e.g.*, SEQ ID NO: 122). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3833 (*e.g.*, SEQ ID NO: 121); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3833 (*e.g.*, SEQ ID NO: 122).

In an embodiment the antibody molecule is monoclonal antibody 3833. In an embodiment, monoclonal antibody 3833 is a humanized monoclonal antibody 3833. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NO: 246-250, a VL comprising the amino acid sequence of any of SEQ ID NO: 251-253, or both.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence

of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 123); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 124); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 127); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 123); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 124); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 127); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises: (i) a VH comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprises the amino acid sequence of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 123); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 124); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125), and (ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 127); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 129); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 130); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 127); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid

residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 129); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 130); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 127); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprises the amino acid sequence of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 129); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 130); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 127); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3631 (*e.g.*, SEQ ID NO: 131). In an embodiment, the antibody molecule comprises

a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3631 (*e.g.*, SEQ ID NO: 132).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3631 (*e.g.*, SEQ ID NO: 131); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3631 (*e.g.*, SEQ ID NO: 132). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3631 (*e.g.*, SEQ ID NO: 131); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3631 (*e.g.*, SEQ ID NO: 132).

In an embodiment the antibody molecule is monoclonal antibody 3631. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3631.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 133); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 134); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 127); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 133); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 134); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 127); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises: (i) a VH comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprises the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 133); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 134); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135), and (ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody

3732 (*e.g.,* SEQ ID NO: 127); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 138); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 139); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 127); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 138); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 139); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 127); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprises the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 138); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 139); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 127); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3732 (*e.g.*, SEQ ID NO: 140). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3732 (*e.g.*, SEQ ID NO: 141).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3732 (*e.g.*, SEQ ID NO: 140); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3732 (*e.g.*, SEQ ID NO: 141). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3732 (*e.g.*,

SEQ ID NO: 140); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3732 (*e.g.*, SEQ ID NO: 141).

In an embodiment the antibody molecule is monoclonal antibody 3732. In an embodiment, monoclonal antibody 3732 is a humanized monoclonal antibody 3732.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 154); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 155); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 156).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116), 4540-063 (*e.g.,* SEQ ID NO: 274), or 4540-033 (*e.g.,* SEQ ID NO: 274); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157), 4540-063 (*e.g.,* SEQ ID NO: 275), or 4540-033 (*e.g.,* SEQ ID NO: 275); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4540, 4540-063,

or 4540-033 (*e.g.,* SEQ ID NO: 154); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 155); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 156), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116), 4540-063 (*e.g.,* SEQ ID NO: 274), or 4540-033 (*e.g.,* SEQ ID NO: 274); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157), 4540-063 (*e.g.,* SEQ ID NO: 275), or 4540-033 (*e.g.,* SEQ ID NO: 275); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises: (i) a VH comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprises the amino acid sequence of the HCDR1 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 154); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 155); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 156), and (ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116), 4540-063 (*e.g.,* SEQ ID NO: 274), or 4540-033 (*e.g.,* SEQ ID NO: 274); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157), 4540-063 (*e.g.,* SEQ ID NO: 275), or 4540-033 (*e.g.,* SEQ ID NO: 275); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3

amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 159), 4540-063 (*e.g.,* SEQ ID NO: 276), or 4540-033 (*e.g.,* SEQ ID NO: 159); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 160), 4540-063 (*e.g.,* SEQ ID NO: 277), or 4540-033 (*e.g.,* SEQ ID NO: 278); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 156).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116), 4540-063 (*e.g.,* SEQ ID NO: 274), or 4540-033 (*e.g.,* SEQ ID NO: 274); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157), 4540-063 (*e.g.,* SEQ ID NO: 275), or 4540-033 (*e.g.,* SEQ ID NO: 275); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 159), 4540-063 (*e.g.,* SEQ ID NO: 276), or 4540-033 (*e.g.,* SEQ ID NO: 159); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 160), 4540-063 (*e.g.,* SEQ ID NO: 277), or 4540-033 (*e.g.,* SEQ ID NO: 278); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 156), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116), 4540-063 (*e.g.,* SEQ ID NO: 274), or 4540-033 (*e.g.,* SEQ ID NO: 274); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157), 4540-063 (*e.g.,* SEQ ID NO: 275), or 4540-033 (*e.g.,* SEQ ID NO: 275); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises: (i) a VH comprising one, two, or all of the following: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 159), 4540-063 (*e.g.,* SEQ ID NO: 276), or 4540-033 (*e.g.,* SEQ ID NO: 159); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 160), 4540-063 (*e.g.,* SEQ ID NO: 277), or 4540-033 (*e.g.,* SEQ ID NO: 278); or an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 156), and (ii) a VL comprising one, two, or all of the following: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116), 4540-063 (*e.g.,* SEQ ID NO: 274), or 4540-033 (*e.g.,* SEQ ID NO: 274); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157), 4540-063 (*e.g.,* SEQ ID NO: 275), or 4540-033 (*e.g.,* SEQ ID NO: 275); or an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4540 (*e.g.*, SEQ ID NO: 161), 4540-063 (*e.g.*, SEQ ID NO: 258), or 4540-033 (*e.g.*, SEQ ID NO: 256). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4540 (*e.g.*, SEQ ID NO: 162), 4540-063 (*e.g.*, SEQ ID NO: 261), or 4540-033 (*e.g.*, SEQ ID NO: 261).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the

VH of monoclonal antibody 4540 (*e.g.*, SEQ ID NO: 161), 4540-063 (*e.g.*, SEQ ID NO: 258), or 4540-033 (*e.g.*, SEQ ID NO: 256); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4540 (*e.g.*, SEQ ID NO: 162), 4540-063 (*e.g.*, SEQ ID NO: 261), or 4540-033 (*e.g.*, SEQ ID NO: 261). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 4540 (*e.g.*, SEQ ID NO: 161), 4540-063 (*e.g.*, SEQ ID NO: 258), or 4540-033 (*e.g.*, SEQ ID NO: 256); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 4540 (*e.g.*, SEQ ID NO: 162), 4540-063 (*e.g.*, SEQ ID NO: 261), or 4540-033 (*e.g.*, SEQ ID NO: 261).

In an embodiment, the antibody molecule is monoclonal antibody 4540, 4540-063, or 4540-033. In an embodiment, monoclonal antibody 4540 is a humanized monoclonal antibody 4540 (*e.g.,* antibodies 4540-063 or 4540-033). In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NO: 254-258, a VL comprising the amino acid sequence of any of SEQ ID NO: 259-261, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, residues within a region of human APRIL as defined in any of **Tables 3-4 or 7**, or Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, residues within a region of human APRIL as defined in **Table 3**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, of the human APRIL residues from **Table 3**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from **Table 3**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises APRIL residues from two monomers, *e.g.,* one or more residues from monomer A and monomer B as shown in **Table 3**.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or more, residues within a region of human APRIL as defined in **Table 4**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or all, of the human APRIL residues from **Table 4**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope

that comprises or consists of all of the human APRIL residues from **Table 4**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises one or more APRIL residues from the C-D loop (*e.g.,* the loop connecting β-sheets C and D), the G-H loop (*e.g.,* the loop connecting β-sheets G and H), or both.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all, residues within a region of human APRIL as defined in **Table 7**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all, of the human APRIL residues from **Table 7**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from **Table 7**.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, residues within a region of human APRIL as defined in Table 8 of International Application Publication No. WO2017/091683, irety. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683y. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) residues of human APRIL from positions 105-114 and/or one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) residues of mouse APRIL from positions 96-105. In an embodiment, the antibody molecule does not bind, or does not substantially bind, to one, two or all of Asp129, Arg233, or His203 of human APRIL. In an embodiment, the epitope is a conformational epitope.

In an embodiment, binding of the antibody molecule to APRIL (*e.g.,* human APRIL) inhibits, or substantially inhibits, the binding of the CRD2 domain of TACI (*e.g.,* human TACI) to APRIL (*e.g.,* human APRIL). In another embodiment, binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, of the APRIL residues from **Table 3**. In yet another embodiment, binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or all, of the human APRIL residues from **Table 4**. In still another embodiment, binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12,

13, 14, 15, 16, 17, or all, of the human APRIL residues from **Table 7**. In still another embodiment, binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683. In another embodiment, binding of the antibody molecule to human APRIL inhibits, or substantially inhibits, the binding of human BCMA, to one or more, *e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, residues within a region of human APRIL as defined in any of **Tables 3-4 or 7**, or Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the anti-APRIL antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, of the human APRIL residues from any of **Tables 3-4 or 7**, or Table 8 of International Application Publication No. WO2017/091683. In an embodiment, the antibody molecule binds, or substantially binds, to a conformational epitope.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, residues within a region of human APRIL as defined in **Table 3**. In an embodiment, the anti-APRIL antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all) of the human APRIL residues from **Table 3.** In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises APRIL residues from two monomers, *e.g.,* one or more residues from monomer A and monomer B as shown in **Table 3**.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or all, residues within a region of human APRIL as defined in **Table 4**. In an embodiment, the epitope comprises consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or all of the APRIL residues from **Table 4**. In an embodiment, the epitope comprises or consists of one or more APRIL residues from the C-D loop (*e.g.,* the loop connecting β-sheets C and D), the G-H loop (*e.g.,* the loop connecting β-sheets G and H), or both.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all, residues within a region of human APRIL as defined

in **Table 7**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all, of the human APRIL residues from **Table 7**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from **Table 7**.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, residues within a region of human APRIL as defined in Table 8 of International Application Publication No. WO2017/091683. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) residues of human APRIL from positions 105-114 and/or one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) residues of mouse APRIL from positions 96-105. In an embodiment, the antibody molecule does not bind, or does not substantially bind, to one, two or all of Asp129, Arg233, or His203 of human APRIL.

In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, or all) of human APRIL residues from Table 6 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more (*e.g.,* 2, 3, 4, 5, or all) of the amino acid residues of human APRIL chosen from V174, F176, Q190, R195, R206, or Y208. In an embodiment, the antibody molecule does not binds, or does not substantially bind, to one or more (*e.g.,* 2, 3, or all) of the amino acid residues of human APRIL chosen from V181, S226, I228, or N237. In an embodiment, the antibody molecule binds, or substantially binds, to one or more (*e.g.,* 2, 3, or all) of the amino acid residues of human APRIL chosen from F176, V181, Q190, or I228. In an embodiment, the antibody molecule does not bind, or does not substantially bind, to one or both of the amino acid residues of human APRIL chosen from Y208 or N237. In an embodiment, the antibody molecule binds, or substantially binds, to one or more (*e.g.,* 2, or all) of the amino acid residues of human APRIL chosen from V174, R206, or Y208. In an embodiment, the antibody molecule does not bind, or

does not substantially bind, to one or more (*e.g.,* 2, 3, or all) of the amino acid residues of human APRIL chosen from F176, V181, Q190, or N237.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL and mouse APRIL. In an embodiment, the antibody molecule binds, or substantially binds to, human APRIL, but does not bind to mouse APRIL, or binds to mouse APRIL with low affinity.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, *e.g.,* between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule binds, or substantially binds, to mouse APRIL at an EC_{50} of 100 nM or less, *e.g.,* 80 nM or less, 60 nM or less, 40 nM or less, 20 nM or less, *e.g.,* 10 nM or less, *e.g.,* 9 nM or less 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 100 nM, *e.g.,* between 0.001 nM and 50 nM, between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, *e.g.,* between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule does not bind to mouse APRIL, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both). In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both), at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less,

0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In an embodiment, binding of the antibody molecule to APRIL (*e.g.,* human APRIL) inhibits, or substantially inhibits, the binding of the CRD2 domain of TACI (*e.g.,* human TACI) to APRIL (*e.g.,* human APRIL). In an embodiment, binding of the antibody molecule to human APRIL inhibits, or substantially inhibits, the binding of human TACI, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, of the human APRIL residues from **Table 3**. In an embodiment, binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or all, of the human APRIL residues from **Table 4**. In an embodiment, binding of the antibody molecule to human APRIL inhibits, or substantially inhibits, the binding of human TACI, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all, of the human APRIL residues from **Table 7**. In an embodiment, binding of the antibody molecule to human APRIL inhibits, or substantially inhibits, the binding of human TACI, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683. In another embodiment, binding of the antibody molecule to human APRIL inhibits, or substantially inhibits, the binding of human BCMA, to one or more, *e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both). In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both), *e.g.,* at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule is a synthetic antibody molecule. In an embodiment, the antibody molecule is an isolated antibody molecule. In an embodiment, the antibody molecule is an IgG antibody molecule, *e.g.,* comprising a heavy chain constant region of IgG, *e.g.,* chosen from IgG1, IgG2 (*e.g.,* IgG2a), IgG3, or IgG4, *e.g.,* IgG2 or IgG4. In an embodiment, the antibody molecule is an IgG1 antibody molecule. In an embodiment, the antibody molecule is an IgG2 antibody molecule. In an embodiment, the antibody molecule comprises a light chain constant region of kappa or lambda light chain.

In an embodiment, the antibody molecule comprises an Fc region. In an embodiment, the Fc region comprises one or more mutations located at the interface between the CH2 and CH3 domains (*e.g.,* to increase the binding affinity to neonatal receptor FcRn and/or the half-life of the antibody molecule). In an embodiment, the Fc region comprises one or more mutations, *e.g.,* one or more (*e.g.,* 2, 3, 4, 6 or all) mutations chosen from T250Q, M252Y, S254T, T256E, M428L, H433K, N434F, or any combination thereof, of IgG1. In an embodiment, the Fc region comprises one or more mutations at positions 233-236 or 322 of human IgG1 or IgG2, or one or more substitutions at positions 327, 330 or 331 of human IgG4 (*e.g.,* to reduce complement-dependent cytotoxicity (CDC)). In an embodiment, the Fc region comprises one or more (*e.g.,* 2, 3, 4, 6 7 or all) mutations chosen from E233P, L234V, L235A, G236, K322A, A327G, A330S, P331S, or any combination thereof.

In an embodiment, the antibody molecule is a humanized antibody molecule, *e.g.,* as described in **Table 1 or 5**, *e.g.,* comprising one or more framework regions derived from human framework germline sequence.

In an embodiment, the antibody molecule comprises two heavy chain variable regions and two light chain variable regions. In an embodiment, the antibody molecule is a Fab, F(ab')2, Fv, Fd, or a single chain Fv fragment (scFv).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 1); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 2); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 3).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 4); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 5); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 6).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 1); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 2); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 3), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 4); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 5); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 6).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 1); an HCDR2 comprising an amino acid sequence that

differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 2); and an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 3), and (ii) a VL comprising: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 4); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 5); and an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 6).

In an embodiment, the antibody molecule comprises a VH comprising one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 7); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 8); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 3).

In an embodiment, the antibody molecule comprises a VL comprising one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 4); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 5); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 6).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 7); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 8); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 3), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 4); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 5); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 6).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 7); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 8); and an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 3), and (ii) a VL comprising: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 4); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 5); and an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 6).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 9). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 10).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 9); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 10). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 9); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 10).

In an embodiment the antibody molecule is monoclonal antibody 2218. In an embodiment, monoclonal antibody 2218 is a humanized monoclonal antibody 2218. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NO: 190-201, a VL comprising the amino acid sequence of any of SEQ ID NO: 202-208, or both.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 11) or a 2419-related antibody; (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 12) or a 2419-related antibody; or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 13) or a 2419-related antibody.

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 14) or a 2419-related antibody; (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 15) or a 2419-related antibody; or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 16) or a 2419-related antibody.

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 11) or a 2419-related antibody; an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 12) or a 2419-related antibody; or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 13) or a 2419-related antibody, and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 14) or a 2419-related antibody; an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 15) or a 2419-related antibody; or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 16) or a 2419-related antibody.

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 11) or a 2419-related antibody; an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal

antibody 2419 (*e.g.,* SEQ ID NO: 12) or a 2419-related antibody; or an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 13) or a 2419-related antibody, and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 14) or a 2419-related antibody; an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 15) or a 2419-related antibody; and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 16) or a 2419-related antibody.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 17) or a 2419-related antibody; (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 18) or a 2419-related antibody; or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 13) or a 2419-related antibody.

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 14) or a 2419-related antibody; (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 15) or a 2419-related antibody; or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 16) or a 2419-related antibody.

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 17) or a 2419-related antibody; an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 18) or a 2419-related antibody; or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 13) or a 2419-related antibody, and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 14) or a 2419-related antibody; an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 15) or a 2419-related antibody; or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 16) or a 2419-related antibody.

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 17) or a 2419-related antibody; an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 18) or a 2419-related antibody; or an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 13) or a 2419-related antibody, and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 14) or a 2419-related antibody; an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 15) or a 2419-related antibody; and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 16) or a 2419-related antibody.

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 19) or a 2419-related antibody. In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 20) or a 2419-related antibody.

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 19) or a 2419-related antibody; and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 20) or a 2419-related antibody.

In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 19) or a 2419-related antibody; and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 20) or a 2419-related antibody.

In an embodiment the antibody molecule is monoclonal antibody 2419. In an embodiment, monoclonal antibody 2419 is a humanized monoclonal antibody 2419. In an embodiment, the antibody molecule is a 2419-related antibody molecule, *e.g.,* any of antibodies 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, or 2419-1406, *e.g.,* as disclosed in **Table 1 or 5**. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NOS: 209-214, 283, 288, 289, 291, 292, 294, 296, or 317, a VL comprising the amino acid sequence of any of SEQ ID NOS: 215-219, 284, 286, 295, or 316, or both.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 21); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 32); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 33).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1,

LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 34); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 35); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 36).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 21); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 32); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 33), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 34); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 35); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 36).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 21); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 32); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 33), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 34); an LCDR2 comprising the amino acid

sequence of the LCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 35); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 36).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 37); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 38); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 33).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 34); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 35); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 36).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 37); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 38); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 33), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 34); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 35); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 36).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 37); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 38); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 33), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 34); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 35); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 36).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 39). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 40).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 39); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 40). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 39); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 40).

In an embodiment the antibody molecule is monoclonal antibody 2922. In an embodiment, the antibody molecule is a humanized monoclonal antibody 2922.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 51); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 52); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 53).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 54); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 55); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 56).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 51); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 52); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 53), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 54); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 55); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 56).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 51); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 52); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 53), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 54); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 55); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 56).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 57); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 58); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 53).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid

residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 54); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 55); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 56).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 57); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 58); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 53), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 54); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 55); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 56).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 57); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 58); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 53), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 54); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 55); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 56).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 59). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 60).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 59); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 60). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 59); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 60).

In an embodiment the antibody molecule is monoclonal antibody 3327. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3327.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 61); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 62); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following:

(i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 61); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 62); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 61); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 62); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); an LCDR2 comprising the amino acid

sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 64); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 65); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 64); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 65); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 64); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 65); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 66). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 70).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 66); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 70). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 66); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 70).

In an embodiment the antibody molecule is monoclonal antibody 3530. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3530.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 61); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 62); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 61); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 62); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63), and

(ii) a VL comprising: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 61); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 62); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 64); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 65); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 64); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 65); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 64); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 65); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of

monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 66). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 50).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 66); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 50). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 66); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 50).

In an embodiment the antibody molecule is monoclonal antibody 3525. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3525.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 21); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 22); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 23).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 24); (ii) an LCDR2 comprising an amino acid

sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 25); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 26).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 21); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 22); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 23), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 24); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 25); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 26).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 21); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 22); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 23), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 24); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 25); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 26).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions

(HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 27); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 28); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 23).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 24); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 25); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 26).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 27); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 28); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 23), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 24); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino

acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 25); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 26).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 27); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 28); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 23), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 24); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 25); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 26).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 29). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 30).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 29); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 30). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 29); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 30).

In an embodiment the antibody molecule is monoclonal antibody 2621. In an embodiment, the antibody molecule is a humanized monoclonal antibody 2621.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 11); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 42); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 43).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 44); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 45); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 11); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 42); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 43), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 11); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 42); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 43), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 45); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 47); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 48); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 43).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 44); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ

ID NO: 45); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 47); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 48); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 43), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO:45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 47); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 48); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 43), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 45); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 49). In an embodiment, the antibody molecule comprises a

VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 50).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 49); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 50). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 49); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 50).

In an embodiment the antibody molecule is monoclonal antibody 3125. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3125.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 93); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 94); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 95).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 96); (ii) an LCDR2 comprising an

amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 97); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 98).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 93); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 94); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 95), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 96); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 97); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 98).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 93); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 94); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 95), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 96); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 97); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 98).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 99); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 100) or 4035-062 (*e.g.,* SEQ ID NO: 273); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 95).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 96); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 97); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 98).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 99); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 100) or 4035-062 (*e.g.,* SEQ ID NO: 273); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 95), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 96); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 97); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 98).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 99); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 100) or 4035-062 (*e.g.,* SEQ ID NO: 273); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 95), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 96); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 97); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 4035 or 4035-062 (*e.g.,* SEQ ID NO: 98).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 101) or 4035-062 (*e.g.,* SEQ ID NO: 225). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 102) or 4035-062 (*e.g.,* SEQ ID NO: 229).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 101) or 4035-062 (*e.g.,* SEQ ID NO: 225); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 102) or 4035-062 (*e.g.,* SEQ ID NO: 229). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino

acid sequence of the VH of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 101) or 4035-062 (*e.g.,* SEQ ID NO: 225); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 102) or 4035-062 (*e.g.,* SEQ ID NO: 229).

In an embodiment, the antibody molecule is monoclonal antibody 4035. In an embodiment, monoclonal antibody 4035 is a humanized monoclonal antibody 4035 (*e.g.,* antibody 4035-062). In another embodiment, the antibody molecule is antibody 4035-062. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NOS: 220-227 or 262-265, a VL comprising the amino acid sequence of any of SEQ ID NOS: 228-234, or both.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 103); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 104); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 105).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 106); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 107); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 108).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 103); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 104); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 105), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 106); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 107); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 108).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 103); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 104); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 105), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 106); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 107); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 108).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 109); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 110); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more

than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 105).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 106); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 107); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 108).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 109); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 110); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 105), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 106); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 107); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 108).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO:

109); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 110); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 105), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 106); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 107); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 108).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 111). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 112).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 111); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 112). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 111); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 112).

In an embodiment the antibody molecule is monoclonal antibody 3934. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3934.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 112); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85,

90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 113); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 114).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 113); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 114); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 118).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 113); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 114); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 118).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 119); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 120); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 118).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 119); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 120); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 118).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 119); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 120); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 118).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 121). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 122).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues

from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 121); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 122). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 121); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 122).

In an embodiment the antibody molecule is monoclonal antibody 3833. In an embodiment, monoclonal antibody 3833 is a humanized monoclonal antibody 3833. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NO: 246-250, a VL comprising the amino acid sequence of any of SEQ ID NO: 251-253, or both.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 123); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 124); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 127); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or

3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 123); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 124); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 127); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 123); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 124); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 127); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3

amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 129); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 130); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 127); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 129); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 130); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO:45); or an LCDR3 comprising an amino acid

sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 129); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 130); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 127); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 131). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 132).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 131); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 132). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 131); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 132).

In an embodiment the antibody molecule is monoclonal antibody 3631. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3631.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions

(HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 133); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 134); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 127); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 133); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 134); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino

acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 127); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 133); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 134); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 127); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 138); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 139); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 127); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or

3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 138); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 139); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 127); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 138); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 139); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 127); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 140). In an embodiment, the antibody molecule comprises

a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 141).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 140); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 141). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 140); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 141).

In an embodiment the antibody molecule is monoclonal antibody 3732. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3732.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 11); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 142); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 143).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 144 or 146); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85,

90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 107 or 147); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 145 or 148).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 11); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 142); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 143), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 144 or 146); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 107 or 147); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 145 or 148).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 11); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 142); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 143), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 144 or 146); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 107 or 147); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 145 or 148).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions

(HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 149); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 150); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 143).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 144 or 146); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 107 or 147); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 145 or 148).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 149); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 150); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 143), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 144 or 146); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or

3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO:107 or 147); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 145 or 148).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 149); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 150); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 143), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 144 or 146); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 107 or 147); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 145 or 148).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 151). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 152 or 153).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 151); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 152 or 153). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 150); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 152 or 153).

In an embodiment the antibody molecule is monoclonal antibody 4338. In an embodiment, the antibody molecule is a humanized monoclonal antibody 4338.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 154); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 155); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 156).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116), 4540-063 (*e.g.,* SEQ ID NO: 274), or 4540-033 (*e.g.,* SEQ ID NO: 274); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157), 4540-063 (*e.g.,* SEQ ID NO: 275), or 4540-033 (*e.g.,* SEQ ID NO: 275); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 154); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 155); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino

acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 156), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116), 4540-063 (*e.g.,* SEQ ID NO: 274), or 4540-033 (*e.g.,* SEQ ID NO: 274); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157), 4540-063 (*e.g.,* SEQ ID NO: 275), or 4540-033 (*e.g.,* SEQ ID NO: 275); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises: (i) a VH comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises: an HCDR1 comprises the amino acid sequence of the HCDR1 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 154); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 155); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 156), and (ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116), 4540-063 (*e.g.,* SEQ ID NO: 274), or 4540-033 (*e.g.,* SEQ ID NO: 274); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157), 4540-063 (*e.g.,* SEQ ID NO: 275), or 4540-033 (*e.g.,* SEQ ID NO: 275); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 159), 4540-063 (*e.g.,* SEQ ID NO: 276), or 4540-033 (*e.g.,* SEQ ID NO: 159); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with,

the amino acid sequence of the HCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 160), 4540-063 (*e.g.,* SEQ ID NO: 277), or 4540-033 (*e.g.,* SEQ ID NO: 278); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 156).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116), 4540-063 (*e.g.,* SEQ ID NO: 274), or 4540-033 (*e.g.,* SEQ ID NO: 274); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157), 4540-063 (*e.g.,* SEQ ID NO: 275), or 4540-033 (*e.g.,* SEQ ID NO: 275); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 159), 4540-063 (*e.g.,* SEQ ID NO: 276), or 4540-033 (*e.g.,* SEQ ID NO: 159); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 160), 4540-063 (*e.g.,* SEQ ID NO: 277), or 4540-033 (*e.g.,* SEQ ID NO: 278); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 156), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116), 4540-063 (*e.g.,* SEQ ID NO: 274), or 4540-033 (*e.g.,* SEQ ID NO: 274); an LCDR2

comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157), 4540-063 (*e.g.,* SEQ ID NO: 275), or 4540-033 (*e.g.,* SEQ ID NO: 275); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises: (i) a VH comprising one, two, or all of the following: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 159), 4540-063 (*e.g.,* SEQ ID NO: 276), or 4540-033 (*e.g.,* SEQ ID NO: 159); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 160), 4540-063 (*e.g.,* SEQ ID NO: 277), or 4540-033 (*e.g.,* SEQ ID NO: 278); or an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 156), and (ii) a VL comprising one, two, or all of the following: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116), 4540-063 (*e.g.,* SEQ ID NO: 274), or 4540-033 (*e.g.,* SEQ ID NO: 274); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157), 4540-063 (*e.g.,* SEQ ID NO: 275), or 4540-033 (*e.g.,* SEQ ID NO: 275); or an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 4540, 4540-063, or 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4540 (*e.g.*, SEQ ID NO: 161), 4540-063 (*e.g.*, SEQ ID NO: 258), or 4540-033 (*e.g.*, SEQ ID NO: 256). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4540 (*e.g.*, SEQ ID NO: 162), 4540-063 (*e.g.*, SEQ ID NO: 261), or 4540-033 (*e.g.*, SEQ ID NO: 261).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4540 (*e.g.*, SEQ ID NO: 161), 4540-063 (*e.g.*, SEQ ID NO: 258), or 4540-033 (*e.g.*, SEQ ID NO: 256); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4540

(*e.g.*, SEQ ID NO: 162), 4540-063 (*e.g.*, SEQ ID NO: 261), or 4540-033 (*e.g.*, SEQ ID NO: 261). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 4540 (*e.g.*, SEQ ID NO: 161), 4540-063 (*e.g.*, SEQ ID NO: 258), or 4540-033 (*e.g.*, SEQ ID NO: 256); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 4540 (*e.g.*, SEQ ID NO: 162), 4540-063 (*e.g.*, SEQ ID NO: 261), or 4540-033 (*e.g.*, SEQ ID NO: 261).

