

ANTI-TCR ANTIBODY MOLECULES AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application 62/957,024 filed on January 3, 2020, and U.S. Provisional Application 63/070,596 filed on August 26, 2020, the entire contents of each of which are hereby incorporated by reference.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on January 29, 2021, is named 53676-736_601_SL.txt and is 1,197,327 bytes in size.

BACKGROUND

Current molecules designed to redirect T cells to promote tumor cell lysis for cancer immunotherapy typically target the CD3 epsilon (CD3e) subunit of the T cell receptor (TCR). However, there are limitations to this approach. Previous studies have shown that, *e.g.*, low doses of anti-CD3e monoclonal antibody (mAb) can cause T cell dysfunction and exert immunosuppressive effects. In addition, anti-CD3e mAbs bind to all T cells and thus activate a large number of T cells. Such non-physiological massive activation of T cells by these anti-CD3e mAbs can result in the production of proinflammatory cytokines such as IFN-gamma, IL-1-beta, IL-6, IL-10 and TNF-alpha, causing a “cytokine storm” known as the cytokine release syndrome (CRS), which is also associated with neurotoxicity (NT). Thus, it might be advantageous to develop antibodies that avoid or reduce CRS and/or NT.

SUMMARY OF THE INVENTION

Disclosed herein are, *inter alia*, antibody molecules directed to the variable chain of the beta subunit of TCR (TCRβV) which bind and, *e.g.*, activate or expand, T cells, *e.g.*, a subset of T cells (“anti-TCRβV antibody molecules”). In some embodiments, the anti-TCRβV antibody molecules disclosed herein result in a cytokine profile, *e.g.*, a cytokine secretion profile, that differs from that of a T cell engager that binds to a receptor or molecule other than a TCRβV region (“a non-TCRβV-binding T cell engager”). In some embodiments, the anti-TCRβV antibody molecules disclosed herein result in lesser, minimal, or no production of cytokines associated with cytokine release syndrome (CRS), *e.g.*, IL-6, IL-1beta, IL-10 and TNF alpha; and enhanced and/or delayed production of IL-2 and IFN-gamma. In some embodiments, the

anti-TCR β V antibodies disclosed herein result in expansion of an immune cell, *e.g.*, a T cell, a tumor infiltrating lymphocyte (TIL), an NK cell, or other immune cells (*e.g.*, as described herein). Also provided herein are methods of making said anti-TCR β V antibody molecules, and methods of using said anti-TCR β V antibody molecules including, methods of using an anti-TCR β V antibody molecule for expanding an immune cell or an immune cell population, and
5 method of using an anti-TCR β V antibody molecule for treating cancer, including the use as

combination therapy with TIL and immune checkpoint therapeutics. This disclosure further provides multispecific molecules, *e.g.*, bispecific molecules, comprising said anti-TCR β V antibody molecules. In some embodiments, compositions comprising anti-TCR β V antibody molecules of the present disclosure, can be used, *e.g.*, to activate and/or redirect T cells to promote tumor cell lysis for cancer immunotherapy. In some embodiments, compositions comprising anti-TCR β V antibody molecules as disclosed herein limit the unwanted side-effects of CRS and/or NT, *e.g.*, CRS and/or NT associated with anti-CD3e targeting.

In some embodiments, the anti-TCR β V antibody molecules disclosed herein result in lesser, minimal, or no production of cytokines associated with cytokine release syndrome (CRS), *e.g.*, IL-6, IL-1 β , IL-10 and TNF α ; and enhanced and/or delayed production of IL-2 and IFN- γ , compared with an anti-CD3 antibody molecule (*e.g.*, a low affinity anti-CD3 antibody molecule). In some embodiments, administration of the anti-TCR β V antibody molecules disclosed herein in a subject results in reduced cytokine release syndrome (CRS) (*e.g.*, lesser duration of CRS or no CRS), a reduced severity of CRS (*e.g.*, absence of severe CRS, *e.g.*, CRS grade 4 or 5), reduced neurotoxicity (NT), or a reduced severity of NT, compared with similar administration of an anti-CD3 antibody molecule (*e.g.*, a low affinity anti-CD3 antibody molecule).

Accordingly, provided herein are, anti-TCR β V antibody molecules, multispecific or multifunctional molecules (*e.g.*, multispecific or multifunctional antibody molecules) (also referred to herein as a “composition”) that comprise anti-TCR β V antibody molecules, nucleic acids encoding the same, methods of producing the aforesaid molecules, pharmaceutical compositions comprising aforesaid molecules, and methods of treating a disease or disorder, *e.g.*, cancer, using the aforesaid molecules. The antibody molecules and pharmaceutical compositions disclosed herein can be used (alone or in combination with other agents or therapeutic modalities) to treat, prevent and/or diagnose disorders and conditions, *e.g.*, cancer, *e.g.*, as described herein.

In one aspect, provided herein is a molecule comprising an antigen binding domain that binds to T cell receptor beta variable region (TCR β V), wherein the antigen binding domain comprises:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (HC CDR1), a heavy chain complementarity determining region 2 (HC CDR2), and a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 1100, and a light chain variable region (VL) comprising a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity

determining region 2 (LC CDR2), and a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 1101;

(ii) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1346, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1347 or SEQ ID NO: 1349;

(iii) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1348, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1349;

(iv) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1350, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1349, SEQ ID NO: 1351, SEQ ID NO: 1353, SEQ ID NO: 1365, SEQ ID NO: 1367, or SEQ ID NO: 1369;

(v) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1356, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1357;

(vi) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1360 or SEQ ID NO: 1362, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1361;

(vii) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1370, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1365, SEQ ID NO: 1367, or SEQ ID NO: 1369;

(viii) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1112, SEQ ID NO: 1113, SEQ ID NO: 1114, SEQ ID NO: 1115, or SEQ ID NO: 1116, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1111;

(ix) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1310 or SEQ ID NO: 1311, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1313;

(x) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1312, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1314;
or

(xi) a single chain variable fragment (scfv) comprising a HC CDR1, a HC CDR2, a HC CDR3, a LC CDR1, a LC CDR2, and a LC CDR3 of any one sequence selected from the group consisting of SEQ ID NOs: 1309, 1326-1337, and 110.

In one aspect, provided herein is a recombinant polynucleotide comprising a sequence encoding the molecule as described herein.

In one aspect, provided herein is a pharmaceutical composition comprising the molecule as described herein, and a pharmaceutically acceptable carrier, excipient, or stabilizer for use in therapy.

5 In one aspect, provided herein is a use of a pharmaceutical composition comprising the molecule as described herein in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein an effective amount of the molecule is to be administered to the subject.

10 In one aspect, provided herein is a of a composition comprising the molecule as described herein in the manufacture of a medicament for modulating an immune response in a subject in need thereof, optionally, wherein an effective amount of the molecule expands an immune cell population, optionally, wherein the expansion occurs *in vivo* or *ex vivo*.

In one aspect, the disclosure provides an antibody molecule, e.g., a non-murine, *e.g.*, a human-like (e.g., a human, or humanized antibody molecule), which binds, *e.g.*, specifically binds, to a T cell receptor beta variable (TCR β V) region.

15 In some embodiments, the anti-TCRBV antibody molecule comprises an antigen binding domain of an antibody disclosed in any of Tables 1-2, or 10-13, or a sequence with at least 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity thereto. In some embodiments, the anti-TCRBV antibody molecule comprises a leader sequence comprising the amino acid sequence of SEQ ID

Table 9: Alignment of TCRBV amino acid sequences (SEQ ID NOS 3457-~~3639~~3516, respectively, in order of appearance)

	FR1-IMGT				CDR1-IMGT				FR2-IMGT				CDR2-IMGT				FR3-IMGT				CDR3-IMGT			
	(1-26)				(27-38)				(39-55)				(56-65)				(66-104)				(105-117)			
Gene	A		B		BC		C		C'		C'C"		C"		D		E		F		FG			
	(1-15)		(16-26)		(27-38)		(39-46)		(47-55)		(56-65)		(66-74)		(75-84)		(85-96)		(97-104)					
	—————>		—————>				—————>		—————>				—————>		—————>		—————>		—————>					
	1	10	15	16	23	26	27	38	3941	46	47	55	56	65	66	74	75	84	85	89	96	97	104	105
																								
TRBV1	DTGITQTPKYLVTAM	GSKRTMKREHL	GH.....DS	MYWYRQKA	KKSLEFMFY	YNC....KEF	IENKTVP.N	HFTPECP.DS	SRLYLHVVALQQ	EDSAAYLC	TSSQ													
TRBV2	EPEVTQTPSHQVTQM	GQEVILRCVPI	SNH.....LY	FYWYRQIL	GQKVEFLVS	FYN....NEI	SEKSEIFDD	QFSVERP.DG	SNFTLKIRSTKL	EDSAMYFC	ASSE													
TRBV3-1	DTAVSQTPKYLVTQM	GNDKSIKCEQN	LGH.....DT	MYWYRQDS	KKFLKIMFS	YNN....KEL	IINETVP.N	RFSPKSP.DK	AHLNLHINSLEL	GDSAVYFC	ASSQ													
TRBV3-2	DTAVSQTPKYLVTQM	GKKESLK*EQN	LGH.....NA	MYWYRQDS	KKFLKTMFI	YSN....KEP	ILNETVP.N	RFSPPDSP.DK	AHLNLHINSLEL	GDSAVYFC	ASSQ													
TRBV4-1	DTEVTQTPKHLVMGM	TNKSLSKCEQH	MGH.....RA	MYWYRQKA	KKPPELMFV	YSY....EKL	SINESVP.S	RFSPECP.NS	SLNLHLHALQP	EDSALYLC	ASSQ													
TRBV4-2	ETGVTQTPRHLVMGM	TNKSLSKCEQH	LGH.....NA	MYWYRQSA	KKPLELMFV	YNF....KEQ	TENNSVP.S	RFSPECP.NS	SHLFLHLHTLQP	EDSALYLC	ASSQ													
TRBV4-3	ETGVTQTPRHLVMGM	TNKSLSKCEQH	LGH.....NA	MYWYRQSA	KKPLELMFV	YSL....EER	VENNSVP.S	RFSPECP.NS	SHLFLHLHTLQP	EDSALYLC	ASSQ													
TRBV5-1	KAGVTQTPRYLIKTR	GQQVTLRCSPI	SGH.....RS	VSWYQQTP	GQGLQFLFE	YFS....ETQ	RNKGNFP.G	RFSGRQF.SN	SRSEMNVSTLEL	GDSALYLC	ASSL													
TRBV5-3	EAGVTQSPTHLIKTR	GQQVTLRCSPI	SGH.....SS	VSWYQQAP	GQGPQFIFE	YAN....ELR	RSEGNFP.N	RFSGRQF.HD	CCSEMNVSALEL	GDSALYLC	ARSL													
TRBV5-4	ETGVTQSPTHLIKTR	GQQVTLRCSQ	SGH.....NT	VSWYQQAL	GQGPQFIFQ	YYR....EEE	NGRGNFP.P	RFSGLQF.PN	YSSELNVNALEL	DDSALYLC	ASSL													
TRBV5-5	DAGVTQSPTHLIKTR	GQQVTLRCSPI	SGH.....KS	VSWYQQVL	GQGPQFIFQ	YYE....KEE	RGRGNFP.D	RFSARQF.PN	YSSELNVNALLL	GDSALYLC	ASSL													
TRBV5-6	DAGVTQSPTHLIKTR	GQQVTLRCSPK	SGH.....DT	VSWYQQAL	GQGPQFIFQ	YYE....EEE	RQGRNFP.D	RFSGHQF.PN	YSSELNVNALLL	GDSALYLC	ASSL													
TRBV5-7	DAGVTQSPTHLIKTR	GQHVTLRCSPI	SGH.....TS	VSSYQQAL	GQGPQFIFQ	YYE....KEE	RGRGNFP.D	QFSGHQF.PN	YSSELNVNALLL	GDSALYLC	ASSL													
TRBV5-8	EAGVTQSPTHLIKTR	GQQATLRCSPI	SGH.....TS	VYWYQQAL	GLGLQFLLW	YDE....GEE	RNRGNFP.P	RFSGRQF.PN	YSSELNVNALEL	EDSALYLC	ASSL													
TRBV6-1	NAGVTQTPKFQVLKT	GQSMTLQCAQD	MNH.....NS	MYWYRQDP	GMGLRLIYY	SAS....EGT	TDKGEVP.N	GYNVSRL.NK	REFSLRLESAAAP	SQTSVYFC	ASSE													
TRBV6-2	NAGVTQTPKFRVLKT	GQSMTLLCAQD	MNH.....EY	MYWYRQDP	GMGLRLIHY	SVG....EGT	TAKGEVP.D	GYNVSRL.KK	QNFLLGLESAAAP	SQTSVYFC	ASSY													
TRBV6-3	NAGVTQTPKFRVLKT	GQSMTLLCAQD	MNH.....EY	MYWYRQDP	GMGLRLIHY	SVG....EGT	TAKGEVP.D	GYNVSRL.KK	QNFLLGLESAAAP	SQTSVYFC	ASSY													
TRBV6-4	IAGITQAPTSQILAA	GRMTLRCQD	MRH.....NA	MYWYRQDL	GLGLRLIHY	SNT....AGT	TDKGEVP.D	GYSVSRA.NT	DDFPLTLASAVP	SQTSVYFC	ASSD													
TRBV6-5	NAGVTQTPKFQVLKT	GQSMTLQCAQD	MNH.....EY	MSWYRQDP	GMGLRLIHY	SVG....AGI	TDQGEVP.N	GYNVSRS.TT	EDFPLRLLSAAP	SQTSVYFC	ASSY													
TRBV6-6	NAGVTQTPKFRILKI	GQSMTLQCQTD	MNH.....NY	MYWYRQDP	GMGLKLIYY	SVG....AGI	TDKGEVP.N	GYNVSRS.TT	EDFPLRLELAAP	SQTSVYFC	ASSY													
TRBV6-7	NAGVTQTPKFHVLT	GQSMTLLCAQD	MNH.....EY	MYRWRQDP	GKGLRLIYY	SVA....AAL	TDKGEVP.N	GYNVSRS.NT	EDFPLKLESAAAP	SQTSVYFC	ASSY													
TRBV6-8	NAGVTQTPKFHILKT	GQSMTLQCAQD	MNH.....GY	MSWYRQDP	GMGLRLIYY	SAA....AGT	TDK.EVP.N	GYNVSRL.NT	EDFPLRLVSAAP	SQTSVYLC	ASSY													
TRBV6-9	NAGVTQTPKFHILKT	GQSMTLQCAQD	MNH.....GY	LSWYRQDP	GMGLRRIHY	SVA....AGI	TDKGEVP.D	GYNVSRS.NT	EDFPLRLESAAAP	SQTSVYFC	ASSY													
TRBV7-1	GAGVSQSLRHVAKK	GKDVALRYDPI	SGH.....NA	LYWYRQSL	GQGLEFPIY	FQG....KDA	ADKSGLPRD	RFSAQRS.EG	SISTLKQRTQQ	GDLAVYLC	ASSS													
TRBV7-2	GAGVSQSPSNKVTEK	GKDVELRCDPI	SGH.....TA	LYWYRQSL	GQGLEFLIY	FQG....NSA	PKSGLPSD	RFSAERT.GG	SVSTLTQRTQQ	EDSAVYLC	ASSL													
TRBV7-3	GAGVSQTPSNKVTEK	GKYVELRCDPI	SGH.....TA	LYWYRQSL	GQGPFLIY	FQG....TGA	ADDSGLPND	RFFAVRP.EG	SVSTLKIQRTER	GDSAVYLC	ASSL													
TRBV7-4	GAGVSQSPRYKVAKR	GRDVALRCDSI	SGH.....VT	LYWYRQTL	GQGEVLTY	SQS....DAQ	RDKSGRPSG	RFSAERP.ER	SVSTLKIQRTEQ	GDSAVYLC	ASSL													
TRBV7-6	GAGVSQSPRYKVTRK	GQDVALRCDPI	SGH.....VS	LYWYRQAL	GQGPFLTY	FNY....EAQ	QDKSGLPND	RFSAERP.EG	SISTLTQRTQQ	RDSAMYRC	ASSL													
TRBV7-7	GAGVSQSPRYKVTRK	GQDVTLRCDPI	SSH.....AT	LYWYQQAL	GQGPFLTY	FNY....EAQ	PKSGLPSD	RFSAERP.EG	SISTLTQRTQQ	RDSAMYRC	ASSL													
TRBV7-8	GAGVSQSPRYKVAKR	GQDVALRCDPI	SGH.....VS	LFWYQQAL	GQGPFLTY	FQN....EAQ	LDKSGLPSD	RFFAERP.EG	SVSTLKIQRTEQ	EDSAVYLC	ASSL													
TRBV7-9	DTGVSQNPRLHKITKR	GQNVTRCDPI	SEH.....NR	LYWYRQTL	GQGPFLTY	FQN....EAQ	LEKSRLLED	RFSAERP.KG	SFSTLEIQRTEQ	GDSAMYLC	ASSL													
TRBV9	DSGVTQTPKHLITAT	GQRVTLRCSPR	SGD.....LS	VYWYQQSL	DQGLQFLIQ	YYN....GEE	RAKNIL.E	RFSAQQF.PD	LHSELNLSLEL	GDSALYFC	ASSV													
TRBV10-1	DAEITQSPRHKITET	GRQVTLACHQT	WNH.....NN	MFWYRQDL	GHGLRLIHY	SYG....VQD	TNKGEVS.D	GYSVRS.NT	EDLPLTLESAAAS	SQTSVYFC	ASSE													
TRBV10-2	DAGITQSPRYKITET	GRQVTLCHQCT	WSH.....SY	MFWYRQDL	GHGLRLIYY	SAA....ADI	TDKGEVP.D	GYVVSRS.KT	ENFPLTLESATR	SQTSVYFC	ASSE													
TRBV10-3	DAGITQSPRHKVTET	GTPVTLRCHQT	ENH.....RY	MYWYRQDP	GHGLRLIHY	SYG....VKD	TDKGEVS.D	GYSVRS.KT	EDFLLTLESATS	SQTSVYFC	AISE													
TRBV11-1	EAEVAQSPRYKITEK	SQAVAFWCNPI	SGH.....AT	LYWYRQIL	GQGPPELLVQ	FQD....ESV	VDSQLPKD	RFSAERL.KG	VDSTLKIQAEL	GDSAMYLC	ASSL													
TRBV11-2	EAGVAQSPRYKIIKE	RQSVAFWCNPI	SGH.....AT	LYWYQQIL	GQGPKLLIQ	FQN....NGV	VDSQLPKD	RFSAERL.KG	VDSTLKIQAEL	EDSAVYLC	ASSL													

