

- bb) Has one or more biological properties of an anti-CD138 monoclonal antibody described herein,
- cc) Has one or more structural properties of an anti-CD138 monoclonal antibody described herein, or
- dd) Has one or more pharmacokinetic properties of an anti-CD138 monoclonal antibody described herein.

In an example, this disclosure features an anti-CD138 antibody molecule, which: (i) binds, or substantially binds, to CD138 in an extracellular region proximal to the transmembrane domain of CD138; and (ii) causes an antibody-dependent cellular cytotoxicity (ADCC) activity on a cell expressing CD138.

In an aspect, there is provided an anti-CD138 antibody molecule, which comprises:
(i) a heavy chain variable region (VH) comprising an HCDR1 comprising an amino acid sequence of GYSFSSY (SEQ ID NO: 355); an HCDR2 comprising an amino acid sequence of HPSTDST (SEQ ID NO: 351); and an HCDR3 comprising an amino acid sequence of FVY; and
(ii) a light chain variable region (VL) comprising an LCDR1 comprising an amino acid sequence of RSSKSLLYKDGKTYLN (SEQ ID NO: 352) or an LCDR1 that differs by no more than 1 conservative amino acid substitution from SEQ ID NO: 352; an LCDR2 comprising an amino acid sequence of VVSTRAS (SEQ ID NO: 353); and an LCDR3 comprising an amino acid sequence of QQLVEYPYT (SEQ ID NO: 354).

In an ~~aspect~~example, there is provided an anti-CD138 antibody molecule, which:
(i) binds to CD138 in an extracellular region proximal to the transmembrane domain of CD138; wherein the C-terminus of the extracellular region proximal to the transmembrane domain is within 70, 65, 60, 55, 50, 45, 40, 35, 30, 25, 20, 15, 10, or 5 amino acids from the N-terminus of the transmembrane domain;

and/or wherein the N-terminus of the extracellular region proximal to the transmembrane domain is within 75, 70, 65, 60, 55, 50, 45, 40, 35, 30, 25, 20, 15, 10, or 5 amino acids from the N-terminus of the transmembrane domain; and

(ii) causes an antibody-dependent cellular cytotoxicity (ADCC) activity on a cell expressing CD138.

In an example, the C-terminus of the extracellular region proximal to the transmembrane domain is within 70, 65, 60, 55, 50, 45, 40, 35, 30, 25, 20, 15, 10, or 5 amino acids from the N-terminus of the transmembrane domain. In an example, the N-terminus of the extracellular region proximal to the transmembrane domain is within 75, 70, 65, 60, 55, 50, 45, 40, 35, 30, 25, 20, 15, 10, or 5 amino acids from the N-terminus of the transmembrane domain.

In an example, the antibody molecule binds to an epitope on CD138 comprising five or more (*e.g.*, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, or more) consecutive amino acid residues in the extracellular region.

In an example, the extracellular region proximal to the transmembrane domain comprises, or consists of, amino acids 210-250 or 220-245 of any of SEQ ID NOS: 1-3 or 450.

In an example, the antibody molecule binds to an Fc receptor (FcR) (*e.g.*, one or more of FcγRI, FcγRIIa, FcγRIIb, FcγRIIc, FcγRIIIa, or FcγRIIIb) on the surface of an immune cell (*e.g.*, a natural killer (NK) cell, a macrophage, a monocyte, or an eosinophil).

In an example, the cell expressing CD138 is a cancer cell or precancerous cell. In an example, the cancer or precancerous cell is a myeloma cell.

In an example, (a) the VH comprises 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, 99 or 100% homology with, the amino acid sequence of the VH of the anti-CD138 antibody; and (b) the VL comprises 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, 99 or 100% homology with, the amino acid sequence of the VH of the anti-CD138 antibody.

In an example, the VH comprises the amino acid sequence of the VH of the anti-CD138 antibody and the VL comprises the amino acid sequence of the VL of the anti-CD138 antibody.

In an example, the antibody molecule comprises an Fc region.

In an example, the disclosure features an antibody molecule, which competes for binding to CD138 with an anti-CD138 monoclonal antibody described herein (*e.g.*, any of antibodies CD001, CD002, CD003, CD004, CD005, CD006, 602, 603, 604, 607, 613, 614, 617, 624, 632, 616, 619, 623, 1610, 2510, 2610, 2710, 2810, 2910, or 1409).