In an embodiment the antibody molecule is monoclonal antibody 4540, 4540-063, or 4540-033. In an embodiment, monoclonal antibody 4540 is a humanized monoclonal antibody 4540 (*e.g.,* antibodies 4540-063 or 4540-033). In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NOS: 254-258, a VL comprising the amino acid sequence of any of SEQ ID NOS: 259-261, or both.

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 163); (ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 164); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 165).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 166); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 167); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 168).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 163); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 164); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 165), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 166); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 167); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 168).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 163); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 164); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 165), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 166); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 167); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 168).

In an embodiment, the antibody molecule comprises a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: (i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 169); (ii) an HCDR2 comprising an

amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 170); or (iii) an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 165).

In an embodiment, the antibody molecule comprises a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: (i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 166); (ii) an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 167); or (iii) an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 168).

In an embodiment, the antibody molecule comprises:

(i) a VH comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 169); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 170); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 165), and

(ii) a VL comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 166); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 167); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 168).

In an embodiment, the antibody molecule comprises: (i) a VH comprising: an HCDR1 comprising the amino acid sequence of the HCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 169); an HCDR2 comprising the amino acid sequence of the HCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 170); and an HCDR3 comprising the amino acid sequence of the HCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 165), and (ii) a VL comprising: an LCDR1 comprising the amino acid sequence of the LCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 166); an LCDR2 comprising the amino acid sequence of the LCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 167); and an LCDR3 comprising the amino acid sequence of the LCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 168).

In an embodiment, the antibody molecule comprises a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 171). In an embodiment, the antibody molecule comprises a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 172).

In an embodiment, the antibody molecule comprises: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 171); and (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 172). In an embodiment, the antibody molecule comprises: (i) a VH comprising the amino acid sequence of the VH of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 171); and (ii) a VL comprising the amino acid sequence of the VL of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 172).

In an embodiment the antibody molecule is monoclonal antibody 4237. In an embodiment, monoclonal antibody 4237 is a humanized monoclonal antibody 4237. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NOS: 235-240, a VL comprising the amino acid sequence of any of SEQ ID NOS: 241-245, or both.

In another embodiment, the anti-APRIL antibody molecule:

(i) binds, or substantially binds, to human APRIL;

(ii) inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both);

(iii) inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both); and

(iv) binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, residues within a region of human APRIL as defined in any of **Tables 3-4 or 7**, or Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule does not bind to mouse APRIL, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both), at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both), *e.g.,* at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4

nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises APRIL residues from two monomers, *e.g.,* one or more residues from monomer A and monomer B as shown in **Table 3**. In an embodiment, the antibody molecule binds, or substantially binds, to one or more APRIL residues from the C-D loop (*e.g.,* the loop connecting β-sheets C and D), the G-H loop (*e.g.,* the loop connecting β-sheets G and H), or both. In an embodiment, the antibody molecule binds, or substantially binds, to one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) residues of human APRIL from positions 105-114 and/or one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) residues of mouse APRIL from positions 96-105. In an embodiment, the antibody molecule does not bind, or binds with low affinity, to one, two or all of Asp129, Arg233, or His203 of human APRIL.

In an embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH) comprising one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of a monoclonal antibody chosen from antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3125, 2621, 4035, 4035-062, 3934, 4338, 4439, or 4237; an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of the (same) monoclonal antibody; or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of the (same) monoclonal antibody, or

(ii) a light chain variable region (VL) comprising one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of the (same) monoclonal antibody; an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of the (same) monoclonal antibody; or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of the (same) monoclonal antibody.

In an embodiment, the antibody molecule comprises one or both of:

(i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of a monoclonal antibody chosen from antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3125, 2621, 4035, 4035-062, 3934, 4338, 4439, or 4237; or

(ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of the (same) monoclonal antibody.

In an embodiment, the antibody molecule is a synthetic antibody molecule. In an embodiment, the antibody molecule is an isolated antibody molecule. In an embodiment, the antibody molecule is a humanized antibody molecule, *e.g.,* comprising one or more framework regions derived from human framework germline sequence.

In an embodiment, the antibody molecule is an IgG antibody molecule, *e.g.,* comprising a heavy chain constant region of IgG, *e.g.,* chosen from IgG1, IgG2 (*e.g.,* IgG2a), IgG3, or IgG4, *e.g.,* IgG2 or IgG4. In an embodiment, the antibody molecule is an IgG1 antibody molecule. In an embodiment, the antibody molecule is an IgG2 antibody molecule. In an embodiment, the antibody molecule comprises a light chain constant region of kappa or lambda light chain.

In an embodiment, the antibody molecule comprises an Fc region. In an embodiment, the Fc region comprises one or more mutations located at the interface between the CH2 and CH3 domains (*e.g.,* to increase the binding affinity to neonatal receptor FcRn and/or the half-life of the antibody molecule). In an embodiment, the Fc region comprises one or more mutations, *e.g.,* one or more (*e.g.,* 2, 3, 4, 6 or all) mutations chosen from T250Q, M252Y, S254T, T256E, M428L, H433K, N434F, or any combination thereof, of IgG1. In an embodiment, the Fc region comprises one or more mutations at positions 233-236 or 322 of human IgG1 or IgG2, or one or more substitutions at positions 327, 330 or 331 of human IgG4 (*e.g.,* to reduce complement-dependent cytotoxicity (CDC)). In an embodiment, the Fc region comprises one or more (*e.g.,* 2, 3, 4, 6 7 or all) mutations chosen from E233P, L234V, L235A, G236, K322A, A327G, A330S, P331S, or any combination thereof.

In an embodiment, the antibody molecule comprises two heavy chain variable regions and two light chain variable regions. In an embodiment, the antibody molecule is a Fab, F(ab')2, Fv, Fd, or a single chain Fv fragment (scFv).

In an embodiment, the anti-APRIL antibody:

a) competes for binding to APRIL with an antibody molecule comprising the heavy chain complementary determining regions (HCDR1, HCDR2 and HCDR3) and the light chain complementary determining regions (LCDR1, LCDR2 and LCDR3) of any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237, *e.g.,* as described in **Table 1 or 5**; or

b) binds, or substantially binds, to an epitope that completely or partially overlaps with the epitope of an antibody molecule comprising the heavy chain complementary determining regions (HCDR1, HCDR2 and HCDR3) and the light chain complementary determining regions (LCDR1, LCDR2 and LCDR3) of any of monoclonal antibodies 2218 (*e.g.,* SEQ ID NOS: 1-6 according to Chothia numbering or SEQ ID NOS: 3-8 according to Kabat numbering), 2419 (*e.g.,* SEQ ID NOS: 11-16 according to Chothia numbering or SEQ ID NOS: 13-18 according to Kabat numbering), 2419-0105 (*e.g.,* SEQ ID NOS: 11-13, 16, 280 and 281 according to Chothia numbering or SEQ ID NOS: 13, 16, 17 and 280-282 according to Kabat numbering), 2419-0205 (*e.g.,* SEQ ID NOS: 11-13, 16, 280 and 281 according to Chothia numbering or SEQ ID NOS: 13, 16, 17 and 280-282 according to Kabat numbering), 2419-0206 (*e.g.,* SEQ ID NOS: 11-13, 16, 280 and 285 according to Chothia numbering or SEQ ID NOS: 13, 16, 17, 280, 282 and 285 according to Kabat numbering), 2419-0406 (*e.g.,* SEQ ID NOS: 11-13, 16, 280 and 285 according to Chothia numbering or SEQ ID NOS: 13, 16, 17, 280, 285 and 290 according to Kabat numbering), 2419-0605 (*e.g.,* SEQ ID NOS: 11-13, 16, 280 and 281 according to Chothia numbering or SEQ ID NOS: 13, 16, 17 and 280-282 according to Kabat numbering), 2419-0805 (*e.g.,* SEQ ID NOS: 11-13, 16, 280 and 281 according to Chothia numbering or SEQ ID NOS: 13, 16, 17, 280, 281 and 287 according to Kabat numbering), 2419-0806 (*e.g.,* SEQ ID NOS: 11-13, 16, 280 and 285 according to Chothia numbering or SEQ ID NOS: 13, 16, 17, 280, 285 and 287 according to Kabat numbering), 2419-1204 (*e.g.,* SEQ ID NOS: 11-13, 16, 280 and 293 according to Chothia numbering or SEQ ID NOS: 13, 16, 17, 280, 282 and 293 according to Kabat numbering), 2419-1205 (*e.g.,* SEQ ID NOS: 11-13, 16, 280 and 281 according to Chothia numbering or SEQ ID NOS: 13, 16, 17 and 280-282 according to Kabat numbering), 2419-1210 (*e.g.,* SEQ ID NOS: 11-13, 16, 314 and 315 according to Chothia numbering or SEQ ID NOS: 13, 16, 17, 282, 314 and 315 according to Kabat numbering), 2419-1305 (*e.g.,* SEQ ID NOS: 11-13, 16, 280 and 281 according to Chothia numbering or SEQ ID NOS: 13, 16, 17 and 280-282 according to Kabat numbering), 2419-1306 (*e.g.,* SEQ ID NOS: 11-13, 16, 280 and 285 according to Chothia numbering or SEQ ID NOS: 13, 16, 17, 280, 282 and 285 according to Kabat numbering), 2419-1310 (*e.g.,* SEQ ID NOS: 11-13, 16, 314 and 315 according to Chothia numbering or

SEQ ID NOS: 13, 16, 17, 282, 314 and 315 according to Kabat numbering), 2419-1406 (*e.g.,* SEQ ID NOS: 11-13, 16, 280 and 285 according to Chothia numbering or SEQ ID NOS: 13, 16, 17, 280, 282 and 285 according to Kabat numbering), 2922 (*e.g.,* SEQ ID NOS: 21 and 32-36 according to Chothia numbering or SEQ ID NOS: 33-38 according to Kabat numbering), 3327 (*e.g.,* SEQ ID NOS: 51-56 according to Chothia numbering or SEQ ID NOS: 53-58 according to Kabat numbering), 3530 (*e.g.,* SEQ ID NOS: 61-63, 67, 45 and 46 according to Chothia numbering or SEQ ID NOS: 63-65, 67, 45 and 46 according to Kabat numbering), 3525 (*e.g.,* SEQ ID NOS: 44-46 and 61-63 according to Chothia numbering or SEQ ID NOS: 44-46 and 63-65 according to Kabat numbering), 3125 (*e.g.,* SEQ ID NOS: 11 and 42-46 according to Chothia numbering or SEQ ID NOS: 43-48 according to Kabat number), 2621 (*e.g.,* SEQ ID NOS: 21-26 according to Chothia numbering or SEQ ID NOS: 23-28 according to Kabat numbering), 4035 (*e.g.,* SEQ ID NOS: 93-98 according to Chothia numbering or SEQ ID NOS: 95-100 according to Kabat numbering), 4035-062 (*e.g.,* SEQ ID NOS: 93-98 according to Chothia numbering or SEQ ID NOS: 95-99 and 273 according to Kabat numbering), 3934 (*e.g.,* SEQ ID NOS: 103-108 according to Chothia numbering or SEQ ID NOS: 105-110 according to Kabat numbering), 3833 (*e.g.,* SEQ ID NOS: 113-118 according to Chothia numbering or SEQ ID NOS: 115-120 according to Kabat numbering), 3631 (*e.g.,* SEQ ID NOS: 123-128 according to Chothia numbering or SEQ ID NOS: 125-130 according to Kabat numbering), 3732 (*e.g.,* SEQ ID NOS: 127 and 133-137 according to Chothia numbering or SEQ ID NOS: 127 and 135-139 according to Kabat numbering), 4338 (*e.g.,* SEQ ID NOS: 11, 107 and 142-145, or SEQ ID NO: 11, 142, 143 and 146-148 according to Chothia numbering; or SEQ ID NOS: 107, 143-145 and 149-150, or SEQ ID NOS: 143 and 146-150 according to Kabat numbering), 4540 (*e.g.,* SEQ ID NOS: 116 and 154-158 according to Chothia numbering or SEQ ID NOS: 116 and 156-160 according to Kabat numbering), 4540-063 (*e.g.,* SEQ ID NOS: 154-156, 158, 274 and 275 according to Chothia numbering or SEQ ID NOS: 156, 158 and 274-277 according to Kabat numbering), 4540-033 (*e.g.,* SEQ ID NOS: 154-156, 158, 274 and 275 according to Chothia numbering or SEQ ID NOS: 156, 158, 159, 274, 275 and 278 according to Kabat numbering), 4439 (*e.g.,* SEQ ID NOS: 146-148 and 266-268 according to Chothia numbering or SEQ ID NOS: 146-148 and 269-270 according to Kabat numbering), or 4237 (*e.g.,* SEQ ID NOS: 163-168 according to Chothia numbering or SEQ ID NOS: 165-170 according to Kabat numbering), *e.g.,* as described in **Table 1 or 5**.

In an embodiment, the antibody molecule is a synthetic antibody molecule. In an embodiment, the antibody molecule is an isolated antibody molecule.

In an embodiment, the antibody molecule competes for binding with two, three, four, five, six, seven, eight, nine, ten, or more of the antibody molecules that comprise the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-

1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that completely or partially overlaps with the epitopes of two, three, four, five, six, seven, eight, nine, ten, or more of the antibody molecules that comprise the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237.

In an embodiment, the antibody molecule that comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 3934, 3833, 3631, 3732, 4338, 4540, 4439, or 4237 comprises a heavy chain variable region and a light chain variable region of any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 3934, 3833, 3631, 3732, 4338, 4540, 4439, or 4237.

In an embodiment, the antibody molecule that comprises the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of any of monoclonal antibodies 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 3934, 3833, 3631, 3732, 4338, 4540, 4439, or 4237 is monoclonal antibody 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 3934, 3833, 3631, 3732, 4338, 4540, 4439, or 4237.

In an embodiment, the antibody molecule is a humanized monoclonal antibody 2218, 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, 2419-1406, 2922, 3327, 3530, 3525, 3125, 2621, 4035, 4035-062, 3934, 3833, 3631, 3732, 4338, 4540, 4540-063, 4540-033, 4439, or 4237. In an embodiment, the antibody molecule comprises a heavy chain variable region (VH) having an amino acid sequence described in **Table 1 or 5**. In an embodiment, the antibody molecule comprises a light chain variable region (VL) having an amino acid sequence described in **Table 1 or 5**. In antibody molecule comprises a heavy chain variable region (VH) having an amino acid sequence described in **Table 1 or 5** and a light chain variable region (VL) having an amino acid sequence described in **Table 1 or 5**.

In an embodiment, the antibody molecule competes for binding to human APRIL, mouse APRIL, or both. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 100 nM, *e.g.,* between 0.001 nM and 50 nM, between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, *e.g.,* between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule binds, or substantially binds, to mouse APRIL at an EC_{50} of 100 nM or less, *e.g.,* 80 nM or less, 60 nM or less, 40 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 100 nM, *e.g.,* between 0.001 nM and 50 nM, between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, *e.g.,* between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule does not bind, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both), inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both), or both.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both), at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between

0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In an embodiment, binding of the antibody molecule to APRIL (*e.g.,* human APRIL) inhibits, or substantially inhibits, the binding of the CRD2 domain of TACI (*e.g.,* human TACI) to APRIL (*e.g.,* human APRIL).

In an embodiment, binding of the antibody molecule to human APRIL inhibits, or substantially inhibits, the binding of human TACI, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all of the human APRIL residues from **Table 3**. In an embodiment, binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or all of the human APRIL residues from **Table 4**. In an embodiment, binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all of the human APRIL residues from **Table 7**. In an embodiment, binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both).

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both), *e.g.,* at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule does not inhibit, or does not substantially inhibit, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both).

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, residues within a region of human APRIL as defined in any of **Tables 3-4 or 7**, or Table 8 of International Application

Publication No. WO2017/091683. In an embodiment, the antibody molecule binds, or substantially binds, to a conformational epitope.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, residues within a region of human APRIL as defined in **Table 3**. In an embodiment, the antibody molecule binds to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all of the human APRIL residues from **Table 3**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises APRIL residues from two monomers, *e.g.,* one or more residues from monomer A and monomer B as shown in **Table 3**.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or more, residues within a region of human APRIL as defined in **Table 4**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises consists of one or more, *e.g.,*2, 3, 4, 5, 6, 7, 8, 9, 10, or all of the APRIL residues from **Table 4**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises one or more APRIL residues from the C-D loop (*e.g.,* the loop connecting β-sheets C and D), the G-H loop (*e.g.,* the loop connecting β-sheets G and H), or both.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all, residues within a region of human APRIL as defined in **Table 7**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all, of the human APRIL residues from **Table 7**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from **Table 7**.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, residues within a region of human APRIL as defined in Table 8 of International Application Publication No. WO2017/091683. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more (*e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, or all) residues of human APRIL from positions 105-114 and/or one or more (*e.g.,* 2, 3, 4,

5, 6, 7, 8, 9, or all) residues of mouse APRIL from positions 96-105. In an embodiment, the antibody molecule does not bind, or does not substantially bind, to one, two or all of Asp129, Arg233, or His203 of human APRIL.

In an embodiment, the antibody molecule is an IgG antibody molecule, *e.g.,* comprising a heavy chain constant region of IgG, *e.g.,* chosen from IgG1, IgG2 (*e.g.,* IgG2a), IgG3, or IgG4, *e.g.,* IgG2 or IgG4. In an embodiment, the antibody molecule is an IgG1 antibody molecule. In another embodiment, the antibody molecule is an IgG2 antibody molecule. In an embodiment, the antibody molecule comprises a light chain constant region of kappa or lambda light chain.

In an embodiment, the antibody molecule comprises an Fc region. In an embodiment, the Fc region comprises one or more mutations located at the interface between the CH2 and CH3 domains (*e.g.,* to increase the binding affinity to neonatal receptor FcRn and/or the half-life of the antibody molecule). In an embodiment, the Fc region comprises one or more mutations, *e.g.,* one or more (*e.g.,* 2, 3, 4, 6 or all) mutations chosen from T250Q, M252Y, S254T, T256E, M428L, H433K, N434F, or any combination thereof, of IgG1. In an embodiment, the Fc region comprises one or more mutations at positions 233-236 or 322 of human IgG1 or IgG2, or one or more substitutions at positions 327, 330 or 331 of human IgG4 (*e.g.,* to reduce complement-dependent cytotoxicity (CDC)). In an embodiment, the Fc region comprises one or more (*e.g.,* 2, 3, 4, 6 7 or all) mutations chosen from E233P, L234V, L235A, G236, K322A, A327G, A330S, P331S, or any combination thereof.

In an embodiment, the antibody molecule is a humanized antibody molecule, *e.g.,* comprising one or more framework regions derived from human framework germline sequence. In an embodiment, the antibody molecule comprises two heavy chain variable regions and two light chain variable regions. In an embodiment, the antibody molecule is a Fab, F(ab')2, Fv, Fd, or a single chain Fv fragment (scFv).

In an embodiment, the anti-APRIL antibody molecule is a synthetic, isolated, or humanized anti-APRIL antibody molecule described herein.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 1 or 7); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 2 or 8); or an HCDR3 comprising an

amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 3), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 4); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 5); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 6).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 9); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 2218 (*e.g.,* SEQ ID NO: 10).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 71 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 72 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 2218. In an embodiment, monoclonal antibody 2218 is humanized monoclonal antibody 2218. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NO: 190-201, a VL comprising the amino acid sequence of any of SEQ ID NO: 202-208, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between

0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 1 nM or less, *e.g.,* about 0.6 nM. In an embodiment, the antibody molecule does not bind to mouse APRIL, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human TACI at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 1 nM or less, *e.g.,* about 0.74 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 0.5 nM or less, *e.g.,* about 0.22 nM.

In an embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence of G-Y-T-F-T-D-Y (SEQ ID NO: 11); an HCDR2 comprising an amino acid sequence of Y-P-

L-R-G-S (SEQ ID NO: 12); or an HCCDR3 comprising an amino acid sequence of H-G-A-Y-Y-S-N-A-F-D-Y (SEQ ID NO: 13), or

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence of X1-X2-S-X4-S-V-D-N-D-G-I-R-F-X14-H (SEQ ID NO: 327), wherein X1 is R or K; X2 is A or S; X4 is E or Q; and X14 is M or L; an LCDR2 comprising an amino acid sequence of R-A-S-X4-X5-X6-X7 (SEQ ID NO: 328), wherein X4 is N or T; X5 is L or R; X6 is E or A; and X7 is S or T; or an LCDR3 comprising an amino acid sequence of Q-Q-S-N-K-D-P-Y-T (SEQ ID NO: 16).

In another embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence of D-Y-T-I-H (SEQ ID NO: 17); an HCDR2 comprising an amino acid sequence of W-I-Y-P-L-R-G-S-I-N-Y-X12-X13-X14-F-X16-X17 (SEQ ID NO: 329), wherein X12 is N, S, or A, X13 is E, P, or Q; X14 is K or S; X16 is K or Q; and X17 is D or G; or an HCCDR3 comprising an amino acid sequence of H-G-A-Y-Y-S-N-A-F-D-Y (SEQ ID NO: 13), or

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence of X1-X2-S-X4-S-V-D-N-D-G-I-R-F-X14-H (SEQ ID NO: 327), wherein X1 is R or K; X2 is A or S; X4 is E or Q; and X14 is M or L; an LCDR2 comprising an amino acid sequence of R-A-S-X4-X5-X6-X7 (SEQ ID NO: 328), wherein X4 is N or T; X5 is L or R; X6 is E or A; and X7 is S or T; or an LCDR3 comprising an amino acid sequence of Q-Q-S-N-K-D-P-Y-T (SEQ ID NO: 16).

In an embodiment, the antibody molecule is any of antibodies 2419, 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, or 2419-1406.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM,

between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 0.01 nM or less, *e.g.,* about 0.001-0.005 nM or 0.002-0.004 nM, *e.g.,* about 0.001, 0.002, 0.003, 0.004, or 0.005 nM. In an embodiment, the antibody molecule does not bind to mouse APRIL, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human TACI at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 0.5 nM or less, *e.g.,* about 0.1-0.5 nM or 0.2-0.4 nM, *e.g.,* about 0.1, 0.2, 0.3, 0.4, or 0.5 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 0.5 nM or less, *e.g.,* about 0.1-0.5 nM or 0.2-0.4 nM, *e.g.,* about 0.1, 0.2, 0.3, 0.4, or 0.5 nM.

In another embodiment, the antibody molecule comprises (i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence

of the HCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 11 or 17); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 12 or 18); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 13), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 14); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 15); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 16).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 19); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 2419 (*e.g.,* SEQ ID NO: 20).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 73 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 74 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 2419. In an embodiment, monoclonal antibody 2419 is humanized monoclonal antibody 2419. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NOS: 209-214, a VL comprising the amino acid sequence of any of SEQ ID NOS: 215-219, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less,

0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 1 nM or less, *e.g.,* about 0.8 nM, about 0.003 nM, or about 0.002 nM. In an embodiment, the antibody molecule does not bind, or bind to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 500 nM or more.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human TACI, at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 1 nM or less, *e.g.,* about 0.74 nM, about 0.4 nM, 0.3 nM, or 0.2 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA, at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 5 nM or less, *e.g.,* about 4 nM, about 2 nM, or about 1 nM, or 0.5 nM or less, *e.g.,* about 0.22 nM, about 1 nM, about 0.7 nM, about 0.3 nM, about 0.2 nM, or about 0.1 nM.

In another embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of a 2419-related antibody (*e.g.,* SEQ ID NO: 11 or 17); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of the 2419-related antibody (*e.g.,* SEQ ID NOS: 12, 282, 287, or 290); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of the 2419-related antibody (*e.g.,* SEQ ID NO: 13), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of the 2419-related antibody (*e.g.,* SEQ ID NOS: 280 or 314); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of the 2419-related antibody (*e.g.,* SEQ ID NOS: 281, 285, 293, or 315); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of the 2419-related antibody (*e.g.,* SEQ ID NO: 16).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of the 2419-related antibody (*e.g.,* SEQ ID NOS: 283, 288, 289, 291, 292, 294, 296, or 317); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of the 2419-related antibody (*e.g.,* SEQ ID NOS: 284, 286, 295, or 316).

In an embodiment, the antibody molecule comprises a VH encoded by the VH nucleotide sequence of the 2419-related antibody (*e.g.,* SEQ ID NOS: 304, 307, 308, 309, 310, 311, 313, or 319) (or a nucleotide sequence substantially identical thereto) or a VL encoded by the VL nucleotide sequence of

the 2419-related antibody (*e.g.,* SEQ ID NOS: 305, 306, 312, or 318) (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the 2419-related antibody molecule is chosen from antibodies 2419-0105, 2419-0205, 2419-0206, 2419-0406, 2419-0605, 2419-0805, 2419-0806, 2419-1204, 2419-1205, 2419-1210, 2419-1305, 2419-1306, 2419-1310, or 2419-1406. In an embodiment, the 2419-related antibody is humanized antibody molecule. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NOS: 209-214, 283, 288, 289, 291, 292, 294, 296, or 317, a VL comprising the amino acid sequence of any of SEQ ID NOS: 215-219, 284, 286, 295, or 316, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, *e.g.,* between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 1 nM or less, *e.g.,* about 0.8 nM, about 0.003 nM, or about 0.002 nM.

In an embodiment, the antibody molecule does not bind, or bind to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 500 nM or more.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human TACI, at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 1 nM or less, *e.g.,* about 0.74 nM, about 0.4 nM, 0.3 nM, or 0.2 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA, at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 5 nM or less, *e.g.,* about 4 nM, about 2 nM, or about 1 nM, or 0.5 nM or less, *e.g.,* about 0.22 nM, about 1 nM, about 0.7 nM, about 0.3 nM, about 0.2 nM, or about 0.1 nM.

In another embodiment, the antibody molecule comprises (i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 21 or 37); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 32 or 38); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 33), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2922 (*e.g.*, SEQ ID NO: 34); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2922 (*e.g.*, SEQ ID NO: 35); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2922 (*e.g.*, SEQ ID NO: 36).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 39); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 2922 (*e.g.,* SEQ ID NO: 40).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 77 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 78 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 2922. In an embodiment, the antibody molecule is humanized monoclonal antibody 2922.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 5 nM or less, *e.g.,* about 3.3 nM. In an embodiment, the antibody molecule does not bind, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human TACI, at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as

determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 50 nM or less, *e.g.,* about 31.64 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA, at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the IC_{50} is 50 nM or less. In an embodiment, the antibody molecule inhibits binding of human TACI to human BCMA at an IC_{50} of 25 nM or less, *e.g.,* about 21.96 nM.

In another embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 51 or 57); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 52 or 58); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 53), and

(ii) a light chain variable region (VH), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 54); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 55); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 56).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 59); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3327 (*e.g.,* SEQ ID NO: 60).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 81 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 82 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 3327. In an embodiment, the antibody molecule is humanized antibody 3327.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 100 nM or less, *e.g.,* 80 nM or less, 60 nM or less, 40 nM or less, 20 nM or less, 10 nM or less, 9 nM or less 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 100 nM, *e.g.,* between 0.001 nM and 50 nM, between 0.01 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM or between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule does not bind, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human TACI, at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and

1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 5 nM or less, *e.g.,* about 3.16 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA, at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the IC_{50} is 50 nM or less. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 5 nM or less, *e.g.,* about 2.35 nM.

In another embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 93 or 99); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 94 or 100); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 95), and

(ii) a light chain variable region (VH), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 96); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 97); or an LCDR3 comprising an amino acid

sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 98).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 101); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4035 (*e.g.,* SEQ ID NO: 102).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 173 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 174 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 4035. In an embodiment, monoclonal antibody 4035 is humanized monoclonal antibody 4035. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NO: 220-227 or 262-265, a VL comprising the amino acid sequence of any of SEQ ID NO: 228-234, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 0.01 nM or less, *e.g.,* about 0.001-0.002 nM. In an embodiment, the antibody molecule does not bind, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human

TACI, at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 5 nM or less, *e.g.,* about 3.16 nM, or about 0.1-0.5 nM or 0.2-0.4 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA, at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 5 nM or less, *e.g.,* about 2.35 nM, or about 0.1-0.5 nM or 0.1-0.2 nM.

