

Bispecific Molecules Comprising an HIV-1 Envelope Targeting Arm

[0001] This invention claims the benefit of and priority to U.S. Serial No. 62/056,834 filed September 29, 2014, and U.S. Serial No. 62/206,586 filed August 18, 2015, the contents of which are hereby incorporated by reference in their entirety.

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[0003] All patents, patent applications and publications cited herein are hereby incorporated by reference in their entirety. The disclosure of these publications in their entirety are hereby incorporated by reference into this application in order to more fully describe the state of the art as known to those skilled therein as of the date of the invention described herein.

GOVERNMENT SUPPORT

[0004] This invention was made with government support under Grant Nos. U19 AI067854 and UM1 AI100645 awarded by the National Institutes of Health. The government has certain rights in the invention.

TECHNICAL FIELD

[0005] The invention is directed to HIV-1 antibodies and bispecific molecules comprising an HIV-1 binding domain and an effector cell binding domain, and their uses.

BACKGROUND

[0006] Highly Active Antiretroviral Therapy (HAART) has been effective in reducing the viral burden and ameliorating the effects of HIV-1 infection in infected individuals. However, despite this therapy the virus persists in the individual due to latent reservoir of HIV infected cells which evade this treatment. Thus, there is a need for therapeutic agents for treatment of HIV-1 infected individuals, as well as agents that target virus infected cells and have to potential to reduce the latent reservoir of HIV-1 infected cells.

SUMMARY

[0007] The present disclosure is directed to bispecific molecules, e.g. covalently linked polypeptide chains to form antibodies, covalent diabodies and/or covalent diabody molecules and their use in the treatment of HIV-1. In certain embodiments, the bispecific molecules of the present disclosure can bind to two different targets or epitopes on two different cells wherein the first epitope is expressed on a different cell type than the second epitope, such that the

bispecific molecules can bring the two cells together. In certain embodiments, the bispecific molecules of the present disclosure can bind to two different cells, wherein the bispecific molecules comprises an arm with the binding specificity of A32, 7B2, CH27, CH28 or CH44, which arm binds to the HIV-1 envelope expressed on a first cell, e.g. HIV infected cell, and a second arm with the binding specificity for an epitope expressed on a different cell type than the first cell, such that the bispecific molecules can bring the two cells together. In certain embodiment, the second cell is in effector cell which expresses CD3 or CD16.

[0008] In certain embodiments an antibody binds specifically to a particular target, even where the specific epitope may not be know, peptide or polysaccharide (such as an antigen present on the surface of a pathogen, for example gp120, gp41, or CD3) and do not bind in a significant amount to other proteins or polysaccharides present in the sample or subject. Specific binding can be determined by methods known in the art. Various competitive binding assays are known in the art. With reference to an antibody antigen complex, in certain embodiments specific binding of the antigen and antibody has a KD of less than about 10^6 Molar, such as less than about 10^6 Molar, 10^7 Molar, 10^8 Molar, 10^9 , or even less than about 10^{10} Molar.

[0009] Disclosed are bispecific molecules 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) having the binding specificity of the A32, 7B2, CH28, or CH44 HIV-1 envelope antibody;

(ii) 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; 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) 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 HIV-1 antibody, 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; and

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); and the domains (B) and (D) associate to form a binding site that binds the epitope (2).

[0010] Disclosed are bispecific molecules 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 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;

(ii) 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;

(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;

(iv) 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 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 HIV-1 antibody, wherein domains (D) and (E) are separated from one another by a peptide linker 1;

(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, a second polypeptide chain, and a third 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 the A32, 7B2, CH28, or CH44 HIV-1 antibody;
- (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;
- (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; and
- (iv) 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 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 the

- A32, 7B2, CH28, or CH44 HIV-1 antibody, 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;
- (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 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;
- peptide linker 2 comprises residues 244-248 of SEQ ID NO: 17; and

the CH2-CH3 domains of the first and third polypeptide form an Fc chain.

