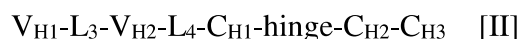


CLAIMS

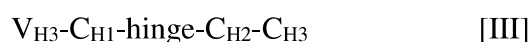
1. A binding protein comprising four polypeptide chains that form the three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L_1 , L_2 , L_3 and L_4 are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair; and

wherein V_{H1} and V_{L1} form a first antigen binding site;

wherein V_{H2} and V_{L2} form a second antigen binding site that binds a CD3 polypeptide, wherein the V_{H2} domain comprises a CDR-H1 sequence comprising the amino acid sequence of

GFTFTKAW (SEQ ID NO:55), a CDR-H2 sequence comprising the amino acid sequence of IKDKSNSYAT (SEQ ID NO:56), and a CDR-H3 sequence comprising the amino acid sequence of RGVYYALSPFDY (SEQ ID NO:57), and the V_{L2} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSLVHX₁NX₂X₃TY, wherein X₁ is E or Q, X₂ is A or L, and X₃ is Q, R, or F (SEQ ID NO:180), a CDR-L2 sequence comprising the amino acid sequence of KVS (SEQ ID NO:64), and a CDR-L3 sequence comprising the amino acid sequence of GQGTQYPFT (SEQ ID NO:65); and

wherein V_{H3} and V_{L3} form a third antigen binding site.

2. The binding protein of claim 1, wherein the first binding site binds a CD28 polypeptide.

3. The binding protein of claim 2, wherein the V_{H1} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYTFTSYY (SEQ ID NO:49), a CDR-H2 sequence comprising the amino acid sequence of IYPGNVNT (SEQ ID NO:50), and a CDR-H3 sequence comprising the amino acid sequence of TRSHYGLDWNFDV (SEQ ID NO:51), and the V_{L1} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QNIYVW (SEQ ID NO:52), a CDR-L2 sequence comprising the amino acid sequence of KAS (SEQ ID NO:53), and a CDR-L3 sequence comprising the amino acid sequence of QQGQTYPY (SEQ ID NO:54); and wherein optionally the V_{H1} domain comprises the amino acid sequence of QVQLVQSGAEVVKPGASVKVSCKASGYTFTSYYIHWRQAPGQGLEWIGSIYPGNVNT NYAQKFQGRATLTVDTSISTAYMELSRRLSDDTAVYYCTRSHYGLDWNFDVWGKGT VTVSS (SEQ ID NO:91), and/or the V_{L1} domain comprises the amino acid sequence of DIQMTQSPSSLSASVGDRVTITCQASQNIYVWLNWYQQKPGKAPKLLIYKASNLHTGVP SRFSGSGSGTDFTLTISLQPEDATYYCQQGQTYPYTFGQGTKLEIK (SEQ ID NO:92).

4. The binding protein of any one of claims 1-3, wherein the CDR-L1 sequence of the V_{L2} domain comprises an amino acid sequence selected from the group consisting of QSLVHQNAQTY (SEQ ID NO:59), QSLVHENLQTY (SEQ ID NO:60), QSLVHENLFTY (SEQ ID NO:61), and QSLVHENLRTY (SEQ ID NO:62); and wherein optionally the V_{H2} domain comprises the amino acid sequence of QVQLVESGGGVVQPGRSLRLSCAASGFTFTKAWMHWRQAPGKQLEWVAQIKDKSNS YATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCRGVYYALSPFDYWGQG

TLVTVSS (SEQ ID NO:93) or

QVQLVESGGGVVQPGRSLRLSCAASGFTFTKAWMHWRQAPGKQLEWVAQIKDKSNS
YATYYASSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCRGVYYALSPFDYWGQG
TLVTVSS (SEQ ID NO:302), and/or the V_{L2} domain comprises an amino acid sequence

selected from the group consisting of

DIVMTQTPLSLSVTPGQPASISCKSSQSLVHQNAQTYLSWYLQKPGQSPQSLIYKVSNRFS
SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK (SEQ ID
NO:95),

DIVMTQTPLSLSVTPGQPASISCKSSQSLVHENLQTYLSWYLQKPGQSPQSLIYKVSNRFS
GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK (SEQ ID
NO:96),

DIVMTQTPLSLSVTPGQPASISCKSSQSLVHENLFTYLSWYLQKPGQSPQSLIYKVSNRFS
GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK (SEQ ID
NO:97), and

DIVMTQTPLSLSVTPGQPASISCKSSQSLVHENLRTYLSWYLQKPGQSPQSLIYKVSNRFS
GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK (SEQ ID
NO:98).

5. The binding protein of any one of claims 1-4, wherein the third antigen binding site binds a tumor target protein.

6. The binding protein of any one of claims 1-4, wherein the third antigen binding site binds a human CD38 polypeptide.

7. The binding protein of claim 6, wherein:

(a) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYTFTSYA (SEQ ID NO:13), a CDR-H2 sequence comprising the amino acid sequence of IYPGQGGT (SEQ ID NO:14), and a CDR-H3 sequence comprising the amino acid sequence of ARTGGLRRAYFTY (SEQ ID NO:15), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSVSSYGQGF (SEQ ID NO:16), a CDR-L2 sequence comprising the amino acid sequence of GAS (SEQ ID NO:17), and a CDR-L3 sequence comprising the amino acid sequence of QQNKEDPWT (SEQ ID NO:18);

(b) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYTLTEFS (SEQ ID NO:19), a CDR-H2 sequence comprising the amino acid sequence of FDPEDGET (SEQ ID NO:20), and a CDR-H3 sequence comprising the amino acid sequence of TTGRFFDWF (SEQ ID NO:21), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSVISRF (SEQ ID NO:22), a CDR-L2 sequence comprising the amino acid sequence of GAS (SEQ ID NO:23), and a CDR-L3 sequence comprising the amino acid sequence of QQDSNLPIT (SEQ ID NO:24);