In another embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4035-062 (*e.g.,* SEQ ID NO: 93 or 99); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4035-062 (*e.g.,* SEQ ID NO: 94 or 273); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4035-062 (*e.g.,* SEQ ID NO: 95), and

(ii) a light chain variable region (VH), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain

variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4035-062 (*e.g.,* SEQ ID NO: 96); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4035-062 (*e.g.,* SEQ ID NO: 97); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4035-062 (*e.g.,* SEQ ID NO: 98).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4035-062 (*e.g.,* SEQ ID NO: 225); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4035-062 (*e.g.,* SEQ ID NO: 229).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 299 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 300 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 4035-062.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 0.01 nM or less, *e.g.,* about 0.001-0.002 nM. In an embodiment, the antibody molecule does not bind, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human TACI, at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 1 nM or less, *e.g.,* about 0.1-0.5 nM or 0.2-0.4 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA, at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 1 nM or less, *e.g.,* about 0.1-0.5 nM or 0.1-0.2 nM.

In another embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising the amino acid sequence of I-Y-D-V-H (SEQ ID NO: 99); an HCDR2 comprising the amino acid sequence of V-I-W-S-D-G-S-T-D-Y-N-X12-X13-X14-X15-S (SEQ ID NO: 342), X12 is A or P, X13 is A or S, X14 is F or L, and X15 is I or K; or an HCDR3 comprising the amino acid sequence of N-W-V-D-Q-A-W-F-A-Y (SEQ ID NO: 95), and

(ii) a light chain variable region (VH), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising the amino acid sequence of R-A-S-K-N-I-Y-S-Y-L-A (SEQ ID NO: 96); an LCDR2 comprising the amino acid sequence

of N-A-K-T-L-P-E (SEQ ID NO: 97); or an LCDR3 comprising the amino acid sequence of Q-H-H-Y-G-T-P-L-T (SEQ ID NO: 98).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of SEQ ID NO: 101 or 225; or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of SEQ ID NO: 102 or 229.

In an embodiment, the antibody molecule is monoclonal antibody 4035. In an embodiment, the antibody molecule is monoclonal antibody 4035-062.

In another embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 103 or 109); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 104 or 110); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 105), and

(ii) a light chain variable region (VH), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 106); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 107); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 108).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 111); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3934 (*e.g.,* SEQ ID NO: 112).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 175 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 176 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 3934. In an embodiment, the antibody molecule is humanized monoclonal antibody 3934.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule does not bind, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human TACI, at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as

determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 5 nM or less, *e.g.,* about 3.16 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA, at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 5 nM or less, *e.g.,* about 2.35 nM.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 11 or 149); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 142 or 150); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 143), and

(ii) a light chain variable region (VH), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 144 or 146); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 107 or 147); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or

has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 145 or 148).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 151); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4338 (*e.g.,* SEQ ID NO: 152 or 153).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 183 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 184 or 185 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 4338. In an embodiment, the antibody molecule is humanized monoclonal antibody 4338.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule does not bind, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human TACI, at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM,

between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 5 nM or less, *e.g.,* about 3.16 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA, at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 5 nM or less, *e.g.,* about 2.35 nM.

In another embodiment, the antibody molecule comprises (i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 163 or 169); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 164 or 170); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 165), and

(ii) a light chain variable region (VH), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 166); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 167); or an LCDR3 comprising an amino acid

sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 168).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 171); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4237 (*e.g.,* SEQ ID NO: 172).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 188 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 189 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 4237. In an embodiment, monoclonal antibody 4237 is humanized monoclonal antibody 4237. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NO: 235-240, a VL comprising the amino acid sequence of any of SEQ ID NO: 241-245, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule does not bind, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human TACI, at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM

or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 5 nM or less, *e.g.,* about 3.16 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA, at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 5 nM or less, *e.g.,* about 2.35 nM.

In another embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence of G-Y-X3-X4-T-X6-X7-Y (SEQ ID NO: 330), wherein X3 is S or T; X4 is I or F; X6 is S or absent; and X7 is G, D or S; an HCDR2 comprising an amino acid sequence of X3-X4-X5-X6-X7-X8 (SEQ ID NO: 331), wherein X3 is absent, N or Y; X4 is S or P, X5 is Y, L or R; X6 is D, N or R; X7 is G or S; and X8 is Y, D or S; or an HCCDR3 comprising an amino acid sequence of X1-X2-X3-X4-Y-X6-X7-X8-X9-F-X11-X12 (SEQ ID NO: 332), wherein X1 is Y, E or H; X2 is absent or G; X3 is Y, D or A; X4 is D, G or Y; X6 is E, absent or D; X7 is D, Y, S or K; X8 is W, N or R; X9 is Y, A or G; X11 is G or D; and X12 is V or Y, or

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence of X1-A-S-X4-S-V-X7-X8-X9-G-X11-X12-X13-X14-X15 (SEQ ID NO: 333), wherein X1 is R or K; X4 is E or Q; X7 is D or S; X8 is N, F, I or N; X9 is Y, A, I or D; X11 is I or T; X12 is S, N or R;

X13 is F, L or S; X14 is M or I; and X15 is N or H; an LCDR2 comprising an amino acid sequence of X1-A-S-N-X5-X6-X7 (SEQ ID NO: 334), wherein X1 is A, R or H; X5 is Q or L; X6 is G or E; and X7 is S, P or T; or an LCDR3 comprising an amino acid sequence of X1-Q-S-X4-X5-X6-P-X8-T (SEQ ID NO: 335), wherein X1 is Q or L; X4 is K, R or N; X5 is E or K; X6 is V, Y, I or D; and X8 is R, W or Y.

In an embodiment, the antibody molecule is any of monoclonal antibodies 2218, 2419, 2922, or 3327.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule does not bind, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human TACI, at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, or 0.1 nM or less, *e.g.,* between 0.1 and 50 nM, *e.g.,* between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA, at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In another embodiment, the antibody molecule comprises one or both of:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence of X6-X7-Y-X9-X10-X11 (SEQ ID NO: 336), wherein X6 is S or absent; X7 is G, D or S; X9 is Y, F, T or D; X10 is W, M, I or V; and X11 is N, H or F; an HCDR2 comprising an amino acid sequence of X1-I-X3-X4-X5-X6-X7-X8-X9-X10-Y-N-X13-X14-X15-K-X17 (SEQ ID NO: 337), wherein X1 is Y, R or W; X3 is absent, N or Y; X4 is S or P, X5 is Y, L or R; X6 is D, N or R; X7 is G or S; X8 is Y, D or S; X9 is N, T or I; X10 is N, F or K; X13 is P, Q or E; X14 is S or K; X15 is L or F; and X17 is N, G or D; or an HCCDR3 comprising an amino acid sequence of X1-X2-X3-X4-Y-X6-X7-X8-X9-F-X11-X12 (SEQ ID NO: 332), wherein X1 is Y, E or H; X2 is absent or G; X3 is Y, D or A; X4 is D, G or Y; X6 is E, absent or D; X7 is D, Y, S or K; X8 is W, N or R; X9 is Y, A or G; X11 is G or D; and X12 is V or Y, or

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence of X1-A-S-X4-S-V-X7-X8-X9-G-X11-X12-X13-X14-X15 (SEQ ID NO: 333), wherein X1 is R or K; X4 is E or Q; X7 is D or S; X8 is N, F, I or N; X9 is Y, A, I or D; X11 is I or T; X12 is S, N or R; X13 is F, L or S; X14 is M or I; and X15 is N or H; an LCDR2 comprising an amino acid sequence of X1-A-S-N-X5-X6-X7 (SEQ ID NO: 334), wherein X1 is A, R or H; X5 is Q or L; X6 is G or E; and X7 is S, P or T; or an LCDR3 comprising an amino acid sequence of X1-Q-S-X4-X5-X6-P-X8-T (SEQ ID NO: 335), wherein X1 is Q or L; X4 is K, R or N; X5 is E or K; X6 is V, Y, I or D; and X8 is R, W or Y.

In an embodiment, the antibody molecule is any of monoclonal antibodies 2218, 2419, 2922, or 3327. In an embodiment, the antibody molecule is a humanized monoclonal antibody 2218, 2419, 2922, or 3327.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM,

between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule does not bind, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human TACI, at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of human APRIL to human BCMA, at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In another embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 61 or 64); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 62 or 65); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85,

90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 63), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 67); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 66); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3530 (*e.g.,* SEQ ID NO: 70).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 83 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 84 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 3530. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3530.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL, mouse APRIL, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM,

between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 5 nM or less, *e.g.,* about 2.7 nM.

In an embodiment, the antibody molecule binds, or substantially binds, to mouse APRIL at an EC_{50} of 100 nM or less, *e.g.,* 80 nM or less, 60 nM or less, 40 nM or less, 20 nM or less, 10 nM or less, 9 nM or less 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 100 nM, *e.g.,* between 0.001 nM and 50 nM, between 0.01 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM or between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both), at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 5 nM or less, *e.g.,* about 4.95 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both), at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the

antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 1 nM or less, *e.g.,* about 0.68 nM.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 61 or 64); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 62 or 65); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 63), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 66); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3525 (*e.g.,* SEQ ID NO: 50).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 83 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 80 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 3525. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3525.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL, mouse APRIL, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 5 nM or less, *e.g.,* about 2.5 nM.

In an embodiment, the antibody molecule binds, or substantially binds, to mouse APRIL at an EC_{50} of 100 nM or less, *e.g.,* 80 nM or less, 60 nM or less, 40 nM or less, 20 nM or less, 10 nM or less, 9 nM or less 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 100 nM, *e.g.,* between 0.001 nM and 50 nM, between 0.01 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM or between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both), at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM,

between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 5 nM or less, *e.g.,* about 4.05 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both), at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 1 nM or less, *e.g.,* about 0.85 nM.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 113 or 119); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 114 or 120); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 115), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 116); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino

acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 117); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 118).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 121); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3833 (*e.g.,* SEQ ID NO: 122).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 177 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 178 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 3833. In an embodiment, monoclonal antibody 3833 is a humanized monoclonal antibody 3833. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NO: 246-250, a VL comprising the amino acid sequence of any of SEQ ID NO: 251-253, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL, mouse APRIL, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 5 nM or less, *e.g.,* about 2.5 nM.

In an embodiment, the antibody molecule binds, or substantially binds, to mouse APRIL at an EC_{50} of 100 nM or less, *e.g.,* 80 nM or less, 60 nM or less, 40 nM or less, 20 nM or less, 10 nM or less, 9

nM or less 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 100 nM, *e.g.,* between 0.001 nM and 50 nM, between 0.01 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM or between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both), at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 5 nM or less, *e.g.,* about 4.05 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both), at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 1 nM or less, *e.g.,* about 0.85 nM.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy

chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 123 or 129); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 124 or 130); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 125), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 126); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 127); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 128).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 131); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3631 (*e.g.,* SEQ ID NO: 132).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 179 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 180 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 3631. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3631.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL, mouse APRIL, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 5 nM or less, *e.g.,* about 2.5 nM.

In an embodiment, the antibody molecule binds, or substantially binds, to mouse APRIL at an EC_{50} of 100 nM or less, *e.g.,* 80 nM or less, 60 nM or less, 40 nM or less, 20 nM or less, 10 nM or less, 9 nM or less 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 100 nM, *e.g.,* between 0.001 nM and 50 nM, between 0.01 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM or between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both. In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both), at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 5 nM or less, *e.g.,* about 4.05 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both), at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 1 nM or less, *e.g.,* about 0.85 nM.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 133 or 138); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 134 or 139); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 135), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 136); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 127); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or

100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 137).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 140); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3732 (*e.g.,* SEQ ID NO: 141).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 181 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 182 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 3732. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3732.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL, mouse APRIL, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 5 nM or less, *e.g.,* about 2.5 nM.

In an embodiment, the antibody molecule binds, or substantially binds, to mouse APRIL at an EC_{50} of 100 nM or less, *e.g.,* 80 nM or less, 60 nM or less, 40 nM or less, 20 nM or less, 10 nM or less, 9 nM or less 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 100 nM, *e.g.,* between 0.001 nM and 50 nM, between 0.01 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM or between 1 nM and 5 nM, between 0.001

nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both), at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 5 nM or less, *e.g.,* about 4.05 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both), at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 1 nM or less, *e.g.,* about 0.85 nM.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 154 or 159); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid

sequence of the HCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 155 or 160); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 156), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 116); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 157); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 161); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4540 (*e.g.,* SEQ ID NO: 162).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 186 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 187 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 4540. In an embodiment, monoclonal antibody 4540 is a humanized monoclonal antibody 4540. In an embodiment, the antibody molecule comprises a VH comprising the amino acid sequence of any of SEQ ID NO: 254-258, a VL comprising the amino acid sequence of any of SEQ ID NO: 259-261, or both.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid

sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4540-063 (*e.g.,* SEQ ID NO: 154 or 276); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4540-063 (*e.g.,* SEQ ID NO: 155 or 277); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4540-063 (*e.g.,* SEQ ID NO: 156), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4540-063 (*e.g.,* SEQ ID NO: 274); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4540-063 (*e.g.,* SEQ ID NO: 275); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4540-063 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4540-063 (*e.g.,* SEQ ID NO: 258); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4540-063 (*e.g.,* SEQ ID NO: 261).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 301 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 302 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 4540-063.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy

chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4540-033 (*e.g.,* SEQ ID NO: 154 or 159); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4540-033 (*e.g.,* SEQ ID NO: 155 or 278); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4540-033 (*e.g.,* SEQ ID NO: 156), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4540-033 (*e.g.,* SEQ ID NO: 274); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4540-033 (*e.g.,* SEQ ID NO: 275); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4540-033 (*e.g.,* SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4540-033 (*e.g.,* SEQ ID NO: 256); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4540-033 (*e.g.,* SEQ ID NO: 261).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 303 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 302 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 4540-033.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the VH comprises one, two, or all of the following: an HCDR1 comprising the amino acid sequence of D-Y-Y-X4-N (SEQ ID NO: 343), where X4 is I or M; an HCDR2 comprising the amino acid sequence of W-I-F-P-G-S-G-S-T-Y-Y-X12-X13-K-X15-X16-G, where X12 is N or A, X13 is E or Q, X15 is F or L, and X16 is K or Q (SEQ ID NO: 344); or an HCDR3 comprising the amino acid sequence of G-D-S-G-R-A-M-D-Y (SEQ ID NO: 156), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the VL comprises one, two, or all of the following: an LCDR1 comprising the amino acid sequence of X1-A-S-Q-D-I-N-K-Y-I-A, wherein X1 is K or Q (SEQ ID NO: 345); an LCDR2 comprising the amino acid sequence of Y-T-S-T-L-X6-X7, wherein X_6 is Q or E, and X7 is S or T (SEQ ID NO: 346); or an LCDR3 comprising the amino acid sequence of L-Q-Y-D-N-L-L-T (SEQ ID NO: 158).

In another embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the VH comprises one, two, or all of the following: an HCDR1 comprising the amino acid sequence of G-Y-T-F-A-D-Y (SEQ ID NO: 154); an HCDR2 comprising the amino acid sequence of F-P-G-S-G-S (SEQ ID NO: 155); or an HCDR3 comprising the amino acid sequence of G-D-S-G-R-A-M-D-Y (SEQ ID NO: 156), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the VL comprises one, two, or all of the following: an LCDR1 comprising the amino acid sequence of X1-A-S-Q-D-I-N-K-Y-I-A, wherein X1 is K or Q (SEQ ID NO: 345); an LCDR2 comprising the amino acid sequence of Y-T-S-T-L-X6-X7 (SEQ ID NO: 346), wherein X6 is Q or E, and X7 is S or T; or an LCDR3 comprising the amino acid sequence of L-Q-Y-D-N-L-L-T (SEQ ID NO: 158).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of SEQ ID NOS: 161, 256 or 258; or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of SEQ ID NO: 162 or 261.

In an embodiment, the antibody molecule is monoclonal antibody 4540. In another embodiment, the antibody molecule is monoclonal antibody 4540-063. In yet another embodiment, the antibody molecule is monoclonal antibody 4540-033.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL, mouse APRIL, or both.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, or 0.1 nM or less, *e.g.,* between 0.1 nM and 20 nM, *e.g.,* between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 5 nM or less, *e.g.,* about 2.5 nM.

In an embodiment, the antibody molecule binds, or substantially binds, to mouse APRIL at an EC_{50} of 100 nM or less, *e.g.,* 80 nM or less, 60 nM or less, 40 nM or less, 20 nM or less, 10 nM or less, 9 nM or less or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, or 0.1 nM or less, *e.g.,* between 0.1 nM and 20 nM, *e.g.,* between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), BCMA (*e.g.,* human BCMA), or both.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to TACI (*e.g.,* human TACI, mouse TACI, or both), at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 5 nM or less, *e.g.,* about 4.05 nM.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL, mouse APRIL, or both) to BCMA (*e.g.,* human BCMA, mouse BCMA, or both), at an IC_{50} of 200 nM or less, 150 nM or less, 100 nM or less, 50 nM or less, 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or

less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human BCMA at an IC_{50} of 1 nM or less, *e.g.,* about 0.85 nM.

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 21 or 27); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 22 or 28); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 23), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 24); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 25); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 26).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid

sequence of the VH of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 29); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 2621 (*e.g.,* SEQ ID NO: 30).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 75 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 76 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 2621. In an embodiment, the antibody molecule is a humanized monoclonal antibody 2621.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 1 nM or less, *e.g.,* about 0.7 nM. In an embodiment, the antibody molecule does not bind, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI). In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of about 1 nM or less.

In an embodiment, the antibody molecule does not inhibit, or does not substantially inhibit, binding of APRIL (*e.g.,* human APRIL) to BCMA (*e.g.,* human BCMA).

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 11 or 47); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 42 or 48); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 43), and

(ii) a light chain variable region (VH), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 44); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 45); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 46).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 49); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 3125 (*e.g.,* SEQ ID NO: 50).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 79 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 80 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 3125. In an embodiment, the antibody molecule is a humanized monoclonal antibody 3125.

In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL. In an embodiment, the antibody molecule binds, or substantially binds, to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, 0.01 nM or less, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, *e.g.,* between 0.001 nM and 20 nM, *e.g.,* between 0.01 nM and 20 nM, between 0.1 nM and 20 nM, between 0.1 nM and 10 nM, between 0.5 nM and 5 nM, between 1 nM and 5 nM, between 0.001 nM and 0.1 nM, between 0.001 nM and 0.01 nM, between 0.001 nM and 0.005 nM, between 0.01 nM and 0.05 nM, or between 0.01 nM and 0.1 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule binds to human APRIL at an EC_{50} of 20 nM or less, *e.g.,* about 13 nM. In an embodiment, the antibody molecule does not bind, or binds to mouse APRIL with low affinity, *e.g.,* at an EC_{50} of 1000 nM or more, *e.g.,* 2000 nM or more, *e.g.,* as determined by a method described herein.

In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI). In an embodiment, the antibody molecule inhibits, or substantially inhibits, binding of APRIL (*e.g.,* human APRIL) to TACI (*e.g.,* human TACI), at an IC_{50} of 50 nM or less, *e.g.,* 40 nM or less, 30 nM or less, 20 nM or less, 10 nM or less, 9 nM or less, 8 nM or less, 7 nM or less, 6 nM or less, 5 nM or less, 4 nM or less, 3 nM or less, 2 nM or less, 1 nM or less, 0.8 nM or less, 0.6 nM or less, 0.4 nM or less, 0.2 nM or less, 0.1 nM or less, 0.05 nM or less, 0.02 nM or less, or 0.01 nM or less, *e.g.,* between 0.01 nM and 50 nM, between 0.1 nM and 50 nM, between 0.1 nM and 25 nM, between 0.1 nM and 10 nM, between 0.1 nM and 5 nM, between 0.1 nM and 1 nM, between 0.1 nM and 0.5 nM, between 0.5 nM and 5 nM, or between 1 nM and 5 nM, *e.g.,* as determined by a method described herein. In an embodiment, the antibody molecule inhibits binding of human APRIL to human TACI at an IC_{50} of 150 nM or less, *e.g.,* about 112.97 nM. In an embodiment, the antibody molecule does not inhibit, or does not substantially inhibit, binding of APRIL (*e.g.,* human APRIL) to BCMA (*e.g.,* human BCMA).

In an embodiment, the antibody molecule comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the heavy chain variable region comprises one, two, or all of the following: an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of monoclonal antibody 4439 (*e.g.,* SEQ ID NO: 266 or 269); an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of monoclonal antibody 4439 (*e.g.,* SEQ ID NO: 267 or 270); or an HCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR3 of monoclonal antibody 4439 (*e.g.,* SEQ ID NO: 268), and

(ii) a light chain variable region (VL), wherein the light chain variable region comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the light chain variable region comprises one, two, or all of the following: an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of monoclonal antibody 4439 (*e.g.,* SEQ ID NO: 146); an LCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR2 of monoclonal antibody 4439 (*e.g.,* SEQ ID NO: 147); or an LCDR3 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR3 of monoclonal antibody 4439 (*e.g.,* SEQ ID NO: 148).

In an embodiment, the antibody molecule comprises one or both of: (i) a VH comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VH of monoclonal antibody 4439 (*e.g.,* SEQ ID NO: 271); or (ii) a VL comprising an amino acid sequence that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 amino acid residues from, or has at least 85, 90, 95, 96, 97, 98, 99, or 100% homology with, the amino acid sequence of the VL of monoclonal antibody 4439 (*e.g.,* SEQ ID NO: 272).

In an embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 297 (or a nucleotide sequence substantially identical thereto) or a VL encoded by the nucleotide sequence of SEQ ID NO: 298 (or a nucleotide sequence substantially identical thereto), or both.

In an embodiment, the antibody molecule is monoclonal antibody 4439. In an embodiment, monoclonal antibody 4439 is humanized monoclonal antibody 4439.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, residues within a region of human APRIL as defined in any of **Tables 3-4 or 7**, or Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, residues within a region of human APRIL as defined in **Table 3**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, of the human APRIL residues from **Table 3**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from **Table 3**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises APRIL residues from two monomers, *e.g.,* one or more residues from monomer A and monomer B as shown in **Table 3**.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or more, residues within a region of human APRIL as defined in **Table 4**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, or all, of the human APRIL residues from **Table 4**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from **Table 4**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises one or more APRIL residues from the C-D loop (*e.g.,* the loop connecting β-sheets C and D), the G-H loop (*e.g.,* the loop connecting β-sheets G and H), or both.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all, residues within a region of human APRIL as defined in **Table 7**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or all, of the human APRIL residues from **Table 7**. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from **Table 7**.

In an embodiment, the antibody molecule binds, or substantially binds, to one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or more, residues within a

region of human APRIL as defined in Table 8 of International Application Publication No. WO2017/091683. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises or consists of one or more, *e.g.,* 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or all, of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that overlaps an epitope that comprises or consists of all of the human APRIL residues from Table 8 of International Application Publication No. WO2017/091683. In an embodiment, the antibody molecule binds, or substantially binds, to an epitope that comprises APRIL residues from two monomers, *e.g.,* one or more residues from monomer A and monomer B as shown in Table 8 of International Application Publication No. WO2017/091683.

In an embodiment, the antibody molecule is an IgG antibody molecule, *e.g.,* comprising a heavy chain constant region of IgG, *e.g.,* chosen from IgG1, IgG2 (*e.g.,* IgG2a), IgG3, or IgG4, *e.g.,* IgG2 or IgG4. In an embodiment, the antibody molecule is an IgG1 antibody molecule. In another embodiment, the antibody molecule is an IgG2 antibody molecule. In an embodiment, the antibody molecule comprises a light chain constant region of kappa or lambda light chain.

In an embodiment, the antibody molecule comprises an Fc region. In an embodiment, the Fc region comprises one or more mutations located at the interface between the CH2 and CH3 domains (*e.g.,* to increase the binding affinity to neonatal receptor FcRn and/or the half-life of the antibody molecule). In an embodiment, the Fc region comprises one or more mutations, *e.g.,* one or more (*e.g.,* 2, 3, 4, 6 or all) mutations chosen from T250Q, M252Y, S254T, T256E, M428L, H433K, N434F, or any combination thereof, of IgG1. In an embodiment, the Fc region comprises one or more mutations at positions 233-236 or 322 of human IgG1 or IgG2, or one or more substitutions at positions 327, 330 or 331 of human IgG4 (*e.g.,* to reduce complement-dependent cytotoxicity (CDC)). In an embodiment, the Fc region comprises one or more (*e.g.,* 2, 3, 4, 6 7 or all) mutations chosen from E233P, L234V, L235A, G236, K322A, A327G, A330S, P331S, or any combination thereof.

In an embodiment, the antibody molecule is a humanized antibody molecule, *e.g.,* as described in **Table 5**, *e.g.,* comprising one or more framework regions derived from human framework germline sequence.

In an embodiment, the antibody molecule comprises two heavy chain variable regions and two light chain variable regions. In an embodiment, the antibody molecule is a Fab, F(ab')2, Fv, Fd, or a single chain Fv fragment (scFv).

Animal Models

The antibody molecules described herein can be evaluated *in vivo*, *e.g.*, using various animal models. For example, an animal model can be used to test the efficacy of an antibody molecule described herein in inhibiting APRIL and/or in treating or preventing a disorder described herein, *e.g.,* IgA nephropathy. Animal models can also be used, *e.g.*, to investigate for side effects, measure concentrations of antibody molecules *in situ*, demonstrate correlations between an APRIL function and a disorder described herein (*e.g.,* IgA nephropathy).

Exemplary animal models for IgA nephropathy that can be used for evaluating an antibody molecule described herein include, but are not limited to, a ddY mouse model for spontaneous IgA nephritis (Imai *et al. Kidney Int.* 1985; 27(5):756-761); a mouse model utilizing inert proteins or a common viral pathogen as the inciting antigen (Emancipator *et al. Curr. Protoc. Immunol.* 2001 May; Chapter 15: Unit 15.11), a rat model by noninfectious protein antigens (Emancipator et al. *Curr. Protoc. Immunol.* 2001 May; Chapter 15: Unit 15.11); a chronic mouse model of IgA immune-complex-associated nephropathy (Montinaro *et al. Nephrol. Dial. Transplant.* 1995; 10(11): 2035-2042); the Gne M712T mouse as a model for human glomerulopathy (Kakani *et al. Am. J. Pathol.* 2012; 180(4):1431-1440); a mouse IgA nephropathy model with the MBP-20-peptide fusion protein (Zhang *et al. Anat. Rec. (Hoboken).* 2010; 293(10): 1729-1737); and a mouse model for IgA immune complex nephritis (Rifai *et al. J Exp Med.* 1979; 150(5):1161-1173). Other animal models for IgA nephropathy are described, *e.g.,* in Tomino *et al. J. Nephrol.* 2008; 21(4):463-467; Endo *Ren. Fail.* 1997; 19(3):347-371; and Rifai *Kidney Int.* 1987; 31(1):1-7.

Exemplary animal models for other disorders described herein are also known in the art. Exemplary types of animals that can be used to evaluate the antibody molecules described herein include, but are not limited to, mice, rats, rabbits, guinea pigs, and monkeys.

Pharmaceutical Compositions and Kits

In some aspects, this disclosure provides compositions, *e.g.,* pharmaceutically acceptable compositions, which include an antibody molecule described herein (*e.g.,* a humanized antibody molecule described herein), formulated together with a pharmaceutically acceptable carrier.

As used herein, "pharmaceutically acceptable carrier" includes any and all solvents, dispersion media, isotonic and absorption delaying agents, and the like that are physiologically compatible. The carrier can be suitable for intravenous, intramuscular, subcutaneous, parenteral, rectal, spinal or epidermal administration (*e.g.,* by injection or infusion). In certain embodiments, less than about 5%, *e.g.,* less than about 4%, 3%, 2%, or 1% of the antibody molecules in the pharmaceutical composition are present as aggregates. In other embodiments, at least about 95%, *e.g.,* at least about 96%, 97%, 98%, 98.5%, 99%,

99.5%, 99.8%, or more of the antibody molecules in the pharmaceutical composition are present as monomers. In some embodiments, the level of aggregates or monomers is determined by chromatography, *e.g.,* high performance size exclusion chromatography (HP-SEC).

The compositions set out herein may be in a variety of forms. These include, for example, liquid, semi-solid and solid dosage forms, such as liquid solutions (*e.g.,* injectable and infusible solutions), dispersions or suspensions, liposomes, and suppositories. A suitable form depends on the intended mode of administration and therapeutic application. Typical suitable compositions are in the form of injectable or infusible solutions. One suitable mode of administration is parenteral (*e.g.,* intravenous, subcutaneous, intraperitoneal, intramuscular). In some embodiments, the antibody molecule is administered by intravenous infusion or injection. In certain embodiments, the antibody is administered by intramuscular or subcutaneous injection.

