MULTI-SPECIFIC ANTIGEN BINDING MOLECULES TARGETING HIV AND METHODS OF USE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application No. 63/070,141, filed on August 25, 2020 and U.S. Provisional Application No. 63/163,713, filed on March 19, 2021, which are hereby incorporated herein by reference in their entireties for all purposes.

FIELD

[0002] Provided are multi-specific antigen binding molecules and antigen binding fragments thereof for one or both of the treatment and the prevention of human immunodeficiency virus (HIV) infection.

SEQUENCE LISTING

[0003] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on June 25, 2021, is named 1337-WO-PCT_SL.txt and is 1,167,237 bytes in size.

BACKGROUND

[0004] Human immunodeficiency virus (HIV) infection and related diseases are a major public health problem worldwide. Most currently approved therapies for HIV infection target the viral reverse transcriptase, protease enzymes, and integrase. Yet resistance of HIV to these existing drugs, long-term toxicity, and lack of patient adherence to daily dosing regimens have been associated with these therapies. Therefore, it is important to discover and develop new anti-HIV antibodies with advantageous properties suitable for therapeutic uses.

[0005] WO 2005/058963; WO 2010/107939; WO 2012/030904; WO 2012/158948; WO 2013/090644; WO 2013/016468; WO 2013/192589; WO 2014/063059 and WO 2018/125813 describe human anti-HIV antibodies derived from memory B cells of HIV-infected donors, which are capable of inhibiting infection by HIV-1 species from a plurality of clades. The therapeutic use of the antibodies is limited due to their intra-patient viral coverage, pharmacokinetics, induction of anti-drug antibodies, off-target binding (*i.e.*, polyspecificity), and other properties that interfere with efficient manufacturing and storage, however.

[0006] Multi-specific antigen binding molecules are single molecules that can bind at least two different antigens. Bispecific antigen binding molecules are single molecules that can bind two different antigens. This property can be leveraged in a number of ways to improve the efficacy and/or selectivity of biotherapeutics, for example, by neutralizing the activity of two disease mediators instead of one, enhancing selective binding to disease over normal tissue, generating novel functions (*e.g.* Factor VIII mimicry of Emicizumab) or by directly recruiting immune cells for targeted killing (*e.g.* Blinatumomab recruitment of CD3+ T-cells to kill CD19+ B-cells). As such, the field of bispecific antibodies is rapidly growing, with potential applications in nearly every therapeutic area. There are currently three approved bispecific products (Blinatumomab, Ebmicizumab and Catumaxomab) and more than 50 clinical trials underway (antibodysociety.org).

[0007] A large number of different bispecific antibody formats have been described, with many of these being used to develop therapeutic molecules (*e.g.*, reviewed in Spiess and Carter, 2015, Mol. Immunol, 67: 95-106). Production of bispecific antibodies is typically more complex than that of conventional antibodies. For instance, generation of Fab-arm exchanged bispecifics such as the Genmab Duobody platform (Labrijn et. al., 2013, PNAS, 110: 5145-5150) requires separate production of each half-antibody (as an IgG), then mixing these together under special conditions that enables Fab arm exchange of the two half antibodies to generate the desired bispecific molecule. The need for separate cell lines to produce each half antibody (or parental unreacted reduced antibody) IgG, purification of these intermediates, and optimization of the Fab arm exchange reaction and process to purify the target bispecific away from residual half antibody IgG adds significant time and complexity to research and development.

[0008] Other bispecific format strategies, such as those that pair an scFv fusion protein with a Fab-Fc fusion protein (*e.g.*, WO 2016/086196; WO 2016/071004), ensure that there is only a single light chain as a strategy to avoid Fab arm exchange. Challenges with bispecific formats that include an scFv arise because the scFv moiety oftentimes does not bind the target antigen with desired affinity, can have undesirable off-target binding, and can contribute to a bispecific molecule that does not express well, is difficult to purify and has insufficient serum half-life to allow efficacy for an intended indication.

SUMMARY

[0009] In one aspect, provided is are multi-specific (*e.g.*, bispecific) antigen binding molecules that binds to human CD3 and an HIV antigen.

[0010] In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule comprises:(a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises: (i) a first VH-complementarity determining region (CDR) 1 comprising the amino acid sequence of TYAMN (SEQ ID NO:1); (ii) a first VH-CDR2 comprising the amino acid sequence of RIRSKYNNYATYYAX$_1$SVKX$_2$, wherein X$_1$ is A or D and X$_2$ is G or S (SEQ ID NO:2); (iii) a first VH-CDR3 comprising the amino acid sequence of HGNFGX$_3$SYVSWFAY, wherein X$_3$ is H or N (SEQ ID NO:3); (iv) a first VL-CDR1 comprising the amino acid sequence of GSSTGAVTTGHYAN (SEQ ID NO: 4); (v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$X$_5$RAP, wherein X$_4$X$_5$ is SN or NK (SEQ ID NO:5); and (vi) a first VL-CDR3 comprising the amino acid sequence of ALWYSNX$_6$WV, wherein X$_6$ is L or R (SEQ ID NO:6), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Kabat; and (b) a second antigen binding domain that binds to an HIV antigen. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule that binds to human CD3 and a second antigen, wherein the antigen binding molecule comprises: (a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises: (i) a first VH-complementarity determining region (CDR) 1 comprising the amino acid sequence of TYAMN (SEQ ID NO:1); (ii) a first VH-CDR2 comprising the amino acid sequence of RIRSKYNNYATYYAX$_1$SVKX$_2$, wherein X$_1$ is A or D and X$_2$ is G or S (SEQ ID NO:2); (iii) a first VH-CDR3 comprising the amino acid sequence of HGNFGX$_3$SYVSWFAY, wherein X$_3$ is H or N (SEQ ID NO:3); (iv) a first VL-CDR1 comprising the amino acid sequence of GSSTGAVTTGHYAN (SEQ ID NO: 4); (v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$X$_5$RAP, wherein X$_4$X$_5$ is SN or NK (SEQ ID NO:5); and (vi) a first VL-CDR3 comprising the amino acid sequence of ALWYSNX$_6$WV, wherein X$_6$ is L or R (SEQ ID NO:6), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Kabat; and (b) a second antigen binding domain that binds to a second antigen. In some embodiments (i) the first VH-complementarity determining region (CDR) 1 comprises the amino acid sequence of TYAMN (SEQ ID NO:1); (ii) the first VH-CDR2 comprises the amino acid sequence of RIRSKYNNYATYYADSVKX$_2$, wherein X$_2$ is G or S (SEQ ID NO:7); (iii) the first VH-CDR3 comprises the amino acid sequence of HGNFGHSYVSWFAY (SEQ ID NO:8); (iv) the first VL-CDR1 comprises the amino acid sequence of GSSTGAVTTGHYAN (SEQ ID NO: 4); (v)

the first VL-CDR2 comprises the amino acid sequence of GTSNRAP (SEQ ID NO:9); and (vi) the first VL-CDR3 comprises the amino acid sequence of ALWYSNRWV (SEQ ID NO:10). In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Kabat): (i) SEQ ID NOs: 1, 11, 8, 4, 5 and 10; (ii) SEQ ID NOs: 1, 11, 8, 4, 9 and 10; (iii) SEQ ID NOs: 1, 12, 8, 4, 9 and 10; (iv) SEQ ID NOs: 1, 13, 8, 4, 14 and 15; (v) SEQ ID NOs: 1, 13, 16, 4, 14 and 15; or (vi) SEQ ID NOs: 1, 11, 8, 4, 14 and 10. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Kabat): (i) SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or (ii) SEQ ID NOs: 1, 12, 8, 4, 9 and 10. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10.

[0011] In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule comprises: (a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises: (i) a first VH-CDR1 comprising the amino acid sequence of GFTFNTY (SEQ ID NO:17); (ii) a first VH-CDR2 comprising the amino acid sequence of SKYNNY (SEQ ID NO:18); (iii) a first VH-CDR3 comprising the amino acid sequence of GNFGX_3SYVSWFA, wherein X_3 is H or N (SEQ ID NO:19); (iv) a first VL-CDR1 comprising the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 20); (v) a first VL-CDR2 comprising the amino acid sequence of GTX_4, wherein X_4 is N or S (SEQ ID NO:21); and (vi) a first VL-CDR3 comprising the amino acid sequence of WYSNX_6W, wherein X_6 is L or R (SEQ ID NO:22), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Chothia; and (b) a second antigen binding domain that binds to an HIV antigen. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule comprises: (a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises: (i) a first VH-CDR1 comprising the amino acid sequence of GFTFNTY (SEQ ID NO:17); (ii) a first VH-CDR2 comprising the amino acid sequence of SKYNNY (SEQ ID NO:18); (iii) a first VH-

CDR3 comprising the amino acid sequence of GNFGX$_3$SYVSWFA, wherein X$_3$ is H or N (SEQ ID NO:19); (iv) a first VL-CDR1 comprising the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 20); (v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$, wherein X$_4$ is N or S (SEQ ID NO:21); and (vi) a first VL-CDR3 comprising the amino acid sequence of WYSNX$_6$W, wherein X$_6$ is L or R (SEQ ID NO:22), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Chothia; and (b) a second antigen binding domain that binds to a second antigen. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Chothia): (i) SEQ ID NOs: 17, 18, 23, 20, 21 and 25; (ii) SEQ ID NOs: 17, 18, 23, 20, 24 and 25; (iii) SEQ ID NOs: 17, 18, 23, 20, 26 and 27; (iv) SEQ ID NOs: 17, 18, 75, 20, 26 and 27; or (v) SEQ ID NOs: 17, 18, 23, 20, 26 and 25. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25.

[0012] In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule comprises: (a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises: (i) a first VH-CDR1 comprising the amino acid sequence of GFTFNTYA (SEQ ID NO:28); (ii) a first VH-CDR2 comprising the amino acid sequence of IRSKYNNYAT (SEQ ID NO:29); (iii) a first VH-CDR3 comprising the amino acid sequence of VRHGNFGX$_3$SYVSWFAY, wherein X$_3$ is H or N (SEQ ID NO:30); (iv) a first VL-CDR1 comprising the amino acid sequence of TGAVTTGHY (SEQ ID NO:31); (v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$, wherein X$_4$ is N or S (SEQ ID NO:21); and (vi) a first VL-CDR3 comprising the amino acid sequence of ALWYSNX$_6$WV, wherein X$_6$ is L or R (SEQ ID NO:6), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to IMGT; and (b) a second antigen binding domain that binds to an HIV antigen. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule comprises: (a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises: (i) a first VH-CDR1 comprising the amino acid sequence of GFTFNTYA (SEQ ID NO:28); (ii) a first VH-CDR2 comprising the amino acid sequence of IRSKYNNYAT (SEQ ID NO:29); (iii) a first VH-CDR3 comprising the amino acid sequence of

VRHGNFGX$_3$SYVSWFAY, wherein X$_3$ is H or N (SEQ ID NO:30); (iv) a first VL-CDR1 comprising the amino acid sequence of TGAVTTGHY (SEQ ID NO:31); (v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$, wherein X$_4$ is N or S (SEQ ID NO:21); and (vi) a first VL-CDR3 comprising the amino acid sequence of ALWYSNX$_6$WV, wherein X$_6$ is L or R (SEQ ID NO:6), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to IMGT; and (b) a second antigen binding domain that binds to a second antigen. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to IMGT): (i) SEQ ID NOs: 28, 29, 32, 31, 21 and 10; (ii) SEQ ID NOs: 28, 29, 32, 31, 24 and 10; (iii) SEQ ID NOs: 28, 29, 32, 31, 26 and 15; (iv) SEQ ID NOs: 28, 29, 33, 31, 26 and 15; or (v) SEQ ID NOs: 28, 29, 32, 31, 26 and 10. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10.

[0013] In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule comprises: (a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises: (i) a first VH-CDR1 comprising the amino acid sequence of ASGFTFNTYA (SEQ ID NO:34); (ii) a first VH-CDR2 comprising the amino acid sequence of IRSKYNNYATYYAX$_1$SVKX$_2$R, wherein X$_1$ is A or D and X$_2$ is G or S (SEQ ID NO:35); (iii) a first VH-CDR3 comprising the amino acid sequence of HGNFGX$_3$SYVSWFA, X$_3$ is H or N (SEQ ID NO:36); (iv) a first VL-CDR1 comprising the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 37); (v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$NRAPX$_7$VPAR, wherein X$_4$ is N or S and X$_7$ is G or W (SEQ ID NO:38); and (vi) a first VL-CDR3 comprising the amino acid sequence of WYSNX$_6$W, wherein X$_6$ is L or R (SEQ ID NO:22), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Honegger; and (b) a second antigen binding domain that binds to an HIV antigen. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule comprises: (a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises: (i) a first VH-CDR1 comprising the amino acid sequence of ASGFTFNTYA (SEQ ID NO:34); (ii) a first VH-CDR2 comprising the amino acid sequence of IRSKYNNYATYYAX$_1$SVKX$_2$R, wherein X$_1$ is A or D

and X_2 is G or S (SEQ ID NO:35); (iii) a first VH-CDR3 comprising the amino acid sequence of HGNFGX$_3$SYVSWFA, X_3 is H or N (SEQ ID NO:36); (iv) a first VL-CDR1 comprising the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 37); (v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$NRAPX$_7$VPAR, wherein X_4 is N or S and X_7 is G or W (SEQ ID NO:38); and (vi) a first VL-CDR3 comprising the amino acid sequence of WYSNX$_6$W, wherein X_6 is L or R (SEQ ID NO:22), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Honegger; and (b) a second antigen binding domain that binds to a second antigen. In some embodiments, (i) the first VH-CDR1 comprises the amino acid sequence of ASGFTFNTYA (SEQ ID NO:34); (ii) the first VH-CDR2 comprises the amino acid sequence of IRSKYNNYATYYADSVKX$_2$R, wherein X_2 is G or S (SEQ ID NO:39); (iii) the first VH-CDR3 comprises the amino acid sequence of HGNFGHSYVSWFA (SEQ ID NO:40); (iv) the first VL-CDR1 comprises the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 37); (v) the first VL-CDR2 comprises the amino acid sequence of GTSNRAPGVPAR (SEQ ID NO:41); and (vi) the first VL-CDR3 comprises the amino acid sequence of WYSNRW (SEQ ID NO:25). In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Honegger): (i) SEQ ID NOs: 34, 39, 40, 37, 41 and 25; (ii) SEQ ID NOs: 34, 42, 40, 37, 41 and 25; (iii) SEQ ID NOs: 34, 43, 40, 37, 41 and 25; (iv) SEQ ID NOs: 34, 44, 40, 37, 45 and 27; (v) SEQ ID NOs: 34, 44, 46, 37, 45 and 27; or (vi) SEQ ID NOs: 34, 42, 40, 37, 47 and 25. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Honegger): (i) SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or (ii) SEQ ID NOs: 34, 43, 40, 37, 41 and 25. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the

following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25.

[0014] With respect to further embodiments of the first antigen binding domain of the multi-specific (*e.g.*, bispecific) antigen binding molecules targeting or binding to CD3, in some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule comprises one or more of the following amino acid substitutions (numbering according to Kabat): position 81 of the first VH is Q or E; position 83 of the first VH is K or R; position 89 of the first VH is M or V; position 100 of the first VH is H; position 57 of the first VL is G or W; and/or position 75 of the first VL is I or L. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule comprises: one or more of the following amino acid substitutions (numbering according to Kabat): (i) position 81 of the first VH is Q or E; (ii) position 83 of the first VH is R; (iii) position 89 of the first VH is V; (iv) position 100 of the first VH is H; (v) position 57 of the first VL is G; and/or (vi) position 75 of the first VL is I. In some embodiments, position 81 of the first VH (numbering according to Kabat) is E. In some embodiments, position 81 of the first VH (numbering according to Kabat) is Q. In some embodiments, position 100 of the first VH (numbering according to Kabat) is H. In some embodiments, the first VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 48-53, or comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 48-53. In some embodiments, the first VH comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 50. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 50. In some embodiments, the first VH comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 51. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 51. In some embodiments, the first VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 54-58, or comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 54-58. In some embodiments, the first VL comprises an amino acid sequence that is at least 80%, at least 85%,

at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 48-53, or comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 48-53 and wherein the first VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 54-58, or comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 54-58. In some embodiments, the first VH and the first VL comprise the amino acid sequences set forth, respectively, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 48 and 54; SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; SEQ ID NOs: 51 and 56; SEQ ID NOs: 52 and 56; SEQ ID NOs: 53 and 57; or SEQ ID NOs: 50 and 58. In some embodiments, the first VH and the first VL comprise the amino acid sequences set forth, respectively, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56. In some embodiments, the first VH and the first VL comprise the amino acid sequences set forth, respectively, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first VH and the first VL comprise the amino acid sequences set forth, respectively, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, at least one of the first antigen binding domain and the second antigen binding domain independently

comprise a Fab, an F(ab)2, Fv, a scFv, a sc(Fv)2, or a diabody. In some embodiments, the first antigen binding domain comprises a scFv and the second antigen binding domain comprises a Fab. In some embodiments, the first antigen binding domain comprises a scFv and the second antigen binding domain comprises a Fab, wherein the first VH and the first VL comprise the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first antigen binding domain comprises a Fab and the second antigen binding domain comprises a scFv. In some embodiments, the first antigen binding domain comprises a Fab and the second antigen binding domain comprises a Fab. In some embodiments, the first antigen binding domain comprises a scFv and the second antigen binding domain comprises a scFv. In some embodiments, the first antigen binding domain comprises a Fab and the second antigen binding domain comprises an extracellular domain of CD4. In some embodiments, the first antigen binding domain comprises a Fab and the second antigen binding domain comprises an extracellular domain of CD4, wherein the first VH and the first VL comprise the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, the first antigen binding domain comprises a scFv and the second antigen binding domain comprises an extracellular domain of CD4. In some embodiments, the first antigen binding domain is a scFv comprising a cysteine (C) at position 44 in the scFv variable heavy domain; and a cysteine (C) at position 100 in the scFv variable light domain. In some embodiments, the first antigen binding domain is a scFv comprising a VH and a VL, the scFv comprising an amino acid sequence selected from SEQ ID NOs: 59-66, or comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from SEQ ID NOs: 59-66. In some embodiments, the first antigen binding domain is a scFv comprising a VH and a VL, the scFv comprising an amino acid sequence selected from SEQ ID NOs: 59-63, or comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from SEQ ID NOs: 59-63. In some embodiments, the first antigen binding domain is a scFv comprising a VH and a VL, the scFv comprising an amino acid sequence selected from SEQ ID NOs: 62-63, or comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from SEQ ID NOs: 62-63.

[0015] With respect to further embodiments of the second antigen binding domain of the multi-specific (*e.g.*, bispecific) antigen binding molecules targeting or binding to an HIV

antigen, in some embodiments, the second antigen binding domain binds to an HIV envelope protein selected from the group consisting of gp120 and gp41. In some embodiments, the second antigen binding domain competes with or comprises VH and VL variable domains of a broadly neutralizing antibody (bNAb) that binds to an HIV antigen. In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 selected from the group consisting of: third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan; second variable loop (V2) (*e.g.*, Env trimer apex); CD4 binding site (CD4bs); gp120/gp41 interface; or silent face of gp120. In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the second variable loop (V2) (*e.g.*, Env trimer apex) and competes with or comprises VH and VL regions from an antibody selected from the group consisting of PG9, PG16, PGC14, PGG14, PGT-142, PGT-143, PGT-144, PGT-145, CH01, CH59, PGDM1400, CAP256, CAP256-VRC26.08, CAP256-VRC26.09, CAP256-VRC26.25, PCT64-24E and VRC38.01. In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises one or more extracellular (EC) domains of CD4. In some embodiments, the one or more EC domains of CD4 comprise a sequence as set forth below, or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from the group consisting of:

(i) KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRVDSRRS LWDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVG (SEQ ID NO: 746);

(ii) KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRVDSRRS LWDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVGGGGSGKKVVYGKKGDTVELTC TASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRVDSRRSLWDQGNFPLIIKNLKP EDSDTYICEVEDQKEEVQLVVVG (SEQ ID NO: 747);

(iii) KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRRS LWDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFG (SEQ ID NO: 748); or

(iv) KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRRS LWDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFGGGGSGKKVVLGKKGDTVELTC TASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRRSLWDQGNFPLIIKNLKI EDSDTYICEVEDQKEEVQLLVFG(SEQ ID NO: 749).

In some embodiments, the EC domain of CD4 comprises a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 95% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises the sequence of SEQ ID NO: 746. In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the gp120/gp41 interface and competes with or comprises VH and VL regions from an antibody selected from the group consisting of PGT-151, CAP248-2B, 35O22, 8ANC195, ACS202, VRC34 and VRC34.01. In some embodiments, the second antigen binding domain binds to an epitope or region of the gp120 silent face and competes with or comprises VH and VL regions from an antibody selected from VRC-PG05 and SF12.In some embodiments, the second antigen binding domain binds to an epitope or region of gp41 in the membrane proximal region (MPER). In some embodiments, the second antigen binding domain binds to an epitope or region of gp41 in the membrane proximal region (MPER) and competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10E8, 10E8v4, 10E8-5R-100cF, 4E10, DH511.11P, 2F5, 7b2, and LN01. In some embodiments, the second antigen binding domain binds to an epitope or region of the gp41 fusion peptide and competes with or comprises VH and VL regions from an antibody selected from the group consisting of VRC34 and ACS202. In some embodiments, the second antigen binding domain comprises a second VH comprising a second VH-CDR1, a second VH-CDR2, and a second VH-CDR3; and a

second VL comprising a second VL-CDR1, a second VL-CDR2, and a second VH-CDR3; comprising the amino acid sequences (according to Kabat) set forth, respectively, in: SEQ ID NOs: 76, 77, 78, 79, 80 and 81; SEQ ID NOs: 76, 82, 78, 79, 80 and 81; SEQ ID NOs: 83, 84, 85, 86, 80 and 87; SEQ ID NOs: 83, 88, 85, 86, 80 and 87; SEQ ID NOs: 90, 91, 92, 93, 94 and 95; SEQ ID NOs: 90, 91, 96, 93, 94 and 95; SEQ ID NOs: 97, 98, 99, 100, 101 and 102; SEQ ID NOs: 103, 104, 105, 106, 94 and 107; SEQ ID NOs: 108, 109, 110, 111, 112 and 113; SEQ ID NOs: 114, 115, 116, 117, 118 and 119; SEQ ID NOs: 114, 120, 121, 122, 118 and 123; SEQ ID NOs: 124, 125, 126, 127, 128 and 113; SEQ ID NOs: 129, 115, 131, 127, 118 and 113; SEQ ID NOs: 132, 133, 134, 135, 136 and 137; SEQ ID NOs: 138, 139, 140, 141, 142 and 143; SEQ ID NOs: 144, 145, 146, 147, 148 and 143; SEQ ID NOs: 149, 150, 151, 152, 153 and 143; SEQ ID NOs: 154, 155, 156, 157, 158 and 159; SEQ ID NOs: 160, 161, 162, 163, 164 and 165; SEQ ID NOs: 166, 161, 167, 163, 164 and 165; SEQ ID NOs: 168, 169, 170, 171, 172 and 173; SEQ ID NOs: 168, 174, 170, 171, 172 and 173; SEQ ID NOs: 175, 176, 177, 171, 172 and 173; SEQ ID NOs: 178, 179, 180, 181, 182 and 183; SEQ ID NOs: 184, 185, 186, 187, 188 and 189; SEQ ID NOs: 190, 191, 192, 193, 194 and 195; SEQ ID NOs: 196, 197, 198, 199, 200 and 201; SEQ ID NOs: 202, 203, 204, 205, 206 and 207; SEQ ID NOs: 208, 209, 210, 211, 212 and 213; SEQ ID NOs: 214, 215, 216, 217, 218 and 219; SEQ ID NOs: 214, 220, 216, 221, 218 and 219; SEQ ID NOs: 214, 220, 222, 221, 218 and 219; SEQ ID NOs: 223, 224, 225, 226, 227 and 228; SEQ ID NOs: 229, 230, 231, 232, 233 and 234; SEQ ID NOs: 902, 903, 904, 905, 906 and 907; SEQ ID NOs: 908, 909, 910, 911, 912 and 913; SEQ ID NOs: 914, 915, 916, 917, 918 and 919; or SEQ ID NOs: 920, 921, 922, 923, 924 and 925. In some embodiments, the second antigen binding domain comprises a second VH comprising a second VH-CDR1, a second VH-CDR2, and a second VH-CDR3; and a second VL comprising a second VL-CDR1, a second VL-CDR2, and a second VH-CDR3; comprising the amino acid sequences (according to Chothia) set forth, respectively, in: SEQ ID NOs: 235, 236, 237, 238, 239 and 240; SEQ ID NOs: 241, 242, 243, 244, 239 and 245; SEQ ID NOs: 246, 242, 247, 244, 239 and 245; SEQ ID NOs: 248, 249, 250, 251, 239 and 252; SEQ ID NOs: 248, 249, 253, 251, 239 and 252; SEQ ID NOs: 254, 255, 256, 257, 258 and 259; SEQ ID NOs: 260, 261, 262, 263, 239 and 264; SEQ ID NOs: 265, 266, 267, 268, 269 and 270; SEQ ID NOs: 271, 272, 273, 274, 275 and 270; SEQ ID NOs: 271, 276, 277, 278, 275 and 279; SEQ ID NOs: 280, 281, 282, 283, 284 and 270; SEQ ID NOs: 285, 272, 286, 283, 275 and 270; SEQ ID NOs: 287, 288, 289, 290, 291 and 292; SEQ ID NOs: 293, 294, 295, 296, 297 and 298; SEQ ID NOs: 299, 300, 301, 302, 303 and 298; SEQ ID NOs: 304, 300, 305, 406, 307 and 298; SEQ ID NOs: 308, 309, 310, 311, 312 and 313; SEQ ID NOs: 314, 315, 316, 317, 318 and 165; SEQ ID NOs: 320, 315, 321, 317, 318 and 165; SEQ ID NOs: 322, 323, 324,

325, 326 and 327; SEQ ID NOs: 322, 328, 324, 325, 326 and 327; SEQ ID NOs: 329, 323, 330, 325, 326 and 327; SEQ ID NOs: 331, 332, 333, 334, 335 and 336; SEQ ID NOs: 337, 338, 339, 340, 341 and 342; SEQ ID NOs: 343, 344, 345, 346, 341 and 347; SEQ ID NOs:348, 349, 350, 351, 352 and 353; SEQ ID NOs: 354, 355, 356, 357, 358 and 359; SEQ ID NOs: 360, 361, 362, 363, 364 and 365; SEQ ID NOs: 366, 367, 368, 369, 370 and 371; SEQ ID NOs: 366, 361, 368, 369, 370 and 371; SEQ ID NOs: 372, 361, 373, 369, 370 and 371; SEQ ID NOs: 374, 375, 376, 377, 378 and 379; SEQ ID NOs: 380, 381, 382, 383, 384 and 385; SEQ ID NOs: 926, 927, 928, 929, 930 and 931; SEQ ID NOs: 932, 933, 934, 935, 936 and 937; SEQ ID NOs: 938, 939, 940, 941, 942 and 943; or SEQ ID NOs: 944, 945, 946, 947, 948 and 949. In some embodiments, the second antigen binding domain comprises a second VH comprising a second VH-CDR1, a second VH-CDR2, and a second VH-CDR3; and a second VL comprising a second VL-CDR1, a second VL-CDR2, and a second VH-CDR3; comprising the amino acid sequences (according to IMGT) set forth, respectively, in: SEQ ID NOs: 386, 387, 388, 389, 239 and 81; SEQ ID NOs: 390, 391, 392, 393, 239 and 87; SEQ ID NOs: 390, 391, 394, 393, 239 and 87; SEQ ID NOs: 395, 396, 397, 393, 239 and 87; SEQ ID NOs: 398, 399, 400, 401, 239 and 95; SEQ ID NOs: 398, 399, 402, 401, 239 and 95; SEQ ID NOs: 403, 404, 405, 406, 258 and 102; SEQ ID NOs: 407, 408, 409, 410, 239 and 107; SEQ ID NOs: 411, 412, 413, 414, 269 and 113; SEQ ID NOs: 415, 416, 417, 418, 275 and 119; SEQ ID NOs: 415, 419, 420, 421, 275 and 123; SEQ ID NOs: 422, 423, 424, 425, 275 and 113; SEQ ID NOs: 426, 416, 427, 425, 275 and 113; SEQ ID NOs: 428, 429, 430, 431, 291 and 137; SEQ ID NOs: 432, 433, 434, 435, 297 and 143; SEQ ID NOs: 436, 437, 438, 439, 303 and 143; SEQ ID NOs: 440, 437, 441, 442, 307 and 143; SEQ ID NOs: 443, 444, 445, 446, 312 and 159; SEQ ID NOs: 447, 448, 449, 450, 318 and 165; SEQ ID NOs: 451, 448, 452, 450, 318 and 165; SEQ ID NOs: 453, 454, 455, 456, 326 and 173; SEQ ID NOs: 453, 457, 455, 456, 326 and 173; SEQ ID NOs: 458, 459, 460, 456, 326 and 173; SEQ ID NOs: 461, 462, 463, 464, 335 and 183; SEQ ID NOs: 465, 466, 467, 468, 341 and 189; SEQ ID NOs: 469, 470, 471, 472, 341 and 195; SEQ ID NOs: 473, 474, 475, 476, 352 and 201; SEQ ID NOs: 477, 478, 479, 480, 358 and 207; SEQ ID NOs: 481, 482, 483, 484, 364 and 213; SEQ ID NOs: 485, 486, 487, 488, 370 and 219; SEQ ID NOs: 485, 482, 487, 488, 370 and 219; SEQ ID NOs: 489, 482, 490, 488, 370 and 219; SEQ ID NOs: 491, 492, 493, 494, 378 and 228; SEQ ID NOs: 495, 496, 497, 498, 384 and 234; SEQ ID NOs: 950, 951, 952, 953, 930 and 907; SEQ ID NOs: 954, 955, 956, 957, 936 and 913; SEQ ID NOs: 958, 959, 960, 961, 942 and 919; or SEQ ID NOs: 962, 963, 964, 965, 948 and 925. In some embodiments, the second antigen binding domain comprises a second VH comprising a second VH-CDR1, a second VH-CDR2, and a second VH-CDR3; and a second VL comprising a second VL-CDR1, a

second VL-CDR2, and a second VH-CDR3; comprising the amino acid sequences (according to Honegger) set forth, respectively, in: SEQ ID NOs: 499, 500, 501, 238, 502 and 240; SEQ ID NOs: 499, 503, 501, 238, 502 and 240; SEQ ID NOs: 505, 506, 507, 244, 502 and 245; SEQ ID NOs: 508, 509, 510, 244, 502 and 245; SEQ ID NOs: 511, 512, 513, 251, 514 and 252; SEQ ID NOs: 511, 512, 515, 251, 514 and 252; SEQ ID NOs: 516, 517, 518, 257, 519 and 259; SEQ ID NOs: 520, 521, 522, 264, 523 and 264; SEQ ID NOs: 524, 525, 526, 268, 527 and 270; SEQ ID NOs: 528, 529, 530, 274, 531 and 270; SEQ ID NOs: 528, 532, 533, 278, 531 and 279; SEQ ID NOs: 534, 535, 536, 283, 537 and 270; SEQ ID NOs: 1090, 529, 538, 283, 531 and 270; SEQ ID NOs: 539, 540, 541, 290, 542 and 292; SEQ ID NOs: 543, 544, 545, 546, 547 and 298; SEQ ID NOs: 548, 549, 550, 1091, 551 and 298; SEQ ID NOs: 552, 553, 554, 555, 556 and 298; SEQ ID NOs: 557, 558, 559, 311, 560 and 313; SEQ ID NOs: 561, 562, 563, 564, 565 and 165; SEQ ID NOs: 566, 562, 1092, 564, 567 and 165; SEQ ID NOs: 568, 569, 570, 571, 572 and 327; SEQ ID NOs: 568, 573, 570, 571, 572 and 327; SEQ ID NOs: 574, 575, 576, 571, 572 and 327; SEQ ID NOs: 577, 578, 579, 580, 581 and 336; SEQ ID NOs: 582, 583, 584, 340, 585 and 342; SEQ ID NOs: 586, 587, 588, 346, 589 and 347; SEQ ID NOs: 590, 591, 592, 351, 593 and 353; SEQ ID NOs: 594, 595, 596, 597, 598 and 359; SEQ ID NOs: 599, 600, 601, 602, 603 and 365; SEQ ID NOs: 604, 605, 606, 607, 608 and 371; SEQ ID NOs: 604, 609, 606, 607, 608 and 371; SEQ ID NOs: 610, 609, 611, 607, 608 and 371; SEQ ID NOs: 612, 613, 614, 615, 616 and 379; SEQ ID NOs: 617, 618, 619, 620, 621 and 385; SEQ ID NOs: 966, 967, 968, 969, 970 and 931; SEQ ID NOs: 971, 972, 973, 974, 975 and 937; SEQ ID NOs: 976, 977, 978, 941, 979 and 943; or SEQ ID NOs: 980, 981, 982, 983, 984 and 949. In some embodiments, the second VH and the second VL comprise the amino acid sequences set forth, respectively, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 622 and 623; SEQ ID NOs: 624 and 625; SEQ ID NOs: 624 and 626; SEQ ID NOs: 627 and 628; SEQ ID NOs: 629 and 630; SEQ ID NOs: 631 and 632; SEQ ID NOs: 633 and 634; SEQ ID NOs: 635 and 636; SEQ ID NOs: 637 and 638; SEQ ID NOs: 639 and 640; SEQ ID NOs: 641 and 642; SEQ ID NOs: 643 and 644; SEQ ID NOs: 645 and 646; SEQ ID NOs: 647 and 648; SEQ ID NOs: 649 and 650; SEQ ID NOs: 651 and 652; SEQ ID NOs: 653 and 654; SEQ ID NOs: 655 and 656; SEQ ID NOs: 657 and 658; SEQ ID NOs: 659 and 660; SEQ ID NOs: 661 and 662; SEQ ID NOs: 663 and 664; SEQ ID NOs: 665 and 666; SEQ ID NOs: 667 and 668; SEQ ID NOs: 669 and 670; SEQ ID NOs:671 and 672; SEQ ID NOs:673 and 670; SEQ ID NOs: 674 and 675; SEQ ID NOs: 676 and 677; SEQ ID NOs: 678 and 679; SEQ ID NOs: 680 and 681; SEQ

ID NOs: 682 and 683; SEQ ID NOs: 684 and 685; SEQ ID NOs: 686 and 687; SEQ ID NOs: 688 and 689; SEQ ID NOs: 690 and 691; SEQ ID NOs: 692 and 693; SEQ ID NOs: 694 and 695; SEQ ID NOs: 985 and 986; SEQ ID NOs: 987 and 988; SEQ ID NOs: 989 and 990; or SEQ ID NOs: 991 and 992. In some embodiments, the second VH and the second VL comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, and comprising the following amino acids at the indicated positions (position numbering according to Kabat): (i) SEQ ID NOs: 622, 624 or 627, comprising one or more of: Ser-Ser-Val (SSV) or Thr-Gly-Val (TGV) at positions 82a-82c, Gln (Q) at position 39, Asn (N) at position 60, His (H) at position 68, any one of Lys (K), His (H) or Thr (T) at position 105, Leu (L) at position 2, Ala (A) at position 32, and Ala (A) at position 95; and SEQ ID NOs: 623, 625, 626 or 628, comprising one or more of: Gly (G) at position 67, Tyr (Y), Phe (F) or Thr (T) at position 67a, Arg (R) at position 67b, Pro (P) at position 67c, and Lys (K) at position 103; or (ii) SEQ ID NOs: 663, 665 or 667, comprising one or more of: His (H) at position 3, Ser (S) or Val (V) at position 5, Glu (E) at position 10, Lys (K) at position 12, Lys (K) at position 23, Asn (N) at position 28, Arg (R) at position 30, Tyr (Y) at position 32, Thr (T) at position 68, Met (M) at position 69, Gln (Q) or His (H) at position 72, Tyr (Y), Phe (F) at position 74a, Phe (F) or Ser (S) at position 76, Ser (S) at position 77, Ala (A) at position 78, Ser (S) at position 82a, Arg (R) at position 82b, Val (V) at position 82c, Ile (I) or Thr (T) at position 89, Phe (F) at position 98, Tyr (Y) or Gly (G) at position 99, Gln (Q) at position 105, Met (M) at position 108, Phe-Asp-Phe-Asp (FDFD) (SEQ ID NO: 1040) at positions 74a, 74b, 74c, and 74d and Trp-Asp-Phe-Asp (WDFD) (SEQ ID NO: 1042) at positions 74a, 74b, 74c, and 74d; and SEQ ID NOs: 664, 666 or 668, comprising one or more of Arg (R) at position 14, Arg (R) at position 18, Ala (A) at position 19, Lys (L) at position 39, Pro (P) at position 40, Thr (T) at position 56, Ala (A) at position 60, Ser (S) at position 65, Thr (T) or His (H) at position 72, Lys (K) at position 74, Ser (S) at position 76, Ser (S) at position 77, Val (V) at position 83, Ile (I) or Phe (F) at position 98, Thr (T) or Gly (G) at position 99, Asn (N) at position 103, and Ile (I) at position 106. In some embodiments, the second VH and the second VL comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, and comprising the following amino acids at the indicated positions (position numbering according to Kabat): (i) SEQ ID NOs: 622, 624 or 627, comprising one or more of: Thr-Gly-Val (TGV) at positions 82a-82c, Asn (N) at position 60, His (H) at position 68, any one of Lys (K), His (H)

and Thr (T) at position 105; and SEQ ID NOs: 623, 625, 626 or 628, comprising one or more of: Gly (G) at position 67, Tyr (Y), Phe (F) or Thr (T) at position 67a, Arg (R) at position 67b, Pro (P) at position 67c; or (ii) SEQ ID NOs: 663, 665 or 667, comprising Phe (F) at position 74a; and SEQ ID NOs: 664, 666 or 668, comprising Ala (A) at position 19.

[0016] With respect to the first and second Fc regions or domains of the multi-specific antigen binding molecules some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1 or IgG4, comprising a first Fc region and a second Fc region. In some embodiments, the first Fc region and the second Fc region are derived from IgG1m17. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1 or IgG4, comprising a first Fc region and a second Fc region, wherein one or both of the first and second Fc regions comprise one or more of the following amino acids at the indicated positions (EU numbering): alanine at position 234, alanine at position 235; and serine at position 331. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, wherein both of the first and second Fc regions comprise one or more of the following amino acids at the indicated positions (EU numbering): alanine at position 234, alanine at position 235; and serine at position 331. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, wherein both of the first and second Fc regions comprise the following amino acids at the indicated positions (EU numbering): alanine at position 234, alanine at position 235; and serine at position 331. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1 or IgG4, comprising a first Fc region and a second Fc region, wherein one or both of the first and second Fc regions comprise the following amino acids at the indicated positions (EU numbering): tyrosine at position 252, threonine at position 254 and glutamic acid at position 256 (YTE); or leucine at position 428 and serine at position 434 (LS). In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, wherein one of the first and second Fc regions comprise the following amino acids at the indicated positions (EU numbering): tyrosine at position 252, threonine at position 254 and glutamic acid at position 256 (YTE). In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, wherein the second Fc region comprises the following amino acids at the indicated positions (EU numbering): tyrosine at position 252, threonine at position 254 and glutamic acid

at position 256 (YTE). In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1 or IgG4, comprising a first Fc region and a second Fc region, comprising the following amino acids at the indicated positions (EU numbering): the first Fc region comprises a tryptophan at position 366 (T366W); and the second Fc region comprises a serine at position 366 (T366S), an alanine at position 368 (L368A) and a valine at position 407 (Y407V); the first Fc region comprises a serine at position 366 (T366S), an alanine at position 368 (L368A) and a valine at position 407 (Y407V); and the second Fc region comprises a tryptophan at position 366 (T366W); the first Fc region comprises a cysteine at position 354 (S354C), a tryptophan at position 366 (T366W); and the second Fc region comprises a cysteine at position 349 (Y349C), a serine at position 366 (T366S), an alanine at position 368 (L368A) and a valine at position 407 (Y407V); the first Fc region comprises cysteine at position 349 (Y349C), a serine at position 366 (T366S), an alanine at position 368 (L368A) and a valine at position 407 (Y407V); and the second Fc region comprises a cysteine at position 354 (S354C), a tryptophan at position 366 (T366W). In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising the following amino acids at the indicated positions (EU numbering): the first Fc region comprises a tryptophan at position 366 (T366W); and the second Fc region comprises a serine at position 366 (T366S), an alanine at position 368 (L368A) and a valine at position 407 (Y407V); or the first Fc region comprises a serine at position 366 (T366S), an alanine at position 368 (L368A) and a valine at position 407 (Y407V); and the second Fc region comprises a tryptophan at position 366 (T366W). In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising the following amino acids at the indicated positions (EU numbering): the first Fc region comprises a serine at position 366 (T366S), an alanine at position 368 (L368A) and a valine at position 407 (Y407V); and the second Fc region comprises a tryptophan at position 366 (T366W). In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1 or IgG4, comprising a first hinge region and a second hinge region, wherein one or both of the first and second hinge regions comprise a serine at position 220 (C220S) (EU numbering). In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1 or IgG4, comprising a first Fc region and a second Fc region, wherein one of the first Fc region or the second Fc region comprise the following amino acids at the indicated positions (EU numbering): arginine at position 435 (H435R); or arginine at position 435 (H435R) and phenylalanine at position 436 (Y436F). In

some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, wherein one of the first Fc region or the second Fc region comprise the following amino acids at the indicated positions (EU numbering): arginine at position 435 (H435R). In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, wherein the first Fc region comprises arginine at position 435 (H435R). In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1 or IgG4, comprising a first Fc region and a second Fc region, comprising the following amino acids at the indicated positions (EU numbering): the first Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S) and a tryptophan at position 366 (T366W); and the second Fc region comprises an alanine a position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a serine at position 366 (T366S), an alanine at position 368 (L368A), a valine at position 407 (Y407V), and an arginine at position 435 (H435R); the first Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S) and a tryptophan at position 366 (T366W); and the second Fc region comprises an alanine a position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a serine at position 366 (T366S), an alanine at position 368 (L368A), a valine at position 407 (Y407V), an arginine at position 435 (H435R) and a phenylalanine at position 436 (Y436F); the first Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a serine at position 366 (T366S), an alanine at position 368 (L368A), and a valine at position 407 (Y407V); and the second Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S) and a tryptophan at position 366 (T366W); the first Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a tryptophan at position 366 (T366W), a leucine at position 428 (M428L) and a serine at position 434 (N434S); and the second Fc region comprises an alanine a position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a serine at position 366 (T366S), an alanine at position 368 (L368A), a valine at position 407 (Y407V), and an arginine at position 435 (H435R); or the first Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a tryptophan at position 366 (T366W), a tyrosine at position 252 (M252Y), a threonine at position 254 (S254T) and a glutamic acid at position 256 (T256E); and the second Fc region comprises an alanine a position 234 (L234), an alanine at position 235

(L235A), a serine at position 331 (P331S), a serine at position 366 (T366S), an alanine at position 368 (L368A), a valine at position 407 (Y407V), and an arginine at position 435 (H435R). In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising the following amino acids at the indicated positions (EU numbering): the first Fc region comprises an alanine a position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a serine at position 366 (T366S), an alanine at position 368 (L368A), a valine at position 407 (Y407V), and an arginine at position 435 (H435R); and the second Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a tryptophan at position 366 (T366W), a tyrosine at position 252 (M252Y), a threonine at position 254 (S254T) and a glutamic acid at position 256 (T256E). In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 696 and 697; SEQ ID NOs.: 697 and 696; SEQ ID NOs.: 696 and 698; SEQ ID NOs.: 698 and 696; SEQ ID NOs.: 699 and 700; SEQ ID NOs.: 700 and 699; SEQ ID NOs.: 701 and 698; SEQ ID NOs.: 698 and 701; SEQ ID NOs.: 702 and 703; SEQ ID NOs.: 703 and 702; SEQ ID NOs.: 704 and 698; SEQ ID NOs.: 698 and 704; SEQ ID NOs.: 705 and 703; SEQ ID NOs.: 703 and 705; SEQ ID NOs.: 706 and 704; SEQ ID NOs.: 704 and 706; SEQ ID NOs.: 707 and 703; SEQ ID NOs.: 703 and 707; SEQ ID NOs.: 708 and 704; SEQ ID NOs.: 704 and 708; SEQ ID NOs.: 709 and 710; or SEQ ID NOs.: 710 and 709. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705 . In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising amino acid sequences that are at

least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecules comprise a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705.

[0017] With respect to further embodiments of the multi-specific (*e.g.*, bispecific) antigen binding molecules, in some embodiments, the first antigen binding domain is a scFv that binds to CD3 and the second antigen binding domain is a Fab that binds to HIV gp120, wherein the first antigen binding domain comprises a first heavy chain (HC), and the second antigen binding domain comprises a second HC and a light chain (LC), the first HC, the second HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 800, 801 and 802; SEQ ID NOs: 800, 803 and 802; SEQ ID NOs: 804, 803 and 802; SEQ ID NOs: 804, 805 and 802; SEQ ID NOs: 806, 801 and 802; SEQ ID NOs: 806, 803 and 802; SEQ ID NOs: 807, 803 and 802; SEQ ID NOs: 807, 805 and 802; SEQ ID NOs: 808, 809 and 802; SEQ ID NOs: 808, 810 and 802; SEQ ID NOs: 811, 801 and 802; SEQ ID NOs: 812, 809 and 802; SEQ ID NOs: 812, 810 and 802; SEQ ID NOs: 813, 805 and 802; SEQ ID NOs: 812, 814 and 802; SEQ ID NOs: 815, 801 and 802; SEQ ID NOs: 816, 805 and 802; SEQ ID NOs: 817, 801 and 802; SEQ ID NOs: 818, 805 and 802; SEQ ID NOs: 819, 810 and 802; SEQ ID NOs: 820, 810 and 802; SEQ ID NOs: 821, 822 and 823; SEQ ID NOs: 824, 825 and 823; SEQ ID NOs: 826, 825 and 823; SEQ ID NOs: 826, 827 and 823; SEQ ID NOs: 828, 829 and 823; SEQ ID NOs: 830, 822 and 823; SEQ ID NOs: 830, 825 and 823; SEQ ID NOs: 831, 825 and 823; SEQ ID NOs: 831, 827 and 823; SEQ ID NOs: 832, 833 and 823; SEQ ID NOs: 832, 829 and 823; SEQ ID NOs: 834, 827 and 823; SEQ ID NOs: 835, 829 and 823; SEQ ID NOs: 836, 829 and 823; SEQ ID NOs: 837, 833 and 823; SEQ ID NOs: 837, 838 and 823; SEQ ID NOs: 839, 840 and 823; SEQ ID NOs: 841, 829 and 823; SEQ ID NOs: 842, 829 and 823; SEQ ID NOs: 843, 829 and 823; SEQ ID NOs: 844, 829 and 823; SEQ ID NOs: 845, 829 and 823; SEQ ID NOs: 846, 829 and 823; SEQ ID NOs: 846, 833 and 823; SEQ ID NOs: 846, 838 and 823; SEQ ID NOs: 847, 827 and 823; SEQ ID NOs: 848, 829 and 823; SEQ ID NOs: 849, 829 and 823; SEQ ID NOs: 850, 829 and 823; SEQ ID NOs: 851, 829 and 823; SEQ ID NOs: 852, 829 and 823; SEQ ID NOs: 853, 829 and 823; SEQ ID NOs: 854, 829 and 823; SEQ ID NOs: 855, 829 and 823; SEQ ID NOs: 856, 829 and 823; SEQ ID NOs: 857, 829 and 823; SEQ ID NOs: 858, 829 and 823; SEQ ID NOs: 859, 829 and 823; SEQ ID NOs: 860, 829 and 823; SEQ ID NOs: 861,

862 and 863; SEQ ID NOs: 861, 864 and 863; SEQ ID NOs: 865, 864 and 863; SEQ ID NOs: 865, 866 and 863; SEQ ID NOs: 867, 868 and 863; SEQ ID NOs: 869, 862 and 863; SEQ ID NOs: 869, 864 and 863; SEQ ID NOs: 870, 864 and 863; SEQ ID NOs: 870, 866 and 863; SEQ ID NOs: 871, 872 and 863; SEQ ID NOs: 871, 868 and 863; SEQ ID NOs: 873, 862 and 863; SEQ ID NOs: 874, 866 and 863; SEQ ID NOs: 875, 872 and 863; SEQ ID NOs: 875, 868 and 863; SEQ ID NOs: 875, 876 and 863; SEQ ID NOs: 877, 862 and 863; SEQ ID NOs: 878, 866 and 863; SEQ ID NOs: 879, 862 and 863; SEQ ID NOs: 880, 866 and 863; SEQ ID NOs: 881, 882 and 883; SEQ ID NOs: 881, 884 and 883; SEQ ID NOs: 885, 884 and 883; SEQ ID NOs: 885, 886 and 883; SEQ ID NOs: 887, 888 and 883; SEQ ID NOs: 889, 882 and 883; SEQ ID NOs: 889, 884 and 883; SEQ ID NOs: 890, 884 and 883; SEQ ID NOs: 890, 886 and 883; SEQ ID NOs: 891, 892 and 883; SEQ ID NOs: 891, 888 and 883; SEQ ID NOs: 893, 882 and 883; SEQ ID NOs: 894, 886 and 883; SEQ ID NOs: 895, 892 and 883; SEQ ID NOs: 895, 888 and 883; SEQ ID NOs: 895, 896 and 883; SEQ ID NOs: 897, 882 and 883; SEQ ID NOs: 898, 886 and 883; SEQ ID NOs: 899, 882 and 883; or SEQ ID NOs: 900, 886 and 883. In some embodiments, the first antigen binding domain is a scFv that binds to CD3 and the second antigen binding domain is a Fab that binds to HIV gp120, wherein the first antigen binding domain comprises a first heavy chain (HC), and the second antigen binding domain comprises a second HC and a light chain (LC), the first HC, the second HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 800, 801 and 802; SEQ ID NOs: 800, 803 and 802; SEQ ID NOs: 804, 803 and 802; SEQ ID NOs: 804, 805 and 802; SEQ ID NOs: 806, 801 and 802; SEQ ID NOs: 806, 803 and 802; SEQ ID NOs: 807, 803 and 802; SEQ ID NOs: 807, 805 and 802; SEQ ID NOs: 808, 809 and 802; SEQ ID NOs: 808, 810 and 802; SEQ ID NOs: 821, 822 and 823; SEQ ID NOs: 824, 825 and 823; SEQ ID NOs: 826, 825 and 823; SEQ ID NOs: 826, 827 and 823; SEQ ID NOs: 828, 829 and 823; SEQ ID NOs: 830, 822 and 823; SEQ ID NOs: 830, 825 and 823; SEQ ID NOs: 831, 825 and 823; SEQ ID NOs: 831, 827 and 823; SEQ ID NOs: 832, 833 and 823; SEQ ID NOs: 832, 829 and 823; SEQ ID NOs: 861, 862 and 863; SEQ ID NOs: 861, 864 and 863; SEQ ID NOs: 865, 864 and 863; SEQ ID NOs: 865, 866 and 863; SEQ ID NOs: 867, 868 and 863; SEQ ID NOs: 869, 862 and 863; SEQ ID NOs: 869, 864 and 863; SEQ ID NOs: 870, 864 and 863; SEQ ID NOs: 870, 866 and 863; SEQ ID NOs: 871, 872 and 863; SEQ ID NOs: 871, 868 and 863; SEQ ID NOs: 881, 882 and 883; SEQ ID NOs: 881, 884 and 883; SEQ ID NOs: 885, 884 and 883; SEQ ID NOs: 885, 886 and 883; SEQ ID

NOs: 887, 888 and 883; SEQ ID NOs: 889, 882 and 883; SEQ ID NOs: 889, 884 and 883; SEQ ID NOs: 890, 884 and 883; SEQ ID NOs: 890, 886 and 883; SEQ ID NOs: 891, 892 and 883; or SEQ ID NOs: 891, 888 and 883. In some embodiments, the first antigen binding domain is a scFv that binds to CD3 and the second antigen binding domain is a Fab that binds to HIV gp120, wherein the first antigen binding domain comprises a first heavy chain (HC), and the second antigen binding domain comprises a second HC and a light chain (LC), the first HC, the second HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 800, 801 and 802; SEQ ID NOs: 800, 803 and 802; SEQ ID NOs: 804, 803 and 802; SEQ ID NOs: 804, 805 and 802; SEQ ID NOs: 821, 822 and 823; SEQ ID NOs: 824, 825 and 823; SEQ ID NOs: 826, 825 and 823; SEQ ID NOs: 826, 827 and 823; SEQ ID NOs: 828, 829 and 823; SEQ ID NOs: 861, 862 and 863; SEQ ID NOs: 861, 864 and 863; SEQ ID NOs: 865, 864 and 863; SEQ ID NOs: 865, 866 and 863; SEQ ID NOs: 867, 868 and 863; SEQ ID NOs: 881, 882 and 883; SEQ ID NOs: 881, 884 and 883; SEQ ID NOs: 885, 884 and 883; SEQ ID NOs: 885, 886 and 883; or SEQ ID NOs: 887, 888 and 883. In some embodiments, the first antigen binding domain is a scFv that binds to CD3 and the second antigen binding domain is a Fab that binds to HIV gp120, wherein the first antigen binding domain comprises a first heavy chain (HC), and the second antigen binding domain comprises a second HC and a light chain (LC), the first HC, the second HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 800, 801 and 802; SEQ ID NOs: 800, 803 and 802; SEQ ID NOs: 804, 803 and 802; SEQ ID NOs: 804, 805 and 802; SEQ ID NOs: 821, 822 and 823; SEQ ID NOs: 824, 825 and 823; SEQ ID NOs: 826, 825 and 823; SEQ ID NOs: 826, 827 and 823; SEQ ID NOs: 828, 829 and 823; SEQ ID NOs: 861, 862 and 863; SEQ ID NOs: 861, 864 and 863; SEQ ID NOs: 865, 864 and 863; SEQ ID NOs: 865, 866 and 863; or SEQ ID NOs: 867, 868 and 863.