(c) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYAFTTYL (SEQ ID NO:25), a CDR-H2 sequence comprising the amino acid sequence of INPGSGST (SEQ ID NO:26), and a CDR-H3 sequence comprising the amino acid sequence of ARYAYGY (SEQ ID NO:27), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QNVGTA (SEQ ID NO:28), a CDR-L2 sequence comprising the amino acid sequence of SAS (SEQ ID NO:29), and a CDR-L3 sequence comprising the amino acid sequence of QQYSTYPFT (SEQ ID NO:30);

(d) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYSFTNYA (SEQ ID NO:31), a CDR-H2 sequence comprising the amino acid sequence of ISPYYGDT (SEQ ID NO:32), and a CDR-H3 sequence comprising the amino acid sequence of ARRFEGFYYSMDY (SEQ ID NO:33), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSLVHSNGNTY (SEQ ID NO:34), a CDR-L2 sequence comprising the amino acid sequence of KVS (SEQ ID NO:35), and a CDR-L3 sequence comprising the amino acid sequence of SQSTHVPLT (SEQ ID NO:36);

(e) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFTFSSYG (SEQ ID NO:37), a CDR-H2 sequence comprising the amino acid sequence of IWYDGSNK (SEQ ID NO:38), and a CDR-H3 sequence comprising the amino acid sequence of ARDPGLRYFDGGMDV (SEQ ID NO:39), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QGISSY (SEQ ID NO:40), a CDR-L2 sequence comprising the amino acid sequence of AAS (SEQ ID NO:41), and a CDR-L3 sequence comprising the amino acid sequence of QQLNSFPYT (SEQ ID NO:42);

(f) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFTFSSYG (SEQ ID NO:43), a CDR-H2 sequence comprising the amino acid sequence of IWYDGSNK (SEQ ID NO:44), and a CDR-H3 sequence comprising the amino acid sequence of ARMFRGAFDY (SEQ ID NO:45), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QGIRND (SEQ ID NO:46), a CDR-L2 sequence comprising the amino acid sequence of AAS (SEQ ID NO:47), and a CDR-L3 sequence comprising the amino acid sequence of LQDYIYYPT (SEQ ID NO:48);

(g) the V_{H3} domain comprises the amino acid sequence of QVQLVQSGAEVVKPGASVKVSCASGYTFTSYAMHWVKEAPGQRLEWIGYIYPGQGG TNYNQKFQGRATLTADTSASTAYMELSSLRSEDVAVYFCARTGGLRRAYFTYWGQGT LVTVSS (SEQ ID NO:79), and/or the V_{L3} domain comprises the amino acid sequence of DIVLTQSPATLSLSPGERATISCRASQSVSSYGQGFMHWYQQKPGQPPRLLIYGASSRAT GIPARFSGSGSGTDFTLTISPLEDFAVYYCQQNKEDPWTFGGGKLEIK (SEQ ID NO:80);

(h) the V_{H3} domain comprises the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKVSQGYTLTEFSIHVVRQAPGQGLEWMGGFDPEDGE TIYAQKFQGRVIMTEDTSTD TAYMEMNSLRSEDTAIYYCTTGRFFDWFVGQGT LVTVSS (SEQ ID NO:81), and/or the V_{L3} domain comprises the amino acid sequence of EIILTQSPAILSLSPGERATLSCRASQSVISRFLSWYQVKPGLAPRLLIYGASTRATGIPVRF SGSGSGTDFTLTISLQPEDCAVYYCQQDSNLPITFGQGTRLEIK (SEQ ID NO:82);

(i) the V_{H3} domain comprises the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCASGYAFTTYLVEWIRQRPQGLEWMGVINPGSGST NYAQKFQGRVTMTVDRSSTTAYMELSRLRSDDTAVYYCARYAYGYWGQGT LVTVSS (SEQ ID NO:83), and/or the V_{L3} domain comprises the amino acid sequence of DIQMTQSPSSLSASVGDRTITCRASQNVGTAVAWYQQKPGKSPKQLIYSASNRYTGVP SRFSGSGSGTDFTLTISLQPEDLATYYCQQYSTYPFTFGQGTKLEIK (SEQ ID NO:84);

(j) the V_{H3} domain comprises the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCASGYSTNYAVHWVRQAPGQGLEWMGVISPYYG DTTYAQKFQGRVTMTVDKSSSTAYMELSRLRSDDTAVYYCARRFEGFYYSMDYWGQG

TLVTVSS (SEQ ID NO:85), and/or the V_{L3} domain comprises the amino acid sequence of DVVMTQSPLSLPVTLGQPASISCRPSQSLVHSNGNTYLNWYQQRPGQSPKLLIYKVS KRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPLTFGGGTKVEIK (SEQ ID NO:86);

(k) the V_{H3} domain comprises the amino acid sequence of QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMWVRQAPGKGLEWVAVIWYDGSN KYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYHCARDPGLRYFDGGM DVWGQ GTTVTVSS (SEQ ID NO:87), and/or the V_{L3} domain comprises the amino acid sequence of DIQLTQSPSFLSASVGDRVTITCRASQGISSYLA WYQQKPGKAPKLLIFAASTLHSGVPSR FSGSGSGTEFTLTISSLQPEDFATYYCQQLNSFPYTFGQGGTKLEIK (SEQ ID NO:88); or

(l) the V_{H3} domain comprises the amino acid sequence of QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVIWYDGSN KYYADSVKGRFTISGDNSKNTLYLQMNSLRAEDTAVYYCARMFRGAFDYWGQGT LVT VSS (SEQ ID NO:89), and/or the V_{L3} domain comprises the amino acid sequence of AIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISGLQPEDSATYYCLQDYIYYPTFGQGGTKVEIK (SEQ ID NO:90).

8. The binding protein of claim 6, wherein:

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:156 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:156; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:157 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:157; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:158 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:158; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:159 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:159;

(b) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:160 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:160; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:161 or

an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:161; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:162 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:162; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:163 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:163;

(c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:164 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:164; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:165 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:165; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:166 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:166; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:167 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:167;

(d) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:168 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:168; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:169 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:169; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:170 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:170; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:171 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:171;

(e) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:172 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:172; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:173 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:173; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:174 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:174; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:175 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:175;

(f) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:176 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:176; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:177 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:177; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:178 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:178; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:179 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:179;

(g) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:181 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:181; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:182 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:182; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:183 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:183; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:184 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:184; or

(h) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:185 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:185; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:186 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:186; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:187 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:187; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:188 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:188.