a VL domain comprising the amino acid sequence of SEQ ID NO: 29, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 29, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 29.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

10 a VL domain comprising the amino acid sequence of SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 30.

15 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24 [or 25](#), an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24 [or 25](#), or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24 [or 25](#); and

a VL domain comprising the amino acid sequence of SEQ ID NO: 26, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 26, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24 [or 25](#), an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24 [or 25](#), or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24 [or 25](#); and

a VL domain comprising the amino acid sequence of SEQ ID NO: 27, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 27, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 27.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24 [or 25](#), an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24 [or 25](#), or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24 [or 25](#); and

a VL domain comprising the amino acid sequence of SEQ ID NO: 28, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 28, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 28.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24 [or 25](#), an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24 [or 25](#), or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24 [or 25](#); and

a VL domain comprising the amino acid sequence of SEQ ID NO: 29, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 29, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 29.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24 [or 25](#), an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24 [or 25](#), or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24 [or 25](#); and

a VL domain comprising the amino acid sequence of SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 30.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 25 [or 23](#), an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ

ID NO: 25 [or 23](#), or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25 [or 23](#); and

5 a VL domain comprising the amino acid sequence of SEQ ID NO: 26, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 26, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

10 a VH domain comprising the amino acid sequence of SEQ ID NO: 25 [or 23](#), an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25 [or 23](#), or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25 [or 23](#); and

15 a VL domain comprising the amino acid sequence of SEQ ID NO: 27, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 27, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 27.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

20 a VH domain comprising the amino acid sequence of SEQ ID NO: 25 [or 23](#), an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25 [or 23](#), or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25 [or 23](#); and

25 a VL domain comprising the amino acid sequence of SEQ ID NO: 28, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 28, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 28.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

30 a VH domain comprising the amino acid sequence of SEQ ID NO: 25 [or 23](#), an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25 [or 23](#), or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25 [or 23](#); and

a VL domain comprising the amino acid sequence of SEQ ID NO: 29, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ

ID NO: 29, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 29.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

5 a VH domain comprising the amino acid sequence of SEQ ID NO: 25 or 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25 or 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25 or 23; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 30, an amino acid
10 sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 30.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule is a full antibody or fragment thereof (*e.g.*, a Fab, F(ab')₂, Fv, or a single
15 chain Fv fragment (scFv)). In embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule is a monoclonal antibody or an antibody with single specificity. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, can also be a humanized, chimeric, camelid, shark, or an *in vitro*-generated antibody molecule. In some embodiments, the anti-TCR β V antibody
20 molecule, *e.g.*, anti-TCR β V12 antibody molecule is a humanized antibody molecule. The heavy and light chains of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule can be full-length (*e.g.*, an antibody can include at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains) or can include an antigen-binding fragment (*e.g.*, a Fab, F(ab')₂, Fv, a single chain Fv fragment, a single domain antibody,
25 a diabody (dAb), a bivalent antibody, or bispecific antibody or fragment thereof, a single domain variant thereof, or a camelid antibody).

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule is in the form of a multispecific molecule, *e.g.*, a bispecific molecule, *e.g.*, as described herein.

30 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule has a heavy chain constant region (Fc) chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE. In some embodiments, the Fc region is chosen from the heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4. In some embodiments, the Fc region is chosen from the heavy chain constant

		YISSGSSTIYYADTLKGRFTISRDNK NSLYLQMNSLRAEDTAVYYCARRGE GAMDYWGQGTTVTVSS
SEQ ID NO: 31	DNA VH	GAGGTGCAGCTGGTTGAATCTGGC GGAGGATTGGTTCAGCCTGGCGGC TCTCTGAGACTGTCTTGTGCCGCTT CTGGCTTCACCTTCTCCAACCTTCGG CATGCACTGGGTCCGACAGGCCCC TGGAAAAGGACTGGAATGGGTGTC CTACATCTCCTCCGGCTCCTCCACC ATCTACTACGCTGACACCCTGAAG GGCAGATTCACCATCTCTCGGGAC AACGCCAAGAAGTCCCTGTACCTG CAGATGAACAGCCTGAGAGCCGA GGACACCGCCGTGTACTACTGTGC TAGAAGAGGCGAGGGCGCCATGG ATTATTGGGGCCAGGGAACACAG TGACCGTGTCTAGC
Antibody B-H.1B HC-2		
SEQ ID NO: 17	HC CDR1 (Combined)	GFTFSNFGMH
SEQ ID NO: 18	HC CDR2 (Combined)	YISSGSSTIYYADTLKG
SEQ ID NO: 19	HC CDR3 (Combined)	RGEGAMDY
SEQ ID NO: 254	VH	EVQLVESGGGLVQPGGSLRLSCAAS GFTFSNFGMHWVRQAPGKGLEWVS YISSGSSTIYYADTLKGRFTISRDNK NTLYLQMNSLRAEDTAVYYCARRG EGAMDYWGQGTTVTVSS
SEQ ID NO: 32	DNA VH	GAGGTGCAGCTGGTTGAATCTGGC GGAGGATTGGTTCAGCCTGGCGGC TCTCTGAGACTGTCTTGTGCCGCTT CTGGCTTCACCTTCTCCAACCTTCGG CATGCACTGGGTCCGACAGGCCCC TGGAAAAGGACTGGAATGGGTGTC CTACATCTCCTCCGGCTCCTCCACC ATCTACTACGCTGACACCCTGAAG GGCAGATTCACCATCAGCCGGGAC AACTCCAAGAACACCCTGTACCTG CAGATGAACTCCCTGAGAGCCGAG GACACCGCCGTGTACTACTGTGCT AGAAGAGGCGAGGGCGCCATGGA TTATTGGGGCCAGGGAACACAGT GACCGTGTCTAGC
Antibody B-H.1C HC-3		
SEQ ID NO: 17	HC CDR1 (Combined)	GFTFSNFGMH
SEQ ID NO: 18	HC CDR2 (Combined)	YISSGSSTIYYADTLKG
SEQ ID NO: 19	HC CDR3 (Combined)	RGEGAMDY
SEQ ID NO: 235	VH	QVQLVESGGGVVQPGSRSLRLSCAAS GFTFSNFGMHWVRQAPGKGLEWVA YISSGSSTIYYADTLKGRFTISRDNK NTLYLQMNSLRAEDTAVYYCARRG EGAMDYWGQGTTVTVSS

		YVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKA LPAPIEKTISKAKGQPREPQVCTLP PSREEMTKNQVSLTSCAVKGFP SDIAVEWESNGQPENNYKTT PPVLDSDGSFFLVSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQK SLSLSPGKGGGSGGGGSGGLND IFEAQKIEWHE
SEQ ID NO: ~~3500~~ 3642	scFv	EVQLVESGGGLVQPGGSLRLSCAAS GFTFSNFGMHWRQAPGKGLEWVS YISSGSSTIYYADTLKGRFTISR DNSKNTLYLQMNSLRAEDTAVY YCARRGEGAMDYWGQGTTVTVS SGGGSGGGSGGGGSDNQLTQSP SFLSASVGDRVTITCRASSSVN IYIYWYQKQPGKAPKLLIYYTS NLAPGVPSRFSGSGSGNEYTLT ISSLQPEDFATYYCQQTSSPFT FGQGTKLEIK
Antibody B-H.2		
SEQ ID NO: 1338	scFv	EVQLVESGGGLVQPGGSLRLSCAAS GFTFSNFGMHWRQAPGKGLEWVS YISSGSSTIYYADTLKGRFTISR DNSKNTLYLQMNSLRAEDTAVY YCARRGEGAMDYWGQGTTVTVS SGGGSGGGSGGGGSDNQLTQSP SSLASVGDRVTITCRASSSVN IYIYWYQKQPGKAPKLLIYYTS NLAPGVPSRFSGSGSGNDYTLT ISSLQPEDFATYYCQQTSSPFT FGQGTKLEIK
Antibody B-H.3		
SEQ ID NO: 1339	scFv	EVQLVESGGGLVQPGGSLRLSCAAS GFTFSNFGMHWRQAPGKGLEWVS YISSGSSTIYYADTLKGRFTISR DNSKNTLYLQMNSLRAEDTAVY YCARRGEGAMDYWGQGTTVTVS SGGGSGGGSGGGGSSNELTQPP SVSVSPGQTARITCRASSSVN IYIYWYQQKSGQAPVLVIYYTS NLAPGIPERFSGSGSGNMYTLT ISGAQVEDEADYYCQQTSSPFT FGTGKVTVL
Antibody B-H.4		
SEQ ID NO: 1340	scFv	QVQLVESGGGVVQPGRSRLSCAAS GFTFSNFGMHWRQAPGKGLEWVA YISSGSSTIYYADTLKGRFTISR DNSKNTLYLQMNSLRAEDTAVY YCARRGEGAMDYWGQGTTVTVS SGGGSGGGSGGGGSDNQLTQSP SFLSASVGDRVTITCRASSSVN IYIYWYQKQPGKAPKLLIYYTS NLAPGVPSRFSGSGSGNEYTLT ISSLQPEDFATYYCQQTSSPFT FGQGTKLEIK

IMMU 222 binds human TCR β V 6-5, TCR β V 6-6, or TCR β V 6-9 (TCR β V13.1 per old nomenclature). REA1062 binds human TCR β V 5-1). JOVI-3 binds human TCR β V 28 (TCR β V3.1 per old nomenclature). IMMU546 binds human TCR β V 2.

