

(iii) a domain (F) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (F) and domain (E) are separated by a peptide linker 2;

(III) the third polypeptide chain comprises in the N- to C-terminal direction:

(i) a peptide linker 3,

(ii) a CH2-CH3 domain, and wherein:

the domains (A) and (B) do not associate with one another to form an epitope binding site;
the domains (D) and (E) do not associate with one another to form an epitope binding site;
the domains (A) and (E) associate to form a binding site that binds the HIV-1 envelope like A32, 7B2, CH28, or CH44 antibody (1);
the domains (B) and (D) associate to form a binding site that binds the epitope (2); and
the CH2-CH3 domains of the first and third polypeptide form an Fc chain.

[0010a] In one aspect, there is provided a bispecific molecule comprising a first polypeptide chain, and a second polypeptide chain covalently bonded to one another, wherein:

(I) the first polypeptide chain comprises in the N- to C-terminal direction:

- (i) a domain (A) comprising a binding region of the light chain variable domain of a first immunoglobulin (VL1) comprising the VL CDR3, CDR2 and CDR1 of HIV-1 antibody A32 (SEQ ID NO:78), 7B2 (SEQ ID NO:55), CH28 (SEQ ID NO:68), or CH44 (SEQ ID NO:74);
- (ii) a domain (B) comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) comprising the VH CDR3, CDR2 and CDR1 of an antibody specific for an epitope of CD3 or CD16, wherein domains (A) and (B) are separated from one another by a peptide linker 1; and
- (iii) a domain (C) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (C) and domain (B) are separated by a peptide linker 2;

(II) the second polypeptide chain comprises in the N- to C-terminal direction:

- (i) a domain (D) comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) comprising the VL CDR3, CDR2 and CDR1 of an antibody specific for the epitope of CD3 or CD16;
- (ii) a domain (E) comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) comprising the VH CDR3, CDR2, and CDR1 of

HIV-1 antibody A32 (SEQ ID NO:77), 7B2 (SEQ ID NO:56), CH28 (SEQ ID NO:67), or CH44 (SEQ ID NO:73), wherein domains (D) and (E) are separated from one another by a peptide linker 1; and

- (iii) a domain (F) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (F) and domain (E) are separated by a peptide linker 2;

and wherein:

the domains (A) and (B) do not associate with one another to form an epitope binding site; the domains (D) and (E) do not associate with one another to form an epitope binding site;

the domains (A) and (E) associate to form a binding site that binds the HIV-1 envelope like the A32, 7B2, CH28, or CH44 antibody (1);

the domains (B) and (D) associate to form a binding site that binds the epitope of CD3 or CD16;

the K coil comprises residues 240-267 of SEQ ID NO: 19, and the E coil comprises residues 249-276 of SEQ ID NO: 17; and

peptide linker 2 comprises residues 244-248 of SEQ ID NO: 17.

[0011] A bispecific molecule comprising a first polypeptide chain, a second polypeptide chain, and a third polypeptide chain, wherein some of the polypeptides are covalently bonded (See Figure 8), and wherein:

(I) the first polypeptide chain comprises in the N- to C-terminal direction:

(i) a peptide linker 3 followed by a CH2-CH3 domain;

(ii) a domain (A) comprising a binding region of the light chain variable domain of a first immunoglobulin (VL1) having the binding specificity of the A32, 7B2, CH28, or CH44 HIV-1 antibody, wherein the CH2-CH3 domain and domain (A) are separated by a peptide linker 4;

(iii) a domain (B) comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) specific for an epitope (2), wherein domains (A) and (B) are separated from one another by a peptide linker 1;

(iv) a domain (C) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (C) and domain B are separated by a peptide linker 2;

(II) the second polypeptide chain comprises in the N- to C-terminal direction:

(i) a domain (D) comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) specific for the epitope (2);

(ii) a domain (E) comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) having the binding specificity of the A32, 7B2, CH28, or CH44

comprising any one of the bispecific molecules of the disclosure, or a combination thereof in a therapeutically sufficient amount. In certain embodiments, the methods further comprise administering a latency activating agent.