9. The binding protein of any one of claims 1-8, wherein the third antigen binding site binds a human HER2 polypeptide.

10. The binding protein of claim 9, wherein:

(a) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFNIKDTY (SEQ ID NO:1) or GFNIRDTY (SEQ ID NO:2), a CDR-H2 sequence comprising the amino acid sequence of IYPTNGYT (SEQ ID NO:3), IYPTQGYT (SEQ ID NO:4), or IYPTNAYT (SEQ ID NO:5), and a CDR-H3 sequence comprising the amino acid sequence of SRWGGDGFYAMDY (SEQ ID NO:6), SRWGGEGFYAMDY (SEQ ID NO:7), or SRWGGSGFYAMDY (SEQ ID NO:8), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QDVNTA (SEQ ID NO:9) or QDVQTA (SEQ ID NO:10), a CDR-L2 sequence comprising the amino acid sequence of SAS (SEQ ID NO:11), and a CDR-L3 sequence comprising the amino acid sequence of QQHYTTP (SEQ ID NO:12);

(b) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFNIKDTY (SEQ ID NO:1), a CDR-H2 sequence comprising the amino acid sequence of IYPTNGYT (SEQ ID NO:3), and a CDR-H3 sequence comprising the amino acid sequence of SRWGGDGFYAMDY (SEQ ID NO:6), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QDVNTA (SEQ ID NO:9), a CDR-L2 sequence comprising the amino acid sequence of SAS (SEQ ID NO:11), and a CDR-L3 sequence comprising the amino acid sequence of QQHYTTP (SEQ ID NO:12);

(c) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFNIRDTY (SEQ ID NO:2), a CDR-H2 sequence comprising the amino acid sequence of IYPTQGYT (SEQ ID NO:4), and a CDR-H3 sequence comprising the amino acid sequence of SRWGGEGFYAMDY (SEQ ID NO:7), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QDVNTA (SEQ ID NO:9), a CDR-L2 sequence comprising the amino acid sequence of SAS (SEQ ID NO:11), and a CDR-L3 sequence comprising the amino acid sequence of QQHYTTP (SEQ ID NO:12);

(d) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFNIRDTY (SEQ ID NO:2), a CDR-H2 sequence comprising the amino acid sequence of IYPTNAYT (SEQ ID NO:5), and a CDR-H3 sequence comprising the amino acid sequence of SRWGGSGFYAMDY (SEQ ID NO:8), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QDVNTA (SEQ ID NO:9), a CDR-L2 sequence

comprising the amino acid sequence of SAS (SEQ ID NO:11), and a CDR-L3 sequence comprising the amino acid sequence of QQHYTTP (SEQ ID NO:12);

(e) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFNIRDY (SEQ ID NO:2), a CDR-H2 sequence comprising the amino acid sequence of IYPTQGYT (SEQ ID NO:4), and a CDR-H3 sequence comprising the amino acid sequence of SRWGGSGFYAMDY (SEQ ID NO:8), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QDVNTA (SEQ ID NO:9), a CDR-L2 sequence comprising the amino acid sequence of SAS (SEQ ID NO:11), and a CDR-L3 sequence comprising the amino acid sequence of QQHYTTP (SEQ ID NO:12);

(f) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFNIRDY (SEQ ID NO:2), a CDR-H2 sequence comprising the amino acid sequence of IYPTNAYT (SEQ ID NO:5), and a CDR-H3 sequence comprising the amino acid sequence of SRWGGEGFYAMDY (SEQ ID NO:7), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QDVNTA (SEQ ID NO:9), a CDR-L2 sequence comprising the amino acid sequence of SAS (SEQ ID NO:11), and a CDR-L3 sequence comprising the amino acid sequence of QQHYTTP (SEQ ID NO:12);

(g) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFNIKDY (SEQ ID NO:1), a CDR-H2 sequence comprising the amino acid sequence of IYPTNGYT (SEQ ID NO:3), and a CDR-H3 sequence comprising the amino acid sequence of SRWGGDGFYAMDY (SEQ ID NO:6), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QDVQTA (SEQ ID NO:10), a CDR-L2 sequence comprising the amino acid sequence of SAS (SEQ ID NO:11), and a CDR-L3 sequence comprising the amino acid sequence of QQHYTTP (SEQ ID NO:12);

(h) the V_{H3} domain comprises the amino acid sequence of
EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYT
RYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGT
LVTVSS (SEQ ID NO:72),
EVQLVESGGGLVQPGGSLRLSCAASGFNIRDYIHWVRQAPGKGLEWVARIYPTQGYTR
YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGEGFYAMDYWGQGT

VTVSS (SEQ ID NO:73),
 EVQLVESGGGLVQPGGSLRLSCAASGPNIRDTYIHWRQAPGKGLEWVARIYPTQGYTR
 YADSVKGRFTISADTSKNTAYLQMNSLRADTAVYYCSRWGSGGFYAMDYWGQGTL
 VTVSS (SEQ ID NO:74),
 EVQLVESGGGLVQPGGSLRLSCAASGPNIRDTYIHWRQAPGKGLEWVARIYPTNAYTR
 YADSVKGRFTISADTSKNTAYLQMNSLRADTAVYYCSRWGSGGFYAMDYWGQGTL
 VTVSS (SEQ ID NO:75), or
 EVQLVESGGGLVQPGGSLRLSCAASGPNIRDTYIHWRQAPGKGLEWVARIYPTNAYTR
 YADSVKGRFTISADTSKNTAYLQMNSLRADTAVYYCSRWGSGGFYAMDYWGQGTL
 VTVSS (SEQ ID NO:76), and/or the V_{L3} domain comprises the amino acid sequence of
 DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVP
 SRFSGSRSGTDFTLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:77) or
 DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVP
 SRFSGSRSGTDFTLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:78);

