

CLAIMS

WHAT IS CLAIMED IS:

1. ~~An isolated composition comprising an~~ antibody molecule that binds to NKp30, wherein the antibody molecule comprises:
 - ~~(a)(i) a heavy chain variable region (VH) comprising~~ a heavy chain complementarity determining region 1 (VHCDR1) comprising the sequence of SEQ ID NO: 19, a heavy chain complementarity determining region 2 (VHCDR2) comprising the sequence of SEQ ID NO: 21, and a heavy chain complementarity determining region 3 (VHCDR3) ~~described in Table 8A~~ comprising the sequence of SEQ ID NO: 23; and/or
 - ~~(b)(ii) a light chain variable region (VL) comprising~~ a light chain complementarity determining region 1 (VLCDR1) comprising the sequence of SEQ ID NO: 26, a light chain complementarity determining region 2 (VLCDR2) comprising the sequence of SEQ ID NO: 28, and a light chain complementarity determining region 3 (VLCDR3) ~~described in Table 8B~~ comprising the sequences of SEQ ID NO: 30, SEQ ID NO: 7395, or SEQ ID NO: 113; or
 - ~~(b)(i) a VH comprising a VHCDR1 comprising the sequence of SEQ ID NO: 19, a VHCDR2 comprising the sequence of SEQ ID NO: 7399, and a VHCDR3 comprising the sequence of the sequence of SEQ ID NO: 23; and~~
 - ~~(ii) a VL comprising a VLCDR1 comprising the sequence of SEQ ID NO: 26, a VLCDR2 comprising the sequence of SEQ ID NO: 28, and a VLCDR3 comprising the sequences of SEQ ID NO: 30, SEQ ID NO: 7395, SEQ ID NO: 86, or SEQ ID NO: 113.~~
- ~~2. The antibody molecule of claim 1, wherein the VHCDR1 comprises the amino acid sequence of any one of SEQ ID NOs: C019, C033, C047, C061, C075, C089, C103, and C116.~~
- ~~3. The antibody molecule of claim 1 or 2, wherein the VHCDR2 comprises the amino acid sequence of any one of SEQ ID NOs: C021, C035, C049, C063, C077, C091, C105, or C118.~~
- ~~4. The antibody molecule of any one of claims 1-3, wherein the VHCDR3 comprises the amino acid sequence of any one of SEQ ID NOs: C023, C037, C051, C065, C079, C093, C107, and C120.~~
- ~~5. The antibody molecule of any one of claims 1-4, wherein the VLCDR1 comprises the amino acid sequence of any one of SEQ ID NOs: C026, C040, C054, C068, C082, C096, C110, and C123.~~
- ~~6. The antibody molecule of any one of claims 1-5, wherein the VLCDR2 comprises the amino acid sequence of any one of SEQ ID NOs: C028, C042, C056, C070, C084, C098, C112, and C125.~~
- ~~7. The antibody molecule of any one of claims 1-6, wherein the VLCDR3 comprises the amino acid sequence of any one of SEQ ID NOs: C030, C044, C058, C072, C086, C100, C113, and C127.~~
- ~~8. The antibody molecule of any one of claims 1-7, comprising:~~
 - ~~(a) a heavy chain framework region 1 (VHFWR1), a heavy chain framework region 2 (VHFWR1), a heavy chain framework region 3 (VHFWR3), and/or a heavy chain framework~~

region 4 (VHFWR4) described in Table 8A, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions; and/or

(b) a light chain framework region 1 (VLFWR1), a light chain framework region 2 (VLFWR2), a light chain framework region 3 (VLFWR3), and/or a light chain framework region 4 (VLFWR4) described in Table 8B, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

9.2. The antibody molecule composition of any one of claims 1-8, wherein the antibody molecule comprises:

(a)(i) ~~a heavy chain variable region (VH) described in Table 9, e.g., a VH comprising an~~ amino acid sequence ~~of any one of SEQ ID NOs: C001-C008, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to the sequence of SEQ ID NO: 1 or SEQ ID NO: 2~~thereto; and/or

(ii)(b) ~~a light chain variable region (VL) described in Table 9, e.g., a VL comprising an~~ amino acid sequence ~~of any one of SEQ ID NOs: C009-C016, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to any one sequence selected from the group consisting of SEQ ID NOs: 9-16~~thereto.