MPB2D5 (murine), also referred to here as BJ1188, BJ1190 and REA654; or Antibody G		
Binds to human TCRVβ 20-1		
SEQ ID NO: 1102	HC CDR1 (Kabat)	SAYMH
SEQ ID NO: 1103	HC CDR2 (Kabat)	RIDPATGKTKYAPKFQA
SEQ ID NO: 1104	HC CDR3 (Kabat)	SLNWDYGLDY
SEQ ID NO: 1105	HC CDR1 (Chothia)	GFNIKSA
SEQ ID NO: 1106	HC CDR2 (Chothia)	DPATGK
SEQ ID NO: 1104	HC CDR3 (Chothia)	SLNWDYGLDY
SEQ ID NO: ~~1107~~ 3640	HC CDR1 (Combined)	GFNIKSAYMH
SEQ ID NO: 1103	HC CDR2 (Combined)	RIDPATGKTKYAPKFQA
SEQ ID NO: 1104	HC CDR3 (Combined)	SLNWDYGLDY
SEQ ID NO: 1107	LC CDR1 (Kabat)	RASKSVSILGTHLIH
SEQ ID NO: 1108	LC CDR2 (Kabat)	AASNLES
SEQ ID NO: 1109	LC CDR3 (Kabat)	QQSIEDPWT
SEQ ID NO: 1110	LC CDR1 (Chothia)	SKSVSILGTHL
SEQ ID NO: 1108	LC CDR2 (Chothia)	AASNLES
SEQ ID NO: 1109	LC CDR3 (Chothia)	QQSIEDPWT
SEQ ID NO: 1107	LC CDR1 (Combined)	RASKSVSILGTHLIH
SEQ ID NO: 1108	LC CDR2 (Combined)	AASNLES
SEQ ID NO: 1109	LC CDR3(Combined)	QQSIEDPWT

		FSGSGSETDFTLTISRLEPEDFAVYFCQQSIEDP FGGGTKVEIK
CAS1.1.3 (murine) also referred to herein as BJ1460; or Antibody H Binds to human TCRVβ 27		
SEQ ID NO: 1120	HC CDR1 (Kabat)	DTYMY
SEQ ID NO: 1121	HC CDR2 (Kabat)	RIDPANGNTKYDPKFQD
SEQ ID NO: 1122	HC CDR3 (Kabat)	GSYYYAMDY
SEQ ID NO: 1123	HC CDR1 (Chothia)	GFKTEDT
SEQ ID NO: 1124	HC CDR2 (Chothia)	DPANGN
SEQ ID NO: 1122	HC CDR3 (Chothia)	GSYYYAMDY
SEQ ID NO: 1125	HC CDR1 (Combined)	GFKTEDTYMY
SEQ ID NO: 1121	HC CDR2 (Combined)	RIDPANGNTKYDPKFQD
SEQ ID NO: 1122	HC CDR3(Combined)	GSYYYAMDY
SEQ ID NO: 1126	LC CDR1 (Kabat)	RASESVDSYGNSFMH
SEQ ID NO: 1127	LC CDR2 (Kabat)	RASNLES
SEQ ID NO: 1128	LC CDR3 (Kabat)	QQSNEDPYT
SEQ ID NO: 3641 ~~1129~~	LC CDR1 (Chothia)	SESVDSYGNSF
SEQ ID NO: 1127	LC CDR2 (Chothia)	RASNLES
SEQ ID NO: 1128	LC CDR3 (Chothia)	QQSNEDPYT
SEQ ID NO: 1126	LC CDR1 (Combined)	RASESVDSYGNSFMH
SEQ ID NO: 1127	LC CDR2 (Combined)	RASNLES
SEQ ID NO: 1128	LC CDR3(Combined)	QQSNEDPYT
SEQ ID NO: 1129	VL	DIVLTQSPASLAVSLGQRATISCRASESVDSYGN SFMHWYQQKPGQPPLLIYRASNLESGIPARFS GSGSRTDFTLTINPVEADDVATYYCQQS

	CDR3(Combined)	
SEQ ID NO: 1168	LC CDR1 (Kabat)	SASSSVSYMH
SEQ ID NO: 1169	LC CDR2 (Kabat)	EISKLAS
SEQ ID NO: 1170	LC CDR3 (Kabat)	QQWNYPLLT
SEQ ID NO: ~~1171~~ 1297	LC CDR1 (Chothia)	SSSVSY
SEQ ID NO: 1169	LC CDR2 (Chothia)	EISKLAS
SEQ ID NO: 1170	LC CDR3 (Chothia)	QQWNYPLLT
SEQ ID NO: 1168	LC CDR1 (Combined)	SASSSVSYMH
SEQ ID NO: 1169	LC CDR2 (Combined)	EISKLAS
SEQ ID NO: 1170	LC CDR3(Combined)	QQWNYPLLT
SEQ ID NO: 1171	VL	EIVLTQSPAITAASLGQKVTITCSASSSVSYMH WYQQKSGTSPKPWIYEISKLASGVPARFSGSG SGTSYSLTISSMEAEDAAIYYCQQWNYPLLTF GAGTKLELK
SEQ ID NO: 1172	VH	EVQLQQSGPVLVKPGASVRMSCKASGYTFTD YNIHWVKQSHGRSLEWVGYNPYNGRTGYN QKFKAKATLTVDKSSSTAYMDLRSLSLSEDTA VYYCARWDGSSYFDYWGQGTTTLTVSS
VH for REA1062 (humanized) also referred to as Antibody J-H Binds to human TCRVβ 5-1		
SEQ ID NO: 1173	VH - 1	QVQLVQSGAEVKKPGSSVKVSKASGYTFTD YNIHWVRQAPGQGLEWVGYNPYNGRTGYN QKFKARATLTVDKSTSTAYMELSSLRSEDTA VYYCARWDGSSYFDYWGQGTTTVTVSS
SEQ ID NO: 1174	VH - 2	QVQLVQSGAEVKKPGASVKVSKASGYTFT DYNIHWVRQAPGQGLEWVGYNPYNGRTGY NQKFKARATLTVDKSTSTAYMELRSLRSDDM AVYYCARWDGSSYFDYWGQGTTTVTVSS
SEQ ID NO: 1175	VH - 3	QVQLVQSGAEVKKPGASVKVSKASGYTFT DYNIHWVRQATGQGLEWVGYNPYNGRTGY NQKFKARATLTVNKSISTAYMELSSLRSEDTA

binds to TRVβ 11-2		
SEQ ID NO: 1283	VH-1	QVTLKESGPVLVKPTETLTLTCTVSGFSLTN YGVHWVRQPPGKALEWLGVIWSDGSTDYD TAFISRLTISKDNSKSQVVLMTNMDPVDTA TYYCARRAVVADFDYWGQGTTVTVSS
SEQ ID NO: 1284	VH-2	QVQLQESGPGLVKPSGTLSTCAVSGFSLTN YGVHWVRQPPGKGLEWLGVIWSDGSTDYD TAFISRLTISKDNSKSQVSLKLSSVTAADTAV YYCARRAVVADFDYWGQGTTVTVSS
SEQ ID NO: 1285	VH-3	QVQLQQSGPGLVKPSQTLSTCAVSGFSLTN YGVHWVRQSPSRGLEWLGVIWSDGSTDYDT AFISRLTINKDNSKSQVSLQLNSVTPEDTAVY YCARRAVVADFDYWGQGTTVTVSS
SEQ ID NO: 1286	VH-4	EVQLVESGGGLVQPGPSLRLSCTVSGFSLTN YGVHWVRQAPGKGLEWLGVIWSDGSTDYD TAFISRLTISKDNSKSIVYLQMNSLKTEDTAV YYCARRAVVADFDYWGQGTTVTVSS
SEQ ID NO: 1287	VH-5	EVQLVQSGAEVKKPGESLRISCKVSGFSLTN YGVHWVRQMPGKGLEWLGVIWSDGSTDYD TAFISQLTISKDNSISTVYLQWSSLKASDTAM YYCARRAVVADFDYWGQGTTVTVSS
MR5-2 (murine), Binds to human TCRVβ 13-2		
SEQ ID NO: 1376A	SCFV (VH + VL)	QVQLQQSGTELMKPGASVKISCKASGYTFSN YWIEWIKRPGHGLEWVGEILPGAGPTNYN EKFKGKATFTADSSSNTAYMQLSSLTSEDSA VYYCARTDYDYDWFAYWGQGLTVTSAG GGGSGGGSGGGSGGGGSDIVMSQSPSSL AVSVGEKVTMSCKSSQSLLYSGNQKNYLAW YQQKPGQSPKLLIYWASTRESGVPDRFTGSG SGTDFTLTINSVKAEDLTVYYCQQYYGYPRT FGGGTKVEIK

Anti-TCRVβ antibody effector function and Fc variants

In some embodiments, an anti-TCRVβ antibody disclosed herein comprises an Fc region, e.g., as described herein. In some embodiments, the Fc region is a wildtype Fc region, e.g., a wildtype human Fc region. In some embodiments, the Fc region comprises a variant, e.g., an Fc region comprising an addition, substitution, or deletion of at least one amino acid residue in the Fc region which results in, e.g., reduced or ablated affinity for at least one Fc receptor.

~~What is claimed is:~~

- ~~1. A multispecific molecule (e.g., a bispecific molecule), comprising a first moiety (e.g., a first immune cell engager) comprising an antibody molecule which binds (e.g., specifically binds) to a T-cell receptor beta variable region (TCR β V) (“anti-TCR β V antibody molecule”), wherein binding of the first moiety to the TCR β V region results in a cytokine profile that differs from a cytokine profile of a T-cell engager that binds to a receptor or molecule other than a TCR β V region (“a non-TCR β V binding T cell engager”).~~
- ~~2. The multispecific molecule of claim 1, comprising a second moiety which comprises one or more of: a tumor targeting moiety, a cytokine molecule, a stromal modifying moiety, or an anti-TCR β V antibody molecule other than the first moiety.~~
- ~~3. The multispecific molecule of claim 1 or 2, wherein the first moiety comprising the anti-TCR β V antibody molecule comprises an Fc region comprising a variant, e.g., an Fc variant described in Table 21, e.g., an Asn297Ala (N297A) mutation or a Leu234Ala/Leu235Ala (LALA) mutation.~~
- ~~4. The multispecific molecule of claim 3, wherein the non-TCR β V binding T cell engager comprises an antibody that binds to a CD3 molecule (e.g., CD3 epsilon (CD3 ϵ) molecule); or a TCR alpha (TCR α) molecule.~~
- ~~5. The multispecific molecule of claim 3 or 4, wherein the cytokine profile of the first moiety comprises, one, two, three, four, five, six, seven, or all of the following:
 - ~~(i) increased level, e.g., expression level, and/or activity of IL-2;~~
 - ~~(ii) reduced level, e.g., expression level, and/or activity of IL-1 β ;~~
 - ~~(iii) reduced level, e.g., expression level, and/or activity of IL-6;~~
 - ~~(iv) reduced level, e.g., expression level, and/or activity of TNF α ;~~
 - ~~(v) reduced level, e.g., expression level, and/or activity of IL-10;~~
 - ~~(vi) a delay, e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more hours delay, in increased level, e.g., expression level, and/or activity of IL-2;~~
 - ~~(vii) a delay, e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 hours delay, in increased level, e.g., expression level, and/or activity of IFN γ ; or~~
 - ~~(viii) increased level, e.g., expression level, and/or activity of IL-15;~~~~

e.g., wherein (i)–(viii) are relative to the cytokine profile of the non-TCR β V binding T cell engager.

6. The multispecific molecule of any of the preceding claims, wherein binding of the first moiety to the TCR β V region results in reduced cytokine storm, e.g., reduced cytokine release syndrome (CRS), as measured by an assay of Example 3, e.g., relative to the cytokine storm induced by the non-TCR β V binding T cell engager.

7. The multispecific molecule of any of the preceding claims, wherein binding of the first moiety to the TCR β V region results in one, two, three or all of:

- (ix) reduced T cell proliferation kinetics;
- (x) cell killing, e.g., target cell killing, e.g. cancer cell killing, e.g., as measured by an assay of Example 4;
- (xi) increased Natural Killer (NK) cell proliferation, e.g., expansion; or
- (xii) expansion, e.g., at least about 1.1–10 fold expansion (e.g., at least about 1.1, 1.2, 1.3, 1.4, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold expansion), of a population of T cells having a memory-like phenotype;

e.g., wherein (ix)–(xii) are relative to the non-TCR β V binding T cell engager.

8. The multispecific molecule of claim 7, wherein the population of T cells having a memory-like phenotype comprises CD45RA⁺ CCR7[–] T cells, e.g., CD4⁺ and/or CD8⁺ T cells.

9. The multispecific molecule of any of the preceding claims, wherein the first moiety binds to one or more of a TCR β V subfamily chosen from:

- (i) TCR β V6 subfamily comprising, e.g., one or more of TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01;
- (ii) TCR β V10 subfamily comprising, e.g., one or more of TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01;
- (iii) TCR β V5 subfamily comprising, e.g., one or more of TCR β V5-6*01, TCR β V5-4*01, TCR β V5-1*01 or TCR β V5-8*01;
- (iv) TCR β V12 subfamily comprising, e.g., one or more of TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01;
- (v) TCR β V27 subfamily;

- ~~—— (vi) TCR β V28 subfamily;~~
- ~~—— (vii) TCR β V4 subfamily comprising, e.g., one or more of TCR β V4 1, TCR β V4 2 or TCR β V4 3;~~
- ~~—— (viii) TCR β V19 subfamily;~~
- ~~—— (ix) TCR β V9 subfamily; or~~
- ~~—— (x) TCR β V11 subfamily comprising, e.g., TCR β V11 2.~~

~~10. The multispecific molecule of any of the preceding claims, wherein the anti TCR β V antibody molecule:~~

- ~~—— (i) binds specifically to an epitope on TCR β V, e.g., the same or similar epitope as the epitope recognized by an anti TCR β V antibody molecule as described herein, e.g., a second anti TCR β V antibody molecule;~~
- ~~—— (ii) shows the same or similar binding affinity or specificity, or both, as an anti TCR β V antibody molecule as described herein, e.g., a second anti TCR β V antibody molecule;~~
- ~~—— (iii) inhibits, e.g., competitively inhibits, the binding of an anti TCR β V antibody molecule as described herein, e.g., a second anti TCR β V antibody molecule;~~
- ~~—— (iv) binds the same or an overlapping epitope with an anti TCR β V antibody molecule as described herein, e.g., a second anti TCR β V antibody molecule; or~~
- ~~—— (v) competes for binding, and/or binds the same epitope, with an anti TCR β V antibody molecule as described herein, e.g., a second anti TCR β V antibody molecule;~~
- ~~—— wherein the second anti TCR β V antibody molecule comprises an antigen binding domain comprising a heavy chain complementarity determining region 1 (HC CDR1), a heavy chain complementarity determining region 2 (HC CDR2) and/or a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 1 or SEQ ID NO: 9; and/or a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and/or a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 2, SEQ ID NO: 10 or SEQ ID NO: 11.~~

~~11. The multispecific molecule of any of the preceding claims, wherein the anti TCR β V antibody molecule comprises an antigen binding domain comprising:~~

- ~~—— (i) (a) a HC CDR1, a HC CDR2 and/or a HC CDR3 of SEQ ID NO: 15, SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25; and/or (b) a LC CDR1, a LC CDR2, and/or a LC CDR3 of SEQ ID NO: 16, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29 or SEQ ID NO: 30; or~~

~~—— (ii) (a) a LC CDR1, a LC CDR2 and/or a LC CDR3 of SEQ ID NO: 2, SEQ ID NO: 10 or SEQ ID NO: 11; and/or (b) a HC CDR1, a HC CDR2 and/or a HC CDR2 of SEQ ID NO: 1 or SEQ ID NO: 9.~~

~~12. The multispecific molecule of any of the preceding claims, wherein the anti-TCR β V antibody molecule binds the same or different TCR β V subfamily members.~~

~~13. The multispecific molecule of any of the preceding claims, which comprises an antibody molecule chosen from a bispecific antibody molecule, a bivalent antibody molecule, or a biparatopic antibody molecule.~~

~~14. The multispecific molecule of any of the preceding claims, which comprises a bispecific antibody molecule that binds to two different TCR β V subfamily members.~~

~~15. The multispecific molecule of any of the preceding claims, wherein the anti-TCR β V antibody molecule binds:~~

~~—— (i) one or more of a TCR β V6 subfamily member and one or more of a TCR β V10 subfamily member;~~

~~—— (ii) one or more of a TCR β V6 subfamily member and one or more of a TCR β V5 subfamily member;~~

~~—— (iii) one or more of a TCR β V6 subfamily member and one or more of a TCR β V12 subfamily member;~~

~~—— (iv) one or more of a TCR β V10 subfamily member and one or more of a TCR β V5 subfamily member;~~

~~—— (v) one or more of a TCR β V10 subfamily member and one or more of a TCR β V12 subfamily member; or~~

~~—— (vi) one or more of a TCR β V5 subfamily member and one or more of a TCR β V12 subfamily member.~~

~~16. A multispecific molecule, e.g., a bispecific molecule, comprising the anti-TCR β V antibody molecule of any of claims 1 to 15.~~

17. An antibody molecule which binds, *e.g.*, specifically binds, to a T cell receptor beta variable chain (TCR β V) region, wherein the anti TCR β V antibody molecule comprises an antigen binding domain comprising:

(a) a light chain variable region (VL) comprising:

(i) one, two or all of (*e.g.*, three) a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 10 or SEQ ID NO: 11; and

(ii) a framework region (FR) having at least 95% identity with one, two, three, or all of (*e.g.*, four) a non murine germline framework 1 (FR1), a non murine germline framework region 2 (FR2), a non murine germline framework region 3 (FR3), and a non murine germline framework region 4 (FR4); and/or

(b) a heavy chain variable region (VH) comprising:

(i) one, two or all of (*e.g.*, three) a heavy chain complementarity determining region 1 (HC CDR1), a heavy chain complementarity determining region 2 (HC CDR2) and a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 9; and

(ii) a framework region (FR) having at least 95% identity with one, two, three, or all of (*e.g.*, four) a non murine germline framework 1 (FR1), a non murine germline framework region 2 (FR2), a non murine germline framework region 3 (FR3), and a non murine germline framework region 4 (FR4).