In an example, the disclosure features an antibody molecule, which binds, or substantially binds, to an epitope that completely or partially overlaps with the epitope of an anti-CD138 monoclonal antibody described herein (*e.g.*, any of antibodies CD001, CD002, CD003, CD004, CD005, CD006, 602, 603, 604, 607, 613, 614, 617, 624, 632, 616, 619, 623, 1610, 2510, 2610, 2710, 2810, 2910, or 1409).

In another aspect, there is provided an anti-CD138 antibody molecule, which comprises:

(i) a heavy chain which comprises a heavy chain variable region (VH) and a heavy chain constant region of IgG1,

wherein the VH comprises an HCDR1 comprising an amino acid sequence of GYSFSSY (SEQ ID NO: 355); an HCDR2 comprising an amino acid sequence of HPSDST (SEQ ID NO: 351); and an HCDR3 comprising an amino acid sequence of FVY; and

(ii) a light chain which comprises a light chain variable region (VL) comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 292 and a light chain constant region of kappa,

wherein the VL comprises an LCDR1 comprising an amino acid sequence of RSSKSLLYKDGKTYLN (SEQ ID NO: 352) or an LCDR1 that differs by no more than 1 conservative amino acid substitution from SEQ ID NO: 352; an LCDR2 comprising an amino acid sequence of VVSTRAS (SEQ ID NO: 353); and an LCDR3 comprising an amino acid sequence of QQLVEYPYT (SEQ ID NO: 354).

In another aspect, there is provided an antibody-molecule drug conjugate (ADC) comprising an antibody molecule as described herein.

In an ~~aspect~~example, the disclosure features an antibody-molecule drug conjugate (ADC) comprising an antibody molecule described herein, optionally comprising a cytotoxic agent, further optionally comprising a linker.

In an example, the disclosure features a composition comprising an antibody molecule described herein, or an ADC described herein, optionally, wherein the composition is a pharmaceutical composition.

In another aspect, there is provided a pharmaceutical composition comprising an antibody molecule as described herein, or an ADC as described herein and a pharmaceutically acceptable carrier.

In an ~~aspect~~example, the disclosure features a composition comprising an antibody molecule described herein, or an ADC as described herein, optionally, wherein the composition is a pharmaceutical composition;

optionally wherein the composition further comprises a pharmaceutically acceptable carrier.

In an example, the composition further comprises a pharmaceutically acceptable carrier.

In an other 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 other aspect, the disclosure features a vector comprising a nucleic acid molecule described herein.

In an example, the disclosure features a cell comprising a nucleic acid molecule described herein or a vector described herein, optionally, wherein the cell is an isolated cell.

In another aspect, there is provided a cell comprising a nucleic acid molecule as described herein or a vector as described herein.

5 In an aspectexample, the disclosure features a cell comprising a nucleic acid molecule described herein or a vector described herein, wherein the cell is an isolated cell.

In another aspect, there is provided a kit comprising an antibody molecule as described herein, an ADC as described herein, or a pharmaceutical composition as described herein, and instructions for use of the antibody molecule or composition

10 In an aspectexample, the disclosure features a kit comprising an antibody molecule described herein, an ADC described herein, or a composition described herein, and instructions to use of the antibody molecule or composition.

In another aspect, there is provided a container comprising an antibody molecule as described herein, an ADC as described herein, or a pharmaceutical composition as described herein.

15 In an aspectexample, the disclosure features a container comprising an antibody molecule described herein, an ADC described herein, or a composition described herein.

In an example, the disclosure features a method of producing an anti-CD138 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 another aspect, there is provided a method of producing an anti-CD138 antibody molecule, the method comprising culturing a cell as described herein under conditions that allow production of an antibody molecule, thereby producing the antibody molecule.

In an ~~aspect~~example, the disclosure features a method of producing an anti-CD138 antibody molecule, the method comprising culturing a cell described herein under conditions that allow production of an antibody molecule, thereby producing the antibody molecule; optionally wherein the method further comprises isolating or purifying the antibody molecule.

In an example, the method further comprises isolating or purifying the antibody molecule.

In an example, the disclosure features an antibody molecule of described herein, an ADC described herein, or a composition described herein, for use in a method of treating a cancer in a subject.

In another aspect, there is provided the use of an antibody molecule as defined herein, an ADC as defined herein or a pharmaceutical composition as defined herein, in the manufacture of a medicament for treating a cancer in a subject.

