

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 7-8**. 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.

Accordingly, this disclosure provides an antibody molecule, *e.g.*, an antibody molecule described herein, having 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,

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 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).

The disclosure features an anti-APRIL antibody molecule described herein, e.g., a synthetic or isolated anti-APRIL antibody molecule described herein.

In another aspect, the present disclosure features an anti-APRIL antibody molecule, comprising 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 the HCDR1 of a monoclonal antibody chosen from 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;

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 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 monoclonal antibody, or

(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 the 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 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 monoclonal antibody; and/or

which 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 monoclonal antibody; 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 monoclonal antibody.

In another aspect, the present disclosure features an anti-APRIL antibody molecule, comprising 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 HCDR3 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); or comprising 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);

5 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 HCDR3 comprising an amino acid sequence of H-G-A-Y-Y-S-N-A-F-D-Y (SEQ ID NO: 13), or

10 (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;

15 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 comprises:

(i) a heavy chain variable region (VH), wherein the heavy chain variable region comprises
20 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
25 by no more than 1, 2, 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

30 (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

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 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).

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 another aspect, the present disclosure features a composition comprising an antibody molecule as disclosed herein, optionally, wherein the composition is a pharmaceutical composition, optionally further comprising a pharmaceutically 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 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 or a composition 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.

The disclosure also 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 another aspect, the present disclosure features the use of an antibody molecule described herein, or a composition
5 described herein, in the manufacture of a medicament for treating IgA nephropathy in a subject.

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,
10 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
15 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
20 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
25 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
30 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
35 combination thereof.

The disclosure also 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 another aspect, the present disclosure features the use of an antibody molecule described herein, or a
5 composition described herein, in the manufacture of a medicament for treating diabetic nephropathy in a subject.

The disclosure further 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 another aspect, the present disclosure features the use of an antibody molecule described herein, or a composition described
5 herein, in the manufacture of a medicament for treating cancer in a subject.

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.

10 The disclosure also 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 another aspect, the present disclosure features the use of an antibody molecule as described herein, or a composition of described herein, in the manufacture of a medicament for treating an
15 immunoproliferative disorder in a subject.

In an embodiment, the immunoproliferative disorder is monoclonal IgA hypergammaglobulinemia.

The disclosure also features a method of treating vasculitis, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule described
20 herein or a composition described herein, thereby treating vasculitis. In another aspect, the present disclosure features the use of an antibody molecule as described herein, or a composition of as described herein, in the manufacture of a medicament for treating vasculitis in a subject.

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.

25 The disclosure further 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 yet another aspect, the present disclosure features the use of an antibody molecule described herein, or a composition described herein, in the manufacture of a medicament for treating an autoimmune
30 disorder in a subject.

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).

The disclosure features a method of treating IgA pemphigus, the method comprising
35 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 another aspect, the present disclosure features the use of an antibody molecule described herein, or a

composition described herein, in the manufacture of a medicament for treating IgA pemphigus in a subject.

5 The disclosure also 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 a further aspect, the present disclosure features the use of an antibody molecule described herein, or a composition described herein, in the manufacture of a medicament for treating celiac disease in a subject.

10 The disclosure further 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 another aspect, the present disclosure features the use of an antibody molecule described herein, or a composition described herein, in the manufacture of a medicament for treating alcoholic cirrhosis in a subject.

15 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.

5 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.

10 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.

20 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).

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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.

30 The disclosure also 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.

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What is claimed is:

1. An anti-APRIL antibody molecule, which:

(i) binds, or substantially binds, to human APRIL;

(ii) binds, or substantially binds, to mouse APRIL;

(iii) inhibits, or substantially inhibits, binding of APRIL to TACI; and

(iv) inhibits, or substantially inhibits, binding of APRIL to BCMA.

2. The antibody molecule of claim 1, which binds, or substantially binds, to human APRIL at an EC_{50} of 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, 0.001 nM or less, between 0.001 nM and 20 nM, 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; and/or

which binds, or substantially binds, to mouse APRIL at an EC_{50} of 100 nM or less, 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, between 0.001 nM and 100 nM, , 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.

3. The antibody molecule of claim 1 or 2, which inhibits, or substantially inhibits, binding of APRIL to TACI at an IC_{50} of 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, 0.002 nM or less, or 0.001 nM or less, between 0.001 nM and 50 nM, 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 0.5 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,

optionally, wherein APRIL is human APRIL, mouse APRIL, or both, and wherein TACI is human TACI, mouse TACI, or both and/or which inhibits, or substantially inhibits, binding of APRIL to 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, 0.005 nM or less, 0.002 nM or less, or 0.001 nM or less, between 0.001 nM and 100 nM, 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,

optionally, wherein APRIL is human APRIL, mouse APRIL, or both, and wherein BCMA is human BCMA, mouse BCMA, or both.