18. The anti TCR β V antibody molecule of claim 17, wherein the VL comprises an amino acid sequence having a consensus sequence of SEQ ID NO: 230.

19. The anti TCR β V antibody molecule of claim 17 or 18, wherein the VH comprises an amino acid sequence having a consensus sequence of SEQ ID NO: 231.

20. The anti TCR β V antibody molecule of any of claims 17-19, which binds to TCR β V6, *e.g.*, one or more of TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01, or a variant thereof.

21. The anti TCR β V antibody molecule of any of claims 17-20, wherein the anti TCR β V antibody molecule comprises an antigen binding domain comprising:

- (i) a HC CDR1, a HC CDR2 and a HC CDR3 of SEQ ID NO: 1 or SEQ ID NO: 9, or an amino acid sequence listed in Table 1; or
- (ii) a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 2, SEQ ID NO: 10 or SEQ ID NO: 11, or an amino acid sequence listed in Table 1.

22. The anti-TCR β V antibody molecule of any of claims 17-21, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a light chain variable region (VL) comprising one, two or all (e.g., three) of a LC CDR1, a LC CDR2 and a LC CDR3 of SEQ ID NO: 2, SEQ ID NO: 10 or SEQ ID NO: 11, or an amino acid sequence listed in Table 1.

23. The anti-TCR β V antibody molecule of any of claims 17-22, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a heavy chain variable region (VH) comprising one, two or all (e.g., three) of a HC CDR1, a HC CDR2 and a HC CDR3 of SEQ ID NO:1 or SEQ ID NO: 9, or an amino acid sequence listed in Table 1.

24. The anti-TCR β V antibody molecule of any of claims 17-23, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

- (i) a VL comprising: a LC CDR1 amino acid sequence of SEQ ID NO: 6 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof), a LC CDR2 amino acid sequence of SEQ ID NO:7 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof), and/or a LC CDR3 amino acid sequence of SEQ ID NO:8 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof); and/or
- (ii) a VH comprising: a HC CDR1 amino acid sequence of SEQ ID NO: 3 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof), a HC CDR2 amino acid sequence of SEQ ID NO:4 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof), and/or a HC CDR3 amino acid sequence of SEQ ID NO:5 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof).

25. The anti-TCR β V antibody molecule of any of claims 17-24, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

- a variable heavy chain (VH) of an amino acid sequence listed in Table 1, e.g., SEQ ID NO: 9 or SEQ ID NO: 1312, or a sequence having at least about 85%, 90%, 95%, or 99%

sequence identity to an amino acid sequence listed in Table 1, e.g., SEQ ID NO: 9 or SEQ ID NO: 1312; and/or

—— a variable light chain (VL) of an amino acid sequence listed in Table 1, e.g., SEQ ID NO: 10 or SEQ ID NO: 11 or SEQ ID NO: 1314, or a sequence having at least about 85%, 90%, 95%, or 99% sequence identity to an amino acid sequence listed in Table 1, e.g., SEQ ID NO: 10 or SEQ ID NO: 11 or SEQ ID NO: 1314.

~~26. The anti-TCR β V antibody molecule of any of claims 17-25, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:~~

- ~~—— (i) the VH amino acid sequence of SEQ ID NO: 9 or SEQ ID NO: 1312;~~
- ~~—— (ii) an amino acid sequence having at least about 85%, 90%, 95%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 9 or SEQ ID NO: 1312;~~
- ~~—— (iii) the VL amino acid sequence of SEQ ID NO: 10 or SEQ ID NO: 1314; and/or~~
- ~~—— (iv) an amino acid sequence having at least about 85%, 90%, 95%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 10 or SEQ ID NO: 1314.~~

~~27. The anti-TCR β V antibody molecule of any of claims 17-26, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:~~

- ~~—— (i) the VH amino acid sequence of SEQ ID NO: 9 or SEQ ID NO: 1312;~~
- ~~—— (ii) an amino acid sequence having at least about 85%, 90%, 95%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 9 or SEQ ID NO: 1312;~~
- ~~—— (iii) the VL amino acid sequence of SEQ ID NO: 11 or SEQ ID NO: 1314; and/or~~
- ~~—— (iv) an amino acid sequence having at least about 85%, 90%, 95%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 11 or SEQ ID NO: 1314.~~

~~28. The anti-TCR β V antibody molecule of any of claims 17-27, wherein the anti-TCR β V antibody molecule comprises a heavy chain comprising a framework region, e.g., framework region 3 (FR3), comprising one or both of:~~

- ~~—— (i) a Threonine at position 73, e.g., a substitution at position 73 according to Kabat numbering, e.g., a Glutamic Acid to Threonine substitution; or~~
- ~~—— (ii) a Glycine at position 94, e.g., a substitution at position 94 according to Kabat numbering, e.g., a Arginine to Glycine substitution;~~

~~wherein the substitution is relative to a human germline heavy chain framework region sequence.~~

~~29. The anti-TCR β V antibody molecule of any of claims 17-28, wherein the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, e.g., framework region 1 (FR1), comprising a Phenylalanine at position 10, e.g., a substitution at position 10 according to Kabat numbering, e.g., a Serine to Phenylalanine substitution, wherein the substitution is relative to a human germline light chain framework region sequence.~~

~~30. The anti-TCR β V antibody molecule of any of claims 17-29, wherein the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, e.g., framework region 2 (FR2), comprising one or both of:~~
~~—— (i) a Histidine at position 36, e.g., a substitution at position 36 according to Kabat numbering, e.g., a Tyrosine to Histidine substitution; or~~
~~—— (ii) an Alanine at position 46, e.g., a substitution at position 46 according to Kabat numbering, e.g., a Arginine to Alanine substitution;~~
~~—— wherein the substitution is relative to a human germline light chain framework region sequence.~~

~~31. The anti-TCR β V antibody molecule of any of claims 17-30, wherein the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, e.g., framework region 3 (FR3), comprising a Phenylalanine at position 87, e.g., a substitution at position 87 according to Kabat numbering, e.g., a Tyrosine to Phenylalanine substitution, wherein the substitution is relative to a human germline light chain framework region sequence.~~

~~32. An antibody molecule which binds, e.g., specifically binds, to a T-cell receptor beta variable chain (TCR β V) region, wherein the anti-TCR β V antibody molecule comprises an antigen-binding domain comprising:~~

~~(a) a light chain variable region (VL) comprising:~~

~~(i) one, two or all of (e.g., three) a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and a light chain complementarity determining region 3 (LC CDR3) of a humanized B-H light chain (LC) of Table 2; and~~

~~(ii) a framework region (FR) having at least 95% identity with one, two, three or all (e.g., four) of a framework region 1 (FR1), a framework region 2 (FR2), a framework region 3 (FR3), and a framework region 4 (FR4) of a humanized B-H LC of Table 2; and/or~~

~~(b) a heavy chain variable region (VH) comprising:~~

- (i) one, two or all of (e.g., three) a heavy chain complementarity determining region 1 (HC CDR1), a heavy chain complementarity determining region 2 (HC CDR2) and a heavy chain complementarity determining region 3 (HC CDR3) of a humanized B-H heavy chain (HC) of Table 2; and
- (ii) a framework region (FR) having at least 95% identity with one, two, three or all (e.g., four) of a framework region 1 (FR1), a framework region 2 (FR2), a framework region 3 (FR3), and a framework region 4 (FR4) of a humanized B-H HC of Table 2.

33. The anti-TCR β V antibody molecule of claim 32, which binds to TCR β V12, e.g., TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01, or a variant thereof.

34. The anti-TCR β V antibody molecule of claim 32 or 33, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

- (i) a HC CDR1, a HC CDR2 and a HC CDR3 of Antibody B-H listed in Table 2; or
- (ii) a LC CDR1, a LC CDR2, and a LC CDR3 of Antibody B-H listed in Table 2.

35. The anti-TCR β V antibody molecule of any of claims 32-34, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a light chain variable region (VL) comprising one, two or all (e.g., three) of a LC CDR1, a LC CDR2 and a LC CDR3 of SEQ ID NO: 2, SEQ ID NO: 10 or SEQ ID NO: 11, or an amino acid sequence listed in Table 1.

36. The anti-TCR β V antibody molecule of any of claims 32-35, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a heavy chain variable region (VH) comprising one, two or all (e.g., three) of a HC CDR1, a HC CDR2 and a HC CDR3 of a humanized Antibody B-H listed in Table 2.

37. The anti-TCR β V antibody molecule of any of claims 32-36, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a light chain variable region (VL) comprising one, two or all (e.g., three) of a LC CDR1, a LC CDR2 and a LC CDR3 of a humanized Antibody B-H listed in Table 2.

38. The anti-TCR β V antibody molecule of any of claims 32-37, wherein the anti-TCR β V antibody molecule comprises:

~~—— a VH sequence of a humanized Antibody B-H listed in Table 2, or a sequence having at least about 85%, 90%, 95%, or 99% sequence identity to a VH of a humanized Antibody B-H listed in Table 2; and/or~~

~~—— a VL sequence of a humanized Antibody B-H listed in Table 2, or a sequence having at least about 85%, 90%, 95%, or 99% sequence identity to a VL of a humanized Antibody B-H listed in Table 2.~~

~~39. The anti-TCR β V antibody molecule of any of claims 32-38, wherein the anti-TCR β V antibody molecule comprises a framework region (FR) having at least 95% identity with one of: a FR1, a FR2, a FR3, and a FR4 of a humanized B-H LC of Table 2.~~

~~40. The anti-TCR β V antibody molecule of any of claims 32-39, wherein the anti-TCR β V antibody molecule comprises a framework region (FR) having at least 95% identity with any two of: a FR1, a FR2, a FR3, and a FR4 of a humanized B-H LC of Table 2.~~

~~41. The anti-TCR β V antibody molecule of any of claims 32-40, wherein the anti-TCR β V antibody molecule comprises a framework region (FR) having at least 95% identity with any three of: a FR1, a FR2, a FR3, and a FR4 of a humanized B-H LC of Table 2.~~

~~42. The anti-TCR β V antibody molecule of any of claims 32-41, wherein the anti-TCR β V antibody molecule comprises a framework region (FR) having at least 95% identity with all of: a FR1, a FR2, a FR3, and a FR4 of a humanized B-H LC of Table 2.~~

~~43. The anti-TCR β V antibody molecule of any of claims 32-42, wherein the anti-TCR β V antibody molecule comprises a framework region (FR) having at least 95% identity with one of: a FR1, a FR2, a FR3, and a FR4 of a humanized B-H HC of Table 2.~~

~~44. The anti-TCR β V antibody molecule of any of claims 32-42, wherein the anti-TCR β V antibody molecule comprises a framework region (FR) having at least 95% identity with any two of: a FR1, a FR2, a FR3, and a FR4 of a humanized B-H HC of Table 2.~~

~~45. The anti-TCR β V antibody molecule of any of claims 32-42, wherein the anti-TCR β V antibody molecule comprises a framework region (FR) having at least 95% identity with any three of: a FR1, a FR2, a FR3, and a FR4 of a humanized B-H HC of Table 2.~~

46. The anti-TCR β V antibody molecule of any of claims 32-42, wherein the anti-TCR β V antibody molecule comprises a framework region (FR) having at least 95% identity with all of: a FR1, a FR2, a FR3, and a FR4 of a humanized B-H HC of Table 2.

47. The anti-TCR β V antibody molecule of any of claims 17 to 46, wherein binding of the anti-TCR β V antibody molecule to the TCR β V region results in a cytokine profile that differs from a cytokine profile of a T cell engager that binds to a receptor or molecule other than a TCR β V region (“a non-TCR β V binding T cell engager”).

48. The anti-TCR β V antibody molecule of claim 47, wherein the non-TCR β V binding T cell engager comprises an antibody that binds to a CD3 molecule (*e.g.*, CD3 epsilon (CD3e) molecule); or a TCR alpha (TCR α) molecule.

49. The anti-TCR β V antibody molecule of claim 47 or 48, wherein the cytokine profile of the first moiety comprises, one, two, three, four, five, six, seven, or all of the following:

- (i) increased level, *e.g.*, expression level, and/or activity of IL-2;
- (ii) reduced level, *e.g.*, expression level, and/or activity of IL-1 β ;
- (iii) reduced level, *e.g.*, expression level, and/or activity of IL-6;
- (iv) reduced level, *e.g.*, expression level, and/or activity of TNF α ;
- (v) reduced level, *e.g.*, expression level, and/or activity of IL-10;
- (vi) a delay, *e.g.*, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more hours delay, in increased level, *e.g.*, expression level, and/or activity of IL-2;
- (vii) a delay, *e.g.*, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 hours delay, in increased level, *e.g.*, expression level, and/or activity of IFN γ ; or
- (viii) increased level, *e.g.*, expression level, and/or activity of IL-15,

e.g., wherein (i)-(vii) are relative to the cytokine profile of the non-TCR β V binding T cell engager.

50. The anti-TCR β V antibody molecule of any of claims 17 to 49, wherein binding of the anti-TCR β V antibody molecule to the TCR β V region results in reduced cytokine storm, *e.g.*, reduced cytokine release syndrome (CRS), as measured by an assay of Example 3, *e.g.*, relative to the cytokine storm induced by the non-TCR β V binding T cell engager.