[0018] With respect to further embodiments of the multi-specific (*e.g.*, bispecific) antigen binding molecules, in some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule comprises (a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3; and (b) a second antigen binding domain that binds to HIV gp120

comprising one or more extracellular (EC) domain of CD4, wherein the one or more EC domains of CD4 comprise a sequence as set forth below, or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from the group consisting of:

(i) KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRVDSRRSL WDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVG (SEQ ID NO: 746);

(ii) KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRVDSRRSL WDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVGGGGSGKKVVYGKKGDTVELTCTA SQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRVDSRRSLWDQGNFPLIIKNLKPEDS DTYICEVEDQKEEVQLVVVG (SEQ ID NO: 747);

(iii) KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRRSL WDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFG (SEQ ID NO: 748); or

(iv) KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRRSL WDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFGGGGSGKKVVLGKKGDTVELTCTA SQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRRSLWDQGNFPLIIKNLKIEDS DTYICEVEDQKEEVQLLVFG(SEQ ID NO: 749).

In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749, *e.g.*, SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences,

respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749, *e.g.*, SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the

second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749, *e.g.*, SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749, *e.g.*, SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC

domain of CD4 comprising an amino acid sequence is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749, *e.g.*, SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain is a Fab that binds to CD3 and the second antigen binding domain is a scFv or an EC domain of CD4 that binds to

HIV gp120, wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753; SEQ ID NOs: 754, 752 and 753; SEQ ID NOs: 755, 756 and 753; SEQ ID NOs: 755, 757 and 753; SEQ ID NOs: 758, 757 and 753; SEQ ID NOs: 759, 756 and 753; SEQ ID NOs: 754, 760 and 761; SEQ ID NOs: 762, 760 and 761; SEQ ID NOs: 751, 763 and 753; SEQ ID NOs: 764, 752 and 753; SEQ ID NOs: 765, 752 and 753; SEQ ID NOs: 766, 767 and 753; SEQ ID NOs: 766, 768 and 753; SEQ ID NOs: 769, 768 and 753; SEQ ID NOs: 770, 767 and 753; SEQ ID NOs: 765, 771 and 761; SEQ ID NOs: 772, 771 and 761; SEQ ID NOs: 774, 775 and 776; SEQ ID NOs: 777, 778 and 776; SEQ ID NOs: 779, 778 and 776; SEQ ID NOs: 779, 780 and 776; SEQ ID NOs: 777, 781 and 776; SEQ ID NOs: 782, 752 and 753; SEQ ID NOs: 783, 752 and 753; SEQ ID NOs: 784, 785 and 753; SEQ ID NOs: 784, 786 and 753; SEQ ID NOs: 787, 786 and 753; SEQ ID NOs: 788, 785 and 753; SEQ ID NOs: 783, 789 and 761; SEQ ID NOs: 790, 789 and 761; SEQ ID NOs: 792, 793 and 794; SEQ ID NOs: 795, 796 and 794; SEQ ID NOs: 797, 796 and 794; SEQ ID NOs: 797, 798 and 794; or SEQ ID NOs: 795, 799 and 794. In some embodiments, the first antigen binding domain is a Fab that binds to CD3 and the second antigen binding domain is a scFv or an EC domain of CD4 that binds to HIV gp120, wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753; SEQ ID NOs: 754, 752 and 753; SEQ ID NOs: 755, 756 and 753; SEQ ID NOs: 755, 757 and 753; SEQ ID NOs: 758, 757 and 753; SEQ ID NOs: 759, 756 and 753; SEQ ID NOs: 764, 752 and 753; SEQ ID NOs: 765, 752 and 753; SEQ ID NOs: 766, 767 and 753; SEQ ID NOs: 766, 768 and 753; SEQ ID NOs: 769, 768 and 753; SEQ ID NOs: 770, 767 and 753; SEQ ID NOs: 777, 778 and 776; SEQ ID NOs: 779, 778 and 776; SEQ ID NOs: 779, 780 and 776; SEQ ID NOs: 777, 781 and 776; SEQ ID NOs: 782, 752 and 753; SEQ ID NOs: 783, 752 and 753; SEQ ID NOs: 784, 785 and 753; SEQ ID NOs: 784, 786 and 753; SEQ ID NOs: 787, 786 and 753; SEQ ID NOs: 788, 785 and 753; SEQ ID NOs: 795, 796 and 794; SEQ ID NOs: 797, 796 and 794; SEQ ID NOs: 797, 798 and

794; or SEQ ID NOs: 795, 799 and 794. In some embodiments, the first antigen binding domain is a Fab that binds to CD3 and the second antigen binding domain is a scFv or an EC domain of CD4 that binds to HIV gp120, wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753; SEQ ID NOs: 754, 752 and 753; SEQ ID NOs: 755, 756 and 753; SEQ ID NOs: 755, 757 and 753; SEQ ID NOs: 758, 757 and 753; or SEQ ID NOs: 759, 756 and 753. In some embodiments, the first antigen binding domain is a Fab that binds to CD3 and the second antigen binding domain is a scFv or an EC domain of CD4 that binds to HIV gp120, wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753; or SEQ ID NOs: 755, 756 and 753. In some embodiments, the first antigen binding domain is a Fab that binds to CD3 and the second antigen binding domain is a scFv or an EC domain of CD4 that binds to HIV gp120, wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753. In some embodiments, the first antigen binding domain is a Fab that binds to CD3 and the second antigen binding domain is a scFv or an EC domain of CD4 that binds to HIV gp120, wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 755, 756 and 753.

[0019] With respect to further embodiments of the multi-specific (*e.g.*, bispecific) antigen binding molecules, in some embodiments, the multi-specific antigen binding molecule is a bispecific antigen binding molecule. In some embodiments, the multi-specific antigen binding molecule binds to or targets human CD3 and HIV gp120. In some embodiments, the first VH and the first VL have at least 80%, 81%, 82%, 83%, 84%, 85%, or more, sequence similarity to a human germline VH and a human germline VL, respectively. In some embodiments, the first antigen binding domain has reduced or insignificant or substantially no binding to Protein A, or does not detectably bind to Protein A. In some embodiments, the first antigen binding domain binds to Protein A with a binding equilibrium dissociation constant (K_D) of greater than 10^{-6} M. In some embodiments, the first antigen binding domain binds to CD3 with a K_D of lower than 10 nM, *e.g.*, lower than 9.5 nM, 9.0 nM, 8.5 nM, 8.0 nM, 7.5 nM, 7.0 nM, 6.5 nM, 6.0 nM, 5.5 nM, 5.0 nM, 4.5 nM, 4.0 nM, 3.5 nM, 3.0 nM, or lower. In some embodiments, the first antigen binding domain binds to CD3 with a K_D of lower than 3.0 nM (*e.g.*, 2.5 nM). In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least 3 days, *e.g.*, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, or longer. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least 7 days. In some embodiments, the multi-specific (*e.g.*, bispecific) antigen binding molecule has a serum half-life in a human of at least 7 days. In some embodiments, the first antigen binding domain binds to CD3 with a K_D of lower than 7.0 nM, *e.g.*, lower than 6.5 nM, 6.0 nM, 5.5 nM, 5.0 nM, 4.5 nM, 4.0 nM, 3.5 nM, 3.0 nM, or lower, and the multi-specific (*e.g.*, bispecific) antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least at least 5 days, *e.g.*, at least 5.5 days, at least 6 days, at least 6.5 days, at least 7 days, at least 7.5 days, at least 8 days, at least 8.5 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, or longer. In some embodiments, the first antigen binding domain binds to CD3 with a K_D of lower than 3.0 nM (*e.g.*, 2.5 nM), and the multi-specific (*e.g.*, bispecific) antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least 7 days. In some embodiments, the first antigen binding domain binds to CD3 with a K_D of lower than 3.0 nM (*e.g.*, 2.5 nM), and the multi-specific (*e.g.*, bispecific) antigen binding molecule has a serum half-life in a human of at least 7 days. In some embodiments, at least 50%, at least 60%, at least 70%, least 80%, at least 85%, at least 90%, or more, N-linked glycosylation sites in at least one of the first VH, the first VL, the second VH and the second VL are sialylated. In some embodiments, the N-linked

glycosylation sites in at least one of the first VH, the first VL, the second VH and the second VL have a sialic acid occupancy (*e.g.*, a glycan comprising one or two terminal sialic acid residues) of at least 40%, at least 50%, at least 60%, at least 70%, least 80%, at least 85%, at least 90%, or more. In some embodiments, the sialylated N-linked glycosylation sites in at least one of the first VH, the first VL, the second VH and the second VL comprise from 1 to 5 sialic acid residues, *e.g.*, from 1 to 4 sialic acid residues, *e.g.*, from 1 to 3 sialic acid residues, *e.g.*, from 1 to 2 sialic acid residues. In some embodiments, at least one of the first VH, the first VL, the second VH and the second VL are sialylated with N-acetylneuraminic acid (NANA). In some embodiments, the sialic acid residues are present in biantennary structures. In some embodiments, the sialic acid residues are present in complex N-linked glycan structures. In some embodiments, the sialic acid residues are present in hybrid N-linked glycan structures. In some embodiments, the glycans are terminally sialylated.

[0020] In another aspect, provided is a polynucleotide or multiple polynucleotides encoding at least the first VH and the first VL of the multi-specific (*e.g.*, bispecific) antigen binding molecule, as described herein. In some embodiments, the polynucleotide or polynucleotides, further comprise a polynucleotide or multiple polynucleotides encoding the second VH and the second VL of the multi-specific (*e.g.*, bispecific) antigen binding molecule, as described herein. In some embodiments, the polynucleotide or polynucleotides comprise a polynucleotide or multiple polynucleotides encoding the HC of the first antigen binding domain that is an scFv, and the HC and LC of the second antigen binding domain that is a Fab, of the multi-specific (*e.g.*, bispecific) antigen binding molecule, as described herein. In some embodiments, the polynucleotide or polynucleotides comprise a polynucleotide or multiple polynucleotides encoding the HC and LC of the first antigen binding domain that is a Fab, and the HC of the second antigen binding domain that is an scFv or an EC domain of CD4, of the multi-specific (*e.g.*, bispecific) antigen binding molecule. In some embodiments, the polynucleotide or polynucleotides comprise a polynucleotide or multiple polynucleotides encoding the HC and LC of the first antigen binding domain that is a Fab, and the HC of the second antigen binding domain that is an EC domain of CD4, of the multi-specific (*e.g.*, bispecific) antigen binding molecule. In some embodiments, the polynucleotide or polynucleotides encode a multi-specific antigen binding molecule, as described herein, comprising the following polynucleotide sequences, or polynucleotide sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the polynucleotide sequences set forth, respectively: SEQ ID NOs: 995, 996 and 997; SEQ ID NOs: 998, 999 and

1000; SEQ ID NOs: 1001, 1002 and 1003; SEQ ID NOs: 1004, 1005 and 1000; SEQ ID NOs: 1006, 1002 and 997; SEQ ID NOs: 1007, 1093 and 1000; SEQ ID NOs: 998, 1008 and 1000; SEQ ID NOs: 998, 1009 and 1000; SEQ ID NOs: 1010, 1011 and 1012; SEQ ID NOs: 1013, 1014 and 1015; SEQ ID NOs: 1016, 1017 and 1012; SEQ ID NOs: 1018, 1019 and 1012; SEQ ID NOs: 1018, 1020 and 1012; SEQ ID NOs: 1021, 1022 and 1023; or SEQ ID NOs: 1024, 1025 and 1023. In some embodiments, the polynucleotide or polynucleotides encode a multi-specific antigen binding molecule, as described herein, comprising polynucleotide sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the polynucleotide sequences set forth, respectively: SEQ ID NOs: 995, 996 and 997. In some embodiments, the polynucleotide or polynucleotides encode a multi-specific antigen binding molecule, as described herein, comprising polynucleotide sequences that are at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to the polynucleotide sequences set forth: SEQ ID NOs: 995, 996 and 997. In some embodiments, the polynucleotide or polynucleotides encode a multi-specific antigen binding molecule, as described herein, comprising the following polynucleotide sequences: SEQ ID NOs: 995, 996 and 997. In some embodiments, the polynucleotide or polynucleotides encode a multi-specific antigen binding molecule, as described herein, comprising polynucleotide sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the polynucleotide sequences set forth, respectively: SEQ ID NOs: 998, 999 and 1000. In some embodiments, the polynucleotide or polynucleotides encode a multi-specific antigen binding molecule, as described herein, comprising polynucleotide sequences that are at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to the polynucleotide sequences set forth: SEQ ID NOs: 998, 999 and 1000. In some embodiments, the polynucleotide or polynucleotides encode a multi-specific antigen binding molecule, as described herein, comprising the following polynucleotide sequences: SEQ ID NOs: 998, 999 and 1000. In some embodiments, the polynucleotide or polynucleotides are comprised of DNA or RNA. In some embodiments, the polynucleotide or polynucleotides are comprised of mRNA. In some embodiments, the polynucleotide or polynucleotides comprise codon bias for efficient expression in a human cell. In a further aspect, provided is a lipoplex, *e.g.*, a lipid nanoparticle (LNP), comprising the polynucleotide or polynucleotides, as described herein. In a further aspect, provided is an expression cassette or multiple expression cassettes comprising one or more regulatory sequences operably linked to the polynucleotide or polynucleotides, as described herein.

[0021] In a further aspect, provided is an expression vector or multiple expression vectors comprising one or more regulatory sequences operably linked to the polynucleotide or polynucleotides, or the expression cassette or expression cassettes, as described herein. In some embodiments, the expression vector or expression vectors comprise a plasmid vector or a viral vector. In some embodiments, the expression vector comprises three, four or five expression cassettes or cistrons. In some embodiments, the expression vector comprises, optionally in sequential order from 5′ to 3′: (i) a first expression cassette or cistron comprising a first polynucleotide encoding an anti-HIV gp120 VL-light chain constant domain (CL) fusion protein; (ii) a second expression cassette or cistron comprising a second polynucleotide encoding an anti-HIV gp120 VH-Fc fusion protein; and (iii) a third expression cassette or cistron comprising a third polynucleotide encoding an anti-CD3 scFv-Fc fusion protein. In some embodiments, the anti-HIV gp120 VL-CL fusion protein, the anti-HIV gp120 VH-Fc fusion protein and the anti-CD3 scFv-Fc fusion protein comprise amino acid sequences set forth, respectively, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 802, 801 and 800; SEQ ID NOs: 802, 803 and 800; SEQ ID NOs: 802, 803 and 804; SEQ ID NOs: 802, 805 and 804; SEQ ID NOs: 802, 801 and 806; SEQ ID NOs: 802, 803 and 806; SEQ ID NOs: 802, 803 and 807; SEQ ID NOs: 802, 805 and 807; SEQ ID NOs: 802, 809 and 808; SEQ ID NOs: 802, 810 and 808; SEQ ID NOs: 802, 801 and 811; SEQ ID NOs: 802, 809 and 812; SEQ ID NOs: 802, 810 and 812; SEQ ID NOs: 802, 805 and 813; SEQ ID NOs: 802, 814 and 812; SEQ ID NOs: 802, 801 and 815; SEQ ID NOs: 802, 805 and 816; SEQ ID NOs: 802, 801 and 817; SEQ ID NOs: 802, 805 and 818; SEQ ID NOs: 802, 810 and 819; SEQ ID NOs: 802, 810 and 820; SEQ ID NOs: 823, 822 and 821; SEQ ID NOs: 823, 825 and 824; SEQ ID NOs: 823, 825 and 826; SEQ ID NOs: 823, 827 and 826; SEQ ID NOs: 823, 829 and 828; SEQ ID NOs: 823, 822 and 830; SEQ ID NOs: 823, 825 and 830; SEQ ID NOs: 823, 825 and 831; SEQ ID NOs: 823, 827 and 831; SEQ ID NOs: 823, 833 and 832; SEQ ID NOs: 823, 829 and 832; SEQ ID NOs: 823, 827 and 834; SEQ ID NOs: 823, 829 and 835; SEQ ID NOs: 823, 829 and 836; SEQ ID NOs: 823, 833 and 837; SEQ ID NOs: 823, 838 and 837; SEQ ID NOs: 823, 840 and 839; SEQ ID NOs: 823, 829 and 841; SEQ ID NOs: 823, 829 and 842; SEQ ID NOs: 823, 829 and 843; SEQ ID NOs: 823, 829 and 844; SEQ ID NOs: 823, 829 and 845; SEQ ID NOs: 823, 829 and 846; SEQ ID NOs: 823, 833 and 846; SEQ ID NOs: 823, 838 and 846; SEQ ID NOs: 823, 827 and 847; SEQ ID NOs: 823, 829 and 848; SEQ ID NOs: 823, 829 and 849; SEQ ID NOs: 823, 829 and 850; SEQ ID NOs: 823, 829 and 851; SEQ ID NOs: 823, 829

and 852; SEQ ID NOs: 823, 829 and 853; SEQ ID NOs: 823, 829 and 854; SEQ ID NOs: 823, 829 and 855; SEQ ID NOs: 823, 829 and 856; SEQ ID NOs: 823, 829 and 857; SEQ ID NOs: 823, 829 and 858; SEQ ID NOs: 823, 829 and 859; SEQ ID NOs: 823, 829 and 860; SEQ ID NOs: 863, 862 and 861; SEQ ID NOs: 863, 864 and 861; SEQ ID NOs: 863, 864 and 865; SEQ ID NOs: 863, 866 and 865; SEQ ID NOs: 863, 868 and 867; SEQ ID NOs: 863, 862 and 869; SEQ ID NOs: 863, 864 and 869; SEQ ID NOs: 863, 864 and 870; SEQ ID NOs: 863, 866 and 870; SEQ ID NOs: 863, 872 and 871; SEQ ID NOs: 863, 868 and 871; SEQ ID NOs: 863, 862 and 873; SEQ ID NOs: 863, 866 and 874; SEQ ID NOs: 863, 872 and 875; SEQ ID NOs: 863, 868 and 875; SEQ ID NOs: 863, 876 and 875; SEQ ID NOs: 863, 862 and 877; SEQ ID NOs: 863, 866 and 878; SEQ ID NOs: 863, 862 and 879; SEQ ID NOs: 863, 866 and 880; SEQ ID NOs: 883, 882 and 881; SEQ ID NOs: 883, 884 and 881; SEQ ID NOs: 883, 884 and 885; SEQ ID NOs: 883, 886 and 885; SEQ ID NOs: 883, 888 and 887; SEQ ID NOs: 883, 882 and 889; SEQ ID NOs: 883, 884 and 889; SEQ ID NOs: 883, 884 and 890; SEQ ID NOs: 883, 886 and 890; SEQ ID NOs: 883, 892 and 891; SEQ ID NOs: 883, 888 and 891; SEQ ID NOs: 883, 882 and 883; SEQ ID NOs: 883, 886 and 894; SEQ ID NOs: 883, 892 and 895; SEQ ID NOs: 883, 888 and 895; SEQ ID NOs: 883, 896 and 895; SEQ ID NOs: 883, 882 and 897; SEQ ID NOs: 883, 886 and 898; SEQ ID NOs: 883, 882 and 899; or SEQ ID NOs: 883, 886 and 900. In some embodiments, the expression vector comprises, optionally in sequential order from 5′ to 3′: (i) a first expression cassette or cistron comprising a first polynucleotide encoding an anti-CD3 VL-CL fusion protein; (ii) a second expression cassette or cistron comprising a second polynucleotide encoding an anti-CD3 VH-Fc fusion protein; and (iii) a third expression cassette or cistron comprising a third polynucleotide encoding a CD4 extracellular (EC) domain-Fc fusion protein. In some embodiments, the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences set forth, respectively, below, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below: SEQ ID NOs: 753, 752 and 751; SEQ ID NOs: 753, 752 and 754; SEQ ID NOs: 753, 756 and 755; SEQ ID NOs: 753, 757 and 755; SEQ ID NOs: 753, 757 and 758; SEQ ID NOs: 753, 756 and 759; SEQ ID NOs: 761, 760 and 754; SEQ ID NOs: 761, 760 and 762; SEQ ID NOs: 753, 763 and 751; SEQ ID NOs: 753, 752 and 764; SEQ ID NOs: 753, 752 and 765; SEQ ID NOs: 753, 767 and 766; SEQ ID NOs: 753, 768 and 766; SEQ ID NOs: 753, 768 and 769; SEQ ID NOs: 753, 767 and 770; SEQ ID NOs: 761, 771 and 765; SEQ ID NOs: 761, 771 and 772; SEQ ID NOs: 776, 775 and 774; SEQ ID NOs: 776, 778 and 777; SEQ ID NOs:

776, 778 and 779; SEQ ID NOs: 776, 780 and 779; SEQ ID NOs: 776, 781 and 777; SEQ ID NOs: 753, 752 and 782; SEQ ID NOs: 753, 752 and 783; SEQ ID NOs: 753, 785 and 784; SEQ ID NOs: 753, 786 and 784; SEQ ID NOs: 753, 786 and 787; SEQ ID NOs: 753, 785 and 788; SEQ ID NOs: 761, 789 and 783; SEQ ID NOs: 761, 789 and 790; SEQ ID NOs: 794, 793 and 792; SEQ ID NOs: 794, 796 and 795; SEQ ID NOs: 794, 796 and 797; SEQ ID NOs: 794, 798 and 797; or SEQ ID NOs: 794, 799 and 795. In some embodiments, the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 753, 752 and 751. In some embodiments, the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences set forth, respectively: SEQ ID NOs: 753, 752 and 751. In some embodiments, the first, second and third expression cassettes or cistrons each comprise a promoter of identical or equivalent transcription strength, *e.g.*, a constitutive promoter, *e.g.*, a promoter selected from cytomegalovirus (CMV), SV40, RSV, EF1a, UBC, PGK and CAGG. In some embodiments, the first, second and third expression cassettes or cistrons comprise one or more promoters of different transcription strength. In embodiments, the expression vector further comprises a fourth expression cassette or cistron positioned 5′ to the first expression cassette or cistron comprising a polynucleotide encoding a eukaryotic selection marker protein, *e.g.*, glutamine synthetase (GS). Generally, the fourth expression cassette or cistron, positioned 5′ to the first expression cassette and comprising a polynucleotide encoding a eukaryotic selection marker protein, is translated from the same strand as the first, second and third expression cassettes or cistrons.

[0022] In a further aspect, provided is a cell or population of cells. In various embodiments, the cell or population of cells comprise the polynucleotide or polynucleotides of, the expression cassette or multiple expression cassettes, or the expression vector or expression vectors, as described herein. In some embodiments, the cell or population of cells comprises a eukaryotic cell. In some embodiments, the cell or population of cells comprises a mammalian cell, an insect cell, a plant cell or a yeast cell. In some embodiments, the mammalian cell is a Chinese Hamster Ovary (CHO) cell. In some embodiments, the mammalian cell is a human cell. In some embodiments, the cell is a human embryonic kidney cell. In some embodiments, the cell predominantly sialylates N-linked glycosylation sites in the variable domains (Fv) of expressed antigen binding molecules. In some embodiments, at least 50%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, or more,

N-linked glycosylation sites in the variable domains (Fv) of expressed antigen binding molecules are sialylated.

[0023] In a further aspect, provided is a pharmaceutical composition comprising one or more multi-specific antigen binding molecules, as described herein, and a pharmaceutically acceptable carrier. In a related aspect, provided is a pharmaceutical composition comprising one or more polynucleotides, described herein, encoding one or more multi-specific antigen binding molecule, described herein, or the lipoplex (*e.g.*, LNP) described herein, and a pharmaceutically acceptable carrier. In some embodiments, the pharmaceutical composition comprises an aqueous formulation. In some embodiments, the pharmaceutical composition comprises one or more multi-specific antigen binding molecules, described herein, at a concentration of from 0.1 mg/ml to 150 mg/ml, *e.g.*, from 0.1 mg/ml to 100 mg/ml, *e.g.*, from 1 mg/ml to 100 mg/ml, *e.g.*, from 5 mg/ml to 60 mg/ml, *e.g.*, from 20 mg/ml to 150 mg/ml, or from 10 mg/ml to 50 mg/ml. In some embodiments, the pharmaceutical composition is lyophilized. In some embodiments, the pharmaceutical composition is formulated for intravenous, intramuscular or subcutaneous administration. In some embodiments, the pharmaceutical composition further comprises a second agent for treating an HIV infection. In some embodiments, the pharmaceutical composition further comprises a toll-like receptor (TLR) agonist or an IL-15 receptor agonist. In some embodiments, the pharmaceutical composition comprises a multi-specific antigen binding molecule having a first antigen binding domain that binds to CD3, and a second antigen binding domain that binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises one or more extracellular (EC) domains of CD4, and optionally, an IL-15 receptor agonist. In some embodiments, the one or more EC domains of CD4 comprise a sequence as set forth in SEQ ID NOs: 746-749, or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the EC domain of CD4 comprises a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 95% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises the sequence of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising

the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%,

identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25;

and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the TLR agonist is a TLR2 agonist, a TLR3 agonist, a TLR7 agonist, a TLR8 agonist or a TLR9 agonist. In some

embodiments, the pharmaceutical composition further comprises the TLR7 agonist is selected from the group consisting of vesatolimod, imiquimod, and resiquimod. In some embodiments, the pharmaceutical composition comprises a first multi-specific antigen binding molecule and second or additional antigen binding molecules, wherein the first multi-specific antigen binding molecule and the second or additional antigen binding molecules bind to different epitopes or regions of gp120 selected from the group consisting of: (i) the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan; (ii) the second variable loop (V2) (*e.g.*, Env trimer apex); (iii) the CD4 binding site (CD4bs); (iv) the gp120/gp41 interface; or (v) the silent face of gp120. In some embodiments, the first multi-specific antigen binding molecule binds to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and the second or additional antigen binding molecules bind to the CD4 binding site (CD4bs). In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second or additional antigen binding molecules comprise an EC domain of CD4. In some embodiments, the first multi-specific antigen binding molecule binds to the CD4 binding site (CD4bs) and the second or additional

antigen binding molecules bind to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134. In some embodiments, the pharmaceutical composition further comprises additional antigen binding molecules that compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07,

VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the pharmaceutical composition further comprises additional antigen binding molecules that compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523. In some embodiments, the pharmaceutical composition comprises: (i) a multi-specific (*e.g.* bispecific) antigen binding molecule comprising a EC domain of CD4, as described herein; (ii) an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134; and (iii) an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523. In some embodiments, the pharmaceutical composition comprises an additional multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody that binds to the gp120 second variable loop (V2) (*e.g.*, Env trimer apex). In some embodiments, the pharmaceutical composition comprises an additional multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of PG9, PG16, PGC14, PGG14, PGT-142, PGT-143, PGT-144, PGT-145, CH01, CH59, PGDM1400, CAP256, CAP256-VRC26.08, CAP256-VRC26.09, CAP256-VRC26.25, PCT64-24E and VRC38.01. In some embodiments, the pharmaceutical composition comprises an additional multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody that binds to the gp120/gp41 interface. In some embodiments, the pharmaceutical composition comprises an additional multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of PGT-151, CAP248-2B, 35O22, 8ANC195, ACS202, VRC34 and VRC34.01. In some embodiments, the pharmaceutical composition comprises an additional multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody that binds to an epitope or region of gp41 in the membrane proximal region (MPER). In some embodiments, the pharmaceutical composition comprises an additional multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10E8, 10E8v4, 10E8-5R-100cF, 4E10, DH511.11P, 2F5, 7b2, and LN01. In some embodiments, the pharmaceutical composition comprises an additional antigen binding molecule or antigen binding fragment thereof that at

least one of binds, inhibits, and neutralizes HIV, or a polynucleotide encoding the additional antigen binding molecule or antigen binding fragment thereof, wherein the additional antigen binding molecule or antigen binding fragment does not compete for binding to gp120 with the one or more multi-specific antigen binding molecules.

[0024] In a further aspect, provided is a kit comprising one or more containers comprising one or more of the multi-specific (*e.g.*, bispecific) antigen binding molecules, the polynucleotide or polynucleotides, the lipoplex (*e.g.*, LNP), or the pharmaceutical composition, as described herein. In some embodiments, the kit comprises one or more unitary doses of the one or more multi-specific antigen binding molecules, or the polynucleotide or polynucleotides, in one or more containers (*e.g.*, one or more vials, ampules, syringes). In some embodiments, the kit comprises one or more unitary doses of the one or more multi-specific antigen binding molecules and a second agent for treating an HIV infection in separate containers. In some embodiments, the kit further comprises at least one of a toll-like receptor (TLR) agonist and an IL-15 receptor agonist. In some embodiments, the kit comprises a multi-specific antigen binding molecule having a first antigen binding domain that binds to CD3, and a second antigen binding domain that binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises one or more extracellular (EC) domains of CD4, and optionally, an IL-15 receptor agonist. In some embodiments, the one or more EC domains of CD4 comprise a sequence as set forth in SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746), or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the EC domain of CD4 comprises a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 95% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises the sequence of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least

91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least

90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the TLR agonist is a TLR2 agonist, a TLR3 agonist, a TLR7 agonist, a TLR8 agonist or a TLR9 agonist. In some embodiments, the TLR7 agonist is selected from the group consisting of vesatolimod, imiquimod, and resiquimod. In some embodiments, the kit comprises a first multi-specific antigen binding molecule and second or additional antigen binding molecules, wherein the first multi-specific antigen binding molecule and the second or additional antigen binding molecules bind to different epitopes or regions of gp120 selected from the group consisting of: (i) the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan; (ii) the second variable loop (V2) (*e.g.*, Env trimer apex); (iii) the CD4 binding site (CD4bs); (iv) the gp120/gp41 interface; or (v) the silent face of gp120. In some embodiments, the first multi-specific antigen binding molecule binds to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and the second or additional antigen binding molecules bind to the CD4 binding site (CD4bs). In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 and PGT-121, and

the second or additional antigen binding molecules comprise an EC domain of CD4. In some embodiments, the first multi-specific antigen binding molecule binds to the CD4 binding site (CD4bs) and the second or additional antigen binding molecules bind to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134. In some embodiments, the kits further comprise second or additional antigen binding molecules compete with or comprise VH

and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the kits further comprise second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523. In some embodiments, the kit comprises: (i) a multi-specific antigen binding molecule comprising a EC domain of CD4, described herein; (ii) an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134; and (iii) an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523. In some embodiments, the kit comprises two or more unitary doses, wherein the unitary doses are the same or different.

[0025] In a further aspect, provided are methods of producing a multi-specific (*e.g.*, bispecific) antigen binding molecule, described herein. In some embodiments, the methods of producing comprises: (a) culturing a cell or population of cells, described herein, transformed with the polynucleotide or polynucleotides, described herein, or the expression cassette or multiple expression cassettes, described herein, in a cell culture under conditions sufficient to express the multi-specific antigen binding molecules; and (b) isolating or purifying the antigen binding molecules from the cell culture. In some embodiments, the first antigen binding domain is a scFv and the second antigen binding domain is a Fab. In some embodiments, the first antigen binding domain is a Fab and the second antigen binding domain is a Fab or an EC domain of CD4. In some embodiments, the first antigen binding domain is a Fab and the second antigen binding domain is an EC domain of CD4. In some embodiments, the polypeptide comprising the first antigen binding domain and the polypeptide comprising the second antigen binding domain are expressed and assembled in the same cell. In some embodiments, the isolating or purifying step comprises Protein A affinity chromatography. In some embodiments, at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more, of the multi-specific antigen binding molecules are isolated or purified. In some embodiments, the isolating or purifying step further comprises ion exchange chromatography. In some embodiments, at least 95%, 96%, 97%, 98%, 99%, or more, of the multi-specific antigen binding molecules are

isolated or purified. In some embodiments, at least 95%, 96%, 97%, 98%, 99%, or more, of the multi-specific antigen binding molecules isolate or purify as non-aggregated soluble heterodimer as determined using size exclusion chromatography (SEC). In some embodiments, the isolated or purified multi-specific antigen binding molecules have increased homogeneity as assessed by analytical ion exchange chromatography, wherein the integrated area of a main peak representing an unmodified target species is at least 95%, 96%, 97%, 98%, or more, of the sum of all integrated protein peak areas. In some embodiments, the isolated or purified antigen binding molecules have fewer than 35%, 30%, 25%, 20%, 15%, 10%, 9%, 8%, 7%, or fewer, acidic contaminants. In some embodiments, the cell or population of cells are cultured in a culture volume of at least 2L, *e.g.*, at least 5L, 10L, 50L, 100L, 150L, 200L, 250L, or more. In some embodiments, the methods further comprise formulating the antigen binding molecule into a sterile pharmaceutical composition suitable for administration to a human subject.

[0026] In another aspect, provided are methods of treating or preventing HIV in a human subject in need thereof. In some embodiments, the methods comprise administering to the subject an effective amount of one or more multi-specific (*e.g.*, bispecific) antigen binding molecules, described herein, or the pharmaceutical composition, described herein. In a related aspect, provided are methods of preventing or treating an HIV infection or an HIV-related disease. In some embodiments, the methods comprises the steps of: identifying a patient in need of such prevention or treatment, and administering to said patient a first therapeutic agent comprising a therapeutically effective amount of at least one multi-specific (*e.g.*, bispecific) antigen binding molecules, described herein, or the pharmaceutical composition, described herein. In some embodiments, the methods further comprise administering to the subject a second agent for treating an HIV infection. In some embodiments, the subject is not receiving antiretroviral therapy (ART) or ART is discontinued prior to administration of the one or more multi-specific antigen binding molecules. In some embodiments, ART is discontinued after one or more administrations of the one or more multi-specific antigen binding molecules. In some embodiments, the methods further comprise administering one or more antiretroviral therapy (ART) agents to the subject. In some embodiments, the methods further comprise administering to the subject at least one of a TLR agonist and an IL-15 receptor agonist. In some embodiments, the method comprises administering a multi-specific antigen binding molecule having a first antigen binding domain that binds to CD3, and a second antigen binding domain that binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises one or more extracellular (EC) domains of CD4, and optionally, an IL-15 receptor agonist. In some embodiments, the one or more EC domains of CD4 comprise a sequence as set forth in SEQ ID

NOs: 746-749 (*e.g.*, SEQ ID NO: 746), or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the EC domain of CD4 comprises a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 95% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises the sequence of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO:

746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the TLR agonist is a TLR2 agonist, a TLR3 agonist, a TLR7 agonist, a TLR8 agonist or a TLR9 agonist. In some embodiments, the TLR7 agonist is selected from the group consisting of vesatolimod, imiquimod, and resiquimod. In some embodiments, the method comprises administering a first multi-specific antigen binding molecule and second or additional antigen binding molecules, wherein the first multi-specific antigen binding molecule and the second or additional antigen binding molecules bind to different epitopes or regions of gp120 selected from the group consisting of: (i) the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan; (ii) the second variable loop (V2) (*e.g.*, Env trimer apex); (iii) the CD4 binding site (CD4bs); (iv) the gp120/gp41 interface; or (v) the silent face of gp120. In some embodiments, the first multi-specific antigen binding molecule binds to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and the second or additional antigen binding molecules bind to the CD4 binding site (CD4bs). In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-

124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second or additional antigen binding molecules comprise an EC domain of CD4. In some embodiments, the first multi-specific antigen binding molecule binds to the CD4 binding site (CD4bs) and the second or additional antigen binding molecules bind to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected

from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134. In some embodiments, the method further comprises administering second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the method further comprises administering second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523. In some embodiments, the methods comprise co-administering: (i) a multi-specific antigen binding molecule comprising a EC domain of CD4, described herein; (ii) an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10 1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134; and (iii) an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS 5423, 3BNC117, VRC07 and VRC07-523. In some embodiments, the methods further comprise administering to the human subject an additional antigen binding molecule or antigen binding fragment thereof that at least one of binds, inhibits, and neutralizes HIV or a polynucleotide

encoding the additional antigen binding molecule or antigen binding fragment thereof. In some embodiments, the method comprises administering an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions that bind to the gp120 third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan, and the human subject is infected with an HIV expressing a gp120 comprising the following amino acid residues, wherein the positions and residues are with reference to SEQ ID NO:69: N332glycan, D325 and T63; N332glycan, D325 and L179; N332glycan, D325 and T320; N332glycan, D325 and H330; N332glycan, D325, T63 and L179; N332glycan, D325, T63 and T320; N332glycan, D325, T63 and H330; N332glycan, D325, L179 and T320; N332glycan, D325, L179 and H330; N332glycan, D325, T320 and H330; N332glycan, D325, T63, T320 and H330; N332glycan, D325, T63, L179 and T320; N332glycan, D325, T63, L179 and H330; N332glycan, D325, L179, T320 and H330; or N332glycan, D325, T63, L179, T320 and H330. In some embodiments, the method comprises administering an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions that bind to the gp120 CD4 binding site, and wherein the human subject is infected with an HIV expressing a gp120 comprising the following amino acid residues, wherein the positions and residues are with reference to SEQ ID NO:73: I201 and F353; I201, I108 and F353; I201, I108, A281 and F353; I201, E102, I108, A281 and F353; or I201, E102, I108, A281, Y318 and F353. In some embodiments, the method entails multiple administrations of the one or more multi-specific antigen binding molecules, optionally with a TLR agonist or an IL-15 receptor agonist, at predetermined intervals. In some embodiments, the method comprises administering a multi-specific antigen binding molecule having a first antigen binding domain that binds to CD3, and a second antigen binding domain that binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises one or more extracellular (EC) domains of CD4, and optionally, an IL-15 receptor agonist, wherein the multi-specific antigen binding molecule and the IL-15 receptor agonist are administered independently at predetermined intervals. In some embodiments, the one or more EC domains of CD4 comprise a sequence as set forth in SEQ ID NOs: 746-749, or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding

domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56; and the second antigen

binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the subject is chronically infected with HIV. In some embodiments, the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition are administered systemically or locally. In some embodiments, the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition is administered via a route selected from intravenous, subcutaneous, intramuscular, intradermal and mucosal (*e.g.* buccal, intranasal, intrarectal, intravaginal). In some embodiments, the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition and the one or more additional therapeutic agents are administered by the same routes of administration. In some embodiments, the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition and the one or more additional therapeutic agents are administered by different routes of administration. In some embodiments, the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition and the one or more additional therapeutic agents are co-administered according to the same schedule (*e.g.*, co-administered at the same time intervals). In some embodiments, the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition and the one or more additional therapeutic agents are co-administered according to different schedules (*e.g.*, co-administered at different time intervals). In some embodiments, the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition is administered at a dose in the range of from 1 μg/kg to 5 μg/kg, *e.g.*, from 350 μg/kg to 550 μg/kg, *e.g.*, from 0.3 mg/kg to 30 mg/kg, *e.g.*, from 2 mg/kg to 10 mg/kg, *e.g.*, from 1 μg/kg up to 2 μg/kg, 3 μg/kg, 4 μg/kg, 5 μg/kg, 10 μg/kg, 50 μg/kg, 100 μg/kg, 250 μg/kg, 300 μg/kg, 350 μg/kg, 400 μg/kg, 410 μg/kg, 420 μg/kg, 430 μg/kg, 440 μg/kg, 450 μg/kg, 460 μg/kg, 470 μg/kg, 480 μg/kg, 490 μg/kg, 500 μg/kg, 750 μg/kg, 1 mg/kg, 1.5 mg/kg, 2 mg/kg, 2.5 mg/kg, 3 mg/kg, 3.5 mg/kg, 4 mg/kg, 4.5 mg/kg, 5 mg/kg, 6 mg/kg, 7 mg/kg, 8 mg/kg, 9 mg/kg, 10 mg/kg, 15 mg/kg, 20 mg/kg, 25 mg/kg, 30 mg/kg, 35 mg/kg, 40 mg/kg, 45 mg/kg, or 50 mg/kg, body weight per administration. In some embodiments, the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition is

administered at a dose in the range of 0.05 mg to 1000 mg per administration, *e.g.,* from 0.05 mg to 150 mg per administration, *e.g.,* from 0.05 mg to 0.35 mg per administration, *e.g.,* from 25 mg to 50 mg per administration, *e.g.,* from 30 mg to 35 mg per administration, *e.g.,* from 10 mg to 1000 mg per administration, *e.g.,* from 50 mg to 1000 mg per administration, *e.g.,* from 100 mg to 700 mg per administration, *e.g.*, at least 0.05 mg up to 0.1 mg, 0.2 mg, 0.3 mg, 0.35 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg, 0.8 mg, 1.0 mg, 5 mg, 10 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 200 mg, 300 mg, 400 mg, 500 mg, 600 mg, 700 mg, 800 mg, 900 mg, or 1000 mg per administration. In some embodiments, the method entails multiple administrations of the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition, optionally with one or more additional therapeutic agents, at predetermined intervals. In some embodiments, the method entails administering over a time period of at least about 2 weeks, 3 weeks, 1 month, 6, weeks, 2 months, 10 weeks, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months, 13 months, 14 months, 15 months, 16 months, 17 months, 18 months, 19 months, 20 months, 21 months, 22 months, 23 months, 24 months, or longer. In some embodiments, the method entails administering one or more times at predetermined intervals spaced at least 1 week and up to at least 2 weeks, 3 weeks, 1 month, 2 months, 3 months, 4 months, 5 months or 6 months apart. In some embodiments, the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition is administered once weekly (*i.e.*, QW), once bi-weekly (*i.e.* once every other week, or once every two weeks or Q2W), once thrice-weekly (*i.e.* once every three weeks or Q3W), once monthly (*i.e.*, QM) or once bi-monthly dosing (*i.e.* once every other month, or once every two months or Q2M), once every three months (Q3M), once every four months (Q4M), once every five months (Q5M), once every six months (Q6M), or less often. In some embodiments, the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition is administered two, three, four, five, or more, times intravenously or subcutaneously at an interval or at intervals between once bi-weekly (*i.e.* once every other week, or once every two weeks or Q2W) to once thrice-weekly (*i.e.* once every three weeks or Q3W). In some embodiments, the method entails the one or more multi-specific antigen binding molecules have a serum half-life in a human of at least 3 days, *e.g.*, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, or longer. In some embodiments, the subject or the mammal is a human. In some embodiments, the subject does not exhibit symptoms of HIV or AIDS in the

absence of anti-retroviral treatment (ART) for at least 6 months, at least 1 year, at least 2 years, at least 3 years, or more. In some embodiments, the subject has a viral load of copies/ml blood of less than 500, *e.g.*, less than 400, less than 300, less than 200, less than 100, less than 50, in the absence of anti-retroviral treatment (ART) for at least 6 months, at least 1 year, at least 2 years, at least 3 years, or more.

[0027] In a related aspect, provided are methods of treating or preventing HIV in a human subject in need thereof. In some embodiments, the methods comprise: (a) Identifying a human subject who is infected with an HIV expressing a gp120 comprising the following amino acid residues, wherein the positions and residues are with reference to SEQ ID NO:69: N332glycan, D325 and T63; N332glycan, D325 and L179; N332glycan, D325 and T320; N332glycan, D325 and H330; N332glycan, D325, T63 and L179; N332glycan, D325, T63 and T320; N332glycan, D325, T63 and H330; N332glycan, D325, L179 and T320; N332glycan, D325, L179 and H330; N332glycan, D325, T320 and H330; N332glycan, D325, T63, T320 and H330; N332glycan, D325, T63, L179 and T320; N332glycan, D325, T63, L179 and H330; N332glycan, D325, L179, T320 and H330; or N332glycan, D325, T63, L179, T320 and H330; and (b) Administering to the subject an effective amount of the multi-specific antigen binding molecule, described herein, or the pharmaceutical composition, described herein, wherein the second binding domain competes with or comprises VH and VL regions that bind to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan. In some embodiments, the methods comprise identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues: N332glycan, D325 and T63; N332glycan, D325 and L179; N332glycan, D325 and T320; or N332glycan, D325 and H330. In some embodiments, the methods comprise identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues: N332glycan, D325, T63 and L179; N332glycan, D325, T63 and T320; N332glycan, D325, T63 and H330; N332glycan, D325, L179 and T320; N332glycan, D325, L179 and H330; or N332glycan, D325, T320 and H330. In some embodiments, the methods comprise identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues: N332glycan, D325, L179, T320 and H330; N332glycan, D325, T63, T320 and H330; N332glycan, D325, T63, L179 and T320; or N332glycan, D325, T63, L179 and H330. In some embodiments, the methods comprise identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues: N332glycan, D325, T63 and H330; N332glycan, D325, T320 and H330; N332glycan, D325, L179, T320 and H330; or N332glycan, D325, T63,

L179, T320 and H330. In some embodiments, the second antigen binding domain competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-9721, GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the second antigen binding domain competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-9721, GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134. In some embodiments, the method entails treating or preventing HIV in a human subject in need thereof, the method comprising: (a) Identifying a human subject who is infected with an HIV expressing a gp120 comprising the following amino acid residues, wherein the positions and residues are with reference to SEQ ID NO:73: (i) I201 and F353; (ii) I201, I108 and F353; (iii) I201, I108, A281 and F353; (iv) I201, E102, I108, A281 and F353; or (v) I201, E102, I108, A281, Y318 and F353; and (b) Administering to the subject an effective amount of the multi-specific antigen binding molecule, or the pharmaceutical composition of any one of claims 123 to 154, wherein the second binding domain competes with or comprises VH and VL regions that bind to the gp120 CD4 binding site (CD4bs). In some embodiments, the second antigen binding domain competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the second antigen binding domain competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, VRC01, VRC07 and VRC07-523. In some embodiments, the methods further comprise administering to the subject a second agent for treating an HIV infection. In some embodiments, the subject is not receiving antiretroviral therapy (ART) or ART is discontinued prior to administration of the one or more multi-specific antigen binding molecules. In some embodiments, ART is discontinued after one or more administrations of the one or more multi-specific antigen binding molecules. In some embodiments, the methods further comprise administering one or more antiretroviral therapy (ART) agents to the subject. In some embodiments, the methods further comprise administering to the subject at least one of a TLR agonist and an IL-15 receptor agonist. In

some embodiments, the method comprises administering a multi-specific antigen binding molecule having a first antigen binding domain that binds to CD3, and a second antigen binding domain that binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises one or more extracellular (EC) domains of CD4, and optionally, an IL-15 receptor agonist. In some embodiments, the one or more EC domains of CD4 comprise a sequence as set forth in SEQ ID NOs: 746-749, or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the

following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the TLR agonist is a TLR2 agonist, a TLR3 agonist, a TLR7 agonist, a TLR8 agonist or a TLR9 agonist. In some embodiments, the TLR7 agonist is selected from the group consisting of vesatolimod, imiquimod, and resiquimod. In some embodiments, the methods entail multiple administrations of the one or more multi-specific antigen binding molecules, optionally with the TLR agonist, at predetermined intervals. In some embodiments, the subject does not exhibit symptoms of HIV or AIDS in the absence of anti-retroviral treatment (ART) for at least 6 months, at least 1 year, at least 2 years, at least 3 years, or more. In some embodiments, the subject has a viral load copies/ml blood of less than 500, *e.g.*, less than 400, less than 300, less than 200, less than 100, less than 50, in the absence of anti-retroviral treatment (ART) for at least 6 months, at least 1 year, at least 2 years, at least 3 years, or more.

[0028] In a further aspect, provided is the use of the multi-specific (*e.g.*, bispecific) antigen binding molecules or antigen binding fragment thereof, or the pharmaceutical compositions, as described herein, in a method of at least one of treating, preventing and inhibiting HIV in a human subject in need thereof. In a further aspect, provided are the multi-specific (*e.g.*, bispecific) antigen binding molecules or antigen binding fragment thereof, or the pharmaceutical compositions, as described herein, for use in a method of at least one of treating, preventing and inhibiting HIV in a human subject in need thereof. In some embodiments, the

use further comprises administering to the subject a second agent for treating an HIV infection. In some embodiments, the use further comprises administering to the subject at least one of a TLR agonist and an IL-15 receptor agonist. In some embodiments, the use entails administering a multi-specific antigen binding molecule having a first antigen binding domain that binds to CD3, and a second antigen binding domain that binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises one or more extracellular (EC) domains of CD4, and optionally, an IL-15 receptor agonist. In some embodiments, the one or more EC domains of CD4 comprise a sequence as set forth in SEQ ID NOs: 746-749, or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID

NO: 746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO: 746). In some embodiments, the TLR agonist is a TLR2 agonist, a TLR3 agonist, a TLR7 agonist, a TLR8 agonist or a TLR9 agonist. In some embodiments, the TLR7 agonist is selected from the group consisting of vesatolimod, imiquimod, and resiquimod. In some embodiments, the use comprises administering a first multi-specific antigen binding molecule and second or additional antigen binding molecules, wherein the first multi-specific antigen binding molecule and the second or additional antigen binding molecules bind to different first and second epitopes or regions of gp120 selected from the group consisting of: (i) third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan; (ii) second variable loop (V2) (*e.g.*, Env trimer apex); (iii) CD4 binding site (CD4bs); (iv) gp120/gp41 interface; or (v) silent face of gp120. In some embodiments, the first multi-specific antigen binding molecule binds to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan, and the second antigen binding molecule binds to the CD4 binding site (CD4bs). In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124,

PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, 3BNC117, 3BNC60, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second antigen binding molecule competes with or comprises VH and VL regions from 3BNC117, GS-9723, VRC07 or VRC07-523. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second antigen binding molecule comprises an EC domain of CD4. In some embodiments, the first multi-specific antigen binding molecule binds to the CD4 binding site (CD4bs) and the second or additional antigen binding molecules bind to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and

VRC07-523, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134. In some embodiments, the use further comprises administering second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the use further comprises administering second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523. In some embodiments, the use comprises co-administering: (i) a multi-specific antigen binding molecule comprising an EC domain of CD4, as described herein; (ii) an antibody that competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10 1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134; and (iii) an antibody that competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS 5423, 3BNC117, VRC07 and VRC07-523. In some embodiments, the use further comprises administering to the human subject an additional antigen binding molecule or antigen binding fragment thereof that at least one of binds, inhibits, and neutralizes HIV or a polynucleotide encoding the additional antigen binding molecule or antigen binding fragment thereof. In some embodiments, the human subject is infected with an HIV expressing a gp120 comprising the

following amino acid residues: N332/D325; N332/D325/H330; N332/D325/H330/T320; N332/D325/H330/T63; N332/D325/H330/T63/T320; or N332/D325/H330/T63/T320/L179.

[0029] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present bispecific molecules described herein, the exemplary methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present application, including definitions, will control. The materials, methods, and examples are illustrative only and not intended to be limiting.

[0030] Other features and advantages of the invention will be apparent from the following detailed description and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0031] Figures 1A and 1B illustrate a homology model of mSP34. The sidechains of potential solvent exposed sequence liabilities are shown as spheres and labelled using single letter amino acid nomenclature and numbered according to Kabat.

[0032] Figures 2A-2B. Figure 2A illustrates a sequence alignment of the mSP34 heavy chain variable domain and five comparators found in clinical stage antibodies. Potential solvent exposed sequence liabilities (Figure 1) are underlined. Figure 2A depicts SEQ ID NOs: 1044-1049, respectively, in order of appearance. Figure 2B illustrates a sequence alignment of the mSP34 light chain variable domain and five comparators found in clinical stage antibodies. Figure 2B depicts SEQ ID NOs: 1050-1055, respectively, in order of appearance.

[0033] Figure 3 illustrates a structural superposition of homology models of mSP34 (white) and the closest human germline (black) found using the IMGT domain gap align server. The models were created using Discovery Studio 2017r2 (Biovia) and superposed using PyMOL (Schrödinger, Inc.). The Cα backbone trace is shown.

[0034] Figures 4A-4B. Figure 4A illustrates a heavy chain (HC) sequence alignment of mSP34, the closest human germline and the first round of huSP34 heavy chain variants (SEQ ID NOs: 1064-1075, respectively, in order of appearance). Figure 4B illustrates a light chain (LC) sequence alignment of mSP34, the closest human germline and the first round of huSP34 light chain variants (SEQ ID NOs: 1056-1063, respectively, in order of appearance).

[0035] Figures 5A-5B. Figure 5A illustrates a heavy chain (HC) sequence alignment of mSP34, the closest human germline and the second round of huSP34 heavy chain variants ((SEQ ID NOs: 1082-1087, respectively, in order of appearance). Figure 5B illustrates a light chain (LC) sequence alignment of mSP34, the closest human germline and the second round of huSP34 light chain variants (SEQ ID NOs: 1076-1081, respectively, in order of appearance).

[0036] Figures 6A-6D illustrate an analysis of anti-CD3 affinity (Octet BLI) (Fig. 6A), charge homogeneity (CX-1) (Fig. 6B), aggregation propensity (size exclusion column (SEC)) (Fig. 6C) and match to the human germline (Fig. 6D) for the first and second round huSP34 Fab variants, mSP34 human chimeric Fab and comparator huSP34 Fab molecules.

[0037] Figures 7A-7D. Figure 7A illustrates examples of scFv-Fc/Fab-Fc bispecific antibodies designed as part of the present bispecific molecules. Figure 7B illustrates examples of CD4 ECD-Fc/Fab-Fc bispecific fusion proteins designed as part of the present bispecific molecules. Figure 7C illustrates examples of CD4 ECD-Fc/scFv-Fc bispecific fusion proteins designed as part of the present bispecific molecules. Figure 7D illustrates examples of CD4 ECD-Fc/scFv-Fc or CD4 ECD-Fc/Fab-Fc bispecific fusion proteins incorporating bivalent or tandem CD4 ECDs and designed as part of the present bispecific molecules. All technologies illustrated are optional and may be omitted or used in combinations beyond what is shown in these figures. Key: ΔEF = remove effector function (*e.g.*, FcγR binding reduced or eliminated with at least one of L234A and L235A (LALA) mutations; C1q binding reduced or eliminated with P331S mutation; collectively "AAS"); knob and hole = engineered Fc heterodimer (*e.g.*, "hole" (H) mutations include T366S, L368A and Y407V ("SAV"); "knob" (K) mutations include T366W ("W"); HLE = half-life extension (*e.g.*, M252Y, S254T and T256E ("YTE") or M428L and N434S ("LS")); ΔProA = reduce or eliminate Protein A binding (*e.g.*, H435R or H435R+Y436F ("RF")); linker = scFv linker (*e.g.*, $(GGGS)_4$ (SEQ ID NO: 711) or $(GGGGS)_4$ (SEQ ID NO: 750)).