(i) the V_{H3} domain comprises the amino acid sequence of
 EVQLVESGGGLVQPGGSLRLSCAASGPNIRDTYIHWRQAPGKGLEWVARIYPTNGYT
 RYADSVKGRFTISADTSKNTAYLQMNSLRADTAVYYCSRWGGDGFYAMDYWGQGT
 LVTVSS (SEQ ID NO:72), and/or the V_{L3} domain comprises the amino acid sequence of
 DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVP
 SRFSGSRSGTDFTLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:77);

(j) the V_{H3} domain comprises the amino acid sequence of
 EVQLVESGGGLVQPGGSLRLSCAASGPNIRDTYIHWRQAPGKGLEWVARIYPTQGYTR
 YADSVKGRFTISADTSKNTAYLQMNSLRADTAVYYCSRWGSGGFYAMDYWGQGTL
 VTVSS (SEQ ID NO:73), and/or the V_{L3} domain comprises the amino acid sequence of
 DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVP
 SRFSGSRSGTDFTLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:77);

(k) the V_{H3} domain comprises the amino acid sequence of
 EVQLVESGGGLVQPGGSLRLSCAASGPNIRDTYIHWRQAPGKGLEWVARIYPTNAYTR
 YADSVKGRFTISADTSKNTAYLQMNSLRADTAVYYCSRWGSGGFYAMDYWGQGTL

VTVSS (SEQ ID NO:75), and/or the V_{L3} domain comprises the amino acid sequence of DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVP SRFSGSRSGTDFTLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:77);

(l) the V_{H3} domain comprises the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFNIRDYIHWVRQAPGKGLEWVARIYPTQGYTR YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGSGFYAMDYWGQGT L VTVSS (SEQ ID NO:74), and/or the V_{L3} domain comprises the amino acid sequence of DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVP SRFSGSRSGTDFTLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:77);

(m) the V_{H3} domain comprises the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFNIRDYIHWVRQAPGKGLEWVARIYPTNAYTR YADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGEGFYAMDYWGQGT L VTVSS (SEQ ID NO:76), and/or the V_{L3} domain comprises the amino acid sequence of DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVP SRFSGSRSGTDFTLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:77); or

(n) the V_{H3} domain comprises the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYT RYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGT L VTVSS (SEQ ID NO:72), and/or the V_{L3} domain comprises the amino acid sequence of DIQMTQSPSSLSASVGDRVTITCRASQDVQTA VAWYQQKPGKAPKLLIYSASFLYSGVP SRFSGSRSGTDFTLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:78).

11. The binding protein of claim 9, wherein:

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:100 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:100; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:101 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:101; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:102 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:102;

and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:103 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:103;

(b) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:104 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:104; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:105 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:105; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:106 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:106; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:107 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:107;

(c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:112 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:112; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:113 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:113; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:114 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:114; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:115 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:115;

(d) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:116 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:116; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:117 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:117; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:118 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:118; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:119 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:119;

(e) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:120 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:120; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:121 or

an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:121; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:122 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:122; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:123 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:123;

(f) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:124 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:124; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:125 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:125; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:126 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:126; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:127 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:127;

(g) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:128 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:128; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:129 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:129; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:130 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:130; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:131 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:131;

(h) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:132 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:132; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:133 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:133; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:134 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:134; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:135 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:135;

(i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:136 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:136; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:137 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:137; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:138 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:138; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:139 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:139;

(j) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:140 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:140; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:141 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:141; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:142 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:142; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:143 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:143;

(k) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:144 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:144; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:145 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:145; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:146 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:146; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:147 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:147;

(l) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:148 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:148; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:149 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:149; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:150 or an amino acid

sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:150; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:151 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:151;

(m) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:152 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:152; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:153 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:153; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:154 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:154; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:155 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:155;

(n) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:286 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:286; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:287 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:287; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:288 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:288; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:289 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:289;

(o) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:290 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:290; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:291 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:291; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:292 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:292; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:293 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:293;

(p) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:294 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID

NO:294; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:295 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:295; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:296 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:296; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:297 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:297; or

(q) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:298 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:298; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:299 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:299; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:300 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:300; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:301 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:301.

12. The binding protein of any one of claims 1-11, wherein:

(a) at least one of L₁, L₂, L₃ or L₄ is independently 0 amino acids in length;

(b) L₁, L₂, L₃ and L₄ each independently are zero amino acids in length or comprise a sequence selected from the group consisting of GGGGSGGGGS (SEQ ID NO:69), GGGGSGGGGSGGGGS (SEQ ID NO: 70), S, RT, TKGPS (SEQ ID NO: 68), GQPKAAP (SEQ ID NO: 67), and GGSGSSGSGG (SEQ ID NO: 71);

(c) L₁, L₂, L₃ and L₄ each independently comprise a sequence selected from the group consisting of GGGGSGGGGS (SEQ ID NO:69), GGGGSGGGGSGGGGS (SEQ ID NO:70), S, RT, TKGPS (SEQ ID NO:68), GQPKAAP (SEQ ID NO: 67), and GGSGSSGSGG (SEQ ID NO:71);

(d) L₁ comprises the sequence GQPKAAP (SEQ ID NO: 67), L₂ comprises the sequence TKGPS (SEQ ID NO:68), L₃ comprises the sequence S, and L₄ comprises the sequence RT;

(e) at least one of L₁, L₂, L₃ or L₄ comprises the sequence DKTHT (SEQ ID NO:66), wherein optionally L₁, L₂, L₃ and L₄ comprise the sequence DKTHT (SEQ ID NO:66).