~~51. The anti-TCR β V antibody molecule of any of claims 17 to 50, wherein binding of the anti-TCR β V antibody molecule to the TCR β V region results in one, two, three or all of:~~

- ~~(ix) reduced T cell proliferation kinetics;~~
- ~~(x) cell killing, e.g., target cell killing, e.g. cancer cell killing, e.g., as measured by an assay of Example 4;~~
- ~~(xi) increased Natural Killer (NK) cell proliferation, e.g., expansion; or~~
- ~~(xii) expansion, e.g., at least about 1.1-10 fold expansion (e.g., at least about 1.1, 1.2, 1.3, 1.4, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold expansion), of a population of T cells having a memory-like phenotype,~~

~~e.g., relative to the non-TCR β V binding T cell engager.~~

~~52. The anti-TCR β V antibody molecule of claim 51, wherein the population of T cells having a memory-like phenotype comprises CD45RA⁺ CCR7⁻ T cells, e.g., CD4⁺ and/or CD8⁺ T cells.~~

~~53. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein binding of the anti-TCR β V antibody molecule to a TCR β V region results in a reduction of at least 2, 5, 10, 20, 50, 100, or 200 fold, or at least 2-200 fold (e.g., 5-150, 10-100, 20-50 fold) in the expression level and or activity of IL-1 β as measured by an assay of Example 3.~~

~~54. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein binding of the anti-TCR β V antibody molecule to a TCR β V region results in a reduction of at least 2, 5, 10, 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, or 1000 fold, or at least 2-1000 fold (e.g., 5-900, 10-800, 20-700, 50-600, 100-500, or 200-400 fold) in the expression level and or activity of IL-6 as measured by an assay of Example 3.~~

~~55. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, binding of the anti-TCR β V antibody molecule to a TCR β V region results in a reduction of at least 2, 5, 10, 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, or 2000 fold, or at least 2-2000 fold (e.g., 5-1000, 10-900, 20-800, 50-700, 100-600, 200-500, or 300-400 fold) in the expression level and or activity of TNF α as measured by an assay of Example 3.~~

~~56. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein binding of the anti-TCR β V antibody molecule to a TCR β V region results in an~~

increase of at least 2, 5, 10, 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, or 2000 fold, or at least 2-2000 fold (e.g., 5-1000, 10-900, 20-800, 50-700, 100-600, 200-500, or 300-400 fold) in the expression level and/or activity of IL-2 as measured by an assay of Example 3.

57. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a single chain Fv (scFv) or a Fab.

58. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein the anti-TCR β V antibody molecule binds to a conformational or a linear epitope on the T cell.

59. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein the anti-TCR β V antibody 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 fragment, a single domain antibody, a diabody (dAb), a bivalent antibody, or bispecific antibody or fragment thereof, a single domain variant thereof, or a camelid antibody).

60. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein the anti-TCR β V antibody molecule comprises one or more heavy chain constant regions chosen from IgG1, IgG2, IgG3, IgGA1, IgGA2, IgG4, IgJ, IgM, IgD, or IgE, or a fragment thereof, e.g., as described in Table 3.

61. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein the anti-TCR β V antibody molecule comprises a heavy chain constant region of an IgM or a fragment thereof, optionally wherein the IgM heavy chain constant region comprises the sequence of SEQ ID NO: 73, or a sequence with at least 85%, 90%, 95%, or 99% sequence identity thereto.

62. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein the anti-TCR β V antibody molecule comprises a heavy chain constant region of an IgJ or a fragment thereof, optionally wherein the IgJ heavy chain constant region comprises

the sequence of SEQ ID NO: 76 or a sequence with at least 85%, 90%, 95%, or 99% sequence identity thereto.

63. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein the anti-TCR β V antibody molecule comprises a heavy chain constant region of an IgGA1, or a fragment thereof, optionally wherein the IgGA1 heavy chain constant region comprises the sequence of SEQ ID NO: 74, or a sequence with at least 85%, 90%, 95%, or 99% sequence identity thereto.

64. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein the anti-TCR β V antibody molecule comprises a heavy chain constant region of an IgGA2, or a fragment thereof, optionally wherein the IgGA2 heavy chain constant region comprises a sequence listed in Table 3, e.g., SEQ ID NO: 75, or a sequence with at least 85%, 90%, 95%, or 99% sequence identity thereto.

65. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein the anti-TCR β V antibody molecule comprises a light chain constant region chosen from the light chain constant regions of kappa or lambda, or a fragment thereof, e.g., as described in Table 3.

66. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein the anti-TCR β V antibody molecule comprises a light chain constant region of a kappa chain, or a fragment thereof, optionally wherein the kappa chain constant region comprises the sequence of SEQ ID NO: 39, or a sequence with at least 85%, 90%, 95%, or 99% sequence identity thereto.

67. The multispecific molecule or the anti-TCR β V antibody molecule of any of the preceding claims, wherein the anti-TCR β V antibody molecule comprises:

—— (i) one or more heavy chain constant regions comprising a heavy chain constant region chosen from IgG1, IgG2, IgG3, IgGA1, IgGA2, IgG4, IgJ, IgM, IgD, or IgE, or a fragment thereof, e.g., as described in Table 3; and

—— (ii) a light chain constant region comprising a light chain constant region chosen from the light chain constant regions of kappa or lambda, or a fragment thereof, e.g., as described in Table 3.

~~68. The multispecific molecule or the anti TCR β V antibody molecule of any of the preceding claims, wherein the anti TCR β V antibody molecule comprises:~~

~~—— (i) a heavy chain constant region comprising:~~

~~—— (a) an IgM heavy chain constant region or a fragment thereof, comprising the sequence of SEQ ID NO: 73, or a sequence with at least 85%, 90%, 95%, or 99% sequence identity thereto;~~

~~—— (b) an IgGA1 heavy chain constant region or a fragment thereof, comprising the sequence of SEQ ID NO: 74, or a sequence with at least 85%, 90%, 95%, or 99% sequence identity thereto; or~~

~~—— (c) an IgGA2 heavy chain constant region or a fragment thereof, comprising the sequence of SEQ ID NO: 75, or a sequence with at least 85%, 90%, 95%, or 99% sequence identity thereto; and~~

~~—— (ii) a light chain constant region comprising a kappa chain constant region comprising the sequence of SEQ ID NO: 39, or a sequence with at least 85%, 90%, 95%, or 99% sequence identity thereto,~~

~~—— optionally wherein, the anti TCR β V antibody molecule further comprises an IgJ heavy chain constant region or a fragment thereof, wherein the IgJ heavy chain constant region comprises the sequence of SEQ ID NO: 76 or a sequence with at least 85%, 90%, 95%, or 99% sequence identity thereto.~~

~~69. The multispecific molecule of any one of claims 1-16 or 53-68, wherein the second moiety is a tumor-targeting moiety.~~

~~70. The multispecific molecule of any one of claims 1-16 or 53-68, wherein the second moiety is a cytokine molecule.~~

~~71. The multispecific molecule of any one of claims 1-16 or 53-68, wherein the second moiety is a stromal-modifying moiety.~~

~~72. The multispecific molecule of any one of claims 1-16 or 53-68, wherein the second moiety is an anti TCR β V antibody molecule other than the first moiety.~~

73. The multispecific molecule of any one of claims 1-16 or 53-72, wherein the first and/or second moiety binds to and activates an immune cell, e.g., an effector cell.
74. The multispecific molecule of any one of claims 1-16 or 53-72, wherein the first and/or second moiety binds to, but does not activate an immune cell, e.g., an effector cell.
75. The multispecific molecule of any one of claims 1-16 or 53-74, wherein the second moiety is chosen from an NK cell engager, a T cell engager other than an anti-TCR β V antibody molecule, a B cell engager, a dendritic cell engager, or a macrophage cell engager, or a combination thereof.
76. The multispecific molecule of any one of claims 1-16 or 53-69, wherein the tumor-targeting moiety comprises an antibody molecule (e.g., Fab or scFv), a receptor molecule (e.g., a receptor, a receptor fragment or functional variant thereof), or a ligand molecule (e.g., a ligand, a ligand fragment or functional variant thereof), or a combination thereof, that binds to a cancer antigen.
77. The multispecific molecule of any one of claims 1-16, 53-69 or 76, wherein the tumor-targeting moiety binds to a cancer antigen present on a cancer, e.g., a hematological cancer, a solid tumor, a metastatic cancer, soft tissue tumor, metastatic lesion, or a combination thereof.
78. The multispecific molecule of claim 77, wherein the cancer antigen is a tumor antigen or stromal antigen, or a hematological antigen.
79. The multispecific molecule of claim 77 or 78, wherein the cancer antigen is chosen from: BCMA, CD19, CD20, CD22, FcRH5, PDL1, CD47, ganglioside 2 (GD2), prostate stem cell antigen (PSCA), prostate specific membrane antigen (PMSA), prostate specific antigen (PSA), carcinoembryonic antigen (CEA), Ron Kinase, c-Met, Immature laminin receptor, TAG-72, BING-4, Calcium-activated chloride channel 2, Cyclin-B1, 9D7, Ep-CAM, EphA3, Her2/neu, Telomerase, SAP-1, Survivin, NY-ESO-1/LAGE-1, PRAME, SSX-2, Melan-A/MART-1, Gp100/pmel17, Tyrosinase, TRP-1/2, MC1R, β -catenin, BRCA1/2, CDK4, CML66, Fibronectin, p53, Ras, TGF- β receptor, AFP, ETA, MAGE, MUC-1, CA-125, BAGE, GAGE, NY-ESO-1, β -catenin, CDK4, CDC27, α -actinin-4, TRP1/gp75, TRP2, gp100, Melan-A/MART1, gangliosides, WT1, EphA3, Epidermal growth factor receptor (EGFR), MART-2, MART-1, MUC1, MUC2, MUM1, MUM2, MUM3, NA88-1, NPM, OA1, OGT, RCC, RUI1, RUI2, SAGE, TRG, TRP1, TSTA, Folate receptor alpha, L1-CAM, CAIX, gpA33, GD3, GM2,

VEGFR, Integrins (Integrin alphaVbeta3, Integrin alpha5Beta1), Carbohydrates (Le), IGF1R, EPHA3, TRAILR1, TRAILR2, RANKL, (FAP), TGF-beta, hyaluronic acid, collagen, e.g., collagen IV, tenascin C, or tenascin W.

80. The multispecific molecule of any one of claims 1-16, 53-69 or 76-79, wherein the tumor-targeting moiety is a BCMA targeting moiety or a FcRH5 targeting moiety.

81. The multispecific molecule of any one of claims 77-80, wherein the cancer is a solid tumor including but not limited to: pancreatic (e.g., pancreatic adenocarcinoma) cancer, breast cancer, colorectal cancer, lung cancer (e.g., small or non-small cell lung cancer), skin cancer, ovarian cancer, or liver cancer.

82. The multispecific molecule of any one of claims 77-80, wherein the cancer is a hematological cancer including, but not limited to: a B-cell or T-cell malignancy, e.g., Hodgkin's lymphoma, Non-Hodgkin's lymphoma (e.g., B-cell lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, chronic lymphocytic leukemia, mantle cell lymphoma, marginal zone B-cell lymphoma, Burkitt lymphoma, lymphoplasmacytic lymphoma, hairy cell leukemia), acute myeloid leukemia (AML), chronic myeloid leukemia, myelodysplastic syndrome, multiple myeloma, and acute lymphocytic leukemia.

83. The multispecific molecule of any one of claims 1-16, 53-68 or 70, wherein the cytokine molecule is chosen from interleukin 2 (IL-2), interleukin 7 (IL-7), interleukin 12 (IL-12), interleukin 15 (IL-15), interleukin 18 (IL-18), interleukin 21 (IL-21), or interferon gamma, or a fragment, variant or combination thereof.

84. The multispecific molecule of any one of claims 1-16, 53-68, 70 or 83, wherein the cytokine molecule is a monomer or a dimer.

85. The multispecific molecule of any one of claims 1-16, 53-68, 70 or 83-84 wherein the cytokine molecule further comprises a receptor dimerizing domain, e.g., an IL15Ralpha dimerizing domain.

86. The multispecific molecule of any one of claims 1-16, 53-68, 70 or 83-85, wherein the cytokine molecule (e.g., IL-15) and the receptor dimerizing domain (e.g., an IL15Ralpha dimerizing domain) are not covalently linked, e.g., are non-covalently associated.

87. The multispecific molecule of any one of claims 1-16, or 53-86, further comprising an immunoglobulin constant region (e.g., Fc region) chosen from the heavy chain constant regions of IgG1, IgG2, IgG3, IgGA1, IgGA2, IgG4, IgJ, IgM, IgD, or IgE, or a fragment thereof, optionally wherein, the heavy chain constant region comprises the heavy chain constant region of human IgG1, IgG2 or IgG4.

88. The multispecific molecule of claim 87, wherein the immunoglobulin constant region (e.g., an Fc region) is linked, e.g., covalently linked to, one or more of tumor-targeting moiety, the cytokine molecule, or the stromal modifying moiety.

89. The multispecific molecule of claim 87 or 88, wherein an interface of a first and second immunoglobulin chain constant regions (e.g., Fc region) is altered, e.g., mutated, to increase or decrease dimerization, e.g., relative to a non-engineered interface.

90. The multispecific molecule of claim 89, wherein the dimerization of the immunoglobulin chain constant region (e.g., Fc region) is enhanced by providing an Fc interface of a first and a second Fc region 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, e.g., relative to a non-engineered interface.

91. The multispecific molecule of any one of claims 1-16, or 53-90, further comprising a linker, e.g., a linker described herein, optionally 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.

92. An isolated nucleic acid molecule comprising a nucleotide sequence encoding the anti-TCRβV antibody molecule of any of claims 17-53, or a nucleotide sequence having at least 75%, 80%, 85%, 90%, 95%, or 99% identity thereto.

- ~~93. An isolated nucleic acid molecule comprising a nucleotide sequence encoding the multispecific molecule of any of claims 1-16, or 53-91, or a nucleotide sequence having at least 75%, 80%, 85%, 90%, 95%, or 99% identity thereto.~~
- ~~94. A vector, e.g., an expression vector, comprising one or more of the nucleic acid molecules of any one of claims 92 or 93.~~
- ~~95. A cell, e.g., host cell, comprising the nucleic acid molecule of any of claims 92 or 93, or the vector of claim 94.~~
- ~~96. A method of making, e.g., producing or manufacturing, the anti-TCR β V antibody molecule of any of claims 17-53, or the multispecific molecule of any of claims 1-16, or 53-91, comprising culturing the host cell of claim 95, under suitable conditions, e.g., conditions suitable expression of the anti-TCR β V antibody molecule or the multispecific molecule.~~
- ~~97. A pharmaceutical composition comprising the anti-TCR β V antibody molecule of any of claims 17-53, or the multispecific molecule of any of claims 1-16, or 53-91, and a pharmaceutically acceptable carrier, excipient, or stabilizer.~~
- ~~98. A method of modulating, e.g., enhancing, an immune response in a subject comprising administering to the subject an effective amount of an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) (“anti-TCR β V antibody molecule”).~~
- ~~99. A method of modulating, e.g., enhancing, an immune response in a subject comprising administering to the subject an effective amount of the multispecific molecule of any of claims 1-16, or 53-91.~~
- ~~100. The method of claim 98 or 99, wherein the method comprises expanding, e.g., increasing the number of, an immune cell population in the subject.~~
- ~~101. A method of expanding, e.g., increasing the number of, an immune cell population comprising, contacting the immune cell population with an effective amount of an antibody~~

molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) (“anti TCR β V antibody molecule”).