4. The antibody molecule of any of claims 1-3, wherein binding of the antibody molecule to APRIL inhibits, or substantially inhibits, the binding of the CRD2 domain of TACI to APRIL,

optionally, wherein APRIL is human APRIL, and wherein TACI is human TACI; and/or wherein binding of the antibody molecule to human APRIL, inhibits, or substantially inhibits, the binding of human TACI, to 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, or more, of the human APRIL residues from any of Tables 3-4 or 7-8.

5. The antibody molecule of any of claims 1-4, which 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 3525, 3530, 3833, 3631, 3732, 4540, 4540-063, or 4540-033;

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 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 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 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 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 monoclonal antibody; and/or which 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 3525, 3530, 3833, 3631, 3732, 4540, 4540-063, or 4540-033; 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 monoclonal antibody.

6. An anti-APRIL antibody molecule, which binds, or substantially binds, to 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, or more, residues within a region of human APRIL as defined in any of Tables 3-4 or 7-8.

7. The antibody molecule of claim 6, which has one, two, or all of the following properties:

(i) binds, or substantially binds, to an epitope that comprises APRIL residues from two monomers, optionally, wherein the epitope comprises one or more residues from monomer A and one or more residues from monomer B as shown in Table 3 or 8;

(ii) binds, or substantially binds, to one or more APRIL residues from the C-D loop, the G-H loop, or both; or

(iii) does not bind, or binds with low affinity, to one, two or all of Asp129, Arg233, or His203 of human APRIL.

8. The antibody molecule of claim 6 or 7, which binds, or substantially binds, to 1, 2, 3, 4, 5, or all of the amino acid residues of human APRIL chosen from V174, F176, Q190, R195, R206, or Y208; optionally, does not binds, or binds with low affinity, to 1, 2, 3, or all of the amino acid residues of human APRIL chosen from V181, S226, I228, or N237,

optionally, wherein the antibody molecule binds, or substantially binds, to 1, 2, or all of the amino acid residues of human APRIL chosen from V174, R206, or Y208; optionally, does not bind, or does not substantially bind, to 1, 2, 3, or all of the amino acid residues of human APRIL chosen from F176, V181, Q190, or N237; or

5 which binds, or substantially binds, to 1, 2, 3, or all of the amino acid residues of human APRIL chosen from F176, V181, Q190, or I228; optionally, 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.

9. The antibody molecule of claim 6 or 7, which binds, or substantially binds, to 1, 2, 3, 4, 5, 6,
10 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, or P230 in monomer A, and V121, I123, Q139, P140, A141, L142, N237, S239, P240, or H241 in monomer B,

optionally, wherein the antibody molecule binds, or substantially binds to, 1, 2, 3, 4, 5, or all of
15 the amino acid residues of human APRIL chosen from V181, Q190, T192, or I228 in monomer A and A141 or H241 in monomer B.

10. The antibody molecule of any of claims 6-9, which binds, or substantially binds, to a conformational epitope.

11. The antibody molecule of any of claims 6-10, which 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:

25 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 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,
30 4338, 4540, 4540-063, 4540-033, 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 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 monoclonal antibody; 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 the 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 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 monoclonal antibody; and/or

which 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 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;

(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 monoclonal antibody.

12. An anti-APRIL antibody molecule, which:

(i) binds, or substantially binds, to human APRIL;

(ii) inhibits, or substantially inhibits, binding of APRIL to TACI;

(iii) inhibits, or substantially inhibits, binding of APRIL to BCMA; and

(iv) binds, or substantially binds, to 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, or more, residues within a region of human APRIL as defined in any of Tables 3-4 or 7-8.

13. The antibody molecule of claim 12, which binds, or substantially binds, to human APRIL at an EC₅₀ of 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, 0.001 nM or less, between 0.001 nM and 20 nM, 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; and/or

which does not bind to mouse APRIL, or binds to mouse APRIL at an EC₅₀ of 1000 nM or more, 2000 nM or more.

14. The antibody molecule of claim 12 or 13, which inhibits, or substantially inhibits, binding of APRIL to TACI at an IC₅₀ of 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, 0.002 nM or less, 0.001 nM or less, between 0.001 nM and 50 nM, 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 0.5 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,

optionally, wherein APRIL is a human APRIL, mouse APRIL, or both, and wherein TACI is human TACI, mouse TACI, or both; and/or

which inhibits, or substantially inhibits, binding of APRIL to BCMA at an IC₅₀ 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, 0.005 nM or less, 0.002 nM or less, 0.001 nM or less, between 0.001 nM and 100 nM, 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,

optionally, wherein APRIL is a human APRIL, mouse APRIL, or both, and wherein BCMA is human BCMA, mouse BCMA, or both.

