

What is claimed is:

1. An anti-CD138 antibody molecule comprising:

(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:

(i) an HCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR1 of any of antibodies 3820, 3821, 3826, 4221, 4226, 4320, 4321, 4322, 4326, 4421, 4520, 4521, 4526, 3522, 3621, 3822, 3825, or 4422;

(ii) an HCDR2 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the HCDR2 of 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% homology with, the amino acid sequence of the HCDR3 of the anti-CD138 antibody; 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:

(i) an LCDR1 comprising an amino acid sequence that differs by no more than 1, 2, or 3 amino acid residues from, or has at least 85, 90, 95, 99 or 100% homology with, the amino acid sequence of the LCDR1 of 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% homology 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% homology with, the amino acid sequence of the LCDR3 of the anti-CD138 antibody.

2. The antibody molecule of claim 1, comprising:

(a) a VH comprising: (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, and

(b) a VL comprising: (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.

3. The antibody molecule of claim 1 or 2, wherein 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.

4. The antibody molecule of any of claims 1-3, wherein the VH comprises the amino acid sequence of the VH of the anti-CD138 antibody.

5. The antibody molecule of any of claims 1-4, wherein 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 VL of the anti-CD138 antibody.

6. The antibody molecule of any of claims 1-5, wherein the VL comprises the amino acid sequence of the VL of the anti-CD138 antibody.

7. The antibody molecule of any of claims 1-6, wherein:

(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.

8. The antibody molecule of any of claims 1-7, wherein 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.

9. The antibody molecule of any of claims 1-8, comprising an Fc region.

10. The antibody molecule of any of claims 1-9, comprising a heavy chain (HC) comprising an amino acid sequence of 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 HC of the anti-CD138 antibody.

11. The antibody molecule of claim 10, wherein the HC comprises the amino acid sequence of the HC of the anti-CD138 antibody.

12. The antibody molecule of any of claims 1-11, comprising a light chain (LC) comprising an amino acid sequence of 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 LC of the anti-CD138 antibody.

13. The antibody molecule of claim 12, wherein the LC comprises the amino acid sequence of the LC of the anti-CD138 antibody.

14. The antibody molecule of any of claims 1-13, comprising:

(a) a heavy chain (HC) comprising an amino acid sequence of 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 HC of the anti-CD138 antibody; and

(b) a light chain (LC) comprising an amino acid sequence of 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 LC of the anti-CD138 antibody.

15. The antibody molecule of claim 14, wherein the HC comprises the amino acid sequence of the HC of the anti-CD138 antibody and the LC comprises the amino acid sequence of the LC of the anti-CD138 antibody.

16. An anti-CD138 antibody molecule comprising:

(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 one, two, or all of: (i) an HCDR1 comprising an amino acid sequence of G-Y-N/S/T-F-A/S/T-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 (SEQ ID NO: 508); 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 K/R-A/S-S-K/Q-S-L-L-Y-K-D-G-K-T-Y-L-N (SEQ ID NO: 522); (ii) an LCDR2 comprising an amino acid sequence of V-L/V-S-S/T-L/R-A/Q-S (SEQ ID NO: 523); or (iii) an LCDR3 comprising an amino acid sequence of Q-Q-L-V-E/Q-Y-P-Y-T (SEQ ID NO: 524); 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 one, two, or all of: (i) an HCDR1 comprising an amino acid sequence of S-Y-Y-I/M-H (SEQ ID NO: 525); (ii) an HCDR2 comprising an amino acid sequence of T-I-H-P-S-D-S-T-A/T-N-Y-A/N-Q-K-F-K/Q-G (SEQ ID NO: 526); or (iii) an HCDR3 comprising an amino acid sequence of F-V-Y (SEQ ID NO: 508); 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 K/R-A/S-S-K/Q-S-L-L-Y-K-D-G-K-T-Y-L-N (SEQ ID NO: 522); (ii) an LCDR2 comprising an amino acid sequence of V-L/V-S-S/T-L/R-A/Q-S (SEQ ID NO: 523); or (iii) an LCDR3 comprising an amino acid sequence of Q-Q-L-V-E/Q-Y-P-Y-T (SEQ ID NO: 524).

17. The antibody molecule of any of claims 1-16, comprising two VHs and two VLs.

18. The antibody molecule of any of claims 1-17, which is a synthetic antibody molecule or an isolated antibody molecule.

19. The antibody molecule of any of claims 1-18, which is a monovalent antibody molecule, a multivalent (*e.g.*, bivalent, trivalent, or tetravalent) antibody molecule, a monospecific molecule, or a multispecific (*e.g.*, bispecific, trispecific, or tetraspecific) antibody molecule.

20. The antibody molecule of any of claims 1-19, which is a humanized antibody molecule.

21. The antibody molecule of any of claims 1-20, comprising one or more framework regions derived from human framework germline sequence.

