

CLAIMS

What is claimed is:

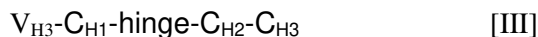
1. A binding protein comprising four polypeptide chains that form three antigen binding sites, wherein a first polypeptide chain comprises a structure represented by the formula:



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 T cell target protein;

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:20), a CDR-H2 sequence comprising the amino acid sequence of IKDKSNSYAT (SEQ ID NO:21), and a CDR-H3 sequence comprising the amino acid sequence of RGVYYALSPFDY (SEQ ID NO:22), 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:293), a CDR-L2 sequence comprising the amino acid sequence of KVS (SEQ ID NO:29), and a CDR-L3 sequence comprising the amino acid sequence of GQGTQYPFT (SEQ ID NO:30); and

wherein V_{H3} and V_{L3} form a third antigen binding site that binds an HIV target protein.

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:31), a CDR-H2 sequence comprising the amino acid sequence of IYPGNVNT (SEQ ID NO:32), and a CDR-H3 sequence comprising the amino acid sequence of TRSHYGLDWNFDV (SEQ ID NO:33), and the V_{L1} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QNIYVW (SEQ ID NO:34), a CDR-L2 sequence comprising the amino acid sequence of KAS (SEQ ID NO:35), and a CDR-L3 sequence comprising the amino acid sequence of QQGQTPY (SEQ ID NO:36).

4. The binding protein of claim 3, wherein the V_{H1} domain comprises the amino acid sequence of
 QVQLVQSGAEVVKPGASVKVCKASGYTFTSYYIHWVRQAPGQGLEWIGSIYPGN
 VNTNYAQKFQGRATLTVDTSISTAYMELSRLRSDDTAVYYCTRSHYGLDWNFDV
 WGKGTTVTVSS (SEQ ID NO:59), and/or the V_{L1} domain comprises the amino acid sequence of
 DIQMTQSPSSLSASVGDRVTITCQASQNIYVWLNWYQQKPGKAPKLLIYKASNLHT
 GVPSRFGSGSGTDFTLTISLQPEDIATYYCQQGQTPYTFGQGTKLEIK (SEQ ID NO:60).

5. The binding protein of any one of claims 1-4, 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:24), QSLVHENLQTY (SEQ ID NO:25), QSLVHENLFTY (SEQ ID NO:26), and QSLVHENLRTY (SEQ ID NO:27).

6. The binding protein of claim 5, wherein the V_{H2} domain comprises the amino acid sequence of

QVQLVESGGGVVQPGRSLRLSCAASGFTFTKAWMHWRQAPGKQLEWVAQIKD
KSNSYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVYYCRGVYYALSPF
DYWGQGTLVTVSS (SEQ ID NO:52), and/or the V_{L2} domain comprises an amino acid
sequence selected from the group consisting of
DIVMTQTPLSLSVTPGQPASISCKSSQSLVHQNAQTYLSWYLQKPGQSPQSLIYKVS
NRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK
(SEQ ID NO:54),
DIVMTQTPLSLSVTPGQPASISCKSSQSLVHENLQTYLSWYLQKPGQSPQSLIYKVS
NRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK
(SEQ ID NO:55),
DIVMTQTPLSLSVTPGQPASISCKSSQSLVHENLFTYLSWYLQKPGQSPQSLIYKVS
NRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK
(SEQ ID NO:56), and
DIVMTQTPLSLSVTPGQPASISCKSSQSLVHENLRTYLSWYLQKPGQSPQSLIYKVS
NRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCGQGTQYPFTFGSGTKVEIK
(SEQ ID NO:57).

7. The binding protein of any one of claims 1-6, wherein the third antigen binding site binds an HIV target protein selected from the group consisting of glycoprotein 120, glycoprotein 41 and glycoprotein 160.

8. The binding protein of claim 7, wherein:

(a) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of NCPIN (SEQ ID NO:1) a CDR-H2 sequence comprising the amino acid

sequence of WMKPRHGAVSYARQLQG (SEQ ID NO:2), and a CDR-H3 sequence comprising the amino acid sequence of GKYCTARDYYNWDFEH (SEQ ID NO:3), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of RTSQYGSLA (SEQ ID NO:4), a CDR-L2 sequence comprising the amino acid sequence of SGSTRAA (SEQ ID NO:5), and a CDR-L3 sequence comprising the amino acid sequence of QQYEF (SEQ ID NO:6);