In an ~~aspect~~example, there is provided the use of an antibody molecule as defined herein, an ADC as defined herein or a composition as defined herein, in the manufacture of a medicament for treating a cancer in a subject.

In an example, the cancer is a hematological cancer. In an example, the cancer is a multiple myeloma. In an example, the cancer is a solid tumor, *e.g.*, a solid tumor described herein.

In an example, the antibody molecule, ADC, or composition is administered to the subject intravenously.

In an example, the antibody molecule, ADC, or composition is administered to the subject 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.

In an example, the antibody molecule, ADC, or composition is administered to the subject 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.

In an example, the antibody molecule, ADC, or composition is administered once a week, twice a week, once every two weeks, once every three weeks, or once every four weeks.

In an example, the disclosure features a method of causing an ADCC activity, the method comprising contacting a cell or subject an antibody molecule described herein, an ADC described herein, or a composition described herein, thereby causing the ADCC activity.

In an example, the disclosure features a method of treating a cancer, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule described herein, an ADC described herein, or a composition described herein, thereby treating the cancer.

In an example, the disclosure features a method of treating a precancerous condition or preventing a cancer, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule described herein, an ADC described herein, or a composition described herein, thereby treating the precancerous condition or preventing the cancer.

In another aspect, there is provided the use of an antibody molecule as described herein, an ADC as described herein, or a pharmaceutical composition as described herein, in the manufacture of a medicament for treating a precancerous condition or preventing a cancer.

In an ~~aspect~~example, there is provided the use of an antibody as defined herein, an ADC as defined herein, or a composition as defined herein, in the manufacture of a medicament for treating a precancerous condition or preventing a cancer, optionally wherein:

(i) the precancerous condition is smoldering myeloma or monoclonal gammopathy of undetermined significance (MGUS); or

(ii) the cancer is multiple myeloma.

In another aspect, there is provided a method of detecting a CD138 molecule, the method comprising contacting a cell or a subject with an antibody molecule as described herein, thereby detecting the CD138 molecule.

In an ~~aspect~~example, there is provided a method of detecting an anti-CD138 molecule, the method comprising contacting a cell or a subject with an antibody molecule as defined herein, thereby detecting the CD138 molecule; optionally wherein:

(i) the antibody molecule is coupled with a detectable label; and/or

(ii) the CD138 molecule is detected *in vitro*, *ex vivo*, or *in vivo*.

In an example, the disclosure features, a method of detecting an anti-CD138 molecule, the method comprising contacting a cell or a subject with an antibody molecule described herein, thereby detecting the CD138 molecule.

In an example, the antibody molecule is coupled with a detectable label. In an example, the CD138 molecule is detected *in vitro*, *ex vivo*, or *in vivo*.

The disclosure contemplates all combinations of any one or more of the foregoing aspects and/or examples, as well as combinations with any one or more of the examples 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.

What is claimed is:

1. An anti-CD138 antibody molecule, which comprises:

(i) a heavy chain variable region (VH) comprising an HCDR1 comprising an amino acid sequence of GYSFSSY (SEQ ID NO: 355); an HCDR2 comprising an amino acid sequence of HPSDST (SEQ ID NO: 351); and an HCDR3 comprising an amino acid sequence of FVY; and

(ii) a light chain variable region (VL) comprising an LCDR1 comprising an amino acid sequence of RSSKSLLYKDGKTYLN (SEQ ID NO: 352) or an LCDR1 that differs by no more than 1 conservative amino acid substitution from SEQ ID NO: 352; an LCDR2 comprising an amino acid sequence of VVSTRAS (SEQ ID NO: 353); and an LCDR3 comprising an amino acid sequence of QQLVEYPYT (SEQ ID NO: 354).

~~(i) binds to CD138 in an extracellular region proximal to the transmembrane domain of CD138; wherein the C-terminus of the extracellular region proximal to the transmembrane domain is within 70, 65, 60, 55, 50, 45, 40, 35, 30, 25, 20, 15, 10, or 5 amino acids from the N-terminus of the transmembrane domain;~~

~~and/or wherein the N-terminus of the extracellular region proximal to the transmembrane domain is within 75, 70, 65, 60, 55, 50, 45, 40, 35, 30, 25, 20, 15, 10, or 5 amino acids from the N-terminus of the transmembrane domain; and~~

~~(ii) causes an antibody-dependent cellular cytotoxicity (ADCC) activity on a cell expressing CD138.~~

