

ANTIBODY MOLECULES THAT BIND TO NKP30 AND USES THEREOF

RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/070,782 filed on August 26, 2020, the entire contents of which are hereby incorporated by reference.

BACKGROUND

[0002] Natural Killer (NK) cells recognize and destroy tumors and virus-infected cells in an antibody-independent manner. The regulation of NK cells is mediated by activating and inhibiting receptors on the NK cell surface. One family of activating receptors is the natural cytotoxicity receptors (NCRs) which include NKp30, NKp44 and NKp46.

[0003] Given the importance of immune checkpoint pathways in regulating an immune response, the need exists for developing novel agents that modulate the activity of immunoinhibitory proteins, such as PD-1, thus leading to activation of immune system. Such agents can be used, *e.g.*, for cancer immunotherapy and treatment of other conditions, such as chronic infection.

SUMMARY OF THE INVENTION

[0003a] In one aspect, provided herein is a 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) comprising the sequence of SEQ ID NO: 23; and (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) 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.

[0003b] In another aspect, provided herein is a recombinant polynucleotide comprising a sequence encoding the antibody molecule of the composition as described herein.

[0003c] In another aspect, provided herein is a pharmaceutical composition comprising the composition as described herein, and a pharmaceutically acceptable carrier, excipient, diluent, or stabilizer for use in therapy.

[0003d] In another aspect, provided herein is use of a pharmaceutical composition comprising the composition of any one of claims 1-24 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 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

[0004] Provided herein, *inter alia*, in an aspect, is an isolated antibody molecule that binds to NKp30, comprising:

(a) a heavy chain complementarity determining region 1 (VHCDR1), a heavy chain complementarity determining region 2 (VHCDR2), and/or a heavy chain complementarity determining region 3 (VHCDR3) described in Table 8A, or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions; and/or

(b) a light chain complementarity determining region 1 (VLCDR1), a light chain complementarity determining region 2 (VLCDR2), and/or a light chain complementarity determining region 3 (VLCDR3) described in Table 8B, or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

[0005] In some embodiments, the VHCDR1 comprises the amino acid sequence of any one of SEQ ID NOs: ~~C019~~, ~~C033~~, ~~C047~~, ~~C061~~, ~~C0757397~~, ~~C089~~, ~~C1103~~, and ~~C1116~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions

[0006] In some embodiments, the VHCDR2 comprises the amino acid sequence of any one of SEQ ID NOs: ~~C021~~, ~~C035~~, ~~C049~~, ~~C063~~, ~~C0777399~~, ~~C091~~, ~~C1105~~, or ~~C1118~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

[0007] In some embodiments, the VHCDR3 comprises the amino acid sequence of any one of SEQ ID NOs: ~~C023~~, ~~C037~~, ~~C051~~, ~~C065~~, ~~C079~~, ~~C093~~, ~~C1107~~, and ~~C1120~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

[0008] In some embodiments, the VLCDR1 comprises the amino acid sequence of any one of SEQ ID NOs: ~~C026~~, ~~C040~~, ~~C054~~, ~~C068~~, ~~C082~~, ~~C096~~, ~~C1110~~, and ~~C1123~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

[0009] In some embodiments, the VLCDR2 comprises the amino acid sequence of any one of SEQ ID

NOs: ~~C028~~, ~~C0427393~~, ~~C056~~, ~~C070~~, ~~C084~~, ~~C098~~, ~~C112~~, and ~~C125~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

[0010] In some embodiments, the VLCDR3 comprises the amino acid sequence of any one of SEQ ID NOs: ~~C030~~, ~~C0447395~~, ~~C058~~, ~~C072~~, ~~C086~~, ~~C1100~~, ~~C1113~~, and ~~C1127~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

[0011] In some embodiments, the antibody molecule as described herein comprises:

(a) a heavy chain framework region 1 (VHFWR1), a heavy chain framework region 2 (VHFWR2), 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.

[0012] In some embodiments, the antibody molecule as described herein comprises:

(a) a heavy chain variable region (VH) described in Table 9, e.g., a VH comprising the 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 thereto; and/or

(b) a light chain variable region (VL) described in Table 9, e.g., a VL comprising the 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 thereto.

[0013] In some embodiments, the antibody molecule as described herein comprises an amino acid sequence described in Table 10, e.g., 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 thereto.

[0014] In another aspect, provides herein is a composition comprising a polypeptide molecule comprising the antibody molecule as described herein.

[0015] In some embodiments, the polypeptide molecule is a multifunctional polypeptide molecule.

[0016] In some embodiments, the polypeptide molecule is a multispecific polypeptide molecule.

[0017] In some embodiments, the polypeptide molecule further comprises a targeting moiety.

[0018] In some embodiments, 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.

[0019] In some embodiments, the targeting moiety that targets the autoreactive T cell binds to an antigen present on the surface of the autoreactive T cell.

[0020] In some embodiments, the antigen present on the surface of the autoreactive T cell is associated with an inflammatory or autoimmune disorder.