15. The antibody molecule of any of claims 12-14, which has one, two or all of the following properties:

(i) binds, or substantially binds, to an epitope that comprises APRIL residues from two monomers, optionally, wherein the epitope comprises one or more residues from monomer A and one or more residues from monomer B as shown in Table 3 or 8;

(ii) binds, or substantially binds, to one or more APRIL residues from the C-D loop, the G-H loop, or both;

(iii) does not bind, or binds with low affinity, to one, two or all of Asp129, Arg233, or His203 of human APRIL.

16. The antibody molecule of any of claims 12-15, which 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 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 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 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 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 monoclonal antibody; and/or

which 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 monoclonal antibody.

17. An anti-APRIL antibody molecule, which competes for binding to APRIL with 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.

18. An anti-APRIL antibody molecule, which binds, or substantially binds, to an epitope that completely or partially overlaps with the epitope 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.

19. The antibody molecule of claim 17 or 18, which binds, or substantially binds, to human APRIL and mouse APRIL; and/or

which does not bind, or binds with low affinity, to mouse APRIL.

20. The antibody molecule of any of claims 17-19, which inhibits, or substantially inhibits, binding of APRIL to TACI, optionally, wherein APRIL is human APRIL, mouse APRIL, or both, and wherein TACI is human TACI, mouse TACI, or both; and/or

which inhibits, or substantially inhibits, binding of APRIL to BCMA, optionally, wherein APRIL is human APRIL, mouse APRIL, or both, and wherein BCMA is human BCMA, mouse BCMA, or both.

21. The antibody molecule of any of claims 17-20, which binds, or substantially binds, to 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, or more, residues within a region of human APRIL as defined in any of Tables 3-4 or 7-8.

5 22. An anti-APRIL antibody molecule, comprising 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:

10 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 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;

15 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 monoclonal antibody; or

20 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 monoclonal antibody, or

(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:

25 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 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 monoclonal antibody; or

30 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 monoclonal antibody; and/or

 which 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 monoclonal antibody; 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 monoclonal antibody.

23. An anti-APRIL antibody molecule, comprising 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); or comprising 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-

5 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).

10 24. The antibody molecule of any of claims 1-23, which is a synthetic or isolated antibody molecule, and/or a humanized antibody molecule, optionally, wherein the antibody molecule comprises one or more framework regions derived from human framework germline sequence.

15 25. The antibody molecule of any of claims 1-24, which comprises a heavy chain constant region of IgG1, IgG2, IgG3, or IgG4, optionally, wherein the antibody molecule comprises a heavy chain constant region of IgG2; and/or

which comprises a light chain constant region of kappa or lambda light chain.

20 26. The antibody molecule of any of claims 1-25, wherein an Fc region of the antibody molecule comprises one, two or three, or all of the following:

(i) one or more mutations located at the interface between the CH2 and CH3 domains, optionally, wherein the one or more mutations increase the binding affinity to neonatal receptor FcRn, the half-life of the antibody molecule, or both;

25 (ii) 1, 2, 3, 4, 6 or all of the mutations chosen from T250Q, M252Y, S254T, T256E, M428L, H433K, or N434F, of IgG1;

(iii) 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, optionally, wherein the one or more mutations reduce complement-dependent cytotoxicity (CDC); or

30 (iv) 1, 2, 3, 4, 6 7 or all of the mutations chosen from E233P, L234V, L235A, G236, K322A, A327G, A330S, or P331S.

27. The antibody molecule of any of claims 1-26, which comprises two heavy chain variable regions and two light chain variable regions, or is a Fab, F(ab')2, Fv, Fd, or a single chain Fv fragment (scFv).

28. A composition comprising an antibody molecule of any of claims 1-27, optionally, wherein the composition is a pharmaceutical composition, optionally further comprising a pharmaceutically acceptable carrier.

5

29. A nucleic acid molecule encoding a heavy chain variable region (VH), a light chain variable region (VL), or both, of an antibody molecule of any of claims 1-27.

30. A vector comprising a nucleic acid molecule of claim 29.

10

31. A cell comprising a nucleic acid molecule of claim 29 or a vector of claim 30, optionally, wherein the cell is an isolated cell.

32. A kit comprising an antibody molecule of any of claims 1-27 and instructions to use of the antibody molecule.

15

33. A container comprising an antibody molecule of any of claims 1-27, or a composition of claim 28.

34. A method of producing an anti-APRIL antibody molecule, the method comprising culturing a cell of claim 31 under conditions that allow production of an antibody molecule, thereby producing the antibody molecule.