[0038] Figures 8A and 8B. Figure 8A illustrates representative HiTrap® SP HP (Cytiva Life Sciences) cation exchange chromatography (employed to isolate the bispecific antibody or fusion protein Fc heterodimer from Fc homodimer or other contaminants with low isoelectric points (pI) using a gradient of 0-30% 1M NaCl in 20 mM sodium phosphate pH 7.0) to separate the desired bispecific antibody or fusion protein Fc heterodimer from Fc homodimer or other contaminants with low isoelectric points (pI)) and SDS-PAGE analysis for purification of the hPGT121.66 (*see*, *e.g.*, WO 2018/237148) AAS+W/huSP34.13.10scFv AAS+SAV+RF Fab-scFv-Fc bispecific antibody (Ab 265; SEQ ID NOs: 848, 829 and 823) (bispecific molecules

described herein are summarized in Table 53). Figure 8B illustrates representative HiTrap® SP HP (Cytiva Life Sciences) cation exchange chromatography results and SDS-PAGE analysis for purification of the hCD4 D1.22 Fc AAS+SAV+YTE/huSP34.3.13 AAS+W+YTE Fab-Fc-fusion bispecific molecule 185.

[0039] Figure 9 illustrates the analytical CX-1 % main peak values for all round 1 huSP34 Fab variants. The variants containing asparagine (N) at heavy chain (HC) position 100 were compared with those containing histidine at heavy chain position 100 using an unpaired t test. The results suggest that H100 contributed significantly to improved charge homogeneity.

[0040] Figure 10 illustrates representative binding of a bispecific to immobilized CD3 obtained from SPR experiments. Black lines denote injection of the bispecific 249 at various concentrations for a period of 120 seconds. Dissociation was then monitored for 80 seconds except for the highest concentration where dissociation was monitored for 10.5 minutes. Smoothed gray lines represent the fit to this data as obtained from a simple kinetic model. This model was used to derive k_{on}, k_{off}. and K_D for these interactions.

[0041] Figure 11 illustrates a representative binding concentration-response curve of PGT121.66 x huSP34 bispecific antibodies 265 (circle), 251 (square), 259 (upright triangle; dotted line). 258 (inverted triangle; solid line) and 260 (diamond) to CD4+ T cells (from Donor 4574). Bispecific molecules described herein are summarized in Table 53.

[0042] Figure 12 illustrates a representative binding concentration-response curve of PGT121.66 x huSP34 bispecific antibodies 265 (circle), 251 (square), 259 (upright triangle; dotted line). 258 (inverted triangle; solid line) and 260 (diamond) to CD8+ T cells (from Donor 4574).

[0043] Figures 13A-13B illustrate a representative binding concentration-response curve of (A) PGT121.66 x huSP34 bispecific antibodies 257 (solid circle), 274 (solid square), 273 (solid, upright triangle), 275 (solid inverted triangle), 256 (solid diamond), 243 (half-solid circle), 251 (half-solid square) and 261 (half-solid upright triangle) to human CD4+ T cells in PBMCs (from Donor hu 151) and (B) CD4 x huSP34 bispecific 180 to human CD4+ T cells in PBMCs (from Donor hu 921).

[0044] Figures 14A-14B illustrate a representative binding concentration-response curve of (A) PGT121.66 x huSP34 bispecific antibodies 257 (solid circle), 274 (solid square), 273 (solid, upright triangle), 275 (solid inverted triangle), 256 (solid diamond), 243 (half-solid circle), 251 (half-solid square) and 261 (half-solid upright triangle) to monkey CD4+ T cells in

PBMCs (from rhesus Donor rh 3563) and (B) CD4 x huSP34 bispecific 180 to monkey CD4+ T cells in PBMCs (from cynomolgus Donor cy 2177).

[0045] Figures 15A-15B illustrate a representative binding concentration-response curve of (A) PGT121.66 x huSP34 bispecific antibodies 257 (solid circle), 274 (solid square), 273 (solid, upright triangle), 275 (solid inverted triangle), 256 (solid diamond), 243 (half-solid circle), 251 (half-solid square) and 261 (half-solid upright triangle) to human CD8+ T cells in PBMCs (from Donor hu 151) and (B) CD4 x huSP34 bispecific 180 to human CD8+ T cells in PBMCs (from Donor hu 921).

[0046] Figures 16A-16B illustrates a representative binding concentration-response curve of (A) PGT121.66 x huSP34 bispecific antibodies 257 (solid circle), 274 (solid square), 273 (solid, upright triangle), 275 (solid inverted triangle), 256 (solid diamond), 243 (half-solid circle), 251 (half-solid square) and 261 (half-solid upright triangle) to rhesus CD8+ PBMCs (from Donor rh 3563) and (B) CD4 x huSP34 bispecific 180 to monkey CD8+ T cells in PBMCs (from cynomolgus Donor cy 2177).

[0047] Figure 17 illustrates EC_{50} values derived from concentration-response curves of PGT121.66 x huSP34 bispecific antibodies 257 (solid circle), 274 (solid square), 273 (solid, upright triangle), 275 (solid inverted triangle), 256 (solid diamond), 243 (open circle), 251 (open square) and 261 (open upright triangle) binding to human (hu) and rhesus (rh) CD4+ PBMCs.

[0048] Figure 18 illustrates EC_{50} values derived from concentration-response curves of PGT121.66 x huSP34 bispecific antibodies 257 (solid circle), 274 (solid square), 273 (solid, upright triangle), 275 (solid inverted triangle), 256 (solid diamond), 243 (open circle), 251 (open square) and 261 (open upright triangle) binding to human (hu) and rhesus (rh) CD8+ PBMCs.

[0049] Figure 19 illustrates a representative killing concentration-response curve by PGT121.66 x huSP34 bispecific antibodies 265 (solid circle), 259 (upright triangle), 258 (inverted triangle), 251 (square), and 260 (half-solid circle) using PBMC effector cells.

[0050] Figure 20 illustrates a Pearson correlation of PGT121.66 x huSP34 bispecific antibodies (from highest to lowest PBMC killing EC_{50} value) 258, 260, 259, 251 and 265. huSP34 variant CD3 binding affinity vs. PBMC killing EC_{50} values. The killing EC_{50} value is the geometric mean EC_{50} value of the 5 viruses tested with two donors.

[0051] Figure 21 illustrates a Pearson correlation of PGT121.66 x huSP34 bispecific antibodies (from highest to lowest T cell killing EC_{50} value) 260, 258, 259, 251 and 265.

huSP34 variant CD3 binding affinity vs. isolated T cell killing EC_{50} values. The killing EC_{50} value is the geometric mean EC_{50} value of the 5 viruses tested with two donors.

[0052] Figure 22 illustrates a representative concentration-response curve of killing by 3BNC117.52.64 x huSP34 bispecific antibodies 237 (circle), 230 (square) and 232 (triangle) using PBMC effector cells.

[0053] Figure 23 illustrates a Pearson correlation of 3BNC117.52.64 x CD3 bispecific antibodies (from highest to lowest PBMC cell killing EC_{50} value) 238, 230 and 237. huSP34 variant CD3 binding affinity vs. PBMC killing EC_{50} values. The killing EC_{50} value is the geometric mean EC_{50} value of the 5 viruses tested with two donors.

[0054] Figure 24 illustrates a representative killing concentration-response curve of primary HIV-infected (virus 657) CD4+ cells by PGT121.66 x huSP34 bispecific molecules 265 (circle) 251 (square) and 259 (triangle) using PBMC effector cells (E:T = 3:1).

[0055] Figure 25 illustrates a representative killing concentration-response curve of primary HIV-infected (virus 7552) CD4+ cells by PGT121.66 x huSP34 bispecific molecules 265 (circle) 251 (square) and 259 (triangle) using PBMC effector cells (E:T = 3:1).

[0056] Figure 26 illustrates EC_{50} values of killing curves plotted across CD4 ECD x α-CD3 bispecific molecules (from right-to-left: 212, 211, 213, 198, 187, 199 and 186). The geomean EC_{50} value for each molecule (—) calculated from all viruses/donors are shown.

[0057] Figure 27 illustrates antibody- and bispecific- mediated killing of primary CD4+ T cells infected with different HIV isolates. Primary CD4+ T cells were infected with a panel of 32 HIV isolates and incubated with the antibodies or antibody combinations indicated and autologous PBMCs as effector cells. Data on the graph represents the EC_{50} values determined in the killing assay for each HIV isolate and antibody, bispecific or antibody/bispecific combination (from left to right: PGT121.42, h3BNC117.52.64, bispecific 180, PGT121.42 + h3BNC117.52.64 combination, PGT121.42 + h3BNC117.52.64 + bispecific 180 combination. Horizontal bars indicate the median and 95% confidence intervals.

[0058] Figure 28 EC_{50} values of binding curves for 24 virus isolate-infected cells plotted across test bispecific molecules 186, 255 and 230.

[0059] Figure 29 illustrates pharmacokinetic (PK) profiles for PGT121.66 x huSP34 bispecific molecules 250 (circle), 252 (square), and 251 (triangle) dosed at 1 mg/kg IV to naïve male cynomolgus monkeys (n=3). For comparison, dose normalized individual monkey PK

profiles for Comparator #7 bispecific (dashed lines) dosed at 30 mg/kg IV on Day 0 and 7. Each symbol is the measured mean ± standard deviation (SD) serum concentration.

[0060] Figure 30 illustrates PK profiles for PGT121.66 x huSP34 bispecific molecules 264 (solid circle), 265 (solid square), 261 (solid triangle), 262 (open circle), and 263 (open square) following 1 mg/kg IV dosing to naïve male cynomolgus monkeys (n=3). Each symbol is the measured mean ± SD serum concentration.

[0061] Figure 31 illustrates PK profiles for PGT121.66 x huSP34 bispecific molecules 257 (solid circle), 274 (open circle), 273 (solid square), 275 (open square), 256 (solid triangle), and 243 (open triangle) following 1 mg/kg IV dosing to naïve male cynomolgus monkeys (n=2). Each symbol is the measured mean serum concentration.

[0062] Figure 32 illustrates PK profiles for PGT121.66 x huSP34 bispecific molecules 249 (solid circle), 276 (solid square), 277 (solid triangle), and 218 (open circle) following 1 mg/kg IV dosing to naïve male cynomolgus monkeys (n=2 or 3). Each symbol is the measured mean ± SD serum concentration.

[0063] Figure 33 illustrates PK profiles for CD4 ECD x huSP34 bispecific molecules 186 (solid circle), 187 (solid square), 180 (open circle), 182 (open square), and 185 (open triangle) following 1 mg/kg IV dosing to naïve male cynomolgus monkeys (n=3). Bispecific molecules 186 and 187 were dosed on Day 0 and 14. Each symbol is the measured mean ± SD serum concentration.

[0064] Figure 34 illustrates organization of an expression vector having polynucleotide sequences encoding the expression of the three polypeptide chains of an asymmetric bispecific molecule having an anti-HIV gp120 Fab and an anti-CD3 scFv. The vector was designed to drive the expression of three polypeptide chains: heavy chain and light chain of anti-gp120 Fab and scFv of anti-CD3 from three separate expression cassettes, each driven by its own promoter of equal transcription strength (*e.g.*, a cytomegalovirus (CMV) promotor). An additional DNA cassette having a polynucleotide encoding a eukaryotic selection marker (*e.g.*, glutamine synthetase (GS)) using a promoter of relatively weaker transcription strength (*e.g.*, an SV40 promoter) was included in the expression vector. DNA encoding for a bacterial origin of replication (*e.g.*, Ori) and an antibiotic selection marker (*e.g.*, ampicillin (AmpR)) were utilized for expression vector production in *E. coli*.

[0065] Figure 35 illustrates an evaluation of expression performance of cell lines expressing asymmetric bispecific molecules having an anti-HIV gp120 Fab and an anti-CD3

scFv. The expression performance was assessed by culturing the cells expressing the bispecific molecules in a fed-batch process and evaluating their performance at baseline (D0) and upon aging (D30). Expression of multiple species including the bispecific molecule of interest was measured using a ProA based Bio-layer interferometry and the relative levels of the heterotrimer (Het%, heterotrimer%) comprising the asymmetric bispecific molecule was monitored using size separation methods (non-reduced capillary electrophoresis).

[0066] Figure 36 illustrates organization of an expression vector having polynucleotide sequences encoding the expression of the three polypeptide chains of an asymmetric bispecific molecule having an anti-CD3 Fab and a CD4 extracellular (EC) domain-Fc fusion protein. The vector was designed to drive the expression of three polypeptide chains: heavy chain and light chain of anti-CD3 Fab and CD4-Fc fusion protein from three separate expression cassettes, each driven by its own promoter of equal transcription strength (*e.g.*, a cytomegalovirus (CMV) promotor). An additional DNA cassette having a polynucleotide encoding a eukaryotic selection marker (*e.g.*, glutamine synthetase (GS)) using a promoter of relatively weaker transcription strength (*e.g.*, an SV40 promoter) was included in the expression vector. DNA encoding for a bacterial origin of replication (*e.g.*, Ori) and an antibiotic selection marker (*e.g.*, ampicillin (AmpR)) were utilized for expression vector production in *E. coli*.

[0067] Figure 37 illustrates an evaluation of expression performance of cell lines expressing asymmetric bispecific molecules having an anti-CD3 Fab and a CD4-Fc fusion protein. The expression performance was assessed by culturing the cells under the production mode (fed-batch process). Each dot represents the selected clones, where the ratio of the desired species (Het%, heterotrimer%) was monitored by size separation method (non-reduced capillary electrophoresis). The amounts of desired heterotrimer comprising the asymmetric bispecific molecule were calculated as the amount of total bispecific molecule (detected via ProA Biosensors) and then multiplied by the heterotrimer % (specific titer in g/L).

[0068] Figure 38 illustrates PGT121/anti-CD3 bispecific antibody pharmacokinetics in serum before ART discontinuation. Peak serum antibody levels are shown following each of the twelve infusions (2 infusions first with anti-CD3KO version followed by 10 of anti-CD3 version) of antibody and during the washout period. Dotted lines indicate limit of detection. Dotted line indicates limit of detection.

[0069] Figure 39 illustrates SHIV viral loads following ART discontinuation. Plasma viral load for 168 days following ART discontinuation. Numbers and percentages of animals that did not show viral rebound are shown. Limit of detection is 1.7 log RNA copies per ml.

[0070] Figure 40 illustrates plasma viral loads before and after CD8+ cell depletion in animals with no viral rebound (n=1) and animals with viral rebound (n=4) following ART discontinuation. Numbers of animals that remained aviremic and total number of animals are shown. Arrows indicate CD8+ cell depletion on day 245 (week 77) after ART discontinuation. Limit of detection is 1.7 log RNA copies per ml.

DETAILED DESCRIPTION

1. Introduction

[0071] Provided are multi-specific or bispecific antigen binding molecules, targeting CD3 and an HIV antigen (*e.g.*, gp120 or gp41), designed for improved manufacturing efficiency, reduced cost, improved drug-like properties (*e.g.*, increased sequence identity to human germline and reduced off-target binding and inducement of anti-drug antibodies (ADAs)). The Fc-containing multi-specific or bispecific molecules described herein can be efficiently produced at high yield using a single cell line with a simplified purification process. We have developed multi-specific or bispecific molecules having an anti-CD3 antibody variable domain with (1) a high affinity for human and non-human primate (NHP) (*e.g.*, to facilitate pre-clinical toxicity studies) CD3, (2) a high sequence similarity to the human germline (*e.g.*, to reduce or eliminate risk of immunogenicity and anti-drug antibody (ADA) reactions in human patients), (3) IgG-like pharmacokinetic (PK) properties with no evidence of ADA in non-human primates (*e.g.*, to facilitate pre-clinical efficacy and toxicity studies) (4) reduced product heterogeneity via removal of sequence liabilities (*e.g.*, deamidation, aspartate isomerization) to improve manufacturing, (5) high thermodynamic stability (*e.g.*, to ensure product stability), (6) low aggregate content (*e.g.*, to reduce risk of immunogenicity), (7) low polyspecificity (to reduce the risk of immunogenicity and improve PK properties), and (8) a heavy chain variable region (VH) with low or no binding to Protein A affinity chromatography resin (*e.g.*, to facilitate efficient purification of bispecific antibody heterodimers). Further the anti-CD3 antibody variable domain possesses all the foregoing desirable properties in both scFv and Fab formats, such that it can be incorporated into a variety of bispecific antibody formats containing three or fewer polypeptide chains, *e.g.*, to limit light chain miss-pairing or other sources of bispecific antibody product heterogeneity.

[0072] In some embodiments, the multi-specific or bispecific molecules comprise a first antigen binding domain, targeting human CD3, that is a single chain variable fragment (scFv) fused to Fc, while the second antigen binding domain, targeting an HIV antigen (*e.g.*, gp120 or gp41) is comprised of a Fab antigen binding fragment fused to Fc. The resulting molecules have

three polypeptide chains (*i.e.*, scFv heavy chain, Fab heavy chain, Fab light chain), which are co-expressed in a single cell line. Formation of the desired bispecific heterodimeric molecule is facilitated through use of mutations in the Fc region that limits unwanted homodimerization of either half molecule, while the use of a scFv fragment as one of the antigen binding arms eliminates the need to co-express two different light chains that can otherwise lead to heterogeneity resulting from incorrect light chain pairing. Purification of the multi-specific antigen binding molecules is simplified and improved by eliminating the ability of the variable regions and one the of Fc regions to bind Protein A. Employing this design strategy, one of the two possible homodimer impurities is not retained during Protein A-based capture of the bispecific from cell culture media.

[0073] In various embodiments of the present multi-specific antigen binding molecules the first and second Fc regions of native human IgG sequences can be modified to promote heavy chain heterodimerization, allow for simplified and efficient purification, and to reduce or remove binding to FcγR and C1q.

[0074] Heterodimerization of the first and second Fc regions can be facilitated by introduction of 'knobs-into-holes' mutations (Atwell *et al.* 1997. JMB 270:26-35). The 'hole' mutations (T366S, L368A and Y407V) are incorporated into one Fc-containing chain, the T366W 'knob' mutation is used in the other chain (Atwell *et al.*, *supra*). In addition, the C220S mutation can be incorporated into the IgG1 hinge region of the scFv-containing arm to eliminate the free cysteine, which would otherwise form a disulfide bond with a corresponding cysteine in an immunoglobulin light chain. Co-transfection of such constructs into a single host cell promotes formation of a heterodimeric Fc, with low levels of homodimer contaminants. The S354C (made in the Fc containing the 'knob' mutations) and Y349C (made in the Fc containing the 'hole' mutations) mutations can optionally be incorporated to generate a covalent bond between the two halves of the heterodimeric Fc if additional thermodynamic stability is desired (Merchant *et al.* 1998. Nat. Biotechnol. 16: 677-81). As described herein, numbering of amino acid positions for substitutions in the first and second Fc regions is according to Eu index.

[0075] Purification of the heterodimeric molecule away from contaminating homodimeric products can be facilitated by introducing into the first or the second Fc region H435R or H435R+Y436F mutations to reduce or eliminate Protein A binding (Jendeberg, L. et al. 1997 J. Immunol. Methods 201:25–34), optionally combined with mutations in any variable heavy (VH) region of the same chain should such VH be derived from a human VH3 germline. For example, additional VH mutations can be made at one or more of positions R19, T57, G65,

Q81 and N82a, as numbered according to the Kabat numbering system. Incorporation of such amino acid substitutions in the Fc region, and optionally in the VH region, can reduce or eliminate Protein A binding of the homodimer contaminants, and greatly simplifies purification of the desired heterodimer away from remaining homodimer contaminant via additional chromatography steps (*e.g.*, ion exchange).

[0076] In certain embodiments, the first and second Fc domain or Fc region incorporate amino acid substitutions to reduce or eliminate one or more of effector function (antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and complement-dependent cytotoxicity (CDC)). In these contexts, at least one of the first and second Fc region can incorporate one or both of the L234A and L235A mutations to reduce or eliminate FcγR binding (Chappel, M. S *et al.* 1991 PNAS 88:9036-9040), and/or the P331S mutation to reduce or eliminate C1q binding (Xu Y, *et al.* J Biol Chem. 1994. 269:3469-74).

[0077] scFv fragments represent a minimal antibody-derived antigen binding unit, and are generated by direct fusion of a variable heavy and variable light domain via a flexible polypeptide linker (Huston *et al.*, 1988, PNAS 85:5879-5883). The sequence of this linker can contain 3 or 4 repeats of a GGGGS motif (SEQ ID NO: 712) (Desplancq *et al.* 1994, Protein Engineering 7:1027-1033). In various embodiments, the G44C mutation (variable heavy domain) and the G100C mutation (variable light domain) can be incorporated to generate a covalent disulfide bond between the VH and VL domains of the scFv if additional thermodynamic stability is desired (Brinkmann, U *et al.*, 1993, PNAS 90: 7538-7542).

[0078] In embodiments comprising a first antigen binding domain in the form of a scFv, and a second antigen binding domain in the form of a Fab, the three polypeptide chains can co-expressed in a single host cell and purified via Protein A chromatography. The desired Fab-scFv-Fc heterodimer is the dominant species observed in non-reducing SDS-PAGE analysis. Contaminating homodimeric species can be further mitigated using the H435R or H435R+Y436F mutations in the first or second Fc regions. Subsequent polishing using ion exchange chromatography and dialysis into a standard formulation buffer generates final material with high purity and homogeneity, *e.g.*, that is at least 90%, *e.g.*, at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more, pure.

2. Anti-CD3 Effector Arm

[0079] Cluster of Differentiation (CD3) is a multimeric protein complex that is composed of four distinct polypeptide chains: epsilon (ε) (CD3E; NCBI Gene ID: 916), gamma

(γ) (CD3G; NCBI Gene ID: 917), delta (δ) (CD3D; NCBI Gene ID: 915) and zeta (ζ) (CD247; NCBI Gene ID: 919), that assemble and function as three pairs of dimers (εγ, εδ, ζζ). CD3 proteins have an N-terminal extracellular region, a transmembrane domain, and a cytoplasmic tail where the immunoreceptor tyrosine activation motifs (ITAMs) are located. The extracellular domains of CD3 ε, γ and δ contain an immunoglobulin-like domain and thus are considered part of the immunoglobulin superfamily. The CD3/T-cell co-receptor helps to activate both $CD8^+$ T-cells and also $CD4^+$ T-cells.

[0080] The amino acid sequence of human CD3ε can be found at UNiProtKB-P07766 and is provided below (the signal sequence is underlined):

MQSGTHWRVL GLCLLSVGVW GQDGNEEMGG ITQTPYKVSI SGTTVILTCP
QYPGSEILWQ HNDKNIGGDE DDKNIGSDED HLSLKEFSEL EQSGYYVCYP
RGSKPEDANF YLYLRARVCE NCMEMDVMSV ATIVIVDICI TGGLLLLVYY
WSKNRKAKAK PVTRGAGAGG RQRGQNKERP PPVPNPDYEP IRKGQRDLYS
GLNQRRI (SEQ ID NO: 130)

[0081] The amino acid sequence of human CD3δ can be found at UNiProtKB-P04234 and is provided below (the signal sequence is underlined):

MEHSTFLSGL VLATLLSQVS PFKIPIEELE DRVFVNCNTS ITWVEGTVGT
LLSDITRLDL GKRILDPRGI YRCNGTDIYK DKESTVQVHY RMCQSCVELD
PATVAGIIVT DVIATLLLAL GVFCFAGHET GRLSGAADTQ ALLRNDQVYQ
PLRDRDDAQY SHLGGNWARN K (SEQ ID NO: 319)

[0082] Antibodies that bind human CD3 have been described, *e.g.*, in Kuhn & Weiner, Immunotherapy, 8(8):889-906 (2016); WO 2015/001085; WO 2015/104346. OKT3 (Muromonab-CD3), an anti-CD3 antibody directed against CD3ε, has been clinically approved for use in humans for the induction of immunosuppression in solid organ transplantation for the prevention and treatment of rejection (Norman, *Therapeutic Drug Monitoring*, 17, 615-620 (1995)). Teplizumab, also known under the names hOKT3γ1 (Ala-Ala) and MGA031, is a humanized IgG1 antibody that was developed by grafting the complementarity determining region of OKT3 into a human IgG1 backbone. Introduction of two point mutations in its Fc portion decreases binding to FcR. Otelixizumab (ChAglyCD3, TRX4, GSK2136525) was derived from the rat antibody YTH12.5. This humanized IgG1 bears a single mutation in the γ1 Fc portion to avoid glycosylation and thus inhibit FcR binding. Visilizumab (Nuvion, HuM291)

is a humanized IgG2 antibody that is rendered non-mitogenic by two point mutations in its Fc region. Foralumab (28F11-AE; NI-0401) is an entirely human anti-CD3 mAb; the Fc portion of this human IgG1 was mutated such that the mAb is non FcR binding *in vitro* and exhibits only minor cytokine release *in vivo* while maintaining modulation of the CD3/TCR and T-cell depletion. Non-limiting examples of anti-CD3 antibodies are also disclosed in US 2016/0333095A1.

[0083] In certain embodiments, the anti-CD3 antigen binding domains described herein bind human CD3. In some instances, the anti-CD3 antigen binding domains described herein bind human CD3ε. In some embodiments, the anti-CD3 antigen binding domains described herein bind human CD3δ.

Exemplary anti-CD3 Antigen Binding Domain Sequences

[0084] In various embodiments, the first antigen binding domain, targeting or binding to, or specifically binding to human CD3, comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), comprising: (i) a first VH-complementarity determining region (CDR) 1 comprising the amino acid sequence of TYAMN (SEQ ID NO:1); (ii) a first VH-CDR2 comprising the amino acid sequence of RIRSKYNNYATYYAX$_1$SVKX$_2$, wherein X$_1$ is A or D and X$_2$ is G or S (SEQ ID NO:2); (iii) a first VH-CDR3 comprising the amino acid sequence of HGNFGX$_3$SYVSWFAY, wherein X$_3$ is H or N (SEQ ID NO:3); (iv) a first VL-CDR1 comprising the amino acid sequence of GSSTGAVTTGHYAN (SEQ ID NO: 4); (v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$X$_5$RAP, wherein X$_4$X$_5$ is SN or NK (SEQ ID NO:5); and (vi) a first VL-CDR3 comprising the amino acid sequence of ALWYSNX$_6$WV, wherein X$_6$ is L or R (SEQ ID NO:6), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Kabat. In some embodiments, (i) the first VH-complementarity determining region (CDR) 1 comprises the amino acid sequence of TYAMN (SEQ ID NO:1); (ii) the first VH-CDR2 comprises the amino acid sequence of RIRSKYNNYATYYADSVKX$_2$, wherein X$_2$ is G or S (SEQ ID NO:7); (iii) the first VH-CDR3 comprises the amino acid sequence of HGNFGHSYVSWFAY (SEQ ID NO:8); (iv) the first VL-CDR1 comprises the amino acid sequence of GSSTGAVTTGHYAN (SEQ ID NO: 4); (v) the first VL-CDR2 comprises the amino acid sequence of GTSNRAP (SEQ ID NO:9); and (vi) the first VL-CDR3 comprises the amino acid sequence of ALWYSNRWV (SEQ ID NO:10). In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 1, 11, 8, 4, 5 and 10; SEQ ID NOs: 1, 11, 8, 4, 9 and 10; SEQ ID NOs: 1, 12, 8, 4, 9 and 10; SEQ ID NOs: 1, 13, 8, 4, 14 and 15; SEQ ID NOs: 1, 13, 16, 4, 14 and 15; or SEQ ID NOs: 1, 11, 8, 4, 14 and 10. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 1, 11, 8, 4, 9 and 10. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 1, 12, 8, 4, 9 and 10.

[0085] In various embodiments, the first antigen binding domain, targeting or binding to, or specifically binding to human CD3, comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), comprising: (i) a first VH-CDR1 comprising the amino acid sequence of GFTFNTY (SEQ ID NO:17); (ii) a first VH-CDR2 comprising the amino acid sequence of SKYNNY (SEQ ID NO:18); (iii) a first VH-CDR3 comprising the amino acid sequence of GNFGX_3SYVSWFA, wherein X_3 is H or N (SEQ ID NO:19); (iv) a first VL-CDR1 comprising the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 20); (v) a first VL-CDR2 comprising the amino acid sequence of GTX_4, wherein X_4 is N or S (SEQ ID NO:21); and (vi) a first VL-CDR3 comprising the amino acid sequence of WYSNX_6W, wherein X_6 is L or R (SEQ ID NO:22), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Chothia. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 17, 18, 23, 20, 21 and 25; SEQ ID NOs: 17, 18, 23, 20, 24 and 25; SEQ ID NOs: 17, 18, 23, 20, 26 and 27; SEQ ID NOs: 17, 18, 75, 20, 26 and 27; or SEQ ID NOs: 17, 18, 23, 20, 26 and 25. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 17, 18, 23, 20, 24 and 25.

[0086] In various embodiments, the first antigen binding domain, targeting or binding to, or specifically binding to human CD3, comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), comprising: (i) a first VH-CDR1 comprising the amino acid sequence of GFTFNTYA (SEQ ID NO:28); (ii) a first VH-CDR2 comprising the amino acid sequence of IRSKYNNYAT (SEQ ID NO:29); (iii) a first VH-CDR3 comprising the amino acid sequence of VRHGNFGX_3SYVSWFAY, wherein X_3 is H or N (SEQ ID NO:30); (iv) a first VL-CDR1 comprising the amino acid sequence of TGAVTTGHY (SEQ ID NO:31); (v) a first VL-CDR2 comprising the amino acid sequence of GTX_4, wherein X_4 is N or S (SEQ ID NO:21); and (vi) a first VL-CDR3 comprising the amino acid sequence of ALWYSNX_6WV, wherein X_6 is L or R (SEQ ID NO:6), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to IMGT. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 28, 29, 32, 31, 21 and 10; SEQ ID NOs: 28, 29, 32, 31, 24 and 10; SEQ ID NOs: 28, 29, 32, 31, 26 and 15; SEQ ID NOs: 28, 29, 33, 31, 26 and 15; or SEQ ID NOs: 28, 29, 32, 31, 26 and 10. In some embodiments, the first VH-CDR1, the first

VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 28, 29, 32, 31, 24 and 10.

[0087] In various embodiments, the first antigen binding domain, targeting or binding to, or specifically binding to human CD3, comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), comprising: (i) a first VH-CDR1 comprising the amino acid sequence of ASGFTFNTYA (SEQ ID NO:34); (ii) a first VH-CDR2 comprising the amino acid sequence of IRSKYNNYATYYAX$_1$SVKX$_2$R, wherein X$_1$ is A or D and X$_2$ is G or S (SEQ ID NO:35); (iii) a first VH-CDR3 comprising the amino acid sequence of HGNFGX$_3$SYVSWFA, X$_3$ is H or N (SEQ ID NO:36); (iv) a first VL-CDR1 comprising the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 37); (v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$NRAPX$_7$VPAR, wherein X$_4$ is N or S and X$_7$ is G or W (SEQ ID NO:38); and (vi) a first VL-CDR3 comprising the amino acid sequence of WYSNX$_6$W, wherein X$_6$ is L or R (SEQ ID NO:22), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Honegger. In some embodiments, (i) the first VH-CDR1 comprises the amino acid sequence of ASGFTFNTYA (SEQ ID NO:34); (ii) the first VH-CDR2 comprises the amino acid sequence of IRSKYNNYATYYADSVKX$_2$R, wherein X$_2$ is G or S (SEQ ID NO:39); (iii) the first VH-CDR3 comprises the amino acid sequence of HGNFGHSYVSWFA (SEQ ID NO:40); (iv) the first VL-CDR1 comprises the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 37); (v) the first VL-CDR2 comprises the amino acid sequence of GTSNRAPGVPAR (SEQ ID NO:41); and (vi) the first VL-CDR3 comprises the amino acid sequence of WYSNRW (SEQ ID NO:25). In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 34, 39, 40, 37, 41 and 25; SEQ ID NOs: 34, 42, 40, 37, 41 and 25; SEQ ID NOs: 34, 43, 40, 37, 41 and 25; SEQ ID NOs: 34, 44, 40, 37, 45 and 27; SEQ ID NOs: 34, 44, 46, 37, 45 and 27; or SEQ ID NOs: 34, 42, 40, 37, 47 and 25. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 34, 42, 40, 37, 41 and 25. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1,

the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 34, 43, 40, 37, 41 and 25.

[0088] Illustrative sequences of complementarity determining regions (CDRs) of exemplary first antigen binding domains of the multi-specific antigen binding molecules, targeting human CD3, according to the Kabat definition, the Chothia definition, the IMGT definition and Honegger definition are provided in Tables A1, A2, A3 and A4, respectively. Multi-specific antigen binding molecules comprising the CDRs identified herein are encompassed by the present application. It is to be understood that this disclosure also encompasses multi-specific antigen binding molecules (*e.g.*, anti-CD3/anti-HIV antigen bi-specific antibodies) comprising the CDRs according to any other CDR definition (*e.g.*, Honegger definition, enhanced Chothia definition, Martin definition, Gelfand definition, AbM definition, contact definition, *see, e.g.*, bioinf.org.uk/abs/#cdrdef and Dondelinger, *et al.*, *Front Immunol.* (2018) 9:2278) of the anti-CD3/anti-HIV multi-specific antigen binding molecules disclosed herein.

TABLE A1 – CDRs for anti-CD3 binding arm (Kabat)

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
400	TYAMN SEQ ID NO:1	RIRSKYNNYATYYAX$_1$SVKX$_2$ X$_1$ is A or D X$_2$ is G or S SEQ ID NO:2	HGNFGX$_3$SYVSWFAY X$_3$ is H or N SEQ ID NO:3	GSSTGAVTTGHYAN SEQ ID NO: 4	GTX$_4$X$_5$RAP X$_4$X$_5$ is SN or NK SEQ ID NO:5	ALWYSNX$_6$WV X$_6$ is L or R SEQ ID NO:6
401	TYAMN SEQ ID NO:1	RIRSKYNNYATYYADSVKX$_2$ X$_2$ is G or S SEQ ID NO:7	HGNFGHSYVSWFAY SEQ ID NO:8	GSSTGAVTTGHYAN SEQ ID NO: 4	GTSNRAP SEQ ID NO:9	ALWYSNRWV SEQ ID NO:10
402	TYAMN SEQ ID NO:1	RIRSKYNNYATYYADSVKG SEQ ID NO:11	HGNFGHSYVSWFAY SEQ ID NO:8	GSSTGAVTTGHYAN SEQ ID NO: 4	GTX$_4$X$_5$RAP X$_4$X$_5$ is SN or NK SEQ ID NO:5	ALWYSNRWV SEQ ID NO:10
403	TYAMN SEQ ID NO:1	RIRSKYNNYATYYADSVKG SEQ ID NO:11	HGNFGHSYVSWFAY SEQ ID NO:8	GSSTGAVTTGHYAN SEQ ID NO: 4	GTSNRAP SEQ ID NO:9	ALWYSNRWV SEQ ID NO:10
404	TYAMN SEQ ID NO:1	RIRSKYNNYATYYADSVKS SEQ ID NO:12	HGNFGHSYVSWFAY SEQ ID NO:8	GSSTGAVTTGHYAN SEQ ID NO: 4	GTSNRAP SEQ ID NO:9	ALWYSNRWV SEQ ID NO:10
405	TYAMN SEQ ID NO:1	RIRSKYNNYATYYAASVKG SEQ ID NO:13	HGNFGHSYVSWFAY SEQ ID NO:8	GSSTGAVTTGHYAN SEQ ID NO: 4	GTNKRAP SEQ ID NO:14	ALWYSNLWV SEQ ID NO:15
406	TYAMN SEQ ID NO:1	RIRSKYNNYATYYAASVKG SEQ ID NO:13	HGNFGNSYVSWFAY SEQ ID NO:16	GSSTGAVTTGHYAN SEQ ID NO: 4	GTNKRAP SEQ ID NO:14	ALWYSNLWV SEQ ID NO:15
407	TYAMN SEQ ID NO:1	RIRSKYNNYATYYADSVKG SEQ ID NO:11	HGNFGHSYVSWFAY SEQ ID NO:8	GSSTGAVTTGHYAN SEQ ID NO: 4	GTNKRAP SEQ ID NO:14	ALWYSNRWV SEQ ID NO:10

TABLE A2 – CDRs for anti-CD3 binding arm (Chothia)

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
408	GFTFNTY SEQ ID NO:17	SKYNNY SEQ ID NO:18	GNFGX$_3$SYVSWFA X_3 is H or N SEQ ID NO:19	SSTGAVTTGHY SEQ ID NO: 20	GTX$_4$ X_4 is N or S SEQ ID NO:21	WYSNX$_6$W X_6 is L or R SEQ ID NO:22
409	GFTFNTY SEQ ID NO:17	SKYNNY SEQ ID NO:18	GNFGHSYVSWFA SEQ ID NO:23	SSTGAVTTGHY SEQ ID NO:20	GTX$_4$ X_4 is N or S SEQ ID NO:21	WYSNRW SEQ ID NO:25
410	GFTFNTY SEQ ID NO:17	SKYNNY SEQ ID NO:18	GNFGHSYVSWFA SEQ ID NO:23	SSTGAVTTGHY SEQ ID NO:20	GTS SEQ ID NO:24	WYSNRW SEQ ID NO:25
411	GFTFNTY SEQ ID NO:17	SKYNNY SEQ ID NO:18	GNFGHSYVSWFA SEQ ID NO:23	SSTGAVTTGHY SEQ ID NO:20	GTN SEQ ID NO:26	WYSNLW SEQ ID NO:27
412	GFTFNTY SEQ ID NO:17	SKYNNY SEQ ID NO:18	GNFGNSYVSWFA SEQ ID NO:75	SSTGAVTTGHY SEQ ID NO:20	GTN SEQ ID NO:26	WYSNLW SEQ ID NO:27
413	GFTFNTY SEQ ID NO:17	SKYNNY SEQ ID NO:18	GNFGHSYVSWFA SEQ ID NO:23	SSTGAVTTGHY SEQ ID NO:20	GTN SEQ ID NO:26	WYSNRW SEQ ID NO:25

TABLE A3 – CDRs for anti-CD3 binding arm (IMGT)

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
414	GFTFNTYA SEQ ID NO:28	IRSKYNNYAT SEQ ID NO:29	VRHGNFGX$_3$SYVSWFAY X_3 is H or N SEQ ID NO:30	TGAVTTGHY SEQ ID NO:31	GTX$_4$ X_4 is N or S SEQ ID NO:21	ALWYSNX$_6$WV X_6 is L or R SEQ ID NO:6
415	GFTFNTYA SEQ ID NO:28	IRSKYNNYAT SEQ ID NO:29	VRHGNFGHSYVSWFAY SEQ ID NO:32	TGAVTTGHY SEQ ID NO: 31	GTX$_4$ X_4 is N or S SEQ ID NO:21	ALWYSNRWV SEQ ID NO:10
416	GFTFNTYA SEQ ID NO:28	IRSKYNNYAT SEQ ID NO:29	VRHGNFGHSYVSWFAY SEQ ID NO:32	TGAVTTGHY SEQ ID NO: 31	GTS SEQ ID NO:24	ALWYSNRWV SEQ ID NO:10
417	GFTFNTYA SEQ ID NO:28	IRSKYNNYAT SEQ ID NO:29	VRHGNFGHSYVSWFAY SEQ ID NO:32	TGAVTTGHY SEQ ID NO: 31	GTN SEQ ID NO:26	ALWYSNLWV SEQ ID NO:15

TABLE A3 – CDRs for anti-CD3 binding arm (IMGT)						
Ab Name	**VH – CDR1**	**VH – CDR2**	**VH – CDR3**	**VL – CDR1**	**VL – CDR2**	**VL – CDR3**
418	GFTFNTYA SEQ ID NO:28	IRSKYNNYAT SEQ ID NO:29	VRHGNFGNSYVSWFAY SEQ ID NO:33	TGAVTTGHY SEQ ID NO: 31	GTN SEQ ID NO:26	ALWYSNLWV SEQ ID NO:15
419	GFTFNTYA SEQ ID NO:28	IRSKYNNYAT SEQ ID NO:29	VRHGNFGHSYVSWFAY SEQ ID NO:32	TGAVTTGHY SEQ ID NO: 31	GTN SEQ ID NO:26	ALWYSNRWV SEQ ID NO:10

TABLE A4 – CDRs for anti-CD3 binding arm (Honegger)						
Ab Name	**VH – CDR1**	**VH – CDR2**	**VH – CDR3**	**VL – CDR1**	**VL – CDR2**	**VL – CDR3**
420	ASGFTFNTYA SEQ ID NO:34	IRSKYNNYATYYAX$_1$SVKX$_2$R X$_1$ is A or D X$_2$ is G or S SEQ ID NO:35	HGNFGX$_3$SYVSWFA X$_3$ is H or N SEQ ID NO:36	SSTGAVTTGHY SEQ ID NO: 37	GTX$_4$NRAPX$_7$VPAR X$_4$ is N or S X$_7$ is G or W SEQ ID NO:38	WYSNX$_6$W X$_6$ is L or R SEQ ID NO:22
421	ASGFTFNTYA SEQ ID NO:34	IRSKYNNYATYYADSVKX$_2$R X$_2$ is G or S SEQ ID NO:39	HGNFGHSYVSWFA SEQ ID NO:40	SSTGAVTTGHY SEQ ID NO: 37	GTSNRAPGVPAR SEQ ID NO:41	WYSNRW SEQ ID NO:25
422	ASGFTFNTYA SEQ ID NO:34	IRSKYNNYATYYADSVKX$_2$R X$_2$ is G or S SEQ ID NO:39	HGNFGHSYVSWFA SEQ ID NO:40	SSTGAVTTGHY SEQ ID NO: 37	GTSNRAPGVPAR SEQ ID NO:41	WYSNRW SEQ ID NO:25
423	ASGFTFNTYA SEQ ID NO:34	IRSKYNNYATYYADSVKGR SEQ ID NO:42	HGNFGHSYVSWFA SEQ ID NO:40	SSTGAVTTGHY SEQ ID NO: 37	GTSNRAPGVPAR SEQ ID NO:41	WYSNRW SEQ ID NO:25
424	ASGFTFNTYA SEQ ID NO:34	IRSKYNNYATYYADSVKSR SEQ ID NO:43	HGNFGHSYVSWFA SEQ ID NO:40	SSTGAVTTGHY SEQ ID NO: 37	GTSNRAPGVPAR SEQ ID NO:41	WYSNRW SEQ ID NO:25
425	ASGFTFNTYA SEQ ID NO:34	IRSKYNNYATYYAASVKGR SEQ ID NO:44	HGNFGHSYVSWFA SEQ ID NO:40	SSTGAVTTGHY SEQ ID NO: 37	GTNKRAPWTPAR SEQ ID NO:45	WYSNLW SEQ ID NO:27
426	ASGFTFNTYA SEQ ID NO:34	IRSKYNNYATYYAASVKGR SEQ ID NO:44	HGNFGNSYVSWFA SEQ ID NO:46	SSTGAVTTGHY SEQ ID NO: 37	GTNKRAPWTPAR SEQ ID NO:45	WYSNLW SEQ ID NO:27
427	ASGFTFNTYA SEQ ID NO:34	IRSKYNNYATYYADSVKGR SEQ ID NO:42	HGNFGHSYVSWFA SEQ ID NO:40	SSTGAVTTGHY SEQ ID NO: 37	GTNKRAPGVPAR SEQ ID NO:47	WYSNRW SEQ ID NO:25

[0089] Additionally, it has been reported that heavy chain variable domains derived from VH3 family germlines can exhibit direct binding to Protein A affinity chromatography resins (Bach, *et al.*, J Chromatogr A. (2015) 1409:60-9). Accordingly, in certain embodiments, to reduce, or substantially or completely eliminate, binding to Protein A by one heavy chain-containing subunit of a multi-specific or bispecific antigen binding molecule, a H435R or H435R+Y436F mutation in the Fc region of the first or second heavy chain can be combined with one or more amino acid substitutions in the VH of the same heavy chain, should that VH region be derived from a human VH3 family germline. In some embodiments, the first VH (and/or a second VH derived from a human VH3 family germline) comprises one or more of the following amino acids at the indicated positions (as described herein, numbering of amino acid positions for substitutions in the first and second VH and VL regions is according to Kabat): the position corresponding to 19 is A, S, T or K; the position corresponding to 57 is A, E or T; the position corresponding to 65 is G, S or T; the position corresponding to 81 is E, K or T; and the position corresponding to 82a is S, T or R. In some embodiments, the first (and/or a second VH derived from a human VH3 family germline) VH comprises one or more of the following amino acids at the indicated positions (position numbering according to Kabat): the position corresponding to 19 is A or S; the position corresponding to 57 is A or E; the position corresponding to 65 is S; and the position corresponding to 81 is E. In some embodiments, the first VH (and/or a second VH derived from a human VH3 family germline) comprises one or more of the following amino acids at the indicated positions (position numbering according to Kabat): the position corresponding to 19 is S and the position corresponding to 57 is A; the position corresponding to 19 is A or S and the position corresponding to 57 is E; the position corresponding to 19 is A and the position corresponding to 57 is E; the position corresponding to 19 is S and the position corresponding to 57 is E; the position corresponding to 19 is S and the position corresponding to 65 is S; the position corresponding to 19 is S and the position corresponding to 81 is E; the position corresponding to 19 is K and the position corresponding to 81 is E; the position corresponding to 57 is A and the position corresponding to 81 is E; the position corresponding to 57 is A and the position corresponding to 65 is S; the position corresponding to 57 is E and the position corresponding to 65 is S; the position corresponding to 57 is E and the position corresponding to 81 is E; the position corresponding to 65 is S and the position corresponding to 81 is E; or the position corresponding to 81 is E and the position corresponding to 82a is S.

[0090] In some embodiments, the first antigen binding domain has reduced or insignificant or substantially no binding to Protein A, or does not detectably bind to Protein A.

In some embodiments, the first antigen binding domain binds to Protein A with a K_D of greater than 10^{-6} M. Protein binding affinity can be determined by any method known in the art, *e.g.*, by surface plasmon resonance (SPR), *e.g.*, using Octet as described herein.

[0091] As used herein, numbering of a given amino acid polymer or nucleic acid polymer "corresponds to", is "corresponding to" or is "relative to" the numbering of a selected or reference amino acid polymer or nucleic acid polymer when the position of any given polymer component (*e.g.*, amino acid, nucleotide, also referred to generically as a "residue") is designated by reference to the same or to an equivalent position (*e.g.*, based on an optimal alignment or a consensus sequence) in the selected amino acid or nucleic acid polymer, rather than by the actual numerical position of the component in the given polymer.

[0092] In some embodiments, the first VH and the first VL comprise one or more of the following amino acid substitutions (numbering according to Kabat): position 81 of the first VH is Q or E; position 83 of the first VH is K or R; position 89 of the first VH is M or V; position 100 of the first VH is H; position 57 of the first VL is G or W; and/or position 75 of the first VL is I or L. In some embodiments, position 81 of the first VH is Q or E. In some embodiments, position 81 of the first VH is E. In some embodiments, position 81 of the first VH is Q. In some embodiments, one or more of position 81 of the first VH is Q or E; position 83 of the first VH is R; position 89 of the first VH is V; position 100 of the first VH is H; position 57 of the first VL is G; and/or position 75 of the first VL is I.

[0093] In some embodiments, the first VH comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to an amino acid sequence selected from the group consisting of SEQ ID NOs: 48-53. In some embodiments, the first VH comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 50. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 50. In some embodiments, the first VH comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 51. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 51. In some embodiments, the first VL comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at

least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to an amino acid sequence of SEQ ID NO: 54-58. In some embodiments, the first VL comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to an amino acid sequence selected from the group consisting of SEQ ID NOs: 48-53 and wherein the first VL comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to an amino acid sequence of SEQ ID NO: 54-58.

[0094] In some embodiments, the first VH comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 50 and wherein the first VL comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 50 and the first VL comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 50 and the first VL comprises an amino acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 50 and the first VL comprises an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 50 and the first VL comprises an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 50 and the first VL comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid

sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprises the amino acid sequence of SEQ ID NO: 56.

[0095] In some embodiments, the first VH comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and wherein the first VL comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 51 and the first VL comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 51 and the first VL comprises an amino acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 51 and the first VL comprises an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 51 and the first VL comprises an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 51 and the first VL comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In

some embodiments, the first VH comprises an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprises the amino acid sequence of SEQ ID NO: 56.

[0096] In various embodiments, the first VH and the first VL comprise the amino acid sequences set forth, respectively, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 48 and 54; SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; SEQ ID NOs: 51 and 56; SEQ ID NOs: 52 and 56; SEQ ID NOs: 53 and 57; or SEQ ID NOs: 50 and 58. In various embodiments, the first VH and the first VL comprise the amino acid sequences set forth, respectively, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56. In various embodiments, the first VH and the first VL comprise the amino acid sequences set forth, respectively, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56; or SEQ ID NOs: 51 and 56. In some embodiments, position 100 of the first VH (numbering according to Kabat) is a histidine (H).

[0097] In some embodiments, the first VH comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 50 and wherein the first VL comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 50 and the first VL comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 50 and the first VL comprises an amino

acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 50 and the first VL comprises an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 50 and the first VL comprises an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 50 and the first VL comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH and the first VL comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first VH and the first VL comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first VH and the first VL comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first VH and the first VL comprise the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10, and the first VH and the first VL comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first VH-CDR1, the

first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10, and the first VH and the first VL comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25, and the first VH and the first VL comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25, and the first VH and the first VL comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10, and the first VH and the first VL comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10, and the first VH and the first VL comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25, and the first VH and the first VL comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25, and the first VH and the first VL comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56.

[0098] In some embodiments, the first VH comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and wherein the first VL comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 51 and the first VL comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 51 and the first VL comprises an amino acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 51 and the first VL comprises an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 51 and the first VL comprises an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises the amino acid sequence of SEQ ID NO: 51 and the first VL comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprises the amino acid sequence of SEQ ID NO: 56. In some embodiments, the first VH and the first VL comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, the first VH and the first VL comprise amino

acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, the first VH and the first VL comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, the first VH and the first VL comprise the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10, and the first VH and the first VL comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10, and the first VH and the first VL comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25, and the first VH and the first VL comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25, and the first VH and the first VL comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10, and the first VH and the first VL comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10, and the first VH and the first VL comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-

CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25, and the first VH and the first VL comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56. In some embodiments, the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25, and the first VH and the first VL comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56.

[0099] Illustrative sequences of the VH and VL of the first antigen binding domains of the multi-specific antigen binding molecules, targeting human CD3, are provided in Tables B1 and B2.

SEQ ID NO:	TABLE B1 –anti–CD3 binding HC variable regions (VH)
48	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYAX$_1$SVKX$_2$RFTISRDDSKNSLY LX$_8$MNSLX$_9$TEDTAX$_{10}$YYCVRHGNFGX$_3$SYVSWFAYWGQGTLVTVSS X$_1$ is A or D; X$_2$ is G or S; X$_3$ is H or N; X$_8$ is E or Q; X$_9$ is K or R; and X$_{10}$ is M or V
49	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKX$_2$RFTISRDDSKNSLYL X$_8$MNSLRTEDTAVYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS X$_2$ is G or S; and X$_8$ is E or Q
50 VH3	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNSLYLQ MNSLRTEDTAVYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS
51 VH39	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKSRFTISRDDSKNSLYLE MNSLRTEDTAVYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS
52 VH34	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQ MNSLKTEDTAMYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS
53 VH1	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQ MNSLKTEDTAMYYCVRHGNFGNSYVSWFAYWGQGTLVTVSS

SEQ ID NO:	TABLE B2 – anti-CD3 binding LC variable regions (VL)
54	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAPRGLIGGTX$_4$X$_5$RAPX$_7$VPARFSGSLLGGKAALTX$_{11}$SGAQ PEDEAEYYCALWYSNX$_6$WVFGGGTKLTVL X$_4$X$_5$ is SN or NK; X$_6$ is L or R; X$_7$ is G or W; and X$_{11}$ is I or L
55	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAPRGLIGGTX$_4$X$_5$RAPGVPARFSGSLLGGKAALTISGAQPE DEAEYYCALWYSNRWVFGGGTKLTVL X$_4$X$_5$ is SN or NK
56 VL13	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAPRGLIGGTSNRAPGVPARFSGSLLGGKAALTISGAQPED EAEYYCALWYSNRWVFGGGTKLTVL
57 VL3	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAPRGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGAQPED EAEYYCALWYSNLWVFGGGTKLTVL
58 VL8	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPED EAEYYCALWYSNRWVFGGGTKLTVL

[0100] "Homology" or "identity" or "similarity" as used herein in the context of nucleic acids and polypeptides refers to the relationship between two polypeptides or two nucleic acid molecules based on an alignment of the amino acid sequences or nucleic acid sequences, respectively. Homology and identity can each be determined by comparing a position in each sequence which may be aligned for purposes of comparison. When an equivalent position in the compared sequences is occupied by the same base or amino acid, then the molecules are identical at that position; when the equivalent site occupied by the same or a similar amino acid residue (*e.g.*, similar in steric and/or electronic nature), then the molecules can be referred to as homologous (similar) at that position. Expression as a percentage of homology/similarity or identity refers to a function of the number of identical or similar amino acids at positions shared by the compared sequences. In comparing two sequences, the absence of residues (amino acids or nucleic acids) or presence of extra residues also decreases the identity and homology/similarity.

[0101] As used herein, "identity" means the percentage of identical nucleotide or amino acid residues at corresponding positions in two or more sequences when the sequences are aligned to maximize sequence matching, *i.e.*, taking into account gaps and insertions. Sequences are generally aligned for maximum correspondence over a designated region, *e.g.*, a region at least 20, 25, 30, 35, 40, 45, 50, 55, 60, 65 or more amino acids or nucleotides in length, and can be up to the full length of the reference polypeptide or polynucleotide sequence. For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are input into a computer program, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. Otherwise, standard parameters can be used. The sequence comparison algorithm then calculates the percent sequence identity for the test sequence(s) relative to the reference sequence, based on the designated program parameters.

[0102] When comparing polynucleotide and polypeptide sequences, two sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least 20 contiguous positions, usually 30 to 75, 40 to 50, or the full length of a sequence, in which a sequence

may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

[0103] Optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) Add. APL. Math 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48:443, by the search for similarity methods of Pearson and Lipman (1988) Proc. Natl. Acad. Sci. USA 85: 2444, by computerized implementations of these algorithms (*e.g.*, GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

[0104] One example of algorithms that are suitable for determining percent sequence identity are the Basic Local Alignment Search Tool (BLAST), BLAST 2.0 and PSI-BLAST algorithms, which are described in Altschul, *et al., J. Mol. Biol.* (1990) 215: 403-410, Altschul, *et al., Nucleic Acids Res.* (1977) 25: 3389-3402, and Altschul, *et al., Nucleic Acids Res.* (1997) 25(17):3389-402, respectively. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (blast.ncbi.nlm.nih.gov/Blast.cgi).