~~102. A method of expanding, e.g., increasing the number of, an immune cell population comprising, contacting the immune cell population with an effective amount of the multispecific molecule of any of claims 1-16, or 53-91.~~

~~103. The method of any of claims 100 to 102, wherein the expansion occurs in vivo or ex vivo (e.g., in vitro).~~

~~104. The method of any of claims 100 to 103, wherein the immune cell population comprises a TCR β V expressing cell, e.g., a TCR β V⁺ cell.~~

~~105. The method of claim 104, wherein the TCR β V expressing cell is a T cell, e.g., a CD8⁺ T cell, a CD3⁺ T cell or a CD4⁺ T cell.~~

~~106. The method of any of claims 100 to 105, wherein the immune cell population comprises a T cell (e.g., a CD4 T cell, a CD8 T cell (e.g., an effector T cell, a T cell having a memory-like phenotype or a memory T cell (e.g., a memory effector T cell (e.g., TEM cell, e.g., TEMRA cell), or a tumor infiltrating lymphocyte (TIL).~~

~~107. The method of any of claims 100-106, wherein the immune cell population comprises a T cell, a Natural Killer cell, a B cell, or a myeloid cell.~~

~~108. The method of any of claims 100-107, wherein the immune cell population is obtained from a healthy subject.~~

~~109. The method of any of claims 100-108, wherein the immune cell population is obtained from a subject (e.g., from an apheresis sample from the subject) having a disease, e.g., a cancer, e.g., as described herein, optionally wherein the immune cell population comprises a tumor infiltrating lymphocyte (TIL).~~

~~110. The method of any of claims 100-109, wherein the method results in an expansion of at least 1.1-10 fold (e.g., at least 1.1, 1.2, 1.3, 1.4, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold expansion).~~

~~111. The method of any of claims 100-110, further comprising contacting the population of cells with an agent that promotes, e.g., increases, immune cell expansion.~~

~~112. The method of any of claims 100-111, further comprising contacting the population of cells with an immune checkpoint inhibitor, e.g., a PD-1 inhibitor.~~

~~113. The method of any of claims 100-112, further comprising contacting the population of cells with a 4-1BB (CD127) agonist, e.g., an anti-4-1BB antibody.~~

~~114. The method of any of claims 100-113, further comprising contacting the population of cells with a non-dividing population of cells, e.g., feeder cells, e.g., irradiated allogenic human PBMCs.~~

~~115. The method of any of claims 100-114, wherein the population of cells is expanded in an appropriate media (e.g., media described herein) that includes one or more cytokines, e.g., IL-2, IL-7, IL-15, or a combination thereof.~~

~~116. The method of any of claims 100-115, wherein the population of cells is expanded for a period of at least about 4 hours, 6 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 22 hours, or for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21 days, or for at least about 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks or 8 weeks.~~

~~117. The method of method of any of claims 100-116, wherein expansion of the population of immune cells, is compared to expansion of a similar population of cells with an antibody that binds to: a CD3 molecule, e.g., CD3 epsilon (CD3e) molecule; or a TCR alpha (TCR α) molecule.~~

~~118. The method of claim of any of claims 100-117, wherein expansion of the population of immune cells, is compared to expansion of a similar population of cells not contacted with the anti-TCR β V antibody molecule, or multispecific molecule comprising the anti-TCR β V antibody molecule.~~

~~119. The method of claim of any of claims 100-118, wherein expansion of the population of T cells having a memory-like phenotype, e.g., CD45RA⁺CCR7⁻ cells (e.g., memory effector T~~

cells, e.g., TEM cells, e.g., TEMRA cells), is compared to expansion of a similar population of cells with an antibody that binds to: a CD3 molecule, e.g., CD3 epsilon (CD3e) molecule; or a TCR alpha (TCR α) molecule.

120. The method of claim of claim 119, wherein the population of expanded T cells having a memory-like phenotype, e.g., effector memory cells, comprises cells which:

(i) have a detectable level of CD45RA, e.g., express or re-express CD45RA;

(ii) have low or no expression of CCR7; and/or

(iii) have a detectable level of CD95, e.g., express CD95,

e.g., a population of CD45RA⁺, CCR7⁻, CD95⁺ T cells, optionally wherein the T cells comprise CD3⁺, CD4⁺ or CD8⁺ T cells.

121. The method of any of claims 100-120, wherein the method results in expansion of, e.g., selective or preferential expansion of, T cells expressing a T cell receptor (TCR) comprising a TCR alpha and/or TCR beta molecule, e.g., TCR alpha beta T cells ($\alpha\beta$ T cells).

122. The method of claim 121, wherein the method results in expansion of $\alpha\beta$ T cells over expansion of T cells expressing a TCR comprising a TCR gamma and/or TCR delta molecule, e.g., TCR gamma delta T cells ($\gamma\delta$ T cells).

123. A method of treating a disease, e.g., cancer, in a subject comprising administering to the subject an effective amount of an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) ("anti-TCR β V antibody molecule"), thereby treating the cancer.

124. A composition comprising an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) ("anti-TCR β V antibody molecule"), for use in treating a disease, e.g., cancer, in a subject.

125. A composition comprising an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) ("anti-TCR β V antibody molecule"), for use in the manufacture of a medicament for treating a disease, e.g., cancer, in a subject.

~~126. A method of treating a disease, e.g., cancer, in a subject comprising administering to the subject an effective amount of the multispecific molecule of any of claims 1-16, or 53-91, thereby treating the cancer.~~

~~127. A composition comprising the multispecific molecule of any of claims 1-16, or 53-91, for use in treating a disease, e.g., cancer, in a subject.~~

~~128. A composition comprising the multispecific molecule of any of claims 1-16, or 53-91, for use in the manufacture of a medicament for treating a disease, e.g., cancer, in a subject.~~

~~129. A method of treating, e.g., preventing or reducing, cytokine release syndrome (CRS) and/or neurotoxicity (NT) in a subject, e.g., CRS and/or NT associated with a treatment, e.g., a previously administered treatment, comprising administering to the subject an effective amount of an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) (“anti-TCR β V antibody molecule”), thereby preventing CRS and/or NT in the subject.~~

~~130. A method of treating, e.g., preventing or reducing, cytokine release syndrome (CRS) and/or neurotoxicity (NT) in a subject, e.g., CRS and/or NT associated with a treatment, e.g., a previously administered treatment, comprising administering to the subject an effective amount the multispecific molecule of any of claims 1-16, or 53-91, thereby preventing CRS and/or NT in the subject.~~

~~131. A method of targeting a therapy, e.g., treatment, to a T cell in a subject having a disease, e.g., cancer, comprising administering an effective amount of:~~

~~(i) an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) (“anti-TCR β V antibody molecule”); and~~

~~(ii) the therapy, e.g., a tumor targeting therapy (e.g., an antibody that binds to a cancer antigen), e.g., as described herein,~~

~~thereby targeting the therapy to the T cell in the subject.~~

~~132. A method of targeting a therapy, e.g., treatment, to a T cell in a subject having a disease, e.g., cancer, comprising administering an effective amount of:~~

~~(i) the multispecific molecule of any of claims 1-16, or 53-91; and~~

(ii) the therapy, e.g., a tumor targeting therapy (e.g., an antibody that binds to a cancer antigen), e.g., as described herein,
thereby targeting the therapy to the T cell in the subject.

~~133. The method of claim 131 or 132, wherein the method results in: reduced cytokine release syndrome (CRS) (e.g., lesser duration of CRS or no CRS), or a reduced severity of CRS (e.g., absence of severe CRS, e.g., CRS grade 4 or 5) compared to administration of (ii) alone.~~

~~134. The method of any one of claims 131-133, wherein the anti-TCR β V antibody or the multispecific molecule is administered concurrently with or after the administration of the treatment associated with CRS.~~

~~135. A method of treating a subject having a cancer, the method comprising:
—— acquiring a value of the status of a TCR β V subfamily for the subject, wherein said value comprises a measure of the presence of, e.g., level or activity of, a TCR β V molecule in a sample from the subject, and
—— administering an effective amount of an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) (“anti-TCR β V antibody molecule”); to the subject,
thereby treating the subject.~~

~~136. A method of treating a subject having a cancer, the method comprising:
—— acquiring a value of the status of a TCR β V subfamily for the subject, wherein said value comprises a measure of the presence of, e.g., level or activity of, a TCR β V molecule in a sample from the subject, and
—— administering an effective amount of the multispecific molecule of any of claims 1-16, or 53-91 to the subject,
thereby treating the subject.~~

~~137. A method of treating a subject having a cancer, the method comprising administering an effective amount of an antibody molecule which binds (e.g., specifically binds) to a T cell receptor beta variable region (TCR β V) (“anti-TCR β V antibody molecule”) to the subject, wherein the subject has a higher, e.g., increased, level or activity of one or more TCR β V~~

subfamilies, *e.g.*, as described herein, compared to a reference level or activity of one or more TCR β V subfamilies, *e.g.*, in a healthy subject, *e.g.*, a subject not having a cancer.

138. A method of treating a subject having a cancer, the method comprising administering an effective amount of the multispecific molecule of any of claims 1-16, or 53-91 to the subject, wherein the subject has a higher, *e.g.*, increased, level or activity of one or more TCR β V subfamilies, *e.g.*, as described herein, compared to a reference level or activity of one or more TCR β V subfamilies, *e.g.*, in a healthy subject, *e.g.*, a subject not having a cancer.

139. A method of expanding a population of immune effector cells from a subject having a cancer, the method comprising:

- (i) isolating a biological sample comprising a population of immune effector cells from the subject; *e.g.*, a peripheral blood sample, biopsy sample, or bone marrow sample;
- (ii) acquiring a value of the status of one or more TCR β V subfamilies for the subject, *e.g.*, in the biological sample from the subject, wherein said value comprises a measure of the presence of, *e.g.*, level or activity of, a TCR β V subfamily in a sample from the subject compared to a reference value, *e.g.*, a sample from a healthy subject, wherein a value that is higher, *e.g.*, increased, in the subject relative to the reference, *e.g.*, healthy subject, is indicative of the presence of cancer in the subject, and
- (iii) contacting the biological sample comprising a population of immune effector cells with an anti-TCR β V antibody molecule, *e.g.*, as described herein.

140. The method of claim 139, further comprising administering the population of immune effector cells contacted with the anti-TCR β V antibody molecule to the subject.

141. A method of expanding a population of immune effector cells from a subject having a cancer, the method comprising:

- (i) isolating a biological sample comprising a population of immune effector cells from the subject; *e.g.*, a peripheral blood sample, biopsy sample, or bone marrow sample;
- (ii) acquiring a value of the status of one or more TCR β V subfamilies for the subject, *e.g.*, in the biological sample from the subject, wherein said value comprises a measure of the presence of, *e.g.*, level or activity of, a TCR β V subfamily in a sample from the subject compared to a reference value, *e.g.*, a sample from a healthy subject, wherein a value that is higher, *e.g.*,

increased, in the subject relative to the reference, e.g., healthy subject, is indicative of the presence of cancer in the subject, and

—— (iii) contacting the biological sample comprising a population of immune effector cells with the multispecific molecule of any of claims 1-16, or 53-91.

142. The method of claim 141, further comprising administering the population of immune effector cells contacted with the multispecific molecule to the subject.

143. The method of any one of claims 139-142, comprising measuring T cell function (e.g., cytotoxic activity, cytokine secretion, or degranulation) in the population of immune effector cells, e.g., compared to a reference population, e.g., an otherwise similar population not contacted with the anti-TCR β V antibody molecule or a population of immune effector cells obtained from a healthy subject (e.g., a subject that does not have a cancer).

144. The method of any one of claims 139-143, wherein the biological sample comprising the population of immune effector cells is contacted with an anti-TCR β V antibody molecule or a multispecific molecule that binds to the one or more TCR β V subfamilies (e.g., the same TCR β V subfamily) identified as being higher, e.g., increased, in the biological sample.

145. The method of any one of claims 139-144, wherein the biological sample comprising the population of immune effector cells is contacted with an anti-TCR β V antibody molecule or a multispecific molecule that does not bind to the one or more TCR β V subfamilies (e.g., a different TCR β V subfamily) identified as being higher, e.g., increased, in the biological sample.

146. The method of any one of claims 139-145, wherein the cancer is a solid tumor including but not limited to: melanoma, pancreatic (e.g., pancreatic adenocarcinoma) cancer, breast cancer, colorectal cancer (CRC), lung cancer (e.g., small or non-small cell lung cancer), skin cancer, ovarian cancer, or liver cancer.

147. The method of any one of claims 139-145, wherein the cancer is a hematological cancer including, but not limited to: a B cell or T cell malignancy, e.g., Hodgkin's lymphoma, Non-Hodgkin's lymphoma (e.g., B cell lymphoma, diffuse large B cell lymphoma (DLBCL), follicular lymphoma, chronic lymphocytic leukemia (B-CLL), mantle cell lymphoma, marginal zone B cell lymphoma, Burkitt lymphoma, lymphoplasmacytic lymphoma, hairy cell leukemia), acute

myeloid leukemia (AML), chronic myeloid leukemia, myelodysplastic syndrome, multiple myeloma, and acute lymphocytic leukemia.