(b) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of GYTFTAHI (SEQ ID NO:7) a CDR-H2 sequence comprising the amino acid sequence of IKPQYGAV (SEQ ID NO:8) or IKPQYGAT (SEQ ID NO:9), and a CDR-H3 sequence comprising the amino acid sequence of DRSYGDSSWALDA (SEQ ID NO:10), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of QGVGSD (SEQ ID NO:11), a CDR-L2 sequence comprising the amino acid sequence of HTS (SEQ ID NO:12), and a CDR-L3 sequence comprising the amino acid sequence of CQVLQF (SEQ ID NO:13); or

(c) the V_{H3} domain comprises a CDR-H1 sequence comprising the amino acid sequence of DCTLN (SEQ ID NO:14) a CDR-H2 sequence comprising the amino acid sequence of WLKPRWGAVNYARPLQG (SEQ ID NO:15), and a CDR-H3 sequence comprising the amino acid sequence of GKNCDYNWDFEH (SEQ ID NO:16), and the V_{L3} domain comprises a CDR-L1 sequence comprising the amino acid sequence of RTSQYGSLA (SEQ ID NO:17), a CDR-L2 sequence comprising the amino acid sequence of SGSTRAA (SEQ ID NO:18), and a CDR-L3 sequence comprising the amino acid sequence of QQYEF (SEQ ID NO:19).

9. The binding protein of claim 8, wherein:

(a) the V_{H3} domain comprises the amino acid sequence of QVRLSQSGGQMKKPGDSMRISCASGYEFINCPINWIRLAPGKRPEWMGWMKPRH GAVSYARQLQGRVTMTRDMYSETAFLELRSLTSDDTAVYFCTRGKYCTARDYYN WDFEHWGQGTPVTVSS (SEQ ID NO:43), and/or the V_{L3} domain comprises the amino acid sequence of

SLTQSPGTLSLSPGETAIISCRTSQYGSLAWYQQRPGQAPRLVIYSGSTRAAGIPDRF
SGSRWGPDPYNTISNLESGDFGVYYCQQYEFFGQGTKVQVDIK (SEQ ID NO:45);

(b) the V_{H3} domain comprises the amino acid sequence of
QVRLSQSGGQMKKPGDSMRISCRASGYEFINCPINWIRLAPGKRPEWMGWMKPRH
GAVSYARQLQGRVTMTRQLSQDPDDPDWGTAFLRLSLTSDDTAVYFCTRGKYC
TARDYYNWDFEHWGQGTPVTVSS (SEQ ID NO:44), and/or the V_{L3} domain comprises
the amino acid sequence of
SLTQSPGTLSLSPGETAIISCRTSQYGSLAWYQQRPGQAPRLVIYSGSTRAAGIPDRF
SGSRWGPDPYNTISNLESGDFGVYYCQQYEFFGQGTKVQVDIK (SEQ ID NO:45);

(c) the V_{H3} domain comprises the amino acid sequence of
RAHLVQSGTAMKKPGASVRVSCQTSQYTGFTAHILFWFRQAPGRGLEWVGWIKPQ
YGAVNFGGGFRDRVTLTRDVYREIAYMDIRGLKPDDTAVYYCARDRSYGDSSWA
LDAWGQGTTVVVSA (SEQ ID NO:46), and/or the V_{L3} domain comprises the amino acid
sequence of
YIHVTQSPSSLSVSIQDRVTINCQTSQGVGSDLHWYQHKPGRAPKLLIHHTSSVEDG
VPSRFSGSGFHTSFNLTISDLQADDIATYYCQVLQFFGRGSRLLHIK (SEQ ID NO:49);

(d) the V_{H3} domain comprises the amino acid sequence of
RAHLVQSGTAMKKPGASVRVSCQTSQYTGFTAHILFWFRQAPGRGLEWVGWIKPQ
YGATNFGGGFRDRVTLTRDVYREIAYMDIRGLKPDDTAVYYCARDRSYGDSSWA
LDAWGQGTTVVVSA (SEQ ID NO:47), and/or the V_{L3} domain comprises the amino acid
sequence of
YIHVTQSPSSLSVSIQDRVTINCQTSQGVGSDLHWYQHKPGRAPKLLIHHTSSVEDG
VPSRFSGSGFHTSFNLTISDLQADDIATYYCQVLQFFGRGSRLLHIK (SEQ ID NO:49);

(e) the V_{H3} domain comprises the amino acid sequence of
RAHLVQSGTAMKKPGASVRVSCQTSQYTGFTAHILFWFRQAPGRGLEWVGWIKPQ
YGAVNFGGGFRDRVTLTRQLSQDPDDPDWGIA YMDIRGLKPDDTAVYYCARDRS
YGDSSWALDAWGQGTTVVVSA (SEQ ID NO:48), and/or the V_{L3} domain comprises the
amino acid sequence of