13. The binding protein of any one of claims 1-12, wherein:

(a) the hinge-C_{H2}-C_{H3} domains of the second and the third polypeptide chains are human IgG4 hinge-C_{H2}-C_{H3} domains, and wherein the hinge-C_{H2}-C_{H3} domains each comprise amino acid substitutions at positions corresponding to positions 234 and 235 of human IgG4 according to EU Index, wherein the amino acid substitutions are F234A and L235A;

(b) the hinge-C_{H2}-C_{H3} domains of the second and the third polypeptide chains are human IgG4 hinge-C_{H2}-C_{H3} domains, and wherein the hinge-C_{H2}-C_{H3} domains each comprise amino acid substitutions at positions corresponding to positions 233-236 of human IgG4 according to EU Index, wherein the amino acid substitutions are E233P, F234V, L235A, and a deletion at 236;

(c) the hinge-C_{H2}-C_{H3} domains of the second and the third polypeptide chains are human IgG1 hinge-C_{H2}-C_{H3} domains, and wherein the hinge-C_{H2}-C_{H3} domains each comprise amino acid substitutions at positions corresponding to positions 234, 235, and 329 of human IgG1 according to EU Index, wherein the amino acid substitutions are L234A, L235A, and P329A; or

(d) the hinge-C_{H2}-C_{H3} domains of the second and the third polypeptide chains are human IgG1 hinge-C_{H2}-C_{H3} domains, and wherein the hinge-C_{H2}-C_{H3} domains each comprise amino acid substitutions at positions corresponding to positions 298, 299, and 300 of human IgG1 according to EU Index, wherein the amino acid substitutions are S298N, T299A, and Y300S.

14. The binding protein of any one of claims 1-13, wherein the hinge-C_{H2}-C_{H3} domains of the second and the third polypeptide chains are human IgG4 hinge-C_{H2}-C_{H3} domains, and wherein the hinge-C_{H2}-C_{H3} domains each comprise amino acid substitutions at positions corresponding to positions 228 and 409 of human IgG4 according to EU Index, wherein the amino acid substitutions are S228P and R409K.

15. The binding protein of any one of claims 1-14, wherein:

(a) the hinge-C_{H2}-C_{H3} domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 or

IgG4 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V; and wherein the hinge-CH₂-CH₃ domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 or IgG4 according to EU Index, wherein the amino acid substitutions are S354C and T366W; or

(b) the hinge-CH₂-CH₃ domain of the second polypeptide chain comprises amino acid substitutions at positions corresponding to positions 354 and 366 of human IgG1 or IgG4 according to EU Index, wherein the amino acid substitutions are S354C and T366W; and wherein the hinge-CH₂-CH₃ domain of the third polypeptide chain comprises amino acid substitutions at positions corresponding to positions 349, 366, 368, and 407 of human IgG1 or IgG4 according to EU Index, wherein the amino acid substitutions are Y349C, T366S, L368A, and Y407V.

16. An isolated nucleic acid molecule comprising a nucleotide sequence encoding the binding protein of any one of claims 1-15.

17. An expression vector comprising the nucleic acid molecule of claim 16.

18. An isolated host cell comprising the nucleic acid molecule of claim 16 or the expression vector of claim 17; wherein optionally the host cell is a mammalian or insect cell.

19. A pharmaceutical composition comprising the binding protein of any one of claims 1-15 and a pharmaceutically acceptable carrier.

20. The binding protein of any one of claims 5-15 or the pharmaceutical composition of claim 19 for use in preventing and/or treating cancer in a patient.

21. The binding protein for use or the composition for use of claim 20, wherein the at least one binding protein is to be co-administered with a chemotherapeutic agent.

22. The binding protein for use or the composition for use of claim 20 or claim 21, wherein the patient is a human.

23. The binding protein for use or the composition for use of any one of claims 20-22, wherein the third antigen binding site binds a human CD38 polypeptide, and wherein cancer cells from the patient express CD38; wherein optionally the cancer is multiple myeloma, acute myeloid leukemia

(AML), acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), or a B cell lymphoma.

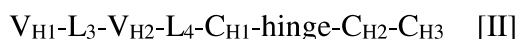
24. The binding protein for use or the composition for use of claim 23, wherein, prior to administration of the binding protein, the patient has been treated with daratumumab without a wash-out period.

25. The binding protein for use or the composition for use of any one of claims 20-22, wherein the third antigen binding site binds a human HER2 polypeptide, and wherein cancer cells from the patient express HER2; wherein optionally the cancer is breast cancer, colorectal cancer, gastric cancer, or non-small cell lung cancer (NSCLC).

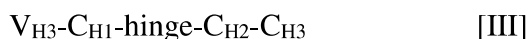
26. A binding protein for use in expanding T cells, wherein the binding protein is to be contacted with a T cell, wherein the binding protein comprises four polypeptide chains that form the three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L₁, L₂, L₃ and L₄ are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair; and

wherein V_{H1} and V_{L1} form a first antigen binding site that binds a CD28 polypeptide;

wherein V_{H2} and V_{L2} form a second antigen binding site that binds a CD3 polypeptide, wherein the V_{H2} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFTFTKAW (SEQ ID NO:55), a CDR-H2 sequence comprising the amino acid sequence of IKDKSNSYAT (SEQ ID NO:56), and a CDR-H3 sequence comprising the amino acid sequence of RGVYYALSPFDY (SEQ ID NO:57), and the V_{L2} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSLVHX₁NX₂X₃TY, wherein X₁ is E or Q, X₂ is A or L, and X₃ is Q, R, or F (SEQ ID NO:180), a CDR-L2 sequence comprising the amino acid sequence of KVS (SEQ ID NO:64), and a CDR-L3 sequence comprising the amino acid sequence of GQGTQYPFT (SEQ ID NO:65); and

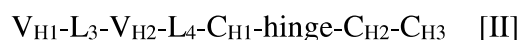
wherein V_{H3} and V_{L3} form a third antigen binding site that binds a CD38 polypeptide.

27. The binding protein for use of claim 26, wherein the T cell expresses a chimeric antigen receptor (CAR) on its cell surface or comprises a polynucleotide encoding a CAR; and/or wherein the T cell is a memory T cell or an effector T cell.