3. The composition of claim 1 or 2, wherein the antibody molecule comprises:

(i) a VH comprising the amino acid sequence of SEQ ID NO: 1; and/or

(ii) a VL comprising any one of the amino acid sequences selected from the group consisting of SEQ ID NOs: 9-12, 15, and 16.

4. The composition of claim 1 or 2, wherein the antibody molecule comprises:

(i) a VH comprising the amino acid sequence of SEQ ID NO: 2; and/or

(ii) a VL comprising any one of the amino acid sequences selected from the group consisting of SEQ ID NOs: 9-16.

10.5. The ~~composition~~antibody molecule of any one of claims 1-49, wherein the antibody molecule comprises an amino acid sequence ~~described in Table 10, optionally wherein the amino acid sequence is the amino acid sequence of any one of SEQ ID NOs: C017-C024, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to any one sequence selected from the group consisting of SEQ ID NOs: 17 and 7386-7392~~thereto.

6. The composition of any one of claims 1-5, wherein the antibody molecule comprises any one amino acid sequences selected from the group consisting of SEQ ID NOs: 17 and 7386-7392.

11. ~~A composition comprising a polypeptide molecule comprising the antibody molecule of any one of claims 1-10.~~

12.7. The composition of any one of claims 1-611, wherein the ~~antibody~~polypeptide molecule is a multifunctional ~~antibody~~polypeptide molecule.

~~13.8.~~ The composition of any one of claims 1-7~~11 or 12~~, wherein the antibody~~polypeptide~~ molecule is a multispecific antibody~~polypeptide~~ molecule.

~~14.~~—The composition of any one of claims 11-13, wherein the polypeptide molecule further comprises a targeting moiety.

~~15.~~—The composition of claim 14, wherein the targeting moiety is selected from a tumor targeting moiety, a targeting moiety that targets an autoreactive T cell, and a targeting moiety that targets an infected cell.

~~16.~~—The composition of claim 15, wherein the targeting moiety that targets the autoreactive T cell binds to an antigen present on the surface of the autoreactive T cell.

~~17.~~—The composition of claim 16, wherein the antigen present on the surface of the autoreactive T cell is associated with an inflammatory or autoimmune disorder.

~~18.~~—The composition of claim 16 or 17, wherein the antigen present on the surface of the autoreactive T cell is selected from the group consisting of CD3, TCR α , TCR β , TCR γ , TCR ζ , ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, and CD226.

~~19.~~—The composition of claim 15, wherein the targeting moiety that targets the infected cell binds to an antigen associated with a viral infection or a bacterial infection.

~~20.~~—The composition of any one of claims 11-19, wherein the polypeptide molecule further comprises a cytokine molecule.

~~21.~~—The composition of any one of claims 11-13, wherein the polypeptide molecule further comprises one, two, three, four or more of:

- (a) a tumor targeting moiety;
- (b) a cytokine molecule;
- (c) a T cell engager; or
- (d) a stromal modifying moiety.

~~22.~~—The composition of claim 20 or 21, wherein the cytokine molecule is a cytokine molecule selected from the group consisting of GM-CSF, IL-1 α , IL-1 β , IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-15, IL-18, IL-21, IFN- α , IFN- β , IFN- γ , MIP-1 α , MIP-1 β , TGF- β , TNF- α , and TNF β .

~~23.~~—The antibody molecule of any one of claims 1-10, or the composition of any one of claims 11-22, wherein the antibody molecule is a monospecific antibody molecule, a bispecific antibody molecule, or a trispecific antibody molecule.

~~24.~~—The antibody molecule of any one of claims 1-10, or the composition of any one of claims 11-22, wherein the antibody molecule is a monovalent antibody molecule, a bivalent antibody molecule, or a trivalent antibody molecule.