22. The antibody molecule of any of claims 1-21, which is an IgG antibody.
23. The antibody molecule of any of claims 1-22, comprising a heavy chain constant region of IgG chosen from IgG1, IgG2, IgG3, or IgG4.
24. The antibody molecule of any of claims 1-23, comprising a light chain constant region of kappa or lambda light chain.
25. The antibody molecule of any of claims 1-24, comprising 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.
26. The antibody molecule of any of claims 1-25, comprising an Fc region comprising one or more mutations described herein, *e.g.*, to increase one or more of half-life, ADCC, CDC, or ADCP.
27. An antibody molecule, which competes for binding to CD138 with any of antibodies 3820, 3821, 3826, 4221, 4226, 4320, 4321, 4322, 4326, 4421, 4520, 4521, 4526, 3522, 3621, 3822, 3825, or 4422.
28. An antibody molecule, which binds, or substantially binds, to an epitope that completely or partially overlaps with the epitope of any of antibodies 3820, 3821, 3826, 4221, 4226, 4320, 4321, 4322, 4326, 4421, 4520, 4521, 4526, 3522, 3621, 3822, 3825, or 4422.
29. An antibody-molecule drug conjugate (ADC) comprising an antibody molecule of any of claims 1-28, optionally comprising a cytotoxic agent, further optionally comprising a linker.
30. A composition comprising an antibody molecule of any of claims 1-28, or an ADC of claim 29, optionally, wherein the composition is a pharmaceutical composition.
31. The composition of claim 30, further comprising a pharmaceutically acceptable carrier.
32. 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 1-28.

33. A vector comprising a nucleic acid molecule of claim 32.
34. A cell comprising a nucleic acid molecule of claim 32 or a vector of claim 33, optionally, wherein the cell is an isolated cell.
35. A kit comprising an antibody molecule of any of claims 1-28, an ADC of claim 29, or a composition of claim 30 or 31, and instructions to use of the antibody molecule or composition.
36. A container comprising an antibody molecule of any of claims 1-28, an ADC of claim 29, or a composition of claim 30 or 31.
37. A method of producing an anti-CD138 antibody molecule, the method comprising culturing a cell of claim 34 under conditions that allow production of an antibody molecule, thereby producing the antibody molecule.
38. The method of claim 37, further comprising isolating or purifying the antibody molecule.
39. An antibody molecule of any of claims 1-28, an ADC of claim 29, or a composition of claim 30 or 31, for use in a method of treating a cancer in a subject.
40. The antibody molecule, ADC, or composition for use of claim 39, wherein the cancer is a hematological cancer.
41. The antibody molecule, ADC, or composition for use of claim 39 or 40, wherein the cancer is a multiple myeloma.
42. The antibody molecule, ADC, or composition for use of claim 39, wherein the cancer is a solid tumor, *e.g.*, a solid tumor described herein.
43. The antibody molecule, ADC, or composition for use of any of claims 39-42, wherein the antibody molecule, ADC, or composition is administered to the subject intravenously.
44. The antibody molecule, ADC, or composition for use of any of claims 39-43, wherein 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.

45. The antibody molecule, ADC, or composition for use of any of claims 39-44, wherein 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.

46. The antibody molecule, ADC, or composition for use of any of claims 39-45, wherein 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.

47. The antibody molecule, ADC, or composition for use of any of claims 39-46, further comprising determining the level of CD138 in a sample from the subject.

48. The antibody molecule, ADC, or composition for use of any of claims 39-47, further comprising administering to the subject a second therapy for cancer.

49. An antibody molecule of any of claims 1-28, an ADC of claim 29, or a composition of claim 30 or 31, for use in a method of treating a precancerous condition or preventing a cancer.

50. The antibody molecule, ADC, or composition for use of claim 49, wherein the precancerous condition is smoldering myeloma or monoclonal gammopathy of undetermined significance (MGUS).

51. The antibody molecule, ADC, or composition for use of claim 49, wherein the cancer is multiple myeloma.

52. A method of causing an ADCC activity, the method comprising contacting a cell or subject with an antibody molecule of any of claims 1-28, an ADC of claim 29, or a composition of claim 30 or 31, thereby causing the ADCC activity.

53. A method of treating a cancer, the method comprising administering to a subject in need thereof an effective amount of an antibody molecule of any of claims 1-28, an ADC of claim 29, or a composition of claim 30 or 31, thereby treating the cancer.

54. 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 of any of claims 1-28, an ADC of claim 29, or a composition of claim 30 or 31, thereby treating the precancerous condition or preventing the cancer.

55. A method of detecting an anti-CD138 molecule, the method comprising contacting a cell or a subject with an antibody molecule of any of claims 1-28, thereby detecting the CD138 molecule.

56. The method of claim 55, wherein the antibody molecule is coupled with a detectable label.

57. The method of claim 55 or 56, wherein the CD138 molecule is detected *in vitro*, *ex vivo*, or *in vivo*.

58. The antibody molecule, ADC, or composition for use of any of claims 39-51, or the method of claim 53 or 54, wherein the antibody molecule is used or administered in combination with a second therapeutic agent or modality.

59. The antibody molecule, ADC, or composition for use of claim 58, or the method of claim 58, wherein the second therapeutic agent or modality comprises a proteasome inhibitor.

60. The antibody molecule, ADC, or composition for use of claim 59, or the method of claim 59, wherein the proteasome inhibitor comprises bortezomib.