[0037a] In another aspect, there is provided a use of a latency activating agent in the manufacture of a medicament for treating or preventing HIV-1 infection in a subject in need thereof, wherein the medicament is to be administered with a composition comprising a bispecific molecule, wherein the bispecific molecule comprises a first polypeptide chain and a second polypeptide chain covalently bonded to one another, wherein:

- (I) the first polypeptide chain comprises in the N- to C-terminal direction:
 - (i) a domain (A) comprising a binding region of the light chain variable domain of a first immunoglobulin (VL1) comprising the VL CDR3, CDR2 and CDR1 of HIV-1 antibody A32 (SEQ ID NO:78), 7B2 (SEQ ID NO:55), CH28 (SEQ ID NO:68), or CH44 (SEQ ID NO:74);
 - (ii) a domain (B) comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) comprising the VH CDR3, CDR2 and CDR1 of an antibody specific for an epitope of CD3 or CD16, wherein domains (A) and (B) are separated from one another by a peptide linker 1; and
 - (iii) a domain (C) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (C) and domain (B) are separated by a peptide linker 2;
- (II) the second polypeptide chain comprises in the N- to C-terminal direction:
 - (i) a domain (D) comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) comprising the VL CDR3, CDR2 and CDR1 of an antibody specific for the epitope of CD3 or CD16;
 - (ii) a domain (E) comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) comprising the VH CDR3, CDR2, and CDR1 of HIV-1 antibody A32 (SEQ ID NO:77), 7B2 (SEQ ID NO:56), CH28 (SEQ ID NO:67), or CH44 (SEQ ID NO:73), wherein domains (D) and (E) are separated from one another by a peptide linker 1; and
 - (iii) a domain (F) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (F) and domain (E) are separated by a peptide linker 2;

and wherein:

the domains (A) and (B) do not associate with one another to form an epitope binding site; the

domains (D) and (E) do not associate with one another to form an epitope binding site;
the domains (A) and (E) associate to form a binding site that binds the HIV-1 envelope like A32, 7B2, CH28, or CH44 antibody (1);
the domains (B) and (D) associate to form a binding site that binds an epitope of CD3 or CD16;
the K coil comprises residues 240-267 of SEQ ID NO: 19, and the E coil comprises residues 249-276 of SEQ ID NO: 17; and
peptide linker 2 comprises residues 244-248 of SEQ ID NO: 17.

[0037b] In another aspect, there is provided use of a latency activating agent and a composition comprising a bispecific molecule in the manufacture of a medicament for treating or preventing HIV-1 infection in a subject in need thereof, wherein the bispecific molecule comprises a first polypeptide chain and a second polypeptide chain covalently bonded to one another, wherein:

- (I) the first polypeptide chain comprises in the N- to C-terminal direction:
 - (i) a domain (A) comprising a binding region of the light chain variable domain of a first immunoglobulin (VL1) comprising the VL CDR3, CDR2 and CDR1 of HIV-1 antibody A32 (SEQ ID NO:78), 7B2 (SEQ ID NO:55), CH28 (SEQ ID NO:68), or CH44 (SEQ ID NO:74);
 - (ii) a domain (B) comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) comprising the VH CDR3, CDR2 and CDR1 of an antibody specific for an epitope of CD3 or CD16, wherein domains (A) and (B) are separated from one another by a peptide linker 1; and
 - (iii) a domain (C) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (C) and domain (B) are separated by a peptide linker 2;
- (II) the second polypeptide chain comprises in the N- to C-terminal direction:
 - (i) a domain (D) comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) comprising the VL CDR3, CDR2 and CDR1 of an antibody specific for the epitope of CD3 or CD16;
 - (ii) a domain (E) comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) comprising the VH CDR3, CDR2, and CDR1 of HIV-1 antibody A32 (SEQ ID NO:77), 7B2 (SEQ ID NO:56), CH28 (SEQ ID NO:67), or CH44 (SEQ ID NO:73), wherein domains (D) and (E) are separated from one another by a peptide linker 1; and
 - (iii) a domain (F) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (F) and domain (E) are separated by a peptide linker 2;

and wherein:

the domains (A) and (B) do not associate with one another to form an epitope binding site; the domains (D) and (E) do not associate with one another to form an epitope binding site; the domains (A) and (E) associate to form a binding site that binds the HIV-1 envelope like A32, 7B2, CH28, or CH44 antibody (1);

the domains (B) and (D) associate to form a binding site that binds an epitope of CD3 or CD16;

the K coil comprises residues 240-267 of SEQ ID NO: 19, and the E coil comprises residues 249-276 of SEQ ID NO: 17; and

peptide linker 2 comprises residues 244-248 of SEQ ID NO: 17.