20

35. The method of claim 34, further comprising isolating or purifying the antibody molecule.

25

36. Use of an antibody molecule of any of claims 1-27, or a composition of claim 28, in the manufacture of a medicament for treating IgA nephropathy in a subject.

37. The use of claim 36, wherein the antibody molecule is used intravenously.

30

38. The use of claim 36 or 37, wherein the antibody molecule is used at a dose between 0.1 mg/kg and 50 mg/kg, 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, or

at a fixed dose between 10 mg and 1000 mg, 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,

optionally, wherein the antibody molecule is used once a week, twice a week, once every two weeks, or once every four weeks.

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39. The use of any of claims 36-38, wherein the use reduces the level of IgA in a peripheral tissue, optionally, wherein the peripheral tissue is serum, mucosal tissue, bone marrow, or any combination thereof; and/or wherein the use reduces the level of a variant of IgA, optionally, wherein the variant of IgA is IgA1, IgA1 in polymeric form (pIgA1), IgA1 with an O-linked glycosylation variant, or any combination thereof.

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40. The use of any of claims 36-39, further comprising determining the level of IgA in a peripheral tissue sample from the subject, optionally, wherein the peripheral tissue is serum, mucosal tissue, or bone marrow.

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41. The use of any of claims 36-40, wherein the use further comprises a second therapy for IgA nephropathy.

42. The use of any of claims 36-41, wherein the second therapy is chosen from an angiotensin-converting enzyme (ACE) inhibitor, an angiotensin receptor blocker (ARB), omega-3 fatty acids, an immunosuppressant, a statin, mycophenolate mofetil, or any combination thereof, optionally, wherein the immunosuppressant is a corticosteroid.

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43. Use of an antibody molecule of any of claims 1-27, or a composition of claim 28, in the manufacture of a medicament for treating diabetic nephropathy in a subject.

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44. Use of an antibody molecule of any of claims 1-27, or a composition of claim 28, in the manufacture of a medicament for treating cancer in a subject.

45. The use of claim 44, wherein the cancer is a hematological cancer, optionally, wherein the hematological cancer is chosen from B-cell non-Hodgkin's lymphoma, chronic lymphocytic leukemia (CLL), Hodgkin's lymphoma, multiple myeloma, Waldenström's macroglobulinemia, or lymphoplasmacytic lymphoma.

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46. Use of an antibody molecule of any of claims 1-27, or a composition of claim 28, in the manufacture of a medicament for treating an immunoproliferative disorder in a subject.

47. The use of claim 46, wherein the immunoproliferative disorder is monoclonal IgA hypergammaglobulinemia in a subject.

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48. Use of an antibody molecule of any of claims 1-27, or a composition of claim 28, in the manufacture of a medicament for treating vasculitis in a subject.

49. The use of claim 48, wherein the vasculitis is kidney vasculitis and/or an IgA associated vasculitis or post-streptococcal glomerulonephritis.

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50. Use of an antibody molecule of any of claims 1-27, or a composition of claim 28, in the manufacture of a medicament for treating an autoimmune disorder in a subject.

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51. The use of claim 50, wherein the autoimmune disorder is chosen from rheumatoid arthritis, systemic lupus erythematosus, a linear IgA bullous disease, or IgA-mediated epidermolysis bullosa acquisita, optionally, wherein the linear IgA bullous disease is linear immunoglobulin A (IgA) dermatosis.

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52. Use of an antibody molecule of any of claims 1-27, or a composition of claim 28, in the manufacture of a medicament for treating IgA pemphigus in a subject.

53. Use of an antibody molecule of any of claims 1-27, or a composition of claim 28, in the manufacture of a medicament for treating celiac disease in a subject.

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54. Use of an antibody molecule of any of claims 1-27, or a composition of claim 28, in the manufacture of a medicament for treating alcoholic cirrhosis in a subject.

55. A method of reducing the level of IgA in a cell or subject, the method comprising contacting the cell or subject an antibody molecule of any of claims 1-27 or a composition of claim 28, thereby reducing the level of IgA.

5 56. Use of an antibody molecule of any of claims 1-27, or a composition of claim 28, in the manufacture of a medicament for treating a disorder, optionally, wherein the disorder is IgA nephropathy.

10 57. A method of detecting an APRIL molecule, the method comprising contacting a cell or a sample from a subject with an antibody molecule of any of claims 1-27, thereby detecting the APRIL molecule.

58. The method of claim 57, wherein the antibody molecule is coupled with a detectable label; and/or wherein the APRIL molecule is detected *in vitro*, *ex vivo*, or *in vivo*.

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