[0021] In some embodiments, the antigen present on the surface of the autoreactive T cell is selected

Humanized variant_VL 2	ARITC (SEQ ID NO: 6089)	NO: 7326)	(SEQ ID NO: 6090)	ID NO: 7327)	RIEAGD EADYFC (SEQ ID NO: 7337)	NO: 7329)	NO: 6080)
15E1_Humanized variant_VL 3	QSVTTQ PPSASG TPGQRV TISC (SEQ ID NO: 6081)	SGEKLS DKYVH (SEQ ID NO: 7326)	WYQQL PGTAPK MLIY (SEQ ID NO: 6078)	ENDRRP S (SEQ ID NO: 7327)	GVPDRF SGSNSG NSASLA ISGLRSE DEADYFC (SEQ ID NO: 7338)	QFWDS TNSAV (SEQ ID NO: 7329)	FGGGTQ LTVL (SEQ ID NO: 6080)
15E1_Humanized variant_VL 4	QSVTTQ PPSVSG APGQR VTISC (SEQ ID NO: 6077)	SGEKLS DKYVH (SEQ ID NO: 7326)	WYQQL PGTAPK MLIY (SEQ ID NO: 6078)	ENDRRP S (SEQ ID NO: 7327)	GVPDRF SGSNSG NSASLA ITGLQA EDEAD YFC (SEQ ID NO: 7339)	QFWDS TNSAV (SEQ ID NO: 7329)	FGGGTQ LTVL (SEQ ID NO: 6080)
15E1_Humanized variant_VL 5	DSVTTQ SPLSLP VTLGQP ASISC (SEQ ID NO: 7340)	SGEKLS DKYVH (SEQ ID NO: 7326)	WYQQR PGQSPR MLIY (SEQ ID NO: 7341)	ENDRRP S (SEQ ID NO: 7327)	GVPDRF SGSNSG NDATL KISRVE AEDVG VYFC (SEQ ID NO: 7342)	QFWDS TNSAV (SEQ ID NO: 7329)	FGGGTK VEIK (SEQ ID NO: 233)

Table 8A. Exemplary heavy chain CDRs and FWRs of NKp30-targeting antigen binding domains

Ab ID	VHFWR1	VHCDR1	VHFWR2	VHCDR2	VHFWR3	VHCDR3	VHFWR4
BKM 0138	EIQLLES GGGLVQ PGGLSLR LSCAVS GFS (SEQ ID NO: ~~6018~~)	ITTTGYH WN (SEQ ID NO: ~~6019~~)	WVRQAP GKGLEW VG (SEQ ID NO: ~~6020~~)	YIYSSGS TSYNPSL KS (SEQ ID NO: ~~6021~~)	RFTISRD TSKNTF YLQMNS LRAEDT AVYYCA R (SEQ ID NO: ~~6022~~)	GDWHY FDY (SEQ ID NO: ~~6023~~)	WGQGT MVTVSS (SEQ ID NO: ~~6024~~)
BKM 0139	EIQLLES GGGLVQ PGGLSLR LSCAVS GFS (SEQ ID NO: ~~6032~~)	ITTTGYH WN (SEQ ID NO: ~~6033~~)	WVRQAP GKGLEW VG (SEQ ID NO: ~~6034~~)	YIYSSGS TSYNPSL KS (SEQ ID NO: ~~6035~~)	RFTISRD TSKNTF YLQMNS LRAEDT AVYYCA R (SEQ ID NO: ~~6036~~)	GDWHY FDY (SEQ ID NO: ~~6037~~)	WGQGT MVTVSS (SEQ ID NO: ~~6038~~)
BKM 0140	EIQLLES GGGLVQ PGGLSLR LSCAVS GFS (SEQ	ITTTGYH WN (SEQ ID NO: ~~6047~~)	WVRQAP GKGLEW VG (SEQ ID NO: ~~6048~~)	YIYSSGS TSYNPSL KS (SEQ ID NO: ~~6049~~)	RFTISRD TSKNTF YLQMNS LRAEDT AVYYCA	GDWHY FDY (SEQ ID NO: ~~6051~~)	WGQGT MVTVSS (SEQ ID NO: ~~6052~~)

	ID NO: C046)				R (SEQ ID NO: C050)		
BKM 0141	EIQLLES GGGLVQ PGGSLR LSCAVS GFS (SEQ ID NO: C060)	ITTTGYH WN (SEQ ID NO: C061)	WVRQAP GKGGLEW VG (SEQ ID NO: C062)	YIYSSGS TSYNPSL KS (SEQ ID NO: C063)	RFTISRD TSKNTF YLQMNS LRAEDT AVYYCA R (SEQ ID NO: C064)	GDWHY FDY (SEQ ID NO: C065)	WGQGT MVTVSS (SEQ ID NO: C066)
BKM 0142	EIQLLES GGGLVQ PGGSLR LSCAVS GFS (SEQ ID NO: C074)	ITTTGYH WN (SEQ ID NO: C0757397)	WVRQAP GKGGLEW VG (SEQ ID NO: C0767398)	YIYSSGS TSYAPSL KS (SEQ ID NO: C0777399)	RFTISRD TSKNTF YLQMNS LRAEDT AVYYCA R (SEQ ID NO: C0787400)	GDWHY FDY (SEQ ID NO: C079)	WGQGT MVTVSS (SEQ ID NO: C080)
BKM 0143	EIQLLES GGGLVQ PGGSLR LSCAVS GFS (SEQ ID NO: C088)	ITTTGYH WN (SEQ ID NO: C089)	WVRQAP GKGGLEW VG (SEQ ID NO: C090)	YIYSSGS TSYAPSL KS (SEQ ID NO: C091)	RFTISRD TSKNTF YLQMNS LRAEDT AVYYCA R (SEQ ID NO: C092)	GDWHY FDY (SEQ ID NO: C093)	WGQGT MVTVSS (SEQ ID NO: C094)
BKM 0144	EIQLLES GGGLVQ PGGSLR LSCAVS GFS (SEQ ID NO: C1102)	ITTTGYH WN (SEQ ID NO: C1103)	WVRQAP GKGGLEW VG (SEQ ID NO: C1104)	YIYSSGS TSYAPSL KS (SEQ ID NO: C1105)	RFTISRD TSKNTF YLQMNS LRAEDT AVYYCA R (SEQ ID NO: C1106)	GDWHY FDY (SEQ ID NO: C1107)	WGQGT MVTVSS (SEQ ID NO: C1108)
BKM 0145	EIQLLES GGGLVQ PGGSLR LSCAVS GFS (SEQ ID NO: C1115)	ITTTGYH WN (SEQ ID NO: C1116)	WVRQAP GKGGLEW VG (SEQ ID NO: C1117)	YIYSSGS TSYAPSL KS (SEQ ID NO: C1118)	RFTISRD TSKNTF YLQMNS LRAEDT AVYYCA R (SEQ ID NO: C1119)	GDWHY FDY (SEQ ID NO: C1120)	WGQGT MVTVSS (SEQ ID NO: C1121)