[0105] In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a word length (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) Proc. Natl. Acad. Sci. USA 89: 10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

[0106] For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The

BLASTP algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

[0107] In one approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residues occur in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

[0108] Residue positions which are not identical can differ by conservative amino acid substitutions. Conservative amino acid substitutions refer to the interchangeability of residues having similar side chains. For example, a group of amino acids having aliphatic side chains is glycine (Gly, G), alanine (Ala, A), valine (Val, V), leucine (Leu, L), and isoleucine (Ile, I); a group of amino acids having aliphatic-hydroxyl side chains is serine (Ser, S) and threonine (Thr, T); a group of amino acids having amide-containing side chains is asparagine (Asn, N) and glutamine (Gln, Q); a group of amino acids having aromatic side chains is phenylalanine (Phe, F), tyrosine (Tyr, Y), and tryptophan (Trp, W); a group of amino acids having basic side chains is lysine (Lys, K), arginine (Arg, R), and histidine (His, H); and a group of amino acids having sulfur-containing side chains is cysteine (Cys, C) and methionine (Met, M). Further, glutamic acid (Glu, E) and aspartic acid (Asp, D) are conservative amino acid substitutions.

[0109] In various embodiments, one or both of the first antigen binding domain and the second antigen binding domain independently comprise a Fab, an F(ab)2, Fv, a scFv, a sc(Fv)2, or a diabody. In some embodiments, the first antigen binding domain comprises a scFv and the second antigen binding domain comprises a Fab. In some embodiments, the first antigen binding domain comprises a Fab and the second antigen binding domain comprises a scFv. In some embodiments, the first antigen binding domain comprises a Fab and the second antigen binding domain comprises a Fab. In some embodiments, the first antigen binding domain comprises a scFv and the second antigen binding domain comprises

a scFv. In some embodiments, the first antigen binding domain comprises a Fab and the second antigen binding domain comprises one or more extracellular domains of CD4, *e.g.*, as set forth herein. In some embodiments, the first antigen binding domain comprises a scFv and the second antigen binding domain comprises one or more extracellular domains of CD4, *e.g.*, as set forth herein. Embodiments comprising an scFv can have one or both of the following amino acid substitutions (numbering according to Kabat): (i) a cysteine (C) at position 44 in the scFv variable heavy domain; and (ii) a cysteine (C) at position 100 in the scFv variable light domain.

[0110] In some embodiments, the first antigen binding domain is a scFv comprising a VH and a VL, the scFv comprises an amino acid sequence selected from SEQ ID NOs: 59-66, or that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from SEQ ID NOs: 59-66. In some embodiments, the first antigen binding domain is a scFv comprising a VH and a VL, the scFv comprises an amino acid sequence selected from SEQ ID NOs: 59-63, or that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from SEQ ID NOs: 59-63. In some embodiments, the first antigen binding domain is a scFv comprising a VH and a VL, the scFv comprising an amino acid sequence selected from SEQ ID NOs: 59-66, *e.g.*, SEQ ID NOs: 59-63, *e.g.*, SEQ ID NOs: 61, 62 or 63, *e.g.*, SEQ ID NOs: 62 or 63. Illustrative sequences of scFv of the first antigen binding domains of the multi-specific antigen binding molecules, targeting human CD3, are provided in Table C.

SEQ ID NO: Ab name	**TABLE C – scFv for anti-CD3 binding arm**
59	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEW VGRIRSKYNNYATYYAX$_1$SVKX$_2$RFTISRDDSKNSLYLX$_8$MNSLX$_9$TED TAX$_{10}$YYCVRHGNFGX$_3$SYVSWFAYWGQGTLVTVSSGGGGSGGGGSGG GGSGGGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQ QKPGQAPRGLIGGTX$_4$X$_5$RAPX$_7$VPARFSGSLLGGKAALTX$_{11}$SGAQPE DEAEYYCALWYSNX$_6$WVFGGGTKLTVL X$_1$ is A or D; X$_2$ is G or S; X$_3$ is H or N; X$_8$ is E or Q;

SEQ ID NO: Ab name	TABLE C – scFv for anti-CD3 binding arm
	X_9 is K or R; X_{10} is M or V; X_4X_5 is SN or NK; X_6 is L or R; X_7 is G or W; and X_{11} is I or L
60	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEW VGRIRSKYNNYATYYADSVKX$_2$RFTISRDDSKNSLYLX$_8$MNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGS GGGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKP GQAPRGLIGGTX$_4$X$_5$RAPGVPARFSGSLLGGKAALTISGAQPEDEAEY YCALWYSNRWVFGGGTKLTVL X_2 is G or S; X_4X_5 is SN or NK; and X_8 is E or Q
61	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEW VGRIRSKYNNYATYYADSVKX$_2$RFTISRDDSKNSLYLX$_8$MNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGS GGGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKP GQAPRGLIGGTSNRAPGVPARFSGSLLGGKAALTISGAQPEDEAEYY CALWYSNRWVFGGGTKLTVL X_2 is G or S; and X_8 is E or Q
62 3.13	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEW VGRIRSKYNNYATYYADSVKGRFTISRDDSKNSLYLQMNSLRTEDTA VYYCVRHGNFGHSYVSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGSG GGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPG QAPRGLIGGTSNRAPGVPARFSGSLLGGKAALTISGAQPEDEAEYYC ALWYSNRWVFGGGTKLTVL
63 39.13	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEW VGRIRSKYNNYATYYADSVKSRFTISRDDSKNSLYLEMNSLRTEDTA VYYCVRHGNFGHSYVSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGSG GGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPG QAPRGLIGGTSNRAPGVPARFSGSLLGGKAALTISGAQPEDEAEYYC ALWYSNRWVFGGGTKLTVL
64 34.3	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEW VGRIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTEDTA MYYCVRHGNFGHSYVSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGSG GGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPG QAPRGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGAQPEDEAEYYC ALWYSNLWVFGGGTKLTVL

SEQ ID NO: Ab name	TABLE C – scFv for anti-CD3 binding arm
65 1.3	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEW VGRIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTEDTA MYYCVRHGNFGNSYVSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGSG GGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPG QAPRGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGAQPEDEAEYYC ALWYSNLWVFGGGTKLTVL
66 3.8	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEW VGRIRSKYNNYATYYADSVKGRFTISRDDSKNSLYLQMNSLRTEDTA VYYCVRHGNFGHSYVSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGSG GGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPG QAPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAEYYC ALWYSNRWVFGGGTKLTVL

[0111] In some embodiments, the first antigen binding domain, *e.g.*, in scFv or Fab format, binds to CD3 with a K_D of lower than 10 nM, *e.g.*, lower than 9.5 nM, 9.0 nM, 8.5 nM, 8.0 nM, 7.5 nM, 7.0 nM, 6.5 nM, 6.0 nM, 5.5 nM, 5.0 nM, 4.5 nM, 4.0 nM, 3.5 nM, 3.0 nM, or lower. In some embodiments, the first antigen binding domain binds to CD3 with a K_D of lower than 10 nM, *e.g.*, lower than 5.0 nM, 4.5 nM, 4.0 nM, 3.5 nM, 3.0 nM, or lower. Protein binding affinity can be determined by any method known in the art, *e.g.*, by surface plasmon resonance (SPR), *e.g.*, using Octet as described herein.

3. Anti-HIV Antigen Arm

[0112] HIV-1 is the main family of HIV and accounts for 95% of all infections worldwide. HIV-2 is mainly seen in a few West African countries.

[0113] HIV viruses are divided into specific groups, M, N, O and P, of which M is the "major" group and responsible for majority of HIV/AIDS globally. Based on their genetic sequence, Group M is further subdivided into subtypes (also called clades) with prevalence in distinct geographical locations.

[0114] A Group M "subtype" or "clade" is a subtype of HIV-1 group M defined by genetic sequence data. Examples of Group M subtypes include Subtypes A-K. Some of the subtypes are known to be more virulent or are resistant to different medications. There are also "circulating recombinant forms" or CRFs derived from recombination between viruses of different subtypes, which are each given a number. CRF12_BF, for example, is a recombination between subtypes B and F. Subtype A is common in West Africa. Subtype B

is the dominant form in Europe, the Americas, Japan, Thailand, and Australia. Subtype C is the dominant form in Southern Africa, Eastern Africa, India, Nepal, and parts of China. Subtype D is generally only seen in Eastern and central Africa. Subtype E has never been identified as a nonrecombinant, only recombined with subtype A as CRF01_AE. Subtype F has been found in central Africa, South America and Eastern Europe. Subtype G (and the CRF02_AG) have been found in Africa and central Europe. Subtype H is limited to central Africa. Subtype I was originally used to describe a strain that is now accounted for as CRF04_cpx, with the cpx for a "complex" recombination of several subtypes. Subtype J is primarily found in North, Central and West Africa, and the Caribbean Subtype K is limited to the Democratic Republic of Congo and Cameroon. These subtypes are sometimes further split into sub-subtypes such as A1 and A2 or F1 and F2. In 2015, the strain CRF19, a recombinant of subtype A, subtype D, and subtype G, with a subtype D protease was found to be strongly associated with rapid progression to AIDS in Cuba.

[0115] This disclosure provides, *inter alia*, multi-specific antigen binding molecules comprising second antigen binding domains derived from human anti-HIV neutralizing antibodies (*e.g.*, broadly neutralizing Abs) that target the gp120 polypeptide on the surface of HIV-infected cells. Neutralizing antibodies against viral envelope proteins provide adaptive immune defense against HIV-1 exposure by blocking the infection of susceptible cells. Broad neutralization indicates that the antibodies can neutralize HIV-1 isolates from different clades. Thus, the multi-specific antigen binding molecules described herein have cross-clade binding activity.

gp120

[0116] Envelope glycoprotein gp120 (or gp120) is a 120 kDa glycoprotein that is part of the outer layer of HIV. It presents itself as viral membrane spikes consisting of three molecules of gp120 linked together and anchored to the membrane by gp41 protein. Gp120 is essential for viral infection as it facilitates HIV entry into the host cell through its interaction with cell surface receptors. These receptors include DC-SIGN, Heparan Sulfate Proteoglycan, and the CD4 receptor. Binding to CD4 on helper T-cells induces the start of a cascade of conformational changes in gp120 and gp41 that lead to the fusion of the virus with the host cell membrane.

[0117] Gp120 is encoded by the HIV *env* gene. The *env* gene encodes a gene product of around 850 amino acids. The primary *env* product is the protein gp160, which

gets cleaved to gp120 (about 480 amino acids) and gp41 (about 345 amino acids) in the endoplasmic reticulum by the cellular protease furin.

[0118] The amino acid sequence of an exemplary gp160 polypeptide of HIV clone WITO is provided below (the V3 hypervariable loop is boldened and the N332 potential N-linked glycosylation site is boldened and underlined):

MKVMGTKKNYQHLWRWGIMLLGMLMMSSAAEQLWVTVYYGVPVWREANTTLFCASDAKAYD
TEVHNVWATHACVPTDPNPQEVVMGNVTEDFNMWKNNMVEQMHEDIISLWDQSLKPCVKLT
PLCVTLHCTNVTISSTNGSTANVTMREEMKNCSFNTTTVIRDKIQKEYALFYKLDIVPIEG
KNTNTSYRLINCNTSVITQACPKVSFEPIPIHYCAPAGFAILKCNNKTFNGKGPCRNVSTV
QCTHGIKPVVSTQLLLNGSLAEEDIIIRSENFTNNGKNIIVQLKEPVKIN**CTRPGNNTRRS**
INIGPGRAFYATGAIIGDIRKAHCNISTEQWNNTLTQIVDKLREQFGNKTIIFNQSSGGDP
EVVMHTFNCGGEFFYCNSTQLFNSTWFNNGTSTWNSTADNITLPCRIKQVINMWQEVGKAM
YAPPIRGQIDCSSNITGLILTRDGGSNSSQNETFRPGGGNMKDNWRSELYKYKVVKIEPLG
IAPTRAKRRVVQREKRAVTLGAVFLGFLGAAGSTMGAASLTLTVQARLLLSGIVQQQSNLL
RAIEAQQHMLQLTVWGIKQLQARVLAIERYLKDQQLLGIWGCSGKLICTTTVPWNTSWSNK
SYDYIWNNMTWMQWEREIDNYTGFIYTLIEESQNQQEKNELELLELDKWASLWNWFNITNW
LWYIKLFIMIIGGLVGLRIVCAVLSIVNRVRQGYSPLSFQTRLPNPRGPDRPEETEGEGGE
RDRDRSARLVNGFLAIIWDDLRSLCLFSYHRLRDLLLIVARVVEILGRRGWEILKYWWNLL
KYWSQELKNSAVSLLNVTAIAVAEGTDRVIEIVQRAVRAILHIPTRIRQGFERALL (SEQ
ID NO: 67)

[0119] The amino acid sequence of an exemplary gp160 polypeptide of HIV clone identified in NCBI Ref Seq No. NP_057856.1 is provided below (the V3 hypervariable loop is boldened and the N332 potential N-linked glycosylation site is boldened and underlined):

MRVKEKYQHLWRWGWRWGTMLLGMLMICSATEKLWVTVYYGVPVWKEATTTLFCASDAKAY
DTEVHNVWATHACVPTDPNPQEVVLVNVTENFNMWKNDMVEQMHEDIISLWDQSLKPCVKL
TPLCVSLKCTDLKNDTNTNSSSGRMIMEKGEIKNCSFNISTSIRGKVQKEYAFFYKLDIIP
IDNDTTSYKLTSCNTSVITQACPKVSFEPIPIHYCAPAGFAILKCNNKTFNGTGPCTNVST
VQCTHGIRPVVSTQLLLNGSLAEEEVVIRSVNFTDNAKTIIVQLNTSVEIN**CTRPNNNTRK**
RIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLREQFGNNKTIIFKQSSG
GDPEIVTHSFNCGGEFFYCNSTQLFNSTWFNSTWSTEGSNNTEGSDTITLPCRIKQIINMW
QKVGKAMYAPPISGQIRCSSNITGLLLTRDGGNSNNESEIFRPGGGDMRDNWRSELYKYKV
VKIEPLGVAPTKAKRRVVQREKRAVGIGALFLGFLGAAGSTMGAASMTLTVQARQLLSGIV
QQQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGIWGCSGKLICTTAVPW
NASWSNKSLEQIWNHTTWMEWDREINNYTSLIHSLIEESQNQQEKNEQELLELDKWASLWN
WFNITNWLWYIKLFIMIVGGLVGLRIVFAVLSIVNRVRQGYSPLSFQTHLPTPRGPDRPEG
IEEEGGERDRDRSIRLVNGSLALIWDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEAL
KYWWNLLQYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQGACRAIRHIPRRIRQGLERI
LL (SEQ ID NO: 68)

[0120] The amino acid sequence of an exemplary gp120 polypeptide of HXB2 subtype B HIV-1 isolate (GenBank Accession No. K0345; corresponding to residues 1-511 of NCBI Ref Seq No. NP_057856.1) is provided below (the V3 hypervariable loop is boldened and the N332 potential N-linked glycosylation site is boldened and underlined; signal peptide is underlined):

MRVKEKYQHLWRWGWRWGTMLLGMLMICSATEKLWVTVYYGVPVWKEATTTLFCASDAKAY
DTEVHNVWATHACVPTDPNPQEVVLVNVTENFNMWKNDMVEQMHEDIISLWDQSLKPCVKL
TPLCVSLKCTDLKNDTNTNSSSGRMIMEKGEIKNCSFNISTSIRGKVQKEYAFFYKLDIIP
IDNDTTSYKLTSCNTSVITQACPKVSFEPIPIHYCAPAGFAILKCNNKTFNGTGPCTNVST
VQCTHGIRPVVSTQLLLNGSLAEEEVVIRSVNFTDNAKTIIVQLNTSVEIN**CTRPNNNTRK**
RIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLREQFGNNKTIIFKQSSG
GDPEIVTHSFNCGGEFFYCNSTQLFNSTWFNSTWSTEGSNNTEGSDTITLPCRIKQIINMW
QKVGKAMYAPPISGQIRCSSNITGLLLTRDGGNSNNESEIFRPGGGDMRDNWRSELYKYKV
VKIEPLGVAPTKAKRRVVQREKR (SEQ ID NO: 69)

[0121] The amino acid sequence of an exemplary gp120 polypeptide is provided below:

AEQLWVTVYYGVPVWREANTTLFCASDAKAYDTEVHNVWATHACVPTDPNPQEVVMGNVTE
DFNMWKNNMVEQMHEDIISLWDQSLKPCVKLTPLCVTLHCTNVTISSTNGSTANVTMREEM
KNCSFNTTTVIRDKIQKEYALFYKLDIVPIEGKNTNTSYRLINCNTSVITQACPKVSFEPI
PIHYCAPAGFAILKCNNKTFNGKGPCRNVSTVQCTHGIKPVVSTQLLLNGSLAEEDIIIRS
ENFTNNGKNIIVQLKEPVKIN**CTRPGNNTRRSINIGPGRAFYATGAIIGDIRKAHCN**ISTE
QWNNTLTQIVDKLREQFGNKTIIFNQSSGGDPEVVMHTFNCGGEFFYCNSTQLFNSTWFNN
GTSTWNSTADNITLPCRIKQVINMWQEVGKAMYAPPIRGQIDCSSNITGLILTRDGGSNSS
QNETFRPGGGNMKDNWRSELYKYKVVKIEPLGIAPTRAKRRVVQREKR (SEQ ID NO:
70).

[0122] The amino acid sequence of another exemplary gp120 polypeptide (see, bioafrica.net/proteomics/ENV-GP120prot.html) is provided below:

TEKLWVTVYY GVPVWKEATT TLFCASDAKA YDTEVHNVWA THACVPTDPN
PQEVVLVNVT ENFNMWKNDM VEQMHEDIIS LWDQSLKPCV KLTPLCVSLK
CTDLKNDTNT NSSSGRMIME KGEIKNCSFN ISTSIRGKVQ KEYAFFYKLD
IIPIDNDTTS YKLTSCNTSV ITQACPKVSF EPIPIHYCAP AGFAILKCNN
KTFNGTGPCT NVSTVQCTHG IRPVVSTQLL LNGSLAEEEV VIRSVNFTDN
AKTIIVQLNT SVEINCTRPN NNTRKRIRIQ RGPGRAFVTI GKIGNMRQAH
CNISRAKWNN TLKQIASKLR EQFGNNKTII FKQSSGGDPE IVTHSFNCGG
EFFYCNSTQL FNSTWFNSTW STEGSNNTEG SDTITLPCRI KQIINMWQKV
GKAMYAPPIS GQIRCSSNIT GLLLTRDGGN SNNESEIFRP GGGDMRDNWR
SELYKYKVVK IEPLGVAPTK AKRRVVQREK R (SEQ ID NO: 71)

[0123] Genomic diversity among independent human immunodeficiency virus type 1 (HIV-1) isolates, to a lesser degree among sequential isolates from the same patients, and even within a single patient isolate is a well-known feature of HIV-1. Although this sequence heterogeneity is distributed throughout the genome, most of the heterogeneity is located in the *env* gene. Comparison of predicted amino acid sequences from several different isolates has shown that sequence heterogeneity is clustered in five variable regions (designated V1 through V5) of the surface glycoprotein, gp120. The V3 region, although only 35 amino acids long, exhibits considerable sequence variability. Interestingly, in spite of this variability, the V3 region includes determinants that mediate interactions with $CD4^+$ cells. The increase in gp120 variability results in higher levels of viral replication, suggesting an increase in viral fitness in individuals infected by diverse HIV-1 variants. Variability in potential N-linked glycosylation sites (PNGSs) also result in increased viral fitness. PNGSs allow for the binding of long-chain carbohydrates to the high variable regions of gp120. Thus, the number of PNGSs in *env* might affect the fitness of the virus by providing more or less sensitivity to neutralizing antibodies.

[0124] A consensus sequence of the V3 region of gp120 (Milich et al., *J Virol.*, (1993) 67(9):5623-5634) is provided below:

CTRPNNNTRKSIHIGPGRAFYTTGEIIGDIRQAHC (SEQ ID NO: 72).

Anti-gp120 and Anti-gp41 Antigen Binding Domains

[0125] This disclosure features anti-gp120 or anti-gp41 multi-specific antigen binding molecules comprising a second antigen binding domain that targets and binds to gp120 or gp41, respectively. In certain embodiments, these multi-specific antigen binding molecules bind to HIV-1 antigens expressed on a cell surface and eliminate or kill the infected cell.

[0126] In certain embodiments, the second antigen binding domains in the herein described multi-specific antigen binding molecules are derived from human neutralizing antibodies (*e.g.*, monoclonal) that target HIV-1. A "neutralizing antibody" is one that can neutralize the ability of HIV to at least one of initiate and perpetuate an infection in at least one of a host *in vivo* and in target cells *in vitro*. The disclosure provides neutralizing monoclonal human antibodies, wherein the antibody recognizes an antigen from HIV, *e.g.*, a gp120 polypeptide. In certain embodiments, a "neutralizing antibody" may inhibit the entry

of HIV-1 virus, *e.g.*, SF162 and/or JR-CSF, with a neutralization index >1.5 or >2.0 (Kostrikis LG et al., *J. Virol.*,70(1): 445-458 (1996)).

[0127] In some embodiments, the second antigen binding domains in the herein described multi-specific antigen binding molecules are derived from human broadly neutralizing antibodies (*e.g.*, monoclonal) that target HIV-1. By "broadly neutralizing antibodies" are meant antibodies that neutralize more than one HIV-1 virus species (from diverse clades and different strains within a clade) in a neutralization assay. A broad neutralizing antibody may neutralize at least 2, 3, 4, 5, 6, 7, 8, 9 or more different strains of HIV-1, the strains belonging to the same or different clades. In particular embodiments, a broad neutralizing antibody may neutralize multiple HIV-1 species belonging to at least 2, 3, 4, 5, or 6 different clades. In certain embodiments, the inhibitory concentration of the multi-specific antigen binding molecule may be less than 0.0001 μg/ml, less than 0.001 μg/ml, less than 0.01 μg/ml, less than 0.1 μg/ml, less than 0.5 μg/ml, less than 1.0 μg/ml, less than 5 μg/ml, less than 10 μg/ml, less than 25 μg/ml, less than 50 μg/ml, or less than 100 μg/ml to neutralize 50% of the input virus in the neutralization assay.

[0128] In some embodiments, the second antigen binding domain of the multi-specific antigen binding molecules binds to an epitope or region of gp120 selected from the group consisting of: (i) third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan; (ii) second variable loop (V2) (*e.g.*, Env trimer apex); (iii) CD4 binding site (CD4bs); (iv) gp120/gp41 interface; or (v) silent face of gp120. The foregoing epitopes or regions of gp120 bound by broadly neutralizing antibodies are described, *e.g.*, in McCoy, *Retrovirology* (2018) 15:70; Sok and Burton, *Nat Immunol.* 2018 19(11):1179-1188; Possas, *et al., Expert Opin Ther Pat.* 2018 Jul;28(7):551-560; and Stephenson and Barouch, *Curr HIV/AIDS Rep* (2016) 13:31–37, which are hereby incorporated herein by reference in their entirety for all purposes.

[0129] In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12,

VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. Additional broadly neutralizing antibodies that bind to gp120 in the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and which can be used in the second antigen binding domain of the herein described multi-specific antigen binding molecules are described, *e.g.*, in WO 2012/030904; WO 2014/063059; WO 2016/149698; WO 2017/106346; WO 2018/075564, WO 2018/125813; WO 2018/237148, WO 2019/226829, WO 2020/023827, WO2020/056145 and Kerwin, *et al.*, *J Pharm Sci.* 2020 Jan;109(1):233-246, which are hereby incorporated herein by reference in their entireties for all purposes.

[0130] In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the second variable loop (V2) (*e.g.*, Env trimer apex) and competes with or comprises VH and VL regions from an antibody selected from the group consisting of PG9, PG16, PGC14, PGG14, PGT-142, PGT-143, PGT-144, PGT-145, CH01, CH59, PGDM1400, CAP256, CAP256-VRC26.08, CAP256-VRC26.09, CAP256-VRC26.25, PCT64-24E and VRC38.01. Additional broadly neutralizing antibodies that bind to gp120 in the second variable loop (V2) (*e.g.*, Env trimer apex) and which can be used in the second antigen binding domain of the herein described multi-specific antigen binding molecules are described, *e.g.*, in WO 2010/107939; WO 2012/030904; WO 2018/075564 and WO 2018/125813, which are hereby incorporated herein by reference in their entireties for all purposes.

gp120 CD4 Binding Site

[0131] Antibody variants described herein bind to the CD4 binding site (CD4bs) of HIV gp120. The CD4 binding site (CD4bs) involves structurally conserved sites located within the β1-α1, loop D, β20-β21 (bridging sheet) and β24-α5 of gp120, which determine the CD4 binding and are involved in the epitopes of CD4bs-directed antibodies (Qiao, *et al.*, *Antiviral Res.* 2016 Aug;132:252-61). The CD4bs of gp120 forms conformational epitopes recognized by anti-CD4bs antibodies involving one or more amino acid residues selected from Thr278, Asp279, Ala281, Thr283, Asp368, Trp427, Glu460, Ser461, Glu462, Leu452, Leu453 and Arg476. The amino acid residues and position numbering is with reference to HXB2 subtype B HIV-1 isolate, which corresponds to residues 1-511 of NCBI Ref Seq No. NP_057856.1, provided below. Residues Thr278, Asp279, Asn280, Ala281, Thr283, Asp368, Trp427, Leu452, Leu453, Gly459, Glu464, Ser465, Glu466, Ile467, Gly472,

Gly473 and Arg476, which can contribute to the gp120 CD4bs, are boldened and underlined:

MRVKEKYQHLWRWGWRWGTMLLGMLMICSATEKLWVTVYYGVPVWKEATTTLFCAS
DAKAYDTEVHNVWATHACVPTDPNPQEVVLVNVTENFNMWKNDMVEQMHEDIISLW
DQSLKPCVKLTPLCVSLKCTDLKNDTNTNSSSGRMIMEKGEIKNCSFNISTSIRGK
VQKEYAFFYKLDIIPIDNDTTSYKLTSCNTSVITQACPKVSFEPIPIHYCAPAGFA
ILKCNNKTFNGTGPCTNVSTVQCTHGIRPVVSTQLLLNGSLAEEEVVIRSVNF**TDN**
AK**T**IIVQLNTSVEINCTRPNNNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRA
KWNNTLKQIASKLREQFGNNKTIIFKQSSGG**D**PEIVTHSFNCGGEFFYCNSTQLFN
STWFNSTWSTEGSNNTEGSDTITLPCRIKQIINM**W**QKVGKAMYAPPISGQIRCSSN
ITG**LL**LTRDG**G**NSNN**ESEI**FRPG**GG**DM**R**DNWRSELYKYKVVKIEPLGVAPTKAKRR
VVQREKR (SEQ ID NO: 73).

[0132] Tridimensional models depicting amino acid residues contributing to the gp120 CD4bs are provided, *e.g.*, in Canducci, *et al.*, *Retrovirology*. 2009 Jan 15;6:4; Falkowska, *et al.*, *J Virol*. 2012 Apr;86(8):4394-403; and Li, *et al.*, *J. Virol*. 2012 Oct;86(20):11231–41; Gristick, *et al., Nat Struct Mol Biol*. 2016 Oct;23(10):906-915; Kwon, *et* al., *Nat Struct Mol Biol*. 2015 Jul;22(7):522-31; Liu, *et* al., *Nat Struct Mol Biol*. 2017 Apr;24(4):370-378; Chen, *et al., Science*. 2009 Nov 20;326(5956):1123-7 and Lyumkis, *et al., Science*. 2013 Dec 20;342(6165):1484-90. In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, b12, CH103, 1NC9, 12A12, VRC01, VRC07, VRC07-523, N6, NIH45-46 and PGV04 (*a.k.a.*, VRC-PG04) for binding to gp120 CD4bs. In some embodiments, the antibody variants described herein bind to an overlapping or identical epitope to the epitope bound by one or more of anti-CD4bs antibodies 3BNC117, GS-9723, GS-5423, 3BNC60, b12, CH103, 1NC9, 12A12, VRC01, VRC07, VRC07-523, N6, NIH45-46 and PGV04 (*a.k.a.*, VRC-PG04).

[0133] In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises immunoglobulin VH and VL (*e.g.*, in Fab or scFv format) that compete with or comprise VH and VL regions from an antibody selected from the group consisting of b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, 3BNC117, GS-9723, GS-5423, 3BNC60, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9,

12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. Additional broadly neutralizing antibodies that bind to gp120 in the CD4 binding site (CD4bs) and which can be used in the second antigen binding domain of the herein described multi-specific antigen binding molecules are described, *e.g.*, in WO 2011/038290; WO 2012/158948; WO 2013/016468; WO 2013/192589; WO 2013/086533; WO 2015/128846; WO 2016/149698; WO 2016/149695; WO 2018/075564; WO 2018/125813; WO 2018/237357, WO 2020/010107, WO 2020/086446 and U.S. Patent Nos. 9,493,549 and 9,879,068, which are hereby incorporated herein by reference in their entireties for all purposes.

[0134] In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and competes with or comprises VH and VL regions from 3BNC117 and comprises Phe-Asp-Phe-Asp (FDFD) (SEQ ID NO: 1040) at positions 74a, 74b, 74c, and 74d of the VH (position numbering according to Kabat). In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and competes with or comprises VH and VL regions from 3BNC117 and comprises a framework region 3 (FR3) of the VH comprising the following amino acid sequence RVSLTRHASFDFDTFSFYMDLKALRSDDTAVYFCAR (SEQ ID NO: 74). Crystallographic studies have shown that framework region 3 at VH Kabat position numbers 74a, 74b, 74c and 74d form part of the paratope of 3BNC117 variants, directly contacting the antigen target, gp120. *See*, *e.g.*, Lee, *et al.*, *Immunity* (2017) 46(4): 690–702 (Figure 1G, identifying residue W71d); Klein, *et al.*, *Cell.* (2013) 153(1):126-38 (Figures 4 and 5); and Zhou, *et al.*, (2013) *Immunity* (2013) 39 245-258 (Table 1); ribbon diagrams of crystallized structures of 5V8L, 5V8M, 4JPV and 4LSV can be viewed at rcsb.org. In some embodiments, at least 50%, at least 60%, at least 70%, least 80%, at least 85%, at least 90%, or more, N-linked glycosylation sites in at least one of the first VH, the first VL, the second VH and the second VL are sialylated. In some embodiments, the N-linked glycosylation sites in at least one of the first VH, the first VL, the second VH and the second VL have a sialic acid occupancy (*e.g.*, a glycan comprising one or two terminal sialic acid residues) of at least 40%, at least 50%, at least 60%, at least 70%, least 80%, at least 85%, at least 90%, or more. In some embodiments, the N-linked glycosylation site at VL asparagine amino acid position 72 (N72) according to Kabat numbering is sialylated. In some embodiments, the sialylated N-linked glycosylation sites in at least one of the first VH, the first VL, the second VH and the second VL comprise from 1 to 5 sialic acid residues, *e.g.*, from 1 to 4

sialic acid residues, *e.g.*, from 1 to 3 sialic acid residues, *e.g.*, from 1 to 2 sialic acid residues. In some embodiments, at least one of the first VH, the first VL, the second VH and the second VL are sialylated with N-acetylneuraminic acid (NANA). In some embodiments, the sialic acid residues are present in biantennary structures. In some embodiments, the sialic acid residues are present in complex N-linked glycan structures. In some embodiments, the sialic acid residues are present in hybrid N-linked glycan structures.

[0135] In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises an EC domain of CD4 (*e.g.*, domain 1 (D1), D1-D1 (tandem), D1-D2, D1-D2-D3-D3, or D1-D2-D3-D4). Illustrative CD4 extracellular domains that can be used in the herein described multi-specific antigen binding molecules are described, *e.g.*, in WO2011146891, WO2014150748 and WO2016153572. In some embodiments, the one or more EC domains of CD4 comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or 100% identical, to a CD4 EC domain selected from:

(i) KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRV DSRRSLWDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVG (SEQ ID NO: 746; see, *e.g.*, Chen, *et al.*, *J Virol.* 2014 Jan;88(2):1125-39);

(ii) KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRV DSRRSLWDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVGGGGSGKKVVYG KKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRVDSRRSL WDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVG (SEQ ID NO: 747);

(iii) KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRA DSRRSLWDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFG (SEQ ID NO: 748); or

(iv) KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRA DSRRSLWDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFGGGGSGKKVVLG KKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRRSL WDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFG(SEQ ID NO: 749).

[0136] In some embodiments, the EC domain of CD4 comprises a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least

94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 95% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises the sequence of SEQ ID NO: 746. In some embodiments, provided is a multi-specific antigen binding molecule comprising a first antigen binding domain that binds to human CD3 and a second antigen binding domain that binds to HIV gp120, wherein the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749, *e.g.*, SEQ ID NO: 746.

[0137] In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC

domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO: 746.

[0138] In some embodiments, provided is a multi-specific antigen binding molecule comprising a first antigen binding domain that binds to human CD3 and a second antigen binding domain that binds to HIV gp120, wherein the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749, *e.g.*, SEQ ID NO: 746.

[0139] In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO: 746.

[0140] In some embodiments, provided is a multi-specific antigen binding molecule comprising a first antigen binding domain that binds to human CD3 and a second antigen binding domain that binds to HIV gp120, wherein the first antigen binding domain

comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749, *e.g.*, SEQ ID NO: 746.

[0141] In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO: 746.

[0142] In some embodiments, provided is a multi-specific antigen binding molecule comprising a first antigen binding domain that binds to human CD3 and a second antigen binding domain that binds to HIV gp120, wherein the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749, *e.g.*, SEQ ID NO: 746.

[0143] In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO: 746.

[0144] In some embodiments, provided is a multi-specific antigen binding molecule comprising a first antigen binding domain that binds to human CD3 and a second antigen binding domain that binds to HIV gp120, wherein the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749, *e.g.*, SEQ ID NO: 746.

[0145] In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99%

identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 50 and a first VL comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746 . In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 50 and a first VL comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 50 and a first VL comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 50 and a first VL comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 50 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 50 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 50 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4

comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 50 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence of SEQ ID NO: 746.

[0146] In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and

the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746 . In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4

comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence of SEQ ID NO: 746.

[0147] In some embodiments, the second antigen binding domain binds to an epitope or region of gp120 in the gp120/gp41 interface and competes with or comprises VH and VL regions from an antibody selected from the group consisting of PGT-151, CAP248-2B, 35O22, 8ANC195, ACS202, VRC34 and VRC34.01. Additional broadly neutralizing antibodies that bind to gp120 in the gp120/gp41 interface and which can be used in the second antigen binding domain of the herein described multi-specific antigen binding molecules are described, *e.g.*, in WO 2011/038290; WO 2012/030904 and WO2017/079479, which are hereby incorporated herein by reference in their entireties for all purposes.

[0148] In some embodiments, the second antigen binding domain binds to an epitope or region of the gp120 silent face and competes with or comprises VH and VL regions from an antibody selected from VRC-PG05 and SF12. *See*, *e.g.*, Schoofs, *et al.*, *Immunity*. (2019) 50(6):1513-1529.

[0149] In some embodiments, the second antigen binding domain binds to an epitope or region of gp41 in the membrane proximal region (MPER). Additional broadly neutralizing antibodies that bind to gp41 in the MPER and which can be used in the second antigen binding domain of the herein described multi-specific antigen binding molecules are described, *e.g.*, in WO 2011/034582; WO 2011/038290; WO 2011/046623 and WO 2013/070776, which are hereby incorporated herein by reference in their entireties for all purposes.

[0150] In some embodiments, the second antigen binding domain binds to an epitope or region of gp41 in the membrane proximal region (MPER) and competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10E8, 10E8v4, 10E8-5R-100cF, 4E10, DH511.11P, 2F5, 7b2, and LN01.

[0151] In some embodiments, the second antigen binding domain binds to an epitope or region of the gp41 fusion peptide and competes with or comprises VH and VL regions from an antibody selected from the group consisting of VRC34 and ACS202.

[0152] Additional broadly neutralizing antibodies which can be used in the second antigen binding domain of the herein described multi-specific antigen binding molecules are described, *e.g.*, in U.S. Patent Nos. 8,673,307; 9,493,549; 9,783,594; 10,239,935; and patent publications numbers US2018371086, US2020223907, WO 2012/154312; WO2012/158948; WO 2013/086533; WO 2013/142324; WO2014/063059; WO 2014/089152, WO 2015/048462; WO 2015/103549; WO 2015/117008; WO2016/014484; WO 2016/154003; WO 2016/196975; WO 2016/149710; WO2017/096221; WO 2017/133639; and WO 2017/133640, which are hereby incorporated herein by reference in their entireties for all purposes. Additional examples include those described in Sajadi, *et al.*, Cell. (2018) 173(7):1783-1795; Sajadi, *et al.*, J Infect Dis. (2016) 213(1):156-64; Klein *et al.*, Nature, 492(7427): 118-22 (2012), Horwitz *et al.*, Proc Natl Acad Sci U S A, 110(41): 16538-43 (2013), Scheid, *et al.*, Science, 333 : 1633-1637 (2011), Scheid, *et al.*, Nature, 458:636-640 (2009), Eroshkin *et al*, Nucleic Acids Res., 42 (Database issue):Dl 133-9 (2014), Mascola *et al.*, Immunol Rev., 254(l):225-44 (2013), such as 2F5, 4E10, M66.6, CAP206-CH12, 10E8, 10E8v4, 10E8-5R-100cF, DH511.11P, 7b2, and LN01 (all of which bind the MPER of gp41); PG9, PG16, CAP256, CAP256-VRC26, CAP256-VRC26.25, CH01-04 (all of which bind V1V2-glycan), 2G12 (which binds to outer domain glycan); b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, 3BNC117, 3BNC60, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-

VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25 (all of which bind to the CD4 binding site), which are hereby incorporated herein by reference in their entireties for all purposes.

[0153] In some embodiments, the second antigen binding domain comprises a second VH comprising a second VH-CDR1, a second VH-CDR2, and a second VH-CDR3; and a second VL comprising a second VL-CDR1, a second VL-CDR2, and a second VH-CDR3; comprising the amino acid sequences (according to Kabat) set forth, respectively, in: SEQ ID NOs: 76, 77, 78, 79, 80 and 81; SEQ ID NOs: 76, 82, 78, 79, 80 and 81; SEQ ID NOs: 83, 84, 85, 86, 80 and 87; SEQ ID NOs: 83, 88, 85, 86, 80 and 87; SEQ ID NOs: 90, 91, 92, 93, 94 and 95; SEQ ID NOs: 90, 91, 96, 93, 94 and 95; SEQ ID NOs: 97, 98, 99, 100, 101 and 102; SEQ ID NOs: 103, 104, 105, 106, 94 and 107; SEQ ID NOs: 108, 109, 110, 111, 112 and 113; SEQ ID NOs: 114, 115, 116, 117, 118 and 119; SEQ ID NOs: 114, 120, 121, 122, 118 and 123; SEQ ID NOs: 124, 125, 126, 127, 128 and 113; SEQ ID NOs: 129, 115, 131, 127, 118 and 113; SEQ ID NOs: 132, 133, 134, 135, 136 and 137; SEQ ID NOs: 138, 139, 140, 141, 142 and 143; SEQ ID NOs: 144, 145, 146, 147, 148 and 143; SEQ ID NOs: 149, 150, 151, 152, 153 and 143; SEQ ID NOs: 154, 155, 156, 157, 158 and 159; SEQ ID NOs: 160, 161, 162, 163, 164 and 165; SEQ ID NOs: 166, 161, 167, 163, 164 and 165; SEQ ID NOs: 168, 169, 170, 171, 172 and 173; SEQ ID NOs: 168, 174, 170, 171, 172 and 173; SEQ ID NOs: 175, 176, 177, 171, 172 and 173; SEQ ID NOs: 178, 179, 180, 181, 182 and 183; SEQ ID NOs: 184, 185, 186, 187, 188 and 189; SEQ ID NOs: 190, 191, 192, 193, 194 and 195; SEQ ID NOs: 196, 197, 198, 199, 200 and 201; SEQ ID NOs: 202, 203, 204, 205, 206 and 207; SEQ ID NOs: 208, 209, 210, 211, 212 and 213; SEQ ID NOs: 214, 215, 216, 217, 218 and 219; SEQ ID NOs: 214, 220, 216, 221, 218 and 219; SEQ ID NOs: 214, 220, 222, 221, 218 and 219; SEQ ID NOs: 223, 224, 225, 226, 227 and 228; or SEQ ID NOs: 229, 230, 231, 232, 233 and 234; SEQ ID NOs: 902, 903, 904, 905, 906 and 907; SEQ ID NOs: 908, 909, 910, 911, 912 and 913; SEQ ID NOs: 914, 915, 916, 917, 918 and 919; or SEQ ID NOs: 920, 921, 922, 923, 924 and 925.

[0154] In some embodiments, the second antigen binding domain comprises a second VH comprising a second VH-CDR1, a second VH-CDR2, and a second VH-CDR3; and a second VL comprising a second VL-CDR1, a second VL-CDR2, and a second VH-CDR3; comprising the amino acid sequences (according to Chothia) set forth, respectively, in: SEQ ID NOs: 235, 236, 237, 238, 239 and 240; SEQ ID NOs: 241, 242, 243, 244, 239 and 245; SEQ ID NOs: 246, 242, 247, 244, 239 and 245; SEQ ID NOs: 248, 249, 250, 251,

239 and 252; SEQ ID NOs: 248, 249, 253, 251, 239 and 252; SEQ ID NOs: 254, 255, 256, 257, 258 and 259; SEQ ID NOs: 260, 261, 262, 263, 239 and 264; SEQ ID NOs: 265, 266, 267, 268, 269 and 270; SEQ ID NOs: 271, 272, 273, 274, 275 and 270; SEQ ID NOs: 271, 276, 277, 278, 275 and 279; SEQ ID NOs: 280, 281, 282, 283, 284 and 270; SEQ ID NOs: 285, 272, 286, 283, 275 and 270; SEQ ID NOs: 287, 288, 289, 290, 291 and 292; SEQ ID NOs: 293, 294, 295, 296, 297 and 298; SEQ ID NOs: 299, 300, 301, 302, 303 and 298; SEQ ID NOs: 304, 300, 305, 406, 307 and 298; SEQ ID NOs: 308, 309, 310, 311, 312 and 313; SEQ ID NOs: 314, 315, 316, 317, 318 and 165; SEQ ID NOs: 320, 315, 321, 317, 318 and 165; SEQ ID NOs: 322, 323, 324, 325, 326 and 327; SEQ ID NOs: 322, 328, 324, 325, 326 and 327; SEQ ID NOs: 329, 323, 330, 325, 326 and 327; SEQ ID NOs: 331, 332, 333, 334, 335 and 336; SEQ ID NOs: 337, 338, 339, 340, 341 and 342; SEQ ID NOs: 343, 344, 345, 346, 341 and 347; SEQ ID NOs:348, 349, 350, 351, 352 and 353; SEQ ID NOs: 354, 355, 356, 357, 358 and 359; SEQ ID NOs: 360, 361, 362, 363, 364 and 365; SEQ ID NOs: 366, 367, 368, 369, 370 and 371; SEQ ID NOs: 366, 361, 368, 369, 370 and 371; SEQ ID NOs: 372, 361, 373, 369, 370 and 371; SEQ ID NOs: 374, 375, 376, 377, 378 and 379; SEQ ID NOs: 380, 381, 382, 383, 384 and 385; SEQ ID NOs: 926, 927, 928, 929, 930 and 931; SEQ ID NOs: 932, 933, 934, 935, 936 and 937; SEQ ID NOs: 938, 939, 940, 941, 942 and 943; or SEQ ID NOs: 944, 945, 946, 947, 948 and 949.

[0155] In some embodiments, the second antigen binding domain comprises a second VH comprising a second VH-CDR1, a second VH-CDR2, and a second VH-CDR3; and a second VL comprising a second VL-CDR1, a second VL-CDR2, and a second VH-CDR3; comprising the amino acid sequences (according to IMGT) set forth, respectively, in: SEQ ID NOs: 386, 387, 388, 389, 239 and 81; SEQ ID NOs: 390, 391, 392, 393, 239 and 87; SEQ ID NOs: 390, 391, 394, 393, 239 and 87; SEQ ID NOs: 395, 396, 397, 393, 239 and 87; SEQ ID NOs: 398, 399, 400, 401, 239 and 95; SEQ ID NOs: 398, 399, 402, 401, 239 and 95; SEQ ID NOs: 403, 404, 405, 406, 258 and 102; SEQ ID NOs: 407, 408, 409, 410, 239 and 107; SEQ ID NOs: 411, 412, 413, 414, 269 and 113; SEQ ID NOs: 415, 416, 417, 418, 275 and 119; SEQ ID NOs: 415, 419, 420, 421, 275 and 123; SEQ ID NOs: 422, 423, 424, 425, 275 and 113; SEQ ID NOs: 426, 416, 427, 425, 275 and 113; SEQ ID NOs: 428, 429, 430, 431, 291 and 137; SEQ ID NOs: 432, 433, 434, 435, 297 and 143; SEQ ID NOs: 436, 437, 438, 439, 303 and 143; SEQ ID NOs: 440, 437, 441, 442, 307 and 143; SEQ ID NOs: 443, 444, 445, 446, 312 and 159; SEQ ID NOs: 447, 448, 449, 450, 318 and 165; SEQ ID NOs: 451, 448, 452, 450, 318 and 165; SEQ ID NOs: 453, 454, 455, 456, 326 and 173; SEQ ID NOs: 453, 457, 455, 456, 326 and 173; SEQ ID NOs: 458, 459, 460, 456,

326 and 173; SEQ ID NOs: 461, 462, 463, 464, 335 and 183; SEQ ID NOs: 465, 466, 467, 468, 341 and 189; SEQ ID NOs: 469, 470, 471, 472, 341 and 195; SEQ ID NOs: 473, 474, 475, 476, 352 and 201; SEQ ID NOs: 477, 478, 479, 480, 358 and 207; SEQ ID NOs: 481, 482, 483, 484, 364 and 213; SEQ ID NOs: 485, 486, 487, 488, 370 and 219; SEQ ID NOs: 485, 482, 487, 488, 370 and 219; SEQ ID NOs: 489, 482, 490, 488, 370 and 219; SEQ ID NOs: 491, 492, 493, 494, 378 and 228; SEQ ID NOs: 495, 496, 497, 498, 384 and 234; SEQ ID NOs: 950, 951, 952, 953, 930 and 907; SEQ ID NOs: 954, 955, 956, 957, 936 and 913; SEQ ID NOs: 958, 959, 960, 961, 942 and 919; or SEQ ID NOs: 962, 963, 964, 965, 948 and 925.

[0156] In some embodiments, the second antigen binding domain comprises a second VH comprising a second VH-CDR1, a second VH-CDR2, and a second VH-CDR3; and a second VL comprising a second VL-CDR1, a second VL-CDR2, and a second VH-CDR3; comprising the amino acid sequences (according to Honegger) set forth, respectively, in: SEQ ID NOs: 499, 500, 501, 238, 502 and 240; SEQ ID NOs: 499, 503, 501, 238, 502 and 240; SEQ ID NOs: 505, 506, 507, 244, 502 and 245; SEQ ID NOs: 508, 509, 510, 244, 502 and 245; SEQ ID NOs: 511, 512, 513, 251, 514 and 252; SEQ ID NOs: 511, 512, 515, 251, 514 and 252; SEQ ID NOs: 516, 517, 518, 257, 519 and 259; SEQ ID NOs: 520, 521, 522, 264, 523 and 264; SEQ ID NOs: 524, 525, 526, 268, 527 and 270; SEQ ID NOs: 528, 529, 530, 274, 531 and 270; SEQ ID NOs: 528, 532, 533, 278, 531 and 279; SEQ ID NOs: 534, 535, 536, 283, 537 and 270; SEQ ID NOs: 1090, 529, 538, 283, 531 and 270; SEQ ID NOs: 539, 540, 541, 290, 542 and 292; SEQ ID NOs: 543, 544, 545, 546, 547 and 298; SEQ ID NOs: 548, 549, 550, 1091, 551 and 298; SEQ ID NOs: 552, 553, 554, 555, 556 and 298; SEQ ID NOs: 557, 558, 559, 311, 560 and 313; SEQ ID NOs: 561, 562, 563, 564, 565 and 165; SEQ ID NOs: 566, 562, 1092, 564, 567 and 165; SEQ ID NOs: 568, 569, 570, 571, 572 and 327; SEQ ID NOs: 568, 573, 570, 571, 572 and 327; SEQ ID NOs: 574, 575, 576, 571, 572 and 327; SEQ ID NOs: 577, 578, 579, 580, 581 and 336; SEQ ID NOs: 582, 583, 584, 340, 585 and 342; SEQ ID NOs: 586, 587, 588, 346, 589 and 347; SEQ ID NOs: 590, 591, 592, 351, 593 and 353; SEQ ID NOs: 594, 595, 596, 597, 598 and 359; SEQ ID NOs: 599, 600, 601, 602, 603 and 365; SEQ ID NOs: 604, 605, 606, 607, 608 and 371; SEQ ID NOs: 604, 609, 606, 607, 608 and 371; SEQ ID NOs: 610, 609, 611, 607, 608 and 371; SEQ ID NOs: 612, 613, 614, 615, 616 and 379; SEQ ID NOs: 617, 618, 619, 620, 621 and 385; SEQ ID NOs: 966, 967, 968, 969, 970 and 931; SEQ ID NOs: 971, 972, 973, 974, 975 and 937; SEQ ID NOs: 976, 977, 978, 941, 979 and 943; or SEQ ID NOs: 980, 981, 982, 983, 984 and 949.

[0157] In some embodiments, the second VH and the second VL comprise the amino acid sequences set forth, respectively, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, in: SEQ ID NOs: 622 and 623; SEQ ID NOs: 624 and 625; SEQ ID NOs: 624 and 626; SEQ ID NOs: 627 and 628; SEQ ID NOs: 629 and 630; SEQ ID NOs: 631 and 632; SEQ ID NOs: 633 and 634; SEQ ID NOs: 635 and 636; SEQ ID NOs: 637 and 638; SEQ ID NOs: 639 and 640; SEQ ID NOs: 641 and 642; SEQ ID NOs: 643 and 644; SEQ ID NOs: 645 and 646; SEQ ID NOs: 647 and 648; SEQ ID NOs: 649 and 650; SEQ ID NOs: 651 and 652; SEQ ID NOs: 653 and 654; SEQ ID NOs: 655 and 656; SEQ ID NOs: 657 and 658; SEQ ID NOs: 659 and 660; SEQ ID NOs: 661 and 662; SEQ ID NOs: 663 and 664; SEQ ID NOs: 665 and 666; SEQ ID NOs: 667 and 668; SEQ ID NOs: 669 and 670; SEQ ID NOs:671 and 672; SEQ ID NOs:673 and 670; SEQ ID NOs: 674 and 675; SEQ ID NOs: 676 and 677; SEQ ID NOs: 678 and 679; SEQ ID NOs: 680 and 681; SEQ ID NOs: 682 and 683; SEQ ID NOs: 684 and 685; SEQ ID NOs: 686 and 687; SEQ ID NOs: 688 and 689; SEQ ID NOs: 690 and 691; SEQ ID NOs: 692 and 693; SEQ ID NOs: 694 and 695; SEQ ID NOs: 985 and 986; SEQ ID NOs: 987 and 988; SEQ ID NOs: 989 and 990; or SEQ ID NOs: 991 and 992.

[0158] Illustrative sequences of complementarity determining regions (CDRs) of the first antigen binding domains of the multi-specific antigen binding molecules, targeting HIV gp120, are provided in Tables D1, D2, D3 and D4. Illustrative sequences of the VH and VL of the second antigen binding domains of the multi-specific antigen binding molecules, targeting HIV gp120, are provided in Table E.