~~148. The method of any one of claims 139-147, wherein the cancer is B-CLL and the TCR β V molecule comprises:~~

- ~~—— (i) TCR β V6 subfamily comprising, e.g., TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01;~~
- ~~—— (ii) TCR β V5 subfamily comprising TCR β V5-6*01, TCR β V5-4*01, or TCR β V5-8*01;~~
- ~~—— (iii) TCR β V3 subfamily comprising TCR β V3-1*01;~~
- ~~—— (iv) TCR β V2 subfamily comprising TCR β V2*01; or~~
- ~~—— (v) TCR β V19 subfamily comprising TCR β V19*01, or TCR β V19*02.~~

~~149. The method of any one of claims 139-147, wherein the cancer is melanoma and the TCR β V molecule comprises the TCR β V6 subfamily comprising, e.g., TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01.~~

~~150. The method of any one of claims 139-147, wherein the cancer is DLBCL and the TCR β V molecule comprises:~~

- ~~—— (i) TCR β V13 subfamily comprising TCR β V13*01;~~
- ~~—— (ii) TCR β V3 subfamily comprising TCR β V3-1*01; or~~
- ~~—— (iii) TCR β V23 subfamily.~~

~~151. The method of any one of claims 139-147, wherein the cancer is CRC and the TCR β V molecule comprises:~~

- ~~—— (i) TCR β V19 subfamily comprising TCR β V19*01, or TCR β V19*02~~
- ~~—— (ii) TCR β V12 subfamily comprising TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01~~
- ~~—— (iii) TCR β V16 subfamily comprising TCR β V16*01; or~~
- ~~—— (iv) TCR β V21 subfamily.~~

~~152. The method of any one of claims 139-151, wherein:~~

~~the tumor comprises an antigen, e.g., a tumor antigen, e.g., a tumor associated antigen or a neoantigen; and/or~~

~~the one or more TCR β V subfamilies recognize, e.g., bind to, the tumor antigen.~~

~~153. The method of any one of claims 139-152, wherein the sample comprises a blood sample, e.g., a peripheral blood sample, a biopsy, e.g., a tumor biopsy, or a bone marrow sample.~~

~~154. The method of any one of claims 139-152, wherein the sample comprises a biological sample comprising immune cells, e.g., TCRBV expressing cells (e.g., TCRBV⁺ cells), T cells, or NK cells.~~

~~155. The method of claim 154, wherein the T cells comprise a CD4 T cell, a CD8 T cell, (e.g., an effector T cell or a memory T cell (e.g., a memory effector T cell (e.g., T_{EM} cell, e.g., T_{EMRA} cell), or a tumor infiltrating lymphocyte (TIL).~~

~~156. The method of any of claims 139-155, wherein the method results in an expansion, e.g., in vivo or ex vivo expansion, of at least 1.1-1000 fold, e.g., 1.1-10, 10-100, 100-200, 200-300, 300-400, 400-500, 500-600, 600-700, 700-800, 800-900, or 900-1000 fold expansion of an immune effector cell population comprising a TCRVB expressing immune effector cell, e.g., T cell.~~

~~157. The method of any of claims 139-156, wherein the population of cells is expanded in an appropriate media (e.g., media described herein) that includes one or more cytokines, e.g., IL-2, IL-7, IL-15, or a combination thereof.~~

~~158. The method of any of claims 139-157, wherein the population of cells is expanded for a period of at least about 4 hours, 6 hours, 10 hours, 12 hours, 15 hours, 18 hours, 20 hours, or 22 hours, or for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21 days, or for at least about 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks or 8 weeks.~~

~~159. The method of any of claims 139-158, wherein expansion of the population of immune cells, is compared to expansion of a similar population of cells with an antibody that binds to: a CD3 molecule, e.g., CD3 epsilon (CD3 ϵ) molecule; or a TCR alpha (TCR α) molecule.~~

~~160. The method of any of claims 139-159, expansion of the population of immune cells, is compared to expansion of a similar population of cells not contacted with the anti-TCR β V antibody molecule.~~

~~161. The method of any of claims 139-160, wherein expansion of the population of T cells having a memory-like phenotype, e.g., memory effector T cells, e.g., TEM cells, e.g., TEMRA cells, is compared to expansion of a similar population of cells with an antibody that binds to: a CD3 molecule, e.g., CD3 epsilon (CD3e) molecule; or a TCR alpha (TCR α) molecule.~~

~~162. The method of any of claims 133-161, wherein the population of expanded T cells having a memory-like phenotype, e.g., effector memory cells, comprises cells which:~~

~~(i) have a detectable level of CD45RA, e.g., express or re-express CD45RA;~~

~~(ii) have low or no expression of CCR7; and/or~~

~~(iii) have a detectable level of CD95, e.g., express CD95,~~

~~e.g., a population of CD45RA⁺, CCR7⁻, CD95⁺ T cells, optionally wherein the T cells comprise CD3⁺, CD4⁺ or CD8⁺ T cells.~~

~~163. The method of any of claims 139-162, wherein the method results in expansion of, e.g., selective or preferential expansion of, T cells expressing a T cell receptor (TCR) comprising a TCR alpha and/or TCR beta molecule, e.g., TCR alpha beta T cells ($\alpha\beta$ T cells).~~

~~164. The method of claim 163, wherein the method results in expansion of $\alpha\beta$ T cells over expansion of T cells expressing a TCR comprising a TCR gamma and/or TCR delta molecule, e.g., TCR gamma delta T cells ($\gamma\delta$ T cells).~~

~~165. The method, or composition for use of any one of claims 98-164, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a light chain variable region (VL) comprising one, two or all of a LC CDR1, a LC CDR2 and a LC CDR3 of a VL disclosed in **Tables 1, 2, 10, 11, 12 or 13**, e.g., SEQ ID NO: 1314, SEQ ID NO: 2, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 16, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29 or SEQ ID NO:30~~

~~166. The method, or composition for use of any one of claims 98-165, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising a heavy chain variable~~

region (VH) comprising one, two or all of a HC CDR1, a HC CDR2 and a HC CDR3 of a VH disclosed in **Tables 1, 2, 10, 11, 12 or 13**, e.g., SEQ ID NO: 1312, SEQ ID NO: 1, SEQ ID NO: 9, SEQ ID NO: 15, SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25.

167. The method, or composition for use of any one of claims 98-166, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

—— (i) a VL comprising: a LC CDR1 amino acid sequence of SEQ ID NO: 20 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof), a LC CDR2 amino acid sequence of SEQ ID NO: 21 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof), and/or a LC CDR3 amino acid sequence of SEQ ID NO: 22 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof); and/or

—— (ii) a VH comprising: a HC CDR1 amino acid sequence of SEQ ID NO: 17 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof), a HC CDR2 amino acid sequence of SEQ ID NO: 18 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof), and/or a HC CDR3 amino acid sequence of SEQ ID NO: 19 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof).

168. The method, or composition for use of any one of claims 98-167, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

a variable heavy chain (VH) of SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25, or a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto; and/or

a variable light chain (VL) of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29 or SEQ ID NO: 30, or a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto.

169. The method, or composition for use of any one of claims 98-168, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising

—— (i) a VL comprising: a LC CDR1 amino acid sequence of SEQ ID NO: 6 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof), a LC CDR2 amino acid sequence of SEQ ID NO: 7 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof),

and/or a LC CDR3 amino acid sequence of SEQ ID NO: 8 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof); and/or
—— (ii) a VH comprising: a HC CDR1 amino acid sequence of SEQ ID NO: 3 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof), a HC CDR2 amino acid sequence of SEQ ID NO: 4 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof), and/or a HC CDR3 amino acid sequence of SEQ ID NO: 5 (or an amino acid sequence with not more than 1, 2, 3 or 4 modifications, e.g., substitutions, additions or deletions thereof).

170. The method, or composition for use of any one of claims 98-169, wherein the anti-TCR β V antibody molecule comprises an antigen binding domain comprising:

a variable heavy chain (VH) of SEQ ID NO: 1 or SEQ ID NO: 9 or SEQ ID NO: 1312, or a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto; and/or

a variable light chain (VL) of SEQ ID NO: 2, SEQ ID NO: 10 or SEQ ID NO: 11 or SEQ ID NO: 1314, or a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto.

171. The method, or composition for use of any one of claims 98-170, wherein the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, e.g., framework region 1 (FR1), comprising one, two or all (e.g., three) of:

(i) an Aspartic Acid at position 1, e.g., a substitution at position 1 according to Kabat numbering, e.g., a Alanine to Aspartic Acid substitution; or

(ii) an Asparagine at position 2, e.g., a substitution at position 2 according to Kabat numbering, e.g., a Isoleucine to Asparagine, a Serine to Asparagine, or a Tyrosine to Asparagine substitution; or

or

(iii) a Leucine at position 4, e.g., a substitution at position 4 according to Kabat numbering, e.g., a Methionine to Leucine substitution;

wherein the substitution is relative to a human germline light chain framework region sequence.

172. The method, or composition for use of any one of claims 98-171, wherein the anti-TCR β V antibody molecule comprises a light chain comprising a framework region, e.g., framework region 3 (FR3), comprising one, two or all (e.g., three) of:

(i) a Glycine at position 66, e.g., a substitution at position 66 according to Kabat numbering, e.g., a Lysine to Glycine, or a Serine to Glycine substitution; or

(ii) an Asparagine at position 69, e.g., a substitution at position 69 according to Kabat numbering, e.g., a Threonine to Asparagine substitution; or
(iii) a Tyrosine at position 71, e.g., a substitution at position 71 according to Kabat numbering, e.g., a Phenylalanine to Tyrosine, or Alanine to Tyrosine substitution,
wherein the substitution is relative to a human germline light chain framework region sequence.

~~173. The method, or composition for use of any one of claims 98-171, wherein binding of the anti-TCR β V antibody molecule to the TCR β V region results in a cytokine profile that differs from a cytokine profile of a T cell engager that binds to a receptor or molecule other than a TCR β V region (“a non-TCR β V binding T cell engager”).~~

~~174. The method, or composition for use of claim 173, wherein the non-TCR β V binding T cell engager comprises an antibody that binds to a CD3 molecule (e.g., CD3-epsilon (CD3e) molecule); or a TCR alpha (TCR α) molecule.~~

~~175. The method, or composition for use of claim 173 or 174, wherein the cytokine profile of the first moiety comprises, one, two, three, four, five, six, seven, or all of the following:~~

- ~~(i) increased level, e.g., expression level, and/or activity of IL-2;~~
- ~~(ii) reduced level, e.g., expression level, and/or activity of IL-1 β ;~~
- ~~(iii) reduced level, e.g., expression level, and/or activity of IL-6;~~
- ~~(iv) reduced level, e.g., expression level, and/or activity of TNF α ;~~
- ~~(v) reduced level, e.g., expression level, and/or activity of IL-10;~~
- ~~(vi) a delay, e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more hours delay, in increased level, e.g., expression level, and/or activity of IL-2;~~
- ~~(vii) a delay, e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 hours delay, in increased level, e.g., expression level, and/or activity of IFN γ ; or~~
- ~~(viii) increased level, e.g., expression level, and/or activity of IL-15;~~

~~e.g., wherein (i)-(vii) are relative to the cytokine profile of the non-TCR β V binding T cell engager.~~

~~176. The method, or composition for use of any one of claims 173-175, wherein binding of the anti-TCR β V antibody molecule to the TCR β V region results in reduced cytokine storm, e.g., reduced cytokine release syndrome (CRS), as measured by an assay of Example 3, e.g., relative to the cytokine storm induced by the non-TCR β V binding T cell engager.~~

~~177. The method, or composition for use of any one of claims 173-176, wherein binding of the anti-TCR β V antibody molecule to the TCR β V region results in one, two, three or all of:~~

- ~~(ix) reduced T cell proliferation kinetics;~~
- ~~(x) cell killing, e.g., target cell killing, e.g. cancer cell killing, e.g., as measured by an assay of Example 4;~~
- ~~(xi) increased Natural Killer (NK) cell proliferation, e.g., expansion; or~~
- ~~(xii) expansion, e.g., at least about 1.1-10 fold expansion (e.g., at least about 1.1, 1.2, 1.3, 1.4, 1.5, 2, 3, 4, 5, 6, 7, 8, 9, or 10 fold expansion), of a population of T cells having a memory-like phenotype;~~

~~e.g., relative to the non-TCR β V binding T cell engager.~~

~~178. The method, or composition for use of any one of claims 98-177, wherein the anti-TCR β V antibody molecule binds to an outward-facing region (e.g., epitope) on a TCR β V protein, e.g., as depicted by the circled area in FIG. 24A.~~

~~179. The method, or composition for use of claim 178, wherein the outward-facing region on the TCR β V protein comprises a structurally conserved region of TCR β V, e.g., a region of TCR β V having a similar structure across one or more TCR β V subfamilies.~~

~~180. The method, or composition for use of any one of claims 98-179, the method further comprises administering (e.g., sequentially, simultaneously or concurrently) a second agent, e.g., therapeutic agent, e.g., as described herein.~~

~~181. The method, or composition for use of claim 180, wherein the second agent, e.g., therapeutic agent, comprises a chemotherapeutic agent, a biologic agent, hormonal therapy), radiation, or surgery.~~

~~182. The method, or composition for use of any one of claims 98 to 134, wherein the disease is a cancer, e.g., a solid tumor or a hematological cancer, or a metastatic lesion.~~

~~183. The method of claim 175, wherein the cancer antigen is BCMA or FcRH5.~~

CLAIMS

WHAT IS CLAIMED IS:

1. A molecule comprising an antigen binding domain that binds to T cell receptor beta variable region (TCR β V), wherein the antigen binding domain comprises:

- (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (HC CDR1), a heavy chain complementarity determining region 2 (HC CDR2), and a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 1100, and a light chain variable region (VL) comprising a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 1101;
- (ii) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1346, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1347 or SEQ ID NO: 1349;
- (iii) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1348, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1349;
- (iv) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1350, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1349, SEQ ID NO: 1351, SEQ ID NO: 1353, SEQ ID NO: 1365, SEQ ID NO: 1367, or SEQ ID NO: 1369;
- (v) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1356, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1357;
- (vi) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1360 or SEQ ID NO: 1362, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1361;
- (vii) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1370, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1365, SEQ ID NO: 1367, or SEQ ID NO: 1369;
- (viii) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1112, SEQ ID NO: 1113, SEQ ID NO: 1114, SEQ ID NO: 1115, or SEQ ID NO: 1116, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1111;

(ix) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1310 or SEQ ID NO: 1311, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1313;

(x) a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3 of SEQ ID NO: 1312, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3 of SEQ ID NO: 1314; or

(xi) a single chain variable fragment (scfv) comprising a HC CDR1, a HC CDR2, a HC CDR3, a LC CDR1, a LC CDR2, and a LC CDR3 of any one sequence selected from the group consisting of SEQ ID NOs: 1309, 1326-1337, and 110.