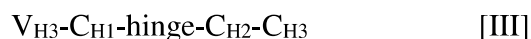
28. A binding protein for use in expanding virus-specific memory T cells, wherein the binding protein is to be contacted with a virus-specific memory T cell, wherein the binding protein comprises four polypeptide chains that form the three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

- V_{L1} is a first immunoglobulin light chain variable domain;
- V_{L2} is a second immunoglobulin light chain variable domain;
- V_{L3} is a third immunoglobulin light chain variable domain;
- V_{H1} is a first immunoglobulin heavy chain variable domain;
- V_{H2} is a second immunoglobulin heavy chain variable domain;
- V_{H3} is a third immunoglobulin heavy chain variable domain;
- C_L is an immunoglobulin light chain constant domain;
- C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain;
- C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;
- C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;
- hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and
- L_1 , L_2 , L_3 and L_4 are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair; and

wherein V_{H1} and V_{L1} form a first antigen binding site that binds a CD28 polypeptide;

wherein V_{H2} and V_{L2} form a second antigen binding site that binds a CD3 polypeptide, wherein the V_{H2} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFTFTKAW (SEQ ID NO:55), a CDR-H2 sequence comprising the amino acid sequence of IKDKSNSYAT (SEQ ID NO:56), and a CDR-H3 sequence comprising the amino acid sequence of RGVYYALSPFDY (SEQ ID NO:57), and the V_{L2} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSLVHX₁NX₂X₃TY, wherein X₁ is E or Q, X₂ is A or L, and X₃ is Q, R, or F (SEQ ID NO:180), a CDR-L2 sequence comprising the amino acid sequence of KVS (SEQ ID NO:64), and a CDR-L3 sequence comprising the amino acid sequence of GQGTQYPFT (SEQ ID NO:65); and

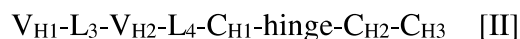
wherein V_{H3} and V_{L3} form a third antigen binding site that binds a CD38 polypeptide.

29. The binding protein for use of claim 28, wherein the virus-specific memory T cell is to be contacted with the binding protein *in vitro* or *ex vivo*; and/or wherein contacting the virus-specific memory T cell with the trispecific binding protein causes activation and/or proliferation of virus-specific memory T cells.

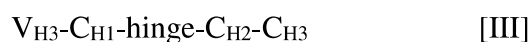
30. A binding protein for use in treating chronic viral infection, wherein the binding protein is to be administered to a patient in need thereof, wherein the binding protein comprises four polypeptide chains that form the three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



and a second polypeptide chain comprises a structure represented by the formula:



and a third polypeptide chain comprises a structure represented by the formula:



and a fourth polypeptide chain comprises a structure represented by the formula:



wherein:

V_{L1} is a first immunoglobulin light chain variable domain;

V_{L2} is a second immunoglobulin light chain variable domain;

V_{L3} is a third immunoglobulin light chain variable domain;

V_{H1} is a first immunoglobulin heavy chain variable domain;

V_{H2} is a second immunoglobulin heavy chain variable domain;

V_{H3} is a third immunoglobulin heavy chain variable domain;

C_L is an immunoglobulin light chain constant domain;

C_{H1} is an immunoglobulin C_{H1} heavy chain constant domain;

C_{H2} is an immunoglobulin C_{H2} heavy chain constant domain;

C_{H3} is an immunoglobulin C_{H3} heavy chain constant domain;

hinge is an immunoglobulin hinge region connecting the C_{H1} and C_{H2} domains; and

L_1 , L_2 , L_3 and L_4 are amino acid linkers;

wherein the polypeptide of formula I and the polypeptide of formula II form a cross-over light chain-heavy chain pair; and

wherein V_{H1} and V_{L1} form a first antigen binding site that binds a CD28 polypeptide;

wherein V_{H2} and V_{L2} form a second antigen binding site that binds a CD3 polypeptide, wherein the V_{H2} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFTFTKAW (SEQ ID NO:55), a CDR-H2 sequence comprising the amino acid sequence of IKDKSNSYAT (SEQ ID NO:56), and a CDR-H3 sequence comprising the amino acid sequence of RGVYYALSPFDY (SEQ ID NO:57), and the V_{L2} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSLVHX₁NX₂X₃TY, wherein X₁ is E or Q, X₂ is A or L, and X₃ is Q, R, or F (SEQ ID NO:180), a CDR-L2 sequence comprising the amino acid sequence of KVS (SEQ ID NO:64), and a CDR-L3 sequence comprising the amino acid sequence of GQGTQYPFT (SEQ ID NO:65); and

wherein V_{H3} and V_{L3} form a third antigen binding site that binds a CD38 polypeptide.

31. The binding protein for use of claim 30, wherein the patient is a human.

32. The binding protein for use of claim 30 or claim 31, wherein the binding protein is to be administered to the patient in pharmaceutical formulation comprising the binding protein and a pharmaceutically acceptable carrier; and/or wherein administration of the binding protein results in activation and/or proliferation of virus-specific memory T cells in the patient.

33. The binding protein for use of any one of claims 27-29 and 32, wherein the memory T cells are CD8+ or CD4+ memory T cells; wherein optionally the memory T cells are central memory T cells (T_{CM}) or effector memory T cells (T_{EM}).

34. The binding protein for use of any one of claims 28-33, wherein the virus is a human immunodeficiency virus (HIV), influenza virus, cytomegalovirus (CMV), hepatitis B virus (HBV), human papillomavirus (HPV), Epstein-barr virus (EBV), human foamy virus (HFV), herpes simplex virus 1 (HSV-1), or herpes simplex virus 1 (HSV-2).

35. The binding protein for use of any one of claims 26-34, wherein the CD28 polypeptide is a human CD28 polypeptide, wherein the CD3 polypeptide is a human CD3 polypeptide, and wherein the CD38 polypeptide is a human CD38 polypeptide.