- [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

[0019] In certain embodiments, the bispecific molecule comprises the first polypeptide of SEQ ID NO: 9, and the complementary second polypeptide of SEQ ID NO: 11. In certain embodiments, the bispecific molecule comprises the first polypeptide of SEQ ID NO: 13, and the complementary second polypeptide of SEQ ID NO: 15. In certain embodiments, the bispecific molecule comprises the first polypeptide of SEQ ID NO: 17, and the complementary second polypeptide of SEQ ID NO: 19. In certain embodiments, the bispecific molecule comprises the first polypeptide of SEQ ID NO: 21, and the complementary second polypeptide of SEQ ID NO: 23. In certain embodiments, the bispecific molecule comprises the first polypeptide of SEQ ID NO: 25, and the complementary second polypeptide of SEQ ID NO: 27.

[0020] In certain embodiments, the bispecific molecule comprises consisting essentially of the first polypeptide of SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 17, SEQ ID NO: 21, SEQ ID NO: 25, or SEQ ID NO: 44 and the second polypeptide of SEQ ID NO: 11, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 23, SEQ ID NO: 27, or SEQ ID NO: 45.

[0021] In certain embodiments, the bispecific molecule comprises consisting of the first polypeptide of SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 17, SEQ ID NO: 21, SEQ ID NO: 25, or SEQ ID NO: 44 and the second polypeptide of SEQ ID NO: 11, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 23, SEQ ID NO: 27, or SEQ ID NO: 45.

[0022] In certain embodiments, the bispecific molecule comprises SEQ ID NO: 46, 47 and 48. In certain embodiments, the bispecific molecule consists essentially of SEQ ID NO: 46, 47 and 48. In certain embodiments, the bispecific molecule consists of SEQ ID NO: 46, 47 and 48. In certain embodiments, the first polypeptide of the bispecific molecule comprises SEQ ID NO: 46, the second polypeptide of the bispecific molecule comprises SEQ ID NO: 47, and the third polypeptide of the bispecific molecule comprises SEQ ID NO: 48.

[0023] In another aspect, there is provided a composition comprising any one of the bispecific molecules or any combination thereof. In certain embodiments, the composition comprises a composition comprising a bispecific 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 CD16. In certain embodiment, the bispecific molecule comprises an Fc portion or any other modification which extends its serum half-life. In certain embodiments, the composition further comprises a second

bispecific molecule comprising a first arm with the binding specificity of the HIV-1 antibody A32, HIV-1 antibody 7B2, HIV-1 antibody CH28, HIV-1 antibody CH44 and a second arm targeting CD3 or CD16, wherein the first and second bispecific molecules are different.

[0024] Disclosed is a method to treat or prevent HIV-1 infection in a subject in need thereof comprising administering to the subject a composition comprising any one of the bispecific molecules of the disclosure or a combination of any one of the bispecific molecules in a therapeutically effective amount. In another aspect, there is provided use of a composition comprising any one of the bispecific molecules described herein 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. In certain embodiments, the methods of claim further comprise administering a latency activating agent. In some embodiments, the latency activating agent is vorinostat, romidepsin, panobinostat, disulfiram, JQ1, bryostatin, PMA, inonomecin, or any combination thereof.

[0025] Disclosed are nucleic acids comprising nucleotides encoding the bispecific molecules of the disclosure. In another aspect, there is provided a vector comprising nucleic acids comprising nucleotides encoding the bispecific molecules of the disclosure. In another aspect, there is provided a composition comprising a vector comprising a nucleic acid encoding the bispecific molecules described herein. Disclosed is a cell line comprising vectors or nucleic acids encoding the bispecific molecules of the disclosure, wherein the vectors encode polypeptide chains for expression of the bispecific molecules of the disclosure, e.g., polypeptide chain 1 and polypeptide chain 2, or polypeptide chain 1, polypeptide chain 2 and polypeptide chain 3. In certain embodiments, the vector is suitable for gene delivery and expression. In certain embodiment, the vector is an adenoviral vector, an adeno associated virus based vector, or a combination thereof.