2. The molecule of claim 1, wherein the antigen binding domain comprises:

(i) a VH comprising a HC CDR1 sequence, a HC CDR2 sequence, and a HC CDR3 sequence comprising the sequence of SEQ ID NO: 3, the sequence of SEQ ID NO: 4, and the sequence of SEQ ID NO: 5, respectively, and a VL comprising a LC CDR1 sequence, a LC CDR2 sequence, and a LC CDR3 sequence comprising the sequence of SEQ ID NO: 6, the sequence of SEQ ID NO: 7, and the sequence of SEQ ID NO: 8, respectively;

(ii) a VH comprising a HC CDR1 sequence, a HC CDR2 sequence, and a HC CDR3 sequence comprising the sequence of SEQ ID NO: 45, the sequence of SEQ ID NO: 46, and the sequence of SEQ ID NO: 47, respectively, and a VL comprising a LC CDR1 sequence, a LC CDR2 sequence, and a LC CDR3 sequence comprising the sequence of SEQ ID NO: 51, the sequence of SEQ ID NO: 52, and the sequence of SEQ ID NO: 53, respectively;

(iii) a VH comprising a HC CDR1 sequence, a HC CDR2 sequence, and a HC CDR3 sequence comprising the sequence of SEQ ID NO: 48, the sequence of SEQ ID NO: 49, and the sequence of SEQ ID NO: 50, respectively, and a VL comprising a LC CDR1 sequence, a LC CDR2 sequence, and a LC CDR3 sequence comprising the sequence of SEQ ID NO: 54, the sequence of SEQ ID NO: 55, and the sequence of SEQ ID NO: 56, respectively;

(iv) a VH comprising a HC CDR1 sequence, a HC CDR2 sequence, and a HC CDR3 sequence comprising the sequence of SEQ ID NO: 3640, the sequence of SEQ ID NO: 1103, and the sequence of SEQ ID NO: 1104, respectively, and a VL comprising a LC CDR1 sequence, a LC CDR2 sequence, and a LC CDR3 sequence comprising the sequence of SEQ ID NO: 1107, the sequence of SEQ ID NO: 1108, and the sequence of SEQ ID NO: 1109, respectively;

(v) a VH comprising a HC CDR1 sequence, a HC CDR2 sequence, and a HC CDR3

sequence comprising the sequence of SEQ ID NO: 1102, the sequence of SEQ ID NO: 1103, and the sequence of SEQ ID NO: 1104, respectively, and a VL comprising a LC CDR1 sequence, a LC CDR2 sequence, and a LC CDR3 sequence comprising the sequence of SEQ ID NO: 1107, the sequence of SEQ ID NO: 1108, and the sequence of SEQ ID NO: 1109, respectively; or

(vi) a VH comprising a HC CDR1 sequence, a HC CDR2 sequence, and a HC CDR3 sequence comprising the sequence of SEQ ID NO: 1105, the sequence of SEQ ID NO: 1106, and the sequence of SEQ ID NO: 1104, respectively, and a VL comprising a LC CDR1 sequence, a LC CDR2 sequence, and a LC CDR3 sequence comprising the sequence of SEQ ID NO: 1110, the sequence of SEQ ID NO: 1108, and the sequence of SEQ ID NO: 1109, respectively.

3. The molecule of claim 1 or 2, wherein the antigen binding domain comprises:

(i) a VH comprising a sequence having at least 80% sequence identity to any one sequence selected from the group consisting of SEQ ID NOs: 1100, 1310, 1311, 1312, 1346, 1348, 1350, 1356, 1360, 1362, and 1370, and/or a VL comprising a sequence having at least 80% sequence identity to any one sequence selected from the group consisting of SEQ ID NOs: 1101, 1313, 1314, 1347, 1349, 1351, 1353, 1365, 1367, 1369, 1357, 1361, 1365, 1367, and 1369; or

(ii) a VH comprising a sequence having at least 80% sequence identity to any one sequence selected from the group consisting of SEQ ID NOs: 1112, 1113, 1114, 1115, and 1116, and/or a VL comprising a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1111.

4. The molecule of any one of claims 1-3, wherein the antigen binding domain comprises:

(i) a VH comprising a sequence selected from the group consisting of SEQ ID NOs: 1100, 1310, 1311, 1312, 1346, 1348, 1350, 1356, 1360, 1362, and 1370, and/or a VL comprising a sequence selected from the group consisting of SEQ ID NOs: 1101, 1313, 1314, 1347, 1349, 1351, 1353, 1365, 1367, 1369, 1357, 1361, 1365, 1367, and 1369; or

(ii) a VH comprising a sequence selected from the group consisting of SEQ ID NOs: 1112, 1113, 1114, 1115, and 1116, and/or a VL comprising the sequence of SEQ ID NO: 1111.

5. The molecule of any one of claims 1-4, wherein the antigen binding domain comprises:

- (i) a VH and a VL comprising a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1100, and a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1101, respectively;
- (ii) a VH and a VL comprising a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1346, and a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1347 or SEQ ID NO: 1349, respectively;
- (iii) a VH and a VL comprising a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1348, and a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1349, respectively;
- (iv) a VH and a VL comprising a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1350, and a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1349, SEQ ID NO: 1351, SEQ ID NO: 1353, SEQ ID NO: 1365, SEQ ID NO: 1367, or SEQ ID NO: 1369, respectively;
- (v) a VH and a VL comprising a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1356, and a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1357, respectively;
- (vi) a VH and a VL comprising a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1360 or SEQ ID NO: 1362, and a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1361, respectively;
- (vii) a VH and a VL comprising a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1370, and a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1365, SEQ ID NO: 1367, SEQ ID NO: 1369, respectively;
- (viii) a VH and a VL comprising a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1310 or SEQ ID NO: 1311, and a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1313, respectively;
- (ix) a VH and a VL comprising a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1312, and a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1314, respectively; or
- (x) a VH and a VL comprising a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1112, SEQ ID NO: 1113, SEQ ID NO: 1114, SEQ ID NO: 1115, or SEQ ID NO: 1116, and a sequence having at least 80% sequence identity to the sequence of SEQ ID NO: 1111, respectively.

6. The molecule of any one of claims 1-5, wherein the antigen binding domain comprises:

- (i) a VH and a VL comprising the sequence of SEQ ID NO: 1100, and the sequence of SEQ ID NO: 1101, respectively;
- (ii) a VH and a VL comprising the sequence of SEQ ID NO: 1346, and the sequence of SEQ ID NO: 1347 or SEQ ID NO: 1349, respectively;
- (iii) a VH and a VL comprising the sequence of SEQ ID NO: 1348, and the sequence of SEQ ID NO: 1349, respectively;
- (iv) a VH and a VL comprising the sequence of SEQ ID NO: 1350, and the sequence of SEQ ID NO: 1349, SEQ ID NO: 1351, SEQ ID NO: 1353, SEQ ID NO: 1365, SEQ ID NO: 1367, or SEQ ID NO: 1369, respectively;
- (v) a VH and a VL comprising the sequence of SEQ ID NO: 1356, and the sequence of SEQ ID NO: 1357, respectively;
- (vi) a VH and a VL comprising the sequence of SEQ ID NO: 1360 or SEQ ID NO: 1362, and the sequence of SEQ ID NO: 1361, respectively;
- (vii) a VH and a VL comprising the sequence of SEQ ID NO: 1370, and the sequence of SEQ ID NO: 1365, SEQ ID NO: 1367, SEQ ID NO: 1369, respectively;
- (viii) a VH and a VL comprising the sequence of SEQ ID NO: 1310 or SEQ ID NO: 1311, and the sequence of SEQ ID NO: 1313, respectively;
- (ix) a VH and a VL comprising the sequence of SEQ ID NO: 1312, and the sequence of SEQ ID NO: 1314, respectively; or
- (x) a VH and a VL comprising the sequence of SEQ ID NO: 1112, SEQ ID NO: 1113, SEQ ID NO: 1114, SEQ ID NO: 1115, or SEQ ID NO: 1116, and the sequence of SEQ ID NO: 1111, respectively.

7. The molecule of claim 1, wherein the antigen binding domain comprises a sequence having at least 80% sequence identity to any one sequence selected from the group consisting of SEQ ID NOs: 1309, 1326-1337, and 110.

8. The molecule of claim 1 or 7, wherein the antigen binding domain comprises a sequence selected from the group consisting of SEQ ID NOs: 1309, 1326-1337, and 110.

9. The molecule of any one of claims 1-8, wherein the molecule further comprises:

- (i) one or more heavy chain constant regions selected from the group consisting of IgG1 heavy chain constant region or fragment thereof, IgG2 heavy chain constant region or

fragment thereof, IgG3 heavy chain constant region or fragment thereof, IgGA1 heavy chain constant region or fragment thereof, IgGA2 heavy chain constant region or fragment thereof, IgG4 heavy chain constant region or fragment thereof, IgJ heavy chain constant region or fragment thereof, IgM heavy chain constant region or fragment thereof, IgD heavy chain constant region or fragment thereof, and IgE heavy chain constant region or fragment thereof;

(ii) a kappa light chain constant region or fragment thereof, or a lambda light chain constant region or fragment thereof; or

(iii) a combination thereof.

10. The molecule of any one of claims 1-9, wherein the molecule is a multispecific molecule that further comprises one or more of a tumor-targeting moiety, a cytokine molecule, a stromal modifying moiety, or an immune cell engager, and

optionally, wherein the immune cell engager is selected from the group consisting of a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, a macrophage cell engager, and any combination thereof.

11. The molecule of claim 10, wherein the molecule comprises the following configuration:

A-, B-[dimerization module]-C, -D,

wherein:

(A) the dimerization module comprises immunoglobulin constant domains;

(B) A, B, C, and D are independently (i) absent; (ii) the antigen binding domain; (iii) the tumor targeting moiety, (iv) the cytokine molecule; (v) the stromal modifying moiety; or (vi) the immune cell engager; and

wherein at least one, two, or three of A, B, C, and D comprises the antigen binding domain.

12. The molecule of claim 10 or 11, wherein the cytokine molecule is selected from the group consisting of interleukin-2 (IL-2) or functional variant thereof, interleukin-7 (IL-7) or functional variant thereof, interleukin-12 (IL-12) or functional variant thereof, interleukin-15 (IL-15) or functional variant thereof, interleukin-18 (IL-18) or functional variant thereof, interleukin-21 (IL-21) or functional variant thereof, interferon gamma or functional variant thereof, and any combination thereof.

13. The molecule of any one of claims 10-12, wherein the tumor-targeting moiety binds to a cancer antigen, wherein:

(i) the cancer antigen is present on a hematological cancer, a solid tumor, a metastatic cancer, a soft tissue tumor, a metastatic lesion, or any combination thereof;

(ii) the cancer antigen is a tumor antigen, a stromal antigen, or a hematological antigen; or

(iii) the cancer antigen is selected from the group consisting of BCMA, CD19, CD20, CD22, FcRH5, PDL1, CD47, ganglioside 2 (GD2), prostate stem cell antigen (PSCA), prostate specific membrane antigen (PMSA), prostate-specific antigen (PSA), carcinoembryonic antigen (CEA), Ron Kinase, c-Met, Immature laminin receptor, TAG-72, BING-4, Calcium-activated chloride channel 2, Cyclin-B1, 9D7, Ep-CAM, EphA3, Her2/neu, Telomerase, SAP-1, Survivin, NY-ESO-1/LAGE-1, PRAME, SSX-2, Melan-A/MART-1, Gp100/pmel17, Tyrosinase, MC1R, β -catenin, BRCA1/2, CDK4, CML66, Fibronectin, p53, Ras, TGF-B receptor, AFP, ETA, MAGE, CA-125, BAGE, GAGE, CDC27, α actinin-4, TRP1/gp75, TRP2, gangliosides, WT1, Epidermal growth factor receptor (EGFR), MART-2, MUC1, MUC2, MUM1, MUM2, MUM3, NA88-1, NPM, OA1, OGT, RCC, RU11, RU12, SAGE, TRG, TSTA, Folate receptor alpha, L1-CAM, CAIX, gpA33, GD3, GM2, VEGFR, Integrins, Carbohydrates, IGF1R, TRAILR1, TRAILR2, RANKL, FAP, TGF-beta, hyaluronic acid, collagen, tenascin C, and tenascin W.

14. The molecule of any one of claims 1-13, wherein the antigen binding domain is a full antibody or an antigen-binding fragment thereof, a bivalent antibody, a bispecific antibody, or a biparatopic antibody, and

optionally, wherein the antigen-binding fragment is a Fab, a F(ab')₂, a Fv, a single chain Fv (scFv), a single domain antibody, a diabody (dAb), a single domain antibody, or a camelid antibody.

15. The molecule of any one of claims 1-14, wherein binding of the molecule to the TCR β V region results in one, two, three or all of:

(i) reduced T cell proliferation kinetics;

(ii) target cell killing;

(iii) increased Natural Killer (NK) cell proliferation; or

(iv) expansion of a population of T cells having a memory-like phenotype,

relative to a non-TCR β V-binding T cell engager, optionally, wherein the non-TCR β V-binding T cell engager comprises an antibody that binds to a CD3 molecule or a TCR α (TCR α) molecule.

16. A recombinant polynucleotide comprising a sequence encoding the molecule of any one of claims 1-15.

17. A pharmaceutical composition comprising the molecule of any one of claims 1-15, and a pharmaceutically acceptable carrier, excipient, or stabilizer for use in therapy.

18. Use of a pharmaceutical composition comprising the molecule of any one of claims 1-15 in the manufacture of a medicament for treating cancer in a subject in need thereof,

wherein an effective amount of the molecule is to be administered to the subject.

19. The use of claim 18, wherein the administration of the effective amount of the molecule treats or reduces cytokine release syndrome (CRS) and/or neurotoxicity (NT) in the subject.

20. The use of claim 19, wherein the administration of the effective amount of the molecule results in a cytokine profile that differs from a cytokine profile induced by a non-TCR β V-binding T cell engager, and

optionally, wherein the non-TCR β V-binding T cell engager comprises an antibody that binds to a CD3 molecule or a TCR alpha (TCR α) molecule.

21. The use of claim 20, wherein the cytokine profile of the molecule comprises one, two, three, four, five, six, seven, or all of:

(i) an increased level and/or activity of IL-2;

(ii) a reduced level and/or activity of IL-1 β ;

(iii) a reduced level and/or activity of IL-6;

(iv) a reduced level and/or activity of TNF α ;

(v) a reduced level and/or activity of IL-10;

(vi) a delay in increased level and/or activity of IL-2;

(vii) a delay in increased level and/or activity of IFN γ ; or

(viii) an increased level and/or activity of IL-15;

relative to the cytokine profile of the non-TCR β V-binding T cell engager.

22. The use of any one of claims 18-21, wherein the cancer is a solid tumor or a hematological cancer.

23. The use of claim 22, wherein:

(i) the solid tumor is melanoma, pancreatic, optionally pancreatic adenocarcinoma, cancer, breast cancer, colorectal cancer, lung cancer, skin cancer, ovarian cancer, or liver cancer; or

(ii) the hematological cancer is a B-cell malignancy or T cell malignancy, wherein the B-cell malignancy or T cell malignancy is Hodgkin's lymphoma, Non-Hodgkin's lymphoma, hairy cell leukemia, acute myeloid leukemia (AML), chronic myeloid leukemia, myelodysplastic syndrome, multiple myeloma, or acute lymphocytic leukemia,

optionally, wherein the Non-Hodgkin's lymphoma is B cell lymphoma, diffuse large B cell lymphoma (DLBCL), follicular lymphoma, chronic lymphocytic leukemia (B-CLL), mantle cell lymphoma, marginal zone B-cell lymphoma, Burkitt lymphoma, or lymphoplasmacytic lymphoma.

24. Use of a composition comprising the molecule of any one of claims 1-15 in the manufacture of a medicament for modulating an immune response in a subject in need thereof,

optionally, wherein an effective amount of the molecule expands an immune cell population,
optionally, wherein the expansion occurs *in vivo* or *ex vivo*.