The phrases "parenteral administration" and "administered parenterally" as used herein means modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal, epidural and intrasternal injection and infusion.

Therapeutic compositions typically should be sterile and stable under the conditions of manufacture and storage. The composition can be formulated as a solution, microemulsion, dispersion, liposome, or other ordered structure suitable to high antibody concentration. Sterile injectable solutions can be prepared by incorporating the active compound (*i.e.*, antibody or antibody portion) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof. The proper fluidity of a solution can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prolonged absorption of injectable compositions can be brought about by including in the composition an agent that delays absorption, for example, monostearate salts and gelatin.

The antibody molecules described herein can be administered by a variety of methods. Several are known in the art, and for many therapeutic, prophylactic, or diagnostic applications, an appropriate route/mode of administration is intravenous injection or infusion. For example, the antibody molecules can be administered by intravenous infusion at a rate of less than 10mg/min; preferably less than or equal

to 5 mg/min to reach a dose of about 1 to 100 mg/m^2, preferably about 5 to 50 mg/m^2, about 7 to 25 mg/m^2 and more preferably, about 10 mg/m^2. As will be appreciated by the skilled artisan, the route and/or mode of administration will vary depending upon the desired results. In certain embodiments, the active compound may be prepared with a carrier that will protect the compound against rapid release, such as a controlled release formulation, including implants, transdermal patches, and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Many methods for the preparation of such formulations are patented or generally known to those skilled in the art. See, *e.g.*, *Sustained and Controlled Release Drug Delivery Systems*, J. R. Robinson, ed., Marcel Dekker, Inc., New York, 1978.

In certain embodiments, an antibody molecule can be orally administered, for example, with an inert diluent or an assimilable edible carrier. The antibody molecule (and other ingredients, if desired) may also be enclosed in a hard or soft shell gelatin capsule, compressed into tablets, or incorporated directly into the subject's diet. For oral therapeutic administration, the antibody molecule may be incorporated with excipients and used in the form of ingestible tablets, buccal tablets, troches, capsules, elixirs, suspensions, syrups, wafers, and the like. To administer an antibody molecule by other than parenteral administration, it may be necessary to coat the compound with, or co-administer the compound with, a material to prevent its inactivation. Therapeutic, prophylactic, or diagnostic compositions can also be administered with medical devices, and several are known in the art.

Dosage regimens are adjusted to provide the desired response (*e.g.,* a therapeutic, prophylactic, or diagnostic response). For example, a single bolus may be administered, several divided doses may be administered over time or the dose may be proportionally reduced or increased as indicated by the exigencies of the therapeutic situation. It is especially advantageous to formulate parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subjects to be treated; each unit contains a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms are dictated by and directly dependent on (a) the unique characteristics of the antibody molecule and the particular therapeutic, prophylactic, or diagnostic effect to be achieved, and (b) the limitations inherent in the art of compounding such an antibody molecule for the treatment of sensitivity in individuals.

An exemplary, non-limiting range for a therapeutically, prophylactically, or diagnostically effective amount of an antibody molecule is about 0.1-50 mg/kg body weight of a subject, *e.g.,* about 0.1-30 mg/kg, *e.g.*, about 1-30, 1-15, 1-10, 1-5, 5-10, or 1-3 mg/kg, *e.g.*, about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, or 50 mg/kg. The antibody molecule can be administered by intravenous infusion at a rate of

less than 10 mg/min, *e.g.*, less than or equal to 5 mg/min to reach a dose of about 1 to 100 mg/m^2, *e.g.*, about 5 to 50 mg/m^2, about 7 to 25 mg/m^2, *e.g.*, about 10 mg/m^2. It is to be noted that dosage values may vary with the type and severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that dosage ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed compositions.

The pharmaceutical compositions herein may include a "therapeutically effective amount," "prophylactically effective amount," or "diagnostically effectively amount" of an antibody molecule described herein.

A "therapeutically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired therapeutic result. A therapeutically effective amount of the antibody molecule may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the antibody or antibody portion to elicit a desired response in the individual. A therapeutically effective amount is also one in which any toxic or detrimental effect of the antibody molecule is outweighed by the therapeutically beneficial effects. A "therapeutically effective dosage" typically inhibits a measurable parameter by at least about 20%, *e.g.*, by at least about 40%, by at least about 60%, or by at least about 80% relative to untreated subjects. The measurable parameter may be, *e.g.,* hematuria, colored urine, foamy urine, pain, swelling (edema) in the hands and feet, or high blood pressure. The ability of an antibody molecule to inhibit a measurable parameter can be evaluated in an animal model system predictive of efficacy in treating or preventing IgA nephropathy. Alternatively, this property of a composition can be evaluated by examining the ability of the antibody molecule to inhibit APRIL, *e.g.,* by an *in vitro* assay.

A "prophylactically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired prophylactic result. Typically, since a prophylactic dose is used in subjects prior to or at an earlier stage of disease, the prophylactically effective amount will be less than the therapeutically effective amount.

A "diagnostically effective amount" refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired diagnostic result. Typically, a diagnostically effective amount is one in which a disorder, *e.g.,* a disorder described herein, *e.g.,* IgA nephropathy, can be diagnosed *in vitro*, *ex vivo*, or *in vivo*.

Also within this disclosure is a kit that comprises an antibody molecule, described herein. The kit can include one or more other elements including: instructions for use; other reagents, *e.g.,* a label, a therapeutic agent, or an agent useful for chelating, or otherwise coupling, an antibody molecule to a label

or therapeutic agent, or a radioprotective composition; devices or other materials for preparing the antibody molecule for administration; pharmaceutically acceptable carriers; and devices or other materials for administration to a subject.

Nucleic Acids

The present disclosure also features nucleic acids comprising nucleotide sequences that encode the antibody molecules (*e.g.*, heavy and light chain variable regions and CDRs of the antibody molecules), as described herein.

For example, the present disclosure features a first and second nucleic acid encoding heavy and light chain variable regions, respectively, of an antibody molecule chosen from one or more of the antibody molecules disclosed herein, *e.g.,* an antibody molecule of **Table 1 or 5**, or a portion of an antibody molecule, *e.g.,* the variable regions of **Table 2**. The nucleic acid can comprise a nucleotide sequence encoding any one of the amino acid sequences in the tables herein, or a sequence substantially identical thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 3, 6, 15, 30, or 45 nucleotides from the sequences shown in the tables herein).

In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs from a heavy chain variable region having an amino acid sequence as set forth in the tables herein, or a sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one or more substitutions, *e.g.,* conserved substitutions). In some embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs from a light chain variable region having an amino acid sequence as set forth in the tables herein, or a sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one or more substitutions, *e.g.,* conserved substitutions). In some embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, three, four, five, or six CDRs from heavy and light chain variable regions having an amino acid sequence as set forth in the tables herein, or a sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or having one or more substitutions, *e.g.,* conserved substitutions).

In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs from a heavy chain variable region having the nucleotide sequence as set forth in **Table 2**, a sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In some embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs from a light chain variable region having the nucleotide sequence as set forth in

Table 2, or a sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, three, four, five, or six CDRs from heavy and light chain variable regions having the nucleotide sequence as set forth in **Table 2**, or a sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein).

In certain embodiments, the nucleic acid comprises a nucleotide sequence as set forth in **Table 2** or a sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). In some embodiments, the nucleic acid comprises a portion of a nucleotide sequence as set forth in **Table 2** or a sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein). The portion may encode, for example, a variable region (*e.g.,* VH or VL); one, two, or three or more CDRs; or one, two, three, or four or more framework regions.

The nucleic acids disclosed herein include deoxyribonucleotides or ribonucleotides, or analogs thereof. The polynucleotide may be either single-stranded or double-stranded, and if single-stranded may be the coding strand or non-coding (antisense) strand. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. The nucleic acid may be a recombinant polynucleotide, or a polynucleotide of genomic, cDNA, semisynthetic, or synthetic origin which either does not occur in nature or is linked to another polynucleotide in a non-natural arrangement.

In some aspects, the application features host cells and vectors containing the nucleic acids described herein. The nucleic acids may be present in a single vector or separate vectors present in the same host cell or separate host cell, as described in more detail below.

Vectors

Further provided herein are vectors that comprise nucleotide sequences encoding an antibody molecule described herein.

In an embodiment, the vector comprises a nucleotide encoding an antibody molecule described herein, *e.g.,* as described in **Table 1 or 5**. In another embodiment, the vector comprises a nucleotide sequence described herein, *e.g.,* in **Table 2**. The vectors include, but are not limited to, a virus, plasmid, cosmid, lambda phage or a yeast artificial chromosome (YAC).

Numerous vector systems can be employed. For example, one class of vectors utilizes DNA elements which are derived from animal viruses such as, for example, bovine papilloma virus, polyoma virus, adenovirus, vaccinia virus, baculovirus, retroviruses (Rous Sarcoma Virus, MMTV or MOMLV) or SV40 virus. Another class of vectors utilizes RNA elements derived from RNA viruses such as Semliki Forest virus, Eastern Equine Encephalitis virus and Flaviviruses.

Additionally, cells which have stably integrated the DNA into their chromosomes may be selected by introducing one or more markers which allow for the selection of transfected host cells. The marker may provide, for example, prototropy to an auxotrophic host, biocide resistance (*e.g.,* antibiotics), or resistance to heavy metals such as copper, or the like. The selectable marker gene can be either directly linked to the DNA sequences to be expressed, or introduced into the same cell by cotransformation. Additional elements may also be needed for optimal synthesis of mRNA. These elements may include splice signals, as well as transcriptional promoters, enhancers, and termination signals.

Once the expression vector or DNA sequence containing the constructs has been prepared for expression, the expression vectors may be transfected or introduced into an appropriate host cell. Various techniques may be employed to achieve this, such as, for example, protoplast fusion, calcium phosphate precipitation, electroporation, retroviral transduction, viral transfection, gene gun, lipid based transfection or other conventional techniques. In the case of protoplast fusion, the cells are grown in media and screened for the appropriate activity.

Methods and conditions for culturing the resulting transfected cells and for recovering the antibody molecule produced are known to those skilled in the art, and may be varied or optimized depending upon the specific expression vector and mammalian host cell employed, based upon the present description.

Cells

The present disclosure also provides cells (*e.g.,* host cells) comprising a nucleic acid encoding an antibody molecule as described herein. For example, the host cells may comprise a nucleic acid molecule having a nucleotide sequence described in **Table 2**, a sequence substantially homologous thereto (*e.g.,* a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, and/or capable of hybridizing under the stringency conditions described herein), or a portion of one of said nucleic acids. Additionally, the host cells may comprise a nucleic acid molecule encoding an amino acid sequence of **Table 1 or 5**, a sequence substantially homologous thereto (*e.g.,* a sequence at least about 80%, 85%, 90%, 95%, 99% or more identical thereto), or a portion of one of said sequences.

In some embodiments, the host cells are genetically engineered to comprise nucleic acids encoding the antibody molecule described herein.

In certain embodiments, the host cells are genetically engineered by using an expression cassette. The phrase "expression cassette," refers to nucleotide sequences, which are capable of affecting expression of a gene in hosts compatible with such sequences. Such cassettes may include a promoter, an open reading frame with or without introns, and a termination signal. Additional factors necessary or helpful in effecting expression may also be used, such as, for example, an inducible promoter.

The disclosure also provides host cells comprising the vectors described herein.

The cell can be, but is not limited to, a eukaryotic cell, a bacterial cell, an insect cell, or a human cell. Suitable eukaryotic cells include, but are not limited to, Vero cells, HeLa cells, COS cells, CHO cells, HEK293 cells, BHK cells and MDCKII cells. Suitable insect cells include, but are not limited to, Sf9 cells. In an embodiment, the cell (*e.g.,* host cell) is an isolated cell.

Uses of Antibody Molecules

The antibody molecules disclosed herein, as well as the pharmaceutical compositions disclosed herein, have *in vitro*, *ex vivo*, and *in vivo* therapeutic, prophylactic, and/or diagnostic utilities.

In an embodiment, the antibody molecule reduces (*e.g.,* inhibits, blocks, or neutralizes) one or more biological activities of APRIL. For example, these antibodies molecules can be administered to cells in culture, *in vitro* or *ex vivo*, or to a subject, *e.g.,* a human subject, *e.g., in vivo*, to reduce (*e.g.,* inhibits, blocks, or neutralizes) one or more biological activities of APRIL. In an embodiment, the antibody molecule inhibits, or substantially inhibit, binding of APRIL, *e.g.,* human APRIL, to TACI, BCMA, or both. Accordingly, in an aspect, the disclosure provides a method of treating, preventing, or diagnosing a disorder, *e.g.,* a disorder described herein (*e.g.,* IgA nephropathy (IgAN) or disorders associated with IgAN (e.g., an advanced chronic kidney disease (CKD), post-transplant IgAN, pediatric IgAN, Henoch-Schonlein purpura (HSP) or cutaneous vasculitis, IgAN with crescentic glomerulonephritis (GN)), IgA vasculitis, IgA dermatitis (e.g., IgA dermatitis herpetiformis, IgA bullous dermatosis), IgM mediated neuropathy (e.g., anti-MAG peripheral neuropathy or IgM mediated neuropathy associated with anti-GM1 antibodies), Waldenstrom's Macroglobulinemia (WM), or lupus nephritis), in a subject, comprising administering to the subject an antibody molecule described herein, such that the disorder is treated, prevented, or diagnosed. For example, the disclosure provides a method comprising contacting the antibody molecule described herein with cells in culture, *e.g. in vitro* or *ex vivo*, or administering the antibody molecule described herein to a subject, *e.g., in vivo*, to treat, prevent, or diagnose a disorder, *e.g.,* a disorder associated with APRIL (*e.g.,* IgA nephropathy (IgAN) or a disorder associated with IgAN (e.g., an advanced chronic kidney disease (CKD), post-transplant IgAN, pediatric

IgAN, Henoch-Schonlein purpura (HSP) or cutaneous vasculitis, IgAN with crescentic glomerulonephritis (GN)), IgA vasculitis, IgA dermatitis (e.g., IgA dermatitis herpetiformis, IgA bullous dermatosis), IgM mediated neuropathy (e.g., anti-MAG peripheral neuropathy or IgM mediated neuropathy associated with anti-GM1 antibodies), Waldenstrom's Macroglobulinemia (WM), or lupus nephritis).

As used herein, the term "subject" is intended to include human and non-human animals. In some embodiments, the subject is a human subject, *e.g.,* a human patient having a disorder described herein (*e.g.,* IgA nephropathy (IgAN) or a disorder associated with IgAN (e.g., an advanced chronic kidney disease (CKD), post-transplant IgAN, pediatric IgAN, Henoch-Schonlein purpura (HSP) or cutaneous vasculitis, IgAN with crescentic glomerulonephritis (GN))), or at risk of having a disorder described herein (*e.g.,* IgA nephropathy (IgAN) or disorders associated with IgAN (e.g., an advanced chronic kidney disease (CKD), post-transplant IgAN, pediatric IgAN, Henoch-Schonlein purpura (HSP) or cutaneous vasculitis, IgAN with crescentic glomerulonephritis (GN)), IgA vasculitis, IgA dermatitis (e.g., IgA dermatitis herpetiformis, IgA bullous dermatosis), IgM mediated neuropathy (e.g., anti-MAG peripheral neuropathy or IgM mediated neuropathy associated with anti-GM1 antibodies), Waldenstrom's Macroglobulinemia (WM), or lupus nephritis). The term "non-human animals" includes mammals and non-mammals, such as non-human primates. In some embodiments, the subject is a human. The methods and compositions described herein are suitable for treating human patients a disorder described herein (*e.g.,* IgA nephropathy (IgAN) or a disorder associated with IgAN (e.g., an advanced chronic kidney disease (CKD), post-transplant IgAN, pediatric IgAN, Henoch-Schonlein purpura (HSP) or cutaneous vasculitis, IgAN with crescentic glomerulonephritis (GN)), IgA vasculitis, IgA dermatitis (e.g., IgA dermatitis herpetiformis, IgA bullous dermatosis), IgM mediated neuropathy (e.g., anti-MAG peripheral neuropathy or IgM mediated neuropathy associated with anti-GM1 antibodies), Waldenstrom's Macroglobulinemia (WM), or lupus nephritis).

Patients having a disorder described herein (*e.g.,* IgA nephropathy (IgAN) or a disorder associated with IgAN (e.g., an advanced chronic kidney disease (CKD), post-transplant IgAN, pediatric IgAN, Henoch-Schonlein purpura (HSP) or cutaneous vasculitis, IgAN with crescentic glomerulonephritis (GN)), IgA vasculitis, IgA dermatitis (e.g., IgA dermatitis herpetiformis, IgA bullous dermatosis), IgM mediated neuropathy (e.g., anti-MAG peripheral neuropathy or IgM mediated neuropathy associated with anti-GM1 antibodies), Waldenstrom's Macroglobulinemia (WM), or lupus nephritis) include those who have developed the disorder, but are (at least temporarily) asymptomatic, patients who have exhibited a symptom of the disorder, or patients having a disorder related to or associated with the disorder.

Methods of Treating or Preventing Disorders

The antibody molecules described herein can be used to treat or prevent disorders associated with APRIL or symptoms thereof.

Exemplary disorders or conditions that can be associated with APRIL include, but are not limited to IgA nephropathy (IgAN) or a disorder associated with IgAN (e.g., an advanced chronic kidney disease (CKD), post-transplant IgAN, pediatric IgAN, Henoch-Schonlein purpura (HSP) or cutaneous vasculitis, IgAN with crescentic glomerulonephritis (GN)), diabetic nephropathy, IgM mediated neuropathy (e.g., anti-MAG peripheral neuropathy or IgM mediated neuropathy associated with anti-GM1 antibodies), cancer (*e.g.,* hematological cancer (*e.g.,* B-cell non-Hodgkin's lymphoma, chronic lymphocytic leukemia, Hodgkin's lymphoma, multiple myeloma, Waldenström macroglobulinemia, and lymphoplasmacytic lymphoma) or solid tumors (*e.g.,* colorectal cancer, breast cancer (*e.g.,* breast carcinoma), esophageal cancer (*e.g.,* esophageal adenocarcinoma), brain cancer (*e.g.,* glioblastoma), and kidney cancer (*e.g.,* renal cell carcinoma)), immunoproliferative disorders (*e.g.,* monoclonal IgA hypergammaglobulinemia), vasculitis (*e.g.,* kidney vasculitis, Henoch-Schonlein purpura (IgA associated vasculitis), and post-streptococcal glomerulonephritis), autoimmune disorders (*e.g.,* rheumatoid arthritis, systemic lupus erythematosus, lupus nephritis, IgA dermatitis (e.g., IgA dermatitis herpetiformis, linear IgA bullous disease/linear immunoglobulin A (IgA) dermatosis, and IgA-mediated epidermolysis bullosa acquisita), IgA pemphigus, celiac disease, and alcoholic cirrhosis. In an embodiment, the disorder is associated with aberrant expression of IgA. In an embodiment, the antibody molecule is used to treat a subject having a disorder described herein, or is at risk of developing a disorder described herein.

In an embodiment, the disorder associated with APRIL is IgA nephropathy (IgAN) or a disorder associated with IgAN (e.g., an advanced chronic kidney disease (CKD), post-transplant IgAN, pediatric IgAN, Henoch-Schonlein purpura (HSP) or cutaneous vasculitis, IgAN with crescentic glomerulonephritis (GN)), IgA vasculitis, IgA dermatitis (e.g., IgA dermatitis herpetiformis, IgA bullous dermatosis), IgM mediated neuropathy (e.g., anti-MAG peripheral neuropathy or IgM mediated neuropathy associated with anti-GM1 antibodies), Waldenstrom's Macroglobulinemia (WM), or lupus nephritis. In an embodiment, the disorder is IgA nephropathy (IgAN). In an embodiment, the disorder is IgA nephropathy in a subject with more advanced chronic kidney disease (CKD) (eGFR $\geq$ 30 or 45). In an embodiment, the disorder is a post-transplant IgA nephropathy. In an embodiment, the disorder is a pediatric IgA nephropathy. In an embodiment, the disorder is Henoch-Schonlein purpura or cutaneous vasculitis). In an embodiment, the disorder is IgA nephropathy in a subject with crescentic glomerulonephritis (GN). In an embodiment, the disorder is IgA vasculitis. In an embodiment, the disorder is IgA bullous dermatosis. In an embodiment, the disorder is IgA dermatitis (e.g., IgA dermatitis herpetiformis, IgA bullous dermatosis). In an embodiment, the disorder is IgM mediated neuropathy

(e.g., anti-MAG peripheral neuropathy or IgM mediated neuropathy associated with anti-GM1 antibodies). In an embodiment, the disorder is Waldenstrom's Macroglobulinemia (WM). In an embodiment, the disorder is lupus nephritis.

The antibody molecules described herein are typically administered at a frequency that keeps a therapeutically effective level of antibody molecules in the patient's system until the patient recovers. For example, the antibody molecules may be administered at a frequency that achieves a serum concentration sufficient for at least about 1, 2, 5, 10, 20, 30, or 40 antibody molecules to bind each APRIL molecule. In an embodiment, the antibody molecules are administered every 1, 2, 3, 4, 5, 6, or 7 days, every 1, 2, 3, 4, 5, or 6 weeks, or every 1, 2, 3, 4, 5, or 6 months.

Methods of administering various antibody molecules are known in the art and are described below. Suitable dosages of the antibody molecules used will depend on the age and weight of the subject and the particular drug used.

In an embodiment, the antibody molecule is administered to the subject (*e.g.,* a human subject) intravenously. In an embodiment, the antibody molecule is administered to the subject at a dose between 0.1 mg/kg and 50 mg/kg, *e.g.,* between 0.2 mg/kg and 25 mg/kg, between 0.5 mg/kg and 10 mg/kg, between 0.5 mg/kg and 5 mg/kg, between 0.5 mg/kg and 3 mg/kg, between 0.5 mg/kg and 2.5 mg/kg, between 0.5 mg/kg and 2 mg/kg, between 0.5 mg/kg and 1.5 mg/kg, between 0.5 mg/kg and 1 mg/kg, between 1 mg/kg and 1.5 mg/kg, between 1 mg/kg and 2 mg/kg, between 1 mg/kg and 2.5 mg/kg, between 1 mg/kg and 3 mg/kg, between 1 mg/kg and 2.5 mg/kg, or between 1 mg/kg and 5 mg/kg. In an embodiment, the antibody molecule is administered to the subject at a fixed dose between 10 mg and 1000 mg, *e.g.,* between 10 mg and 500 mg, between 10 mg and 250 mg, between 10 mg and 150 mg, between 10 mg and 100 mg, between 10 mg and 50 mg, between 250 mg and 500 mg, between 150 mg and 500 mg, between 100 mg and 500 mg, between 50 mg and 500 mg, between 25 mg and 250 mg, between 50 mg and 150 mg, between 50 mg and 100 mg, between 100 mg and 150 mg. between 100 mg and 200 mg, or between 150 mg and 250 mg. In an embodiment, the antibody molecule is administered to the subject at a dose of about 100 mg, about 200 mg, about 400 mg, about 600 mg, about 800 mg, or about 1000 mg, or about 1200 mg, e.g., subcutaneously. In an embodiment, the antibody molecule is administered subcutaneously to the subject at a dose of about 200 mg. In an embodiment, the antibody molecule is administered subcutaneously to the subject at a dose of about 400 mg. In an embodiment, the antibody molecule is administered subcutaneously to the subject at a dose of about 600 mg. In an embodiment, the antibody molecule is administered subcutaneously to the subject at a dose of about 800 mg. In an embodiment, the antibody molecule is administered at a unit dose of 100 mg/mL to 300 mg/mL, e.g., 200 mg/mL. In an embodiment, the antibody molecule is administered by a subcutaneous injection of about 0.5 mL to 5 mL, e.g., 1 mL, 1.5 mL, 2 mL, 2.5 mL, 3 mL, 3.5 mL, 4 mL, 4.5 mL, 5

mL, 5.5 mL, or 6 mL. In an embodiment, the antibody molecule is administered at a dose of 200 mg by one 1 mL subcutaneous injection. In an embodiment, the antibody molecule is administered at a dose of 400 mg by one 2 mL subcutaneous injection. In an embodiment, the antibody molecule is administered at a dose of 600 mg by one 2 mL subcutaneous injection and one 1 mL subcutaneous injection. In an embodiment, the antibody molecule is administered once a week, twice a week, once every two weeks, once every three weeks, once every four weeks, once every eight weeks, once a month, once every two months, or once every three months. In an embodiment the antibody molecule is administered as a single subcutaneous dose, e.g., in a period of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, or 36 weeks. In an embodiment, the antibody molecule is administered between 0.5 mg/kg and 3 mg/kg or between 50 mg and 150 mg, once a week, twice a week, once every two weeks, or once every four weeks.

The antibody molecules can be used by themselves or conjugated to a second agent, *e.g.,* a bacterial agent, toxin, or protein, *e.g.,* a second anti-APRIL antibody molecule. This method includes: administering the antibody molecule, alone or conjugated to a second agent, to a subject requiring such treatment. The antibody molecules can be used to deliver a variety of therapeutic agents, *e.g.,* a toxin, or mixtures thereof.

IgA Nephropathy

IgA nephropathy (also known as Berger's disease, Berger disease, Berger's syndrome, Berger syndrome, IgA nephritis, IgAN, or synpharyngitic glomerulonephritis) is the most prevalent, chronic glomerular disease worldwide. Conservative epidemiological estimates cite a global incidence of approximately 5-50 cases/million (children) and 10-40 cases /million (adults). This incidence of disease presents a regional bias with a higher prevalence in Asia and the Americas, with a particularly higher disease burden in Japan and regions of China. Biopsy confirmed cases of IgA nephropathy in Japan are projected at approximately 350,000. In the US, this projection is approximately 100,000—as such, it is the most frequently diagnosed 1° glomerular disease in adults. While a relatively indolent disease, IgA nephropathy leads to end stage renal disease (ESRD), *i.e.,* renal failure in 20-50% of patients within a 20-30 year span. These numbers are likely grossly underreported given the need to confirm the disease by kidney biopsy, a protocol that is variably practiced in various clinical settings. The disease has a complex pathogenesis with genetic, epidemiological, and potentially environmental components to disease etiology, pathology, and progression. It likewise has a variable clinical presentation ranging from asymptomatic to end-stage renal failure (ESRD). There are currently no disease-specific treatments to address primary disease or progression.

The etiology of this disease, as its name implies, has been established. In brief, the disease is caused by the deposition of IgA, typically in the form of immune complexes in the mesangium of the kidney. A molecular characterization of these particular immunoglobulins has been carried out. These IgAs are of the A1 subclass (IgA1 vs. IgA2), predominantly polymeric (with J chain-mediated linkages), and apparently differentially o-glycosylated in the hinge region that is intervening between CH1 and CH2 domains. In particular, these o-glycans are heterogeneously lacking β1,3 galactose linkages and, as such, are commonly referred to as galactose-deficient IgA1 (or gdIgA1). As the pathogenesis of this disease can involve a polygenic, multi-hit mechanism for inducing renal pathology and aberrant physiology, IgA1 may be viewed as the so-called auto-antigen representing this first critical "hit" in a multi-hit model for IgA nephropathy. A set of autoantibodies for this disease has likewise been defined and it relates to immunoglobulins (predominantly IgG) that specifically recognize this differentially glycosylated epitope and promote the formation of immune complexes (representing so-called "hit 2"). It should also be noted that IgA itself is subject to aggregation due to misfolding, conformational changes, and potential changes in the N-glycosylation state of the CH2/CH3 glycans.

Without wishing to be bound by theory, it is believed that in an embodiment, aberrantly glycosylated IgA1 levels correlate with disease and clinical outcomes in IgA nephropathy. Aberrantly glycosylated IgA1 has been characterized directly from kidney biopsies and increased production of aberrantly glycosylated IgA1 was observed in B cells (tonsillar, PBMC) in IgA nephropathy patients. The level of galactose-deficient IgA1 in the sera of patients with IgA nephropathy is associated with disease progression (Zhao *et al. Kidney Int.* 2012; 82(7):790-6). Differential lectin staining demonstrated elevated levels of aberrantly glycosylated IgA1 in serum and glomeruli of IgA nephropathy patients relative to healthy controls (Allen *et al. Kidney Int.* 2001; 60(3):969-73).