BRIEF DESCRIPTION OF THE DRAWINGS

[0038] Figure 1 shows potency of ADCC-mediating mAbs. The ADCC activity of the 5 CHAVI mAbs against the 22 HIV-1 IMC is reported as maximum percentage of specific killing. Each dot represent the average activity of all the positive results for each group of mAbs against the individual IMCs. The lines represent the mean $\pm$ standard deviation. The black line represent the cut-off for positive response.

[0039] Figure 2 shows anti-HIV-1-DARTs-mediated cytotoxic activity. Activated CD4+ T cells from a HIV-1 seronegative donor were infected with HIV-1 subtype B BaL, AE CM235, and C 1086.c IMC (top to bottom). The cells were incubated with autologous resting CD8 T cells in the presence of six concentrations of the anti-HIV-1 (A32xCD3 $\blacklozenge$ and 7B2xCD3 $\blacksquare$) and control (4420xCD3 $\bullet$) DARTs for 6, 24, and 48 hours at an effector to target cell ratio of 33:1. The results are reported as maximum percentage of specific killing observed at each time point.

[0040] Figure 3 shows dose dependence of anti-HIV-1 BaL DARTs-mediated cytotoxic activity. Activated CD4+ T cells from a HIV-1 seronegative donor were infected with HIV-1 subtype B BaL. The cells were incubated with autologous resting CD8 T cells in the presence of six concentrations of the anti-HIV-1 (A32xCD3 $\blacklozenge$ and 7B2xCD3 $\blacksquare$) and control (4420xCD3 $\bullet$) DARTs for 48 hours at an effector to target cell ratio of 33, 11, and 3:1 (top to bottom). The results are reported as percentage of specific killing.

[0041] Figure 4. shows DART concentration to reach 50% Specific Killing. Activated CD4+ T cells from a HIV-1 seronegative donor were infected with HIV-1 subtype B BaL, AE CM235, and C 1086.c IMC. The cells were incubated with autologous resting CD8 T cells in the presence of six concentrations of the anti-HIV (A32xCD3, red; 7B2xCD3, blue) and control (4420xCD3, black) DARTs for 48 hours at an effector to target cell ratio of 33:1. Each bar represent the concentration required to detect 50% specific killing against each infected target population.

[0042] Figure 5 shows the sequences of CH27, CH28 and CH44 HIV-1 antibodies. CDRs are indicated in the sequences (SEQ ID Nos: 57-74).

What is claimed is:

1. A bispecific molecule comprising a first polypeptide chain, and a second polypeptide chain covalently bonded to one another, wherein:
 - (I) the first polypeptide chain comprises in the N- to C-terminal direction:
 - (i) a domain (A) comprising a binding region of the light chain variable domain of a first immunoglobulin (VL1) comprising the VL CDR3, CDR2 and CDR1 of HIV-1 antibody A32 (SEQ ID NO:78), 7B2 (SEQ ID NO:55), CH28 (SEQ ID NO:68), or CH44 (SEQ ID NO:74);
 - (ii) a domain (B) comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) comprising the VH CDR3, CDR2 and CDR1 of an antibody specific for an epitope of CD3 or CD16, wherein domains (A) and (B) are separated from one another by a peptide linker 1; and
 - (iii) a domain (C) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (C) and domain (B) are separated by a peptide linker 2;
 - (II) the second polypeptide chain comprises in the N- to C-terminal direction:
 - (i) a domain (D) comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) comprising the VL CDR3, CDR2 and CDR1 of an antibody specific for the epitope of CD3 or CD16;
 - (ii) a domain (E) comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) comprising the VH CDR3, CDR2, and CDR1 of HIV-1 antibody A32 (SEQ ID NO:77), 7B2 (SEQ ID NO:56), CH28 (SEQ ID NO:67), or CH44 (SEQ ID NO:73), wherein domains (D) and (E) are separated from one another by a peptide linker 1; and
 - (iii) a domain (F) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (F) and domain (E) are separated by a peptide linker 2;