2. The antibody molecule of claim 1, wherein the antibody molecule has one, two, three, or all of (i)-(iv):

(i) ~~the antibody molecule binds to an epitope on CD138 comprising five or more consecutive amino acid residues in the extracellular region;~~

(ii) ~~the extracellular region proximal to the transmembrane domain comprises, or consists of, amino acids 210-250 or 220-245 of any of SEQ ID NOS: 1-3 or 450;~~

(iii) ~~the antibody molecule binds to an Fc receptor (FcR) on the surface of an immune cell;~~
~~and/or~~

(iv) ~~the cell expressing CD138 is a cancer cell or precancerous cell, optionally wherein the cancer or precancerous cell is a myeloma cell.~~

3. The antibody molecule of claim 1 or 2, which has one, two, or all of (i)-(iii):

~~(i) (a) does not bind, or binds with low affinity, to an extracellular region of CD138 distant from the transmembrane domain; or~~

~~(b) binds, an epitope on CD138 comprising five or more consecutive amino acid residues in an extracellular region distant from the transmembrane domain;~~

5 ~~(ii) does not bind to an epitope on CD138 comprising five or more consecutive amino acid residues in an extracellular region distant from the transmembrane domain;~~
~~optionally wherein:~~

~~(a) the C terminus of the extracellular region distant from the transmembrane domain is at least 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, or 200 amino acids away from the N terminus of the transmembrane domain; and/or~~

10 ~~(b) the extracellular region distant from the transmembrane domain comprises amino acids 23-50, 51-95, 88-121, or 111-150 of any of SEQ ID NOS: 1-3 or 450; and/or~~

~~(iii) (a) does not bind, or binds with low affinity, to the integrin binding domain (IBD) of CD138, a region N-terminal to the IBD of CD138, or both; or (b) binds to the IBD of CD138, a region N-terminal to the IBD of CD138, or both.~~

15 4. The antibody molecule of any of claims 1-3, which has one, two, three, four, five, six, seven, eight, nine, or all of (i) (x):

20 ~~(i) binds to CD138 with a disassociation constant (K_D) of less than 100, 90, 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, or 10-0.001, 10-0.01, 5-0.01, 3-0.05, or 1-0.1 nM;~~

~~(ii) the binding affinity of the antibody molecule to a membrane bound CD138 is at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 50, 100, 200, or 500 fold higher than the binding affinity to a soluble CD138;~~

25 ~~(iii) binds to a membrane bound CD138 with a K_D less than 100, 90, 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, or 10-0.001, 10-0.01, 5-0.01, 3-0.05, or 1-0.1 nM;~~

~~(iv) binds to a soluble CD138 with a K_D less than 100, 90, 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, or 10-0.001, 10-0.01, 5-0.01, 3-0.05, or 1-0.1 nM, or with a K_D of more than 100, 200, 300, 400, or 500 nM;~~

30 ~~(v) binds to a membrane bound CD138 preferably over a soluble CD138, optionally wherein the binding affinity to a membrane bound CD138 is at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold higher than the binding affinity to a soluble CD138; or binds with similar affinity to a membrane bound CD138 and a soluble CD138, or the binding affinity to a membrane bound CD138 is less than 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% higher than the binding affinity to a soluble CD138;~~

(vi) binds to C1q and causes a complement dependent cytotoxicity (CDC) activity on a cell expressing CD138;

(vii) reduces one or more biological activities of a cell expressing CD138 *in vitro*, *ex vivo*, or *in vivo*;

(viii) mediates homotypic adhesion of one or more CD138-expressing cells;

(ix) inhibits the action of a protease on a membrane bound CD138; and/or

(x) reduces proliferation of a cancer or precancerous cell expressing CD138.

52. The antibody molecule of ~~any of claims 1-4~~, comprising:

(i) ~~one or more heavy chain CDRs and/or one or more light chain CDRs of an anti-CD138 monoclonal antibody described herein;~~

(ii) ~~a heavy chain variable region (VH) and/or light chain variable region (VL) of an anti-CD138 monoclonal antibody described herein; and/or~~

(iii) an Fc region.