Table 8B. Exemplary light chain CDRs and FWRs of NKp30-targeting antigen binding domains

Ab ID	VLFWR1	VLCDR1	VLFWR2	VLCDR2	VLFWR3	VLCDR3	VLFWR4
BKM 0138	DSVTTQ SPLSLPV TLGQPA SISC (SEQ ID NO: C025)	SGEKLS DKYVH (SEQ ID NO: C026)	WYQQR GQSPRM LIY (SEQ ID NO: C027)	ENDRRP S (SEQ ID NO: C028)	GVPDRF SGSNSG NDATLK ISRVEAE DVG VYF C (SEQ ID NO: C029)	QFWDST ASAV (SEQ ID NO: C030)	FGGGTK VEIK (SEQ ID NO: C031)

BKM 0139	DSVTTQ SPLSLPV TLGQPA	SGEKLS DKYVH (SEQ ID	WYQQR GQSPRM LIY (SEQ	ENDRRP S (SEQ ID	GVPDRF SGSNSG NDATLK	QFWAST NSAV (SEQ ID	FGGGTK VEIK (SEQ ID
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	SISC (SEQ ID NO: C039)	NO: C040)	ID NO: C041)	NO: C0427393)	ISRVEAE DVGIFY C (SEQ ID NO: C0437394)	NO: C0447395)	NO: C0457396)
BKM 0140	SSETTQP PSVSVSP GQTASIT C (SEQ ID NO: C053)	SGEKL DKYVH (SEQ ID NO: C054)	WYQQK PGQSPV MVIY (SEQ ID NO: C055)	ENDRRP S (SEQ ID NO: C056)	GIPERFS GSNSGN TATLTIS GTQAM DEADYF C (SEQ ID NO: C057)	QFWAST NSAV (SEQ ID NO: C058)	FGGGTQ LTVL (SEQ ID NO: C059)
BKM 0141	SSETTQP PSVSVSP GQTASIT C (SEQ ID NO: C067)	SGEKL DKYVH (SEQ ID NO: C068)	WYQQK PGQSPV MVIY (SEQ ID NO: C069)	ENDRRP S (SEQ ID NO: C070)	GIPERFS GSNSGN TATLTIS GTQAM DEADYF C (SEQ ID NO: C071)	QFWDST ASAV (SEQ ID NO: C072)	FGGGTQ LTVL (SEQ ID NO: C073)
BKM 0142	DSVTTQ SPLSLPV TLGQPA SISC (SEQ ID NO: C081)	SGEKL DKYVH (SEQ ID NO: C082)	WYQQR GQSPRM LIY (SEQ ID NO: C083)	ENDRRP S (SEQ ID NO: C084)	GVPDRF SGSNSG NDATLK ISRVEAE DVGIFY C (SEQ ID NO: C085)	QFWDST NSAV (SEQ ID NO: C086)	FGGGTK VEIK (SEQ ID NO: C087)
BKM 0143	SSETTQP PSVSVSP GQTASIT C (SEQ ID NO: C095)	SGEKL DKYVH (SEQ ID NO: C096)	WYQQK PGQSPV MVIY (SEQ ID NO: C097)	ENDRRP S (SEQ ID NO: C098)	GIPERFS GSNSGN TATLTIS GTQAM DEADYF C (SEQ ID NO: C099)	QFWDST NSAV (SEQ ID NO: C100)	FGGGTQ LTVL (SEQ ID NO: C101)
BKM 0144	DSVTTQ SPLSLPV TLGQPA SISC (SEQ ID NO: C109)	SGEKL DKYVH (SEQ ID NO: C110)	WYQQR GQSPRM LIY (SEQ ID NO: C111)	ENDRRP S (SEQ ID NO: C112)	GVPDRF SGSNSG NDATLK ISRVEAE DVGIFY C (SEQ ID NO: C085)	QFWAST ASAV (SEQ ID NO: C113)	FGGGTK VEIK (SEQ ID NO: C114)
BKM 0145	SSETTQP PSVSVSP GQTASIT C (SEQ ID NO: C122)	SGEKL DKYVH (SEQ ID NO: C123)	WYQQK PGQSPV MVIY (SEQ ID NO: C124)	ENDRRP S (SEQ ID NO: C125)	GIPERFS GSNSGN TATLTIS GTQAM DEADYF C (SEQ ID NO: C126)	QFWAST ASAV (SEQ ID NO: C127)	FGGGTQ LTVL (SEQ ID NO: C128)