Based on this evolving disease model, IgA nephropathy may be appropriately viewed as an autoimmune disease with strong and critical extra-renal involvement. The identification and validation of select immune-based targets proposed to play a critical role in disease pathogenesis, namely the production of IgA and subsequent production of autoreactive antibodies to this target, represent a logical therapeutic strategy for treatment. APRIL (TNFSF13) represents particular area of focus for this reason. Additional rationale for targeting APRIL include emerging genetic data based on multiple, comprehensive genome wide association (GWAS) studies along with IgA related genetic disorders *e.g.,* IgA hypogammaglobulinemia related common variable immunoglobulin deficiency (CVID) whose locus maps to defects in TNFRSF13B (TACI) with direct implications of the role of APRIL-TACI interactions in regulating IgA synthesis.

IgA nephropathy often does not cause symptoms in the early stages. The disease can go unnoticed for years and is sometimes first diagnosed when routine tests reveal protein and red blood cells

in urine that cannot be seen without a microscope (microscopic hematuria). Signs and symptoms of IgA nephropathy when kidney function is impaired include, *e.g.,* cola- or tea-colored urine (caused by red blood cells in the urine); repeated episodes of cola- or tea-colored urine, sometimes even visible blood in the urine, usually during or after an upper respiratory or other type of infection; pain in the side(s) of the back below the ribs (flank); foam in the toilet water from protein in the urine; swelling (edema) in the hands and feet; and high blood pressure. In an embodiment, the sign or symptom includes, *e.g.,* one or more of hematuria, proteinuria, albuminuria, hypertension, or an early stage kidney disease (*e.g.,* requiring dialysis or transplantation). In an embodiment, the sign or symptom is associated with, *e.g.,* one or more of aberrantly glycosylated IgA1, auto-antibody formation, deposition of nephritogenic immune complexes in the kidney, or inflammation and loss of kidney function.

The classic presentation (in about 40-50% of the cases, more common in younger adults) of IgA nephropathy is episodic hematuria which usually starts within a day or two of a non-specific upper respiratory tract infection (hence synpharyngitic). Less commonly gastrointestinal or urinary infection can be the inciting agent. All of these infections have in common the activation of mucosal defenses and hence IgA antibody production. These episodes can occur on an irregular basis every few months and in most patients eventually subsides. Renal function usually remains normal, though rarely, acute kidney failure may occur.

A smaller proportion (in about 20-30% of the cases, usually the older population) of IgA nephropathy patients have microscopic hematuria and proteinuria (less than 2 gram/day). These patients may not have any symptoms and are only clinically found if a doctor decides to take a urine sample. Hence, the disease is more commonly diagnosed in situations where screening of urine is compulsory, *e.g.*, school children in Japan.

Some (about 5% each) IgA nephropathy patients have the following disease presentation: nephrotic syndrome (*e.g.,* 3-3.5 grams of protein loss in the urine, associated with a poorer prognosis); acute kidney failure (*e.g.,* either as a complication of the frank hematuria, when it usually recovers, or due to rapidly progressive glomerulonephritis which often leads to chronic kidney failure); chronic kidney failure (*e.g.,* no previous symptoms, presents with anemia, hypertension and other symptoms of kidney failure, in people who probably had longstanding undetected microscopic hematuria and/or proteinuria).

A variety of systemic diseases can be associated with IgA nephropathy such as liver failure, celiac disease, rheumatoid arthritis, reactive arthritis, ankylosing spondylitis and HIV. Diagnosis of IgA nephropathy and a search for any associated disease occasionally reveals such an underlying serious systemic disease. Occasionally, there are simultaneous symptoms of Henoch-Schönlein purpura. Some HLA alleles have been suspected along with complement phenotypes as being genetic factors.

IgA nephropathy can be diagnosed by various tests, *e.g.,* urine test, blood tests (*e.g.,* to show increased blood levels of the waste product creatinine), iothalamate clearance test, kidney imaging (*e.g.,* ultrasound, X-rays, or cystoscopy), kidney biopsy, or a combination thereof.

For an adult patient with isolated hematuria, tests such as ultrasound of the kidney and cystoscopy are usually done first to pinpoint the source of the bleeding. These tests would rule out kidney stones and bladder cancer, two other common urological causes of hematuria. In children and younger adults, the history and association with respiratory infection can raise the suspicion of IgA nephropathy. A kidney biopsy is often necessary to confirm the diagnosis. The biopsy specimen shows proliferation of the mesangium, with IgA deposits on immunofluorescence and electron microscopy. However, patients with isolated microscopic hematuria (*i.e.,* without associated proteinuria and with normal kidney function) are not usually biopsied since this is associated with an excellent prognosis. A urinalysis will show red blood cells, usually as red cell urinary casts. Proteinuria, usually less than 2 grams per day, also may be present. Other renal causes of isolated hematuria include, *e.g.,* thin basement membrane disease and Alport syndrome, the latter being a hereditary disease associated with hearing impairment and eye problems. Other blood tests done to aid in the diagnosis include CRP or ESR, complement levels, ANA, and LDH. Protein electrophoresis and immunoglobulin levels can show increased IgA in 50% of all patients.

Treatment with a number of medications can slow the progress of the disease and help manage symptoms such as high blood pressure, protein in the urine (proteinuria), and swelling (edema) in the hands and feet. Exemplary therapies for IgA nephropathy include, *e.g.,* high blood pressure medications (*e.g.,* angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs)), omega-3 fatty acids**,** immunosuppressants (*e.g.,* corticosteroid medications, such as prednisone), statin therapy, mycophenolate mofetil, ciclosporin, mizoribine, cyclophosphamide (*e.g.,* in combination with anti-platelet/anticoagulants, or in combination with steroids and azathioprine), kidney dialysis, or kidney transplantation. Exemplary therapies for IgA nephropathy are also described in Floege and Eitner *J. Am. Soc. Nephrol.* 22: 1785-1794, 2011. Other exemplary therapies for IgA nephropathy are described in the section of "Combination Therapies" herein.

Without wishing to be bound by theory, it is believed that in an embodiment, targeting APRIL selectively reduces IgA. APRIL-/- mice have normal T and B lymphocyte development, normal T and B cell proliferation *in vitro*, but decreased serum IgA levels (Castigli *et al. Proc Natl Acad Sci U S A.* 2004; 101(11):3903-8). Discovery of new risk loci for IgA nephropathy implicates genes involved in immunity against intestinal pathogens (Kiryluk *et al. Nat Genet.* 2014; 46(11):1187-96). Serum levels and B cell production of APRIL are elevated in patients with IgA nephropathy and correlate with aberrantly glycosylated IgA levels (Zhai *et al. Medicine* (Baltimore). 2016; 95(11):e3099). Plasma levels of APRIL (TNFSF13) correlate with progression of chronic kidney disease in IgA nephropathy (Han *et al. J Am Soc*

Nephrol. 2016; 27(2):439-53). Treatment with anti-APRIL antibody results in reduction of serum IgA, clearing of kidney mesangium, and reduction of inflammatory cell infiltration and glomerular injury, in mice (Kim *et al. PLoS One.* 2015; 10(9):e0137044). Anti-APRIL antibody preserves immune cell homeostasis in bone marrow and spleen (Kim *et al. PLoS One.* 2015; 10(9):e0137044).

APRIL (TNFSF13) represents a logical biological and therapeutic target for the treatment of IgA nephropathy. Without wishing to be bound by theory, it is believed that in an embodiment, the efficacy of the antibody molecules described herein with respect to the targeted modulation of APRIL-mediated immunobiolgocial mechanisms is directly relevant to treatment of IgA nephropathy. The anti-APRIL antibody molecules described herein (*e.g.,* humanized anti-APRIL antibody molecules), *e.g.,* with high biological potency and/or low complement activation, can be used to treat IgA nephropathy. In an embodiment, the antibody molecule has picomolar APRIL binding affinity and sub-nanomolar receptor blocking activity to both TACI and BCMA, *e.g., in vitro.* In another embodiment, the antibody molecule functionally interfere with APRIL mediated downstream cellular signaling, *e.g.,* through the canonical NFκB activation pathway. In an embodiment, the antibody molecule is engineered, *e.g.,* as an IgG2 subtype, for purposes of clinically mitigating against antibody-dependent exacerbation of complement recruitment, *e.g.,* in the kidneys of IgA nephropathy patients. In an embodiment, an antibody molecule described herein can have an improved safety profile in comparison to more depletive B cell-based therapeutic approaches, *e.g.,* due to a lesser perturbation of B and T cell homeostasis as shown in a murine model (Kim *et al. PLoS One.* 2015;10(9):e0137044).

The antibody molecules described herein can be used to treat or prevent different stages of IgA nephropathy. In an embodiment, the antibody molecule is used to treat a symptom associated with IgA nephropathy, *e.g.,* hematuria, proteinuria, albuminuria, hypertension, an early stage kidney disease (*e.g.,* requiring dialysis or transplantation), or a combination thereof. In an embodiment, the antibody molecule reduces aberrantly glycosylated IgA1, auto-antibody formation, deposition of nephritogenic immune complexes in the kidney, inflammation and loss of kidney function, or a combination thereof. In an embodiment, the subject is at low risk, *e.g.,* having minor urinary abnormalities (*e.g.,* micro-hematuria), normal glomerular filtration rate (GFR), and/or no hypertension. In another embodiment, the subject is at moderate to high risk, *e.g.*, having proteinuria greater than 0.5-1 g/d and/or GFR reduced (*e.g.,* below 30-50 ml/min) and/or hypertension. In yet another embodiment, the subject has acute or rapid GFR loss, *e.g.*, having nephrotic syndrome or rapidly progressive glomerulonephritis (RPGN), or acute kidney injury (AKI) due to macro-hematuria or other common cause. In an embodiment, the subject has proteinuria greater than 0.5 g/day, *e.g.,* between 0.5-1 g/day or greater than 1 g/day. In an embodiment, the subject treated for IgA nephropathy has glomerular filtration rate (GFR) less than 50 ml/min, *e.g.,* less than 30 ml/min.

The antibody molecules described herein can be used to treat various forms of IgA nephropathy or a disorder or condition associated with IgA nephropathy. In an embodiment, the subject treated for IgA nephropathy has more advanced chronic kidney disease (CKD), wherein the estimated GFR (eGFR) ≥ 30 or 45. In an embodiment, the subject treated for IgA nephropathy has crescentic glomerulonephritis (GN). In an embodiment, the antibody molecule is used to treat a pediatric IgA nephropathy. In an embodiment, the antibody molecule is used to treat a post-transplant IgA nephropathy. In an embodiment, the antibody molecule is used to treat Henoch-Schonlein purpura (HSP) or cutaneous vasculitis. In an embodiment, the antibody molecule does not significantly change (*e.g.,* capable of preserving) immune cell homeostasis. In another embodiment, the antibody molecule results in a reduction of IgA not total ablation of IgA.

Diabetic Nephropathy

The antibody molecule described herein can be used to treat or prevent diabetic nephropathy. Diabetic nephropathy (or known as diabetic kidney disease) is a progressive kidney disease caused, *e.g.,* by damage to the capillaries in the kidneys' glomeruli. It is typically characterized by nephrotic syndrome and diffuse scarring of the glomeruli. It is often due to longstanding diabetes mellitus, and is a prime reason for dialysis. It is classified as a small blood vessel complication of diabetes.

Exemplary symptoms of diabetic nephropathy include, but are not limited to, severe tiredness, headaches, a general feeling of illness, nausea, vomiting, frequent voiding, lack of appetite, itchy skin, or leg swelling. The cause of diabetic nephropathy can include, *e.g.,* high blood sugar, advanced glycation end product formation. Cytokines may be involved in the development of diabetic nephropathy.

Diabetes can cause a number of changes to the body's metabolism and blood circulation, which likely combine to produce excess reactive oxygen species. These changes damage the kidney's glomeruli, which leads to the hallmark feature of albuminuria (Cao and Cooper *J Diabetes Investig.* 2011; 2(4): 243-247). As diabetic nephropathy progresses, the glomerular filtration barrier (GFB), which is composed of the fenestrated endothelium, glomerular basement membrane, and epithelial podocytes, is increasingly damaged (Mora-Fernández *et al. J. Physiol. (Lond.)* 2014; 592 (Pt 18): 3997-4012). Damage to the glomerular basement membrane allows proteins in the blood to leak through, leading to accumulation in Bowman's space as distinct periodic-acid schiff positive nodules (Kimmelstiel–Wilson nodules).

Diagnosis of diabetic nephropathy can be based on the measurement of high levels of albumin in the urine or evidence of reduced kidney function (Lewis and Maxwell Practitioner. 2014; 258(1768):13-7, 2). Albumin measurements can be defined as follows: normal albuminuria: urinary albumin excretion <30 mg/24h; microalbuminuria: urinary albumin excretion in the range of 30–299 mg/24h; clinical (overt) albuminuria: urinary albumin excretion ≥300 mg/24h. To test kidney function, the person's estimated

glomerular filtration rate (eGFR) is measured from a blood sample. Normal eGFR ranges from 90 to 120 ml/min/1.73 m^2.

Other treatments that can be used in combination with the antibody molecule described herein to treat diabetic nephropathy include, *e.g.,* an angiotensin-converting enzyme (ACE) inhibitor (*e.g.,* captopril, enalapril, lisinopril, or ramipril), an angiotensin II receptor blocker (ARB) (*e.g.*, candesartan cilexetil, irbesartan, losartan, or telmisartan), a calcium channel blocker (*e.g.,* amlodipine, diltiazem, or verapamil), a diuretic (*e.g.,* chlorthalidone, hydrochlorothiazide, or spironolactone), a beta-blocker (*e.g.,* atenolol, carvedilol, or metoprolol), and diabetes management (*e.g.,* control of high blood pressure or blood sugar levels, or reduction of dietary salt intake).

Cancer

The antibody molecule described herein can be used to treat or prevent a cancer. Exemplary cancers that can be treated or prevented by the antibody molecules described herein include, but are not limited to, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), adrenocortical carcinoma, Kaposi sarcoma, an AIDS-related lymphoma, primary central nervous system (CNS) lymphoma, anal cancer, appendix cancer, astrocytoma, atypical teratoid/rhabdoid tumor, basal cell carcinoma, bile duct cancer, bladder cancer, bone cancer (*e.g.,* Ewing sarcoma or osteosarcoma and malignant fibrous histiocytoma), brain tumor (*e.g.,* astrocytomas, brain stem glioma, central nervous system atypical teratoid/rhabdoid tumor, central nervous system embryonal tumor, central nervous system germ cell tumor, craniopharyngioma, or ependymoma), breast cancer, bronchial tumor, Burkitt lymphoma, carcinoid tumor (*e.g.,* gastrointestinal carcinoid tumor), cardiac (heart) tumor, embryonal tumor, germ cell tumor, lymphoma, cervical cancer, cholangiocarcinoma, chordoma, chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), chronic myeloproliferative neoplasm, colon cancer, colorectal cancer, craniopharyngioma, cutaneous T-cell lymphoma, ductal carcinoma *in situ* (DCIS), endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, Ewing sarcoma, extracranial germ cell tumor, extragonadal germ cell tumor, eye cancer (*e.g.,* intraocular melanoma or retinoblastoma), fallopian tube cancer, fibrous histiocytoma of bone, osteosarcoma, gallbladder cancer, gastric (stomach) cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumors (GIST), germ cell tumor (*e.g.,* central nervous system tumor, extracranial tumor, extragonadal tumor, ovarian cancer, or testicular cancer), gestational trophoblastic disease, glioma, hairy cell leukemia, head and neck cancer, hepatocellular (liver) cancer, Hodgkin lymphoma, hypopharyngeal cancer, intraocular melanoma, islet cell tumor, pancreatic neuroendocrine tumor, Kaposi sarcoma, kidney cancer (*e.g.,* renal cell cancer or Wilms tumor), Langerhans cell histiocytosis (LCH), laryngeal cancer, leukemia (*e.g.,* acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic

myelogenous leukemia (CML), or hairy cell leukemia), lip and oral cavity cancer, liver cancer, lung cancer (*e.g.,* non-small cell lung cancer (NSCLC) or small cell lung cancer), lymphoma (*e.g.,* aids-related, Burkitt lymphoma, cutaneous T-cell lymphoma, Hodgkin lymphoma, non-Hodgkin lymphoma, or primary central nervous system (CNS) lymphoma), Waldenström macroglobulinemia, male breast cancer, malignant fibrous histiocytoma of bone and osteosarcoma, melanoma (*e.g.,* intraocular (eye) melanoma), Merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer, midline tract carcinoma, mouth cancer, multiple endocrine neoplasia syndrome, multiple myeloma/plasma cell neoplasm, mycosis fungoides, myelodysplastic syndrome, myelodysplastic/myeloproliferative neoplasm, chronic myeloproliferative neoplasm, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, oral cancer, lip and oral cavity cancer, oropharyngeal cancer, osteosarcoma and malignant fibrous histiocytoma of bone, ovarian cancer (*e.g.,* epithelial ovarian cancer or germ cell ovarian tumor), pancreatic cancer, pancreatic neuroendocrine tumors (islet cell tumors), papillomatosis, paraganglioma, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytoma, pituitary tumor, pleuropulmonary blastoma, peritoneal cancer, prostate cancer, rectal cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, sarcoma (*e.g.,* Ewing sarcoma, Kaposi sarcoma, osteosarcoma, rhabdomyosarcoma, soft tissue sarcoma, or uterine sarcoma), Sézary syndrome, skin cancer (*e.g.,* melanoma, Merkel cell carcinoma, or nonmelanoma skin cancer), small intestine cancer, squamous cell carcinoma, testicular cancer, throat cancer, thymoma and thymic carcinoma, thyroid cancer, transitional cell cancer of the renal pelvis and ureter, urethral cancer, endometrial uterine cancer, vaginal cancer, vulvar cancer, or a metastatic lesion thereof.

In an embodiment, the cancer is a hematological cancer, *e.g.,* a lymphoma or leukemia, *e.g.,* chosen from B-cell non-Hodgkin's lymphoma, chronic lymphocytic leukemia (CLL), Hodgkin's lymphoma, multiple myeloma, Waldenström macroglobulinemia, or lymphoplasmacytic lymphoma. In an embodiment, the cancer is a multiple myeloma. In another embodiment, the cancer is a solid tumor, *e.g.,* chosen from colorectal cancer, breast cancer (*e.g.,* breast carcinoma), esophageal cancer (*e.g.,* esophageal adenocarcinoma), brain cancer (*e.g.,* glioblastoma), or kidney cancer (*e.g.,* renal cell carcinoma).

In an embodiment, the antibody molecule is used to treat a lymphoma. Other treatments that can be used in combination with the antibody molecule described herein to treat lymphoma include, *e.g.,* chemotherapy, immunotherapy, targeted drug therapy, radiation therapy, and stem cell transplant. Exemplary targeted drug therapy includes a CD20 inhibitor (*e.g.,* rituximab (RITUXAN® or ibritumomab tiuxetan (ZEVALIN®)).

In an embodiment, the antibody molecule is used to treat a leukemia. Other treatments that can be used in combination with the antibody molecule described herein to treat leukemia include, *e.g.,*

chemotherapy, immunotherapy, targeted drug therapy, radiation therapy, and stem cell transplant. Exemplary targeted drug therapy includes a tyrosine kinase inhibitor (*e.g.,* imatinib (GLEEVEC®).

In an embodiment, the antibody molecule is used to treat a multiple myeloma. Other treatments that can be used in combination with the antibody molecule described herein to treat multiple myeloma include, *e.g.,* chemotherapy, corticosteroids, immunotherapy, targeted drug therapy, radiation therapy, and stem cell transplant. Exemplary targeted drug therapy includes, *e.g.,* a thalidomide analog (*e.g.,* thalidomide (THALOMID®), lenalidomide (REVLIMID®), or pomalidomide (POMALYST®)).

In an embodiment, the antibody molecule is used to treat Waldenström macroglobulinemia. Other treatments that can be used in combination with the antibody molecule described herein to treat Waldenström macroglobulinemia include, *e.g.,* plasma exchange, chemotherapy, immunotherapy, targeted drug therapy, and stem cell transplant.

In an embodiment, the antibody molecule is used to treat a colorectal cancer. Other treatments that can be used in combination with the antibody molecule described herein to treat colorectal cancer include, *e.g.,* surgery, chemotherapy, radiation therapy, immunotherapy, and targeted drug therapy. Exemplary targeted drug therapy includes, *e.g.,* a VEGF inhibitor (*e.g.,* bevacizumab (AVASTIN®)), an EGFR inhibitor (*e.g.,* cetuximab (ERBITUX®), panitumumab (VECTIBIX®)), and dual VEGFR2-TIE2 tyrosine kinase inhibitor (*e.g.,* regorafenib (STIVARGA®)).

In an embodiment, the antibody molecule is used to treat a breast cancer, *e.g.,* a breast carcinoma. Other treatments that can be used in combination with the antibody molecule described herein to treat breast cancer include, *e.g.,* surgery, chemotherapy, radiation therapy, hormone therapy, immunotherapy, and targeted drug therapy. Exemplary target drug therapy includes, *e.g.,* an HER2 inhibitor (*e.g.,* trastuzumab (HERCEPTIN®), pertuzumab (PERJETA®), ado-trastuzumab (KADCYLA®), or lapatinib (TYKERB®)) or a VEGF inhibitor (*e.g.,* bevacizumab (AVASTIN®)).

In an embodiment, the antibody molecule is used to treat an esophageal cancer, *e.g.,* an esophageal adenocarcinoma. Other treatments that can be used in combination with the antibody molecule described herein to treat esophageal cancer include, *e.g.,* surgery, chemotherapy, radiation therapy, and immunotherapy.

In an embodiment, the antibody molecule is used to treat a brain cancer, *e.g.,* a glioblastoma. Other treatments that can be used in combination with the antibody molecule described herein to treat brain cancer include, *e.g.,* surgery, chemotherapy, radiation therapy, radiosurgery, immunotherapy, and targeted drug therapy. Exemplary targeted drug therapy includes, *e.g.,* a VEGF inhibitor (*e.g.,* bevacizumab (AVASTIN®)).

In an embodiment, the antibody molecule is used to treat a kidney cancer, *e.g.,* a renal cell carcinoma. Other treatments that can be used in combination with the antibody molecule described herein

to treat kidney cancer include, *e.g.,* surgery, cryoablation, radiofrequency ablation, radiation therapy, immunotherapy, and targeted drug therapy. Exemplary targeted drug therapy includes, *e.g.,* a VEGF inhibitor (*e.g.,* bevacizumab (AVASTIN®)), a tyrosine kinase inhibitor (*e.g.,* axitinib (INLYTA®), pazopanib (VOTRIENT®), sorafenib (NEXAVAR®), or sunitinib (SUTENT®), or an mTOR inhibitor (*e.g.,* temsirolimus (TORISEL®) or everolimus (AFINITOR®).

Immunoproliferative Disorders

The antibody molecule described herein can be used to treat or prevent an immunoproliferative disorder. Immunoproliferative disorders (also known as immunoproliferative diseases or immunoproliferative neoplasms) are disorders of the immune system that are characterized by the abnormal proliferation of the primary cells of the immune system (*e.g.,* B cells, T cells and Natural killer (NK) cells) or by the excessive production of immunoglobulins (*e.g.,* antibodies).

Exemplary immunoproliferative disorders include, but are not limited to, lymphoproliferative disorders (LPDs), hypergammaglobulinemia, and paraproteinemia. Lymphoproliferative disorders include several conditions in which lymphocytes are produced in excessive quantities. They typically occur in patients who have compromised immune systems. Hypergammaglobulinemia is often characterized by increased levels of immunoglobulins in the blood serum. Paraproteinemia or monoclonal gammopathy is the presence of excessive amounts of a single monoclonal gammaglobulin (*e.g.,* a paraprotein) in the blood. In an embodiment, the antibody molecule is used to treat monoclonal IgA hypergammaglobulinemia.

Vasculitis

The antibody molecule described herein can be used to treat or prevent vasculitis. Vasculitis is a group of disorders that destroy blood vessels by inflammation. Vasculitis is primarily caused by leukocyte migration and resultant damage. Exemplary types of vasculitis include, but are not limited to, microscopic polyarteritis (poly-angiitis), Wegener's granulomatosis, Henoch Schonlein purpura and polyarteritis nodosa.

In an embodiment, the antibody molecule is used to treat IgA vasculitis. In an embodiment, the antibody molecule is used to treat Henoch-Schonlein purpura (IgA associated vasculitis).

Henoch–Schönlein purpura (HSP, also known as anaphylactoid purpura, purpura rheumatica, or Schönlein–Henoch purpura) is a disease of the skin and other organs that most commonly affects children. HSP is a systemic vasculitis (inflammation of blood vessels) and is characterized by deposition of immune complexes of IgA and complement component 3 (C3) on arterioles, capillaries, and venules. In the skin, the disease causes palpable purpura (small hemorrhages); often with joint and abdominal pain.

With kidney involvement, there may be a loss of small amounts of blood and protein in the urine; in a small proportion of cases, the kidney involvement proceeds to chronic kidney disease even irreversible kidney damage. HSP is often preceded by an infection, such as a throat infection.

Symptoms of Henoch–Schönlein purpura include, *e.g.,* rash (purpura), swollen or sore joints (arthritis), gastrointestinal symptoms (*e.g.,* abdominal pain, nausea, vomiting or bloody stools), and kidney involvement (*e.g.,* protein or blood in the urine). Serum levels of IgA are high in HSP patients.

Standards for defining Henoch–Schönlein purpura include, *e.g.,* the 1990 American College of Rheumatology (ACR) classification (Mills *et al.* (1990). Arthritis and Rheumatism 33 (8): 1114–21), the 1994 Chapel Hill Consensus Conference (CHCC) (Jennette *et al.* (1994) Arthritis and Rheumatism 37 (2): 187–92), and the 2006 European League Against Rheumatism (EULAR) and Pediatric Rheumatology Society (PReS) classification, which includes palpable purpura as a mandatory criterion, together with at least one of the following findings: diffuse abdominal pain, predominant IgA deposition (confirmed on skin biopsy), acute arthritis in any joint, and renal involvement (as evidenced by the presence of blood and/or protein in the urine) (Ozen *et al.* (2006) Annals of Rheumatic Diseases 65 (7): 936–41).

Other treatments that can be used in combination with the antibody molecule described herein to treat Henoch–Schönlein purpura include, *e.g.,* analgesics for the abdominal and joint pains, steroids (*e.g.,* oral steroids or a combination of intravenous methylprednisolone (steroid), cyclophosphamide and dipyridamole followed by prednisone). Other regimens also include, *e.g.,* steroids/azathioprine, and steroids/cyclophosphamide (with or without heparin and warfarin), or intravenous immunoglobulin (IVIG).

In another embodiment, the antibody molecule is used to treat acute proliferative glomerulonephritis, *e.g.,* post-streptococcal glomerulonephritis.

Acute proliferative glomerulonephritis is a disorder of the glomeruli (glomerulonephritis), or small blood vessels in the kidneys. It is a common complication of bacterial infections, typically skin infection by *Streptococcus* bacteria types 12, 4 and 1 (impetigo) but also after streptococcal pharyngitis, for which it is also known as postinfectious or poststreptococcal glomerulonephritis. The infection causes blood vessels in the kidneys to develop inflammation, which hampers the renal organs ability to filter urine.

The pathophysiology of this disorder is consistent with an immune complex mediated mechanism. This disorder produces proteins that have different antigenic determinants, which in turn have an affinity for sites in the glomerulus. As soon as binding occurs to the glomerulus, via interaction with properdin, complement is activated. Complement fixation causes the generation of additional inflammatory mediators.

Symptoms of acute proliferative glomerulonephritis include, *e.g.,* hematuria, oliguria, edema, hypertension, fever, headache, malaise, anorexia, and nausea.

Other treatments that can be used in combination with the antibody molecule described herein to treat cute proliferative glomerulonephritis includes, *e.g.,* blood pressure (BP) control and control of the amount of potassium in individuals with oliguric acute kidney injury.