63. The antibody molecule of claim 1 or 2 ~~any of claims 1-5, which wherein the antibody molecule further~~ comprises:

(i) ~~a heavy chain variable region (VH) comprising an HCDR1 comprising an amino acid sequence of GYSFSSY (SEQ ID NO: 355); an HCDR2 comprising an amino acid sequence of HPSDST (SEQ ID NO: 351); and an HCDR3 comprising an amino acid sequence of FVY; and~~

(ii) ~~a light chain variable region (VL) comprising an LCDR1 comprising an amino acid sequence of RSSKSLLYKDGTKTYLN (SEQ ID NO: 352) or an LCDR1 that differs by no more than 1 amino acid residue from SEQ ID NO: 352; an LCDR2 comprising an amino acid sequence of VVSTRAS (SEQ ID NO: 353); and an LCDR3 comprising an amino acid sequence of QQLVEYPYT (SEQ ID NO: 354);~~

~~optionally wherein the antibody molecule further comprises:~~

(iii) a heavy chain variable region (VH) having comprising the amino acid sequence of SEQ ID NO: 296, or a VH region having an amino acid sequence at least 85, 90, 95, or 99% identical to SEQ ID NO: 296; and/or

(ii) a light chain variable region (VL) having comprising the amino acid sequence of SEQ ID NO: 292, or a VL region having an amino acid sequence at least 85, 90, 95, or 99% identical to SEQ ID NO: 292.

~~7. The anti-CD138 antibody molecule of any of claims 1-6, which binds to an epitope on CD138 comprising four or more consecutive amino acid residues in an extracellular region proximal to the transmembrane domain of CD138.~~

5 ~~8. The antibody molecule of claim 7, wherein the antibody molecule has one, two, three, or all of (i)-(iv):~~

~~(i) the C-terminus of the extracellular region proximal to the transmembrane domain is within 70, 65, 60, 55, 50, 45, 40, 35, 30, 25, 20, 15, 10, or 5 amino acids from the N-terminus of the transmembrane domain;~~

10 ~~(ii) the N-terminus of the extracellular region proximal to the transmembrane domain is within 75, 70, 65, 60, 55, 50, 45, 40, 35, 30, 25, 20, 15, 10, or 5 amino acids from the N-terminus of the transmembrane domain;~~

~~(iii) the extracellular region proximal to the transmembrane domain comprises, or consists of, amino acids 176-250 of any of SEQ ID NOS: 1-3 or 450; and/or~~

15 ~~(iv) the antibody molecule does not bind, or binds with low affinity, to an extracellular region of CD138 distant from the transmembrane domain; and/or the epitope does not comprise five or more consecutive amino acid residues in an extracellular region distant from the transmembrane domain; optionally wherein:~~

~~(a) the C-terminus of the extracellular region distant from the transmembrane domain is at least 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, or 200 amino acids away from the N-terminus of the transmembrane domain;~~

20 ~~(b) the extracellular region distant from the transmembrane domain comprises amino acids 23-50, 51-95, 88-121, or 111-150 of any of SEQ ID NOS: 1-3 or 450; and/or~~

25 ~~(c) the antibody molecule (1) does not bind, or binds with low affinity, to the integrin binding domain (IBD) of CD138, a region N-terminal to the IBD of CD138, or both, or (2) binds to the IBD of CD138, a region N-terminal to the IBD of CD138, or both.~~

30 ~~9. The antibody molecule of claim 7 or 8, which:~~

~~(i) binds to an Fc receptor (FcR) on the surface of an immune cell;~~

~~(ii) is capable of causing an ADCC activity on a cell expressing CD138, optionally wherein the cell expressing CD138 is a cancer cell or precancerous cell, further optionally wherein the cancer or precancerous cell is a myeloma cell;~~

(iii) binds to CD138 with a disassociation constant (K_D) of less than 100, 90, 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, or 10-0.001, 10-0.01, 5-0.01, 3-0.05, or 1-0.1 nM;

(iv) has a binding affinity to a membrane-bound CD138 at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 50, 100, 200, or 500 fold higher than the binding affinity to a soluble CD138; or which binds with similar affinity to a membrane-bound CD138 and a soluble CD138, optionally wherein the binding affinity to a membrane-bound CD138 is less than 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% higher than the binding affinity to a soluble CD138;

(v) binds to a membrane-bound CD138 with a K_D less than 100, 90, 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, or 10-0.001, 10-0.01, 5-0.01, 3-0.05, or 1-0.1 nM;

(vi) binds to a soluble CD138 with a K_D of less than 100, 90, 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, or 10-0.001, 10-0.01, 5-0.01, 3-0.05, or 1-0.1 nM, or greater than 100, 200, 300, 400, or 500 nM;