and wherein:

the domains (A) and (B) do not associate with one another to form an epitope binding site; the domains (D) and (E) do not associate with one another to form an epitope binding site;

the domains (A) and (E) associate to form a binding site that binds the HIV-1 envelope like the A32, 7B2, CH28, or CH44 antibody (1);

the domains (B) and (D) associate to form a binding site that binds the epitope of CD3 or CD16;

the K coil comprises residues 240-267 of SEQ ID NO: 19, and the E coil comprises residues 249-276 of SEQ ID NO: 17; and

peptide linker 2 comprises residues 244-248 of SEQ ID NO: 17.

2. The bispecific molecule of claim 23 wherein:

- (i) the CH2-CH3 domain of the first polypeptide chain comprises SEQ ID NO: 42 and the CH2-CH3 domain of the third polypeptide chain comprises SEQ ID NO: 43; or
- (ii) the CH2-CH3 domain of the first polypeptide chain comprises SEQ ID NO: 43 and the CH2-CH3 domain of the third polypeptide chain comprises SEQ ID NO: 42.

3. The bispecific molecule of claim 1, wherein:

- (i) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 52, and the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 51; or
- (ii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 54, and the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 53.

4. The bispecific molecule of claim 1, wherein:

- (I) (i) the VL1 comprises the VLCDR3, CDR2, and CDR1 of SEQ ID NO: 78;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 77;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 52; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 51; or wherein
- (II) (i) the VL1 comprises VL CDR3, CDR2, and CDR1 of SEQ ID NO: 78;

- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 77;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 54; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 53; or
wherein
- (III) (i) the VL1 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 55;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 56;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 52; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 51; or
wherein
- (IV) (i) the VL1 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 55;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 56;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 54; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 53; or
wherein
- (V) (i) the VL1 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 68;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 67;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 52; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 51; or
wherein
- (VI) (i) the VL1 comprises the CDR1, CDR2 and CDR3 of SEQ ID NO: 68;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 67;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 54; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 53; or
wherein
- (VII) (i) the VL1 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 74;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 73;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 52; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 51; or
wherein
- (VIII) (i) the VL1 comprises the VL CDR1, CDR2 and CDR3 of SEQ ID NO: 74;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 73;

- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 54; and
 - (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 53.
5. The bispecific molecule of claim 1 or 3, wherein:
- (i) the domain (A) comprises SEQ ID NO: 78, SEQ ID NO: 55; SEQ ID NO: 68; or SEQ ID NO: 74;
 - (ii) the domain (E) comprises SEQ ID NO: 77, SEQ ID NO: 56; SEQ ID NO: 67; or SEQ ID NO: 73;
 - (iii) the domain (B) comprises SEQ ID NO: 51 or SEQ ID NO: 53; and
 - (iv) the domain (D) comprises SEQ ID NO: 52, or SEQ ID NO: 54.
6. The bispecific molecule of claim 1 or 3, wherein:
- (i) the domain (A) comprises SEQ ID NO: 78, the domain (B) comprises SEQ ID NO: 51, the domain (D) comprises SEQ ID NO: 52, and the domain (E) comprises SEQ ID NO: 77; or wherein
 - (ii) the domain (A) comprises SEQ ID NO: 55, the domain (B) comprises SEQ ID NO: 51, the domain (D) comprises SEQ ID NO: 52, and the domain (E) comprises SEQ ID NO: 56; or wherein
 - (iii) the domain (A) comprises SEQ ID NO: 78, the domain (B) comprises SEQ ID NO: 53, the domain (D) comprises SEQ ID NO: 54, and the domain (E) comprises SEQ ID NO: 77; or wherein
 - (iv) the domain (A) comprises SEQ ID NO: 55, the domain (B) comprises SEQ ID NO: 53, the domain (D) comprises SEQ ID NO: 54, and the domain (E) comprises SEQ ID NO: 56.
7. A composition comprising any one of the bispecific molecules of claims 1-6 or any combination thereof.
8. The composition of claim 7, further comprising a second bispecific molecule comprising a first arm with the binding specificity of HIV-1 antibody A32, HIV-1 antibody 7B2, HIV-1 antibody CH28, or HIV-1 antibody CH44 and a second arm targeting CD3 or CD16, wherein the first and second bispecific molecules are different.
9. Use of a composition comprising any one of the bispecific molecules of claims 1-6 or a