Table D1 – CDRs (Kabat) for illustrative anti-HIV antigen binding arm

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
1	DSYWS SEQ ID NO:76	YVHKSGDTNYSPSLKS SEQ ID NO:77	TLHGRRIYGIVAFN EWFTYFYMDV SEQ ID NO:78	GEKSLGSRAVQ SEQ ID NO:79	NNQDRPS SEQ ID NO:80	HIWDSRVPTKWV SEQ ID NO:81
2	DSYWS SEQ ID NO:76	YVHKSGDTNYNPSLKS SEQ ID NO:82	TLHGRRIYGIVAFN EWFTYFYMDV SEQ ID NO:78	GEKSLGSRAVQ SEQ ID NO:79	NNQDRPS SEQ ID NO:80	HIWDSRVPTKWV SEQ ID NO:81
3	NYYWT SEQ ID NO:83	YISDRESATYNPSLNS SEQ ID NO:84	ARRGQRIYGVVSFG EFFYYYSMDV SEQ ID NO:85	GRQALGSRAVQ SEQ ID NO:86	NNQDRPS SEQ ID NO:80	HMWDSRSGFSWS SEQ ID NO:87
4	NYYWT SEQ ID NO:83	YISDRETTTYNPSLNS SEQ ID NO:88	ARRGQRIYGVVSFG EFFYYYYMDV SEQ ID NO:89	GRQALGSRAVQ SEQ ID NO:86	NNQDRPS SEQ ID NO:80	HMWDSRSGFSWS SEQ ID NO:87
5	GRFWS SEQ ID NO:90	YFSDTDRSEYNPSLRS SEQ ID NO:91	AQQGKRIYGIVSFG EFFYYYYMDA SEQ ID NO:92	GERSRGSRAVQ SEQ ID NO:93	NNQDRPA SEQ ID NO:94	HYWDSRSPISWI SEQ ID NO:95
6	GRFWS SEQ ID NO:90	YFSDTDRSEYNPSLRS SEQ ID NO:91	AQQGKRIYGIVSFG ELFYYYYMDA SEQ ID NO:96	GERSRGSRAVQ SEQ ID NO:93	NNQDRPA SEQ ID NO:94	HYWDSRSPISWI SEQ ID NO:95
7	DNYWS SEQ ID NO:97	YVHDSGDTNYNPSLKS SEQ ID NO:98	TKHGRRIYGVVAFK EWFTYFYMDV SEQ ID NO:99	GEESLGSRSVI SEQ ID NO:100	NNNDRPS SEQ ID NO:101	HIWDSRRPTNWV SEQ ID NO:102
8	DAYWS SEQ ID NO:103	YVHHSGDTNYNPSLKR SEQ ID NO:104	ALHGKRIYGIVALG ELFTYFYMDV SEQ ID NO:105	GKESIGSRAVQ SEQ ID NO:106	NNQDRPA SEQ ID NO:94	HIYDARGGTNWV SEQ ID NO:107
9	ACTYFWG SEQ ID NO:108	SLSHCQSFWGSGWTFH NPSLKS SEQ ID NO:109	FDGEVLVYNHWPKP AWVDL SEQ ID NO:110	NGTATNFVS SEQ ID NO:111	GVDKRPP SEQ ID NO:112	GSLVGNWDVI SEQ ID NO:113
10	ACDYFWG SEQ ID NO:114	GLSHCAGYYNTGWTYH NPSLKS	FDGEVLVYHDWPKP AWVDL	TGTSNRFVS SEQ ID NO:117	GVNKRPS	SSLVGNWDVI

Table D1 – CDRs (Kabat) for illustrative anti-HIV antigen binding arm

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
		SEQ ID NO:115	SEQ ID NO:116		SEQ ID NO:118	SEQ ID NO:119
11	ACDYFWG SEQ ID NO:114	SLSHCAGYYNSGWTYH NPSLKS SEQ ID NO:120	FGGDVLVYHDWPKP AWVDL SEQ ID NO:121	TGNINNFVS SEQ ID NO:122	GVNKRPS SEQ ID NO:118	GSLAGNWDVV SEQ ID NO:123
12	ACNSFWG SEQ ID NO:124	SLSHCASYWNRGWTYH NPSLKS SEQ ID NO:125	FGGEVLRYTDWPKP AWVDL SEQ ID NO:126	TGTSNNFVS SEQ ID NO:127	DVNKRPS SEQ ID NO:128	GSLVGNWDVI SEQ ID NO:113
13	GCDYFWG SEQ ID NO:129	GLSHCAGYYNTGWTYH NPSLKS SEQ ID NO:115	FDGEVLVYNDWPKP AWVDL SEQ ID NO:131	TGTSNNFVS SEQ ID NO:127	GVNKRPS SEQ ID NO:118	GSLVGNWDVI SEQ ID NO:113
14	TGHYYWG SEQ ID NO:132	HIHYTTAVLHNPSLKS SEQ ID NO:133	SGGDILYYYEWQKP HWFSP SEQ ID NO:134	NGTSSDIGGWNFVS SEQ ID NO:135	EVNKRPS SEQ ID NO:136	SSLFGRWDVV SEQ ID NO:137
15	GTDWGENDFHYG SEQ ID NO:138	SIHWRGRTTHYKTSFR S SEQ ID NO:139	HKYHDIFRVVPVAG WFDP SEQ ID NO:140	RASQNVKNNLA SEQ ID NO:141	DASSRAG SEQ ID NO:142	QQYEEWPRT SEQ ID NO:143
16	GGEWGDSDYHWG SEQ ID NO:144	SIHWRGTTHYNAPFRG SEQ ID NO:145	HKYHDIVMVVPIAG WFDP SEQ ID NO:146	RASQSVKNNLA SEQ ID NO:147	DTSSRAS SEQ ID NO:148	QQYEEWPRT SEQ ID NO:143
17	GGEWGDKDYHWG SEQ ID NO:149	SIHWRGTTHYKESLRR SEQ ID NO:150	HRHHDVFMLVPIAG WFDV SEQ ID NO:151	RASQNINKNLA SEQ ID NO:152	ETYSKIA SEQ ID NO:153	QQYEEWPRT SEQ ID NO:143
18	SDHSWT SEQ ID NO:154	DIHYNGATTYNPSLRS SEQ ID NO:155	NAIRIYGVVALGEW FHYGMDV SEQ ID NO:156	SGAPLTSRFTY SEQ ID NO:157	RSSQRSS SEQ ID NO:158	QSSDTSDSYKM SEQ ID NO:159
19	DYFIH SEQ ID NO:160	WINPKTGQPNNPRQFQ G SEQ ID NO:161	QRSDYWDFDV SEQ ID NO:162	QANGYLN SEQ ID NO:163	DGSKLER SEQ ID NO:164	QVYEF SEQ ID NO:165

Table D1 – CDRs (Kabat) for illustrative anti-HIV antigen binding arm

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
20	DHFIH SEQ ID NO:166	WINPKTGQPNNPRQFQG SEQ ID NO:161	QRSDFWDFDV SEQ ID NO:167	QANGYLN SEQ ID NO:163	DGSKLER SEQ ID NO:164	QVYEF SEQ ID NO:165
21	NCPIN SEQ ID NO:168	WMKPRGGAVSYARQLQG SEQ ID NO:169	GKYCTARDYYNWDFEH SEQ ID NO:170	RTSQYGSLA SEQ ID NO:171	SGSTRAA SEQ ID NO:172	QQYEF SEQ ID NO:173
22	NCPIN SEQ ID NO:168	WMKPRHGAVSYARQLQG SEQ ID NO:174	GKYCTARDYYNWDFEH SEQ ID NO:170	RTSQYGSLA SEQ ID NO:171	SGSTRAA SEQ ID NO:172	QQYEF SEQ ID NO:173
23	DCTLN SEQ ID NO:175	WLKPRGGAVNYARPLQGSEQ ID NO:176	GKNCDYNWDFEH SEQ ID NO:177	RTSQYGSLA SEQ ID NO:171	SGSTRAA SEQ ID NO:172	QQYEF SEQ ID NO:173
24	AHILF SEQ ID NO:178	WIKPQYGAVNFGGGFRDSEQ ID NO:179	DRSYGDSSWALDA SEQ ID NO:180	QTSQGVGSDLH SEQ ID NO:181	HTSSVED SEQ ID NO:182	QVLQF SEQ ID NO:183
25	DDDTFTKYWTH SEQ ID NO:902	VISPHFARPIYSYKFRD SEQ ID NO:903	DPFGDRAPHYNYHMDV SEQ ID NO:904	RASQGLDSSHLA SEQ ID NO:905	GTSNRAR SEQ ID NO:906	QRYGGTPIT SEQ ID NO:907
26	RTELIH SEQ ID NO:908	WVKTVTGAVNFGSPDFR SEQ ID NO:909	QKFYTGGQGWYFDL SEQ ID NO:910	TAASYGHMT SEQ ID NO:911	ATSKRAS SEQ ID NO:912	QQLEF SEQ ID NO:913
27	SGFDFSRQGMH SEQ ID NO:184	FIKYDGSEKYHADSVW SEQ ID NO:185	EAGGPDYRNGYNYYDFYDGYYNYHYMDV SEQ ID NO:186	NGTSNDVGGYESVS SEQ ID NO:187	DVSKRPSG SEQ ID NO:188	KSLTSTRRRV SEQ ID NO:189
28	SGFTFHKYGMH SEQ ID NO:190	LISDDGMRKYHSDSMW SEQ ID NO:191	EAGGPIWHDDVKYYDFNDGYYNYHYMDV SEQ ID NO:192	NGTSSDVGGFDSVS SEQ ID NO:193	DVSHRPSG SEQ ID NO:194	SSLTDRSHRI SEQ ID NO:195

Table D1 – CDRs (Kabat) for illustrative anti-HIV antigen binding arm

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
29	DYYLH SEQ ID NO:196	LIDPENGEARYAEKFQG SEQ ID NO:197	GAVGADSGSWFDP SEQ ID NO:198	SGSKLGDKYVS SEQ ID NO:199	ENDRRPS SEQ ID NO:200	QAWETTTTFV SEQ ID NO:201
30	SYAFS SEQ ID NO:202	MITPVFGETKYAPRFQG SEQ ID NO:203	DRRVVPMATDNWLDP SEQ ID NO:204	RASQTIHTYLN SEQ ID NO:205	GASTLQS SEQ ID NO:206	QQSYSTPRT SEQ ID NO:207
31	NHDVH SEQ ID NO:208	WMSHEGDKTGLAQKFQG SEQ ID NO:209	GSKHRLRDYFLYNEYGPNYEEWGDYLATLDV SEQ ID NO:210	KCSHSLQHSTGANYLA SEQ ID NO:211	LATHRAS SEQ ID NO:212	MQGLHSPWT SEQ ID NO:213
32	KYDVH SEQ ID NO:214	WISHERDKTESAQRFKG SEQ ID NO:215	GSKHRLRDYVLYDDYGLINYQEWNDYLEFLDV SEQ ID NO:216	SSTQSLRHSNGANYLA SEQ ID NO:217	LGSQRAS SEQ ID NO:218	MQGLNRPWT SEQ ID NO:219
33	KYDVH SEQ ID NO:214	WMSHEGDKTESAQRFKG SEQ ID NO:220	GSKHRLRDYVLYDDYGLINYQEWNDYLEFLDV SEQ ID NO:216	TSTQSLRHSNGANYLA SEQ ID NO:221	LGSQRAS SEQ ID NO:218	MQGLNRPWT SEQ ID NO:219
34	KYDVH SEQ ID NO:214	WMSHEGDKTESAQRFKG SEQ ID NO:220	GSKHRLRDYVLYDDYGLINQQEWNDYLEFLDV SEQ ID NO:222	TSTQSLRHSNGANYLA SEQ ID NO:221	LGSQRAS SEQ ID NO:218	MQGLNRPWT SEQ ID NO:219
35	GYGMH SEQ ID NO:914	SISHDGIKKYHAEKVWG SEQ ID NO:915	DLREDECEEWWSDYYDFGKQLPCAKSRGGLVGIADN SEQ ID NO:916	SGNTSNIGNNFVS SEQ ID NO:917	ETDKRPS SEQ ID NO:918	ATWAASLSSARV SEQ ID NO:919
36	KYPMY SEQ ID NO:223	AISGDAWHVVYSNSVQG SEQ ID NO:224	MFQESGPPRLDRWSGRNYYYYSGMDV SEQ ID NO:225	KSSESLRQSNGKTSLY SEQ ID NO:226	EVSNRFS SEQ ID NO:227	MQSKDFPLT SEQ ID NO:228

Table D1 – CDRs (Kabat) for illustrative anti-HIV antigen binding arm

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
37	GLYAVN SEQ ID NO:229	QIWRWKSSASHHFRG SEQ ID NO:230	TSTYDKWSGLHHDG VMAFSS SEQ ID NO:231	RASQSITGNWVA SEQ ID NO:232	RGAALLG SEQ ID NO:233	QQYDTYPGT SEQ ID NO:234
38	NDNYYWA SEQ ID NO:920	TIYYSGTTYYNPSLRN SEQ ID NO:921	MPSHGFWSTSFSYW YFDL SEQ ID NO:922	RASQSVTKYLN SEQ ID NO:923	GTYTLLS SEQ ID NO:924	QQAHSTPWT SEQ ID NO:925

Table D2 – CDRs (Chothia) for illustrative anti-HIV antigen binding arm

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
39	GASISD SEQ ID NO:235	KSG SEQ ID NO:236	LHGRRIYGIVAFNEWFT YFYMD SEQ ID NO:237	EKSLGSRA SEQ ID NO:238	NNQ SEQ ID NO:239	WDSRVPTKW SEQ ID NO:240
40	GDSMNNY SEQ ID NO:241	DRE SEQ ID NO:242	RRGQRIYGVVSFGEFFY YYSMD SEQ ID NO:243	RQALGSRA SEQ ID NO:244	NNQ SEQ ID NO:239	WDSRSGFSW SEQ ID NO:245
41	GGSISNY SEQ ID NO:246	DRE SEQ ID NO:242	RRGQRIYGVVSFGEFFY YYYMD SEQ ID NO:247	RQALGSRA SEQ ID NO:244	NNQ SEQ ID NO:239	WDSRSGFSW SEQ ID NO:245
42	NGSVSGR SEQ ID NO:248	DTD SEQ ID NO:249	QQGKRIYGIVSFGEFFY YYYMD SEQ ID NO:250	ERSRGSRA SEQ ID NO:251	NNQ SEQ ID NO:239	WDSRSPISW SEQ ID NO:252
43	NGSVSGR SEQ ID NO:248	DTD SEQ ID NO:249	QQGKRIYGIVSFGELFY YYYMD SEQ ID NO:253	ERSRGSRA SEQ ID NO:251	NNQ SEQ ID NO:239	WDSRSPISW SEQ ID NO:252
44	GTLVRDN SEQ ID NO:254	DSG SEQ ID NO:255	KHGRRIYGVVAFKEWFT YFYMD SEQ ID NO:256	EESLGSRS SEQ ID NO:257	NNN SEQ ID NO:258	WDSRRPTNW SEQ ID NO:259

Table D2 – CDRs (Chothia) for illustrative anti-HIV antigen binding arm

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
45	GASINDA SEQ ID NO:260	HSG SEQ ID NO:261	LHGKRIYGIVALGELFT YFYMD SEQ ID NO:262	KESIGSRA SEQ ID NO:263	NNQ SEQ ID NO:239	YDARGGTNW SEQ ID NO:264
46	GESTGACTY SEQ ID NO:265	HCQSFWGSG SEQ ID NO:266	DGEVLVYNHWPKPAWVD SEQ ID NO:267	GTATNF SEQ ID NO:268	GVD SEQ ID NO:269	LVGNWDV SEQ ID NO:270
47	GDSTAACDY SEQ ID NO: 271	HCAGYYNTG SEQ ID NO:272	DGEVLVYHDWPKPAWVD SEQ ID NO:273	GTSNRF SEQ ID NO:274	GVN SEQ ID NO:275	LVGNWDV SEQ ID NO:270
48	GDSTAACDY SEQ ID NO:271	HCAGYYNSG SEQ ID NO:276	GGDVLVYHDWPKPAWVD SEQ ID NO:277	GNINNF SEQ ID NO:278	GVN SEQ ID NO:275	LAGNWDV SEQ ID NO:279
49	GDSTAACNS SEQ ID NO:280	HCASYWNRG SEQ ID NO:281	GGEVLRYTDWPKPAWVD SEQ ID NO:282	GTSNNF SEQ ID NO:283	DVN SEQ ID NO:284	LVGNWDV SEQ ID NO:270
50	GDSTAGCDY SEQ ID NO:285	HCAGYYNTG SEQ ID NO:272	DGEVLVYNDWPKPAWVD SEQ ID NO:286	GTSNNF SEQ ID NO:283	GVN SEQ ID NO:275	LVGNWDV SEQ ID NO:270
51	GESINTGHY SEQ ID NO:287	YTT SEQ ID NO:288	GGDILYYYEWQKPHWFS SEQ ID NO:289	GTSSDIGGWNF SEQ ID NO:290	EVN SEQ ID NO:291	LFGRWDV SEQ ID NO:292
52	GGSMRGTDWGEND F SEQ ID NO:293	WRGR SEQ ID NO:294	KYHDIFRVVPVAGWFD SEQ ID NO:295	SQNVKNN SEQ ID NO:296	DAS SEQ ID NO:297	YEEWPR SEQ ID NO:298
53	GGSIRGGEWGDSD Y SEQ ID NO:299	WRG SEQ ID NO:300	KYHDIVMVVPIAGWFD SEQ ID NO:301	SQSVKNN SEQ ID NO:302	DTS SEQ ID NO:303	YEEWPR SEQ ID NO:298
54	GDSIRGGEWGDKD Y	WRG SEQ ID NO:300	RHHDVFMLVPIAGWFD SEQ ID NO:305	SQNINKN SEQ ID NO:306	ETY	YEEWPR SEQ ID NO:298

Table D2 – CDRs (Chothia) for illustrative anti-HIV antigen binding arm

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
	SEQ ID NO:304				SEQ ID NO:307	
55	QDSRPSDH SEQ ID NO:308	YNG SEQ ID NO:309	AIRIYGVVALGEWFHYGMD SEQ ID NO:310	GAPLTSRF SEQ ID NO:311	RSS SEQ ID NO:312	SDTSDSYK SEQ ID NO:313
56	GYNIRDY SEQ ID NO:314	PKTG SEQ ID NO:315	RSDYWDFD SEQ ID NO:316	NGY SEQ ID NO:317	DGS SEQ ID NO:318	YE SEQ ID NO:327
57	GYKISDH SEQ ID NO:320	PKTG SEQ ID NO:315	RSDFWDFD SEQ ID NO:321	NGY SEQ ID NO:317	DGS SEQ ID NO:318	YE SEQ ID NO:327
58	GYEFINC SEQ ID NO:322	PRGG SEQ ID NO:323	KYCTARDYYNWDFE SEQ ID NO:324	SQYGS SEQ ID NO:325	SGS SEQ ID NO:326	YE SEQ ID NO:327
59	GYEFINC SEQ ID NO:322	PRHG SEQ ID NO:328	KYCTARDYYNWDFE SEQ ID NO:324	SQYGS SEQ ID NO:325	SGS SEQ ID NO:326	YE SEQ ID NO:327
60	GYEFIDC SEQ ID NO:329	PRGG SEQ ID NO:323	KNCDYNWDFE SEQ ID NO:330	SQYGS SEQ ID NO:325	SGS SEQ ID NO:326	YE SEQ ID NO:327
61	GYTFTAH SEQ ID NO:331	PQYG SEQ ID NO:332	RSYGDSSWALD SEQ ID NO:333	SQGVGSD SEQ ID NO:334	HTS SEQ ID NO:335	LQ SEQ ID NO:336
62	DDPYTDDDTFTKY SEQ ID NO:926	PHFA SEQ ID NO:927	PFGDRAPHYNYHMD SEQ ID NO:928	SQGLDSSH SEQ ID NO:929	GTS SEQ ID NO:930	YGGTPI SEQ ID NO:931
63	EDIFERTE SEQ ID NO:932	TVTG SEQ ID NO:933	KFYTGGQGWYFD SEQ ID NO:934	ASYGH SEQ ID NO:935	ATS SEQ ID NO:936	LE SEQ ID NO:937

Table D2 – CDRs (Chothia) for illustrative anti-HIV antigen binding arm

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
64	GFDFSRQ SEQ ID NO:337	YDGS SEQ ID NO:338	AGGPDYRNGYNYYDFYD GYYNYHYMD SEQ ID NO:339	GTSNDVGGYES SEQ ID NO:340	DVS SEQ ID NO:341	LTSTRRR SEQ ID NO:342
65	GFTFHKY SEQ ID NO:343	DDGM SEQ ID NO:344	AGGPIWHDDVKYYDFND GYYNYHYMD SEQ ID NO:345	GTSSDVGGFDS SEQ ID NO:346	DVS SEQ ID NO:341	LTDRSHR SEQ ID NO:347
66	GYSFIDY SEQ ID NO:348	PENG SEQ ID NO:349	AVGADSGSWFD SEQ ID NO:350	GSKLGDKY SEQ ID NO:351	END SEQ ID NO:352	WETTTTTF SEQ ID NO:353
67	GGAFSSY SEQ ID NO:354	PVFG SEQ ID NO:355	RRVVPMATDNWLD SEQ ID NO:356	SQTIHTY SEQ ID NO:357	GAS SEQ ID NO:358	SYSTPR SEQ ID NO:359
68	GNSFSNH SEQ ID NO:360	HEGD SEQ ID NO:361	SKHRLRDYFLYNEYGPN YEEWGDYLATLD SEQ ID NO:362	SHSLQHSTGANY SEQ ID NO:363	LAT SEQ ID NO:364	GLHSPW SEQ ID NO:365
69	GNTFSKY SEQ ID NO:366	HERD SEQ ID NO:367	SKHRLRDYVLYDDYGLI NYQEWNDYLEFLD SEQ ID NO:368	TQSLRHSNGANY SEQ ID NO:369	LGS SEQ ID NO:370	GLNRPW SEQ ID NO:371
70	GNTFSKY SEQ ID NO:366	HEGD SEQ ID NO:361	SKHRLRDYVLYDDYGLI NYQEWNDYLEFLD SEQ ID NO:368	TQSLRHSNGANY SEQ ID NO:369	LGS SEQ ID NO:370	GLNRPW SEQ ID NO:371
71	GNTFRKY SEQ ID NO:372	HEGD SEQ ID NO:361	SKHRLRDYVLYDDYGLI NQQEWNDYLEFLD SEQ ID NO:373	TQSLRHSNGANY SEQ ID NO:369	LGS SEQ ID NO:370	GLNRPW SEQ ID NO:371
72	QFRFDGY SEQ ID NO:938	HDGI SEQ ID NO:939	LREDECEEWWSDYYDFG KQLPCAKSRGGLVGIAD SEQ ID NO:940	GNTSNIGNNF SEQ ID NO:941	ETD SEQ ID NO:942	WAASLSSAR SEQ ID NO:943
73	DFPFSKY SEQ ID NO:374	GDAW SEQ ID NO:375	FQESGPPRLDRWSGRNY YYYSGMD	SESLRQSNGKTS SEQ ID NO:377	EVS	SKDFPL SEQ ID NO:379

Table D2 – CDRs (Chothia) for illustrative anti-HIV antigen binding arm						
Ab Name	**VH – CDR1**	**VH – CDR2**	**VH – CDR3**	**VL – CDR1**	**VL – CDR2**	**VL – CDR3**
			SEQ ID NO:376		SEQ ID NO:378	
74	GVNTFGLY SEQ ID NO:380	RW SEQ ID NO:381	STYDKWSGLHHDGVMAFS SEQ ID NO:382	SQSITGNW SEQ ID NO:383	RGA SEQ ID NO:384	YDTYPG SEQ ID NO:385
75	GDSVSNDNY SEQ ID NO:944	YSG SEQ ID NO:945	PSHGFWSTSFSYWYFD SEQ ID NO:946	SQSVTKY SEQ ID NO:947	GTY SEQ ID NO:948	AHSTPW SEQ ID NO:949

Table D3 – CDRs (IMGT) for illustrative anti-HIV antigen binding arm						
Ab Name	**VH – CDR1**	**VH – CDR2**	**VH – CDR3**	**VL – CDR1**	**VL – CDR2**	**VL – CDR3**
76	GASISDSY SEQ ID NO:386	VHKSGDT SEQ ID NO:387	ARTLHGRRIYGIVAFNEWFTYFYMDV SEQ ID NO:388	SLGSRA SEQ ID NO:389	NNQ SEQ ID NO:239	HIWDSRVPTKWV SEQ ID NO:81
77	GDSMNNYY SEQ ID NO:390	ISDRESA SEQ ID NO:391	ATARRGQRIYGVVSFGEFFYYYSMDV SEQ ID NO:392	ALGSRA SEQ ID NO:393	NNQ SEQ ID NO:239	HMWDSRSGFSWS SEQ ID NO:87
78	GDSMNNYY SEQ ID NO:390	ISDRESA SEQ ID NO:391	ARARRGQRIYGVVSFGEFFYYYSMDV SEQ ID NO:394	ALGSRA SEQ ID NO:393	NNQ SEQ ID NO:239	HMWDSRSGFSWS SEQ ID NO:87
79	GGSISNYY SEQ ID NO:395	ISDRETT SEQ ID NO:396	ATARRGQRIYGVVSFGEFFYYYYMDV SEQ ID NO:397	ALGSRA SEQ ID NO:393	NNQ SEQ ID NO:239	HMWDSRSGFSWS SEQ ID NO:87
80	NGSVSGRF SEQ ID NO:398	FSDTDRS SEQ ID NO:399	ARAQQGKRIYGIVSFGELFYYYYMDA SEQ ID NO:400	SRGSRA SEQ ID NO:401	NNQ SEQ ID NO:239	HYWDSRSPISWI SEQ ID NO:95
81	NGSVSGRF	FSDTDRS	ARAQQGKRIYGIVSFGEFFYYYYMDA	SRGSRA	NNQ	HYWDSRSPISWI

Table D3 – CDRs (IMGT) for illustrative anti-HIV antigen binding arm

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
	SEQ ID NO:398	SEQ ID NO:399	SEQ ID NO:402	SEQ ID NO:401	SEQ ID NO:239	SEQ ID NO:95
82	GASINDAY SEQ ID NO:403	VHHSGDT SEQ ID NO:404	ARALHGKRIYGIVALGELFTYFYMDV SEQ ID NO:405	SLGSRS SEQ ID NO:406	NNN SEQ ID NO:258	HIWDSRRPTNWV SEQ ID NO:102
83	GTLVRDNY SEQ ID NO:407	VHDSGDT SEQ ID NO:408	ATTKHGRRIYGVVAFKEWFTYFYMDV SEQ ID NO:409	SIGSRA SEQ ID NO:410	NNQ SEQ ID NO:239	HIYDARGGTNWV SEQ ID NO:107
84	GESTGACTYF SEQ ID NO:411	LSHCQSFWGSGWT SEQ ID NO:412	ARFDGEVLVYNHWPKPAWVDL SEQ ID NO:413	ATNF SEQ ID NO:414	GVD SEQ ID NO:269	GSLVGNWDVI SEQ ID NO:113
85	GDSTAACDYF SEQ ID NO:415	LSHCAGYYNTGWT SEQ ID NO:416	ARFDGEVLVYHDWPKPAWVDL SEQ ID NO:417	SNRF SEQ ID NO:418	GVN SEQ ID NO:275	SSLVGNWDVI SEQ ID NO:119
86	GDSTAACDYF SEQ ID NO:415	LSHCAGYYNSGWT SEQ ID NO:419	ARFGGDVLVYHDWPKPAWVDL SEQ ID NO:420	INNF SEQ ID NO:421	GVN SEQ ID NO:275	GSLAGNWDVV SEQ ID NO:123
87	GDSTAACNSF SEQ ID NO:422	LSHCASYWNRGWT SEQ ID NO:423	ARFGGEVLRYTDWPKPAWVDL SEQ ID NO:424	SNNF SEQ ID NO:425	DVN SEQ ID NO:284	GSLVGNWDVI SEQ ID NO:113
88	GDSTAGCDYF SEQ ID NO:426	LSHCAGYYNTGWT SEQ ID NO:416	ARFDGEVLVYNDWPKPAWVDL SEQ ID NO:427	SNNF SEQ ID NO:425	GVN SEQ ID NO:275	GSLVGNWDVI SEQ ID NO:113
89	GESINTGHYY SEQ ID NO:428	IHYTTAV SEQ ID NO:429	VRSGGDILYYYEWQKPHWFSP SEQ ID NO:430	SSDIGGWNF SEQ ID NO:431	EVN SEQ ID NO:291	SSLFGRWDVV SEQ ID NO:137
90	GGSMRGTDWG ENDFH	IHWRGRTT SEQ ID NO:433	ARHKYHDIFRVVPVAGWFDP SEQ ID NO:434	QNVKNN SEQ ID NO:435	DAS SEQ ID NO:297	QQYEEWPRT SEQ ID NO:143

Table D3 – CDRs (IMGT) for illustrative anti-HIV antigen binding arm						
Ab Name	**VH – CDR1**	**VH – CDR2**	**VH – CDR3**	**VL – CDR1**	**VL – CDR2**	**VL – CDR3**
	SEQ ID NO:432					
91	GGSIRGGEWG DSDYH SEQ ID NO:436	IHWRGTT SEQ ID NO:437	VKHKYHDIVMVVPIAGWFDP SEQ ID NO:438	QSVKNN SEQ ID NO:439	DTS SEQ ID NO:303	QQYEEWPRT SEQ ID NO:143
92	GDSIRGGEWG DKDYH SEQ ID NO:440	IHWRGTT SEQ ID NO:437	ARHRHHDVFMLVPIAGWFDV SEQ ID NO:441	QNINKN SEQ ID NO:442	ETY SEQ ID NO:307	QQYEEWPRT SEQ ID NO:143
93	QDSRPSDHS SEQ ID NO:443	IHYNGAT SEQ ID NO:444	NAIRIYGVVALGEWFHYGMDV SEQ ID NO:445	PLTSRF SEQ ID NO:446	RSS SEQ ID NO:312	QSSDTSDSYKM SEQ ID NO:159
94	GYNIRDYF SEQ ID NO:447	INPKTGQP SEQ ID NO:448	ARQRSDYWDFDV SEQ ID NO:449	NGY SEQ ID NO:450	DGS SEQ ID NO:318	QVYEF SEQ ID NO:165
95	GYKISDHF SEQ ID NO:451	INPKTGQP SEQ ID NO:448	ARQRSDFWDFDV SEQ ID NO:452	NGY SEQ ID NO:450	DGS SEQ ID NO:318	QVYEF SEQ ID NO:165
96	GYEFINCP SEQ ID NO:453	MKPRGGAV SEQ ID NO:454	TRGKYCTARDYYNWDFEH SEQ ID NO:455	QYGS SEQ ID NO:456	SGS SEQ ID NO:326	QQYEF SEQ ID NO:173
97	GYEFINCP SEQ ID NO:453	MKPRHGAV SEQ ID NO:457	TRGKYCTARDYYNWDFEH SEQ ID NO:455	QYGS SEQ ID NO:456	SGS SEQ ID NO:326	QQYEF SEQ ID NO:173
98	GYEFIDCT SEQ ID NO:458	LKPRGGAV SEQ ID NO:459	TRGKNCDYNWDFEH SEQ ID NO:460	QYGS SEQ ID NO:456	SGS SEQ ID NO:326	QQYEF SEQ ID NO:173
99	GYTFTAHI	IKPQYGAV	ARDRSYGDSSWALDA	QGVGSD	HTS	QVLQF

Table D3 – CDRs (IMGT) for illustrative anti-HIV antigen binding arm

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
	SEQ ID NO:461	SEQ ID NO:462	SEQ ID NO:463	SEQ ID NO:464	SEQ ID NO:335	SEQ ID NO:183
100	DDPYTDDDTF TKYW SEQ ID NO:950	ISPHFARP SEQ ID NO:951	ARDPFGDRAPHYNYHMDV SEQ ID NO:952	QGLDSSH SEQ ID NO:953	GTS SEQ ID NO:930	QRYGGTPIT SEQ ID NO:907
101	EDIFERTEL SEQ ID NO:954	VKTVTGAV SEQ ID NO:955	ARQKFYTGGQGWYFDL SEQ ID NO:956	SYGH SEQ ID NO:957	ATS SEQ ID NO:936	QQLEF SEQ ID NO:913
102	GFDFSRQG SEQ ID NO:465	IKYDGSEK SEQ ID NO:466	VREAGGPDYRNGYNYYDFYDGYYNYH YMDV SEQ ID NO:467	SNDVGGYES SEQ ID NO:468	DVS SEQ ID NO:341	KSLTSTRRRV SEQ ID NO:189
103	GFTFHKYG SEQ ID NO:469	ISDDGMRK SEQ ID NO:470	AREAGGPIWHDDVKYYDFNDGYYNYH YMDV SEQ ID NO:471	SSDVGGFDS SEQ ID NO:472	DVS SEQ ID NO:341	SSLTDRSHRI SEQ ID NO:195
104	GYSFIDYY SEQ ID NO:473	IDPENGEA SEQ ID NO:474	AAGAVGADSGSWFDP SEQ ID NO:475	KLGDKY SEQ ID NO:476	END SEQ ID NO:352	QAWETTTTTFV SEQ ID NO:201
105	GGAFSSYA SEQ ID NO:477	ITPVFGET SEQ ID NO:478	TRDRRVVPMATDNWLDP SEQ ID NO:479	QTIHTY SEQ ID NO:480	GAS SEQ ID NO:358	QQSYSTPRT SEQ ID NO:207
106	GNSFSNHD SEQ ID NO:481	MSHEGDKT SEQ ID NO:482	LTGSKHRLRDYFLYNEYGPNYEEWGD YLATLDV SEQ ID NO:483	HSLQHSTGAN Y SEQ ID NO:484	LAT SEQ ID NO:364	MQGLHSPWT SEQ ID NO:213
107	GNTFSKYD SEQ ID NO:485	ISHERDKT SEQ ID NO:486	TRGSKHRLRDYVLYDDYGLINYQEWN DYLEFLDV SEQ ID NO:487	QSLRHSNGAN Y SEQ ID NO:488	LGS SEQ ID NO:370	MQGLNRPWT SEQ ID NO:219

Table D3 – CDRs (IMGT) for illustrative anti-HIV antigen binding arm						
Ab Name	**VH – CDR1**	**VH – CDR2**	**VH – CDR3**	**VL – CDR1**	**VL – CDR2**	**VL – CDR3**
108	GNTFSKYD SEQ ID NO:485	MSHEGDKT SEQ ID NO:482	TRGSKHRLRDYVLYDDYGLINYQEWN DYLEFLDV SEQ ID NO:487	QSLRHSNGAN Y SEQ ID NO:488	LGS SEQ ID NO:370	MQGLNRPWT SEQ ID NO:219
109	GNTFRKYD SEQ ID NO:489	MSHEGDKT SEQ ID NO:482	TGGSKHRLRDYVLYDDYGLINQQEWN DYLEFLDV SEQ ID NO:490	QSLRHSNGAN Y SEQ ID NO:488	LGS SEQ ID NO:370	MQGLNRPWT SEQ ID NO:219
110	QFRFDGYG SEQ ID NO:958	ISHDGIKK SEQ ID NO:959	AKDLREDECEEWWSDYYDFGKQLPCA KSRGGLVGIADN SEQ ID NO:960	TSNIGNNF SEQ ID NO:961	ETD SEQ ID NO:942	ATWAASLSSARV SEQ ID NO:919
111	DFPFSKYP SEQ ID NO:491	ISGDAWHV SEQ ID NO:492	ARMFQESGPPRLDRWSGRNYYYYSGM DV SEQ ID NO:493	ESLRQSNGKT S SEQ ID NO:494	EVS SEQ ID NO:378	MQSKDFPLT SEQ ID NO:228
112	GVNTFGLYA SEQ ID NO:495	IWRWKS SEQ ID NO:496	TTTSTYDKWSGLHHDGVMAFSS SEQ ID NO:497	QSITGNW SEQ ID NO:498	RGA SEQ ID NO:384	QQYDTYPGT SEQ ID NO:234
113	GDSVSNDNYY SEQ ID NO:962	IYYSGTT SEQ ID NO:963	VRMPSHGFWSTSFSYWYFDL SEQ ID NO:964	QSVTKY SEQ ID NO:965	GTY SEQ ID NO:948	QQAHSTPWT SEQ ID NO:925

Table D4 – CDRs (Honegger) for illustrative anti-HIV antigen binding arm

Ab Name	VH – CDR1	VH – CDR2	VH – CDR3	VL – CDR1	VL – CDR2	VL – CDR3
114	VSGASISDSY SEQ ID NO:499	VHKSGDTNYSPSLKSR SEQ ID NO:500	TLHGRRIYGIVAF NEWFTYFYMD SEQ ID NO:501	EKSLGSRA SEQ ID NO:238	NNQDRPSGIPER SEQ ID NO:502	WDSRVPTKW SEQ ID NO:240
115	VSGASISDSY SEQ ID NO:499	VHKSGDTNYNPSLKSR SEQ ID NO:503	TLHGRRIYGIVAF NEWFTYFYMD SEQ ID NO:501	EKSLGSRA SEQ ID NO:238	NNQDRPSGIPER SEQ ID NO:502	WDSRVPTKW SEQ ID NO:240
116	VSGDSMNNYY SEQ ID NO:505	ISDRESATYNPSLNSR SEQ ID NO:506	ARRGQRIYGVVSF GEFFYYYSMD SEQ ID NO:507	RQALGSRA SEQ ID NO:244	NNQDRPSGIPER SEQ ID NO:502	WDSRSGFSW SEQ ID NO:245
117	VSGGSISNYY SEQ ID NO:508	ISDRETTTYNPSLNSR SEQ ID NO:509	ARRGQRIYGVVSF GEFFYYYYMD SEQ ID NO:510	RQALGSRA SEQ ID NO:244	NNQDRPSGIPER SEQ ID NO:502	WDSRSGFSW SEQ ID NO:245
118	VSNGSVSGRF SEQ ID NO:511	FSDTDRSEYNPSLRSR SEQ ID NO:512	AQQGKRIYGIVSF GELFYYYYMD SEQ ID NO:513	ERSRGSRA SEQ ID NO:251	NNQDRPAGVSER SEQ ID NO:514	WDSRSPISW SEQ ID NO:252
119	VSNGSVSGRF SEQ ID NO:511	FSDTDRSEYNPSLRSR SEQ ID NO:512	AQQGKRIYGIVSF GEFFYYYYMD SEQ ID NO:515	ERSRGSRA SEQ ID NO:251	NNQDRPAGVSER SEQ ID NO:514	WDSRSPISW SEQ ID NO:252
120	VSGTLVRDNY SEQ ID NO:516	VHDSGDTNYNPSLKSR SEQ ID NO:517	TKHGRRIYGVVAF KEWFTYFYMD SEQ ID NO:518	EESLGSRS SEQ ID NO:257	NNNDRPSGIPDR SEQ ID NO:519	WDSRRPTNW SEQ ID NO:259
121	VSGASINDAY SEQ ID NO:520	VHHSGDTNYNPSLKRR SEQ ID NO:521	ALHGKRIYGIVAL GELFTYFYMD SEQ ID NO:522	KESIGSRA SEQ ID NO:263	NNQDRPAGVPER SEQ ID NO:523	YDARGGTNW SEQ ID NO:264
122	VSGESTGACTYF SEQ ID NO:524	LSHCQSFWGSGWTFHNP SLKSR SEQ ID NO:525	FDGEVLVYNHWPK PAWVD SEQ ID NO:526	GTATNF SEQ ID NO:268	GVDKRPPGVPDR SEQ ID NO:527	LVGNWDV SEQ ID NO:270
123	VSGDSTAACDYF SEQ ID NO:528	LSHCAGYYNTGWTYHNP SLKSR	FDGEVLVYHDWPK PAWVD	GTSNRF	GVNKRPSGVPDR SEQ ID NO:531	LVGNWDV

Table D4 – CDRs (Honegger) for illustrative anti-HIV antigen binding arm						
Ab Name	**VH – CDR1**	**VH – CDR2**	**VH – CDR3**	**VL – CDR1**	**VL – CDR2**	**VL – CDR3**
		SEQ ID NO:529	SEQ ID NO:530	SEQ ID NO:274		SEQ ID NO:270
124	VSGDSTAACDYF SEQ ID NO:528	LSHCAGYYNSGWTYHNP SLKSR SEQ ID NO:532	FGGDVLVYHDWPK PAWVD SEQ ID NO:533	GNINNF SEQ ID NO:278	GVNKRPSGVPDR SEQ ID NO:531	LAGNWDV SEQ ID NO:279
125	VSGDSTAACNSF SEQ ID NO:534	LSHCASYWNRGWTYHNP SLKSR SEQ ID NO:535	FGGEVLRYTDWPK PAWVD SEQ ID NO:536	GTSNNF SEQ ID NO:283	DVNKRPSGVPDR SEQ ID NO:537	LVGNWDV SEQ ID NO:270
126	VSGDSTAGCDYF SEQ ID NO:1090	LSHCAGYYNTGWTYHNP SLKSR SEQ ID NO:529	FDGEVLVYNDWPK PAWVD SEQ ID NO:538	GTSNNF SEQ ID NO:283	GVNKRPSGVPDR SEQ ID NO:531	LVGNWDV SEQ ID NO:270
127	VSGESINTGHYY SEQ ID NO:539	IHYTTAVLHNPSLKSR SEQ ID NO:540	SGGDILYYYEWQK PHWFS SEQ ID NO:541	GTSSDIGGWNF SEQ ID NO:290	EVNKRPSGVPGR SEQ ID NO:542	LFGRWDV SEQ ID NO:292
128	VSGGSMRGTDWGE NDFH SEQ ID NO:543	IHWRGRTTHYKTSFRSR SEQ ID NO:544	HKYHDIFRVVPVA GWFD SEQ ID NO:545	ASQNVKNN SEQ ID NO:546	DASSRAGGIPDR SEQ ID NO:547	YEEWPR SEQ ID NO:298
129	ASGGSIRGGEWGD SDYH SEQ ID NO:548	IHWRGTTHYNAPFRGR SEQ ID NO:549	HKYHDIVMVVPIA GWFD SEQ ID NO:550	ASQSVKNN SEQ ID NO:1091	DTSSRASGIPAR SEQ ID NO:551	YEEWPR SEQ ID NO:298
130	VSGDSIRGGEWGD KDYH SEQ ID NO:552	IHWRGTTHYKESLRRR SEQ ID NO:553	HRHHDVFMLVPIA GWFD SEQ ID NO:554	ASQNINKN SEQ ID NO:555	ETYSKIAAFPAR SEQ ID NO:556	YEEWPR SEQ ID NO:298
131	VSQDSRPSDHS SEQ ID NO:557	IHYNGATTYNPSLRSR SEQ ID NO:558	NAIRIYGVVALGE WFHYGMD SEQ ID NO:559	GAPLTSRF SEQ ID NO:311	RSSQRSSGWSGR SEQ ID NO:560	SDTSDSYK SEQ ID NO:313
132	ASGYNIRDYF SEQ ID NO:561	INPKTGQPNNPRQFQGR SEQ ID NO:562	QRSDYWDFD SEQ ID NO:563	ANGY SEQ ID NO:564	DGSKLERGVPSRF SEQ ID NO:565	YE SEQ ID NO:327

Table D4 – CDRs (Honegger) for illustrative anti-HIV antigen binding arm						
Ab Name	**VH – CDR1**	**VH – CDR2**	**VH – CDR3**	**VL – CDR1**	**VL – CDR2**	**VL – CDR3**
133	ASGYKISDHF SEQ ID NO:566	INPKTGQPNNPRQFQGR SEQ ID NO:562	QRSDFWDFD SEQ ID NO:1092	ANGY SEQ ID NO:564	DGSKLERGVPAR SEQ ID NO:567	YE SEQ ID NO:327
134	ASGYEFINCP SEQ ID NO:568	MKPRGGAVSYARQLQGR SEQ ID NO:569	GKYCTARDYYNWD FE SEQ ID NO:570	TSQYGS SEQ ID NO:571	SGSTRAAGIPDR SEQ ID NO:572	YE SEQ ID NO:327
135	ASGYEFINCP SEQ ID NO:568	MKPRHGAVSYARQLQGR SEQ ID NO:573	GKYCTARDYYNWD FE SEQ ID NO:570	TSQYGS SEQ ID NO:571	SGSTRAAGIPDR SEQ ID NO:572	YE SEQ ID NO:327
136	ASGYEFIDCT SEQ ID NO:574	LKPRGGAVNYARPLQGR SEQ ID NO:575	GKNCDYNWDFE SEQ ID NO:576	TSQYGS SEQ ID NO:571	SGSTRAAGIPDR SEQ ID NO:572	YE SEQ ID NO:327
137	TSGYTFTAHI SEQ ID NO:577	IKPQYGAVNFGGGFRDR SEQ ID NO:578	DRSYGDSSWALD SEQ ID NO:579	TSQGVGSD SEQ ID NO:580	HTSSVEDGVPSR SEQ ID NO:581	LQ SEQ ID NO:336
138	ADDDPYTDDDTFT KYW SEQ ID NO:966	ISPHFARPIYSYKFRDR SEQ ID NO:967	DPFGDRAPHYNYH MD SEQ ID NO:968	ASQGLDSSH SEQ ID NO:969	GTSNRARGTPDR SEQ ID NO:970	YGGTPI SEQ ID NO:931
139	TSEDIFERTEL SEQ ID NO:971	VKTVTGAVNFGSPDFRQ SEQ ID NO:972	QKFYTGGQGWYFD SEQ ID NO:973	AASYGH SEQ ID NO:974	ATSKRASGIPDR SEQ ID NO:975	LE SEQ ID NO:937
140	ASGFDFSRQG SEQ ID NO:582	IKYDGSEKYHADSVWGR SEQ ID NO:583	EAGGPDYRNGYNY YDFYDGYYNYHYM D SEQ ID NO:584	GTSNDVGGYES SEQ ID NO:340	DVSKRPSGVSNR SEQ ID NO:585	LTSTRRR SEQ ID NO:342
141	ASGFTFHKYG SEQ ID NO:586	ISDDGMRKYHSDSMWGR SEQ ID NO:587	EAGGPIWHDDVKY YDFNDGYYNYHYM D SEQ ID NO:588	GTSSDVGGFDS SEQ ID NO:346	DVSHRPSGISNR SEQ ID NO:589	LTDRSHR SEQ ID NO:347

Table D4 – CDRs (Honegger) for illustrative anti-HIV antigen binding arm						
Ab Name	**VH – CDR1**	**VH – CDR2**	**VH – CDR3**	**VL – CDR1**	**VL – CDR2**	**VL – CDR3**
142	VSGYSFIDYY SEQ ID NO:590	IDPENGEARYAEKFQGR SEQ ID NO:591	GAVGADSGSWFD SEQ ID NO:592	GSKLGDKY SEQ ID NO:351	ENDRRPSGIPER SEQ ID NO:593	WETTTTTF SEQ ID NO:353
143	ASGGAFSSYA SEQ ID NO:594	ITPVFGETKYAPRFQGR SEQ ID NO:595	DRRVVPMATDNWLD SEQ ID NO:596	ASQTIHTY SEQ ID NO:597	GASTLQSGVPSR SEQ ID NO:598	SYSTPR SEQ ID NO:359
144	ASGNSFSNHD SEQ ID NO:599	MSHEGDKTGLAQKFQGR SEQ ID NO:600	GSKHRLRDYFLYNEYGPNYEEWGDYLATLD SEQ ID NO:601	CSHSLQHSTGANY SEQ ID NO:602	LATHRASGVPDR SEQ ID NO:603	GLHSPW SEQ ID NO:365
145	ASGNTFSKYD SEQ ID NO:604	ISHERDKTESAQRFKGR SEQ ID NO:605	GSKHRLRDYVLYDDYGLINYQEWNDYLEFLD SEQ ID NO:606	STQSLRHSNGANY SEQ ID NO:607	LGSQRASGVPDR SEQ ID NO:608	GLNRPW SEQ ID NO:371
146	ASGNTFSKYD SEQ ID NO:604	MSHEGDKTESAQRFKGR SEQ ID NO:609	GSKHRLRDYVLYDDYGLINYQEWNDYLEFLD SEQ ID NO:606	STQSLRHSNGANY SEQ ID NO:607	LGSQRASGVPDR SEQ ID NO:608	GLNRPW SEQ ID NO:371
147	ASGNTFRKYD SEQ ID NO:610	MSHEGDKTESAQRFKGR SEQ ID NO:609	GSKHRLRDYVLYDDYGLINQQEWNDYLEFLD SEQ ID NO:611	STQSLRHSNGANY SEQ ID NO:607	LGSQRASGVPDR SEQ ID NO:608	GLNRPW SEQ ID NO:371
148	ASQFRFDGYG SEQ ID NO:976	ISHDGIKKYHAEKVWGR SEQ ID NO:977	DLREDECEEWWSDYYDFGKQLPCAKSRGGLVGIAD SEQ ID NO:978	GNTSNIGNNF SEQ ID NO:941	ETDKRPSGIPDR SEQ ID NO:979	WAASLSSAR SEQ ID NO:943
149	VSDFPFSKYP SEQ ID NO:612	ISGDAWHVVYSNSVQGR SEQ ID NO:613	MFQESGPPRLDRWSGRNYYYYSGMD SEQ ID NO:614	SSESLRQSNGKTS	EVSNRFSGVSDR SEQ ID NO:616	SKDFPL SEQ ID NO:379

Table D4 – CDRs (Honegger) for illustrative anti-HIV antigen binding arm						
Ab Name	**VH – CDR1**	**VH – CDR2**	**VH – CDR3**	**VL – CDR1**	**VL – CDR2**	**VL – CDR3**
				SEQ ID NO:615		
150	AYGVNTFGLYA SEQ ID NO:617	IWRWKSSASHHFRGR SEQ ID NO:618	TSTYDKWSGLHHD GVMAFS SEQ ID NO:619	ASQSITGNW SEQ ID NO:620	RGAALLGGVPSR SEQ ID NO:621	YDTYPG SEQ ID NO:385
151	VSGDSVSNDNYY SEQ ID NO:980	IYYSGTTYYNPSLRNR SEQ ID NO:981	MPSHGFWSTSFSY WYFD SEQ ID NO:982	ASQSVTKY SEQ ID NO:983	GTYTLLSGVSPR SEQ ID NO:984	AHSTPW SEQ ID NO:949

Table E – VH/VL for illustrative anti-HIV binding arm				
Ab Name	**SEQ ID NO**	**VH**	**SEQ ID NO**	**VL**
320	622	QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWSWIRRS PGKGLEWIGYVHKSGDTNYSPSLKSRVNLSLDTSKNQVSL SLVAATAADSGKYYCARTLHGRRIYGIVAFNEWFTYFYMD VWGNGTQVTVSS	623	SDISVAPGETARISCGEKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPSGIPERFSGSPDSPFGT TATLTITSVEAGDEADYYCHIWDSRVPTKWVF GGGTTLTVL
321	624	QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWSWIRRS PGKGLEWIGYVHKSGDTNYNPSLKSRVHLSLDTSKNQVSL SLTGVTAADSGKYYCARTLHGRRIYGIVAFNEWFTYFYMD VWGTGTQVTVSS	625	SDISVAPGETARISCGEKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPSGIPERFSGSPDSRPGT TATLTITSVEAGDEADYYCHIWDSRVPTKWVF GGGTTLTVL
322	624	QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWSWIRRS PGKGLEWIGYVHKSGDTNYNPSLKSRVHLSLDTSKNQVSL SLTGVTAADSGKYYCARTLHGRRIYGIVAFNEWFTYFYMD VWGTGTQVTVSS	626	SDISVAPGETARISCGEKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPSGIPERFSGSPDFRPGT TATLTITSVEAGDEADYYCHIWDSRVPTKWVF GGGTTLTVL
323	627	QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWSWIRQP PGKGLEWIGYVHKSGDTNYSPSLKSRVNLSLDTSKNQVSL SLSAATAADSGVYYCARTLHGRRIYGIVAFNEWFTYFYMD VWGNGTQVTVSS	628	SDISVAPGETARISCGEKSLGSRAVQWYQQRA GQAPSLIIYNNQDRPSGIPERFSGSPDSGFGT TATLTITSVEAGDEADYYCHIWDSRVPTKWVF GGGTTLTVL

Table E – VH/VL for illustrative anti-HIV binding arm

Ab Name	SEQ ID NO	VH	SEQ ID NO	VL
324	629	QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWTWIRQS PGKGLEWIGYISDRESATYNPSLNSRVVISRDTSKNQLSL KLNSVTPADTAVYYCATARRGQRIYGVVSFGEFFYYYSMD VWGKGTTVTVSS	630	SYVRPLSVALGETARISCGRQALGSRAVQWYQ HRPGQAPILLIYNNQDRPSGIPERFSGTPDIN FGTRATLTISGVEAGDEADYYCHMWDSRSGFS WSFGGATRLTVL
325	631	QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWTWIRQS PGKGLEWIGYISDRESATYNPSLNSRVTISRDTSKNQFSL KLNSVTPADTAVYYCARARRGQRIYGVVSFGEFFYYYSMD VWGKGTTVTVSS	632	SPVRPLSVALGETARISCGRQALGSRAVQWYQ HRPGQAPILLIYNNQDRPSGIPERFSGTPDIN FGTRATLTISGVEAGDEADYYCHMWDSRSGFS WSFGGATRLTVL
326	633	QVQLQESGPGLVRPSETLSVTCIVSGGSISNYYWTWIRQS PGKGLEWIGYISDRETTTYNPSLNSRAVISRDTSKNQLSL QLRSVTTADTAIYFCATARRGQRIYGVVSFGEFFYYYYMD VWGKGTAVTVSS	634	SVTSYVSPLSVALGETARISCGRQALGSRAVQ WYQHKPGQAPILLIYNNQDRPSGIPERFSGTP DINFGTTATLTISGVEVGDEADYYCHMWDSRS GFSWSFGGATRLTVL
327	635	QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWSWIRQS PGRGLEWIGYFSDTDRSEYNPSLRSRLTLSVDRSKNQLSL KLKSVTAADSATYYCARAQQGKRIYGIVSFGELFYYYYMD AWGKGTPVTVSS	636	SLNPLSLAPGATAKIPCGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDRPAGVSERFSGNPDVAI GVTATLTISRVEVGDEGDYYCHYWDSRSPISW IFAGGTQLTVL
328	637	QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWSWIRQS PGRGLEWIGYFSDTDRSEYNPSLRSRLTLSVDRSKNQLSL RLKSVTAADSATYYCARAQQGKRIYGIVSFGEFFYYYYMD AWGKGTPVTVSS	638	SLNPLSLAPGATAKIPCGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDRPAGVSERFSGNPDVAI GVTATLTISRVEVGDEADYYCHYWDSRSPISW IFGGGTQLTVL
329	639	QVHLQESGPGLVKPSETLSLTCNVSGTLVRDNYWSWIRQP LGKQPEWIGYVHDSGDTNYNPSLKSRVHLSLDKSKNLVSL RLTGVTAADSAIYYCATTKHGRRIYGVVAFKEWFTYFYMD VWGKGTSVTVSS	640	TFVSVAPGQTARITCGEESLGSRSVIWYQQRP GQAPSLIIYNNNDRPSGIPDRFSGSPGSTFGT TATLTITSVEAGDEADYYCHIWDSRRPTNWVF GEGTTLIVL
330	641	QLHLQESGPGLVKPPETLSLTCSVSGASINDAYWSWIRQS PGKRPEWVGYVHHSGDTNYNPSLKRRVTFSLDTAKNEVSL KLVDLTAADSATYFCARALHGKRIYGIVALGELFTYFYMD VWGKGTAVTVSS	642	SSMSVSPGETAKISCGKESIGSRAVQWYQQKP GQPPSLIIYNNQDRPAGVPERFSASPDFRPGT TATLTITNVDAEDEADYYCHIYDARGGTNWVF DRGTTLTVL