~~25.9. The composition antibody molecule of any one of claims 1-8, 10, 23, and 24, or the composition of any one of claims 11-24, wherein the antibody molecule is a full antibody or an antigen-binding fragment thereof, a bivalent antibody, or a bispecific antibody.~~

~~10. The composition of any one of claims 1-9, wherein the antibody molecule is a Fab, F(ab')₂, Fv, a single chain Fv, a single domain antibody, a diabody, or a camelid antibody.~~

~~11.26. The antibody molecule of any one of claims 1-10 and 23-25, or the composition of any one of claims 1-10, 11-25, wherein the antibody molecule comprises an immunoglobulin heavy chain constant region selected from the group consisting of chosen from IgG1 heavy chain constant region or fragment thereof, IgG2 heavy chain constant region or fragment thereof, IgG3 heavy chain constant region or fragment thereof, and/or IgG4 heavy chain constant region, or a fragment thereof.~~

~~27. The antibody molecule of any one of claims 1-10 and 23-26, or the composition of any one of claims 11-26, wherein the antibody comprises a light chain constant region chosen from the light chain constant regions of kappa or lambda, or a fragment thereof.~~

~~12.28. The antibody molecule of any one of claims 1-10 and 23-27, or the composition of any one of claims 11-27, wherein the immunoglobulin heavy chain constant region is altered to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function.~~

~~29. The antibody molecule of any one of claims 1-10 and 23-28, or the composition of any one of claims 11-28, wherein an interface of a first and second immunoglobulin chain constant regions is altered, e.g., mutated, to increase or decrease dimerization relative to a non-engineered interface.~~

~~13.30. The antibody molecule or the composition of claim 11 or 12, 29, wherein the antibody molecule comprises dimerization of the immunoglobulin chain constant region is enhanced by providing an Fc interface of a first immunoglobulin heavy chain constant region and a second immunoglobulin heavy chain constant region, wherein the first immunoglobulin heavy chain constant region comprises a first Fc region, and the second immunoglobulin heavy chain constant region comprises a second Fc region, and wherein the dimerization of the first immunoglobulin heavy chain constant region and the second immunoglobulin heavy chain constant region is enhanced by providing an Fc interface of the first Fc region and the second Fc region with one or more of: a paired cavity-protuberance, an electrostatic interaction, or a strand-exchange, such that a greater ratio of heteromultimer:homomultimer forms relative to a non-engineered interface with one or more of: a paired cavity-protuberance (“knob-in-a-hole”), an electrostatic interaction, or a strand-exchange, such that a greater ratio of heteromultimer:homomultimer forms relative to a non-engineered interface.~~

~~14.31. The antibody molecule or the composition of claim 13, 29 or 30, wherein the immunoglobulin heavy chain constant region comprises an amino acid substitution at a position chosen from one or more of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397, 398, 399, 405, 407, or 409, e.g., of the Fc region of human IgG1.~~

~~15.32. The antibody molecule or the composition of claim 13 or 1429, wherein the immunoglobulin chain heavy constant region comprises an amino acid substitution selecteddehosen from the group consisting of: (i) T366S, L368A, or Y407V, (ii)or T366W, and (iii)or a combination thereof.~~

~~16.33. The antibody molecule of any one of claims 1-10 and 23-32, or the composition of any one of claims 1344-1532, wherein the first Fc region comprises an amino acid substitution selected from the group consisting of T366S, L368A, Y407V, and any combination thereof, and the second Fc region comprises an amino acid substitution of T366W, or the first Fc region comprises an amino acid substitution of T366W, and the second Fc region comprises an amino acid substitution selected from the group consisting of T366S, L368A, Y407V, and any combination thereofantibody molecule or the polypeptide molecule further comprises a linker, optionally wherein the linker is a linker between one or more of: the targeting moiety and the cytokine molecule or the stromal modifying moiety, the targeting moiety and the immune cell engager, the cytokine molecule or the stromal modifying moiety, and the immune cell engager, the cytokine molecule or the stromal modifying moiety and the immunoglobulin chain constant region, the targeting moiety and the immunoglobulin chain constant region, or the immune cell engager and the immunoglobulin chain constant region.~~

~~34. The antibody molecule or the composition of claim 33, wherein the linker is selected from: a cleavable linker, a non-cleavable linker, a peptide linker, a flexible linker, a rigid linker, a helical linker, or a non-helical linker.~~

~~35. The antibody molecule or the composition of claim 34, wherein the linker is a peptide linker.~~

~~36. The antibody molecule or the composition of claim 35, wherein the peptide linker comprises Gly and Ser.~~

~~37. An isolated or recombinant nucleic acid molecule, which comprises the nucleotide sequence encoding any one of the antibody molecules or the polypeptide molecule described herein, or a nucleotide sequence substantially homologous thereto.~~