(vii) (a) binds to a membrane-bound CD138 preferably over a soluble CD138, optionally wherein the binding affinity to a membrane-bound CD138 is at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold higher than the binding affinity to a soluble CD138; or (b) binds to C1q and causes a complement-dependent cytotoxicity (CDC) activity on a cell expressing CD138;

(viii) reduces one or more biological activities of a cell expressing CD138 *in vitro*, *ex vivo*, or *in vivo*;

(ix) mediates homotypic adhesion of one or more CD138-expressing cells;

(x) inhibits the action of a protease on a membrane-bound CD138;

(xi) reduces proliferation of a cancer or precancerous cell expressing CD138;

(xii) comprises one or more heavy chain CDRs and/or one or more light chain CDRs of an anti-CD138 monoclonal antibody described herein;

(xiii) comprises a heavy chain variable region (VH) and/or light chain variable region (VL) of an anti-CD138 monoclonal antibody described herein; and/or

(xiv) comprises an Fc region.

10. The anti-CD138 antibody molecule of any of claims 1-9, which comprises one or both of:

(a) a heavy chain variable region (VH), wherein the VH comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the VH 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% sequence identity with, the amino acid sequence of the HCDR1 of any of antibodies CD001, CD002, CD003, CD004, CD005, CD006, 602, 603, 604, 607, 613, 614, 617, 624, 632, 616, 619, 623, 1610, 2510, 2610, 2710, 2810, 2910, or 1409;

(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% sequence identity with, the amino acid sequence of the HCDR2 of the anti-CD138 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% sequence identity with, the amino acid sequence of the HCDR3 of the anti-CD138 antibody; or

(b) a light chain variable region (VL), wherein the VL comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the VL 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% sequence identity with, the amino acid sequence of the LCDR1 of the anti-CD138 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% sequence identity with, the amino acid sequence of the LCDR2 of the anti-CD138 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% sequence identity with, the amino acid sequence of the LCDR3 of the anti-CD138 antibody.

11. The antibody molecule of claim 10, wherein the antibody molecule has one, two, or all of (I), (II) and (III):

(I) wherein the antibody molecule has (a), (b) or both (a) and (b):

(a) the VH comprises:

(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% sequence identity with, the amino acid sequence of the HCDR1 of the anti-CD138 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% sequence identity with, the amino acid sequence of the HCDR2 of the anti-CD138 antibody; and

(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% sequence identity with, the amino acid sequence of the HCDR3 of the anti-CD138 antibody;

optionally wherein the VH comprises: (i) an HCDR1 comprising the amino acid sequence of the HCDR1 of the anti-CD138 antibody; (ii) an HCDR2 comprising the amino acid sequence of the HCDR2 of the anti-CD138 antibody; and (iii) an HCDR3 comprising the amino acid sequence of the HCDR3 of the anti-CD138 antibody; or

(b) the VL comprises:

(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% sequence identity with, the amino acid sequence of the LCDR1 of the anti-CD138 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% sequence identity with, the amino acid sequence of the LCDR2 of the anti-CD138 antibody; and

(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% sequence identity with, the amino acid sequence of the LCDR3 of the anti-CD138 antibody;

optionally wherein the VL comprises: (i) an LCDR1 comprising the amino acid sequence of the LCDR1 of the anti-CD138 antibody; (ii) an LCDR2 comprising the amino acid sequence of the LCDR2 of the anti-CD138 antibody; and (iii) an LCDR3 comprising the amino acid sequence of the LCDR3 of the anti-CD138 antibody;

(II) wherein the antibody molecule has (a), (b), or both (a) and (b):

(a) the VH comprises 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, 99 or 100% sequence identity with, the amino acid sequence of the VH of the anti-CD138 antibody;

optionally wherein the VH comprises the amino acid sequence of the VH of the anti-CD138 antibody; or

(b) the VL comprises 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, 99 or 100% sequence identity with, the amino acid sequence of the VL of the anti-CD138 antibody;

optionally wherein the VL comprises the amino acid sequence of the VL of the anti-CD138 antibody; and/or

(III) the antibody molecule comprises an Fc region.