Autoimmune Disorders

The antibody molecule described herein can be used to treat or prevent an autoimmune disorder. Exemplary autoimmune disorders that can be treated or prevented by the antibody molecule described herein include, but are not limited to, acute Disseminated Encephalomyelitis (ADEM), acute necrotizing hemorrhagic leukoencephalitis, Addison's disease, agammaglobulinemia, alopecia areata, amyloidosis, ankylosing spondylitis, anti-GBM/anti-TBM nephritis, antiphospholipid syndrome (APS), autoimmune angioedema, autoimmune aplastic anemia, autoimmune dysautonomia, autoimmune hepatitis, autoimmune hyperlipidemia, autoimmune immunodeficiency, autoimmune inner ear disease (AIED), autoimmune myocarditis, autoimmune oophoritis, autoimmune pancreatitis, autoimmune retinopathy, autoimmune thrombocytopenic purpura (ATP), autoimmune thyroid disease, autoimmune urticaria, axonal & neuronal neuropathies, Balo disease, Behcet's disease, bullous pemphigoid, cardiomyopathy, Castleman disease, celiac disease, Chagas disease, chronic fatigue syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), chronic recurrent multifocal ostomyelitis (CRMO), Churg-Strauss syndrome, cicatricial pemphigoid/benign mucosal pemphigoid, Crohn's disease, Cogans syndrome, cold agglutinin disease, congenital heart block, coxsackie myocarditis, CREST disease, essential mixed cryoglobulinemia, demyelinating neuropathies, dermatitis herpetiformis, dermatomyositis, Devic's disease (neuromyelitis optica), discoid lupus, Dressler's syndrome, endometriosis, eosinophilic esophagitis, eosinophilic fasciitis, Erythema nodosum, experimental allergic encephalomyelitis, Evans syndrome, fibromyalgia, fibrosing alveolitis, giant cell arteritis (temporal arteritis), giant cell myocarditis, glomerulonephritis, Goodpasture's syndrome, granulomatosis with polyangiitis (GPA) (formerly called Wegener's Granulomatosis), Graves' disease, Guillain-Barre syndrome, Hashimoto's encephalitis, Hashimoto's thyroiditis, hemolytic anemia, Henoch-Schonlein purpura, Herpes gestationis, hypogammaglobulinemia, idiopathic thrombocytopenic purpura (ITP), IgA nephropathy, IgG4-related sclerosing disease, immunoregulatory lipoproteins, inclusion body myositis, interstitial cystitis, juvenile arthritis, juvenile diabetes (type 1 diabetes), juvenile myositis, Kawasaki syndrome, Lambert-Eaton syndrome, Leukocytoclastic vasculitis, Lichen planus, Lichen sclerosus, Ligneous conjunctivitis, linear IgA disease (LAD), pupus (SLE), Lyme disease, chronic, Meniere's disease, microscopic polyangiitis, mixed connective tissue disease (MCTD), Mooren's ulcer, Mucha-Habermann disease, multiple sclerosis,

myasthenia gravis, myositis, narcolepsy, neuromyelitis optica (Devic's), neutropenia, ocular cicatricial pemphigoid, optic neuritis, palindromic rheumatism, PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus), paraneoplastic cerebellar degeneration, paroxysmal nocturnal hemoglobinuria (PNH), Parry Romberg syndrome, Parsonnage-Turner syndrome, Pars planitis (peripheral uveitis), pemphigus, peripheral neuropathy, perivenous encephalomyelitis, pernicious anemia, POEMS syndrome, polyarteritis nodosa, Type I, II, & III autoimmune polyglandular syndromes, polymyalgia rheumatica, polymyositis, postmyocardial infarction syndrome, postpericardiotomy syndrome, progesterone dermatitis, primary biliary cirrhosis, primary sclerosing cholangitis, psoriasis, psoriatic arthritis, idiopathic pulmonary fibrosis, pyoderma gangrenosum, pure red cell aplasia, raynauds phenomenon, reactive arthritis, reflex sympathetic dystrophy, reiter's syndrome, relapsing polychondritis, restless legs syndrome, retroperitoneal fibrosis, rheumatic fever, rheumatoid arthritis, sarcoidosis, Schmidt syndrome, scleritis, scleroderma, Sjogren's syndrome, sperm & testicular autoimmunity, stiff person syndrome, subacute bacterial endocarditis (SBE), Susac's syndrome, sympathetic ophthalmia, Takayasu's arteritis, temporal arteritis/Giant cell arteritis, thrombocytopenic purpura (TTP), Tolosa-Hunt syndrome, transverse myelitis, Type 1 diabetes, ulcerative colitis, undifferentiated connective tissue disease (UCTD), uveitis, vasculitis, vesiculobullous dermatosis, vitiligo, Wegener's granulomatosis (also known as Granulomatosis with Polyangiitis (GPA).

In an embodiment, the autoimmune disorder is rheumatoid arthritis, systemic lupus erythematosus, a linear IgA bullous disease (*e.g.,* linear immunoglobulin A (IgA) dermatosis), or IgA-mediated epidermolysis bullosa acquisita.

In an embodiment, the antibody molecule is used to treat rheumatoid arthritis. Other treatments that can be used in combination with the antibody molecule described herein to treat rheumatoid arthritis includes, *e.g.,* an NSAID, a steroid (*e.g.,* corticosteroid), a disease-modifying antirheumatic drug (DMARD) (*e.g.,* methotrexate (TREXALL®), leflunomide (ARAVA®), hydroxychloroquine (PLAQUENIL®), or sulfasalazine (AZULFIDINE®), a biologic response modifier (*e.g.,* abatacept (ORENCIA®), adalimumab (HUMIRA®), anakinra (KINERET®), certolizumab (CIMZIA®), etanercept (ENBREL®), golimumab (SIMPONI®), infliximab (REMICADE®), rituximab (RITUXAN®) and tocilizumab (ACTEMRA®), or Tofacitinib (XELJANZ®)), or surgery.

In an embodiment, the antibody molecule is used to treat systemic lupus erythematosus (SLE). Other treatments that can be used in combination with the antibody molecule described herein to treat SLE, *e.g.,* an NSAID, an antimalarial drug (*e.g.,* hydroxychloroquine (PLAQUENIL®), corticosteroid (*e.g.,* prednisone), an immunosuppressant (*e.g.,* azathioprine (IMURAN®, AZASAN®), mycophenolate (CELLCEPT®), leflunomide (ARAVA®), or methotrexate (TREXALL®)), or a BAFF inhibitor (*e.g.,* belimumab (BENLYSTA®).

In an embodiment, the antibody molecule is used to treat a linear IgA bullous disease (*e.g.,* linear immunoglobulin A (IgA) dermatosis). Other treatments that can be used in combination with the antibody molecule described herein to treat a linear IgA bullous disease (*e.g.,* linear immunoglobulin A (IgA) dermatosis) include, *e.g.,* corticosteroids (*e.g.,* prednisone or prednisolone), an antibiotic (*e.g.,* tetracycline, erythromycin, sulfapyridine), colchicine, or mycophenolate mofetil.

In an embodiment, the antibody molecule is used to treat IgA-mediated epidermolysis bullosa acquisita. Other treatments that can be used in combination with the antibody molecule described herein to treat IgA-mediated epidermolysis bullosa acquisita includes, *e.g.,* an antibiotic, an anti-inflammatory drug (*e.g.,* corticosteroid), or surgery.

Linear IgA Bullous Dermatosis

The antibody molecule described herein can be used to treat or prevent IgA dermatitis, e.g., linear IgA bullous disease/linear immunoglobulin A (IgA) dermatosis, and IgA-mediated epidermolysis bullosa acquisita. Linear IgA bullous dermatosis is a mucocutaneous autoimmune disease characterized by linear deposition of IgA and disruption of the dermoepidermal junction. In an embodiment, linear IgA bullous dermatosis is an autoimmune reaction against basement membrane proteins such as the lamina lucida and sublamina densa. The basement membrane anchors the epidermis to the dermis and helps to stabilize the skin. When IgA antibodies target such proteins, the basement membrane destabilizes resulting in tense blister formation. In an embodiment, linear IgA bullous dermatosis is drug-induced (e.g., induced from antibiotics (e.g., vancomycin), antihypertensives, and nonsteroidal anti-inflammatory agents), associated with another disease or disorder (e.g., a lymphoproliferative disorder, infection, ulcerative colitis, or systemic lupus (SLE)). In an embodiment, linear IgA bullous dermatosis can be of idiopathic origin. In children, the lesions of linear IgA bullous dermatosis are generally localized to the lower abdomen, perineal area, and inner thighs. In adults, the lesions are generally localized to the extensor surfaces, trunk, buttocks, and face.

Exemplary symptoms of linear IgA bullous dermatosis include, but are not limited to, prodromal itching, burning and discharge from the eyes, formation of tense blisters on the base of red or normal-appearing skin, clustering of blisters that results in the classic cluster of jewels sign or linearly along the edge of a blister resulting in the string of beads sign, and/or scattered red bumps or plaques at sites of inflammation.

Linear IgA bullous dermatosis can be diagnosed using clinical, immunological, and histopathological tests. A skin biopsy of a blister is typically performed, and immunofluorescence can also be done, to detect the presence of IgA deposits along the basement membrane zone in a linear pattern, which is typically indicative of linear IgA bullous dermatosis.

Other treatments that can be used in combination with the antibody molecule described herein to treat linear IgA bullous dermatosis include, *e.g.*, dapsone, sulfonamides, sulfapyridine, mycophenolate mofetil, corticosteroids (e.g., prednisone or prednisolone), colchicine), an antibiotic (*e.g.,* tetracycline, erythromycin, sulfapyridine), nicotinamide, or surgery.

IgM Mediated Neuropathy

The antibody molecule described herein can be used to treat or prevent IgM mediated neuropathy, e.g., anti-myelin associated glycoprotein (MAG) peripheral neuropathy or IgM mediated neuropathy associated with anti-GM1 antibodies. In an embodiment, the antibody molecule described herein can be used to treat or prevent anti-MAG. Anti-MAG neuropathy is characterized by the development of autoantibodies to myelin associated glycoprotein (MAG), which is found in the myelin sheath and in Schwann cells. These autoantibodies can impair MAG function and neuronal signaling, leading to loss of nerve function and problems with sensory and motor function. In an embodiment, anti-MAG neuropathy results from monoclonal gammopathy, e.g., IgM monoclonal gammopathy.

Exemplary symptoms of anti-MAG neuropathy include, but are not limited to, sensory loss, e.g., sensory loss in toes and fingers, loss of vibration sensation, unsteady gait, tremors in hands and legs, or weakness.

Anti-MAG neuropathy can be diagnosed using clinical features, electrodiagnostic studies, and measurement of serum IgM protein levels.

Other treatments that can be used in combination with the antibody molecule described herein to treat anti-MAG neuropathy, include cyclophosphamide, rituximab (RITUXAN®), plasma exchange, or intravenous immunoglobulin (IvIg).

In an embodiment, the antibody molecule described herein can be used to treat or prevent IgM mediated neuropathy associated with anti-GM1 ganglioside antibodies, e.g., multifocal motor neuropathy (MMN). MMN is characterized by progressive asymptomatic muscle weakness and atrophy. In an embodiment, a subject treated for MMN has IgM anti GMI1 ganglioside antibodies. Exemplary symptoms include, but are not limited to, functional motor deficit, ganglioside accumulation, increased CSF protein, muscle spasm, reduced tendon reflexes, progressive muscle weakness, weakness in the hands and lower arms, cramping, involuntary contractions or twitching, wrist drop or foot drop, or atrophy of affected muscles. In an embodiment, MMN results from an abnormal immune response. MMN can be diagnosed using clinical features, electrodiagnostic studies, and measurement of serum IgM protein levels. Other treatments that can be used in combination with the antibody molecule described herein to treat MMN include intravenous immunoglobulin (IvIg), rituximab (RITUXAN®), cyclophosphamide, or physical therapy.

Waldenstrom's Macroglobulinemia

The antibody molecule described herein can be used to treat or prevent Waldenstrom's macroglobulinemia. Waldenstrom's macroglobulinemia is a hematological cancer typically characterized by an excess of lymphoplasmacytic cells in the bone marrow. In an embodiment, Waldenstrom's macroglobulinemia is classified as a lymphoplasmacytic lymphoma. These abnormal cells generally comprise characteristics of lymphocytes and B cells and demonstrate aberrant expression of IgM, e.g., they produce excess IgM. In an embodiment, the excess IgM can build up in various organs, e.g., the heart and/or the kidneys, resulting in amyloidosis. In an embodiment, accumulation of lymphoplasmacytic cells in different tissues can result in hepatomegaly, splenomegaly, or enlarged lymph nodes.

Waldenstrom's macroglobulinemia can be a slow growing lymphoma. In an embodiment, Waldenstrom's macroglobulinemia can be clinically insignificant and indolent. In an embodiment, Waldenstrom's macroglobulinemia can be clinically significant. In an embodiment, Waldenstrom's macroglobulinemia results from a combination of genetic mutations, e.g., a mutation in the *MYD88* gene and/or the *CXCR4* gene.

Exemplary symptoms of Waldenstrom's macroglobulinemia include, but are not limited to, easily bruising, nose bleeds, bleeding of the gums, fatigue, weight loss, peripheral neuropathy (numbness in hands and feet), anemia, fever, headache, shortness of breath, changes in vision (e.g., blurring or loss of vision), dizziness, ataxia, cryoglobulinemia, confusion, or night sweats.

Waldenstrom's macroglobulinemia can be diagnosed by a blood test to detect, e.g., blood count, IgM protein levels in the blood, and/or measure organ function, e.g., kidney and/or liver function. Waldenstrom's macroglobulinemia can also be diagnosed and/or prognosed using a bone marrow biopsy and/or imaging tests, e.g., a CT scan or a PET scan.

Other treatments that can be used in combination with the antibody molecule described herein to treat Waldenström macroglobulinemia include, e.g., plasma exchange, chemotherapy, immunotherapy, targeted drug therapy, and stem cell transplant.

Lupus Nephritis

The antibody molecule described herein can be used to treat or prevent lupus nephritis. Lupus nephritis is an autoimmune disorder that is a form of glomerulonephritis that can constitute the most severe organ manifestation of systemic lupus erythematosus (SLE). Lupus nephritis leads to autoantibodies in the kidney which causes inflammation, e.g., inflammation in the nephrons, and impairs kidney function, e.g., waste removal and filtration. It can result in permanent scarring and damage to the

kidneys and possibly end-stage renal disease (ESRD). Lupus nephritis often develops in a subject within five years of developing lupus.

Exemplary symptoms of lupus nephritis include, but are not limited to, blood in the urine (hematuria), proteinuria, foamy urine (e.g., foamy urine due to excess protein in the urine), increased urination, edema, joint pain, high blood pressure, swelling in hands, ankles, and feet, excess levels of creatine in the blood, muscle pain, weight gain, fever of unknown etiology, red rash that is typically localized to the face (e.g., across the nose and face).

Diagnosis of lupus nephritis can be based on urinalysis and the measurement of blood, cell casts (e.g., cell fragments often found in the blood and/or the tubules of the kidneys), and protein levels in the urine. Diagnosis can also be based on a blood test to estimate kidney function, e.g., a creatine blood test with or without a blood urea nitrogen (BUN) test. Additionally, to test kidney function, the person's estimated glomerular filtration rate (eGFR) can be measured from a blood sample. A kidney biopsy can also be performed, which can be used to stage lupus nephritis. In an embodiment, lupus nephritis is classified as one of six stages under the International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification system, which include, minimal mesangial glomerulonephritis (Class I), mesangial proliferative lupus nephritis (Class II), focal lupus nephritis (<50% glomeruli) (Class III), diffuse segmental or global lupus nephritis (>50% glomeruli) (Class IV), membranous nephritis (Class V), or advanced sclerosing lupus nephritis (Class VI).

Other treatments that can be used in combination with the antibody molecule described herein to treat lupus nephritis, including but not limited to cyclophosphamide, mycophenolate mofetil, calcineurin inhibitors (e.g., azathioprine or tacrolimus), cyclosporine A, hydroxychloroquine, rituximab (RITUXAN®), belimumab, dialysis, kidney transplant, corticosteroids angiotensin-converting enzyme (ACE) inhibitors with angiotensin receptor blockers (ARBs), diuretics, beta blockers, and/or calcium channel blockers.

Other Disorders

The antibody molecule described herein can be used to treat or prevent other disorders, *e.g.,* IgA pemphigus, celiac disease, or alcoholic cirrhosis.

In an embodiment, the antibody molecule is used to treat or prevent IgA pemphigus. Other treatments that can be used in combination with the antibody molecule described herein to treat IgA pemphigus include, *e.g.,* corticosteroid, an immunosuppressant (*e.g.,* azathioprine (IMURAN®), methotrexate (TREXALL®), or mycophenolate mofetil (CELLCEPT®)), an CD-20 inhibitor (*e.g.,* rituximab (RITUXAN®), an antibiotic, an antiviral agent, or an antifungal agent.

In an embodiment, the antibody molecule is used to treat or prevent celiac disease. Other treatments that can be used in combination with the antibody molecule described herein to treat celiac disease include, *e.g.,* a gluten-free diet, a vitamin or mineral supplement, or a steroid.

In an embodiment, the antibody molecule is used to treat or prevent alcoholic cirrhosis. Other treatments that can be used in combination with the antibody molecule described herein to treat alcoholic cirrhosis include, *e.g.,* an immunosuppressant (*e.g.,* azathioprine, prednisone, azathioprine, cyclosporine, or methotrexate) or liver transplant.

Combination Therapies

The antibody molecules can be used in combination with other therapies. For example, the combination therapy can include an antibody molecule co-formulated with, and/or co-administered with, one or more additional therapeutic agents, *e.g.,* one or more additional therapeutic agents described herein. In other embodiments, the antibody molecules are administered in combination with other therapeutic treatment modalities, *e.g.,* other therapeutic treatment modalities described herein. Such combination therapies may advantageously utilize lower dosages of the administered therapeutic agents, thus avoiding possible toxicities or complications associated with the various monotherapies.

Administered "in combination", as used herein, means that two (or more) different treatments are delivered to the subject before, or during the course of the subject's affliction with a disorder. In an embodiment, two or more treatments are delivered prophylactically, *e.g.*, before the subject has the disorder or is diagnosed with the disorder. In another embodiment, the two or more treatments are delivered after the subject has developed or diagnosed with the disorder. In some embodiments, the delivery of one treatment is still occurring when the delivery of the second begins, so that there is overlap. This is sometimes referred to herein as "simultaneous" or "concurrent delivery." In other embodiments, the delivery of one treatment ends before the delivery of the other treatment begins. In some embodiments of either case, the treatment is more effective because of combined administration. For example, the second treatment is more effective, *e.g.,* an equivalent effect is seen with less of the second treatment, or the second treatment reduces symptoms to a greater extent, than would be seen if the second treatment were administered in the absence of the first treatment, or the analogous situation is seen with the first treatment. In some embodiments, delivery is such that the reduction in a symptom, or other parameter related to the disorder is greater than what would be observed with one treatment delivered in the absence of the other. The effect of the two treatments can be partially additive, wholly additive, or greater than additive. The delivery can be such that an effect of the first treatment delivered is still detectable when the second is delivered.

In certain embodiments, the additional agent is a second antibody molecule, *e.g.,* an antibody molecule different from a first antibody molecule. Exemplary antibody molecules that can be used in combination include, but are not limited to, any combination of the antibody molecules listed in **Table 1 or 5**.

In an embodiment, the antibody molecule is administered in combination with a second therapy to treat or prevent IgA nephropathy. In an embodiment, the antibody molecule is administered in combination with a second therapy to treat or prevent IgA nephropathy with crescentic glomerulonephritis (GN).

In an embodiment, the antibody molecule is administered in combination with an angiotensin-converting-enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB).

In an embodiment, the antibody molecule is administered in combination with an Fc decoy receptor, *e.g.*, a soluble Fc receptor. In an embodiment, the soluble Fc receptor is a soluble Fc-gamma receptor IIB. In an embodiment, the soluble Fc receptor is SM101/BAX 1810 (Baxalta). In an embodiment, the soluble Fc receptor is administered at a dose between 1 mg/kg and 50 mg/kg, *e.g.,* between 5 mg/kg and 15 mg/kg, between 12 mg/kg and 24 mg/kg, or between 20 mg/kg and 30 mg/kg.

In an embodiment, the antibody molecule is administered in combination with repository corticotropin (ACTHAR®). Repository corticotropin is an adrenocorticotropic hormone (ACTH) analogue. In an embodiment, repository corticotropin is administered at a dose between 50 U and 150 U, *e.g.,* between 80 U and 120 U, by subcutaneous injection, twice or three times a week. In an embodiment, repository corticotropin is administered at a dose of 120 U, by subcutaneous injection, *e.g.,* once, twice, or three times a week.

In an embodiment, the antibody molecule is administered in combination with mycophenolate mofetil (MMF). Mycophenolate mofetil is the 2-morpholinoethyl ester of mycophenolic acid (MPA), an immunosuppressive agent and inosine monophosphate dehydrogenase (IMPDH) inhibitor. In an embodiment, mycophenolate mofetil is administered at a dose of between 0.5 g and 2 g, *e.g.,* between 1 g and 1.5 g or between 1.5 g and 2 g, orally or intravenously, *e.g.,* once, twice, or three times a day.

In an embodiment, the antibody molecule is administered in combination with bortezomib (VELCADE®). Bortezomib, also known as [(1R)-3-methyl-1-({(2S)-3-phenyl-2-[(pyrazin-2-ylcarbonyl)amino]propanoyl}amino)butyl]boronic acid, is a proteasome inhibitor. In an embodiment, bortezomib is administered at a dose at between 0.5 mg/m^2 and 2.5 mg/m^2, *e.g.,* between 1 mg/m^2 and 1.5 mg/m^2, *e.g.* every three days or every week.

In an embodiment, the antibody molecule is administered in combination with allopurinol (ZYLOPRIM®). Allopurinol, also known as 1*H*-pyrazolo[3,4-d]pyrimidin-4(2H)-one, is a purine analog.

In an embodiment, allopurinol is administered at a dose between about 50 mg and 1000 mg, *e.g.,* between 100 mg and 600 mg or between 200 and 300 mg, orally, *e.g.,* once a day or once two days.

In an embodiment, the antibody molecule is administered in combination with prednisone and/or cyclophosphamide. In an embodiment, prednisone is administered at a dose between 0.2 mg/kg and 2 mg/kg, *e.g.,* between 0.5 mg/kg and 1 mg/kg, *e.g.,* once a day. In an embodiment, cyclophosphamide is administered at a dose between 0.2 g and 2 g, *e.g.,* between 0.5 g and 1 g, *e.g.,* once a day.

In an embodiment, the antibody molecule is administered in combination with rituximab (RITUXAN®). Rituximab is a chimeric anti-CD20 monoclonal antibody. In an embodiment, rituximab is administered at a dose between 100 mg/m^2 and 500 mg/m^2, *e.g.,* between 200 mg/m^2 and 450 mg/m^2 or between 300 mg/m^2 and 400 mg/m^2, intravenously, *e.g.,* once weekly, once every two weeks, once every four weeks, or once every eight weeks.

In an embodiment, the antibody molecule is administered in combination with blisibimod. Blisibimod, also known as A-623 or AMG 623, is a selective antagonist of B-cell activating factor (BAFF, also known as B-lymphocyte stimulator or BLyS).

In an embodiment, the antibody molecule is administered with budesonide. In an embodiment, the budesonide is NEFECON®, an oral formulation that releases budesonide.

In an embodiment, the antibody molecule is administered with valsartan and/or probucol. In an embodiment, valsartan is administered at a dose between 50 mg/day and 200 mg/day, *e.g.,* between 80 mg/day and 160 mg/day. In an embodiment, probucol is administered at a dose between 500 mg/day and 1000 mg/day, *e.g.,* between 700 mg/day and 800 mg/day.

In an embodiment, the antibody molecule is administered in combination with OPL-CCL2-LPM. OPL-CCL2-LPM is a recombinant fusion protein comprised of the human CCL2 (monocyte chemoattractant protein-1) chemokine fused to a truncated form of the enzymatically active A1 domain of *Shigella dysenteriae* holotoxin (SA1). In an embodiment, OPL-CCL2-LPM is administered at a dose between 0.001 mg/kg and 1 mg/kg, *e.g.,* between 0.01 mg/kg and 0.5 mg/kg or 0.05 mg/kg and 0.1 mg/kg, *e.g.,* intravenously.

In an embodiment, the antibody molecule is administered in combination with methylprednisolone. In an embodiment, methylprednisolone is administered at a dose between 0.1 mg/kg and 2 mg/kg/day, *e.g.,* between 0.2 mg/kg/day and 1.5 mg/kg/day or 0.5 mg/kg/day and 1 mg/kg/day, *e.g.,* orally.

In an embodiment, the antibody molecule is administered in combination with sirolimus. Sirolimus, also known as rapamycin, can inhibit IL-2 and other cytokines receptor-dependent signal transduction mechanisms, via action on mTOR, and thereby block activation of T and B cells. In an

embodiment, sirolimus is administered at dose between 0.2 mg/day and 2 mg/day, *e.g.,* between 0.5 mg/day and 1 mg/day.

In an embodiment, the antibody molecule is administered in combination with a renin-angiotensin system (RAS) blocker. For example, the RAS blocker can be an angiotensin-converting enzyme (ACE) inhibitor or an AT1 receptor blocker (ARB). Exemplary ACE inhibitors that can be used in combination with the antibody molecule described herein include, *e.g.,* benazepril (LOTENSIN®), captopril, enalapril (VASOTEC®), fosinopril, lisinopril (ZESTRIL®), moexipril (UNIVASC®), perindopril (ACEON®), quinapril (ACCUPRIL®), ramipril (ALTACE®), or trandolapril (MAVIK®). Exemplary AT1 receptor blockers that can be used in combination with the antibody molecule described herein include, *e.g.,* candesartan (ATACAND®), eprosartan (TEVETEN®), irbesartan (AVAPRO®), losartan (COZAAR®), olmesartan (BENICAR®), telmisartan (MICARDIS®), or valsartan (DIOVAN®).

In an embodiment, the antibody molecule is administered in combination with fostamatinib. Fostamatinib is a prodrug of the active compound tamatinib (R-406), which is an inhibitor of the enzyme spleen tyrosine kinase (Syk). In an embodiment, fostamatinib is administered at a dose between about 50 mg and 200 mg, *e.g.,* between 100 mg and 150 mg, *e.g.,* orally, *e.g.,* every day.

In an embodiment, the antibody molecule is administered in combination with paricalcitol. In an embodiment, paricalcitol is administered at a dose between about 0.2 mg and 2 mg, *e.g.,* between 0.5 mg and 1 mg, *e.g.,* every day.

In an embodiment, the antibody molecule is administered in combination with ramipril. In an embodiment, ramipril is administered at a dose between about 0.5 mg and 5 mg, *e.g.,* between 1 mg and 4 mg or between 2 mg and 3 mg, *e.g.,* every day.

In an embodiment, the antibody molecule is administered in combination with an angiotensin-converting-enzyme (ACE) inhibitor. In an embodiment, the ACE inhibitor is enalapril (VASOTEC®).

In an embodiment, the antibody molecule is administered in combination with an immunosuppressant. In an embodiment, the immunosuppressant is tacrolimus. Tacrolimus, also known as FK-506 or fujimycin, is a macrolide calcineurin inhibitor.

In an embodiment, the antibody molecule is administered in combination with omega-3 fatty acids.

In an embodiment, the antibody molecule is administered in combination with CCX168. CCX168 is an orally administered C5aR inhibitor.

Exemplary therapies that can be used in combination with an antibody molecule or composition described herein to treat or prevent other disorders are also described in the section of "Methods of Treating or Preventing Disorders" herein.

Methods of Diagnosis

In some aspects, the present disclosure provides a diagnostic method for detecting the presence of APRIL *in vitro* (*e.g.,* in a biological sample, such as a biopsy or blood sample) or *in vivo* (*e.g., in vivo* imaging in a subject). The method includes: (i) contacting the sample with an antibody molecule described herein, or administering to the subject, the antibody molecule; (optionally) (ii) contacting a reference sample, *e.g.,* a control sample (*e.g.,* a control biological sample, such as a biopsy or blood sample) or a control subject with an antibody molecule described herein; and (iii) detecting formation of a complex between the antibody molecule and APRIL in the sample or subject, or the control sample or subject, wherein a change, *e.g.,* a statistically significant change, in the formation of the complex in the sample or subject relative to the control sample or subject is indicative of the presence of APRIL in the sample. The antibody molecule can be directly or indirectly labeled with a detectable substance to facilitate detection of the bound or unbound antibody. Suitable detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials and radioactive materials, as described above and described in more detail below.