~~17. The composition of any one of claims 1-16, wherein the antibody molecule further comprises a light chain constant region selected from the group consisting of the kappa light chain constant region or fragment thereof, and the lambda light chain constant region or fragment thereof.~~

~~18. The composition of any one of claims 7-17, wherein the antibody molecule further comprises a targeting moiety selected from the group consisting of a tumor targeting moiety, a targeting moiety that targets an autoreactive T cell, and a targeting moiety that targets an infected cell.~~

~~19. The composition of claim 18, wherein the targeting moiety that targets an autoreactive T cell binds to an antigen present on the surface of the autoreactive T cell, wherein the antigen present on the surface of the autoreactive T cell is associated with an inflammatory or autoimmune disorder.~~

~~20. The composition of claim 19, wherein the antigen present on the surface of the autoreactive T cell is selected from the group consisting of CD3, TCR α , TCR β , TCR γ , TCR ζ , ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, and CD226.~~

~~21. The composition of claim 18, wherein the targeting moiety that targets an infected cell binds to~~

an antigen associated with a viral infection or a bacterial infection.

22. The composition of any one of claims 7-21, wherein the antibody molecule further comprises a cytokine molecule.

23. The composition of any one of claims 7-22, wherein the antibody molecule comprises one, two, three, four or more of:

(a) a tumor targeting moiety;

(b) a cytokine molecule;

(c) a T cell engager; or

(d) a stromal modifying moiety.

24. The composition of claim 22 or 23, wherein the cytokine molecule is interleukin-2 (IL-2) or a functional variant thereof, interleukin-12 (IL-12) or a functional variant thereof, interleukin-15 (IL-15) or a functional variant thereof, interleukin-18 (IL-18) or a functional variant thereof, interleukin-21 (IL-21) or a functional variant thereof, interleukin-7 (IL-7) or a functional variant thereof, or interferon gamma or a functional variant thereof.

~~25.38. An isolated or recombinant nucleic acid encoding the antibody molecule of any one of claims 1-10 and 23-36, or the polynucleotide comprising a sequence encoding the antibody molecule of the composition of any one of claims 1-24 molecule of the composition of any one of claims 11-36.~~

~~39. A vector comprising one or more of the nucleic acid molecules of claim 37 or 38.~~

~~40. A host cell comprising the nucleic acid molecule of claim 37 or 38, or the vector of claim 39.~~

~~41. A method of making the antibody molecule of any one of claims 1-10 and 23-36 or the composition of any one of claims 11-36, comprising culturing the host cell of claim 40, under suitable conditions.~~

~~26.42. A pharmaceutical composition comprising the antibody molecule of any one of claims 1-10 and 23-36, the composition of any one of claims 1-11-2436, the nucleic acid molecule of claim 37 or 38, or the host cell of claim 40, and a pharmaceutically acceptable carrier, excipient, diluent, or stabilizer for use in therapy.~~

~~27.43. Use of a A method of treating a cancer, comprising administering to a subject in need thereof the antibody molecule of any one of claims 1-10 and 23-36, the composition of any one of claims 11-36, or the pharmaceutical composition comprising the composition of any one of claims 1-2442 or the pharmaceutical composition of claim 26 in the manufacture of a medicament for treating cancer, an autoimmune or an inflammatory disorder, or an infectious disorder in a subject in need thereof, wherein the antibody molecule, the composition, or the pharmaceutical composition comprises an effective amount of the antibody molecule to treat the cancer, the autoimmune or the inflammatory disorder, or the infectious disorder in the subject-is administered in an amount effective to treat the cancer.~~

28.44. The ~~antibody molecule of any one~~use of claims ~~1-10 and 23-36~~27, wherein the cancer is a solid tumor cancer, a hematological cancer, or a metastatic cancer ~~or the composition of any one of claims 11-36 for use in treating cancer.~~

29.45. The ~~use~~method of claim ~~43 or the use of claim 44~~28, wherein the solid tumor cancer is one or more of pancreatic cancer, breast cancer, colorectal cancer, lung cancer, skin cancer, ovarian cancer, or liver cancer~~a solid tumor cancer, or a metastatic lesion.~~

30. The use of claim 27, wherein the infectious disorder is associated with a viral infection or a bacterial infection.