12. ~~The anti-CD138 antibody molecule of any of claims 1-11, which comprises:~~

~~(I) (a) a heavy chain variable region (VH), wherein the VH comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the VH comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the VH comprises: (i) an HCDR1 comprising an amino acid sequence of G-Y-N/S/T-F-S-S-Y (SEQ ID NO: 438); (ii) an HCDR2 comprising an amino acid sequence of H-P-S-D-S-T (SEQ ID NO: 351); or (iii) an HCDR3 comprising an amino acid sequence of F-V-Y; and (b) a light chain variable region (VL), wherein the VL comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the VL comprises one, two, or all of: (i) an LCDR1 comprising an amino acid sequence of R-S-S-K-S-L-L-Y-K-D-G-K-T-Y-L-N (SEQ ID NO: 352); (ii) an LCDR2 comprising an amino acid sequence of V-V-S-T-R-A-S (SEQ ID NO: 353); or (iii) an LCDR3 comprising an amino acid sequence of Q-Q-L-V-E-Y-P-Y-T (SEQ ID NO: 354); or~~

~~(II) (a) a heavy chain variable region (VH), wherein the VH comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the VH comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3), wherein the VH comprises: (i) an HCDR1 comprising an amino acid sequence of S-Y-Y-M-H (SEQ ID NO: 380); (ii) an HCDR2 comprising an amino acid sequence of T-I-H-P-S-D-S-T-T-N-C/Y-N-Q-K-F-K-G (SEQ ID NO: 439); or (iii) an HCDR3 comprising an amino acid sequence of F-V-Y; and (b) a light chain variable region (VL), wherein the VL comprises three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), wherein the VL comprises one, two, or all of: (i) an LCDR1 comprising an amino acid sequence of R-S-S-K-S-L-L-Y-K-D-G-K-T-Y-L-N (SEQ ID NO: 352); (ii) an LCDR2 comprising an amino acid sequence of V-V-S-T-R-A-S (SEQ ID NO: 353); or (iii) an LCDR3 comprising an amino acid sequence of Q-Q-L-V-E-Y-P-Y-T (SEQ ID NO: 354).~~

134. The antibody molecule of any of claims 1-312, which has one, two, three, four, five, six, seven, eight, nine, ten, or all of (i)-(xi):

- (i) comprises two VHs and two VLs;
- (ii) is a synthetic antibody molecule or an isolated antibody molecule;
- (iii) is a monovalent antibody molecule, a multivalent antibody molecule, a monospecific molecule, or a multispecific antibody molecule;
- (iv) is a humanized antibody molecule;
- (v) comprises one or more framework regions derived from human framework germline sequence;
- (vi) is an IgG antibody;

(vii) comprises a heavy chain constant region of IgG chosen from IgG1, IgG2, IgG3, or IgG4;
(viii) comprises a light chain constant region of kappa or lambda light chain;
(ix) comprises an Fc region comprising one or more mutations to increase the binding affinity to neonatal receptor FcRn and/or the half-life of the antibody molecule; ~~and/or~~
5 (x) comprises an Fc region comprising one or more mutations increase one or more of half-life, ADCC, CDC, or ADCP; ~~and/or~~
~~(xi) the antibody molecule is an afucosylated antibody molecule.~~

5. An anti-CD138 antibody molecule, which comprises:

10 (i) a heavy chain which comprises a heavy chain variable region (VH) and a heavy chain constant region of IgG1,

wherein the VH comprises an HCDR1 comprising an amino acid sequence of GYSFSSY (SEQ ID NO: 355); an HCDR2 comprising an amino acid sequence of HPSDST (SEQ ID NO: 351); and an HCDR3 comprising an amino acid sequence of FVY; and

15 (ii) a light chain which comprises a light chain variable region (VL) comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 292 and a light chain constant region of kappa,

wherein the VL comprises an LCDR1 comprising an amino acid sequence of RSSKSLLYKDGKTYLN (SEQ ID NO: 352) or an LCDR1 that differs by no more than 1 conservative amino acid substitution from SEQ ID NO: 352; an LCDR2 comprising an amino acid sequence of VVSTRAS (SEQ ID NO: 353); and an LCDR3 comprising an amino acid sequence of QQLVEYPYT (SEQ ID NO: 354).