SEQ ID NO: 7303	15E1_Humanized variant_VH 4	15E1 heavy chain variable region humanized variant 4	EIQLVESGGGLVQPGGSLRLSCAVSGFSITTTGYH WNWVRQAPGKGLEWVGYYSSGSTSYNPSLKSR FTISRDTAKNSFYLMNSLRAEDTAVYYCARGD WHYFDYWGQGTMTVSS
SEQ ID NO: 7304	15E1_Humanized variant_VH 5	15E1 heavy chain variable region humanized variant 5	QIQLVQSGAEVKKPGASVKVSVSGFSITTTGY HWNWVRQAPGQGLEWMGYIYSSGSTSYNPSLK SRVTMTRDTSTNTFYMELSSLRSEDTAVYYCAR GDWHYFDYWGQGTMTVSS
SEQ ID NO: 7305	15E1_Humanized variant_VL1 (BJM0407 VL)	15E1 light chain variable region humanized variant 1	SSETTQPPSVSVSPGQTASITCSGEKLSDKYVHW YQQKPGQSPVMVIYENDRRPSGIPERFSGSNSGN TATLTISGTQAMDEADYFCQFWDSTNSAVFGGG TQLTVL
SEQ ID NO: 7306	15E1_Humanized variant_VL2	15E1 light chain variable region humanized variant 2	SSETTQPHSVSVATAQMARITCSGEKLSDKYVH WYQQKPGQDPVMVIYENDRRPSGIPERFSGSNPG NTATLTISRIEAGDEADYFCQFWDSTNSAVFGGG TQLTVL
SEQ ID NO: 7307	15E1_Humanized variant_VL3	15E1 light chain variable region humanized variant 3	QSVTTQPPSASGTPGQRVTISCSGEKLSDKYVHW YQQLPGTAPKMLIYENDRRPSGVPDRFSGSNSGN SASLAISGLRSEDEADYFCQFWDSTNSAVFGGGT QLTVL
SEQ ID NO: 7308	15E1_Humanized variant_VL4	15E1 light chain variable region humanized variant 4	QSVTTQPPSVSGAPGQRVTISCSGEKLSDKYVHW YQQLPGTAPKMLIYENDRRPSGVPDRFSGSNSGN SASLAITGLQAEDEADYFCQFWDSTNSAVFGGGT QLTVL
SEQ ID NO: 7309	15E1_Humanized variant_VL5 (BJM0411 VL)	15E1 light chain variable region humanized variant 5	DSVTTQSPLSLPVTLGQPASISCSGEKLSDKYVH WYQQRPQGSPRMLIYENDRRPSGVPDRFSGSNSG NDATLKISRVEAEDVGVYFCQFWDSTNSAVFGG GTKVEIK
SEQ ID NO: ~~€001~~	BKM0138 VH	BKM0138 heavy chain variable region	EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYH WNWVRQAPGKGLEWVGYYSSGSTSYNPSLKSR FTISRDTSKNTFYLMNSLRAEDTAVYYCARGD WHYFDYWGQGTMTVSS
SEQ ID NO: ~~€002~~	BKM0139 VH	BKM0139 heavy chain variable region	EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYH WNWVRQAPGKGLEWVGYYSSGSTSYNPSLKSR FTISRDTSKNTFYLMNSLRAEDTAVYYCARGD WHYFDYWGQGTMTVSS
SEQ ID NO: ~~€003~~	BKM0140 VH	BKM0140 heavy chain variable region	EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYH WNWVRQAPGKGLEWVGYYSSGSTSYNPSLKSR FTISRDTSKNTFYLMNSLRAEDTAVYYCARGD WHYFDYWGQGTMTVSS
SEQ ID NO: ~~€004~~	BKM0141 VH	BKM0141 heavy chain variable region	EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYH WNWVRQAPGKGLEWVGYYSSGSTSYNPSLKSR FTISRDTSKNTFYLMNSLRAEDTAVYYCARGD WHYFDYWGQGTMTVSS
SEQ ID NO: ~~€005~~	BKM0142 VH	BKM0142 heavy chain variable region	EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYH WNWVRQAPGKGLEWVGYYSSGSTSYAPSLKSR FTISRDTSKNTFYLMNSLRAEDTAVYYCARGD WHYFDYWGQGTMTVSS
SEQ ID NO: ~~€006~~	BKM0143 VH	BKM0143 heavy chain variable region	EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYH WNWVRQAPGKGLEWVGYYSSGSTSYAPSLKSR FTISRDTSKNTFYLMNSLRAEDTAVYYCARGD WHYFDYWGQGTMTVSS