YIHVTQSPSSLSVSIQDRVTINCQTSQGVGSDLHWYQHKPGRAPKLLIHHTSSVEDG
VPSRFSGSGFHTSFNLTISDLQADDIATYYCQVLQFFGRGSRLHIK (SEQ ID NO:49);
or

(f) the V_{H3} domain comprises the amino acid sequence of
QVQLVQSGGQMKKPGESMRISCASGYEFIDCTLNWIRLAPGKRPEWMGWLKPR
WGAVNYARPLQGRVTMTRQLSQDPDDPDWGTAFLRLSLTVDDTAVYFCTRGKN
CDYNWDFEHWGRGTPVIVSS (SEQ ID NO:50), and/or the V_{L3} domain comprises the
amino acid sequence of
LTQSPGTLSPGETAIISCRTSQYGSLAWYQQRPGQAPRLVIYSGSTRAAGIPDRFS
GSRWGPDYNTISNLESGDFGVYYCQQYEFFGQGTKVQVDIK (SEQ ID NO:51).

10. The binding protein of any one of claims 1-9, wherein at least one of L_1 , L_2 , L_3 or L_4 is independently 0 amino acids in length.

11. The binding protein of any one of claims 1-9, wherein (a) L_1 , L_2 , L_3 and L_4 each independently are zero amino acids in length or comprise a sequence selected from the group consisting of GGGGSGGGGS (SEQ ID NO:40), GGGGSGGGSGGGGS (SEQ ID NO: 41), S, RT, TKGPS (SEQ ID NO: 39), GQPKAAP (SEQ ID NO: 38), and GGSGSSGSGG (SEQ ID NO: 42); or (b) L_1 , L_2 , L_3 and L_4 each independently comprise a sequence selected from the group consisting of GGGGSGGGGS (SEQ ID NO:40), GGGGSGGGSGGGGS (SEQ ID NO:41), S, RT, TKGPS (SEQ ID NO:39), GQPKAAP (SEQ ID NO: 38), and GGSGSSGSGG (SEQ ID NO:42).

12. The binding protein of any one of claims 1-9, wherein L_1 comprises the sequence GQPKAAP (SEQ ID NO: 38), L_2 comprises the sequence TKGPS (SEQ ID NO:39), L_3 comprises the sequence S, and L_4 comprises the sequence RT.

13. The binding protein of any one of claims 1-9, wherein at least one of L_1 , L_2 , L_3 or L_4 comprises the sequence DKTHT (SEQ ID NO:37).

14. The binding protein of claim 13, wherein L_1 , L_2 , L_3 and L_4 comprise the sequence DKTHT (SEQ ID NO:37).

15. The binding protein of any one of claims 1-14, wherein the hinge-CH₂-CH₃ domains of the second and the third polypeptide chains are human IgG4 hinge-CH₂-CH₃ domains, and wherein the hinge-CH₂-CH₃ 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.

16. The binding protein of any one of claims 1-14, wherein the hinge-CH₂-CH₃ domains of the second and the third polypeptide chains are human IgG4 hinge-CH₂-CH₃ domains, and wherein the hinge-CH₂-CH₃ 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.

17. The binding protein of any one of claims 1-16, wherein the hinge-CH₂-CH₃ domains of the second and the third polypeptide chains are human IgG4 hinge-CH₂-CH₃ domains, and wherein the hinge-CH₂-CH₃ 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.

18. The binding protein of any one of claims 1-14, wherein the hinge-CH₂-CH₃ domains of the second and the third polypeptide chains are human IgG1 hinge-CH₂-CH₃ domains, and wherein the hinge-CH₂-CH₃ 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.

19. The binding protein of any one of claims 1-14, wherein the hinge-CH₂-CH₃ domains of the second and the third polypeptide chains are human IgG1 hinge-CH₂-CH₃ domains, and wherein the hinge-CH₂-CH₃ 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.

20. The binding protein of any one of claims 1-19, wherein the hinge-CH₂-CH₃ 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.