[0026] Disclosed is a bispecific molecule comprising a polypeptide with a dual affinity retargeting reagent (DART), wherein the DART comprises a diabody molecule comprising a first polypeptide chain and a second polypeptide chain, covalently bonded to one another, wherein:

(A) the first polypeptide chain comprises:

(i) a domain (A) comprising a binding region of the light chain variable domain of a first immunoglobulin (VL1) specific for the first epitope (1); wherein the first VL1 comprises, consists essentially of, consists of the VL or VLCDR1, VLCDR2, and VLCDR3 from A32, 7B2, CH27, CH28, or CH44 HIV-1 antibody,

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

(iii) a domain (C) comprising a heterodimer promoting domain;

(B) the second polypeptide chain comprises:

(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) specific for the first epitope (1); wherein the first VH1 comprises, consists essentially of, consists of the VH or VHCDR1, VHCDR2, and VHCDR3 from A32, 7B2, CH27, CH28, or CH44 HIV-1 antibody, wherein domains (D) and (E) are separated from one another by a peptide linker, and

(iii) a domain (F) comprising a heterodimer promoting 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 A32, 7B2, CH27, CH28, or CH44 HIV-1 antibody epitope (1); the domains (B) and (D) associate to form a binding site that binds the second target, e.g., epitope (2).

[0027] Disclosed are bispecific molecules, wherein the HIV antibodies VH and VL domains, and the CD3 and CD16 VH and VL domains are in a different orientation. For example, in a non-limiting embodiment, the VL1 domain in polypeptide chain 1 is from CD3, and VH2 domain is from an HIV envelope binding antibody. In this embodiment, the VH1 domain of polypeptide 2 is from CD3, and VL2 domain is from is from an HIV envelope binding antibody.

[0028] Disclosed is a bispecific molecule capable of specific binding to HIV-1 envelope and to an epitope of CD3, wherein the bispecific molecule comprises a first polypeptide chain and a second polypeptide chain, covalently bonded to one another, wherein:

A. the first polypeptide chain comprises, in the N-terminal to C-terminal direction:

- i. a Domain 1, comprising
 - (1) a sub-Domain (1A), which comprises a VL Domain of a monoclonal antibody capable of binding to CD3 (VLCD3); and

binds to the 7B2-HIV1 envelope epitope and CD3, or CD16. In certain embodiments, the bispecific molecule binds to the CH27-HIV-1 envelope epitope and CD3, or CD16. In certain embodiments, the bispecific molecule binds to the CH28-HIV-1 envelope epitope and CD3, or CD16. In certain embodiments, the bispecific molecule binds to the CH44-HIV-1 envelope epitope and CD3, or CD16.

[0031] In certain embodiments, the bispecific molecule has the binding specificity of the A32 HIV-1-envelope antibody. In certain embodiments, the bispecific molecule has the binding specificity of the 7B2 HIV-1-envelope antibody. The bispecific molecule has the binding specificity of the CH27 HIV-1-envelope antibody. The bispecific molecule has the binding specificity of the CH28 HIV-1-envelope antibody. In certain embodiments, the bispecific molecule has the binding specificity of the CH44 HIV-1-envelope antibody.

[0032] In certain embodiments a bispecific molecule of the disclosure comprises, consists essentially of or consists of sequences as described herein, e.g. Table 2 and Table 3)

[0033] In certain embodiments a bispecific molecule of the disclosure comprises, consists essentially of or consists of SEQ ID NO: 9 and 11; SEQ ID NO: 13 and 15, SEQ ID NO: 17 and 19; SEQ ID NO: 21 and 23; SEQ ID NO: 25 and 27; SEQ ID NO: 44 and 45 (See Table 2 and Table 3).

[0034] Disclosed are compositions comprising any of the bispecific molecule described herein, or a combination thereof. In certain embodiments, these compositions are formulated as pharmaceutical composition for therapeutic use.

[0035] In certain embodiments, the disclosure is directed to nucleic acids which encode the bispecific molecules of the disclosure. In certain embodiments, these nucleic acids are comprised in a vector, and are operably linked to a promoter. Disclosed are cell lines, or isolated cells, which comprise nucleic acids for the expression of the bispecific molecules of the disclosure.