SEQ ID NO: ~~€007~~	BKM0144 VH	BKM0144 heavy chain variable region	EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYH WNWVRQAPGKGLEWVGYYSSGSTSYAPSLKSR FTISRDTSKNTFYLMNSLRAEDTAVYYCARGD WHYFDYWGQGTMTVSS
SEQ ID NO: ~~€008~~	BKM0145 VH	BKM0145 heavy chain variable region	EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYH WNWVRQAPGKGLEWVGYYSSGSTSYAPSLKSR FTISRDTSKNTFYLMNSLRAEDTAVYYCARGD WHYFDYWGQGTMTVSS
SEQ ID NO: ~~€009~~	BKM0138 VL	BKM0138 light chain variable region	DSVTTQSPLSLPVTLGQPASISCSGEKLSDKYVH WYQQRPGQSPRMLIYENDRRPSGVPDRFSGSNSG NDATLKISRVEAEDVGVYFCQFWASTASAVFGG GTKVEIK
SEQ ID NO: ~~€010~~	BKM0139 VL	BKM0139 light chain variable region	DSVTTQSPLSLPVTLGQPASISCSGEKLSDKYVH WYQQRPGQSPRMLIYENDRRPSGVPDRFSGSNSG NDATLKISRVEAEDVGVYFCQFWASTNSAVFGG GTKVEIK
SEQ ID NO: ~~€011~~	BKM0140 VL	BKM0140 light chain variable region	SSETTQPPSVSVSPGQTASITCSGEKLSDKYVHW YQQKPGQSPVMVIYENDRRPSGIPERFSGSNSGN TATLTISGTQAMDEADYFCQFWASTNSAVFGGG TQLTVL
SEQ ID NO: ~~€012~~	BKM0141 VL	BKM0141 light chain variable region	SSETTQPPSVSVSPGQTASITCSGEKLSDKYVHW YQQKPGQSPVMVIYENDRRPSGIPERFSGSNSGN TATLTISGTQAMDEADYFCQFWASTNSAVFGGG TQLTVL
SEQ ID NO: ~~€013~~	BKM0142 VL	BKM0142 light chain variable region	DSVTTQSPLSLPVTLGQPASISCSGEKLSDKYVH WYQQRPGQSPRMLIYENDRRPSGVPDRFSGSNSG NDATLKISRVEAEDVGVYFCQFWASTNSAVFGG GTKVEIK
SEQ ID NO: ~~€014~~	BKM0143 VL	BKM0143 light chain variable region	SSETTQPPSVSVSPGQTASITCSGEKLSDKYVHW YQQKPGQSPVMVIYENDRRPSGIPERFSGSNSGN TATLTISGTQAMDEADYFCQFWASTNSAVFGGG TQLTVL
SEQ ID NO: ~~€015~~	BKM0144 VL	BKM0144 light chain variable region	DSVTTQSPLSLPVTLGQPASISCSGEKLSDKYVH WYQQRPGQSPRMLIYENDRRPSGVPDRFSGSNSG NDATLKISRVEAEDVGVYFCQFWASTASAVFGG GTKVEIK
SEQ ID NO: ~~€016~~	BKM0145 VL	BKM0145 light chain variable region	SSETTQPPSVSVSPGQTASITCSGEKLSDKYVHW YQQKPGQSPVMVIYENDRRPSGIPERFSGSNSGN TATLTISGTQAMDEADYFCQFWASTASAVFGGG TQLTVL

Table 10. Exemplary NKp30-targeting antigen binding domains/antibody molecules

SEQ ID NO	Ab ID	Description	Sequence
SEQ ID NO: 6148	Ch(anti-NKp30 9G1)HC N297A	9G1 heavy chain	QIQLQESGPGLVKPSQSLSTCSVTGFSINTGGYHWN WIRQFPGKKLEWMGYIYSSGSTSYNPSLKSRISITRDT SKNQFFLQLNSVTTEDTATYYCARGNWHYFDWFGQ GTMVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLV KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS SVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSC DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL PAPIEKTISKAKGQPREPVCTLPSPREEMTKNQVSL CAVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGS

			PSVSVSPGQTASITCSGEKLSDKYVHWYQQKPGQSPV MVIYENDRRPSGIPERFSGSNSGNTATLTISGTQAMDE ADYFCQFWDSTNSAVFGGGTQLTVL
SEQ ID NO: 7311	BJM0860 kappa scFv		EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYHWN WVRQAPGKGLEWVGYYSSGSTSYNPSLKSRTISR TSKNTFYQLQMNSLRAEDTAVYYCARGDWHYFDYWG QGTMTVTVSSGGGGSGGGGSGGGGSGGGGSDSVTTQS PLSLPVTLGQPASISCSGEKLSDKYVHWYQQRPGQSP RMLIYENDRRPSGVPDRFSGSNSGNDATLTKISRVEAE DVG VYFCQFWDSTNSAVFGGGTKVEIK
SEQ ID NO: ~~€017~~	BKM0138 scFv		EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYHWN WVRQAPGKGLEWVGYYSSGSTSYNPSLKSRTISR TSKNTFYQLQMNSLRAEDTAVYYCARGDWHYFDYWG QGTMTVTVSSGGGGSGGGGSGGGGSGGGGSDSVTTQS PLSLPVTLGQPASISCSGEKLSDKYVHWYQQRPGQSP RMLIYENDRRPSGVPDRFSGSNSGNDATLTKISRVEAE DVG VYFCQFWDSTASAVFGGGTKVEIK
SEQ ID NO: ~~€0187~~ <u>386</u>	BKM0139 scFv		EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYHWN WVRQAPGKGLEWVGYYSSGSTSYNPSLKSRTISR TSKNTFYQLQMNSLRAEDTAVYYCARGDWHYFDYWG QGTMTVTVSSGGGGSGGGGSGGGGSGGGGSDSVTTQS PLSLPVTLGQPASISCSGEKLSDKYVHWYQQRPGQSP RMLIYENDRRPSGVPDRFSGSNSGNDATLTKISRVEAE DVG VYFCQFWASTNSAVFGGGTKVEIK
SEQ ID NO: ~~€0197~~ <u>387</u>	BKM0140 scFv		EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYHWN WVRQAPGKGLEWVGYYSSGSTSYNPSLKSRTISR TSKNTFYQLQMNSLRAEDTAVYYCARGDWHYFDYWG QGTMTVTVSSGGGGSGGGGSGGGGSGGGGSSSETTQP PSVSVSPGQTASITCSGEKLSDKYVHWYQQKPGQSPV MVIYENDRRPSGIPERFSGSNSGNTATLTISGTQAMDE ADYFCQFWASTNSAVFGGGTQLTVL
SEQ ID NO: ~~€0207~~ <u>388</u>	BKM0141 scFv		EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYHWN WVRQAPGKGLEWVGYYSSGSTSYNPSLKSRTISR TSKNTFYQLQMNSLRAEDTAVYYCARGDWHYFDYWG QGTMTVTVSSGGGGSGGGGSGGGGSGGGGSSSETTQP PSVSVSPGQTASITCSGEKLSDKYVHWYQQKPGQSPV MVIYENDRRPSGIPERFSGSNSGNTATLTISGTQAMDE ADYFCQFWDSTASAVFGGGTQLTVL
SEQ ID NO: ~~€0217~~ <u>389</u>	BKM0142 scFv		EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYHWN WVRQAPGKGLEWVGYYSSGSTSYAPSLKSRTISR TSKNTFYQLQMNSLRAEDTAVYYCARGDWHYFDYWG QGTMTVTVSSGGGGSGGGGSGGGGSGGGGSDSVTTQS PLSLPVTLGQPASISCSGEKLSDKYVHWYQQRPGQSP RMLIYENDRRPSGVPDRFSGSNSGNDATLTKISRVEAE DVG VYFCQFWDSTNSAVFGGGTKVEIK
SEQ ID NO: ~~€0227~~ <u>390</u>	BKM0143 scFv		EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYHWNWV RQAPGKGLEWVGYYSSGSTSYAPSLKSRTISRDTSKNT FYQLQMNSLRAEDTAVYYCARGDWHYFDYWGQGTMTVT VSSGGGGSGGGGSGGGGSGGGGSSSETTQPPSVSVSPGQ TASITCSGEKLSDKYVHWYQQKPGQSPVMVIYENDRRP SGIPERFSGSNSGNTATLTISGTQAMDEADYFCQFWDST NSAVFGGGTQLTVL
SEQ ID NO: ~~€0237~~ <u>391</u>	BKM0144 scFv		EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYHWNWV RQAPGKGLEWVGYYSSGSTSYAPSLKSRTISRDTSKNT FYQLQMNSLRAEDTAVYYCARGDWHYFDYWGQGTMTVT VSSGGGGSGGGGSGGGGSGGGGSDSVTTQSPLSLPVTL GQPASISCSGEKLSDKYVHWYQQRPGQSP

			RMLIYENDRRPSGVPDRFSGSNSGNDATLKISRVEAE DVGVFYFCQFWASTASAVFGGGTKVEIK
SEQ ID NO: <u>C0247</u> <u>392</u>	BKM0145 scFv		EIQLLESGGGLVQPGGSLRLSCAVSGFSITTTGYHWN WVRQAPGKGLEWVGYYSSGSTSYAPSLKSRFTISRD TSKNTFYLQMNSLRAEDTAVYYCARGDWHYFDYWG QGTMTVTVSSGGGGSGGGGSGGGGSGGGGSSSETTQP PSVSVSPGQTASITCSGEKLSDKYVHWYQQKPGQSPV MVIYENDRRPSGIPERFSGSNSGNTATLTISGTQAMDE ADYFCQFWASTASAVFGGGTQLTVL

[00164] In some embodiments, the NK cell engager is an antigen binding domain that binds to NKp46 (e.g., NKp46 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in Table 15. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to NKp46, to the NK cell activates the NK cell. An antigen binding domain that binds to NKp46 (e.g., NKp46 present, e.g., expressed or displayed, on the surface of an NK cell) may be said to target NKp46, the NK cell, or both.

[00165] In some embodiments, the NK cell engager is an antigen binding domain that binds to NKG2D (e.g., NKG2D present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in Table 15. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to NKG2D, to the NK cell activates the NK cell. An antigen binding domain that binds to NKG2D (e.g., NKG2D present, e.g., expressed or displayed, on the surface of an NK cell) may be said to target NKG2D, the NK cell, or both.

[00166] In some embodiments, the NK cell engager is an antigen binding domain that binds to CD16 (e.g., CD16 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in Table 15. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to CD16, to the NK cell activates the NK cell. An antigen binding domain that binds to CD16 (e.g., CD16 present, e.g., expressed or displayed, on the surface of an NK cell) may be said to target CD16, the NK cell, or both.