combination of any one of the bispecific molecules in the manufacture of a medicament for treating or preventing HIV-1 infection in a subject in need thereof.

10. The use of claim 9, wherein the medicament is to be administered with a latency activating agent.
11. The use of claim 10, wherein the latency activating agent is vorinostat, romidepsin, panobinostat, disulfiram, JQ1, bryostatin, PMA, inonomycin, or any combination thereof.
12. A vector comprising nucleic acids comprising nucleotides encoding the bispecific molecules of any one of claims 1-6.
13. A composition comprising a vector comprising a nucleic acid encoding the bispecific molecules of any one of claims 1-6.
14. Use of a latency activating agent in the manufacture of a medicament for treating or preventing HIV-1 infection in a subject in need thereof, wherein the medicament is to be administered with a composition comprising a bispecific molecule, wherein the bispecific molecule comprises a first polypeptide chain and a second polypeptide chain covalently bonded to one another, wherein:
 - (I) the first polypeptide chain comprises in the N- to C-terminal direction:
 - (i) a domain (A) comprising a binding region of the light chain variable domain of a first immunoglobulin (VL1) comprising the VL CDR3, CDR2 and CDR1 of HIV-1 antibody A32 (SEQ ID NO:78), 7B2 (SEQ ID NO:55), CH28 (SEQ ID NO:68), or CH44 (SEQ ID NO:74);
 - (ii) a domain (B) comprising a binding region of a heavy chain variable domain of a second immunoglobulin (VH2) comprising the VH CDR3, CDR2 and CDR1 of an antibody specific for an epitope of CD3 or CD16, wherein domains (A) and (B) are separated from one another by a peptide linker 1; and
 - (iii) a domain (C) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (C) and domain (B) are separated by a peptide linker 2;
 - (II) the second polypeptide chain comprises in the N- to C-terminal direction:
 - (i) a domain (D) comprising a binding region of a light chain variable domain

of the second immunoglobulin (VL2) comprising the VL CDR3, CDR2 and CDR1 of an antibody specific for the epitope of CD3 or CD16;

- (ii) a domain (E) comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) comprising the VH CDR3, CDR2, and CDR1 of HIV-1 antibody A32 (SEQ ID NO:77), 7B2 (SEQ ID NO:56), CH28 (SEQ ID NO:67), or CH44 (SEQ ID NO:73), wherein domains (D) and (E) are separated from one another by a peptide linker 1; and
- (iii) a domain (F) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (F) and domain (E) are separated by a peptide linker 2;

and wherein:

the domains (A) and (B) do not associate with one another to form an epitope binding site; the domains (D) and (E) do not associate with one another to form an epitope binding site;

the domains (A) and (E) associate to form a binding site that binds the HIV-1 envelope like A32, 7B2, CH28, or CH44 antibody (1);

the domains (B) and (D) associate to form a binding site that binds an epitope of CD3 or CD16;

the K coil comprises residues 240-267 of SEQ ID NO: 19, and the E coil comprises residues 249-276 of SEQ ID NO: 17; and

peptide linker 2 comprises residues 244-248 of SEQ ID NO: 17.