Table E – VH/VL for illustrative anti-HIV binding arm

Ab Name	SEQ ID NO	VH	SEQ ID NO	VL
331	643	QSQLQESGPRLVEASETLSLTCNVSGESTGACTYFWGWVR QAPGKGLEWIGSLSHCQSFWGSGWTFHNPSLKSRLTISLD TPKNQVFLKLTSLTAADTATYYCARFDGEVLVYNHWPKPA WVDLWGRGIPVTVSS	644	QSALTQPPSASGSPGQSITISCNGTATNFVSW YQQFPDKAPKLIIFGVDKRPPGVPDRFSGSRS GTTASLTVSRLQTDDEAVYYCGSLVGNWDVIF GGGTTLTVL
332	645	QPQLQESGPGLVEASETLSLTCTVSGDSTAACDYFWGWVR QPPGKGLEWIGGLSHCAGYYNTGWTYHNPSLKSRLTISLD TPKNQVFLKLNSVTAADTAIYYCARFDGEVLVYHDWPKPA WVDLWGRGTLVTVSS	646	QSALTQPPSASGSPGQSISISCTGTSNRFVSW YQQHPGKAPKLVIYGVNKRPSGVPDRFSGSKS GNTASLTVSGLQTDDEAVYYCSSLVGNWDVIF GGGTKLTVL
333	647	QPQLQESGPGLVEASETLSLTCTVSGDSTAACDYFWGWVR QPPGKGLEWIGSLSHCAGYYNSGWTYHNPSLKSRLTISLD TPKNQVFLKLNSVTAADTAIYYCARFGGDVLVYHDWPKPA WVDLWGRGVLVTVSS	648	QSALTQPPSASGSPGQSITISCTGNINNFVSW YQQHPGKAPKLVIYGVNKRPSGVPDRFSGSKS GNAASLTVSGLQTDDEAVYYCGSLAGNWDVVF GGGTKLTVL
334	649	QPQLQESGPTLVEASETLSLTCAVSGDSTAACNSFWGWVR QPPGKGLEWVGSLSHCASYWNRGWTYHNPSLKSRLTLALD TPKNLVFLKLNSVTAADTATYYCARFGGEVLRYTDWPKPA WVDLWGRGTLVTVSS	650	QSALTQPPSASGSPGQSITISCTGTSNNFVSW YQQHAGKAPKLVIYDVNKRPSGVPDRFSGSKS GNTASLTVSGLQTDDEAVYYCGSLVGNWDVIF GGGTKLTVL
335	651	QPQLQESGPGLVEASETLSLTCTVSGDSTAGCDYFWGWVR QPPGKGLEWIGGLSHCAGYYNTGWTYHNPSLKSRLTISLD TPKNQVFLKLNSVTAADTAIYYCARFDGEVLVYNDWPKPA WVDLWGRGTLVTVSS	652	QSALTQPPSASGSPGQSITISCTGTSNNFVSW YQQHPAKAPKLVIYGVNKRPSGVPDRFSGSKS GNTASLTVSGLQTDDEAVYYCGSLVGNWDVIF GGGTKLTVL
336	653	QVQLQESGPGLVKPAETLSLTCSVSGESINTGHYYWGWVR QVPGKGLEWIGHIHYTTAVLHNPSLKSRLTIKIYTLRNQI TLRLSNVTAADTAVYHCVRSGGDILYYYEWQKPHWFSPWG PGIHVTVSS	654	QSALTQPPSASGSLGQSVTISCNGTSSDIGGW NFVSWYQQFPGRAPRLIIFEVNKRPSGVPGRF SGSKSGNSASLTVSGLQSDDEGQYFCSSLFGR WDVVFGGGTKLTVL
337	655	QLQLQESGPGLVKPSETLSLTCTVSGGSMRGTDWGENDFH YGWIRQSSAKGLEWIGSIHWRGRTTHYKTSFRSRATLSID TSNNRFSLTFSFVTAADTAVYYCARHKYHDIFRVVPVAGW FDPWGQGLLVTVSS	656	EIVMTQSPPTLSVSPGETATLSCRASQNVKNN LAWYQLKPGQAPRLLIFDASSRAGGIPDRFSG SGYGTDFTLTVNSVQSEDFGDYFCQQYEEWPR TFGQGTKVDIK

Table E – VH/VL for illustrative anti-HIV binding arm

Ab Name	SEQ ID NO	VH	SEQ ID NO	VL
338	657	EVHLEESGPGLVRPSETLSLTCTASGGSIRGGEWGDSDYH WGWVRHSPEKGLEWIGSIHWRGTTHYNAPFRGRGRLSIDL SRNQFSLRLTSVTAEDTAVYYCVKHKYHDIVMVVPIAGWF DPWGQGLQVTVSS	658	EIMMTQSPAILSVSPGDRATLSCRASQSVKNN LAWYQKRPGQAPRLLIFDTSSRASGIPARFSG GGSGTEFTLTVNSMQSEDFATYYCQQYEEWPR TFGQGTKVEIK
339	659	QLQMQESGPGLVKPSETLSLSCTVSGDSIRGGEWGDKDYH WGWVRHSAGKGLEWIGSIHWRGTTHYKESLRRRVSMSIDT SRNWFSLRLASVTAADTAVYFCARHRHHDVFMLVPIAGWF DVWGPGVQVTVSS	660	EIVMTQSPDTLSVSPGETVTLSCRASQNINKN LAWYQYKPGQSPRLVIFETYSKIAAFPARFVA SGSGTEFTLTINNMQSEDVAVYYCQQYEEWPR TFGQGTKVDIK
340	661	QVQLRESGPGLVKPSETLSLSCTVSQDSRPSDHSWTWVRQ SPGKALEWIGDIHYNGATTYNPSLRSRVRIELDQSIPRFS LKMTSMTAADTGMYYCARNAIRIYGVVALGEWFHYGMDVW GQGTAVTVSS	662	WASSELTQPPSVSVSPGQTARITCSGAPLTSR FTYWYRQKPGQAPVLIISRSSQRSSGWSGRFS ASWSGTTVTLTIRGVQADDEADYYCQSSDTSD SYKMFGGGTKLTVL
341	663	QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIHWWRQA PGQGLQWVGWINPKTGQPNNPRQFQGRVSLTRHASWDFDT FSFYMDLKALRSDDTAVYFCARQRSDYWDFDVWGSGTQVT VSS	664	DIQMTQSPSSLSASVGDTVTITCQANGYLNWY QQRRGKAPKLLIYDGSKLERGVPSRFSGRRWG QEYNLTINNLQPEDIATYFCQVYEFVVPGTRL DLK
342	665	QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIHWWRQA PGQGLQWVGWINPKTGQPNNPRQFQGRVSLTRHASFDFDT FSFYMDLKALRSDDTAVYFCARQRSDYWDFDVWGSGTQVT VSS	666	DIQMTQSPSSLSASVGDTATITCQANGYLNWY QQRRGKAPKLLIYDGSKLERGVPSRFSGRRWG QEYNLTINNLQPEDIATYFCQVYEFVVPGTRL DLK
343	667	QVHLSQSGAAVTKPGASVRVSCEASGYKISDHFIHWWRQA PGQGLQWVGWINPKTGQPNNPRQFQGRVSLTRQASWDFDT YSFYMDLKAVRSDDTAIYFCARQRSDFWDFDVWGSGTQVT VSS	668	DIQMTQSPSSLSARVGDTVTITCQANGYLNWY QQRRGKAPKLLIYDGSKLERGVPARFSGRRWG QEYNLTINNLQPEDVATYFCQVYEFIVPGTRL DLK
344	669	QVRLSQSGGQMKKPGDSMRISCRASGYEFINCPINWIRLA PGKRPEWMGWMKPRGGAVSYARQLQGRVTMTRDMYSETAF LELRSLTSDDTAVYFCTRGKYCTARDYYNWDFEHWGQGTP VTVSS	670	EIVLTQSPGTLSLSPGETAIISCRTSQYGSLA WYQQRPGQAPRLVIYSGSTRAAGIPDRFSGSR WGPDYNLTISNLESGDFGVYYCQQYEFFGQGT KVQVDIK

Table E – VH/VL for illustrative anti-HIV binding arm

Ab Name	SEQ ID NO	VH	SEQ ID NO	VL
345	671	QVRLSQSGGQMKKPGDSMRISCRASGYEFINCPINWIRLA PGKRPEWMGWMKPRHGAVSYARQLQGRVTMTRDMYSETAF LELRSLTSDDTAVYFCTRGKYCTARDYYNWDFEHWGQGTP VTVSS	672	SLTQSPGTLSLSPGETAIISCRTSQYGSLAWY QQRPGQAPRLVIYSGSTRAAGIPDRFSGSRWG PDYNLTISNLESGDFGVYYCQQYEFFGQGTKV QVDIK
346	673	QVQLVQSGGQMKKPGESMRISCRASGYEFIDCTLNWIRLA PGKRPEWMGWLKPRGGAVNYARPLQGRVTMTRDVYSDTAF LELRSLTVDDTAVYFCTRGKNCDYNWDFEHWGRGTPVIVS S	670	EIVLTQSPGTLSLSPGETAIISCRTSQYGSLA WYQQRPGQAPRLVIYSGSTRAAGIPDRFSGSR WGPDYNLTISNLESGDFGVYYCQQYEFFGQGT KVQVDIK
347	674	RAHLVQSGTAMKKPGASVRVSCQTSGYTFTAHILFWFRQA PGRGLEWVGWIKPQYGAVNFGGGFRDRVTLTRDVYREIAY MDIRGLKPDDTAVYYCARDRSYGDSSWALDAWGQGTTVVV SA	675	YIHVTQSPSSLSVSIGDRVTINCQTSQGVGSD LHWYQHKPGRAPKLLIHHTSSVEDGVPSRFSG SGFHTSFNLTISDLQADDIATYYCQVLQFFGR GSRLHIK
348	985	QGRLFQSGAEVKRPGASVRISCRADDDPYTDDDTFTKYWT HWIRQAPGQRPEWLGVISPHFARPIYSYKFRDRLTLTRDS SLTAVYLELKGLQPDDSGIYFCARDPFGDRAPHYNYHMDV WGGGTAVIVSS	986	EVVLTQSPAILSVSPGDRVILSCRASQGLDSS HLAWYRFKRGQIPTLVIFGTSNRARGTPDRFS GSGSGADFTLTISRVEPEDFATYYCQRYGGTP ITFGGGTTLDKKRTVA
349	987	QVQLVQSGSGVKKPGASVRVSCWTSEDIFERTELIHWVRQ APGQGLEWIGWVKTVTGAVNFGSPDFRQRVSLTRDRDLFT AHMDIRGLTQGDTATYFCARQKFYTGGQGWYFDLWGRGTL IVVSS	988	EIVLTQSPGTLSLSPGETASLSCTAASYGHMT WYQKKPGQPPKLLIFATSKRASGIPDRFSGSQ FGKQYTLTITRMEPEDFARYYCQQLEFFGQGT RLEIRRTVA
350	676	CQRLVESGGGVVQPGSSLRLSCAASGFDFSRQGMHWVRQA PGQGLEWVAFIKYDGSEKYHADSVWGRLSISRDNSKDTLY LQMNSLRVEDTATYFCVREAGGPDYRNGYNYYDFYDGYYN YHYMDVWGKGTTVTVSS	677	QSALTQPASVSGSPGQSITISCNGTSNDVGGY ESVSWYQQHPGKAPKVVIYDVSKRPSGVSNRF SGSKSGNTASLTISGLQAEDEGDYYCKSLTST RRRVFGTGTKLTVL
351	678	QEQLVESGGGVVQPGGSLRLSCLASGFTFHKYGMHWVRQA PGKGLEWVALISDDGMRKYHSDSMWGRVTISRDNSKNTLY LQFSSLKVEDTAMFFCAREAGGPIWHDDVKYYDFNDGYYN YHYMDVWGKGTTVTVSS	679	QSALTQPASVSGSPGQTITISCNGTSSDVGGF DSVSWYQQSPGKAPKVMVFDVSHRPSGISNRF SGSKSGNTASLTISGLHIEDEGDYFCSSLTDR SHRIFGGGTKVTVL

Table E – VH/VL for illustrative anti-HIV binding arm

Ab Name	SEQ ID NO	VH	SEQ ID NO	VL
352	680	DGHLVQSGVEVKKTGATVKISCKVSGYSFIDYYLHWVQRA PGKGLEWVGLIDPENGEARYAEKFQGRVTIIADTSIDTGY MEMRSLKSEDTAVYFCAAGAVGADSGSWFDPWGQGTLVTV SSASTKGPSVFPLAPSS	681	SYELTQPPSVSVSPGQTASITCSGSKLGDKYV SWYQLRPGQSPILVMYENDRRPSGIPERFSGS NSGDTATLTISGTQALDEADFYCQAWETTTTT FVFFGGGTQLTVL
353	682	QVLLVQSGTEVKKPGSSVKVSCQASGGAFSSYAFSWVRQA PGQGLEWMGMITPVFGETKYAPRFQGRLTLTAEESLSTTY MELRSLTSDDTAFYYCTRDRRVVPMATDNWLDPWGQGTLV TVSSASTKGPSVFPLAPSS	683	DIQLTQSPSSLSASVGDRVTVTCRASQTIHTY LNWYQQIPGKAPKLLIYGASTLQSGVPSRFSG SGSGTDFTLTINSLQPEDFATYYCQQSYSTPR TFGQGTRLDIK
354	684	QVQLVQSGAEVKKPGSSVKVSCKASGNSFSNHDVHWVRQA TGQGLEWMGWMSHEGDKTGLAQKFQGRVTITRDSGASTVY MELRGLTADDTAIYYCLTGSKHRLRDYFLYNEYGPNYEEW GDYLATLDVWGHGTAVTVSS	685	EVVITQSPLFLPVTPGEAASLSCKCSHSLQHS TGANYLAWYLQRPGQTPRLLIHLATHRASGVP DRFSGSGSGTDFTLKISRVESDDVGTYYCMQG LHSPWTFGQGTKVEIK
355	686	QVQLVQSGPEVKKPGSSVKVSCKASGNTFSKYDVHWVRQA TGQGLEWVGWISHERDKTESAQRFKGRVTFTRDTSATTAY MELRGLTSDDTAIYYCTRGSKHRLRDYVLYDDYGLINYQE WNDYLEFLDVWGHGTAVTVSS	687	DTVVTQSPLSLPVTPGEAASMSCSSTQSLRHS NGANYLAWYQHKPGQSPRLLIRLGSQRASGVP DRFSGSGSGTHFTLKISRVEAEDAAIYYCMQG LNRPWTFGKGTKLEIK
356	688	QVQLEQSGAEVKKPGSSVKVSCKASGNTFSKYDVHWVRQA TGQGLEWVGWMSHEGDKTESAQRFKGRVTFTRDTSASTAY MELRGLTSDDTAIYYCTRGSKHRLRDYVLYDDYGLINYQE WNDYLEFLDVWGHGTAVTVSS	689	DTVVTQSPLSLPVTPGEAASMSCTSTQSLRHS NGANYLAWYQHKPGQSPRLLIRLGSQRASGVP DRFSGSGSGTHFTLKISRVEPEDAAIYYCMQG LNRPWTFGKGTKLEIK
357	690	QVQLVQSGAEVKKPGSSVKVSCKASGNTFRKYDVHWVRQA TGQGLEWVGWMSHEGDKTESAQRFKGRVSFTRDNSASTAY IELRGLTSDDTAIYYCTGGSKHRLRDYVLYDDYGLINQQE WNDYLEFLDVWGHGTAVTVSS	691	DTVVTQSPLSLSVTPGEAASMSCTSTQSLRHS NGANYLAWYQHKPGQSPRLLIRLGSQRASGVP DRFSGSGSGTHFTLKISRVEADDAAIYYCMQG LNRPWTFGKGTKLEIK
358	989	QVQLVESGGGVVQPGTSLRLSCAASQFRFDGYGMHWVRQA PGKGLEWVASISHDGIKKYHAEKVWGRFTISRDNSKNTLY LQMNSLRPEDTALYYCAKDLREDECEEWWSDYYDFGKQLP CAKSRGGLVGIADNWGQGTMVTVSS	990	QSVLTQPPSVSAAPGQKVTISCSGNTSNIGNN FVSWYQQRPGRAPQLLIYETDKRPSGIPDRFS ASKSGTSGTLAITGLQTGDEADYYCATWAASL SSARVFGTGTKVIVL

Table E – VH/VL for illustrative anti-HIV binding arm

Ab Name	SEQ ID NO	VH	SEQ ID NO	VL
359	692	RVQLVESGGGVVQPGKSVRLSCVVSDFPFSKYPMYWVRQA PGKGLEWVAAISGDAWHVVYSNSVQGRFLVSRDNVKNTLY LEMNSLKIEDTAVYRCARMFQESGPPRLDRWSGRNYYYYS GMDVWGQGTTVTVSS	693	DIVMTQTPLSLSVTPGQPASISCKSSESLRQS NGKTSLYWYRQKPGQSPQLLVFEVSNRFSGVS DRFVGSGSGTDFTLRISRVEAEDVGFYYCMQS KDFPLTFGGGTKVDL
360	694	QIHLVQSGTEVKKPGSSVTVSCKAYGVNTFGLYAVNWVRQ APGQSLEYIGQIWRWKSSASHHFRGRVLISAVDLTGSSPP ISSLEIKNLTSDDTAVYFCTTTSTYDKWSGLHHDGVMAFS SWGQGTLISVSA	695	DIQMTQSPSTLSASIGDTVRISCRASQSITGN WVAWYQQRPGKAPRLLIYRGAALLGGVPSRFS GSAAGTDFTLTIGNLQAEDFGTFYCQQYDTYP GTFGQGTKVEVK
361	991	EVQLVESGPGLVQPWGTLSLTCRVSGDSVSNDNYYWAWIR QTPGRELQVIGTIYYSGTTYYNPSLRNRVTISLDKSVNVV SLRLGSVSAADTAQYYCVRMPSHGFWSTSFSYWYFDLWGR GHFVAVSW	992	DIQMTQSPSSLSASVGDKVTITCRASQSVTKY LNWYQFKTGQAPRILIYGTYTLLSGVSPRFSG AGSGSLYTLTITNIQPEDFATYYCQQAHSTPW TFGQGTHVAANRTVA

4. Fc Domains or Fc Regions

[0159] In certain embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain is from a human IgG. In one embodiment, the Fc region or Fc domain of the multi-specific antigen binding molecule is an IgG1, IgG2, IgG4, or chimeras thereof. In some embodiments, the antibody has a chimeric heavy chain constant region (*e.g.*, having the CH1, hinge, and CH2 regions of IgG4 and CH3 region of IgG1). In some embodiments, the Fc region is from a human IgG1 or IgG4. In some embodiments, the Fc region is from a human IgG1. In some embodiments, the Fc region is from a human IgG4.

[0160] In certain embodiments the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain, is directly linked to, or linked via an intervening amino acid sequence (*e.g.*, a G-S linker), to a human IgG1 (*e.g.*, a wild-type or mutant IgG1m3 sequence), IgG2, IgG3 or IgG4 with 1 to 10 (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) amino acid substitutions. In some embodiments, the Fc modifications can promote one or more of increased serum half-life or decreased antibody effector function of the molecule. In other embodiments, certain of these modifications, decrease antibody effector function and increase half-life of the antibody. In some embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprise two or more, three or more, four or more, five or more, six or more, six or fewer, five or fewer, four or fewer, three or fewer, two or fewer, or one modified Fc amino acid residue(s). As appropriate, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain can be the same or different. In some embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain independently can comprise two or more, three or more, four or more, five or more, six or more, six or fewer, five or fewer, four or fewer, three or fewer, two or fewer, or one modified Fc amino acid residue(s). Illustrative amino acid substitutions are described below.

IgG1 Isotype Fc

[0161] In one embodiment, the Fc region comprises or is derived from a human IgG1. In some embodiments, the antibody has a chimeric heavy chain constant region (*e.g.*, having the CH1, hinge, CH2 regions of IgG4 and CH3 region of IgG1).

[0162] IgG1 antibodies exist in various allotypes and isoallotypes. In various embodiments, one or both of the Fc region or Fc domain of the CD3-targeting heavy chain

and the HIV antigen-targeting heavy chain include an IgG1 heavy chain having an allotype of G1m1; nG1m2; G1m3; G1m17,1; G1m17,1,2; G1m3,1; or G1m17. Each of these allotypes or isoallotypes is characterized by the following amino acid residues at the indicated positions within the IgG1 heavy chain constant region (Fc) (EU numbering):

G1m1: D356, L358;
nG1m1: E356, M358;
G1m3: R214, E356, M358, A431;
G1m17,1: K214, D356, L358, A431;
G1m17,1,2: K214, D356, L358, G431;
G1m3,1: R214, D356, L358, A431; and
G1m17: K214, E356, M358, A431.

[0163] In certain embodiments, the Fc region or Fc domain of the multi-specific antigen binding molecule comprises a wild-type IgG1m3 sequence (*e.g.*, SEQ ID NO: 1089), or has at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a wild-type IgG1m3 sequence (*e.g.*, SEQ ID NO: 1089), as provided below.

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG
LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPS
VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN
QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 1089).

[0164] In certain embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain is from an IgG1 isotype. In some embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain contains a human IgG1 constant region. In some embodiments, the human IgG1 Fc region contains one or more modifications. For example, in some embodiments, the Fc region contains one or more amino acid substitutions (*e.g.*, relative to a wild-type Fc region of the same isotype). In some embodiments, the one or more amino acid substitutions are selected from N297A, N297Q (Bolt S *et al.* (1993) Eur J Immunol 23:403-411), D265A, L234A, L235A (McEarchem *et al.*, (2007) Blood, 109:1185-1192), C226S, C229S (McEarchem *et al.*, (2007) Blood. 109:1185-1192), P238S (Davis *et al.*, (2007) J Rheumatol, 34:2204-2210),

E233P, L234V (McEarchern *et al.*, (2007) Blood, 109:1185-1192), P238A, A327Q, A327G, P329A (Shields R L. *et al.*, (2001) J Biol Chem. 276(9):6591-604), K322A, L234F, L235E (Hezareh, *et al.*, (2001) J Virol 75, 12161-12168; Oganesyan *et al.*, (2008). Acta Crystallographica 64, 700-704), P331S (Oganesyan *et al.*, (2008) Acta Crystallographica 64, 700-704), T394D (Wilkinson *et al.* (2013) MAbs 5(3): 406-417), A330L, M252Y, S254T, and T256E, where the amino acid position is according to the EU numbering convention. In certain embodiments, the Fc region further includes an amino acid deletion at a position corresponding to glycine 236 according to the EU numbering convention.

[0165] In some embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain has an IgG1 isotype with a heavy chain constant region that contains a C220S amino acid substitution according to the EU numbering convention.

[0166] In some embodiments, the Fc region comprises a human IgG1 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: N297A, N297G, N297Q, N297G, D265A, L234A, L235A, C226S, C229S, P238S, E233P, L234V, P238A, A327Q, A327G, P329A, P329G, K322A, L234F, L235E, P331S, T394D, A330L, M252Y, S254T, T256E, M428L, N434S, T366W, T366S, L368A, Y407V and any combination thereof, wherein the numbering of the residues is according to EU numbering. In some embodiments, the Fc region comprises a human IgG1 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: L234A, L234V, L234F, L235A, L235E, A330L, P331S, and any combination thereof, wherein the numbering of the residues is according to EU numbering. In some embodiments, the Fc region comprises a human IgG1 isotype and comprises the amino acid substitutions in the Fc region of L234A, L235A, and P331S, wherein the numbering of the residues is according to EU numbering. In some embodiments, the Fc region comprises a human IgG1 isotype and comprises the amino acid substitutions in the Fc region of M252Y, S254T, T256E, wherein the numbering of the residues is according to EU numbering. In some embodiments, the Fc region comprises a human IgG1 isotype and comprises the amino acid substitutions in the Fc region of T366S, L368A, Y407V, wherein the numbering of the residues is according to EU numbering. In some embodiments, the Fc region comprises a human IgG1 isotype and comprises the amino acid substitutions in the Fc region of L234A, L235A, P331S, T366S, L368A and Y407V, wherein the numbering of the residues is according to EU numbering. In some

embodiments, the Fc region comprises a human IgG1 isotype and comprises the amino acid substitutions in the Fc region of L234A, L235A, P331S, M252Y, S254T and T256E, wherein the numbering of the residues is according to EU numbering.

IgG4 Isotype Fc

[0167] For uses where effector function is to be avoided altogether, *e.g.* when antigen binding alone is sufficient to generate the desired therapeutic benefit, and effector function only leads to (or increases the risk of) undesired side effects, IgG4 antibodies may be used, or antibodies or fragments lacking the Fc region or a substantial portion thereof can be devised, or the Fc may be mutated to eliminate glycosylation altogether (*e.g.* N297A). Alternatively, a hybrid construct of human IgG2 (CH1 domain and hinge region) and human IgG4 (CH2 and CH3 domains) has been generated that is devoid of effector function, lacking the ability to bind the FcγRs (like IgG2) and unable to activate complement (like IgG4). (*see*, Rother *et al.* (2007) Nat. Biotechnol. 25:1256; Mueller *et al.* (1997) Mol. Immunol. 34:441; and Labrijn *et al.* (2008) Curr. Op. Immunol. 20:479, discussing Fc modifications to reduce effector function generally).

[0168] In certain embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain has an IgG4 isotype. In some embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain contains a human IgG4 constant region. In some embodiments, the human IgG4 constant region includes an Fc region. In some embodiments, the Fc region contains one or more modifications. For example, in some embodiments, the Fc region contains one or more amino acid substitutions (*e.g.*, relative to a wild-type Fc region of the same isotype). In some embodiments, the one or more amino acid substitutions are selected from E233P, F234V, F234A, L235A, G237A, E318A, S228P, L235E, T394D, M252Y, S254T, T256E, N297A, N297G, N297Q, T366W, T366S, L368A, Y407V, M428L, N434S, and any combination thereof, where the amino acid position is according to the EU numbering convention. *See, e.g.*, Hutchins *et al.* (1995) *Proc Natl Acad Sci USA*, 92:11980-11984; Reddy *et al.*, (2000) *J Immunol*, 164:1925-1933; Angal *et al.*, (1993) *Mol Immunol.* 30(1):105-8; U.S. Pat. No. 8,614,299 B2; Vafa O. *et al.*, (2014) *Methods* 65:114-126; and Jacobsen *et. al., J. Biol. Chem.*(2017) 292(5):1865-1875. In some embodiments, the Fc region comprises a human IgG4 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group

consisting of: F234V, F234A, L235A, L235E, S228P, and any combination thereof, wherein the numbering of the residues is according to EU numbering.

[0169] In some embodiments, an IgG4 variant of the present disclosure may be combined with at least one of an S228P mutation according to the EU numbering convention (Angal *et al.*, (1993) Mol Immunol, 30:105-108) and with one or more mutations described in Peters *et al.*, (2012) J Biol Chem. 13; 287(29):24525-33) to enhance antibody stabilization.

IgG2 Isotype Fc

[0170] In certain embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain has an IgG2 isotype. In some embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain contains a human IgG2 constant region. In some embodiments, the human IgG2 constant region includes an Fc region. In some embodiments, the Fc region contains one or more modifications. For example, in some embodiments, the Fc region contains one or more amino acid substitutions (*e.g.*, relative to a wild-type Fc region of the same isotype). In some embodiments, the one or more amino acid substitutions are selected from P238S, V234A, G237A, H268A, H268Q, H268E, V309L, N297A, N297G, N297Q, V309L, A330S, P331 S, C232S, C233S, M252Y, S254T, and T256E, where the amino acid position is according to the EU numbering convention (Vafa, *et al.*, (2014) Methods 65:114-126).

Fc Mutations that Increase Serum Half-Life

[0171] In some embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprise amino acid modifications that promote an increased serum half-life of the multi-specific antigen binding molecule. Mutations that increase the half-life of an antibody have been described. In one embodiment, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprise a methionine to tyrosine substitution at position 252 (EU numbering), a serine to threonine substitution at position 254 (EU numbering), and a threonine to glutamic acid substitution at position 256 (EU numbering). See, *e.g.*, U.S. Patent No. 7,658,921. This type of mutant, designated as a "YTE mutant" exhibits a four-fold increased half-life relative to wild-type versions of the same antibody (Dall'Acqua, *et al.*, J Biol Chem, 281: 23514-24 (2006); Robbie, *et al.*,

Antimicrob Agents Chemotherap., 57(12):6147-6153 (2013)). In certain embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprise an IgG constant domain comprising one, two, three or more amino acid substitutions of amino acid residues at positions 251-257, 285-290, 308-314, 385-389, and 428-436 (EU numbering). Alternatively, M428L and N434S ("LS") substitutions can increase the pharmacokinetic (PK) half-life of the multi-specific antigen binding molecule. In other embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprise a M428L and N434S substitution (EU numbering). In other embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprise T250Q and M428L (EU numbering) mutations. In other embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprise H433K and N434F (EU numbering) mutations.

Fc Mutations that Reduce or Eliminate Effector Activity

[0172] In some embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain have amino acid substitutions that reduce or eliminate Fc effector function (including, *e.g.*, antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and complement-dependent cytotoxicity (CDC)).

[0173] In some embodiments, the Fc region is altered by replacing at least one amino acid residue with a different amino acid residue to reduce or eliminate effector function(s) of the antibody. For example, one or more amino acids selected from amino acid residues 234, 235, 236, 237, 297, 318, 320 and 322 (EU numbering) can be replaced with a different amino acid residue such that the multi-specific antigen binding molecule has decreased affinity for an effector ligand. The effector ligand to which affinity is altered can be, for example, an Fc receptor (*e.g.*, at residue positions 234, 235, 236, 237, 297 (EU numbering)) or the C1 component of complement (*e.g.*, at residue positions 297, 318, 320, 322 (EU numbering)). U.S. Pat. Nos. 5,624,821 and 5,648,260, both by Winter *et al.*

[0174] Fc modifications reducing or eliminating effector function include substitutions, insertions, and deletions, *e.g.*, at one or more positions including 234, 235, 236, 237, 267, 269, 325, and 328, *e.g.*, 234G, 235G, 236R, 237K, 267R, 269R, 325L, and

328R (EU numbering). Further, an Fc variant may comprise 236R/328R. Other modifications for reducing FcγR and complement interactions include substitutions at positions 297A, 234A, 235A, 318A, 228P, 236E, 268Q, 309L, 330S, 331S, 220S, 226S, 229S, 238S, 233P, and 234V (EU numbering). These and other modifications are reviewed in Strohl (2009) Current Opinion in Biotechnology 20:685-691. Effector functions (both ADCC and complement activation) can be reduced, while maintaining neonatal FcR binding (maintaining half-life), by mutating IgG residues at one or more of positions 233-236 and 327-331, such as E233P, L234V, L235A, optionally G236A, A327G, A330S and P331S in IgG1; E233P, F234V, L235A, optionally G236A, in IgG4; and A330S and P331S in IgG2 (EU numbering). *See* Armour *et al.* (1999) Eur. J. Immunol. 29:2613; WO 99/58572. Other mutations that reduce effector function include L234A and L235A ("LALA") in IgG1 (Alegre *et al.* (1994) Transplantation 57:1537); V234A and G237A in IgG2 (Cole *et al.* (1997) J. Immunol. 159:3613; see also U.S. Pat. No. 5,834,597); and S228P and L235E for IgG4 (Reddy *et al.* (2000) J. Immunol. 164:1925). Another combination of mutations for reducing effector function in a human IgG1 include L234F, L235E and P331S. Oganesyan *et al.* (2008) Acta Crystallogr. D. Biol. Crystallogr. 64:700. *See generally* Labrijn et gal. (2008) Curr. Op. Immunol. 20:479. Additional mutations found to decrease effector function in the context of an Fc (IgG1) fusion protein (abatacept) include C226S, C229S and P238S (EU numbering). Davis *et al.* (2007) J. Immunol. 34:2204.

[0175] ADCC activity may be reduced by modifying the Fc region. In certain embodiments, sites that affect binding to Fc receptors may be removed, *e.g.*, sites other than salvage receptor binding sites. In other embodiments, an Fc region may be modified to remove an ADCC site. Exemplary ADCC sites have been described with respect to ADCC sites in IgG1 (Sarmay, *et al*, (1992) Molec. Immunol. 29 (5): 633-9). In one embodiment, the G236R and L328R variant of human IgG1 effectively eliminates FcγR binding (Horton, *et al.* (2011) J. Immunol. 186:4223 and Chu, *et al.* (2008) Mol. Immunol. 45:3926). In other embodiments, the Fc having reduced binding to FcγRs comprises the amino acid substitutions L234A, L235E and G237A. Gross, *et al.* (2001) Immunity 15:289. Modifications in the IgG Fc region to decrease binding to FcγRI to decrease ADCC (*e.g.*, 234A; 235E; 236A; G237A) identified in WO 88/007089 can be used in the present fusion proteins. See also Duncan & Winter (1988) Nature 332:563; Chappel *et al.* (1991) Proc. Nat'l Acad. Sci. (USA) 88:9036; and Sondermann *et al.* (2000) Nature 406:267 (discussing

the effects of these mutations on FcγRIII binding). In some embodiments, the Fc having reduced binding to FcγRs comprises the amino acid substitutions L234A and L235A.

[0176] CDC activity may also be reduced by modifying the Fc region. Mutations at IgG1 positions D270, K322, P329 and P331, specifically alanine mutations D270A, K322A, P329A and P331A, significantly reduce the ability of the corresponding antibody to bind C1q and activate complement (Idusogie *et al.* (2000) J. Immunol. 164:4178; WO 99/51642. Modification of position 331 of IgG1 (*e.g.* P331S) has been shown to reduce complement binding (Tao *et al.* (1993) J. Exp. Med. 178:661; Xu Y, *et al.* J Biol Chem. 1994. 269:3469-74; and Canfield & Morrison (1991) J. Exp. Med. 173:1483). In another example, one or more amino acid residues within amino acid positions 231 to 239 are altered to thereby reduce the ability of the antibody to fix complement (WO 94/29351). Modifications in the IgG Fc region identified in WO 88/007089 that reduce or eliminate binding to complement component C1q, and therefore reduce or eliminate CDC (*e.g.*, E318A or V/K320A and K322A/Q) can be used in the present fusion proteins.

[0177] In some embodiments, the Fc with reduced complement fixation has the amino acid substitutions A330S and P331S. Gross *et al.* (2001) Immunity 15:289. In some embodiments, the Fc with reduced complement fixation has the amino acid substitution P331S.

[0178] In certain embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain have essentially no effector function, *e.g.*, one or both of the Fc domains have reduced or eliminated binding to FcγRs and reduced or eliminated complement fixation, *e.g.*, is effectorless. An exemplary IgG1 Fc that is effectorless comprises the following five mutations: L234A, L235E, G237A, A330S and P331S (EU numbering) (Gross *et al.* (2001) Immunity 15:289). These five substitutions may be combined with N297A to eliminate glycosylation as well.

[0179] In certain embodiments, the multi-specific antigen binding molecules comprise the L234F, L235E, D264A mutations, which are collectively referred to as "FEA." The FEA mutations decrease or abrogate effector function. In certain embodiments, the multi-specific antigen binding molecules comprise the L234F, L235E, D264A, and F405L mutations, which are collectively referred to as "FEAL." In certain embodiments, the multi-specific antigen binding molecules comprise the L234F, L235E, D264A, and a mutation selected from the group consisting of F405L, F405A, F405D, F405E, F405H, F405I, F405K, F405M, F405N, F405Q, F405S, F405T, F405V, F405W,

and F405Y. In certain embodiments, the multi-specific antigen binding molecules comprise the L234F, L235E, D264A, and K409R mutations, which are collectively referred to as "FEAR." In certain embodiments, FEAL and FEAR are comprised in a multi-specific antigen binding molecule described herein. In certain embodiments, the multi-specific antigen binding molecules additionally comprise the M428L and N434S mutations, which are collectively referred to as LS. In certain embodiments, the multi-specific antigen binding molecules comprise the L234F, L235E, D264A, F405L, M428L, and N434S mutations, which are collectively referred to as "FEALLS." In certain embodiments, the multi-specific antigen binding molecules comprise the L234F, L235E, D264A, M428L, and N434S mutations along with one further mutation selected from the group consisting of F405L, F405A, F405D, F405E, F405H, F405I, F405K, F405M, F405N, F405Q, F405S, F405T, F405V, F405W, and F405Y. In certain embodiments, the multi-specific antigen binding molecules comprise the L234F, L235E, D264A, K409R, M428L, and N434S mutations which are collectively referred to as "FEARLS." In certain embodiments, FEALLS and FEARLS are comprised in a multi-specific antigen binding molecule described herein.

[0180] Other Fc variants having one or both of reduced ADCC and reduced CDC are disclosed at Glaesner *et al.* (2010) Diabetes Metab. Res. Rev. 26:287 (F234A and L235A to decrease ADCC and ADCP in an IgG4); Hutchins *et al.* (1995) Proc. Nat'l Acad. Sci. (USA) 92:11980 (F234A, G237A and E318A in an IgG4); An *et al.* (2009) MAbs 1:572 and U.S. Pat. App. Pub. 2007/0148167 (H268Q, V309L, A330S and P331S in an IgG2); McEarchern *et al.* (2007) Blood 109:1185 (C226S, C229S, E233P, L234V, L235A in an IgG1); Vafa *et al.* (2014) Methods 65:114 (V234A, G237A, P238S, H268A, V309L, A330S, P331S in an IgG2) (EU numbering).

[0181] By reducing or abrogating effector function on the Fc domains of the CD3 X gp120 multi-specific/bispecific antigen binding molecule (i) T-cells bound by the molecule, including those not infected with HIV, are not killed by innate effector cells *e.g.*, NK cells, macrophages; and (ii) T-cells are not activated in the absence of target cells due to reduced binding to FcγRs on innate effector cells. Activation of T-cells in the absence of target cells could lead to an intolerable cytokine response. Binding of the bispecific molecule to FcγRs on innate effector cells could lead to clustering of the CD3 molecules on the T-cells, resulting in antigen-independent T-cell activation.

Fc Mutations that Facilitate Heterodimerization

[0182] In some embodiments, first and second Fc domains have mutations to facilitate heterodimerization. Mutations in Fc domain pairs that facilitate or promote heterodimerization are reviewed in Ha, *et al.*, Front. Immunol. (2016) 7:394. In some embodiments, the first Fc domain and the second Fc domain comprise the following amino acid substitutions (EU numbering), respectively (or vice versa): T366W and T366S/L368A/Y407V; T366W/S354C and T366S/L368A/Y407V/Y349C; S364H/F405A and Y349T/T394; T350V/L351Y/F405A/Y407V and T350V/T366L/K392L/T394W; K360D/D399M/Y407A and E345R/Q347R/T366V/K409V; K409D/K392D and D399K/E356K; K360E/K409W and Q347R/D399V/F405T; K360E/K409W/Y349C and Q347R/D399V/F405T/S354C; or K370E/K409W and E357N/D399V/F405T. In some embodiments, the first Fc domain and the second Fc domain comprise the following amino acid substitutions (EU numbering), respectively (or vice versa): T366W and T366S/L368A/Y407V.

[0183] In some embodiments, Fc region heterodimerization of the two different heavy chain-containing species can be facilitated by so-called 'knobs-into-holes' mutations (Atwell *et al.* 1997. JMB 270:26-35). The 'hole' mutations (T366S, L368A and Y407V ("SAV")) are incorporated into one Fc-containing chain, the T366W 'knob' ("W") mutation is incorporated into the other chain. In addition, a C220S mutation can be incorporated into an IgG1 hinge region of a scFv-containing arm to eliminate a free cysteine that otherwise forms a disulfide bond with a corresponding cysteine in the light chain in a wild-type IgG1. Co-transfection of such constructs leads to preferential formation of a heterodimeric Fc, with low levels of homodimer contaminants. Additionally, incorporating a S354C mutation can be incorporated into the Fc containing the 'knob' mutations and a Y349C mutation into the Fc containing the 'hole' mutations can optionally be used to generate a covalent bond between the two halves of the heterodimeric Fc if additional thermodynamic stability is desired (Merchant *et al.* 1998. Nat. Biotechnol. 16: 677-81).

[0184] To facilitate purification of the heterodimeric molecule away from contaminating homodimeric products, the H435R ("R") or H435R+Y436F ("RF") mutations to reduce or eliminate Protein A binding can be introduced into one but not both of the Fc-containing chains (Jendeberg, L. *et al.* 1997 J. Immunol. Methods 201:25–34). This reduces or eliminates Protein A binding of the homodimer contaminant containing these mutations, and greatly simplifies purification of the desired heterodimer away from remaining homodimer contaminant via additional chromatography steps (*e.g.* ion

exchange). In embodiments incorporating H435R (or H435R+Y436F) mutations in the first or second Fc region of a heavy chain, if the VH region in the same heavy chain is from a VH3 family variable region, this VH region can also include amino acid substitutions, as described herein, to reduce or eliminate Protein A binding of the entire heavy chain. In some embodiments, the H435R is introduced into one of the Fc-containing chains.

[0185] In certain embodiments, the one or more modifications are selected from the following Fc amino acid substitutions (EU numbering) or combinations thereof: L234F; L235E; G236A; S239D; F243L; D265E; D265A; S267E; H268F; R292P; N297Q; N297A; S298A; S324T; I332E; S239D; A330L; L234F; L235E; P331S; F243L; Y300L; V305I; P396L; S298A; E333A; K334A; E345R; L235V; F243L; R292P; Y300L; P396L; M428L; E430G; N434S; G236A, S267E, H268F, S324T, and I332E; G236A, S239D, and I332E; S239D, A330L, I332E; L234F, L235E, and P331S; F243L, R292P, Y300L, V305I, and P396L; G236A, H268F, S324T, and I332E; S239D, H268F, S324T, and I332E; S298A, E333A, and K334A; L235V, F243L, R292P, Y300L, and P396L; S239D, I332E; S239D, S298A, and I332E; G236A, S239D, I332E, M428L, and N434S; G236A, S239D, A330L, I332E, M428L, and N434S; S239D, I332E, G236A and A330L; M428L and N4343S; M428L, N434S; G236A, S239D, A330L, and I332E; and G236A and I332E. In certain embodiments, the one or more modifications is selected from the group consisting of: N297A, D265A, L234F, L235E, N297Q, and P331S. In certain embodiments, the one or more modifications is N297A or D265A. In certain embodiments the one or more modifications are L234F and L235E. In certain embodiments, the one or more modifications are L234F, L234E, and D265A. In certain embodiments, the one or more modifications are L234F, L234E, and N297Q. In certain embodiments, the one or more modifications are L234F, L235E, and P331S. In certain embodiments, the one or more modifications are D265A and N297Q. In certain embodiments, the one or more modifications are L234F, L235E, D265A, N297Q, and P331S. In some embodiments the modifications are L234A, L235A, P331S, T366S, L368A, Y407V and H435R. In some embodiments the modifications are L234A, L235A, P331S, T366W, M252Y, S254T and T256E.

[0186] Combined mutations that reduce Fc-receptor binding and find use in the present antigen binding molecules include, for example, N297A; N297Q; D265A; L234F/L235E; L234F/L235E/N297Q; L234F/L235E/P331S; D265A/N297Q; and L234F/L235E/ D265A/N297Q/P331S (all EU numbering). In certain embodiments the

multi-specific antigen binding molecules described herein comprise L234F and L235E mutations. In certain embodiments the multi-specific antigen binding molecules described herein comprise L234F, L235E, and D265A mutations. In certain embodiments the multi-specific antigen binding molecules described herein comprise L234F, L235E, and N297Q mutations. In certain embodiments the multi-specific antigen binding molecules described herein comprise an N297A or N297Q mutation. In certain embodiments the multi-specific antigen binding molecules described herein comprise an N297A or N297Q mutation as well as L234F, L235E, and D265A mutations. In certain embodiments, one, two, three, four, or more amino acid substitutions are introduced into a Fc region to alter the effector function of the antigen binding molecule. For example, these substitutions are located at positions selected from the group consisting of amino acid residues 234, 235, 236, 237, 265, 297, 318, 320, and 322, (according to EU numbering). These positions can be replaced with a different amino acid residue such that the antigen binding molecule has an altered (*e.g.*, reduced) affinity for an effector ligand (*e.g.*, an Fc receptor or the C1 component of complement), but retains the antigen binding ability of the parent antibody. In certain embodiments, the multi-specific antigen binding molecules described herein comprise one or more of E233P, L234V, L235A, and G236A mutations (EU numbering). In some embodiments, the multi-specific antigen binding molecules comprise one or more of A327G, A330S, and P331S mutations (EU numbering). In some embodiments, the multi-specific antigen binding molecules comprise K322A mutations (EU numbering). In some embodiments the multi-specific antigen binding molecules comprise E318A, K320A, and K322A (EU numbering) mutations. In certain embodiments, the multi-specific antigen binding molecules comprise a L235E (EU numbering) mutation.

[0187] In some embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain does not comprise a hinge region; or the hinge region is truncated or deleted, in whole or in part. The structural hinge region of human IgG1, IgG2 and IgG4 antibodies is a peptide linker of 19 to 23 amino acids containing two to four cysteine residues, is genetically encoded on the hinge exon together with the 5'-end of the CH2 exon, and allows for disulfide bridges between first and second Fc domains (Roux, *et al., J. Immunol.* (1998) 161:4083). The structural hinge region is comprised of amino acid residue positions 216-238 (EU numbering) or 226-251 (Kabat numbering) (identified on imgt.org). In some embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprises or is derived from a human IgG4 isotype and does not comprise the

amino acid sequence ESKYGPPCPPCP (SEQ ID NO: 504). In some embodiments, the Fc region or Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprises or is derived from a human IgG1 isotype and does not comprise the amino acid sequence EPKSCDKTHTCPPCP (SEQ ID NO: 993) or EPKSCDKTHTCPPCPAPELL (SEQ ID NO: 994). As appropriate, the hinge region of the Fc domain of one or both of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain can be the same or different.

[0188] In various embodiments, the Fc region or Fc domain of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprise a heterodimeric human IgG1, comprising amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 696 and 697; SEQ ID NOs.: 697 and 696; SEQ ID NOs.: 696 and 698; SEQ ID NOs.: 698 and 696; SEQ ID NOs.: 699 and 700; SEQ ID NOs.: 700 and 699; SEQ ID NOs.: 701 and 698; SEQ ID NOs.: 698 and 701; SEQ ID NOs.: 702 and 703; SEQ ID NOs.: 703 and 702; SEQ ID NOs.: 704 and 698; SEQ ID NOs.: 698 and 704; SEQ ID NOs.: 705 and 703; SEQ ID NOs.: 703 and 705; SEQ ID NOs.: 706 and 704; SEQ ID NOs.: 704 and 706; SEQ ID NOs.: 707 and 703; SEQ ID NOs.: 703 and 707; SEQ ID NOs.: 708 and 704; SEQ ID NOs.: 704 and 708; SEQ ID NOs.: 709 and 710; or SEQ ID NOs.: 710 and 709.

[0189] In some embodiments, the Fc region or Fc domain of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprise a heterodimeric human IgG1, comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705. In some embodiments the Fc region or Fc domain of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprise a heterodimeric human IgG1, comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705. In some embodiments, the Fc region or Fc domain of the CD3-targeting heavy chain and the HIV antigen-targeting heavy chain comprise a heterodimeric human IgG1, comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705. In some embodiments, the Fc region or Fc domain of the CD3-targeting

heavy chain and the HIV antigen-targeting heavy chain comprise a heterodimeric human IgG1, comprising amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705.

[0190] Illustrative sequences of complementarity first and second Fc domain pairs of the multi-specific antigen binding molecules, targeting HIV gp120, are provided in Table F. In some embodiments, the first Fc domain in a Fc domain pair is fused to the first antigen binding domain, targeting CD3. In such embodiments, the second Fc domain in a Fc domain pair is fused to the second antigen binding domain, targeting an HIV antigen. In some embodiments, the second Fc domain in a Fc domain pair is fused to the first antigen binding domain, targeting CD3. In such embodiments, the first Fc domain in a Fc domain pair is fused to the second antigen binding domain, targeting an HIV antigen.

TABLE F – Fc regions – Heterodimeric pairs

Fc aa subst	SEQ ID NO:		Fc aa subst	SEQ ID NO:	
L234A, L235A, P331S T366W	696	EPKSCDKTHTCPPCPAPEAAGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAS IEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLWCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK	L234A, L235A, P331S T366S, L368A, Y407V H435R, Y436F	697	EPKSSDKTHTCPPCPAPEAAGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSL SCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSC SVMHEALHNRFTQKSLSLSPGK
L234A, L235A, P331S T366W	696	EPKSCDKTHTCPPCPAPEAAGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAS IEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLWCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK	L234A, L235A, P331S T366S, L368A, Y407V H435R	698	EPKSSDKTHTCPPCPAPEAAGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSL SCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSC SVMHEALHNRYTQKSLSLSPGK
L234A, L235A, P331S T366S, L368A, Y407V	699	EPKSCDKTHTCPPCPAPEAAGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAS IEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLSCAVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLVSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK	L234A, L235A, P331S T366W	700	EPKSSDKTHTCPPCPAPEAAGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSL WCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPGK
L234A, L235A, P331S T366W	701	EPKSCDKTHTCPPCPAPEAAGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAS IEKTISKAKGQPREPQVYTLPPSREEMTK	L234A, L235A, P331S T366S, L368A,	698	EPKSSDKTHTCPPCPAPEAAGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSL

TABLE F – Fc regions – Heterodimeric pairs					
Fc aa subst	**SEQ ID NO:**		**Fc aa subst**	**SEQ ID NO:**	
M428L, N434S		NQVSLWCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVLHEALHSHYTQKSLSLSPGK	Y407V H435R		SCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSC SVMHEALHNRYTQKSLSLSPGK
L234A, L235A, P331S T366W M428L, N434S	702	SDKTHTCPPCPAPEAAGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVLHEALHSHYTQKSLSLSPGK	L234A, L235A, P331S T366S, L368A, Y407V H435R	703	EPKSCDKTHTCPPCPAPEAAGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSL SCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSC SVMHEALHNRYTQKSLSLSPGK
L234A, L235A, P331S T366W M252Y, S254T, T256E	704	EPKSCDKTHTCPPCPAPEAAGGPSVFLFP PKPKDTLYITREPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAS IEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLWCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK	L234A, L235A, P331S T366S, L368A, Y407V H435R	698	EPKSSDKTHTCPPCPAPEAAGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSL SCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSC SVMHEALHNRYTQKSLSLSPGK
L234A, L235A, P331S T366W M252Y, S254T, T256E	705	SDKTHTCPPCPAPEAAGGPSVFLFPPKPK DTLYITREPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK	L234A, L235A, P331S T366S, L368A, Y407V H435R	703	EPKSCDKTHTCPPCPAPEAAGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSL SCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSC SVMHEALHNRYTQKSLSLSPGK
L234A, L235A,	706	SDKTHTCPPCPAPEAAGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSHEDPEVKFNW	L234A, L235A,	704	EPKSCDKTHTCPPCPAPEAAGGPSVFLFPP KPKDTLYITREPEVTCVVVDVSHEDPEVKF

TABLE F – Fc regions – Heterodimeric pairs					
Fc aa subst	**SEQ ID NO:**		**Fc aa subst**	**SEQ ID NO:**	
P331S T366S, L368A, Y407V H435R		YVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLVSKLTVDKSRWQQGNV FSCSVMHEALHNRYTQKSLSLSPGK	P331S T366W M252Y, S254T, T256E		NWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSL WCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPGK
L234A, L235A, P331S + T366W	707	SDKTHTCPPCPAPEAAGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK	L234A, L235A, P331S + T366S, L368A, Y407V + H435R	703	EPKSCDKTHTCPPCPAPEAAGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSL SCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSC SVMHEALHNRYTQKSLSLSPGK
L234A, L235A, P331S T366S, L368A, Y407V M252Y, S254T, T256E	708	SDKTHTCPPCPAPEAAGGPSVFLFPPKPK DTLYITREPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLVSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK	L234A, L235A, P331S T366W M252Y, S254T, T256E	704	EPKSCDKTHTCPPCPAPEAAGGPSVFLFPP KPKDTLYITREPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSL WCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPGK
L234A, L235A, P331S T366S,	709	EPKSSDKTHTCPPCPAPEAAGGPSVFLFP PKPKDTLYITREPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAS IEKTISKAKGQPREPQVYTLPPSREEMTK	L234A, L235A, P331S T366W M252Y	710	EPKSCDKTHTCPPCPAPEAAGGPSVFLFPP KPKDTLYITREPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSL

TABLE F – Fc regions – Heterodimeric pairs					
Fc aa subst	**SEQ ID NO:**		**Fc aa subst**	**SEQ ID NO:**	
L368A, Y407V M252Y, S254T, T256E		NQVSLWCLVKGFYPSDIAVEWESNGQPEN NYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK	S254T, T256E		SCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPGK

[0191] In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a scFv and a second antigen binding domain that is a Fab, wherein the first antigen binding domain comprises a first heavy chain (HC), and the second antigen binding domain comprises a second HC and a light chain (LC), the first HC, the second HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 800, 801 and 802; SEQ ID NOs: 800, 803 and 802; SEQ ID NOs: 804, 803 and 802; SEQ ID NOs: 804, 805 and 802; SEQ ID NOs: 806, 801 and 802; SEQ ID NOs: 806, 803 and 802; SEQ ID NOs: 807, 803 and 802; SEQ ID NOs: 807, 805 and 802; SEQ ID NOs: 808, 809 and 802; SEQ ID NOs: 808, 810 and 802; SEQ ID NOs: 811, 801 and 802; SEQ ID NOs: 812, 809 and 802; SEQ ID NOs: 812, 810 and 802; SEQ ID NOs: 813, 805 and 802; SEQ ID NOs: 812, 814 and 802; SEQ ID NOs: 815, 801 and 802; SEQ ID NOs: 816, 805 and 802; SEQ ID NOs: 817, 801 and 802; SEQ ID NOs: 818, 805 and 802 ;SEQ ID NOs: 819, 810 and 802; SEQ ID NOs: 820, 810 and 802; SEQ ID NOs: 821, 822 and 823; SEQ ID NOs: 824, 825 and 823; SEQ ID NOs: 826, 825 and 823; SEQ ID NOs: 826, 827 and 823; SEQ ID NOs: 828, 829 and 823; SEQ ID NOs: 830, 822 and 823; SEQ ID NOs: 830, 825 and 823; SEQ ID NOs: 831, 825 and 823; SEQ ID NOs: 831, 827 and 823; SEQ ID NOs: 832, 833 and 823; SEQ ID NOs: 832, 829 and 823; SEQ ID NOs: 834, 827 and 823; SEQ ID NOs: 835, 829 and 823; SEQ ID NOs: 836, 829 and 823; SEQ ID NOs: 837, 833 and 823; SEQ ID NOs: 837, 838 and 823; SEQ ID NOs: 839, 840 and 823; SEQ ID NOs: 841, 829 and 823; SEQ ID NOs: 842, 829 and 823; SEQ ID NOs: 843, 829 and 823; SEQ ID NOs: 844, 829 and 823; SEQ ID NOs: 845, 829 and 823; SEQ ID NOs: 846, 829 and 823; SEQ ID NOs: 846, 833 and 823; SEQ ID NOs: 846, 838 and 823; SEQ ID NOs: 847, 827 and 823; SEQ ID NOs: 848, 829 and 823; SEQ ID NOs: 849, 829 and 823; SEQ ID NOs: 850, 829 and 823; SEQ ID NOs: 851, 829 and 823; SEQ ID NOs: 852, 829 and 823; SEQ ID NOs: 853, 829 and 823; SEQ ID NOs: 854, 829 and 823; SEQ ID NOs: 855, 829 and 823; SEQ ID NOs: 856, 829 and 823; SEQ ID NOs: 857, 829 and 823; SEQ ID NOs: 858, 829 and 823; SEQ ID NOs: 859, 829 and 823; SEQ ID NOs: 860, 829 and 823; SEQ ID NOs: 861, 862 and 863; SEQ ID NOs: 861, 864 and 863; SEQ ID NOs: 865, 864 and 863; SEQ ID NOs: 865, 866 and 863; SEQ ID NOs: 867, 868 and 863; SEQ ID NOs: 869, 862 and 863; SEQ ID NOs: 869, 864 and 863; SEQ ID NOs: 870, 864 and 863; SEQ ID NOs: 870, 866 and 863; SEQ ID NOs: 871, 872 and 863; SEQ

ID NOs: 871, 868 and 863; SEQ ID NOs: 873, 862 and 863; SEQ ID NOs: 874, 866 and 863; SEQ ID NOs: 875, 872 and 863; SEQ ID NOs: 875, 868 and 863; SEQ ID NOs: 875, 876 and 863; SEQ ID NOs: 877, 862 and 863; SEQ ID NOs: 878, 866 and 863; SEQ ID NOs: 879, 862 and 863; SEQ ID NOs: 880, 866 and 863; SEQ ID NOs: 881, 882 and 883; SEQ ID NOs: 881, 884 and 883; SEQ ID NOs: 885, 884 and 883; SEQ ID NOs: 885, 886 and 883; SEQ ID NOs: 887, 888 and 883; SEQ ID NOs: 889, 882 and 883; SEQ ID NOs: 889, 884 and 883; SEQ ID NOs: 890, 884 and 883; SEQ ID NOs: 890, 886 and 883; SEQ ID NOs: 891, 892 and 883; SEQ ID NOs: 891, 888 and 883; SEQ ID NOs: 893, 882 and 883; SEQ ID NOs: 894, 886 and 883; SEQ ID NOs: 895, 892 and 883; SEQ ID NOs: 895, 888 and 883; SEQ ID NOs: 895, 896 and 883; SEQ ID NOs: 897, 882 and 883; SEQ ID NOs: 898, 886 and 883; SEQ ID NOs: 899, 882 and 883; or SEQ ID NOs: 900, 886 and 883.