36. The binding protein for use of any one of claims 26-35, wherein the V_{H1} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYTFTSYY (SEQ ID NO:49), a CDR-H2 sequence comprising the amino acid sequence of IYPGNVNT (SEQ ID NO:50), and a CDR-H3 sequence comprising the amino acid sequence of TRSHYGLDWNFDV (SEQ ID NO:51), and the V_{L1} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QNIYVW (SEQ ID NO:52), a CDR-L2 sequence comprising the amino acid sequence of KAS (SEQ ID NO:53), and a CDR-L3 sequence comprising the amino acid sequence of QQGQTYPY (SEQ ID NO:54); wherein optionally the V_{H1} domain comprises the amino acid sequence of QVQLVQSGAEVVKPGASVKVSCASGYTFTSYYIHWVRQAPGQGLEWIGSIYPGNVNT NYAQKFQGRATLTVDTSISTAYMELSRLRSDDTAVYYCTRSHYGLDWNFDVWGKGT VTVSS (SEQ ID NO:91), and/or the V_{L1} domain comprises the amino acid sequence of DIQMTQSPSSLSASVGDRVTITCQASQNIYVWLNWYQQKPGKAPKLLIYKASNLHTGVP SRFSGSGSGTDFTLTISLQPEDATYYCQQGQTYPYTFGQGTKLEIK (SEQ ID NO:92).

37. The binding protein for use of any one of claims 26-36, wherein the CDR-L1 sequence of the V_{L2} domain comprises an amino acid sequence selected from the group consisting of QSLVHQNAQTY (SEQ ID NO:59), QSLVHENLQTY (SEQ ID NO:60), QSLVHENLFTY (SEQ ID NO:61), and QSLVHENLRTY (SEQ ID NO:62); wherein optionally the V_{H2} domain comprises the amino acid sequence of QVQLVESGGGVVQPGRSLRLSCAASGFTFTKAWMHWRQAPGKQLEWVAQIKDKSNS YATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCRGVYYALSPFDYWGQG TLVTVSS (SEQ ID NO:93) or QVQLVESGGGVVQPGRSLRLSCAASGFTFTKAWMHWRQAPGKQLEWVAQIKDKSNS YATYYASSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCRGVYYALSPFDYWGQG TLVTVSS (SEQ ID NO:302), and/or the V_{L2} domain comprises an amino acid sequence selected from the group consisting of DIVMTQTPLSLSVTPGQPASISCKSSQSLVHQNAQTYLSWYLQKPGQSPQSLIYKVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK (SEQ ID NO:95), DIVMTQTPLSLSVTPGQPASISCKSSQSLVHENLQTYLSWYLQKPGQSPQSLIYKVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK (SEQ ID NO:96),

DIVMTQTPLSLSVTPGQPASISCKSSQSLVHENLFTYLSWYLQKPGQSPQSLIYKVSNRFS
GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK (SEQ ID
NO:97), and

DIVMTQTPLSLSVTPGQPASISCKSSQSLVHENLRITYLSWYLQKPGQSPQSLIYKVSNRFS
GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK (SEQ ID
NO:98).

38. The binding protein for use of any one of claims 26-37, wherein:

(a) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYTFTSYA (SEQ ID NO:13), a CDR-H2 sequence comprising the amino acid sequence of IYPGQGGT (SEQ ID NO:14), and a CDR-H3 sequence comprising the amino acid sequence of ARTGGLRRAYFTY (SEQ ID NO:15), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSVSSYGQGF (SEQ ID NO:16), a CDR-L2 sequence comprising the amino acid sequence of GAS (SEQ ID NO:17), and a CDR-L3 sequence comprising the amino acid sequence of QQNKEDPWT (SEQ ID NO:18);

(b) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYTLTEFS (SEQ ID NO:19), a CDR-H2 sequence comprising the amino acid sequence of FDPEDGET (SEQ ID NO:20), and a CDR-H3 sequence comprising the amino acid sequence of TTGRFFDWF (SEQ ID NO:21), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSVISRF (SEQ ID NO:22), a CDR-L2 sequence comprising the amino acid sequence of GAS (SEQ ID NO:23), and a CDR-L3 sequence comprising the amino acid sequence of QQDSNLPIT (SEQ ID NO:24);

(c) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYAFTTYL (SEQ ID NO:25), a CDR-H2 sequence comprising the amino acid sequence of INPGSGST (SEQ ID NO:26), and a CDR-H3 sequence comprising the amino acid sequence of ARYAYGY (SEQ ID NO:27), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QNVGTA (SEQ ID NO:28), a CDR-L2 sequence comprising the amino acid sequence of SAS (SEQ ID NO:29), and a CDR-L3 sequence comprising the amino acid sequence of QQYSTYPFT (SEQ ID NO:30);

(d) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYSFTNYA (SEQ ID NO:31), a CDR-H2 sequence comprising the amino acid sequence of ISPYYGDT (SEQ ID NO:32), and a CDR-H3 sequence comprising the amino acid sequence of ARRFEGFYYSMDY (SEQ ID NO:33), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QSLVHSNGNTY (SEQ ID NO:34), a CDR-L2 sequence comprising the amino acid sequence of KVS (SEQ ID NO:35), and a CDR-L3 sequence comprising the amino acid sequence of SQSTHVPLT (SEQ ID NO:36);

(e) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFTFSSYG (SEQ ID NO:37), a CDR-H2 sequence comprising the amino acid sequence of IWYDGSNK (SEQ ID NO:38), and a CDR-H3 sequence comprising the amino acid sequence of ARDPGLRYFDGGMDV (SEQ ID NO:39), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QGISSY (SEQ ID NO:40), a CDR-L2 sequence comprising the amino acid sequence of AAS (SEQ ID NO:41), and a CDR-L3 sequence comprising the amino acid sequence of QQLNSFPYT (SEQ ID NO:42);

(f) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GFTFSSYG (SEQ ID NO:43), a CDR-H2 sequence comprising the amino acid sequence of IWYDGSNK (SEQ ID NO:44), and a CDR-H3 sequence comprising the amino acid sequence of ARMFRGAFDY (SEQ ID NO:45), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QGIRND (SEQ ID NO:46), a CDR-L2 sequence comprising the amino acid sequence of AAS (SEQ ID NO:47), and a CDR-L3 sequence comprising the amino acid sequence of LQDYIYYPT (SEQ ID NO:48);