The term "sample," as it refers to samples used for detecting a polypeptide (*e.g.,* APRIL) or a nucleic acid encoding the polypeptide includes, but is not limited to, cells, cell lysates, proteins or membrane extracts of cells, body fluids such as blood, or tissue samples such as biopsies.

Complex formation between the antibody molecule, and APRIL, can be detected by measuring or visualizing either the antibody molecule bound to APRIL or unbound antibody molecule. Any suitable detection assays can be used, and conventional detection assays include an enzyme-linked immunosorbent assays (ELISA), a radioimmunoassay (RIA) or tissue immunohistochemistry. Alternative to labeling the antibody molecule, the presence of APRIL can be assayed in a sample by a competition immunoassay utilizing standards labeled with a detectable substance and an unlabeled antibody molecule. In this assay, the biological sample, the labeled standards and the antibody molecule are combined and the amount of labeled standard bound to the unlabeled binding molecule is determined. The amount of APRIL in the sample is inversely proportional to the amount of labeled standard bound to the antibody molecule.

The antibody molecules described herein can be used to diagnose disorders that can be treated or prevented by the antibody molecules described herein. The detection or diagnostic methods described herein can be used in combination with other methods described herein to treat or prevent a disorder described herein.

Other Aspects and Embodiments

In an aspect, the disclosure features a composition, *e.g.,* pharmaceutical composition, comprising an antibody molecule described herein. In an embodiment, the composition further comprises a pharmaceutical acceptable carrier.

In an aspect, the disclosure features a nucleic acid molecule encoding a heavy chain variable region (VH), a light chain variable region (VL), or both, of an antibody molecule described herein. In an embodiment, the nucleic acid molecule encodes a heavy chain (HC), a light chain (LC), or both, of an antibody molecule described herein. In an aspect, the disclosure features a vector comprising a nucleic acid molecule described herein. In an aspect, the disclosure features a cell, *e.g.,* an isolated cell, comprising a nucleic acid molecule described herein or a vector described herein.

In an aspect, the disclosure features a kit comprising an antibody molecule described herein and instructions to use of the antibody molecule.

In an aspect, the disclosure features a container comprising an antibody molecule described herein.

In an aspect, the disclosure features a method of producing an anti-APRIL antibody molecule, the method comprising culturing a cell described herein under conditions that allow production of an antibody molecule, thereby producing the antibody molecule.

In an embodiment, the method further comprises isolating the antibody molecule.

In an aspect, the disclosure features a method of treating IgA nephropathy, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule described herein or a composition described herein, thereby treating IgA nephropathy.

In an embodiment, the antibody molecule is administered to the subject intravenously.

In an embodiment, the antibody molecule is administered to the subject at a dose between 0.1 mg/kg and 50 mg/kg, *e.g.,* between 0.2 mg/kg and 25 mg/kg, between 0.5 mg/kg and 10 mg/kg, between 0.5 mg/kg and 5 mg/kg, between 0.5 mg/kg and 3 mg/kg, between 0.5 mg/kg and 2.5 mg/kg, between 0.5 mg/kg and 2 mg/kg, between 0.5 mg/kg and 1.5 mg/kg, between 0.5 mg/kg and 1 mg/kg, between 1 mg/kg and 1.5 mg/kg, between 1 mg/kg and 2 mg/kg, between 1 mg/kg and 2.5 mg/kg, between 1 mg/kg and 3 mg/kg, between 1 mg/kg and 2.5 mg/kg, or between 1 mg/kg and 5 mg/kg.

In an embodiment, the antibody molecule is administered to the subject at a fixed dose between 10 mg and 1000 mg, *e.g.,* between 10 mg and 500 mg, between 10 mg and 250 mg, between 10 mg and 150 mg, between 10 mg and 100 mg, between 10 mg and 50 mg, between 250 mg and 500 mg, between 150 mg and 500 mg, between 100 mg and 500 mg, between 50 mg and 500 mg, between 25 mg and 250 mg, between 50 mg and 150 mg, between 50 mg and 100 mg, between 100 mg and 150 mg. between 100 mg and 200 mg, or between 150 mg and 250 mg.

In an embodiment, the antibody molecule is administered once a week, twice a week, once every two weeks, once every three weeks, once every four weeks, once every eight weeks, once a month, once every two months, or once every three months.

In an embodiment, administration of the antibody molecule reduces the level of IgA in a peripheral tissue, *e.g.,* in serum, mucosal tissue, bone marrow, or any combination thereof.

In an embodiment, administration of the antibody molecule reduces the level of IgA1. In an embodiment, administration of the antibody molecule reduces the level of IgA1 in polymeric form (pIgA1). In an embodiment, administration of the antibody molecule reduces the level of IgA1 with O-linked glycosylation variants (*e.g.,* aberrant or reduced composition of galactose in CH1 hinge region).

In an embodiment, the method further comprises determining the level of IgA in a peripheral tissue sample from the subject, *e.g.,* chosen from serum, mucosal tissue, or bone marrow.

In an embodiment, the method further comprises administering to the subject a second therapy for IgA nephropathy. In an embodiment, the second therapy is chosen from an angiotensin-converting enzyme (ACE) inhibitor, an angiotensin receptor blocker (ARB), omega-3 fatty acids, an immunosuppressant (*e.g.,* a corticosteroid, *e.g.,* prednisone), a statin, mycophenolate mofetil, or any combination thereof.

In an aspect, the disclosure features a method of treating diabetic nephropathy, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule described herein or a composition described herein, thereby treating diabetic nephropathy.

In an aspect, the disclosure features a method of treating cancer, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule described herein or a composition described herein, thereby treating cancer.

In an embodiment, the cancer is a hematological cancer. In an embodiment, the hematological cancer is chosen from B-cell non-Hodgkin's lymphoma, chronic lymphocytic leukemia (CLL), Hodgkin's lymphoma, multiple myeloma, Waldenström macroglobulinemia, or lymphoplasmacytic lymphoma. In an embodiment, the cancer is a multiple myeloma.

In an aspect, the disclosure features a method of treating an immunoproliferative disorder, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule described herein or a composition described herein, thereby treating the immunoproliferative disorder.

In an embodiment, the immunoproliferative disorder is monoclonal IgA hypergammaglobulinemia.

In an aspect, the disclosure features a method of treating vasculitis, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule described herein or a composition described herein, thereby treating vasculitis.

In an embodiment, the vasculitis is kidney vasculitis. In an embodiment, the vasculitis is an IgA associated vasculitis (*e.g.,* Henoch-Schonlein purpura) or post-streptococcal glomerulonephritis.

In an aspect, the disclosure features a method of treating an autoimmune disorder, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule described herein or a composition described herein, thereby treating the autoimmune disorder.

In an embodiment, the autoimmune disorder is chosen from rheumatoid arthritis, systemic lupus erythematosus, a linear IgA bullous disease (*e.g.,* linear immunoglobulin A (IgA) dermatosis), or IgA-mediated epidermolysis bullosa acquisita (EBA).

In an aspect, the disclosure features a method of treating IgA pemphigus, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule described herein or a composition described herein, thereby treating IgA pemphigus.

In an aspect, the disclosure features a method of treating celiac disease, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule described herein or a composition described herein, thereby treating celiac disease.

In an aspect, the disclosure features a method of treating alcoholic cirrhosis, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule described herein or a composition described herein, thereby treating alcoholic cirrhosis.

In an aspect, the disclosure features a method of reducing the level of IgA in a cell or subject, the method comprising contacting the cell or subject, or administering to a subject in need thereof an effective amount of, an antibody molecule described herein or a composition described herein, thereby reducing the level of IgA.

In an embodiment, the antibody molecule is administered to the subject intravenously.

In an embodiment, the antibody molecule is administered to the subject at a dose between 0.1 mg/kg and 50 mg/kg, *e.g.,* between 0.2 mg/kg and 25 mg/kg, between 0.5 mg/kg and 10 mg/kg, between 0.5 mg/kg and 5 mg/kg, between 0.5 mg/kg and 3 mg/kg, between 0.5 mg/kg and 2.5 mg/kg, between 0.5 mg/kg and 2 mg/kg, between 0.5 mg/kg and 1.5 mg/kg, between 0.5 mg/kg and 1 mg/kg, between 1 mg/kg and 1.5 mg/kg, between 1 mg/kg and 2 mg/kg, between 1 mg/kg and 2.5 mg/kg, between 1 mg/kg and 3 mg/kg, between 1 mg/kg and 2.5 mg/kg, or between 1 mg/kg and 5 mg/kg.

In an embodiment, the antibody molecule is administered to the subject at a fixed dose between 10 mg and 1000 mg, *e.g.,* between 10 mg and 500 mg, between 10 mg and 250 mg, between 10 mg and 150 mg, between 10 mg and 100 mg, between 10 mg and 50 mg, between 250 mg and 500 mg, between

150 mg and 500 mg, between 100 mg and 500 mg, between 50 mg and 500 mg, between 25 mg and 250 mg, between 50 mg and 150 mg, between 50 mg and 100 mg, between 100 mg and 150 mg. between 100 mg and 200 mg, or between 150 mg and 250 mg.

In an embodiment, the antibody molecule is administered once a week, twice a week, once every two weeks, once every three weeks, once every four weeks, once every eight weeks, once a month, once every two months, once every three months.

In an embodiment, administration of the antibody molecule reduces the level of IgA in a peripheral tissue, *e.g.,* in serum, mucosal tissue, bone marrow, or any combination thereof.

In an embodiment, administration of the antibody molecule reduces the level of IgA1. In an embodiment, administration of the antibody molecule reduces the level of IgA1 in polymeric form (pIgA1). In an embodiment, administration of the antibody molecule reduces the level of IgA1 with O-linked glycosylation variants (*e.g.,* aberrant or reduced composition of galactose in CH1 hinge region).

In an aspect, the disclosure features use of an antibody molecule described herein or a composition described herein in the treatment, or in the manufacture of a medicament for the treatment, of a disorder described herein.

In another aspect, the disclosure features an antibody molecule described herein or a composition described herein for use in the treatment of a disorder described herein.

In an aspect, the disclosure features a method of detecting an APRIL molecule, the method comprising contacting a cell or a sample from a subject with an antibody molecule described herein, thereby detecting the APRIL molecule.

In an embodiment, the antibody molecule is coupled with a detectable label. In an embodiment, the APRIL molecule is detected *in vitro* or *ex vivo*. In another embodiment, the APRIL molecule is detected *in vivo*.

EXAMPLES

Example 1: Effect of Anti-APRIL Antibody Molecule on Serum Aberrantly Glycosylated IgA Levels

In this study, upon administration of an exemplary anti-APRIL antibody molecule, mAb 2419-1406, a dose-dependent reduction from baseline in serum aberrantly glycosylated Ig A (a-g IgA) levels was observed, and a dose response was generally observed in time to nadirs.

Results

Following antibody dosing, a dose-dependent reduction from baseline in serum a-g IgA by timepoint levels was observed. The maximum mean (median) percent reduction in serum a-g IgA ranged

from -24.35% (-28.13%) in the 0.5 mg/kg group (corresponding to 3.554 [2.730] µg/mL observed) to -71.61% (-68.94%) in the 12.0 mg/kg group (corresponding to 1.920 [1.750] µg/mL observed), and a dose response was generally observed in time to nadirs, which occurred at Week 4 for the 0.5 mg/kg group and Week 12 for the 12.0 mg/kg group (**Table 10**).

Serum a-g IgA level suppression was reversible, with a dose response in time to recovery during the follow-up period: the 0.5, 2.0, 6.0 and 12.0 mg/kg groups' mean (median) percent change at 16 weeks postdose were -18.16% (-21.43%), -15.41% (-8.25%), -9.93% (-21.21%) and -50.05% (-45.65%), respectively (**Table 10**). Overall, trends were generally similar for the Japanese and non-Japanese subjects as for the subjects overall (**FIG. 1**).

Table 10. Aberrantly Glycosylated Immunoglobulin A: Summary by Treatment – Any Ethnicity (Pharmacodynamic Population)

		Week 4		Week 8		Week 12		Week 16	
Statistic	**Baseline**	**Observed**	**% Change**	**Observed**	**% Change**	**Observed**	**% Change**	**Observed**	**% Change**
a-g IgA (µg/mL): placebo									
n	8	8	8	8	8	8	8	8	8
Mean	5.658	5.909	3.80	5.806	2.95	5.289	-4.29	5.355	-4.94
(Med)	(6.130)	(6.285)	(-1.65)	(5.545)	(0.61)	(5.570)	(-4.76)	(5.570)	(-10.37)
SD	1.751	2.177	26.839	1.894	17.083	1.375	14.028	1.982	22.678
Min,	2.750,	1.960,	-28.7,	2.460,	-18.4,	2.840,	-28.3,	2.370,	-33.2,
Max	8.280	8.970	51.8	7.910	32.5	6.870	16.2	8.400	42.1
a-g IgA (µg/mL): antibody 0.5 mg/kg									
n	7	7	7	6	6	7	7	7	7
Mean	4.804	3.554	-24.35	3.965	-20.59	3.719	-18.51	3.814	-18.16
(Med)	(4.100)	(2.730)	(-28.13)	(3.265)	(-20.13)	(3.050)	(-27.08)	(2.730)	(-21.43)
SD	2.674	1.908	14.671	2.155	10.658	1.659	22.408	1.922	18.574
Min,	2.660,	2.270,	-44.6,	2.270,	-36.6,	2.430,	-38.0,	2.600,	-38.2,
Max	10.700	7.690	-5.3	8.120	-5.9	6.680	20.0	7.700	10.8
a-g IgA (µg/mL): antibody 2.0 mg/kg									
n	7	7	7	6	6	5	5	5	5
Mean	5.363	2.517	-53.46	3.615	-34.44	4.310	-24.66	4.836	-15.41
(Med)	(5.160)	(2.580)	(-50.19)	(3.490)	(-32.16)	(4.170)	(-19.65)	(4.670)	(-8.25)
SD	0.985	0.715	7.710	1.246	17.806	1.568	17.060	1.775	19.981
Min,	4.660,	1.510,	-67.6,	2.320,	-54.6,	2.510,	-51.5,	2.820,	-45.6,
Max	7.540	3.870	-44.5	5.310	-8.9	6.740	-10.6	7.560	1.7
a-g IgA (µg/mL): antibody 6 mg/kg									
n	7	7	7	7	7	6	6	7	7
Mean	6.270	3.435	-44.80	2.756	-54.93	5.293	-25.73	5.771	-9.93
(Med)	(6.170)	(4.060)	(-49.89)	(2.910)	(-56.52)	(5.495)	(-20.94)	(7.030)	(-21.21)
SD	3.807	2.030	26.244	1.577	14.598	3.346	24.709	3.817	47.555
Min,	1.150,	0.500,	-79.4, 6.0	0.500,	-73.6,	0.500,	-56.5,	0.515,	-55.2,
Max	11.800	5.280		4.620	-26.1	9.830	11.0	10.700	83.6

		Week 4		Week 8		Week 12		Week 16	
Statistic	**Baseline**	**Observed**	**% Change**	**Observed**	**% Change**	**Observed**	**% Change**	**Observed**	**% Change**
a-g IgA (µg/mL): antibody 12 mg/kg									
n	7	7	7	6	6	7	7	7	7
Mean	6.960	2.913	-56.70	2.518	-62.95	1.920	-71.61	3.374	-50.05
(Med)	(7.980)	(2.590)	(-53.47)	(2.190)	(-66.72)	(1.750)	(-68.94)	(3.880)	(-45.65)
SD	3.312	1.562	10.965	1.683	10.546	0.981	5.432	1.811	11.621
Min,	1.700,	0.791,	-77.4,	0.508,	-74.3,	0.528,	-79.5,	0.976,	-75.6,
Max	11.600	5.610	-42.1	5.600	-48.1	3.670	-64.1	6.350	-42.5
a-g IgA (µg/mL): placebo[2] + vaccine									
n	5	5	5	5	5	5	5	5	5
Mean	4.910	4.510	-5.62	4.684	-1.38	5.008	3.23	4.510	-5.79
(Med)	(4.350)	(4.150)	(-4.75)	(4.890)	(-6.10)	(5.300)	(2.71)	(4.600)	(-14.37)
SD	2.232	1.684	7.965	1.670	12.980	2.052	14.190	1.775	17.310
Min,	2.950,	2.810,	-16.2, 5.9	2.770,	-15,	2.560,	-13.2,	2.280,	-22.7,
Max	8.280	6.940		7.040	-12.4	7.680	21.8	7.090	18.6
a-g IgA (µg/mL): vaccine + antibody 6.0 mg/kg									
n	10	9	9	9	9	9	9	9	9
Mean	5.706	2.920	-53.91	2.241	-65.54	3.502	-44.93	4.511	-26.24
(Med)	(4.375)	(2.460)	(-57.87)	(1.510)	(-67.69)	(3.240)	(-41.36)	(3.100)	(-28.41)
SD	3.314	1.809	10.334	1.604	13.381	2.214	16.720	2.484	8.524
Min,	1.960,	1.030,	-63.9,	0.594,	-80.7,	0.961,	-76.7,	2.110,	-34.2,
Max	12.500	6.420	-33.2	4.810	-33.1	7.330	-25.2	9.090	-8.8

Max = maximum; Med = median; Min = minimum; N = number of subjects in the PD Population; n = number of subjects evaluated; PD = pharmacodynamics; SD = standard deviation
[1] All subjects who received Placebo within Cohorts 1-4.
[2] All subjects who received Placebo within Cohort 5.
[3] % Change: Percent change from baseline.

Analysis

In data from a single-ascending dose study of the exemplary antibody molecule in healthy participants, the antibody molecule reduced serum levels of IgA and aberrantly glycosylated IgA1 (a-g IgA1). Aberrantly glycosylated IgA_1 was measured during the study with a validated ELISA using KM55 [rat anti-(a-g IgA1)] coated plates with bound standards and samples subsequently detected with anti-human IgA.

At baseline, a-g IgA levels ranged from 5.4 to 7.0 µg/mL across cohorts (**Table 11**). In contrast, baseline total IgA levels ranged from 2076 to 2866 µg/mL. Thus, serum a-g IgA in this healthy population comprised roughly 0.19 to 0.27% of total serum IgA at Baseline.

Following antibody dosing in the study, a dose-dependent reduction from baseline in serum a-g IgA1 by timepoint levels was observed. At peak a-g IgA nadir, the ratio of serum a-g IgA to total IgA ranged from 0.17% to 0.23% of total IgA at the corresponding timepoint.

These data demonstrate that a-g IgA comprised approximately 0.19% to 0.27% of total IgA at baseline, at a-g IgA nadir, the ratio of a-g IgA to total IgA ranged from 0.17% to 0.23%, and in healthy volunteers, 2149-1406 significantly lowers both total IgA and a-g IgA, but does not appreciably alter the ratio of aberrantly glycosylated IgA to total IgA.

Table 11. Changes in Serum IgA, a-g IgA, and a-g IgA to total IgA ratios Over Time

	BL IgA (mg/dL)	BL IgA (ug/mL)	BL a-g IgA (ug/mL)	BL Ratio, a-g IgA/IgA	Lowest Observed a-g IgA (ug/mL)	Timepoint of Lowest Observed a-g IgA	IgA level (ug/mL)	Ratio, a-g IgA/IgA
Pooled PBO (n=8)	231.1	2311	5.7	0.0025	5.36	Week 16	2300	0.0023
0.5 mg/kg antibody (n=7)	207.6	2076	4.8	0.0023	3.55	Week 4	1843	0.0019
2.0 mg/kg antibody (n=7)	284.4	2844	5.4	0.0019	2.52	Week 4	1507	0.0017
6.0 mg/kg antibody (n=7)	286.6	2866	6.3	0.0022	2.76	Week 8	1237	0.0022
12.0 mg/kg antibody (n=7)	261	2610	7	0.0027	1.92	Week 12	1154	0.0017
Placebo + vaccine (n=5)	220.3	2203	5.7	0.0026	4.51	Week 4	2208	0.0020
antibody + vaccine (n=10)	226.6	2266	4.9	0.0022	2.24	Week 8	1060	0.0021

Example 2: Study to Assess Pharmacokinetics, Pharmacodynamics, Safety, and Tolerability of Subcutaneously Administered Anti-APRIL Antibody

This phase 1, open-label single ascending single dose (SAD) study assesses the pharmacokinetics (PK), safety and tolerability, and pharmacodynamics (PD) upon subcutaneous (SC) administration of an exemplary anti-APRIL antibody molecule, mAb 2419-1406, in healthy non-Japanese and Japanese male and female participants aged 18 to 55 years. The results can inform the design and dose selection of other studies and provide data relating to the treatment of IgAN.

Inclusion Criteria:

Healthy participants for this study are chosen from 18-55-year-old males and females based on a pre-study medical evaluation (medical history, physical examination, vital signs, 12 lead electrocardiogram (ECG), and clinical laboratory evaluations). Participants must meet the following criteria at the time of initial screening: white blood cells (3,000 to 12,000/mm^3), platelets (>150,000/mm^3), Haemoglobin (>13 gm/dL for males and >11 gm/dL for females), estimated glomerular filtration rate (>80 mL/min/1.73 m^2), serum creatinine (<1.25 × upper limit of normal (ULN)), glucose (<115 mg/dL after 8 hours of fasting), serum IgG (≥6.0 g/L for participants 18 years of age or ≥7.0 g/L for participants ≥ 19 years of age), serum IgM (≥0.4 g/L), serum IgA (≥0.4 g/L for participants 18 years of age or ≥0.8 g/L for participants ≥ 19 years of age) and body mass index (BMI) between 17-32 kg/m^2.

Dosage:

The exemplary antibody molecule is administered subcutaneously (SC) at a starting dose of 200 mg in Cohort 1. Doses in Cohorts 2 and 3 may be administered as either one or two SC injections. The doses in Cohort 2 may be adjusted based on data from Cohort 1 and dosage for Cohort 3 may be adjusted based on data from both Cohort 1 and Cohort 2, with the total dose not to exceed 800 mg. The highest potential single dose is 800 mg administered SC (in the optional Cohort 3), which is approximately equivalent to 9.1 mg/kg based on a body weight of 70 kg and 80% bioavailability.

The starting dose was selected upon consideration of the antibody target and mechanism of action, in vitro/in vivo toxicology data, the no observed-adverse-effect level (NOAEL) observed in a toxicology study in cynomolgus monkeys, and data from a previous first in human study with the exemplary antibody molecule.

The exemplary dose levels for each cohort are summarized in **Table 12**.

Table 12. Exemplary Dose Level for Each Cohort

Cohorts	**Treatment**
Cohort 1	200 mg mAb (1 mL injection)
Cohort 2	400 mg mAb (2 mL injection)
Cohort 3	Not to exceed 800 mg mAb

Doses in Cohorts 2 and 3 can be administered as either 1 or 2 SC injections with the total dose not to exceed 800 mg mAb. The potential dose of 400 mg mAb 2419-1406 administered SC for Cohort 2 may be further adjusted based on the data from Cohort 1 and a decision for Cohort 3 can be made based on data from Cohorts 1 and 2. Doses can be selected such that they do not exceed a maximum allowed dose of 800 mg. Doses in Cohort 2 and 3 can be administered as either 1 or 2 SC injections.

Study Design:

The study is conducted in 3 sequential dosing cohorts. On Day 1, a single dose of the exemplary antibody molecule is administered SC in the morning approximately 30 minutes after a light meal. For the participants in Cohort 1, 2 participants are initially dosed and monitored for 24 hours potential unexpected adverse events (AEs). After a successful observation period, the remaining participants of Cohort I are subsequently be dosed. The dosing level of Cohort 2 participants can be modified based on the data from Cohort 1 study. Cohort 3 represents an optimal cohort which may assess an additional dose level. The dosing level of Cohort 3 can be decided based on data obtained from Cohort 1 and 2. The study intervention that is administered for each cohort in this study are outlined in **Table 13**.

Table 13: Identity of Study Interventions

	Cohort 1	**Cohort 2**	**Cohort 3**
Dose Formulation	Solution	Solution	Solution
Unit Dose Strength	200 mg/mL	200 mg/mL	200 mg/mL
Dosage level	200 mg	400 mg	TBD (not to exceed 800 mg)
Volume of Injection	1.0 mL	2.0 mL	TBD
Route of Administration	SC	SC	SC
Injection Site	Abdomen	Abdomen	Abdomen

Pharmacokinetic sampling starts on Day 1 and samples are collected until the final follow up visit on Day 112. Pharmacodynamic samples (total IgA, IgG, and IgM) and samples for APRIL, a-g IgA, anti-drug antibody (ADA), secretory immunoglobulin A (sIgA), and salivary IgA are also collected during the study.

Participants are monitored to detect AEs and SAEs during the study and followed appropriately to ensure resolution of AEs. The following conditions can result in in discontinuation of the study intervention and participant discontinuation/withdrawal: any AE of severe intensity and related causality or any SAE of related causality; symptomatic hypotension (systolic blood pressure <85 mmHg and/or 20 mmHg decrease in systolic blood pressure based on 3 systolic blood pressure measurement), tachycardia (heart rate> 120 beats per minute lasting longer than 30 minutes or with impaired consciousness), ALT ≥3 × ULN, AST ≥3 × ULN, serum creatinine >1.5 × ULN, a decrease from baseline in hemoglobin concentration >3 g/dL, white blood cell count <1,500/mm^3, and/or platelets <50,000/mm^3.

Sample Collection:

Whole blood samples of approximately 5 mL per timepoint (starting from day 1 to the final follow up visit at day 112) are collected for measurement of serum concentrations of the exemplary antibody molecule for pharmacokinetic studies. Pharmacodynamic samples (total immunoglobulin IgA, IgG, and IgM), and samples for APRIL, aberrantly glycosylated immunoglobulin A (a-g IgA), anti-drug antibody (ADA), secretory immunoglobulin A (sIgA), and salivary IgA are also collected during the study. Salivary IgG is also be collected per timepoint for measuring salivary IgG level. In particular, whole blood samples of approximately 3.5 mL for Ig levels and 5 mL for APRIL, a-g IgA, and sIgA are collected at various time points. For assessing the effect of the exemplary antibody molecule on PD parameters, serum is evaluated for Ig levels (total IgA, IgG and IgM). Serum is also be evaluated for APRIL, a-g IgA, and sIgA. Salivary IgA is also evaluated in saliva samples taken at various time points.

Endpoint parameters measured:

For pharmacokinetics (PK), the following parameters are measured: Cmax (primary), $AUC_{0\text{-}inf}$ (primary), $AUC_{0\text{-}last}$ (primary), C_{last} (secondary), t_{max}(secondary), T_{last}(secondary), $t_{1/2}$(secondary), $AUC_{0\text{-}28d}$(secondary), $AUC_{0\text{-}112d}$(secondary), $\%AUC_{ex}$(secondary), $V_{d/F}$(secondary), and CL/F(secondary).

For safety, the following parameters are measured: physical examination, vital sign (blood pressure, pulse, respiratory rate, and oral temperature), clinical laboratory tests (hematology, clinical chemistry, urianlysis, and Anti-drug antibody response), assessment of injection site, pain visual analog scale and adverse events (AEs).

For pharmacodynamics (PD), the following parameters are measured: Change from baseline in total serum IgG, IgA, and IgM concentrations and time to recovery; changes in serum a-g IgA levels; changes in plasma or serum APRIL levels; changes in the Serum sIgA levels; changes in salivary IgA levels; relationships between PK and PD/exploratory endpoints.

The following additional parameters are also be measured: characterization of ADA levels; assess ADA status impact on mAb 2419-1406 PK parameters.

%AUCex = Percentage of AUC0-inf obtained by extrapolation; AUC = area under the concentration-time curve; $AUC_{0\text{-}28d}$ = area under the concentration-curve from time zero to Day 28; $AUC_{0\text{-}112d}$ = AUC from time zero to Day 112; $AUC_{0\ inf}$ = AUC from time zero extrapolated to infinite time; $AUC_{0\text{-}last}$ = AUC from time zero to the last quantifiable concentration; CL/F = apparent clearance; Cl_{ast} = time of last serum concentration; $t_{1/2}$ = apparent terminal elimination half-life; sIgA = secretory immunoglobulin A; tl_{ast} = time of last quantifiable observed concentration; t_{max} = time of maximum serum concentration; VAS = visual analog scale; and Vd/F = apparent volume of distribution.