[0192] In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a scFv and a second antigen binding domain that is a Fab, wherein the first antigen binding domain comprises a first heavy chain (HC), and the second antigen binding domain comprises a second HC and a light chain (LC), the first HC, the second HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 800, 801 and 802; SEQ ID NOs: 800, 803 and 802; SEQ ID NOs: 804, 803 and 802; SEQ ID NOs: 804, 805 and 802; SEQ ID NOs: 806, 801 and 802; SEQ ID NOs: 806, 803 and 802; SEQ ID NOs: 807, 803 and 802; SEQ ID NOs: 807, 805 and 802; SEQ ID NOs: 808, 809 and 802; SEQ ID NOs: 808, 810 and 802; SEQ ID NOs: 821, 822 and 823; SEQ ID NOs: 824, 825 and 823; SEQ ID NOs: 826, 825 and 823; SEQ ID NOs: 826, 827 and 823; SEQ ID NOs: 828, 829 and 823; SEQ ID NOs: 830, 822 and 823; SEQ ID NOs: 830, 825 and 823; SEQ ID NOs: 831, 825 and 823; SEQ ID NOs: 831, 827 and 823; SEQ ID NOs: 832, 833 and 823; SEQ ID NOs: 832, 829 and 823; SEQ ID NOs: 861, 862 and 863; SEQ ID NOs: 861, 864 and 863; SEQ ID NOs: 865, 864 and 863; SEQ ID NOs: 865, 866 and 863; SEQ ID NOs: 867, 868 and 863; SEQ ID NOs: 869, 862 and 863; SEQ ID NOs: 869, 864 and 863; SEQ ID NOs: 870, 864 and 863; SEQ ID NOs: 870, 866 and 863; SEQ ID NOs: 871, 872 and 863; SEQ ID NOs: 871, 868 and 863; SEQ ID NOs: 881, 882 and 883; SEQ ID NOs: 881, 884 and 883; SEQ ID NOs: 885, 884 and 883; SEQ ID NOs: 885, 886 and 883; SEQ ID NOs: 887, 888 and 883; SEQ ID NOs: 889,

882 and 883; SEQ ID NOs: 889, 884 and 883; SEQ ID NOs: 890, 884 and 883; SEQ ID NOs: 890, 886 and 883; SEQ ID NOs: 891, 892 and 883; or SEQ ID NOs: 891, 888 and 883.

[0193] In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a scFv and a second antigen binding domain that is a Fab, wherein the first antigen binding domain comprises a first heavy chain (HC), and the second antigen binding domain comprises a second HC and a light chain (LC), the first HC, the second HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 800, 801 and 802; SEQ ID NOs: 800, 803 and 802; SEQ ID NOs: 804, 803 and 802; SEQ ID NOs: 804, 805 and 802; SEQ ID NOs: 821, 822 and 823; SEQ ID NOs: 824, 825 and 823; SEQ ID NOs: 826, 825 and 823; SEQ ID NOs: 826, 827 and 823; SEQ ID NOs: 828, 829 and 823; SEQ ID NOs: 861, 862 and 863; SEQ ID NOs: 861, 864 and 863; SEQ ID NOs: 865, 864 and 863; SEQ ID NOs: 865, 866 and 863; SEQ ID NOs: 867, 868 and 863; SEQ ID NOs: 881, 882 and 883; SEQ ID NOs: 881, 884 and 883; SEQ ID NOs: 885, 884 and 883; SEQ ID NOs: 885, 886 and 883; or SEQ ID NOs: 887, 888 and 883.

[0194] In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a scFv and a second antigen binding domain that is a Fab, wherein the first antigen binding domain comprises a first heavy chain (HC), and the second antigen binding domain comprises a second HC and a light chain (LC), the first HC, the second HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 800, 801 and 802; SEQ ID NOs: 800, 803 and 802; SEQ ID NOs: 804, 803 and 802; SEQ ID NOs: 804, 805 and 802; SEQ ID NOs: 821, 822 and 823; SEQ ID NOs: 824, 825 and 823; SEQ ID NOs: 826, 825 and 823; SEQ ID NOs: 826, 827 and 823; SEQ ID NOs: 828, 829 and 823; SEQ ID NOs: 861, 862 and 863; SEQ ID NOs: 861, 864 and 863; SEQ ID NOs: 865, 864 and 863; SEQ ID NOs: 865, 866 and 863; or SEQ ID NOs: 867, 868 and 863.

[0195] In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is a scFv or an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753; SEQ ID NOs: 754, 752 and 753; SEQ ID NOs: 755, 756 and 753; SEQ ID NOs: 755, 757 and 753; SEQ ID NOs: 758, 757 and 753; SEQ ID NOs: 759, 756 and 753; SEQ ID NOs: 754, 760 and 761; SEQ ID NOs: 762, 760 and 761; SEQ ID NOs: 751, 763 and 753; SEQ ID NOs: 764, 752 and 753; SEQ ID NOs: 765, 752 and 753; SEQ ID NOs: 766, 767 and 753; SEQ ID NOs: 766, 768 and 753; SEQ ID NOs: 769, 768 and 753; SEQ ID NOs: 770, 767 and 753; SEQ ID NOs: 765, 771 and 761; SEQ ID NOs: 772, 771 and 761; SEQ ID NOs: 774, 775 and 776; SEQ ID NOs: 777, 778 and 776; SEQ ID NOs: 779, 778 and 776; SEQ ID NOs: 779, 780 and 776; SEQ ID NOs: 777, 781 and 776; SEQ ID NOs: 782, 752 and 753; SEQ ID NOs: 783, 752 and 753; SEQ ID NOs: 784, 785 and 753; SEQ ID NOs: 784, 786 and 753; SEQ ID NOs: 787, 786 and 753; SEQ ID NOs: 788, 785 and 753; SEQ ID NOs: 783, 789 and 761; SEQ ID NOs: 790, 789 and 761; SEQ ID NOs: 792, 793 and 794; SEQ ID NOs: 795, 796 and 794; SEQ ID NOs: 797, 796 and 794; SEQ ID NOs: 797, 798 and 794; or SEQ ID NOs: 795, 799 and 794.

[0196] In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is a scFv or an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753; SEQ ID NOs: 754, 752 and 753; SEQ ID NOs: 755, 756 and 753; SEQ ID NOs: 755, 757 and 753; SEQ ID NOs: 758, 757 and 753; SEQ ID NOs: 759, 756 and 753; SEQ ID NOs: 764, 752 and 753; SEQ ID NOs: 765, 752 and 753; SEQ ID NOs: 766, 767 and 753; SEQ ID NOs: 766, 768 and 753; SEQ ID NOs:

769, 768 and 753; SEQ ID NOs: 770, 767 and 753; SEQ ID NOs: 777, 778 and 776; SEQ ID NOs: 779, 778 and 776; SEQ ID NOs: 779, 780 and 776; SEQ ID NOs: 777, 781 and 776; SEQ ID NOs: 782, 752 and 753; SEQ ID NOs: 783, 752 and 753; SEQ ID NOs: 784, 785 and 753; SEQ ID NOs: 784, 786 and 753; SEQ ID NOs: 787, 786 and 753; SEQ ID NOs: 788, 785 and 753; SEQ ID NOs: 795, 796 and 794; SEQ ID NOs: 797, 796 and 794; SEQ ID NOs: 797, 798 and 794; or SEQ ID NOs: 795, 799 and 794.

[0197] In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is a scFv or an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753; SEQ ID NOs: 754, 752 and 753; SEQ ID NOs: 755, 756 and 753; SEQ ID NOs: 755, 757 and 753; SEQ ID NOs: 758, 757 and 753; or SEQ ID NOs: 759, 756 and 753.

[0198] In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is a scFv or an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753; or SEQ ID NOs: 755, 756 and 753. In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is a scFv or an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least

99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753. In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is a scFv or an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 755, 756 and 753. In various embodiments, the multi-specific antigen binding molecule has a potency, as measured by EC50, of less than 0.15 μg/mL, *e.g.*, less than 0.14 μg/mL, 0.13 μg/mL, 0.12 μg/mL or 0.11 μg/mL, or less, against at least 30 different HIV isolates. In some embodiments, the multi-specific antigen binding molecule has a potency, as measured by EC50, of less than 0.11 μg/mL against at least 30 different HIV isolates.

[0199] In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753. In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753. In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753. In some embodiments, the multi-specific antigen binding molecule comprises

a first antigen binding domain that is a Fab and a second antigen binding domain that is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC comprising an amino acid sequence that is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to the amino acid sequence of SEQ ID NO: 751, and the first HC and the LC comprising amino acid sequences that are at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 752 and 753.

[0200] In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC comprising an amino acid sequence that is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to the amino acid sequence of SEQ ID NO: 751, the first HC comprises an amino acid sequence that is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to the amino acid sequence of SEQ ID NO: 752, and the LC comprises an amino acid sequence that is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to the amino acid sequence of SEQ ID NO: 753. In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC comprising an amino acid sequence that is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to the amino acid sequence of SEQ ID NO: 751, the first HC comprises an amino acid sequence of SEQ ID NO: 752, and the LC comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 753. In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC comprising an amino acid sequence that is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to the amino acid sequence of SEQ ID NO: 751, the first HC comprises an amino acid sequence of SEQ ID NO: 752, and the LC comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 753. In some

embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC comprising an amino acid sequence that is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to the amino acid sequence of SEQ ID NO: 751, the first HC comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 752, and the LC comprises an amino acid sequence of SEQ ID NO: 753. In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC comprising an amino acid sequence that is at least 95% (*e.g.*, at least 96%, at least 97%, at least 98%, or at least 99%) identical to the amino acid sequence of SEQ ID NO: 751, the first HC comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 752, and the LC comprises an amino acid sequence of SEQ ID NO: 753. In some embodiments, the multi-specific antigen binding molecule comprises a first antigen binding domain that is a Fab and a second antigen binding domain that is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753.

[0201] Illustrative sequences of bispecific molecules targeting CD3 and HIV gp120, described herein, are provided in Table G. Bispecific molecules described herein are summarized in Table 53.

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
180 **hCD4 D1.22 Fc AAS+W+YTE/huSP34.39.13 AAS+SAV+R**	SEQ ID NO: 751 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGSDKTHTCPPCPAPEAAGGPSVFLF PPKPKDTLYITREPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLWC LVKGFYPSDIAVEWESNGQPENNYKTTPPVL DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK	SEQ ID NO: 752 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKSRF TISRDDSKNSLYLEMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
181 **hCD4 D1.22 Fc AAS+W/huSP34.39.13 AAS+SAV+R**	SEQ ID NO: 754 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGSDKTHTCPPCPAPEAAGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKTI	SEQ ID NO: 752 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKSRF TISRDDSKNSLYLEMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	SKAKGQPREPQVYTLPPSREEMTKNQVSLWC LVKGFYPSDIAVEWESNGQPENNYKTTPPVL DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK	PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
182 **hCD4 D1.22 Fc AAS+SAV+ R/huSP34 .3.13 AAS+W+YT E**	SEQ ID NO: 755 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGSDKTHTCPPCPAPEAAGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLSC AVKGFYPSDIAVEWESNGQPENNYKTTPPVL DSDGSFFLVSKLTVDKSRWQQGNVFSCSVMH EALHNRYTQKSLSLSPGK	SEQ ID NO: 756 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRF TISRDDSKNSLYLQMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
183 **hCD4 D1.22 Fc AAS+SAV+ R/huSP34 .3.13 AAS+W**	SEQ ID NO: 755 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGSDKTHTCPPCPAPEAAGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLSC AVKGFYPSDIAVEWESNGQPENNYKTTPPVL DSDGSFFLVSKLTVDKSRWQQGNVFSCSVMH EALHNRYTQKSLSLSPGK	SEQ ID NO: 757 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRF TISRDDSKNSLYLQMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
184 **hCD4 D1.22 Fc AAS+SAV/ huSP34.3 .13 AAS+W**	SEQ ID NO: 758 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGSDKTHTCPPCPAPEAAGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLSC	SEQ ID NO: 757 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRF TISRDDSKNSLYLQMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	AVKGFYPSDIAVEWESNGQPENNYKTTPPVL DSDGSFFLVSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK	VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
185 **hCD4 D1.22 Fc AAS+SAV+ YTE/huSP 34.3.13 AAS+W+YT E**	SEQ ID NO: 759 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGSDKTHTCPPCPAPEAAGGPSVFLF PPKPKDTLYITREPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLSC AVKGFYPSDIAVEWESNGQPENNYKTTPPVL DSDGSFFLVSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK	SEQ ID NO: 756 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRF TISRDDSKNSLYLQMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
186 **CD4 D1.22 Fc AAS+W/huSP34.1.3 AAS+SAV+R**	SEQ ID NO: 754 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGSDKTHTCPPCPAPEAAGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLWC LVKGFYPSDIAVEWESNGQPENNYKTTPPVL DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK	SEQ ID NO: 760 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYAASVKGRF TISRDDSKNSLYLQMNSLKTEDTAMYYCVRHGNFG NSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 761 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTNKRAPWTPARF SGSLLGGKAALTLSGA QPEDEAEYYCALWYSN LWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
187 **hCD4 D1.22 Fc AAS+W+LS/huSP34.1.3 AAS+SAV+R**	SEQ ID NO: 762 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGSDKTHTCPPCPAPEAAGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLWC	SEQ ID NO: 760 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYAASVKGRF TISRDDSKNSLYLQMNSLKTEDTAMYYCVRHGNFG NSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE	SEQ ID NO: 761 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTNKRAPWTPARF SGSLLGGKAALTLSGA QPEDEAEYYCALWYSN LWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL

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	LVKGFYPSDIAVEWESNGQPENNYKTTPPVL DSDGSFFLYSKLTVDKSRWQQGNVFSCSVLH EALHSHYTQKSLSLSPGK	VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
190 **hCD4 D1.22(tandem) Fc AAS+W+YTE/huSP34.39.13 AAS+SAV+R**	SEQ ID NO: 764 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGGGSGKKVVYGKKGDTVELTCTASQ KKNIQFHWKNSNQIKILGNQGSFLTKGPSKL NDRVDSRRSLWDQGNFPLIIKNLKPEDSDTY ICEVEDQKEEVQLVVVGGSDKTHTCPPCPAP EAAGGPSVFLFPPKPKDTLYITREPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPASIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 752 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKSRF TISRDDSKNSLYLEMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS

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191 **hCD4 D1.22(tandem) Fc AAS+W/huSP34.39.13 AAS+SAV+R**	SEQ ID NO: 765 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGGGSGKKVVYGKKGDTVELTCTASQ KKNIQFHWKNSNQIKILGNQGSFLTKGPSKL NDRVDSRRSLWDQGNFPLIIKNLKPEDSDTY ICEVEDQKEEVQLVVVGGSDKTHTCPPCPAP EAAGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPASIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 752 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKSRF TISRDDSKNSLYLEMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
192 **hCD4 D1.22(tandem) Fc AAS+SAV+R/huSP34.3.13 AAS+W+YTE**	SEQ ID NO: 766 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGGGSGKKVVYGKKGDTVELTCTASQ KKNIQFHWKNSNQIKILGNQGSFLTKGPSKL NDRVDSRRSLWDQGNFPLIIKNLKPEDSDTY ICEVEDQKEEVQLVVVGGSDKTHTCPPCPAP EAAGGPSVFLFPPKPKDTLMISRTPEVTCVV	SEQ ID NO: 767 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRF TISRDDSKNSLYLQMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPE	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL

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	VDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPASIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQ QGNVFSCSVMHEALHNRYTQKSLSLSPGK	VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
193 **hCD4 D1.22(tandem) Fc AAS+SAV+R/huSP34.3.13 AAS+W**	SEQ ID NO: 766 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGGGSGKKVVYGKKGDTVELTCTASQ KKNIQFHWKNSNQIKILGNQGSFLTKGPSKL NDRVDSRRSLWDQGNFPLIIKNLKPEDSDTY ICEVEDQKEEVQLVVVGGSDKTHTCPPCPAP EAAGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPASIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQ QGNVFSCSVMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 768 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRF TISRDDSKNSLYLQMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS

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195 **hCD4 D1.22(tandem) Fc AAS+SAV+ YTE/huSP 34.3.13 AAS+W+YTE**	SEQ ID NO: 770 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGGGSGKKVVYGKKGDTVELTCTASQ KKNIQFHWKNSNQIKILGNQGSFLTKGPSKL NDRVDSRRSLWDQGNFPLIIKNLKPEDSDTY ICEVEDQKEEVQLVVVGGSDKTHTCPPCPAP EAAGGPSVFLFPPKPKDTLYITREPEVTCVV	SEQ ID NO: 767 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRF TISRDDSKNSLYLQMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPE	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL

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Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
197 **hCD4 D1.22(tandem) Fc AAS+W+LS /huSP34.1.3 AAS+SAV+R**	SEQ ID NO: 772 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGGGSGKKVVYGKKGDTVELTCTASQ KKNIQFHWKNSNQIKILGNQGSFLTKGPSKL NDRVDSRRSLWDQGNFPLIIKNLKPEDSDTY ICEVEDQKEEVQLVVVGGSDKTHTCPPCPAP EAAGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPASIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVLHEALHSHYTQKSLSLSPGK	SEQ ID NO: 771 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYAASVKGRF TISRDDSKNSLYLQMNSLKTEDTAMYYCVRHGNFG NSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 761 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTNKRAPWTPARF SGSLLGGKAALTLSGA QPEDEAEYYCALWYSN LWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
198 **hCD4–D1.22(tandem) Fc AAS+W+LS /huSP34.1.3scFv AAS+SAV+R**	SEQ ID NO: 772 KKVVYGKKGDTVELTCTASQKKNIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRVDSRRSLW DQGNFPLIIKNLKPEDSDTYICEVEDQKEEV QLVVVGGGGSGKKVVYGKKGDTVELTCTASQ KKNIQFHWKNSNQIKILGNQGSFLTKGPSKL NDRVDSRRSLWDQGNFPLIIKNLKPEDSDTY ICEVEDQKEEVQLVVVGGSDKTHTCPPCPAP EAAGGPSVFLFPPKPKDTLMISRTPEVTCVV	SEQ ID NO: 773 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYAASVKGRF TISRDDSKNSLYLQMNSLKTEDTAMYYCVRHGNFG NSYVSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGS GGGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVT TGHYANWVQQKPGQAPRGLIGGTNKRAPWTPARFS GSLLGGKAALTLSGAQPEDEAEYYCALWYSNLWVF GGGTKLTVLEPKSSDKTHTCPPCPAPEAAGGPSVF	

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	VDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN KALPASIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVLHEALHSHYTQKSLSLSPGK	LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ DWLNGKEYKCKVSNKALPASIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSR WQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	
199 **hCD4-D1.22(bivalent) AAS+W+LS/huSP34.1.3scFv AAS+SAV+R**	SEQ ID NO: 774 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 775 KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIK ILGNQGSFLTKGPSKLNDRVDSRRSLWDQGNFPLI IKNLKPEDSDTYICEVEDQKEEVQLVVVGGGGSGS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVV TVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRT PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPASIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEA LHSHYTQKSLSLSPGK	SEQ ID NO: 776 KKVVYGKKGDTVELTC TASQKKNIQFHWKNSN QIKILGNQGSFLTKGP SKLNDRVDSRRSLWDQ GNFPLIIKNLKPEDSD TYICEVEDQKEEVQLV VVGGGGSGKRTVAAPS VFIFPPSDEQLKSGTA SVVCLLNNFYPREAKV QWKVDNALQSGNSQES VTEQDSKDSTYSLSST LTLSKADYEKHKVYAC EVTHQGLSSPVTKSFN RGEC

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
200 **hCD4 D1.22(bivalent) AAS+SAV+R/huSP34.3.13scFv AAS+W+YTE**	SEQ ID NO: 777 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 778 KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIK ILGNQGSFLTKGPSKLNDRVDSRRSLWDQGNFPLI IKNLKPEDSDTYICEVEDQKEEVQLVVVGGGGSGS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVV TVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRT PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPASIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEA LHNRYTQKSLSLSPGK	SEQ ID NO: 776 KKVVYGKKGDTVELTC TASQKKNIQFHWKNSN QIKILGNQGSFLTKGP SKLNDRVDSRRSLWDQ GNFPLIIKNLKPEDSD TYICEVEDQKEEVQLV VVGGGGSGKRTVAAPS VFIFPPSDEQLKSGTA SVVCLLNNFYPREAKV QWKVDNALQSGNSQES VTEQDSKDSTYSLSST LTLSKADYEKHKVYAC EVTHQGLSSPVTKSFN RGEC
201 **hCD4 D1.22(bivalent) AAS+SAV+R/huSP34**	SEQ ID NO: 779 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 778 KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIK ILGNQGSFLTKGPSKLNDRVDSRRSLWDQGNFPLI IKNLKPEDSDTYICEVEDQKEEVQLVVVGGGGSGS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVV TVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD	SEQ ID NO: 776 KKVVYGKKGDTVELTC TASQKKNIQFHWKNSN QIKILGNQGSFLTKGP SKLNDRVDSRRSLWDQ GNFPLIIKNLKPEDSD TYICEVEDQKEEVQLV

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
.3.13scFv AAS+W	PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRT PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPASIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEA LHNRYTQKSLSLSPGK	VVGGGGSGKRTVAAPS VFIFPPSDEQLKSGTA SVVCLLNNFYPREAKV QWKVDNALQSGNSQES VTEQDSKDSTYSLSST LTLSKADYEKHKVYAC EVTHQGLSSPVTKSFN RGEC
202 hCD4 D1.22(bivalent) AAS+SAV/ huSP34.3.13scFv AAS+W	SEQ ID NO: 779 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 780 KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIK ILGNQGSFLTKGPSKLNDRVDSRRSLWDQGNFPLI IKNLKPEDSDTYICEVEDQKEEVQLVVVGGGGSGS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVV TVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRT PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPASIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPGK	SEQ ID NO: 776 KKVVYGKKGDTVELTC TASQKKNIQFHWKNSN QIKILGNQGSFLTKGP SKLNDRVDSRRSLWDQ GNFPLIIKNLKPEDSD TYICEVEDQKEEVQLV VVGGGGSGKRTVAAPS VFIFPPSDEQLKSGTA SVVCLLNNFYPREAKV QWKVDNALQSGNSQES VTEQDSKDSTYSLSST LTLSKADYEKHKVYAC

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK		EVTHQGLSSPVTKSFN RGEC
203 **hCD4 D1.22(bivalent) AAS+SAV+YTE/huSP34.3.13scFv AAS+W+YTE**	SEQ ID NO: 777 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 781 KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIK ILGNQGSFLTKGPSKLNDRVDSRRSLWDQGNFPLI IKNLKPEDSDTYICEVEDQKEEVQLVVVGGGGSGS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVV TVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD KTHTCPPCPAPEAAGGPSVFLFPPKPKDTLYITRE PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALPASIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPGK	SEQ ID NO: 776 KKVVYGKKGDTVELTC TASQKKNIQFHWKNSN QIKILGNQGSFLTKGP SKLNDRVDSRRSLWDQ GNFPLIIKNLKPEDSD TYICEVEDQKEEVQLV VVGGGGSGKRTVAAPS VFIFPPSDEQLKSGTA SVVCLLNNFYPREAKV QWKVDNALQSGNSQES VTEQDSKDSTYSLSST LTLSKADYEKHKVYAC EVTHQGLSSPVTKSFN RGEC

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
204 **hCD4 D1D2 Fc AAS+W+YTE/huSP34.39.13 AAS+SAV+R**	SEQ ID NO: 782 KKVVLGKKGDTVELTCTASQKKSIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRADSRRSLW DQGNFPLIIKNLKIEDSDTYICEVEDQKEEV QLLVFGLTANSDTHLLQGQSLTLTLESPPGS SPSVQCRSPRGKNIQGGKTLSVSQLELQDSG TWTCTVLQNQKKVEFKIDIVVLAGSDKTHTC PPCPAPEAAGGPSVFLFPPKPKDTLYITREP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPASIEKTISKAKGQPREPQVYT LPPSREEMTKNQVSLWCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK	SEQ ID NO: 752 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKSRF TISRDDSKNSLYLEMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
205 **hCD4 D1D2 Fc AAS+W/huSP34.39.13 AAS+SAV+R**	SEQ ID NO: 783 KKVVLGKKGDTVELTCTASQKKSIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRADSRRSLW DQGNFPLIIKNLKIEDSDTYICEVEDQKEEV QLLVFGLTANSDTHLLQGQSLTLTLESPPGS SPSVQCRSPRGKNIQGGKTLSVSQLELQDSG TWTCTVLQNQKKVEFKIDIVVLAGSDKTHTC PPCPAPEAAGGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK	SEQ ID NO: 752 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKSRF TISRDDSKNSLYLEMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	TKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPASIEKTISKAKGQPREPQVYT LPPSREEMTKNQVSLWCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK	VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
206 **hCD4 D1D2 Fc AAS+SAV+ R/huSP34 .3.13 AAS+W+YT E**	SEQ ID NO: 784 KKVVLGKKGDTVELTCTASQKKSIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRADSRRSLW DQGNFPLIIKNLKIEDSDTYICEVEDQKEEV QLLVFGLTANSDTHLLQGQSLTLTLESPPGS SPSVQCRSPRGKNIQGGKTLSVSQLELQDSG TWTCTVLQNQKKVEFKIDIVVLAGSDKTHTC PPCPAPEAAGGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPASIEKTISKAKGQPREPQVYT LPPSREEMTKNQVSLSCAVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSL SPGK	SEQ ID NO: 785 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRF TISRDDSKNSLYLQMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
207 **hCD4 D1D2 Fc AAS+SAV+ R/huSP34 .3.13 AAS+W**	SEQ ID NO: 784 KKVVLGKKGDTVELTCTASQKKSIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRADSRRSLW DQGNFPLIIKNLKIEDSDTYICEVEDQKEEV QLLVFGLTANSDTHLLQGQSLTLTLESPPGS SPSVQCRSPRGKNIQGGKTLSVSQLELQDSG TWTCTVLQNQKKVEFKIDIVVLAGSDKTHTC PPCPAPEAAGGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPASIEKTISKAKGQPREPQVYT LPPSREEMTKNQVSLSCAVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSL SPGK	SEQ ID NO: 786 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRF TISRDDSKNSLYLQMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
208 **hCD4 D1D2 Fc AAS+SAV/ huSP34.3 .13 AAS+W**	SEQ ID NO: 787 KKVVLGKKGDTVELTCTASQKKSIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRADSRRSLW DQGNFPLIIKNLKIEDSDTYICEVEDQKEEV QLLVFGLTANSDTHLLQGQSLTLTLESPPGS SPSVQCRSPRGKNIQGGKTLSVSQLELQDSG TWTCTVLQNQKKVEFKIDIVVLAGSDKTHTC PPCPAPEAAGGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK	SEQ ID NO: 786 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRF TISRDDSKNSLYLQMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	TKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPASIEKTISKAKGQPREPQVYT LPPSREEMTKNQVSLSCAVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK	VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
209 **hCD4 D1D2 Fc AAS+SAV+ YTE/huSP 34.3.13 AAS+W+YT E**	SEQ ID NO: 788 KKVVLGKKGDTVELTCTASQKKSIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRADSRRSLW DQGNFPLIIKNLKIEDSDTYICEVEDQKEEV QLLVFGLTANSDTHLLQGQSLTLTLESPPGS SPSVQCRSPRGKNIQGGKTLSVSQLELQDSG TWTCTVLQNQKKVEFKIDIVVLAGSDKTHTC PPCPAPEAAGGPSVFLFPPKPKDTLYITREP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPASIEKTISKAKGQPREPQVYT LPPSREEMTKNQVSLSCAVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK	SEQ ID NO: 785 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYADSVKGRF TISRDDSKNSLYLQMNSLRTEDTAVYYCVRHGNFG HSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 753 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTSNRAPGVPARF SGSLLGGKAALTISGA QPEDEAEYYCALWYSN RWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
210 **CD4 D1D2 Fc AAS W/huSP34 .1.3 AAS+SAV+ R**	SEQ ID NO: 783 KKVVLGKKGDTVELTCTASQKKSIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRADSRRSLW DQGNFPLIIKNLKIEDSDTYICEVEDQKEEV QLLVFGLTANSDTHLLQGQSLTLTLESPPGS SPSVQCRSPRGKNIQGGKTLSVSQLELQDSG TWTCTVLQNQKKVEFKIDIVVLAGSDKTHTC PPCPAPEAAGGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPASIEKTISKAKGQPREPQVYT LPPSREEMTKNQVSLWCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK	SEQ ID NO: 789 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYAASVKGRF TISRDDSKNSLYLQMNSLKTEDTAMYYCVRHGNFG NSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 761 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTNKRAPWTPARF SGSLLGGKAALTLSGA QPEDEAEYYCALWYSN LWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
211 **hCD4–D1D2 Fc AAS+W+LS /huSP34.1.3 AAS+SAV+ R**	SEQ ID NO: 790 KKVVLGKKGDTVELTCTASQKKSIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRADSRRSLW DQGNFPLIIKNLKIEDSDTYICEVEDQKEEV QLLVFGLTANSDTHLLQGQSLTLTLESPPGS SPSVQCRSPRGKNIQGGKTLSVSQLELQDSG TWTCTVLQNQKKVEFKIDIVVLAGSDKTHTC PPCPAPEAAGGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK	SEQ ID NO: 789 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYAASVKGRF TISRDDSKNSLYLQMNSLKTEDTAMYYCVRHGNFG NSYVSWFAYWGQGTLVTVSSASTKGPSVFPLAPSS KSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE	SEQ ID NO: 761 QAVVTQEPSLTVSPGG TVTLTCGSSTGAVTTG HYANWVQQKPGQAPRG LIGGTNKRAPWTPARF SGSLLGGKAALTLSGA QPEDEAEYYCALWYSN LWVFGGGTKLTVLGQP KAAPSVTLFPPSSEEL

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	TKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPASIEKTISKAKGQPREPQVYT LPPSREEMTKNQVSLWCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVLHEALHSHYTQKSLSL SPGK	VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPASIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTV DKSRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	QANKATLVCLISDFYP GAVTVAWKADSSPVKA GVETTTPSKQSNNKYA ASSYLSLTPEQWKSHR SYSCQVTHEGSTVEKT VAPTECS
212 **hCD4-D1D2 Fc AAS+W+LS /huSP34.1.3scFv AAS+SAV+R**	SEQ ID NO: 790 KKVVLGKKGDTVELTCTASQKKSIQFHWKNS NQIKILGNQGSFLTKGPSKLNDRADSRRSLW DQGNFPLIIKNLKIEDSDTYICEVEDQKEEV QLLVFGLTANSDTHLLQGQSLTLTLESPPGS SPSVQCRSPRGKNIQGGKTLSVSQLELQDSG TWTCTVLQNQKKVEFKIDIVVLAGSDKTHTC PPCPAPEAAGGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPASIEKTISKAKGQPREPQVYT LPPSREEMTKNQVSLWCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVLHEALHSHYTQKSLSL SPGK	SEQ ID NO: 791 EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMN WVRQAPGKGLEWVGRIRSKYNNYATYYAASVKGRF TISRDDSKNSLYLQMNSLKTEDTAMYYCVRHGNFG NSYVSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGS GGGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVT TGHYANWVQQKPGQAPRGLIGGTNKRAPWTPARFS GSLLGGKAALTLSGAQPEDEAEYYCALWYSNLWVF GGGTKLTVLEPKSSDKTHTCPPCPAPEAAGGPSVF LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ DWLNGKEYKCKVSNKALPASIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSR WQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
213 **hCD4-D1D2 (bivalent AAS+W+LS/huSP34.1.3scFv AAS+SAV+R**	SEQ ID NO: 792 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 793 KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIK ILGNQGSFLTKGPSKLNDRADSRRSLWDQGNFPLI IKNLKIEDSDTYICEVEDQKEEVQLLVFGLTANSD THLLQGQSLTLTLESPPGSSPSVQCRSPRGKNIQG GKTLSVSQLELQDSGTWTCTVLQNQKKVEFKIDIV VLAGGGSGSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD KKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKP KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPASIEKTISKAKGQPREPQVYTLP PSREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVLHEALHSHYTQKSLSLSPGK	SEQ ID NO: 794 KKVVLGKKGDTVELTC TASQKKSIQFHWKNSN QIKILGNQGSFLTKGP SKLNDRADSRRSLWDQ GNFPLIIKNLKIEDSD TYICEVEDQKEEVQLL VFGLTANSDTHLLQGQ SLTLTLESPPGSSPSV QCRSPRGKNIQGGKTL SVSQLELQDSGTWTCT VLQNQKKVEFKIDIVV LAGGGSGKRTVAAPSV FIFPPSDEQLKSGTAS VVCLLNNFYPREAKVQ WKVDNALQSGNSQESV TEQDSKDSTYSLSSTL TLSKADYEKHKVYACE VTHQGLSSPVTKSFNR GEC
214 **hCD4 D1D2 (biv**	SEQ ID NO: 795 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT	SEQ ID NO: 796 KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIK ILGNQGSFLTKGPSKLNDRADSRRSLWDQGNFPLI IKNLKIEDSDTYICEVEDQKEEVQLLVFGLTANSD	SEQ ID NO: 794 KKVVLGKKGDTVELTC TASQKKSIQFHWKNSN QIKILGNQGSFLTKGP

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
alent) AAS+SAV+ R/huSP34 .3.13scF v AAS+W+YT E	AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	THLLQGQSLTLTLESPPGSSPSVQCRSPRGKNIQG GKTLSVSQLELQDSGTWTCTVLQNQKKVEFKIDIV VLAGGGSGGSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD KKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKP KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPASIEKTISKAKGQPREPQVYTLP PSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNV FSCSVMHEALHNRYTQKSLSLSPGK	SKLNDRADSRRSLWDQ GNFPLIIKNLKIEDSD TYICEVEDQKEEVQLL VFGLTANSDTHLLQGQ SLTLTLESPPGSSPSV QCRSPRGKNIQGGKTL SVSQLELQDSGTWTCT VLQNQKKVEFKIDIVV LAGGGSGKRTVAAPSV FIFPPSDEQLKSGTAS VVCLLNNFYPREAKVQ WKVDNALQSGNSQESV TEQDSKDSTYSLSSTL TLSKADYEKHKVYACE VTHQGLSSPVTKSFNR GEC
215 hCD4 D1D2(biv alent) AAS+SAV+ R/huSP34 .3.13scF v AAS+W	SEQ ID NO: 797 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK	SEQ ID NO: 796 KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIK ILGNQGSFLTKGPSKLNDRADSRRSLWDQGNFPLI IKNLKIEDSDTYICEVEDQKEEVQLLVFGLTANSD THLLQGQSLTLTLESPPGSSPSVQCRSPRGKNIQG GKTLSVSQLELQDSGTWTCTVLQNQKKVEFKIDIV VLAGGGSGSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS	SEQ ID NO: 794 KKVVLGKKGDTVELTC TASQKKSIQFHWKNSN QIKILGNQGSFLTKGP SKLNDRADSRRSLWDQ GNFPLIIKNLKIEDSD TYICEVEDQKEEVQLL VFGLTANSDTHLLQGQ

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD KKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKP KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPASIEKTISKAKGQPREPQVYTLP PSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNV FSCSVMHEALHNRYTQKSLSLSPGK	SLTLTLESPPGSSPSV QCRSPRGKNIQGGKTL SVSQLELQDSGTWTCT VLQNQKKVEFKIDIVV LAGGGSGKRTVAAPSV FIFPPSDEQLKSGTAS VVCLLNNFYPREAKVQ WKVDNALQSGNSQESV TEQDSKDSTYSLSSTL TLSKADYEKHKVYACE VTHQGLSSPVTKSFNR GEC
216 **hCD4 D1D2 (bivalent) AAS+SAV/ huSP34.3 .13scFv AAS+W**	SEQ ID NO: 797 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV	SEQ ID NO: 798 KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIK ILGNQGSFLTKGPSKLNDRADSRRSLWDQGNFPLI IKNLKIEDSDTYICEVEDQKEEVQLLVFGLTANSD THLLQGQSLTLTLESPPGSSPSVQCRSPRGKNIQG GKTLSVSQLELQDSGTWTCTVLQNQKKVEFKIDIV VLAGGGSGGSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD KKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKP KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK	SEQ ID NO: 794 KKVVLGKKGDTVELTC TASQKKSIQFHWKNSN QIKILGNQGSFLTKGP SKLNDRADSRRSLWDQ GNFPLIIKNLKIEDSD TYICEVEDQKEEVQLL VFGLTANSDTHLLQGQ SLTLTLESPPGSSPSV QCRSPRGKNIQGGKTL SVSQLELQDSGTWTCT VLQNQKKVEFKIDIVV

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	EYKCKVSNKALPASIEKTISKAKGQPREPQVYTLP PSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK	LAGGGSGKRTVAAPSV FIFPPSDEQLKSGTAS VVCLLNNFYPREAKVQ WKVDNALQSGNSQESV TEQDSKDSTYSLSSTL TLSKADYEKHKVYACE VTHQGLSSPVTKSFNR GEC
217 **hCD4 D1D2 (bivalent) AAS+SAV+ YTE/huSP 34.3.13s cFv AAS+W+YT E**	SEQ ID NO: 795 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP	SEQ ID NO: 799 KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIK ILGNQGSFLTKGPSKLNDRADSRRSLWDQGNFPLI IKNLKIEDSDTYICEVEDQKEEVQLLVFGLTANSD THLLQGQSLTLTLESPPGSSPSVQCRSPRGKNIQG GKTLSVSQLELQDSGTWTCTVLQNQKKVEFKIDIV VLAGGGSGSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD KKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKP KDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPASIEKTISKAKGQPREPQVYTLP PSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 794 KKVVLGKKGDTVELTC TASQKKSIQFHWKNSN QIKILGNQGSFLTKGP SKLNDRADSRRSLWDQ GNFPLIIKNLKIEDSD TYICEVEDQKEEVQLL VFGLTANSDTHLLQGQ SLTLTLESPPGSSPSV QCRSPRGKNIQGGKTL SVSQLELQDSGTWTCT VLQNQKKVEFKIDIVV LAGGGSGKRTVAAPSV FIFPPSDEQLKSGTAS VVCLLNNFYPREAKVQ WKVDNALQSGNSQESV

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	**unpaired HC**	**Fab Arm – HC (VH-Fc)**	**Fab Arm – LC (VL-CL)**
	PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK		TEQDSKDSTYSLSSTL TLSKADYEKHKVYACE VTHQGLSSPVTKSFNR GEC
218 **h3BNC117 .52.64 AAS+SAV+ YTE/huSP 34.3.13s cFv AAS+W+YT E**	SEQ ID NO: 800 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 801 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC

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220 **h3BNC117 .52.64 AAS+SAV+ R/huSP34 .3.13scF v AAS+W**	SEQ ID NO: 804 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 803 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL

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	PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC
221 **h3BNC117 .52.64 AAS+SAV/ huSP34.3 .13scFv AAS+W**	SEQ ID NO: 804 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 805 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC

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	LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK		
222 **h3BNC117 .52.64 AAS+SAV+ YTE/huSP 34.39.13 scFv AAS+W+YT E**	SEQ ID NO: 806 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 801 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC

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223 **h3BNC117 .52.64 AAS+SAV+ R/huSP34 .39.13sc Fv AAS+W+YT E**	SEQ ID NO: 806 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 803 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC
224 **h3BNC117 .52.64 AAS+SAV+ R/huSP34 .39.13sc Fv AAS+W**	SEQ ID NO: 807 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 803 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL

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226 **h3BNC117 .52.64 AAS+W+YT E/huSP34 .39.13sc Fv AAS+SAV+ R**	SEQ ID NO: 808 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 809 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
227 **h3BNC117.52.64 AAS+W/huSP34.39.13scFv AAS+SAV+R**	SEQ ID NO: 808 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 810 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC
228 **h3BNC117.52.64 AAS+SAV+YTE/huSP34.1.3scFv**	SEQ ID NO: 811 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 801 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL

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229 **h3BNC117.52.64 AAS+W+YTE/huSP34.1.3 scFv AAS+SAV+R**	SEQ ID NO: 812 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 809 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC

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	LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK		
230 **h3BNC117 .52.64 AAS+W/hu SP34.1.3 scFv AAS+SAV+ R**	SEQ ID NO: 812 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 810 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC

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231 **h3BNC117 .52.64 AAS+SAV/ huSP34.1 .3scFv AAS+W**	SEQ ID NO: 813 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 805 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC
232 **h3BNC117 .52.64 AAS+W+LS /huSP34. 1.3 scFv**	SEQ ID NO: 812 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 814 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL

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233 **h3BNC117.52.64 AAS+SAV+YTE/huSP34.3.8scFv AAS+W+YTE**	SEQ ID NO: 815 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 801 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC

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	LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK		
234 **h3BNC117 .52.64 AAS+SAV/ huSP34.3 .8scFv AAS+W**	SEQ ID NO: 816 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 805 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC

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236 **h3BNC117 .52.64 AAS+SAV/ huSP34.3 4.3scFv AAS+W**	SEQ ID NO: 818 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 805 QVQLLQSGAAVTKPGASVRVSCEASGYNIRDYFIH WWRQAPGQGLQWVGWINPKTGQPNNPRQFQGRVSL TRHASFDFDTFSFYMDLKALRSDDTAVYFCARQRS DYWDFDVWGSGTQVTVSSASTKGPSVFPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH	SEQ ID NO: 802 DIQMTQSPSSLSASVG DTATITCQANGYLNWY QQRRGKAPKLLIYDGS KLERGVPSRFSGRRWG QEYNLTINNLQPEDIA TYFCQVYEFVVPGTRL

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	PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	KPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPASIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	DLKRTVAAPSVFIFPP SDEQLKSGTASVVCLL NNFYPREAKVQWKVDN ALQSGNSQESVTEQDS KDSTYSLSSTLTLSKA DYEKHKVYACEVTHQG LSSPVTKSFNRGEC
239 **hPGT121.66 AAS+SAV+YTE/huSP34.3.13s cFv AAS+W+YTE**	SEQ ID NO: 821 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 822 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	QVTHEGSTVEKTVAPT ECS
240 **hPGT121.66 AAS+SAV+R/huSP34.3.13scFv AAS+W+YTE**	SEQ ID NO: 824 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 825 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNRYTQKS LSLSPGK	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC QVTHEGSTVEKTVAPT ECS

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242 **hPGT121.66 AAS+SAV/huSP34.3.13scFv AAS+W**	SEQ ID NO: 826 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 827 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF

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243 **hPGT121.66 AAS+W/huSP34.3.13 scFv AAS+SAV+R**	SEQ ID NO: 828 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 829 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC

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Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	QVTHEGSTVEKTVAPT ECS
244 **hPGT121.66 AAS+SAV+YTE/huSP34.39.13 scFv AAS+W+YTE**	SEQ ID NO: 830 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 822 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC QVTHEGSTVEKTVAPT ECS

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246 **hPGT121.66 AAS+SAV+R/huSP34.39.13scFv AAS+W**	SEQ ID NO: 831 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 825 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF

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247 **hPGT121.66 AAS+SAV/ huSP34.39.13scFv AAS+W**	SEQ ID NO: 831 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 827 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC

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Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	QVTHEGSTVEKTVAPT ECS
248 hPGT121.66 AAS+W+YTE/huSP34.39.13scFv AAS+SAV+R	SEQ ID NO: 832 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 833 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC QVTHEGSTVEKTVAPT ECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
249 **hPGT121.66 AAS+W/huSP34.39.13scFv AAS+SAV+R**	SEQ ID NO: 832 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 829 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC QVTHEGSTVEKTVAPT ECS
250 **hPGT121.66 AAS+SAV/huSP34.1.3scFv AAS+W**	SEQ ID NO: 834 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 827 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
	PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC QVTHEGSTVEKTVAPT ECS
251 **hPGT121.66 AAS+W/huSP34.1.3 scFv AAS+SAV+RF**	SEQ ID NO: 835 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 829 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRFTQKSLSLSPGK	LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	QVTHEGSTVEKTVAPT ECS
252 **hPGT121.66 AAS+W/huSP34.1.3 scFv AAS+SAV+R**	SEQ ID NO: 836 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 829 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC QVTHEGSTVEKTVAPT ECS
253	SEQ ID NO: 837 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY	SEQ ID NO: 833 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
hPGT121.66 AAS+W+YTE/huSP34.1.3 scFv AAS+SAV+R	AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC QVTHEGSTVEKTVAPT ECS
254 **hPGT121.66 AAS+W+LS/huSP34.1.3 scFv AAS+SAV+R**	SEQ ID NO: 837 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV	SEQ ID NO: 838 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGK	VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC QVTHEGSTVEKTVAPT ECS
255 hPGT121.66 W/huSP34.1.3scFv SAV+R	SEQ ID NO: 839 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPAPIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 840 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC QVTHEGSTVEKTVAPT ECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
256 **hPGT121.66 AAS+W/huSP34.3.8 scFv AAS+SAV+R**	SEQ ID NO: 841 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 829 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC QVTHEGSTVEKTVAPT ECS
257 **hPGT121.66 AAS+W/huSP34.34.3scFv**	SEQ ID NO: 842 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 829 QMQLQESGPGLVKPSETLSLTCSVSGASISDSYWS WIRRSPGKGLEWIGYVHKSGDTNYNPSLKSRVHLS LDTSKNQVSLSLTGVTAADSGKYYCARTLHGRRIY GIVAFNEWFTYFYMDVWGTGTQVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 823 SDISVAPGETARISCG EKSLGSRAVQWYQHRA GQAPSLIIYNNQDRPS GIPERFSGSPDFRPGT TATLTITSVEAGDEAD YYCHIWDSRVPTKWVF

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
AAS+SAV+R	PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	GGGTTLTVLGQPKAAP SVTLFPPSSEELQANK ATLVCLISDFYPGAVT VAWKADSSPVKAGVET TTPSKQSNNKYAASSY LSLTPEQWKSHRSYSC QVTHEGSTVEKTVAPT ECS
278 **10-1074 AAS+SAV+ YTE/huSP 34.3.13s cFv AAS+W+YT E**	SEQ ID NO: 861 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 862 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	YSCQVTHEGSTVEKTV APTECS
279 **10-1074 AAS+SAV+ R/huSP34 .3.13scF v AAS+W+YT E**	SEQ ID NO: 861 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 864 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNRYTQKS LSLSPGK	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
280 **10–1074 AAS+SAV+ R/huSP34 .3.13scF v AAS+W**	SEQ ID NO: 865 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 864 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNRYTQKS LSLSPGK	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS
281 **10–1074 AAS+SAV/ huSP34.3 .13scFv AAS+W**	SEQ ID NO: 865 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 866 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS
282 **10-1074 AAS+W/huSP34.3.1 3scFv AAS+SAV+R**	SEQ ID NO: 867 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 868 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	YSCQVTHEGSTVEKTV APTECS
283 **10-1074 AAS+SAV+ YTE/huSP 34.39.13 scFv AAS+W+YT E**	SEQ ID NO: 869 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 862 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS
284	SEQ ID NO: 869 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY	SEQ ID NO: 864 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
10-1074 AAS+SAV+ R/huSP34 .39.13sc Fv AAS+W+YT E	ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNRYTQKS LSLSPGK	HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS
285 **10-1074 AAS+SAV+ R/huSP34 .39.13sc Fv AAS+W**	SEQ ID NO: 870 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV	SEQ ID NO: 864 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNRYTQKS LSLSPGK	AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS
286 **10-1074 AAS+SAV/ huSP34.3 9.13scFv AAS+W**	SEQ ID NO: 870 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 866 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
287 **10–1074 AAS+W+YTE/huSP34.39.13scFv AAS+SAV+R**	SEQ ID NO: 871 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 872 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS
288 **10–1074 AAS+W/huSP34.39.13scFv AAS+SAV+R**	SEQ ID NO: 871 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 868 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS
289 **10-1074 AAS+SAV+ YTE/huSP 34.1.3sc Fv AAS+W+YT E**	SEQ ID NO: 873 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 862 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	YSCQVTHEGSTVEKTV APTECS
290 **10-1074 AAS+SAV/ huSP34.1 .3scFv AAS+W**	SEQ ID NO: 874 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 866 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
291 **10–1074 AAS+W+YTE/huSP34.1.3 scFv AAS+SAV+R**	SEQ ID NO: 875 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 872 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS
292 **10–1074 AAS+W/huSP34.1.3 scFv AAS+SAV+R**	SEQ ID NO: 875 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 868 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS
293 **10-1074 AAS+W+LS /huSP34. 1.3 scFv AAS+SAV+ R**	SEQ ID NO: 875 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 876 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	LYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGK	YSCQVTHEGSTVEKTV APTECS
294 **10-1074 AAS+SAV+ YTE/huSP 34.3.8scFv AAS+W+YT E**	SEQ ID NO: 877 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 862 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
295 **10–1074 AAS+SAV/ huSP34.3 .8scFv AAS+W**	SEQ ID NO: 878 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 866 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS
296 **10–1074 AAS+SAV+ YTE/huSP 34.34.3s cFv**	SEQ ID NO: 879 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 862 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
AAS+W+YTE	PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS YSCQVTHEGSTVEKTV APTECS
297 **10-1074 AAS+SAV/ huSP34.34.3scFv AAS+W**	SEQ ID NO: 880 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 866 QVQLQESGPGLVKPSETLSVTCSVSGDSMNNYYWT WIRQSPGKGLEWIGYISDRESATYNPSLNSRVVIS RDTSKNQLSLKLNSVTPADTAVYYCATARRGQRIY GVVSFGEFFYYYSMDVWGKGTTVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 863 SYVRPLSVALGETARI SCGRQALGSRAVQWYQ HRPGQAPILLIYNNQD RPSGIPERFSGTPDIN FGTRATLTISGVEAGD EADYYCHMWDSRSGFS WSFGGATRLTVLGQPK AAPSVTLFPPSSEELQ ANKATLVCLISDFYPG AVTVAWKADSSPVKAG VETTTPSKQSNNKYAA SSYLSLTPEQWKSHRS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name/ features	**unpaired HC**	**Fab Arm – HC (VH-Fc)**	**Fab Arm – LC (VL-CL)**
	LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	YSCQVTHEGSTVEKTV APTECS
298 **PGT-134 AAS+SAV+ YTE/huSP 34.3.13s cFv AAS+W+YT E**	SEQ ID NO: 881 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 882 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS

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300 **PGT-134 AAS+SAV+ R/huSP34 .3.13scFv AAS+W**	SEQ ID NO: 885 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 884 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNRYTQKS LSLSPGK	IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS
301 **PGT-134 AAS+SAV/ huSP34.3 .13scFv AAS+W**	SEQ ID NO: 885 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 886 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SCQVTHEGSTVEKTVA PTECS
302 **PGT-134 AAS+W/hu SP34.3.1 3scFv AAS+SAV+ R**	SEQ ID NO: 887 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 888 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS

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Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
303 **PGT-134 AAS+SAV+ YTE/huSP 34.39.13 scFv AAS+W+YT E**	SEQ ID NO: 889 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 882 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS
304 **PGT-134 AAS+SAV+ R/huSP34 .39.13sc Fv**	SEQ ID NO: 889 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 884 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW

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305 **PGT-134 AAS+SAV+ R/huSP34 .39.13sc Fv AAS+W**	SEQ ID NO: 890 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 884 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY

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	LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	LVSKLTVDKSRWQQGNVFSCSVMHEALHNRYTQKS LSLSPGK	SCQVTHEGSTVEKTVA PTECS
306 **PGT-134 AAS+SAV/ huSP34.3 9.13scFv AAS+W**	SEQ ID NO: 890 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 886 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
307 **PGT-134 AAS+W+YTE/huSP34.39.13scFv AAS+SAV+R**	SEQ ID NO: 891 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 892 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS
308 **PGT-134 AAS+W/huSP34.39.13scFv AAS+SAV+R**	SEQ ID NO: 891 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKSRFTISRDDSKNSLYLEMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 888 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	PGQAPRGLIGGTSNRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS
309 **PGT-134 AAS+SAV+ YTE/huSP 34.1.3sc Fv AAS+W+YT E**	SEQ ID NO: 893 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 882 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SCQVTHEGSTVEKTVA PTECS
310 **PGT-134 AAS+SAV/ huSP34.1 .3scFv AAS+W**	SEQ ID NO: 894 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 886 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
311 **PGT-134 AAS+W+YTE/huSP34.1.3 scFv AAS+SAV+R**	SEQ ID NO: 895 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	SEQ ID NO: 892 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS
312 **PGT-134 AAS+W/huSP34.1.3 scFv AAS+SAV+R**	SEQ ID NO: 895 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 888 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
	PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS
313 **PGT-134 AAS+W+LS /huSP34. 1.3 scFv AAS+SAV+ R**	SEQ ID NO: 895 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGNSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 896 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH–Fc)	Fab Arm – LC (VL–CL)
	LSCAVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	LYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKS LSLSPGK	SCQVTHEGSTVEKTVA PTECS
314 **PGT–134 AAS+SAV+ YTE/huSP 34.3.8scFv AAS+W+YTE**	SEQ ID NO: 897 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 882 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
315 **PGT-134 AAS+SAV/ huSP34.3 .8scFv AAS+W**	SEQ ID NO: 898 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY ADSVKGRFTISRDDSKNSLYLQMNSLRTEDT AVYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPGVPARFSGSLLGGK AALTISGAQPEDEAEYYCALWYSNRWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	SEQ ID NO: 886 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS
316 **PGT-134 AAS+SAV+ YTE/huSP 34.34.3s cFv**	SEQ ID NO: 899 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK	SEQ ID NO: 882 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name/ features	unpaired HC	Fab Arm – HC (VH-Fc)	Fab Arm – LC (VL-CL)
AAS+W+YTE	PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLYITREPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIE KTISKAKGQPREPQVYTLPPSREEMTKNQVS LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLYITREPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY SCQVTHEGSTVEKTVA PTECS
317 **PGT-134 AAS+SAV/ huSP34.34.3scFv AAS+W**	SEQ ID NO: 900 EVQLVESGGGLVQPGGSLRLSCAASGFTFNT YAMNWVRQAPGKGLEWVGRIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNSLKTEDT AMYYCVRHGNFGHSYVSWFAYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSQAVVTQEPSL TVSPGGTVTLTCGSSTGAVTTGHYANWVQQK PGQAPRGLIGGTNKRAPWTPARFSGSLLGGK AALTLSGAQPEDEAEYYCALWYSNLWVFGGG TKLTVLEPKSSDKTHTCPPCPAPEAAGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRV VSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVS	SEQ ID NO: 886 QVHLQESGPGLVTPSETLSLTCTVSNGSVSGRFWS WIRQSPGRGLEWIGYFSDTDRSEYNPSLRSRLTLS VDRSKNQLSLKLKSVTAADSATYYCARAQQGKRIY GIVSFGELFYYYYMDAWGKGTPVTVSSASTKGPSV FPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNS GALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPASIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFF	SEQ ID NO: 883 SLNPLSLAPGATAKIP CGERSRGSRAVQWYQQ KPGQAPTLIIYNNQDR PAGVSERFSGNPDVAI GVTATLTISRVEVGDE GDYYCHYWDSRSPISW IFAGGTQLTVLGQPKA APSVTLFPPSSEELQA NKATLVCLISDFYPGA VTVAWKADSSPVKAGV ETTTPSKQSNNKYAAS SYLSLTPEQWKSHRSY

TABLE G – amino acid sequences of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name/ features	**unpaired HC**	**Fab Arm – HC (VH-Fc)**	**Fab Arm – LC (VL-CL)**
	LWCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	LVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK	SCQVTHEGSTVEKTVA PTECS

[0202] In some embodiments, one or more of the polypeptides comprising the multispecific antigen binding molecules described herin comprise an N-terminal signal peptide. The signal peptide can be an endogenous signal peptide (*e.g.*, from a native or wild-type immunoglobulin or CD4 ECD protein), or from a heterologous polypeptide. In various embodiments, the signal peptide or leader sequence is from a source protein selected from a serum protein, an immunoglobulin, a cytokine, a chemokine, a chaperone protein, an invariant protein, and a protein that directs proteins to the lysosomal compartment. In various embodiments, the signal peptide or leader sequence is from a source protein selected from colony stimulating factor 2 (CSF2, GM-CSF), tissue type plasminogen activator (PLAT, t-PA), C-C motif chemokine ligand 7 (CCL7, MCP-3), C-X-C motif chemokine ligand 10 (CXCL10, IP-10), catenin beta 1 (CTNNB1), CD74 (p33; DHLAG; HLADG; immunoglobulin Kappa; Ia-GAMMA, invariant chain), serum albumin (ALB), SPARC (osteonectin), cwcv and kazal like domains proteoglycan 1 (SPOCK1); SPARC (osteonectin), cwcv and kazal like domains proteoglycan 2 (SPOCK2); polyubiquitin B/C (UBB/UBC), calreticulin (CALR), vesicular stomatitis virus G protein (VSV-G), lysosomal associated membrane protein 1 (LAMP-1) and lysosomal associated membrane protein 2 (LAMP-2). In some embodiments, the signal peptide is from a serum albumin signal peptide (*e.g.*, comprising the amino acid sequence KWVTFISLLFLFSSAYS (SEQ ID NO: 1026)). In various embodiments, the signal peptide or leader sequence is selected from an amino acid sequence of any one of SEQ ID NOs: 1026-1039, or a sequence that is at least 95%, 96%, 97%, 98%, or 99% identical to any one of SEQ ID NOs: 1026-1039. Illustrative signal sequences that can be used in the present multi-specific binding proteins are provided in Table H.