25 ~~14. The antibody molecule of any of claims 1-13, which competes for binding to CD138 with any of antibodies CD001, CD002, CD003, CD004, CD005, CD006, 602, 603, 604, 607, 613, 614, 617, 624, 632, 616, 619, 623, 1610, 2510, 2610, 2710, 2810, 2910, or 1409.~~

30 ~~15. The antibody molecule of any of claims 1-13, which binds to an epitope that completely or partially overlaps with the epitope of any of antibodies CD001, CD002, CD003, CD004, CD005, CD006, 602, 603, 604, 607, 613, 614, 617, 624, 632, 616, 619, 623, 1610, 2510, 2610, 2710, 2810, 2910, or 1409.~~

~~16. An antibody-molecule drug conjugate (ADC) comprising an antibody molecule of any of claims 1-15, optionally comprising a cytotoxic agent, further optionally comprising a linker.~~

7. The ADC of claim 6, further comprising a cytotoxic agent.

8. The ADC of claim 6 or 7, further comprising a linker.

5 ~~179.~~ A pharmaceutical composition comprising an antibody molecule of any of claims 1-~~15~~, or an ADC of any of claims ~~16-8~~, ~~optionally, wherein the composition is a pharmaceutical composition;~~
~~optionally wherein the composition further comprises and~~ a pharmaceutically acceptable carrier.

10 ~~1810.~~ 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-~~15~~.

~~1911.~~ A vector comprising a nucleic acid molecule of claim ~~1810~~.

15 ~~2012.~~ A cell comprising a nucleic acid molecule of claim ~~18-10~~ or a vector of claim ~~1911~~,
~~optionally, wherein the cell is an isolated cell.~~

13. The cell of claim 12, wherein the cell is an isolated cell.

20 ~~2114.~~ A kit comprising an antibody molecule of any of claims 1-~~15~~, an ADC of any of claims ~~166-8~~, or a pharmaceutical composition of claim ~~179~~, and instructions for use of the antibody molecule or composition.

25 ~~2215.~~ A container comprising an antibody molecule of any of claims 1-~~15~~, an ADC of any of claims ~~166-8~~, or a pharmaceutical composition of claim ~~179~~.

30 ~~2316.~~ A method of producing an anti-CD138 antibody molecule, the method comprising culturing a cell of claim ~~20-12 or 13~~ under conditions that allow production of an antibody molecule, thereby producing the antibody molecule; ~~optionally wherein the method further comprises isolating or purifying the antibody molecule.~~

17. The method of claim 16, wherein the method further comprises isolating or purifying the antibody molecule.

2418. Use of an antibody molecule of any of claims 1-~~15~~, an ADC of any of claims ~~166-8~~, or a pharmaceutical composition of claim ~~179~~, in the manufacture of a medicament for treating a cancer in a subject.

5 2519. The use of claim 2418, wherein the use has one, two, three, four, five, six, or all of (i)-(vii):
(i) the cancer is a hematological cancer, a multiple myeloma, and/or a solid tumor;
(ii) the antibody molecule, ADC, or composition is to be administered to the subject intravenously;

10 (iii) the antibody molecule, ADC, or composition is to be administered to the subject 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;

15 (iv) the antibody molecule, ADC, or composition is to be administered to the subject 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-~~1~~,
20 between 100 mg and 200 mg, or between 150 mg and 250 mg;

 (v) wherein the antibody molecule, ADC, or composition is to be administered once a week, twice a week, once every two weeks, once every three weeks, or once every four weeks;

 (vi) wherein the use further comprises determining the level of CD138 in a sample from the subject; and/or

25 (vii) wherein the use further comprises a second therapy for cancer to be administered to the subject.

2620. Use of an antibody molecule of any of claims 1-~~15~~, an ADC of any of claims ~~166-8~~, or a pharmaceutical composition of claim ~~179~~, in the manufacture of a medicament for treating a precancerous condition or preventing a cancer, ~~optionally wherein:~~

30 ~~(i) the precancerous condition is smoldering myeloma or monoclonal gammopathy of undetermined significance (MGUS); or~~

~~(ii) the cancer is multiple myeloma.~~

21. The use of claim 20, wherein:

(i) the precancerous condition is smoldering myeloma or monoclonal gammopathy of undetermined significance (MGUS); or

(ii) the cancer is multiple myeloma.

5

~~2722.~~ A method of detecting a ~~n-anti~~ CD138 molecule, the method comprising contacting a cell or a subject with an antibody molecule of any of claims 1-~~4~~5, thereby detecting the CD138 molecule; ~~optionally wherein:~~

~~(i) the antibody molecule is coupled with a detectable label; and/or~~

~~(ii) the CD138 molecule is detected *in vitro*, *ex vivo*, or *in vivo*.~~

10

23. The method of claim 22, wherein:

(i) the antibody molecule is coupled with a detectable label; and/or

(ii) the CD138 molecule is detected *in vitro*, *ex vivo*, or *in vivo*.