Table 15. Exemplary variable regions of NKp46, NKG2D, or CD16-targeting antigen binding domains

SEQ ID NO	Ab ID	Description	Sequence
SEQ ID NO: 6175	NKG2D_1 scFV	scFv that binds NKG2D	QVHLQESGPGLVKPSETLSLTCTVSDDSISSYYWSWIR QPPGKGLEWIGHISYSGSANYNPSLKSRTISVDTSKN QFSLKLSSVTAADTAVYYCANWDDAFNIWGQGTMTV VSSGGGGSGGGGSGGGGSGGGGSEIVLTQSPGTLSP GERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYGA SSRATGIPDRFSGSGGTDFTLTISRLEPEDFAVYYCQQ YGSSPWTFGQGTKVEIK

NKp30 antibody molecules are disclosed herein.

[00361] Accordingly, in one aspect, the invention features an antibody molecule (*e.g.*, an isolated or recombinant antibody molecule), comprising one or more sequences according to the following enumerated embodiments. Additional features of any of the disclosed antibody molecules, multifunctional molecules, nucleic acids, vectors, host cells, or methods include one or more of the following enumerated embodiments.

[00362] Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following enumerated embodiments.

[00363] In an aspect, the disclosure features an isolated antibody molecule that binds to NKp30, comprising:

- (a) a heavy chain complementarity determining region 1 (VHCDR1), a heavy chain complementarity determining region 2 (VHCDR2), and/or a heavy chain complementarity determining region 3 (VHCDR3) described in **Table 8A**, or a sequence with no more than 1, 2, 3, or 4 mutations, *e.g.*, substitutions, additions, or deletions; and/or
- (b) a light chain complementarity determining region 1 (VLCDR1), a light chain complementarity determining region 2 (VLCDR2), and/or a light chain complementarity determining region 3 (VLCDR3) described in **Table 8B**, or a sequence with no more than 1, 2, 3, or 4 mutations, *e.g.*, substitutions, additions, or deletions.

[00364] In some embodiments, the VHCDR1 comprises the amino acid sequence of any of SEQ ID NOs: ~~C019~~, ~~C033~~, ~~C047~~, ~~C061~~, ~~C0757397~~, ~~C089~~, ~~C1103~~, or ~~C1116~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, *e.g.*, substitutions, additions, or deletions.

[00365] In some embodiments, the VHCDR2 comprises the amino acid sequence of any of SEQ ID NOs: ~~C021~~, ~~C035~~, ~~C049~~, ~~C063~~, ~~C0777399~~, ~~C091~~, ~~C1105~~, or ~~C1118~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, *e.g.*, substitutions, additions, or deletions.

[00366] In some embodiments, the VHCDR3 comprises the amino acid sequence of any of SEQ ID NOs: ~~C023~~, ~~C037~~, ~~C051~~, ~~C065~~, ~~C079~~, ~~C093~~, ~~C1107~~, or ~~C1120~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, *e.g.*, substitutions, additions, or deletions.

[00367] In some embodiments, the VLCDR1 comprises the amino acid sequence of any of SEQ ID NOs: ~~C026~~, ~~C040~~, ~~C054~~, ~~C068~~, ~~C082~~, ~~C096~~, ~~C1110~~, or ~~C1123~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, *e.g.*, substitutions, additions, or deletions.

[00368] In some embodiments, the VLCDR2 comprises the amino acid sequence of any of SEQ ID NOs: ~~C028~~, ~~C0427393~~, ~~C056~~, ~~C070~~, ~~C084~~, ~~C098~~, ~~C1112~~, or ~~C1125~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, *e.g.*, substitutions, additions, or deletions.

[00369] In some embodiments, the VLCDR3 comprises the amino acid sequence of any of SEQ ID NOs: ~~C030~~, ~~C0447395~~, ~~C058~~, ~~C072~~, ~~C086~~, ~~C1100~~, ~~C1113~~, or ~~C1127~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, *e.g.*, substitutions, additions, or deletions.

[00370] In some embodiments, the antibody molecule comprises:

(a) a heavy chain framework region 1 (VHFWR1), a heavy chain framework region 2 (VHFWR2), 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.

[00371] In some embodiments, the antibody molecule comprises:

(a) a heavy chain variable region (VH) described in **Table 9**, e.g., a VH comprising the amino acid sequence of any of SEQ ID NOs: ~~C001~~-~~C008~~, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto; and/or

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

[00372] In some embodiments, the antibody molecule comprises an amino acid sequence described in **Table 10**, e.g., the amino acid sequence of any of SEQ ID NOs: ~~C017~~-~~C024~~, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

[00373] In an aspect, the disclosure features a multispecific molecule comprising an antibody molecule described herein.

[00374] In some embodiments, the multispecific molecule further comprises one, two, three, four or more of: (a) a tumor targeting moiety, e.g., as described herein; (b) a cytokine molecule, e.g., as described herein; (c) a T cell engager, e.g., as described herein; or (d) a stromal modifying moiety, e.g., as described herein.

[00375] In some embodiments, the multispecific molecule further comprises a binding specificity that binds to an autoreactive T cell, e.g., an antigen present on the surface of an autoreactive T cell that is associated with the inflammatory or autoimmune disorder.

[00376] In some embodiments, the multispecific molecule further comprises a binding specificity that binds to an infected cell, e.g., a viral or bacterial infected cell.