15. Use of a latency activating agent and a composition comprising a bispecific molecule in the manufacture of a medicament for treating or preventing HIV-1 infection in a subject in need thereof, wherein the bispecific molecule comprises a first polypeptide chain and a second polypeptide chain covalently bonded to one another, wherein:

- (I) the first polypeptide chain comprises in the N- to C-terminal direction:

- (i) a domain (A) comprising a binding region of the light chain variable domain of a first immunoglobulin (VL1) comprising the VL CDR3, CDR2 and CDR1 of HIV-1 antibody A32 (SEQ ID NO:78), 7B2 (SEQ ID NO:55), CH28 (SEQ ID NO:68), or CH44 (SEQ ID NO:74);
- (ii) a domain (B) comprising a binding region of a heavy chain variable

domain of a second immunoglobulin (VH2) comprising the VH CDR3, CDR2 and CDR1 of an antibody specific for an epitope of CD3 or CD16, wherein domains (A) and (B) are separated from one another by a peptide linker 1; and

(iii) a domain (C) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (C) and domain (B) are separated by a peptide linker 2;

(II) the second polypeptide chain comprises in the N- to C-terminal direction:

(i) a domain (D) comprising a binding region of a light chain variable domain of the second immunoglobulin (VL2) comprising the VL CDR3, CDR2 and CDR1 of an antibody specific for the epitope of CD3 or CD16;

(ii) a domain (E) comprising a binding region of a heavy chain variable domain of the first immunoglobulin (VH1) comprising the VH CDR3, CDR2, and CDR1 of HIV-1 antibody A32 (SEQ ID NO:77), 7B2 (SEQ ID NO:56), CH28 (SEQ ID NO:67), or CH44 (SEQ ID NO:73), wherein domains (D) and (E) are separated from one another by a peptide linker 1; and

(iii) a domain (F) comprising a heterodimer promoting domain including a K coil or E coil; wherein the heterodimer promoting domain (F) and domain (E) are separated by a peptide linker 2;

and wherein:

the domains (A) and (B) do not associate with one another to form an epitope binding site; the domains (D) and (E) do not associate with one another to form an epitope binding site;

the domains (A) and (E) associate to form a binding site that binds the HIV-1 envelope like A32, 7B2, CH28, or CH44 antibody (1);

the domains (B) and (D) associate to form a binding site that binds an epitope of CD3 or CD16;

the K coil comprises residues 240-267 of SEQ ID NO: 19, and the E coil comprises residues 249-276 of SEQ ID NO: 17; and

peptide linker 2 comprises residues 244-248 of SEQ ID NO: 17.

16. The use of claim 28, wherein:

- (i) the CH2-CH3 domain of the first polypeptide chain comprises SEQ ID NO: 42 and the CH2-CH3 domain of the third polypeptide chain comprises SEQ ID NO: 43; or
- (ii) the CH2-CH3 domain of the first polypeptide chain comprises SEQ ID NO: 43 and the CH2-CH3 domain of the third polypeptide chain comprises SEQ ID NO: 42.

17. The use of claim 14 or 15, wherein:

- (i) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 52, and the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 51;
- (ii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 54, and the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 53.

18. The use of claim 14 or 15, wherein:

- (I) (i) the VL1 comprises the VLCDR3, CDR2, and CDR1 of SEQ ID NO: 78;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 77;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 52; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 51;
- (II) (i) the VL1 comprises VL CDR3, CDR2, and CDR1 of SEQ ID NO: 78;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 77;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 54; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 53;
- (III) (i) the VL1 comprises the VLCDR3, CDR2, and CDR1 of SEQ ID NO: 55;

- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 56;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 52; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 51;
- (IV) (i) the VL1 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 55;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 56;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 54; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 53;
- (V) (i) the VL1 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 68;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 67;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 52; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 51;
- (VI) (i) the VL1 comprises the VL CDR1, CDR2 and CDR3 of SEQ ID NO: 68;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 67;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 54; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 53; or
- (VII) (i) the VL1 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 74;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 73;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 52; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 51;
- (VIII) (i) the VL1 comprises the VL CDR1, CDR2 and CDR3 of SEQ ID NO: 74;
- (ii) the VH1 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 73;
- (iii) the VL2 comprises the VL CDR3, CDR2, and CDR1 of SEQ ID NO: 54; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 53.