Analysis:

Serum are evaluated for Ig levels (total IgA, IgG and IgM) for assessing the effect of the exemplary antibody molecule on PD parameters. Serum are also evaluated for APRIL, a-g IgA, and sIgA. Data collected from the study are statistically analysed. Descriptive statistics for continuous variables are summarized by treatment group and include the number of participants, arithmetic mean, standard deviation, median, minimum and maximum; descriptive statistics for categorical data are summarized by treatment group using frequency counts and percentages. Descriptive statistics for PK parameters include number of observations, arithmetic mean, standard deviation, arithmetic percentage coefficient of variation (%CV), and geometric mean, median, geometric %CV, minimum and maximum. Data grouped by cohorts and overall (all cohorts) are analysed separately if deemed appropriate. All safety analyses are performed using the safety population.

Pharmacokinetic analysis is performed using data from all participants assigned to the PK population. Antibody serum concentrations is listed for each participant. Two sets of summary statistics of antibody serum concentrations are presented by dose level; the first combines the ethnicities and the second set stratifies each dose level by ethnicity group. Individual and mean antibody concentration-time profiles are plotted for each dose level in both linear and logarithmic scales. The PK parameters as described under parameters measured section are summarized by dose level for non-Japanese, Japanese, and all participants using descriptive statistics. The noncompartmental PK parameters are calculated using Phoenix WinNonlin® Version 8.0 or higher. Pharmacokinetic/PD modelling can be used for further characterization of data and reported separately.

Pharmacodynamics for total IgA, IgG, and IgM, and other relevant PD applicable markers in serum or appropriate matrix (using the raw data, change from baseline data and percent change from baseline, as appropriate) are summarized using descriptive statistics and plotted over time. Baseline data are taken as the last measurement prior to dosing or if not available, the screening value is used instead. An exploratory PK/PD analysis between the serum concentrations of the study intervention and PD assessments can be performed, if deemed appropriate.

Serum samples are screened for antibodies binding to the exemplary antibody molecule (ADA) and the titre of confirmed positive samples is reported. A summary table of confirmed positive or negative ADA is presented, by treatment (dose of the antibody molecule), and by study day based on the safety population. In addition, ADA titres are summarized by treatment and study day. The impact of ADA response on PK parameters is also analysed.

Clinical Laboratory Tests

The tests detailed in **Table 14** are performed.

Table 14. Clinical Laboratory Tests

Laboratory Tests	Parameters
Hematology	Basophils (percentage and absolute count)
	Eosinophils (percentage and absolute count)
	Hematocrit
	Hemoglobin
	Lymphocytes (percentage and absolute count)
	Mean corpuscular hemoglobin
	Mean corpuscular hemoglobin concentration
	Mean corpuscular volume
	Monocytes (percentage and absolute count)
	Neutrophils (percentage and absolute count)
	Platelet count
	Red blood cell count
	Red blood cell distribution width
	White blood cell count
Clinical Chemistry	Albumin
	Alkaline phosphatase
	ALT
	AST
	Calcium
	Chloride
	Total cholesterol
	Creatinine
	Gamma glutamyl transferase
	Glomerular filtration rate (calculated using the CKD-EPI equation)
	Glucose (fasting [8 hours])
	Lactate dehydrogenase
	Phosphorus
	Potassium
	Sodium
	Total bilirubin (if out of range, direct and indirect bilirubin are measured)
	Total protein
	Triglycerides
	Uric acid
Urinalysis	Bilirubin
	Blood
	Creatinine
	Glucose
	Ketones
	Leukocytes
	Nitrite
	pH and specific gravity
	Protein
	Urobilinogen
	Microscopic (only for abnormal urine stick test findings)

Serology	HBsAg
	Hepatitis C virus antibody
	HBcAb
	HIV ELISA
Urine drug screening test	Amphetamines
	Barbiturates
	Benzodiazepines
	Cannabinoids
	Cocaine
	Methylenedioxymethamphetamine
	Opiates
	Phencyclidine
	Propoxyphene
Pregnancy testing	Serum/urine β-hCG (WOCBP only)
Other	FSH (screening visit only, limited to female participants in whom nonchildbearing potential needs validation)

Results

The three-cohort study design described in the protocol above were expanded as follows:

The study has enrolled and dosed four sequential cohorts of 12 participants each (48 total, including 9 of Japanese descent). Participants were administered mAb 2419-1406 (200 mg/mL liquid) subcutaneously (SC). Doses for cohorts 1 through 4 were 200 mg (one 1 mL SC injection), 400 mg (two 1 mL SC injections), 400 mg (one 2 mL SC injection), and 600 mg (one 2 mL SC injection + one 1 mL SC injection), respectively. Participants received SC administered study drug on Day 1, were discharged from the institution on Day 2, and are being followed through day 112 on an outpatient basis. Standard safety assessments and blood sampling for PK and PD were performed at regular intervals.

48 participants were enrolled and dosed with study drug. Cohorts 1 and 2 have completed the study visits. Cohorts 3 and 4 have completed dosing, and follow-up visits are currently ongoing. mAb 2419-1406 administered as a SC injection was well tolerated, with no serious adverse events (AEs) or AEs that led to study discontinuation, and no injection site reactions. Treatment Emergent AEs (TEAEs) were all mild and all resolved. There was no clinically relevant effect of treatment on laboratory tests, vital signs, electrocardiogram parameters, or physical examinations. Preliminary PK results showed bioavailability of approximately 75% in comparison to data from intravenous administration of mAb 2419-1406. Single SC doses of either 400 mg or 600 mg suppressed total IgA by up to approximately 60% from baseline values. This indicated a similar degree and trajectory of IgA suppression achieved by the intravenous (IV) formulation of mAb 2419-1406 in the first-in-human Phase 1 study in healthy volunteers (**FIG. 5**).

To summarize, this ongoing Ph1 study of single dose mAb 2419-1406 administered via SC route has, to date, been safe and well tolerated in healthy adults, demonstrated acceptable bioavailability, and

suppressed total IgA by approximately 60% from baseline values at 400 mg and 600 mg doses. Final study data readout will likely support the further clinical development of SC-administered mAb 2419-1406 as a candidate treatment for IgAN.

Example 3: Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Anti-APRIL Antibody Molecule in Healthy Volunteers

This example describes an in-human study to evaluate the safety and tolerability of an exemplary anti-APRIL antibody molecule, mAb 2419-1406, in healthy volunteers and to characterize the pharmacokinetics (PK) and pharmacodynamics (PD) of this antibody molecule.

Briefly, a Phase 1, randomized, double-blind, placebo-controlled, single ascending dose study of mAb 2419-1406 (in the form of humanized IgG2) was performed in healthy adult male and female volunteers. The study was conducted in sequential dosing cohorts. The first four cohorts (0.5, 2.0, 6.0, and 12.0 mg/kg, respectively) each enrolled 9 participants (4 of Japanese descent and 5 of non-Japanese descent) who were randomized to mAb 2419-1406 or placebo in a ratio of 7:2. In addition, a fifth cohort enrolled 15 adults randomized to receive 6.0 mg/kg mAb 2419-1406 or placebo (10:5), followed by tetanus/diphtheria vaccine challenge after 28 days (TENIVAC®, Sanofi Pasteur Limited; the effect of APRIL inhibition on vaccine response is described in a companion abstract). Participants received intravenous administration of 2419-1406 on Day 1, were discharged from the institution on Day 2, and were followed for 16 weeks on an outpatient basis. Standard safety assessments and blood sampling for PK and PD were performed at regular intervals.

Overall, 51 participants were enrolled, randomized and dosed with mAb 2419-1406, of whom 47 (92.2%) completed the study. 2419-1406 was well tolerated, with no deaths, and no serious adverse events (AEs) or AEs that led to study discontinuation. Most treatment-emergent AEs (TEAEs) were mild; the incidence and severity of TEAEs were not dose dependent. One participant in the 2.0 mg/kg group experienced a severe TEAE of syncope following phlebotomy that the investigator considered unlikely to be related to study drug. There was no clinically relevant effect of treatment on laboratory tests, vital signs, electrocardiogram parameters, or physical examinations. Mab 2419-1406 had non-linear PK: half-life (t½) increased with dose, while drug exposure (AUC) increased in a greater than dose proportional manner. Serum immunoglobulins (IgA, a-g IgA1, IgG, and IgM) were reversibly suppressed in a dose-dependent manner following mAb 2419-1406 administration. The mean comparison treatment, by immunoglobulin, is shown in FIG. 2. The maximum mean percentage reductions from baseline occurred at Week 12 for the 12.0 mg/kg dose: IgA, -57.2% (FIG. 2, right panel); a-g IgA1, -71.6% (FIG. 2, left panel); IgG, -33.6%; and IgM, -67.2%. These reductions were reversible, with a dose response in time to recovery. Mean free (non-mAb 2419-1406 bound) serum APRIL levels decreased to the lower limit of

quantification (50 pg/mL) for all mAb 2419-1406 doses at Week 1, and also showed a dose response in time to recovery. No depletions in circulating lymphocyte populations were observed. There were no significant PK or PD differences between Japanese and non-Japanese participants.

In summary, mAb 2419-1406 single doses up to 12.0 mg/kg were safe and well tolerated in healthy adults. A single dose of mAb 2419-1406 was able to suppress free serum APRIL to the lower level of quantification. Serum a-g IgA1 decreased in parallel with total serum IgA and recovered in a dose-dependent manner following detection of free APRIL in serum.

Example 4: Impact of Anti-APRIL Antibody Molecule on Tetanus- and Diphtheria-Toxoid Vaccination-Elicited Immune Responses in Healthy Volunteers

As shown in Example 3, an exemplary anti-APRIL antibody molecule, mAb 2419-1406, was associated with dose-dependent reductions in serum immunoglobulins (IgA, IgG and IgM), which were reversible and had a dose response in time to recovery. This example describes a study to examine whether APRIL suppression by mAb 2419-1406 influences the T-cell dependent antibody responses to tetanus and diphtheria toxoid vaccination was examined.

Briefly, a Phase 1, randomized, double-blind, placebo-controlled, single ascending dose study of mAb 2419-1406 (in the form of humanized IgG2) was conducted in healthy adult male and female volunteers. In one cohort within the study, participants were randomized in a 2:1 ratio to receive intravenous administration of 6.0 mg/kg mAb 2419-1406 or placebo, followed by a vaccine composed of tetanus and diphtheria toxoids (TENIVAC®, Sanofi Pasteur Limited), in order to evaluate the effect of mAb 2419-1406 on recipients' ability to generate a vaccine booster response. Participants received intravenous administration of mAb 2419-1406 on Day 1, were discharged from the institution on Day 2, received a single intramuscular dose of vaccine on Day 28, and were followed for 16 weeks thereafter on an outpatient basis. Blood samples were taken at regular intervals, and anti-tetanus toxoid and anti-diphtheria toxoid IgG, IgM and IgA quantitative ELISA assays were performed. Tetanus and diphtheria anti-toxoid IgG titers $\geq$0.1 IU/mL were generally considered to be protective.

In the vaccination cohort, 15 participants were enrolled, randomized and dosed with mAb 2419-1406, of whom 14 completed the study, and one participant who received mAb 2419-1406 was lost to follow-up prior to receiving the vaccine. Both groups (placebo and mAb 2419-1406) demonstrated increased tetanus anti-toxoid IgG titers following immunization, with a mean 7.9-fold increase in IU/mL at Day 42 for placebo recipients and a mean 6.4-fold increase in IU/mL for mAb 2419-1406 recipients (FIG. 3). Tetanus anti-toxoid IgG titers greater than or equal to 0.1 IU/mL were considered protective. At visits after Day 42, tetanus anti-toxoid IgG titers declined faster in the mAb 2419-1406 group than in the placebo group (consistent with the reduction in total IgG associated with mAb 2419-1406 administration)

but remained above the protective threshold of 0.1 IU/mL for all participants throughout the study (FIG. 3). Similar trends were observed for diphtheria anti-toxoid IgG titers, with a mean 5.5-fold increase in IU/mL at the Day 42 visit for placebo recipients and a mean 5.1-fold increase for mAb 2419-1406 recipients (FIG. 4). Diphtheria anti-toxoid IgG titers greater than or equal to 0.1 IU/mL were considered protective. There was no evidence of tetanus- or diphtheria-toxoid elicited IgM responses in either the placebo or mAb 2419-1406 groups, consistent with the recall nature of the vaccination. In a *post hoc* analysis, pre-existing serum anti-Td IgA titers fell between Day 1 and Day 28 consistent with the overall suppression of total serum IgA, were boosted to similar levels after vaccination in both groups and waned faster in the mAb 2419-1406 recipients thereafter.

In summary, mAb 2419-1406 treatment did not interfere with participants' ability to mount an antigen-specific serum IgG or IgA boost response to tetanus and diphtheria toxoid vaccination. There was no evidence of tetanus- or diphtheria-specific IgM responses in either the placebo or mAb 2419-1406 groups, consistent with recall vaccination exposure. These data indicate that qualitative T-cell dependent antibody responses are preserved during APRIL suppression.

INCORPORATION BY REFERENCE

All publications, patents, and Accession numbers mentioned herein are hereby incorporated by reference in their entirety as if each individual publication or patent was specifically and individually indicated to be incorporated by reference.

EQUIVALENTS

While specific embodiments of the subject invention have been discussed, the above specification is illustrative and not restrictive. Many variations of the invention will become apparent to those skilled in the art upon review of this specification and the claims below. The full scope of the invention should be determined by reference to the claims, along with their full scope of equivalents, and the specification, along with such variations.

What is claimed is:

1. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-APRIL antibody molecule, for use in a method of treating a disorder in a human subject,

wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

wherein the administration reduces the level of aberrantly glycosylated IgA (a-g IgA) by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy.

2. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-APRIL antibody molecule, for use in a method of reducing the level of a-g IgA in a human subject,

wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

wherein the administration reduces the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the subject has, or is at risk of having, a disorder, e.g., IgA nephropathy.

3. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-APRIL antibody molecule, for use in a method of treating a disorder in a human subject,

wherein the method comprises selecting a dose or dosage for the antibody molecule;

wherein administration of the antibody molecule at the selected dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

optionally wherein the disorder is IgA nephropathy.

4. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-APRIL antibody molecule, for use in a method of treating a disorder in a human subject,

wherein the method comprises responsive to a determination that administration of the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject, administering to the subject the antibody molecule at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy.

5. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-APRIL antibody molecule, for use in a method of treating a disorder in a human subject,

wherein the method comprises determining whether administration of an anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject,

if the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%, administration of the antibody molecule at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg is initiated, continued, or maintained; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

optionally wherein the disorder is IgA nephropathy,

optionally wherein if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%, administration of the antibody molecule is terminated, discontinued, or altered, and/or a different therapeutic agent or modality is administered.

6. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-APRIL antibody molecule, for use in a method of treating a disorder in a human subject,

wherein the method comprises determining whether administration of a therapeutic agent or modality other than the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in a subject in need thereof,

if the therapeutic agent or modality does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%, administering the antibody molecule to the subject at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and

a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy.

7. An anti-APRIL antibody molecule, or a pharmaceutical composition comprising the anti-APRIL antibody molecule, for use in a method of treating a disorder in a human subject,

wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

wherein the subject has received, or is going to receive, a vaccine within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks of administration of the antibody molecule, optionally wherein the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®),

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3

comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

optionally wherein administration of the antibody molecule at the selected dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject.

8. A method of treating a disorder, comprising:

administering an anti-APRIL antibody molecule to a human subject in need thereof at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

wherein the administration reduces the level of aberrantly glycosylated IgA (a-g IgA) by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject; and

wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

optionally wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

thereby treating the disorder.

9. A method of reducing the level of a-g IgA, comprising:

administering an anti-APRIL antibody molecule to a human subject in need thereof,

wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg;

wherein the administration reduces the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%,

80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the subject has, or is at risk of having, a disorder, e.g., IgA nephropathy,

thereby reducing the level of a-g IgA.

10. A method of treating a disorder, comprising:

selecting a dose or dosage for an anti-APRIL antibody molecule;

wherein administration of the antibody molecule at the selected dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino

acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

optionally wherein the subject has, or is at risk of having, IgA nephropathy,

thereby threating the disorder.

11. A method of treating a disorder, comprising:

responsive to a determination that administration of the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject, administering to a human subject in need thereof an anti-APRIL antibody molecule at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

thereby treating the disorder.

12. A method of treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%,

99%, or 100% in the subject,

if the antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%, administration of the antibody molecule at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg is initiated, continued, or maintained; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the antibody molecule is administered at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

optionally wherein if the antibody molecule does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%, administration of the antibody molecule is terminated, discontinued, or altered, and/or a different therapeutic agent or modality is administered,

optionally wherein the disorder is IgA nephropathy,

thereby treating the disorder.

13. A method of treating a disorder, comprising:

determining whether administration of a therapeutic agent or modality other than an anti-APRIL antibody molecule reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in a subject in need thereof,

if the therapeutic agent or modality does not reduce, or is not likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100%,

administering the antibody molecule to a human subject at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

thereby treating the disorder.

14. A method of treating a disorder, comprising:

administering an anti-APRIL antibody molecule to a human subject in need thereof at a dose of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg; and

wherein the subject has received, or is going to receive, a vaccine within 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 weeks of administration of the antibody molecule, optionally wherein the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®),

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3

comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

optionally wherein administration of the antibody molecule at the selected dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject,

thereby treating the disorder.

15. A method of selecting an anti-APRIL antibody molecule for treating a disorder, comprising:

determining whether administration of the antibody molecule at a dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in a human subject in need thereof,

wherein the dose is about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

thereby selecting the antibody molecule.

16. A method of selecting a dose or dosage for an anti-APRIL antibody molecule for treating a disorder, comprising:

determining whether administration of the antibody molecule at a dose or dosage reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in a human subject in need thereof,

optionally wherein the dose is about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg,

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

thereby selecting the dose or dosage.

17. A method of selecting a human subject for treating a disorder, comprising:

determining whether administration of an anti-APRIL antibody molecule at a dosage of about 0.5 mg/kg, 2.0 mg/kg, 6 mg/kg, 9 mg/kg, 9.1 mg/kg, 12 mg/kg, or at a fixed dose of about 200 mg, 400 mg, 600 mg, or 800 mg reduces, or is likely to reduce, the level of a-g IgA by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% in the subject,

optionally wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

optionally wherein the disorder is IgA nephropathy,

thereby selecting the subject,

18. The antibody molecule or pharmaceutical composition for use of any of claims 1-7, or the method of any of claims 8-17, wherein the a-g IgA comprises or is a-g IgA1.

19. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18, or the method of any of claims 8-18, wherein the level of a-g IgA is reduced by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% for a predetermined period, e.g., at least one, two, three, or four weeks, or at least one, two, three, four, five, six, seven, eight, nine, ten, eleven, or twelve months.

20. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-19, or the method of any of claims 8-19, wherein the level of a-g IgA is reduced by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% about 4 weeks after the antibody molecule is administered.

21. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-20, or the method of any of claims 8-20, wherein the level of a-g IgA is reduced by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% about 8 weeks after the antibody molecule is administered.

22. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-21, or the method of any of claims 8-21, wherein the level of a-g IgA is reduced by at least 40%, 50%, 60%,

70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% about 12 weeks after the antibody molecule is administered.

23. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-22, or the method of any of claims 8-22, wherein the level of a-g IgA is reduced by at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% about 16 weeks after the antibody molecule is administered.

24. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-23, or the method of any of claims 8-23, wherein the level of a-g IgA is reduced by at least 50%.

25. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-24, or the method of any of claims 8-24, wherein the level of a-g IgA is reduced by at least 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%.

26. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-25, or the method of any of claims 8-25, e.g., in a period of at least 1, 2, 3, 4, 5, 6, 7, 8, 9. 10, 11, 12, 13, 14, 15, 16, 17, or 18 months.

27. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-26, or the method of any of claims 8-26, wherein the antibody molecule is administered as a repeated dose, e.g., in a period of at least 3, 6, 9. 12, 15, 18, 24, 30, or 36 months, optionally wherein the subject is administered one or more additional dosages of the anti-APRIL antibody molecules (e.g., 24 hours, 48 hours, 72 hours, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 1 month, 2 months, 3 months, 4 months, 5 months, or 6 months after the first administration).

28. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-27, or the method of any of claims 8-27, wherein the antibody molecule is administered subcutaneously.

29. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-27, or the method of any of claims 8-27, wherein the antibody molecule is administered intravenously.

30. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-29, or the method of any of claims 8-29, wherein the disorder an APRIL-associated disorder.

31. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-30, or the method of any of claims 8-30, wherein the disorder is associated with an aberrant level of total IgA.

32. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-31, or the method of any of claims 8-31, wherein the disorder is a disorder associated with a-g IgA.

33. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-32, or the method of any of claims 8-32, wherein the disorder is IgA nephropathy (IgAN).

34. The antibody molecule or pharmaceutical composition for use of claim 33, or the method of claim 33, wherein the IgAN is a familial IgAN.

35. The antibody molecule or pharmaceutical composition for use of claim 33, or the method of claim 33, wherein the IgAN is an adult IgAN.

36. The antibody molecule or pharmaceutical composition for use of claim 33, or the method of claim 33, wherein the IgAN is a post-transplant IgAN, a pediatric IgAN, or a crescentic IgAN.

37. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-32, or the method of any of claims 8-32, wherein the disorder is a chronic kidney disease (CKD) or a disorder associated with CKD.

38. The antibody molecule or pharmaceutical composition for use of claim 37, or the method of claim 37, wherein the CKD is an advanced CKD, e.g., with an estimated glomerular filtration rate (eGFR) equal to or greater than about 30 or about 45.

39. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-32, or the method of any of claims 8-32, wherein the disorder is Henoch-Schonlein purpura (HSP).

40. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-32, or the method of any of claims 8-32, wherein the disorder is cutaneous vasculitis or IgA vasculitis.

41. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-32,

or the method of any of claims 8-32, wherein the disorder is IgA dermatitis, e.g., IgA bullous dermatosis.

42. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-32, or the method of any of claims 8-32, wherein the disorder is Waldenström macroglobulinemia (WM).

43. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-32, or the method of any of claims 8-32, wherein the disorder is lupus nephritis.

44. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-43, or the method of any of claims 8-43, wherein the subject is a human patient.

45. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-44, or the method of any of claims 8-44, wherein the subject has, or is identified as having, a level of a-g IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of a-g IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject.

46. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-45, or the method of any of claims 8-45, wherein the subject has, or is identified as having, a level of total IgA that is at least 1, 1.5, 2, 2.5, 3.5, 4, 4.5, or 5-fold higher than the level of total IgA in a reference subject, e.g., a subject who does not have the disorder, e.g., a healthy or normal subject.

47. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-46, or the method of any of claims 8-46, wherein the subject has received, or is receiving, a different therapeutic agent or modality for treating the disorder.

48. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-46, or the method of any of claims 8-46, wherein the subject has not received, or is not receiving, a different therapeutic agent or modality for treating the disorder.

49. The antibody molecule or pharmaceutical composition for use of any of claims 1-6 or 18-43, or the method of any of claims 8-13 or 15-43, wherein the subject has received, is receiving, or is going to receive, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule.

50. The antibody molecule or pharmaceutical composition for use of any of claims 1-6, 18-43 or 49, or the method of any of claims 8-13, 15-43 or 49, wherein the subject is, or is identified as being, in need of receiving, a vaccine, e.g., within 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 weeks, of administration of the antibody molecule.

51. The antibody molecule or pharmaceutical composition for use of claim 49 or 50, or the method of claim 49 or 50, wherein the subject receives the vaccine before, concurrent with, or after administration of the antibody molecule.

52. The antibody molecule or pharmaceutical composition for use of any of claims 1-6, 18-43 or 49-51, or the method of any of claims 8-13, 15-43 or 49-51, wherein administration of the antibody molecule reduces the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine by no more than 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%.

53. The antibody molecule or pharmaceutical composition for use of any of claims 1-6, 18-43 or 49-52, or the method of any of claims 8-13, 15-43 or 49-52, wherein administration of the antibody molecule does not reduce, or does not substantially reduce, the subject's ability to have an effective antigen-specific serum IgG and/or IgA response to the vaccine.

54. The antibody molecule or pharmaceutical composition for use of any of claims 1-6, 18-43 or 49-53, or the method of any of claims 8-13, 15-43 or 49-53, wherein the subject has or maintains an effective (e.g., protective) antigen-specific serum IgG and/or IgA response to the vaccine after administration of the antibody molecule.

55. The antibody molecule or pharmaceutical composition for use of any of claims 1-6, 18-43 or 49-54, or the method of any of claims 8-13, 15-43 or 49-54, wherein the vaccine comprises tetanus toxoid, diphtheria toxoid, or both (e.g., TENIVAC®).

56. The antibody molecule or pharmaceutical composition for use of claim 55, or the method of claim 55, wherein the subject has or maintains an effective (e.g., protective) level of tetanus and/or diphtheria anti-toxoid IgG (e.g., equal to or above 0.1 IU/mL in the blood), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or more weeks after administration of the antibody molecule.

57. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-56,

or the method of any of claims 8-56, wherein the subject has, or is identified as having, a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

58. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-57, or the method of any of claims 8-57, further comprising determining whether the subject has a genomic susceptible locus of the disorder, e.g., IgA nephropathy.

59. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-58, or the method of any of claims 8-58, wherein the antibody molecule comprises a heavy chain variable region (VH) comprising three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and a light chain variable region (VL) comprising three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3),

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 11; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 12, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16; or

wherein the VH comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 282, and an HCDR3 comprising the amino acid sequence of SEQ ID NO: 13; and the VL comprises an LCDR1 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

60. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-59, or the method of any of claims 8-59, wherein the antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 296, and a VL comprising the amino acid sequence of SEQ ID NO: 286,

optionally wherein the antibody molecule is an IgG2.

61. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-60, or the method of any of claims 8-60, wherein the level of a-g IgA is determined in a sample from the subject.

62. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-61, or the method of any of claims 8-61, further comprising determining the level of a-g IgA in a sample from the subject.

63. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-62, or the method of any of claims 8-62, further comprising determining the level of total IgA in the sample.

64. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-63, or the method of any of claims 8-63, further comprising determining the level of IgM and/or IgG in the sample.

65. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-64, or the method of any of claims 8-64, further comprising obtaining a sample from the subject.

66. The antibody molecule or pharmaceutical composition for use of claim 65, or the method of claim 65, wherein the sample is a blood or serum sample.

67. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-66, or the method of any of claims 8-66, further comprising administering a second therapeutic agent or modality to the subject.

68. The antibody molecule or pharmaceutical composition for use of claim 67, or the method of claim 67, wherein the second therapeutic agent or modality is a small molecule.

69. The antibody molecule or pharmaceutical composition for use of claim 67, or the method of claim 67, wherein the second therapeutic agent or modality is an antibody molecule.

70. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-69, or the method of any of claims 8-69, wherein the subject is administered the anti-APRIL antibody molecule at a concentration of about 100, 150, 175, 180, 190, 200, 210, 220, 225, 230, 240, 250, or 300 mg/mL.

71. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-70, or the method of any of claims 8-70, wherein the subject is administered the anti-APRIL antibody molecule at a concentration of about 200 mg/mL.

72. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-71, or the method of any of claims 8-71, wherein the subject is administered the anti-APRIL antibody molecule

at a fixed dose of about 200, 250, 300, 450, 400, 450, 500, 550, 600, 650, 700, 750, or 800 mg.

73. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-72, or the method of any of claims 8-72, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dose of about 200 mg (e.g., at a volume of about 1 mL).

74. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-72, or the method of any of claims 8-72, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dose of about 400 mg (e.g., at a total volume of about 2 mL, e.g., as two administrations of 1 mL volumes or as one administration of a 2 mL volume).

75. The antibody molecule or pharmaceutical composition for use of any of claims 1-7 or 18-72, or the method of any of claims 8-72, wherein the subject is administered the anti-APRIL antibody molecule at a fixed dose of about 600 mg (e.g., at a total volume of about 3 mL, e.g., as one administration of a 2 mL volume and one administration of a 1 mL volume).