[0036] Disclosed are compositions comprising the bispecific molecules of the disclosure or nucleic acids encoding the same for use in methods of treating or preventing HIV infection. In some embodiments, these methods further comprise administering a Latency Activating Reagent. Non-limiting examples of these include HDAC inhibitors, e.g, vorinostat, romidepsin, panobinostat, disulfiram, JQ1, bryostatins, PMA, inonomecin, or any combination thereof. In some embodiments, this combination therapy targets the pool of latently infected HIV cells.

[0037] Disclosed are methods for treating or preventing an HIV infection in a subject, the method comprising administering to the subject a composition

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, a second polypeptide chain, and a third 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 the A32, 7B2, CH28, or CH44 HIV-1 antibody;
 - (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;
 - (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; and
 - (iv) 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 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 the A32, 7B2, CH28, or CH44 HIV-1 antibody, 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;
- (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 an epitope of CD3 or CD16; and

the CH2-CH3 domains of the first and third polypeptide form an Fc chain.

[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, a second polypeptide chain, and a third 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 the A32, 7B2, CH28, or CH44 HIV-1 antibody;
 - (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;
 - (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; and
 - (iv) 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 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 the A32, 7B2, CH28, or CH44 HIV-1 antibody, 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;

(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 an epitope of CD3 or CD16; and

the CH2-CH3 domains of the first and third polypeptide form an Fc chain.

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, a second polypeptide chain, and a third 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 the A32, 7B2, CH28, or CH44 HIV-1 antibody;
 - (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;
 - (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; and
 - (iv) 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 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 the A32, 7B2, CH28, or CH44 HIV-1 antibody, 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;
 - (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 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;
 - peptide linker 2 comprises residues 244-248 of SEQ ID NO: 17; and
 - the CH2-CH3 domains of the first and third polypeptide form an Fc chain.
2. The bispecific molecule of claim 1 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 or 2, 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 or 2, 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 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 CDR3 of SEQ ID NO: 52; and
 - (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 51; or wherein
- (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: 54; and
 - (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 53; or wherein
- (IV) (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
- (V) (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
- (VI) (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
- (VII) (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, 2, 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, a second polypeptide chain, and a third 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 the A32, 7B2, CH28, or CH44 HIV-1 antibody;
 - (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;
 - (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; and
 - (iv) 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 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 the A32, 7B2, CH28, or CH44 HIV-1 antibody, 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;

(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 an epitope of CD3 or CD16; and

the CH2-CH3 domains of the first and third polypeptide form an Fc chain.

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, a second polypeptide chain, and a third 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 the A32, 7B2, CH28, or CH44 HIV-1 antibody;
 - (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;
- (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; and
 - (iv) 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 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 the A32, 7B2, CH28, or CH44 HIV-1 antibody, 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;
- (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 an epitope of CD3 or CD16; and

the CH2-CH3 domains of the first and third polypeptide form an Fc chain.

16. The use of claim 14 or 15, 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 any one of claims 14-16, wherein:

- (i) the K coil comprises SEQ ID NO: 8 and the E coil comprises SEQ ID NO: 7, and the peptide linker 2 comprises SEQ ID NO: 2; or
- (ii) the K coil comprise residues 240-267 of SEQ ID NO: 19, and the E coil comprises residues 249-276 of SEQ ID NO: 17, and the peptide linker 2 comprises residues 244-248 of SEQ ID NO: 17.

18. The use of any one of claims 14-16, 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.

19. The use of any one of claims 14-16, 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;
- (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 CDR3 of SEQ ID NO: 54; and
- (iv) the VH2 comprises the VH CDR3, CDR2, and CDR1 of SEQ ID NO: 53;
- (IV) (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;
- (V) (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
- (VI) (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;
- (VII) (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.

20. The use of any one of claims 14-16, 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.

21. The use of any one of claims 14-16, 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.

22. The use of any one of claims 14-21, 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, wherein the first and second bispecific molecules are different.

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