21. The binding protein of any one of claims 1-19, wherein 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.

22. The binding protein of claim 1, wherein:

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:61 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:61; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:62 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:62; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:63 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:63; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:64 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:64;

(b) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:65 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:65; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:66 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:66; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:67 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:67; and the fourth polypeptide chain comprises the amino acid sequence of

SEQ ID NO:68 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:68;

(c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:69 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:69; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:70 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:70; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:71 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:71; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:72 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:72;

(d) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:73 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:73; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:74 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:74; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:75 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:75; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:76 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:76;

(e) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:77 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:77; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:78 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:78; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:79 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:79; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:80 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:80;

(f) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:81 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:81; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:82 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:82; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:83 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:83; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:84 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:84;

(g) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:85 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:85; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:86 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:86; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:87 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:87; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:88 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:88;

(h) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:89 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:89; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:90 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:90; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:91 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:91; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:92 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:92;

(i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:93 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ

ID NO:93; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:94 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:94; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:95 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:95; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:96 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:96;

(j) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:97 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:97; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:98 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:98; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:99 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:99; and the fourth 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;

(k) the first 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 second 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; the third 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; and the fourth 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;

(l) the first 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 second 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; the third 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; and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:108 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:108;

(m) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:109 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:109; the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:110 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:110; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:111 or an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:111; and the fourth 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;

(n) the first 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 second 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; the third 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; and the fourth 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;

(o) the first 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 second 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; the third 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; and the fourth 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;

(p) the first 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 second 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; the third 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; and the fourth 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;

(q) the first 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 second 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; the third 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; and the fourth 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;

(r) the first 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 second 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; the third 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; and the fourth 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;

(s) the first 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 second 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; the third 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; and the fourth 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;

(t) the first 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 second 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; the third 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; and the fourth 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;

(u) the first 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 second 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; the third 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; and the fourth 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;

(v) the first 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 second 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; the third 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; and the fourth 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;

(x) the first 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 second 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; the third 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; and the fourth 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;

(y) the first 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 second 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; the third 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; and the fourth 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;

(z) the first 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 second 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; the third 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; and the fourth 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;

(aa) the first 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 second 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; the third 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; and the fourth 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;

(bb) the first 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 second 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; the third 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; and the fourth 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; or

(cc) the first 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 second 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; the third 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; and the fourth 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.

23. An isolated nucleic acid molecule comprising a nucleotide sequence encoding the binding protein of any one of claims 1-22.

24. An expression vector comprising the nucleic acid molecule of claim 23.

25. An isolated host cell comprising the nucleic acid molecule of claim 23 or the expression vector of claim 24.

26. The isolated host cell of claim 25, wherein the host cell is a mammalian or insect cell.

27. A pharmaceutical composition comprising the binding protein of any one of claims 1-22 and a pharmaceutically acceptable carrier.

28. Use of the binding protein of any one of claims 1-22 or the pharmaceutical composition of claim 27 in the manufacture of a medicament to prevent and/or treat HIV infection in a patient.

29. The use of claim 28, wherein the medicament is co-administered with standard anti-retroviral therapy.

30. The use of claim 28 or claim 29, wherein administration of the medicament results in the elimination of one or more latently and/or chronically HIV-infected cells in the patient.

31. The use of any one of claims 28-30, wherein the patient is a human.

32. The binding protein of any one of claims 1-22 or the pharmaceutical composition of claim 27 for use in preventing and/or treating HIV infection in a patient.

33. The binding protein for use of claim 32, wherein the binding protein is to be co-administered with standard anti-retroviral therapy.

34. The binding protein for use of claim 32 or claim 33, wherein the binding protein causes the elimination of one or more latently and/or chronically HIV-infected cells in the patient.

35. The binding protein for use of any one of claims 32-34, wherein the patient is a human.

36. A vector system comprising one or more vectors encoding a first, second, third, and fourth polypeptide chain of the binding protein of any one of claims 1-22.

37. The vector system of claim 36, wherein 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.

38. A kit of polynucleotides, comprising:

(a) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:177, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:178, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:179, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:180;

(b) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:181, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:182, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:183, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:184;

(c) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:185, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:186, a third

polynucleotide comprising the polynucleotide sequence of SEQ ID NO:187, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:188;

(d) 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;

(e) 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;

(f) 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;

(g) 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;

(h) 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;

(i) 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;

(j) 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;

(k) 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;

(l) 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;

(m) 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;

(n) 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;

(o) 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;

(p) 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;

(q) 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;

(r) 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;

(s) 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;

(t) 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;

(u) 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;

(v) 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;

(w) 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;

(x) 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;

(y) 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;

(z) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:277, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:278, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:279, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:280;

(aa) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:281, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:282, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:283, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:284;

(bb) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:285, a second polynucleotide comprising the polynucleotide sequence of SEQ ID NO:286, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:287, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:288; or

(cc) a first polynucleotide comprising the polynucleotide sequence of SEQ ID NO:289, a second polynucleotide comprising the polynucleotide sequence of SEQ ID

NO:290, a third polynucleotide comprising the polynucleotide sequence of SEQ ID NO:291, and a fourth polynucleotide comprising the polynucleotide sequence of SEQ ID NO:292.

39. The kit of claim 38, wherein the first, second, third, and fourth polynucleotides are present on one or more expression vectors.