[00377] In some embodiments, the antibody molecule is a monospecific antibody molecule, a bispecific antibody molecule, or a trispecific antibody molecule. In some embodiments, the multispecific molecule is a bispecific antibody molecule, or a trispecific antibody molecule.

[00378] In some embodiments, the antibody molecule or the multispecific molecule is a monovalent antibody molecule, a bivalent antibody molecule, or a trivalent antibody molecule.

[00379] In some embodiments, the antibody molecule or the multispecific molecule is a full antibody (e.g., an antibody that includes at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains), or an antigen-binding fragment (e.g., a Fab, F(ab')₂, Fv, a single chain Fv, a single domain antibody, a diabody (dAb), a bivalent antibody, or bispecific antibody or

[00526] 122. The method of embodiment 121 or the use of embodiment 121, wherein the therapeutic agent is selected from: a chemotherapeutic agent, or a biologic agent.

[00527] 123. A method of treating an autoimmune or an inflammatory disorder, comprising administering to a subject in need thereof the antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments, wherein the multispecific antibody is administered in an amount effective to treat the autoimmune or the inflammatory disorder.

[00528] 124. The antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments for use in treating an autoimmune or an inflammatory disorder.

[00529] 125. A method of treating an infectious disorder, comprising administering to a subject in need thereof the antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments, wherein the multispecific antibody is administered in an amount effective to treat the infectious disorder.

[00530] 126. The antibody molecule or the multispecific or multifunctional molecule polypeptide of any of the preceding embodiments for use in treating an infectious disorder.

Exemplary Embodiment 3

[00531] 1. An isolated antibody molecule that binds to NKp30, comprising:

(a) a heavy chain complementarity determining region 1 (VHCDR1), a heavy chain complementarity determining region 2 (VHCDR2), and/or a heavy chain complementarity determining region 3 (VHCDR3) described in Table 8A, or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions; and/or

(b) a light chain complementarity determining region 1 (VLCDR1), a light chain complementarity determining region 2 (VLCDR2), and/or a light chain complementarity determining region 3 (VLCDR3) described in Table 8B, or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

[00532] 2. The antibody molecule of embodiment 1, wherein the VHCDR1 comprises the amino acid sequence of any of SEQ ID NOs: ~~C019~~, ~~C033~~, ~~C047~~, ~~C061~~, ~~C0757397~~, ~~C089~~, ~~C1103~~, or ~~C1116~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

[00533] 3. The antibody molecule of embodiment 1 or 2, wherein the VHCDR2 comprises the amino acid sequence of any of SEQ ID NOs: ~~C021~~, ~~C035~~, ~~C049~~, ~~C063~~, ~~C0777399~~, ~~C091~~, ~~C1105~~, or ~~C1118~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

[00534] 4. The antibody molecule of any of embodiments 1-3, wherein the VHCDR3 comprises the amino acid sequence of any of SEQ ID NOs: ~~C023~~, ~~C037~~, ~~C051~~, ~~C065~~, ~~C079~~, ~~C093~~, ~~C1107~~, or ~~C1120~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

[00535] 5. The antibody molecule of any of embodiments 1-4, wherein the VLCDR1 comprises the amino acid sequence of any of SEQ ID NOs: ~~C026~~, ~~C040~~, ~~C054~~, ~~C068~~, ~~C082~~, ~~C096~~, ~~C1110~~, or ~~C1123~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or

deletions.

[00536] 6. The antibody molecule of any of embodiments 1-5, wherein the VLCDR2 comprises the amino acid sequence of any of SEQ ID NOs: ~~C028~~, ~~C0427393~~, ~~C056~~, ~~C070~~, ~~C084~~, ~~C098~~, ~~C1112~~, or ~~C1125~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

[00537] 7. The antibody molecule of any of embodiments 1-6, wherein the VLCDR3 comprises the amino acid sequence of any of SEQ ID NOs: ~~C030~~, ~~C0447395~~, ~~C058~~, ~~C072~~, ~~C086~~, ~~C1100~~, ~~C1113~~, or ~~C1127~~, or an amino acid sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions.

[00538] 8. The antibody molecule of any of embodiments 1-7, comprising:

(a) a heavy chain framework region 1 (VHFWR1), a heavy chain framework region 2 (VHFWR2), 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.

[00539] 9. The antibody molecule of any of embodiments 1-8, comprising:

(a) a heavy chain variable region (VH) described in Table 9, e.g., a VH comprising the amino acid sequence of any of SEQ ID NOs: ~~C001-C008~~, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto; and/or

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

[00540] 10. The antibody molecule of any of embodiments 1-9, comprising an amino acid sequence described in Table 10, e.g., the amino acid sequence of any of SEQ ID NOs: ~~C017-C024~~, or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

[00541] 11. A multispecific molecule comprising the antibody molecule of any of embodiments 1-10.

[00542] 12. The multispecific molecule of embodiment 11, further comprising one, two, three, four or more of:

- a. a tumor targeting moiety, e.g., as described herein;
- b. a cytokine molecule, e.g., as described herein;
- c. a T cell engager, e.g., as described herein; or
- d. a stromal modifying moiety, e.g., as described herein.

[00543] 13. The multispecific molecule of embodiment 11, further comprising a binding specificity that binds to an autoreactive T cell, e.g., an antigen present on the surface of an autoreactive T cell that is associated with the inflammatory or autoimmune disorder.