19. The use of claim 14 or 15, wherein:

- (i) the domain (A) comprises SEQ ID NO: 78, SEQ ID NO: 55; SEQ ID NO: 68; or SEQ ID NO: 74;
- (ii) the domain (E) comprises SEQ ID NO: 77, SEQ ID NO: 56; SEQ ID NO: 67; or SEQ ID NO: 73;
- (iii) the domain (B) comprises SEQ ID NO: 51 or SEQ ID NO: 53; and
- (iv) the domain (D) comprises SEQ ID NO: 52, or SEQ ID NO: 54.

20. The use of claim 14 or 15, wherein:

- (i) the domain (A) comprises SEQ ID NO: 78, the domain (B) comprises SEQ ID NO: 51, the domain (D) comprises SEQ ID NO: 52, and the domain (E) comprises SEQ ID NO: 77;
- (ii) the domain (A) comprises SEQ ID NO: 55, the domain (B) comprises SEQ ID NO: 51, the domain (D) comprises SEQ ID NO: 52, and the domain (E) comprises SEQ ID NO: 56;
- (iii) the domain (A) comprises SEQ ID NO: 78, the domain (B) comprises SEQ ID NO: 53, the domain (D) comprises SEQ ID NO: 54, and the domain (E) comprises SEQ ID NO: 77; or
- (iv) the domain (A) comprises SEQ ID NO: 55, the domain (B) comprises SEQ ID NO: 53, the domain (D) comprises SEQ ID NO: 54, and the domain (E) comprises SEQ ID NO: 56.

21. The use of any one of claims 14-20, wherein the composition further comprises a second bispecific binding molecule, comprising a first arm with the binding specificity of HIV-1 antibody A32, HIV-1 antibody 7B2, HIV-1 antibody CH28, HIV-1 antibody CH44 and a second arm targeting CD3 or CD 16, and wherein the first and second bispecific molecules are different.

22. The use of any one of claims 14-21, wherein the latency activating agent is vorinostat, romidepsin, panobinostat, disulfiram, JQ1, bryostatin, PMA, inonomecin, or any combination thereof.

23. The bispecific molecule of claim 1, 3, 4, 5, or 6 wherein:

- (i) the first polypeptide chain further comprises a CH2-CH3 domain, wherein the CH2-CH3 domain and domain (C) are separated by a peptide linker 3 or a spacer-linker 3;
- (ii) the bispecific molecule further comprises a third polypeptide chain comprising in the N- to C-terminal direction a peptide linker 3 and a CH2-CH3 domain; and
- (iii) the CH2-CH3 domains of the first and third polypeptide form an Fc chain.

24. A composition comprising any one of the bispecific molecules of claim 23 or any combination thereof.

25. Use of a composition comprising any one of the bispecific molecules of claim 23 or a combination of any one of the bispecific molecules in the manufacture of a medicament for treating or preventing HIV-1 infection in a subject in need thereof.

26. A vector comprising nucleic acids comprising nucleotides encoding the bispecific molecules of any one of claim 23.
27. A composition comprising a vector comprising a nucleic acid encoding the bispecific molecules of any one of claim 23.
28. The use of claim 14, 15, 17, 18, 19 or 20 wherein:
- (i) the first polypeptide chain further comprises a CH2-CH3 domain, wherein the CH2-CH3 domain and domain (C) are separated by a peptide linker 3 or a spacer-linker 3;
 - (ii) the bispecific molecule further comprises a third polypeptide chain comprising in the N- to C-terminal direction a peptide linker 3 and a CH2-CH3 domain; and
 - (iii) the CH2-CH3 domains of the first and third polypeptide form an Fc chain.
29. The use of claim 28, wherein the composition further comprises a second bispecific binding molecule, comprising a first arm with the binding specificity of HIV-1 antibody A32, HIV-1 antibody 7B2, HIV-1 antibody CH28, HIV-1 antibody CH44 and a second arm targeting CD3 or CD 16, and wherein the first and second bispecific molecules are different.
30. The use of claim 28, wherein the latency activating agent is vorinostat, romidepsin, panobinostat, disulfiram, JQ1, bryostatin, PMA, inonomecin, or any combination thereof.