(g) the V_{H3} domain comprises the amino acid sequence of QVQLVQSGAEVVKPGASVKVSCKASGYTFTSYAMHWVKEAPGQRLEWIGYIYPGQGG TNYNQKFQGRATLTADTSASTAYMELSSLRSEDVAVYFCARTGGLRRAYFTYWGQGTL VTVSS (SEQ ID NO:79), and/or the V_{L3} domain comprises the amino acid sequence of DIVLTQSPATLSLSPGERATISCRASQSVSSYGQGFMHWYQQKPGQPRLLIYGASSRAT GIPARFSGSGSGTDFTLTISPLEDFAVYYCQQNKEDPWTFGGGTKLEIK (SEQ ID NO:80);

(h) the V_{H3} domain comprises the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCVSGYTLTEFSIHVVRQAPGQGLEWMGGFDPEDGE TIYAQKFQGRVIMTEDTSTDYMEMNSLRSEDTAIYYCTTGRFFDWFVGQGLTVTVSS (SEQ ID NO:81), and/or the V_{L3} domain comprises the amino acid sequence of EIILTQSPAILSLSPGERATLSCRASQSVISRFLSWYQVKPGLAPRLLIYGASTRATGIPVRF SGSGSGTDFSLTISSLQPEDCAVYYCQQDSNLPITFGQGTRLEIK (SEQ ID NO:82);

(i) the V_{H3} domain comprises the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKASGYAFTTYLVEWIRQRPQGQGLEWMGVINPGSGST NYAQKFQGRVTMTVDRSSTAYMELSRLRSDDTAVYYCARYAYGYWGQGLTVTVSS (SEQ ID NO:83), and/or the V_{L3} domain comprises the amino acid sequence of DIQMTQSPSSLSASVGDRVTITCRASQNVGTAVAWYQQKPGKSPKQLIYSASNRYTGVP SRFSGSGSGTDFTLTISLQPEDLATYYCQQYSTYPFTFGQGTKLEIK (SEQ ID NO:84);

(j) the V_{H3} domain comprises the amino acid sequence of QVQLVQSGAEVKKPGASVKVSCKASGYSFTNYAVHWVRQAPGQGLEWMGVISPYYG DTTYAQKFQGRVTMTVDKSSSTAYMELSRLRSDDTAVYYCARRFEGFYYSMDYWGQG TLTVTVSS (SEQ ID NO:85), and/or the V_{L3} domain comprises the amino acid sequence of DVVMTQSPLSLPVTLGQPASISCRPSQSLVHSNGNTYLNWYQQRPGQSPKLLIYKVSKRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPLTFGGGKVEIK (SEQ ID NO:86);

(k) the V_{H3} domain comprises the amino acid sequence of QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMWVRQAPGKGLEWVAVIWYDGSN KYYADSVKGRFTISRDN SKNTLYLQMNSLR AEDTAVYHCARDPGLRYFDGGM DVWGQ GTTVTVSS (SEQ ID NO:87), and/or the V_{L3} domain comprises the amino acid sequence of DIQLTQSPSFLSASVGDRVTITCRASQGISSYLAWYQQKPGKAPKLLIFAASTLHSGVPSR FSGSGSGTEFTLTISLQPEDFATYYCQQQLNSFPYTFGQGTKLEIK (SEQ ID NO:88); or

(l) the V_{H3} domain comprises the amino acid sequence of QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVIWYDGSN KYYADSVKGRFTISGDNSKNTLYLQMNSLR AEDTAVYYCARMFRGAFDYWGQGLTVT VSS (SEQ ID NO:89), and/or the V_{L3} domain comprises the amino acid sequence of

AIQMTQSPSSLSASVGDRVTTTCRASQGIRNDLGWYQQKPGKAPKLLIYAASSLQSGVPS
RFSGSGSGTDFTLTISGLQPEDSATYYCLQDYIYYPTFGQGTKVEIK (SEQ ID NO:90).

39. The binding protein for use of any one of claims 26-37, wherein:

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:156 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:156; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:157 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:157; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:158 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:158; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:159 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:159;

(b) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:160 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:160; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:161 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:161; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:162 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:162; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:163 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:163;

(c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:164 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:164; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:165 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:165; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:166 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:166; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:167 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:167;

(d) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:168 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:168; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:169 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:169; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:170 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:170; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:171 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:171;

(e) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:172 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:172; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:173 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:173; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:174 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:174; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:175 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:175;

(f) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:176 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:176; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:177 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:177; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:178 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:178; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:179 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:179;

(g) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:181 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:181; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:182 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:182; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:183 or an

amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:183; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:184 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:184; or

(h) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:185 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:185; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:186 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:186; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:187 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:187; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:188 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:188.

40. A vector system comprising one or more vectors encoding a first, second, third, and fourth polypeptide chain of a binding protein of any one of claims 1-15; wherein optionally the vector system comprises a first vector encoding the first polypeptide chain of the binding protein, a second vector encoding the second polypeptide chain of the binding protein, a third vector encoding the third polypeptide chain of the binding protein, and a fourth vector encoding the fourth polypeptide chain of the binding protein.

41. A kit of polynucleotides, comprising:

(a) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:189, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:190, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:191, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:192;

(b) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:193, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:194, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:195, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:196;

(c) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:197, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:198, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:199, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:200;

(d) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:201, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:202, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:203, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:204;

(e) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:205, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:206, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:207, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:208;

(f) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:209, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:210, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:211, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:212;

(g) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:213, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:214, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:215, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:216;

(h) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:217, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:218, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:219, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:220;

(i) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:221, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:222, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:223, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:224;

(j) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:225, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:226, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:227, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:228;

(k) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:229, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:230, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:231, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:232;

(l) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:233, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:234, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:235, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:236;

(m) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:237, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:238, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:239, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:240;

(n) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:241, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:242, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:243, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:244;

(o) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:245, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:246, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:247, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:248;

(p) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:249, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:250, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:251, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:252;

(q) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:253, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:254, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:255, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:256;

(r) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:257, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:258, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:259, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:260;

(s) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:261, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:262, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:263, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:264;

(t) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:265, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:266, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:267, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:268;

(u) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:269, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:270, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:271, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:272; or

(v) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:273, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:274, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:275, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:276;

wherein optionally the first, second, third, and fourth polynucleotides are present on one or more expression vectors.