TABLE H – illustrative signal sequences

SEQ ID NO:	source protein name	SEQUENCE
1026	albumin	KWVTFISLLFLFSSAYS
1027	IL-2	MYRMQLLSCIALSLALVTNS
1028	SPOCK1	MPAIAVLAAAAAAWCFLQVES
1029	SPOCK2	MRAPGCGRLVLPLLLLAAAALA
1030	Ig Kappa	METDTLLLWVLLLWVPG
1031	CSF2, GM-CSF	MWLQSLLLLGTVACSISV
1032	PLAT, t-PA	MDAMKRGLCCVLLLCGAVFVSAR
1033	CD74	MHRRRSRSCREDQKPV
1034	β-catenin	MRKAAVSHWQQQSYLDSGIHSGATTTAPSLS

TABLE H – illustrative signal sequences		
SEQ ID NO:	**source protein name**	**SEQUENCE**
1035	CCL7, MCP-3	MNPSAAVIFCLILLGLSGTQGILDMAQPVGINTSTTCCYRFI NKKIPKQRLESYRRTTSSHCPREAVIFKTKLDKEICADPTQK WVQDFMKHLDKKTQTPKLASAGA
1036	ubiquitin	MQIFVKTLTGKTITLEVEPSDTIENVKAKIQDKEGIPPDQQR LIFAGKQLEDGRTLSDYNIQKESTLHLVLRLRGG
1037	calreticulin	MLLSVPLLLGLLGLAVA
1038	VSV-G	MKCLLYLAFLFIGVNC
1039	CXCL10, IP-10	MNQTAILICCLIFLTLSGIQG

[0203] The signal peptide can be designed to be cleaved off, *e.g.*, after secretion from the cell, to form a mature fusion protein. A modified human serum albumin signal peptide to secrete proteins in cells that can find use in expressing the present fusion proteins is described, *e.g.*, in Attallah, *et al.*, *Protein Expr Purif.* (2017) 132:27-33. Additional signal peptide sequences for use in expressing the herein described fusion proteins are described, *e.g.*, in Kober, *et al.*, *Biotechnol Bioeng.* (2013) 110(4):1164-73.

[0204] In various embodiments, multi-specific antigen binding molecules described herein, and/or the polynucleotides encoding such polypeptides, are provided in provided in isolated form. This means that such the polypeptide or polynucleotide is at least 50% w/w pure of interfering proteins, cellular and other contaminants arising from its production or purification but does not exclude the possibility that the agent is combined with an excess of pharmaceutical acceptable carrier(s) or other vehicle intended to facilitate its use. The term "isolated," when applied to a polypeptide or polynucleotide, as described herein, denotes that the polypeptide or polynucleotide is essentially free of cellular components with which it is associated in the natural state. It can be, for example, in a homogeneous state and may be in either a dry or aqueous solution. Purity and homogeneity can be determined using known methods, *e.g.*, analytical chemistry techniques such as polyacrylamide gel electrophoresis, column chromatography, thin layer chromatography, or high-performance liquid chromatography (HPLC) analysis. A protein that is the predominant species present in a preparation is substantially purified. An "isolated" or "purified" polypeptide or polynucleotide is substantially free of other cellular material, or culture medium when produced by recombinant techniques, or chemical precursors or other chemicals when chemically synthesized. In various embodiments, purified polypeptides and/or

polynucleotides are at least 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% (w/w), separated from, purified of, or free of interfering proteins and contaminants from production or purification. Often a multi-specific antigen binding molecule is the predominant macromolecular species remaining after its purification.

5. Conjugated Multi-Specific Antigen Binding Molecules

[0205] Any of the multi-specific antigen binding molecules described herein may be conjugated antigen binding molecules which are bound to various molecules (*e.g.*, labels) including without limitation macromolecular substances such as polymers (*e.g.*, polyethylene glycol (PEG), polyethylenimine (PEI) modified with PEG (PEI-PEG), polyglutamic acid (PGA) (N-(2-Hydroxypropyl) methacrylamide (HPMA) copolymers), hyaluronic acid, radioactive materials (*e.g.* ^{90}Y, ^{131}I, ^{125}I, ^{35}S, ^{3}H, ^{121}In, ^{99}Tc), fluorescent substances (*e.g.*, fluorescein and rhodamine), luminescent substances (*e.g.*, luminol), haptens, enzymes (*e.g.*, glucose oxidase), metal chelates, biotin, avidin, and drugs.

[0206] The above-described conjugated multi-specific antigen binding molecules can be prepared according to known methods, *e.g.*, performing chemical modifications on the antigen binding molecules or the lower molecular weight forms thereof described herein. Methods for modifying antibodies are well known in the art (*e.g.*, US 5,057,313 and US 5,156,840).

6. Polynucleotides Encoding Multi-Specific Antigen Binding Molecules

[0207] Provided are polynucleotides encoding the multi-specific antigen binding molecules, described herein, vectors comprising such polynucleotides, and host cells (*e.g.*, mammalian cells, plant cells, yeast cells, bacteria cells including *E. coli* cells) comprising such polynucleotides or expression vectors. Provided herein are polynucleotides comprising nucleotide sequence(s) encoding any of the multi-specific antigen binding molecules provided herein, as well as expression cassettes and vector(s) comprising such polynucleotide sequences, *e.g.*, expression vectors for their efficient expression in host cells, *e.g.*, mammalian cells.

[0208] Further provided are polynucleotides or nucleic acid molecules encoding a multi-specific antigen binding molecule or antigen binding fragment thereof, as described herein. In some embodiments, the polynucleotides encode an immunoglobulin heavy chain variable region (or a fragment thereof) and an immunoglobulin light chain variable region

(or a fragment thereof), of one or both of the anti-CD3 binding domain and an anti-HIV antigen (*e.g.*, anti-gp120, anti-gp41). In other embodiments, the polynucleotides or nucleic acid molecules are DNA, cDNA, or mRNA. In some other embodiments, the polynucleotides or nucleic acid molecules are codon-biased to enhance expression in a desired host cell.

[0209] In some embodiments, provided are polynucleotides encoding the VH, VL, or VH and VL of one or both of the first and second binding domains of the multi-specific antigen binding molecules or antigen binding fragments which bind to gp120. In certain instances, the polynucleotides encode one or more of CDRs, VH, VL, HC, LC and Fc regions comprising the amino acid sequences of the multi-specific antigen binding molecules set forth in one or more of Tables A1-A4, B1-B2, C, D1-D4, E, F and G, as described herein.

[0210] Provided herein are polynucleotides encoding the CDRs, VH, VL, light chain, or heavy chain of a multi-specific antigen binding molecule, described herein. In one embodiment, the polynucleotides can comprise nucleotide sequences encoding a heavy chain or heavy chain variable domain targeting CD3 comprising the VH CDRs of antibodies described herein (see, *e.g.*, Tables A1-A4, B1, C and G, herein). In one embodiment, the polynucleotides can comprise nucleotide sequences encoding a light chain or light chain variable domain targeting CD3 comprising the VL CDRs of multi-specific antigen binding molecules described herein (see, *e.g.*, Tables A1-A4, B2, C and G, herein). In one embodiment, a polynucleotide described herein encodes a heavy chain variable region or a heavy chain comprising VH–CDRs targeting CD3 comprising the amino acid sequences set forth in Tables A1, A2, A3 or A4, respectively. In one embodiment, a polynucleotide described herein encodes a light chain variable region or a light chain comprising VL–CDRs targeting CD3 comprising the amino acid sequences set forth in Tables A1, A2, A3 or A4, respectively. In some embodiments, the polynucleotide or polynucleotides encode a first heavy chain variable domain (VH) and a first light chain variable domain (VL) that target, bind to or specifically bind to CD3, comprising a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences (according to Kabat), respectively: SEQ ID NOs: 1, 11, 8, 4, 9 and 10; SEQ ID NOs: 1, 12, 8, 4, 9 and 10; SEQ ID NOs: 1, 13, 8, 4, 14 and 15; SEQ ID NOs: 1, 13, 16, 4, 14 and 15; or SEQ ID NOs: 1, 11, 8, 4, 14 and 10. In some embodiments, the polynucleotide or polynucleotides encode a first heavy chain variable

domain (VH) and a first light chain variable domain (VL) that target, bind to or specifically bind to CD3, comprising a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences (according to Kabat), respectively: SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10. In some embodiments, the polynucleotide or polynucleotides encode a first heavy chain variable domain (VH) and a first light chain variable domain (VL) that target, bind to or specifically bind to CD3, comprising a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences (according to Kabat), respectively: SEQ ID NOs: 1, 11, 8, 4, 9 and 10. In some embodiments, the polynucleotide or polynucleotides encode a first heavy chain variable domain (VH) and a first light chain variable domain (VL) that target, bind to or specifically bind to CD3, comprising a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences (according to Kabat), respectively: SEQ ID NOs: 1, 12, 8, 4, 9 and 10.

[0211] In some embodiments, the polynucleotide or polynucleotides encode a first heavy chain variable domain (VH) and a first light chain variable domain (VL) that target, bind to or specifically bind to CD3, comprising a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences (according to Chothia), respectively: SEQ ID NOs: 17, 18, 23, 20, 24 and 25; SEQ ID NOs: 17, 18, 23, 20, 26 and 27; SEQ ID NOs: 17, 18, 75, 20, 26 and 27; or SEQ ID NOs: 17, 18, 23, 20, 26 and 25. In some embodiments, the polynucleotide or polynucleotides encode a first heavy chain variable domain (VH) and a first light chain variable domain (VL) that target, bind to or specifically bind to CD3, comprising a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences (according to Chothia), respectively: SEQ ID NOs: 17, 18, 23, 20, 24 and 25.

[0212] In some embodiments, the polynucleotide or polynucleotides encode a first heavy chain variable domain (VH) and a first light chain variable domain (VL) that target, bind to or specifically bind to CD3, comprising a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences (according to IMGT), respectively: SEQ ID NOs: 28, 29, 32, 31, 24 and 10; SEQ ID NOs: 28, 29, 32, 31, 26 and 15; SEQ ID NOs: 28, 29, 33, 31, 26

and 15; or SEQ ID NOs: 28, 29, 32, 31, 26 and 10. In some embodiments, the polynucleotide or polynucleotides encode a first heavy chain variable domain (VH) and a first light chain variable domain (VL) that target, bind to or specifically bind to CD3, comprising a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences (according to IMGT), respectively: SEQ ID NOs: 28, 29, 32, 31, 24 and 10.

[0213] In some embodiments, the polynucleotide or polynucleotides encode a first heavy chain variable domain (VH) and a first light chain variable domain (VL) that target, bind to or specifically bind to CD3, comprising a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences (according to Honegger), respectively: SEQ ID NOs: 34, 42, 40, 37, 41 and 25; SEQ ID NOs: 34, 43, 40, 37, 41 and 25; SEQ ID NOs: 34, 44, 40, 37, 45 and 27; SEQ ID NOs: 34, 44, 46, 37, 45 and 27; or SEQ ID NOs: 34, 42, 40, 37, 47 and 25. In some embodiments, the polynucleotide or polynucleotides encode a first heavy chain variable domain (VH) and a first light chain variable domain (VL) that target, bind to or specifically bind to CD3, comprising a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences (according to Honegger), respectively: SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25. In some embodiments, the polynucleotide or polynucleotides encode a first heavy chain variable domain (VH) and a first light chain variable domain (VL) that target, bind to or specifically bind to CD3, comprising a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences (according to Honegger), respectively: SEQ ID NOs: 34, 42, 40, 37, 41 and 25. In some embodiments, the polynucleotide or polynucleotides encode a first heavy chain variable domain (VH) and a first light chain variable domain (VL) that target, bind to or specifically bind to CD3, comprising a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences (according to Honegger), respectively: SEQ ID NOs: 34, 43, 40, 37, 41 and 25.

[0214] In one embodiment, a polynucleotide described herein encodes a heavy chain variable region or a heavy chain targeting CD3 comprising the amino acid sequences set forth in Table B1. In one embodiment, a polynucleotide described herein encodes a light chain variable region or a light chain targeting CD3 comprising the amino acid sequences

set forth in Table B2. In some embodiments, the polynucleotide encodes a first VH comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to an amino acid sequence selected from the group consisting of SEQ ID NOs: 48-53. In some embodiments, the polynucleotide encodes a first VH comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to the amino acid sequence of SEQ ID NO: 50. In some embodiments, the polynucleotide encodes a first VH comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to the amino acid sequence of SEQ ID NO: 51. In some embodiments, the polynucleotide encodes a first VL comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to an amino acid sequence of SEQ ID NO: 54-58. In some embodiments, the polynucleotide encodes a first VL comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to an amino acid sequence selected from the group consisting of SEQ ID NOs: 48-53 and encode a first VL comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to an amino acid sequence of SEQ ID NO: 54-58. In some embodiments, the polynucleotide or polynucleotides encode a first VH comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to the amino acid sequence of SEQ ID NO: 51 and encode a first VL comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at

least 98%, at least 99% identical, or is 100% identical, to the amino acid sequence of SEQ ID NO: 56.

[0215] In various embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH and the first VL comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to the amino acid sequences set forth, respectively: SEQ ID NOs: 48 and 54; SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; SEQ ID NOs: 51 and 56; SEQ ID NOs: 52 and 56; SEQ ID NOs: 53 and 57; or SEQ ID NOs: 50 and 58. In various embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH and the first VL comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56.

[0216] In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH and the first VL comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to the amino acid sequence set forth, respectively: SEQ ID NO: 50 and 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH and the first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequence set forth, respectively: SEQ ID NO: 50 and 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH and the first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequence set forth, respectively: SEQ ID NO: 50 and 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH and the first VL comprising amino acid sequences that are 100% identical to the amino acid sequence set forth, respectively: SEQ ID NO: 50 and 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising the amino acid sequence of SEQ ID NO: 50 and the first VL comprising an amino acid sequence that is at least 95% identical to the amino acid sequence

of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising the amino acid sequence of SEQ ID NO: 50 and the first VL comprising an amino acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising the amino acid sequence of SEQ ID NO: 50 and the first VL comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising the amino acid sequence of SEQ ID NO: 50 and the first VL comprising an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising the amino acid sequence of SEQ ID NO: 50 and the first VL comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprising the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising an amino acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprising the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprising the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprising the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 50 and the first VL comprising the amino acid sequence of SEQ ID NO: 56.

[0217] In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH and the first VL comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is

100% identical, to the amino acid sequence set forth, respectively: SEQ ID NO: 51 and 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH and the first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequence set forth, respectively: SEQ ID NO: 51 and 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH and the first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequence set forth, respectively: SEQ ID NO: 51 and 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH and the first VL comprising amino acid sequences that are 100% identical to the amino acid sequence set forth, respectively: SEQ ID NO: 51 and 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising the amino acid sequence of SEQ ID NO: 51 and the first VL comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising the amino acid sequence of SEQ ID NO: 51 and the first VL comprising an amino acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising the amino acid sequence of SEQ ID NO: 51 and the first VL comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising the amino acid sequence of SEQ ID NO: 51 and the first VL comprising an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising the amino acid sequence of SEQ ID NO: 51 and the first VL comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprising the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising an amino acid sequence that is at least 96% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprising the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the

first VH comprising an amino acid sequence that is at least 97% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprising the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising an amino acid sequence that is at least 98% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprising the amino acid sequence of SEQ ID NO: 56. In some embodiments, the polynucleotide or polynucleotides encode a first VH and a first VL, the first VH comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and the first VL comprising the amino acid sequence of SEQ ID NO: 56.

[0218] In some embodiments, the polynucleotide encodes a scFv comprising a VH and a VL, the scFv comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100%, identical to an amino acid sequence selected from SEQ ID NOs: 59-66, *e.g.*, SEQ ID NOs: 59-66, *e.g.*, SEQ ID NOs: 59-63, *e.g.*, SEQ ID NOs: 61, 62 or 63, *e.g.*, SEQ ID NOs: 62 or 63.

[0219] Provided herein are polynucleotides encoding the CDRs, VH, VL, light chain, or heavy chain of a multi-specific antigen binding molecule, described herein. In one embodiment, the polynucleotides can comprise nucleotide sequences encoding a heavy chain or heavy chain variable domain targeting an HIV antigen (*e.g.*, HIV gp120) comprising the VH CDRs of antibodies described herein (see, *e.g.*, Tables D1-D4, E and G, herein). In one embodiment, the polynucleotides can comprise nucleotide sequences encoding a light chain or light chain variable domain targeting an HIV antigen (*e.g.*, HIV gp120) comprising the VL CDRs of multi-specific antigen binding molecules described herein (see, *e.g.*, Tables D1-D4, E and G, herein). In one embodiment, a polynucleotide described herein encodes a heavy chain variable region or a heavy chain comprising VH–CDRs targeting an HIV antigen (*e.g.*, HIV gp120) comprising the amino acid sequences set forth in Tables D1, D2, D3 or D4, respectively. In one embodiment, a polynucleotide described herein encodes a light chain variable region or a light chain comprising VL–CDRs targeting an HIV antigen (*e.g.*, HIV gp120) comprising the amino acid sequences set forth in Tables D1, D2, D3 or D4, respectively.

[0220] In one embodiments, the polynucleotide or polynucleotides encode a second heavy chain variable domain (VH) and a second light chain variable domain (VL) that target, bind to or specifically bind to an HIV antigen (*e.g.*, HIV gp120), comprising a

second VH-CDR1, a second VH-CDR2, a second VH-CDR3, a second VL-CDR1, a second VL-CDR2 and a second VL-CDR3 comprising the amino acid sequences (according to Kabat) set forth, respectively, in: SEQ ID NOs: 76, 77, 78, 79, 80 and 81; SEQ ID NOs: 76, 82, 78, 79, 80 and 81; SEQ ID NOs: 83, 84, 85, 86, 80 and 87; SEQ ID NOs: 83, 88, 85, 86, 80 and 87; SEQ ID NOs: 90, 91, 92, 93, 94 and 95; SEQ ID NOs: 90, 91, 96, 93, 94 and 95; SEQ ID NOs: 97, 98, 99, 100, 101 and 102; SEQ ID NOs: 103, 104, 105, 106, 94 and 107; SEQ ID NOs: 108, 109, 110, 111, 112 and 113; SEQ ID NOs: 114, 115, 116, 117, 118 and 119; SEQ ID NOs: 114, 120, 121, 122, 118 and 123; SEQ ID NOs: 124, 125, 126, 127, 128 and 113; SEQ ID NOs: 129, 115, 131, 127, 118 and 113; SEQ ID NOs: 132, 133, 134, 135, 136 and 137; SEQ ID NOs: 138, 139, 140, 141, 142 and 143; SEQ ID NOs: 144, 145, 146, 147, 148 and 143; SEQ ID NOs: 149, 150, 151, 152, 153 and 143; SEQ ID NOs: 154, 155, 156, 157, 158 and 159; SEQ ID NOs: 160, 161, 162, 163, 164 and 165; SEQ ID NOs: 166, 161, 167, 163, 164 and 165; SEQ ID NOs: 168, 169, 170, 171, 172 and 173; SEQ ID NOs: 168, 174, 170, 171, 172 and 173; SEQ ID NOs: 175, 176, 177, 171, 172 and 173; SEQ ID NOs: 178, 179, 180, 181, 182 and 183; SEQ ID NOs: 184, 185, 186, 187, 188 and 189; SEQ ID NOs: 190, 191, 192, 193, 194 and 195; SEQ ID NOs: 196, 197, 198, 199, 200 and 201; SEQ ID NOs: 202, 203, 204, 205, 206 and 207; SEQ ID NOs: 208, 209, 210, 211, 212 and 213; SEQ ID NOs: 214, 215, 216, 217, 218 and 219; SEQ ID NOs: 214, 220, 216, 221, 218 and 219; SEQ ID NOs: 214, 220, 222, 221, 218 and 219; SEQ ID NOs: 223, 224, 225, 226, 227 and 228; SEQ ID NOs: 229, 230, 231, 232, 233 and 234; SEQ ID NOs: 902, 903, 904, 905, 906 and 907; SEQ ID NOs: 908, 909, 910, 911, 912 and 913; SEQ ID NOs: 914, 915, 916, 917, 918 and 919; or SEQ ID NOs: 920, 921, 922, 923, 924 and 925.

[0221] In one embodiments, the polynucleotide or polynucleotides encode a second heavy chain variable domain (VH) and a second light chain variable domain (VL) that target, bind to or specifically bind to an HIV antigen (*e.g.*, HIV gp120), comprising a second VH-CDR1, a second VH-CDR2, a second VH-CDR3, a second VL-CDR1, a second VL-CDR2 and a second VL-CDR3 comprising the amino acid sequences (according to Chothia) set forth, respectively, in: SEQ ID NOs: 235, 236, 237, 238, 239 and 240; SEQ ID NOs: 241, 242, 243, 244, 239 and 245; SEQ ID NOs: 246, 242, 247, 244, 239 and 245; SEQ ID NOs: 248, 249, 250, 251, 239 and 252; SEQ ID NOs: 248, 249, 253, 251, 239 and 252; SEQ ID NOs: 254, 255, 256, 257, 258 and 259; SEQ ID NOs: 260, 261, 262, 263, 239 and 264; SEQ ID NOs: 265, 266, 267, 268, 269 and 270; SEQ ID NOs: 271, 272, 273, 274, 275 and 270; SEQ ID NOs: 271, 276, 277, 278, 275 and 279; SEQ ID NOs: 280, 281, 282, 283, 284 and 270; SEQ ID NOs: 285, 272, 286, 283, 275 and 270; SEQ ID NOs: 287, 288, 289,

290, 291 and 292; SEQ ID NOs: 293, 294, 295, 296, 297 and 298; SEQ ID NOs: 299, 300, 301, 302, 303 and 298; SEQ ID NOs: 304, 300, 305, 406, 307 and 298; SEQ ID NOs: 308, 309, 310, 311, 312 and 313; SEQ ID NOs: 314, 315, 316, 317, 318 and 165; SEQ ID NOs: 320, 315, 321, 317, 318 and 165; SEQ ID NOs: 322, 323, 324, 325, 326 and 327; SEQ ID NOs: 322, 328, 324, 325, 326 and 327; SEQ ID NOs: 329, 323, 330, 325, 326 and 327; SEQ ID NOs: 331, 332, 333, 334, 335 and 336; SEQ ID NOs: 337, 338, 339, 340, 341 and 342; SEQ ID NOs: 343, 344, 345, 346, 341 and 347; SEQ ID NOs:348, 349, 350, 351, 352 and 353; SEQ ID NOs: 354, 355, 356, 357, 358 and 359; SEQ ID NOs: 360, 361, 362, 363, 364 and 365; SEQ ID NOs: 366, 367, 368, 369, 370 and 371; SEQ ID NOs: 366, 361, 368, 369, 370 and 371; SEQ ID NOs: 372, 361, 373, 369, 370 and 371; SEQ ID NOs: 374, 375, 376, 377, 378 and 379; or SEQ ID NOs: 380, 381, 382, 383, 384 and 385.

[0222] In one embodiments, the polynucleotide or polynucleotides encode a second heavy chain variable domain (VH) and a second light chain variable domain (VL) that target, bind to or specifically bind to an HIV antigen (*e.g.*, HIV gp120), comprising a second VH-CDR1, a second VH-CDR2, a second VH-CDR3, a second VL-CDR1, a second VL-CDR2 and a second VL-CDR3 comprising the amino acid sequences (according to IMGT) set forth, respectively, in: SEQ ID NOs: 386, 387, 388, 389, 239 and 81; SEQ ID NOs: 390, 391, 392, 393, 239 and 87; SEQ ID NOs: 390, 391, 394, 393, 239 and 87; SEQ ID NOs: 395, 396, 397, 393, 239 and 87; SEQ ID NOs: 398, 399, 400, 401, 239 and 95; SEQ ID NOs: 398, 399, 402, 401, 239 and 95; SEQ ID NOs: 403, 404, 405, 406, 258 and 102; SEQ ID NOs: 407, 408, 409, 410, 239 and 107; SEQ ID NOs: 411, 412, 413, 414, 269 and 113; SEQ ID NOs: 415, 416, 417, 418, 275 and 119; SEQ ID NOs: 415, 419, 420, 421, 275 and 123; SEQ ID NOs: 422, 423, 424, 425, 275 and 113; SEQ ID NOs: 426, 416, 427, 425, 275 and 113; SEQ ID NOs: 428, 429, 430, 431, 291 and 137; SEQ ID NOs: 432, 433, 434, 435, 297 and 143; SEQ ID NOs: 436, 437, 438, 439, 303 and 143; SEQ ID NOs: 440, 437, 441, 442, 307 and 143; SEQ ID NOs: 443, 444, 445, 446, 312 and 159; SEQ ID NOs: 447, 448, 449, 450, 318 and 165; SEQ ID NOs: 451, 448, 452, 450, 318 and 165; SEQ ID NOs: 453, 454, 455, 456, 326 and 173; SEQ ID NOs: 453, 457, 455, 456, 326 and 173; SEQ ID NOs: 458, 459, 460, 456, 326 and 173; SEQ ID NOs: 461, 462, 463, 464, 335 and 183; SEQ ID NOs: 465, 466, 467, 468, 341 and 189; SEQ ID NOs: 469, 470, 471, 472, 341 and 195; SEQ ID NOs: 473, 474, 475, 476, 352 and 201; SEQ ID NOs: 477, 478, 479, 480, 358 and 207; SEQ ID NOs: 481, 482, 483, 484, 364 and 213; SEQ ID NOs: 485, 486, 487, 488, 370 and 219; SEQ ID NOs: 485, 482, 487, 488, 370 and 219; SEQ ID NOs: 489, 482, 490, 488, 370 and 219; SEQ ID NOs: 491, 492, 493, 494, 378 and 228; SEQ ID NOs: 495, 496,

497, 498, 384 and 234; SEQ ID NOs: 950, 951, 952, 953, 930 and 907; SEQ ID NOs: 954, 955, 956, 957, 936 and 913; SEQ ID NOs: 958, 959, 960, 961, 942 and 919; or SEQ ID NOs: 962, 963, 964, 965, 948 and 925.

[0223] In one embodiments, the polynucleotide or polynucleotides encode a second heavy chain variable domain (VH) and a second light chain variable domain (VL) that target, bind to or specifically bind to an HIV antigen (*e.g.*, HIV gp120), comprising a second VH-CDR1, a second VH-CDR2, a second VH-CDR3, a second VL-CDR1, a second VL-CDR2 and a second VL-CDR3 comprising the amino acid sequences (according to Honegger) set forth, respectively, in: SEQ ID NOs: 499, 500, 501, 238, 502 and 240; SEQ ID NOs: 499, 503, 501, 238, 502 and 240; SEQ ID NOs: 505, 506, 507, 244, 502 and 245; SEQ ID NOs: 508, 509, 510, 244, 502 and 245; SEQ ID NOs: 511, 512, 513, 251, 514 and 252; SEQ ID NOs: 511, 512, 515, 251, 514 and 252; SEQ ID NOs: 516, 517, 518, 257, 519 and 259; SEQ ID NOs: 520, 521, 522, 264, 523 and 264; SEQ ID NOs: 524, 525, 526, 268, 527 and 270; SEQ ID NOs: 528, 529, 530, 274, 531 and 270; SEQ ID NOs: 528, 532, 533, 278, 531 and 279; SEQ ID NOs: 534, 535, 536, 283, 537 and 270; SEQ ID NOs: 1090, 529, 538, 283, 531 and 270; SEQ ID NOs: 539, 540, 541, 290, 542 and 292; SEQ ID NOs: 543, 544, 545, 546, 547 and 298; SEQ ID NOs: 548, 549, 550, 1091, 551 and 298; SEQ ID NOs: 552, 553, 554, 555, 556 and 298; SEQ ID NOs: 557, 558, 559, 311, 560 and 313; SEQ ID NOs: 561, 562, 563, 564, 565 and 165; SEQ ID NOs: 566, 562, 1092, 564, 567 and 165; SEQ ID NOs: 568, 569, 570, 571, 572 and 327; SEQ ID NOs: 568, 573, 570, 571, 572 and 327; SEQ ID NOs: 574, 575, 576, 571, 572 and 327; SEQ ID NOs: 577, 578, 579, 580, 581 and 336; SEQ ID NOs: 582, 583, 584, 340, 585 and 342; SEQ ID NOs: 586, 587, 588, 346, 589 and 347; SEQ ID NOs: 590, 591, 592, 351, 593 and 353; SEQ ID NOs: 594, 595, 596, 597, 598 and 359; SEQ ID NOs: 599, 600, 601, 602, 603 and 365; SEQ ID NOs: 604, 605, 606, 607, 608 and 371; SEQ ID NOs: 604, 609, 606, 607, 608 and 371; SEQ ID NOs: 610, 609, 611, 607, 608 and 371; SEQ ID NOs: 612, 613, 614, 615, 616 and 379; SEQ ID NOs: 617, 618, 619, 620, 621 and 385; SEQ ID NOs: 966, 967, 968, 969, 970 and 931; SEQ ID NOs: 971, 972, 973, 974, 975 and 937; SEQ ID NOs: 976, 977, 978, 941, 979 and 943; or SEQ ID NOs: 980, 981, 982, 983, 984 and 949.

[0224] In one embodiment, a polynucleotide described herein encodes a heavy chain variable region and a heavy chain targeting an HIV antigen (*e.g.*, HIV gp120) comprising the amino acid sequences set forth in Table E. In various embodiments, the polynucleotide or polynucleotides encode a second VH and a second VL, the second VH and the second

VL comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or are 100% identical, to the amino acid sequences set forth, respectively: SEQ ID NOs: 622 and 623; SEQ ID NOs: 624 and 625; SEQ ID NOs: 624 and 626; SEQ ID NOs: 627 and 628; SEQ ID NOs: 629 and 630; SEQ ID NOs: 631 and 632; SEQ ID NOs: 633 and 634; SEQ ID NOs: 635 and 636; SEQ ID NOs: 637 and 638; SEQ ID NOs: 639 and 640; SEQ ID NOs: 641 and 642; SEQ ID NOs: 643 and 644; SEQ ID NOs: 645 and 646; SEQ ID NOs: 647 and 648; SEQ ID NOs: 649 and 650; SEQ ID NOs: 651 and 652; SEQ ID NOs: 653 and 654; SEQ ID NOs: 655 and 656; SEQ ID NOs: 657 and 658; SEQ ID NOs: 659 and 660; SEQ ID NOs: 661 and 662; SEQ ID NOs: 663 and 664; SEQ ID NOs: 665 and 666; SEQ ID NOs: 667 and 668; SEQ ID NOs: 669 and 670; SEQ ID NOs:671 and 672; SEQ ID NOs:673 and 670; SEQ ID NOs: 674 and 675; SEQ ID NOs: 676 and 677; SEQ ID NOs: 678 and 679; SEQ ID NOs: 680 and 681; SEQ ID NOs: 682 and 683; SEQ ID NOs: 684 and 685; SEQ ID NOs: 686 and 687; SEQ ID NOs: 688 and 689; SEQ ID NOs: 690 and 691; SEQ ID NOs: 692 and 693; SEQ ID NOs: 694 and 695; SEQ ID NOs: 985 and 986; SEQ ID NOs: 987 and 988; SEQ ID NOs: 989 and 990; or SEQ ID NOs: 991 and 992.

[0225] In some embodiments, the polynucleotide or polynucleotides encode a first Fc region and a second Fc region, as set forth in Table F. In some embodiments, the polynucleotide or polynucleotides encode a first Fc region and a second Fc region, comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or are 100% identical, to the amino acid sequences set forth, respectively: SEQ ID NOs.: 696 and 697; SEQ ID NOs.: 697 and 696; SEQ ID NOs.: 696 and 698; SEQ ID NOs.: 698 and 696; SEQ ID NOs.: 699 and 700; SEQ ID NOs.: 700 and 699; SEQ ID NOs.: 701 and 698; SEQ ID NOs.: 698 and 701; SEQ ID NOs.: 702 and 703; SEQ ID NOs.: 703 and 702; SEQ ID NOs.: 704 and 698; SEQ ID NOs.: 698 and 704; SEQ ID NOs.: 705 and 703; SEQ ID NOs.: 703 and 705; SEQ ID NOs.: 706 and 704; SEQ ID NOs.: 704 and 706; SEQ ID NOs.: 707 and 703; SEQ ID NOs.: 703 and 707; SEQ ID NOs.: 708 and 704; SEQ ID NOs.: 704 and 708; SEQ ID NOs.: 709 and 710; or SEQ ID NOs.: 710 and 709. In some embodiments, the polynucleotide or polynucleotides encode a first Fc region and a second Fc region, comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or are 100%

identical, to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705. In some embodiments, the polynucleotide or polynucleotides encode a first Fc region and a second Fc region, comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705. In some embodiments, the polynucleotide or polynucleotides encode a first Fc region and a second Fc region, comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705. In some embodiments, the polynucleotide or polynucleotides encode a first Fc region and a second Fc region, comprising amino acid sequences that are 100% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705.

[0226] In some embodiments, the polynucleotide or polynucleotides encode an unpaired heavy chain a Fab arm heavy chain and a Fab arm light chain as set forth in Table G. Illustrative polynucleotide sequences are provided in Table J. In some embodiments, the polynucleotide or polynucleotides encode an unpaired heavy chain a Fab arm heavy chain and a Fab arm light chain comprising amino acid sequences comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to the amino acid sequences set forth, respectively: SEQ ID NOs: 995, 996 and 997; SEQ ID NOs: 998, 999 and 1000; SEQ ID NOs: 1001, 1002 and 1003; SEQ ID NOs: 1004, 1005 and 1000; SEQ ID NOs: 1006, 1002 and 997; SEQ ID NOs: 1007, 1093 and 1000; SEQ ID NOs: 998, 1008 and 1000; SEQ ID NOs: 998, 1009 and 1000; SEQ ID NOs: 1010, 1011 and 1012; SEQ ID NOs: 1013, 1014 and 1015; SEQ ID NOs: 1016, 1017 and 1012; SEQ ID NOs: 1018, 1019 and 1012; SEQ ID NOs: 1018, 1020 and 1012; SEQ ID NOs: 1021, 1022 and 1023; or SEQ ID NOs: 1024, 1025 and 1023.

[0227] In some embodiments, the polynucleotide or polynucleotides encode an unpaired heavy chain a Fab arm heavy chain and a Fab arm light chain comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to the amino acid sequences set forth, respectively: SEQ ID NOs: 995, 996 and 997. In some embodiments, the polynucleotide or polynucleotides encode an unpaired heavy chain a Fab arm heavy chain and a Fab arm light chain comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 995, 996 and 997. In some embodiments,

the polynucleotide or polynucleotides encode an unpaired heavy chain a Fab arm heavy chain and a Fab arm light chain comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 995, 996 and 997. In some embodiments, the polynucleotide or polynucleotides encode an unpaired heavy chain a Fab arm heavy chain and a Fab arm light chain comprising amino acid sequences that are 100% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 995, 996 and 997.

[0228] In some embodiments, the polynucleotide or polynucleotides encode an unpaired heavy chain a Fab arm heavy chain and a Fab arm light chain comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical, or is 100% identical, to the amino acid sequences set forth, respectively: SEQ ID NOs: 998, 999 and 1000. In some embodiments, the polynucleotide or polynucleotides encode an unpaired heavy chain a Fab arm heavy chain and a Fab arm light chain comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 998, 999 and 1000. In some embodiments, the polynucleotide or polynucleotides encode an unpaired heavy chain a Fab arm heavy chain and a Fab arm light chain comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 998, 999 and 1000. In some embodiments, the polynucleotide or polynucleotides encode an unpaired heavy chain a Fab arm heavy chain and a Fab arm light chain comprising amino acid sequences that are 100% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 998, 999 and 1000.

[0229] Also encompassed by this disclosure are polynucleotides encoding an anti-gp120 antigen binding molecule or antigen binding fragment thereof, or an anti-CD3 antigen binding domain or antigen binding fragment thereof, that have at least one of codon-biased sequences for improved expression in a desired host cell, replacement heterologous signal sequences, and reduced or eliminated mRNA instability elements. Methods to generate codon-biased nucleic acids can be carried out by adapting the methods described in, *e.g.*, U.S. Patent Nos. 5,965,726; 6,174,666; 6,291,664; 6,414,132; and 6,794,498. Preferred codon usage for expression of the multi-specific antigen binding molecules in desired host cells is provided, *e.g.*, at kazusa.or.jp/codon/; and genscript.com/tools/codon-frequency-table.

[0230] As appropriate, in certain embodiments, the 3′-end of the polynucleotides encoding the multi-specific antigen binding molecules comprises one or multiple tandem stop codons, *e.g.*, two or more tandem TAG ("amber"), TAA ("ochre") or TGA ("opal" or "umber") stop codons. The multiple tandem stop codons can be the same or different.

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TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
430 **hCD4 D1.22 Fc AAS+W +YTE/ huSP3 4.39. 13 AAS+S AV+R**	SEQ ID NO: 995 AAGAAAGTGGTGTACGGCAAAAAGGGCGACACC GTGGAACTGACCTGTACCGCCAGCCAGAAGAAG AACATCCAGTTCCACTGGAAGAACTCCAACCAG ATCAAGATCCTGGGCAACCAGGGCAGCTTCCTG ACCAAGGGACCTTCCAAGCTGAACGACAGAGTG GACTCCAGACGGTCCCTGTGGGACCAGGGCAAC TTTCCACTGATCATCAAGAACCTGAAGCCTGAG GACTCCGACACCTACATCTGCGAGGTGGAAGAT CAGAAAGAAGAGGTGCAGCTGGTCGTCGTCGGA GGATCTGACAAGACCCACACCTGTCCTCCATGT CCTGCTCCAGAAGCTGCTGGCGGCCCTTCTGTG TTCCTGTTTCCTCCAAAGCCTAAGGACACCCTG TACATCACCCGCGAGCCTGAAGTGACCTGTGTG GTGGTGGATGTGTCCCACGAGGACCCCGAAGTG AAGTTCAATTGGTACGTGGACGGCGTGGAAGTG CACAACGCCAAGACCAAGCCTAGAGAGGAACAG TACAACAGCACCTACAGAGTGGTGTCCGTGCTG ACCGTGCTGCACCAGGATTGGCTGAACGGCAAA GAGTACAAGTGCAAGGTGTCCAACAAGGCCCTG CCTGCCAGCATCGAGAAAACCATCAGCAAGGCC AAGGGCCAGCCTAGGGAACCCCAGGTTTACACA CTGCCTCCAAGCCGGGAAGAGATGACCAAGAAC CAGGTGTCCCTGTGGTGCCTCGTGAAGGGCTTC TACCCTTCCGATATCGCCGTGGAATGGGAGAGC	SEQ ID NO: 996 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCC ATGAACTGGGTCCGACAGGCTCCTGGCAAAGGC CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC AACAATTACGCCACCTACTACGCCGACTCCGTG AAGAGCAGATTCACCATCTCTCGGGACGACTCC AAGAACTCCCTGTACCTGGAGATGAACAGCCTG CGGACCGAGGATACCGCCGTGTACTATTGTGTG CGGCACGGCAACTTCGGCCACTCCTATGTGTCT TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC ACAGTTTCTTCCGCCTCTACAAAGGGCCCTAGT GTGTTCCCTCTGGCTCCCAGCAGCAAGTCTACA TCTGGCGGAACAGCCGCTCTGGGCTGCCTGGTC AAGGATTACTTTCCCGAGCCTGTGACCGTGTCC TGGAATTCTGGCGCTCTGACAAGCGGCGTGCAC ACCTTTCCAGCTGTGCTGCAAAGCAGCGGCCTG TACTCTCTGAGCAGCGTGGTCACAGTGCCTAGC TCTAGCCTGGGCACCCAGACCTACATCTGCAAT GTGAACCACAAGCCTAGCAACACCAAGGTGGAC AAGAAGGTGGAACCCAAGAGCTGCGACAAGACC CACACCTGTCCTCCATGTCCTGCTCCAGAAGCT GCTGGCGGCCCTTCCGTGTTTCTGTTCCCTCCA AAGCCTAAGGACACCCTGATGATCAGCAGAACC	SEQ ID NO: 997 CAAGCTGTTGTGACAC AAGAGCCCAGCCTGAC AGTGTCTCCTGGCGGA ACAGTGACACTGACCT GTGGATCTTCTACAGG CGCCGTGACAACCGGC CACTATGCTAATTGGG TGCAGCAGAAACCCGG ACAGGCCCCTAGAGGA CTGATCGGCGGAACAT CTAATAGAGCCCCTGG CGTGCCAGCCAGATTT TCTGGATCTCTGCTCG GAGGCAAGGCCGCTCT GACAATTTCTGGCGCC CAGCCAGAGGATGAGG CCGAGTATTATTGTGC CCTGTGGTACAGCAAC AGATGGGTGTTCGGCG GAGGCACCAAACTGAC AGTGCTGGGACAACCT AAGGCTGCCCCTAGCG TGACACTGTTTCCTCC AAGCTCTGAGGAACTC

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	AATGGCCAGCCTGAGAACAACTACAAGACAACC CCTCCTGTGCTGGACAGCGACGGCTCATTCTTC CTGTACAGCAAGCTGACAGTGGACAAGTCCAGA TGGCAGCAGGGCAACGTGTTCAGCTGCAGCGTG ATGCACGAGGCCCTGCACAACCACTACACCCAG AAGTCCCTGAGCCTGTCTCCTGGCAAA	CCTGAAGTGACCTGCGTGGTGGTGGATGTGTCC CACGAGGATCCCGAAGTGAAGTTCAATTGGTAC GTGGACGGCGTGGAAGTGCACAACGCCAAGACC AAGCCTAGAGAGGAACAGTACAACAGCACCTAC AGAGTGGTGTCCGTGCTGACCGTGCTGCACCAG GATTGGCTGAACGGCAAAGAGTACAAGTGCAAG GTGTCCAACAAGGCCCTGCCTGCCAGCATCGAG AAAACCATCAGCAAGGCCAAGGGCCAGCCTAGG GAACCCCAGGTTTACACACTGCCTCCAAGCCGG GAAGAGATGACCAAGAACCAGGTGTCCCTGAGC TGTGCCGTGAAGGGCTTCTACCCTTCCGATATC GCCGTGGAATGGGAGAGCAATGGCCAGCCTGAG AACAACTACAAGACAACCCCTCCTGTGCTGGAC AGCGACGGCTCATTCTTCCTGGTGTCCAAGCTG ACAGTGGACAAGTCCAGATGGCAGCAGGGCAAC GTGTTCAGCTGCAGCGTGATGCACGAGGCCCTG CACAACCGGTACACCCAGAAGTCCCTGTCTCTG AGCCCCGGCAAA	CAGGCCAACAAGGCCA CACTCGTGTGCCTGAT CAGCGATTTTTACCCT GGCGCTGTGACAGTGG CCTGGAAGGCTGATAG CTCTCCTGTGAAAGCC GGCGTGGAAACCACCA CACCTAGCAAGCAGAG CAACAACAAATACGCC GCCAGCAGCTACCTGA GCCTGACACCTGAGCA GTGGAAGTCCCACAGA TCCTACAGCTGCCAAG TGACCCACGAGGGCAG CACCGTGGAAAAAACA GTGGCCCCTACCGAGT GCAGC
431 **hCD4 D1.22 Fc AAS+W +YTE/ huSP3**	SEQ ID NO: 998 AAAAAGGTGGTGTACGGCAAGAAGGGCGACACC GTCGAGCTGACCTGTACCGCCTCTCAGAAGAAG AACATCCAGTTCCACTGGAAGAACTCCAACCAG ATCAAGATCCTGGGCAACCAGGGCAGCTTCCTG ACCAAGGGACCTTCCAAGCTGAACGACAGAGTG GACTCCAGACGGTCCCTGTGGGACCAGGGCAAC	SEQ ID NO: 999 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCT ATGAACTGGGTCCGACAGGCCCCTGGCAAAGGA CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC AACAACTACGCCACCTACTACGCCGACTCCGTG	SEQ ID NO: 1000 CAGGCCGTGGTCACCC AAGAGCCTAGCCTGAC AGTTTCTCCTGGCGGC ACCGTGACACTGACCT GTGGATCTTCTACCGG CGCTGTGACCACCGGC

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
4.39.13 AAS+SAV+R	TTTCCACTGATCATCAAGAACCTGAAGCCTGAG GACTCCGACACCTACATCTGCGAGGTGGAAGAT CAGAAAGAAGAGGTGCAGCTGGTCGTCGTCGGC GGCTCTGATAAGACCCATACCTGTCCTCCATGT CCTGCTCCAGAAGCTGCTGGCGGCCCTTCCGTG TTTCTGTTCCCTCCAAAGCCTAAGGACACCCTG TACATCACCCGCGAGCCTGAAGTGACCTGCGTG GTGGTGGATGTGTCTCACGAGGACCCCGAAGTG AAGTTCAATTGGTACGTGGACGGCGTGGAAGTG CACAACGCCAAGACCAAGCCTAGAGAGGAACAG TACAACTCCACCTACAGAGTGGTGTCCGTGCTG ACCGTGCTGCACCAGGATTGGCTGAACGGCAAA GAGTACAAGTGCAAGGTGTCCAACAAGGCCCTG CCTGCCTCCATCGAAAAGACCATCTCCAAGGCC AAGGGCCAGCCTAGGGAACCCCAGGTTTACACC CTGCCACCTAGCCGGGAAGAGATGACCAAGAAC CAGGTGTCACTGTGGTGCCTGGTCAAGGGCTTC TACCCCTCTGATATCGCCGTGGAATGGGAGAGC AATGGCCAGCCTGAGAACAACTACAAGACCACA CCTCCTGTGCTGGACAGCGACGGCTCATTCTTC CTGTACAGCAAGCTGACAGTGGACAAGTCCAGA TGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTG ATGCACGAGGCCCTGCACAATCACTACACCCAG AAGTCCCTGTCTCTGTCCCCTGGCAAA	AAGTCCCGGTTCACCATCTCTCGGGACGACTCC AAGAACTCCCTGTACCTGGAAATGAACAGCCTG CGGACCGAGGACACCGCCGTGTATTATTGTGTG CGGCACGGCAACTTCGGCCACTCCTATGTGTCT TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC ACAGTTTCTTCCGCCTCCACCAAGGGACCCAGC GTTTTCCCTCTGGCTCCATCCTCCAAGTCTACC TCTGGCGGAACAGCTGCTCTGGGCTGCCTGGTC AAGGACTACTTTCCTGAGCCTGTGACCGTGTCC TGGAACTCTGGCGCTCTGACATCTGGCGTGCAC ACCTTTCCAGCTGTGCTGCAGTCCTCCGGCCTG TACTCTCTGTCCTCTGTCGTGACCGTGCCTTCC AGCTCTCTGGGAACCCAGACCTACATCTGCAAT GTGAACCACAAGCCTTCCAACACCAAGGTGGAC AAGAAGGTGGAACCCAAGTCCTGCGACAAGACC CACACCTGTCCTCCATGTCCTGCTCCAGAAGCT GCTGGCGGCCCTTCCGTGTTTCTGTTCCCTCCA AAGCCTAAGGACACCCTGATGATCTCTCGGACC CCTGAAGTGACCTGCGTGGTGGTGGATGTGTCT CACGAGGATCCCGAAGTGAAGTTCAATTGGTAC GTGGACGGCGTGGAAGTGCACAACGCCAAGACC AAGCCTAGAGAGGAACAGTACAACTCCACCTAC AGAGTGGTGTCCGTGCTGACCGTGCTGCACCAG GATTGGCTGAACGGCAAAGAGTACAAGTGCAAG GTGTCCAACAAGGCCCTGCCTGCCTCCATCGAA	CACTACGCTAATTGGG TGCAGCAGAAGCCTGG ACAGGCTCCCAGAGGA CTGATCGGCGGCACCT CTAATAGAGCACCTGG CGTGCCAGCCAGATTC TCCGGATCTCTGCTTG GCGGAAAGGCCGCTCT GACAATCTCTGGTGCT CAGCCTGAGGACGAGG CCGAGTACTATTGTGC CCTGTGGTACTCCAAC AGATGGGTGTTCGGCG GAGGCACCAAGCTGAC AGTTCTGGGACAGCCT AAGGCTGCCCCTTCCG TGACTCTGTTCCCTCC ATCCTCTGAGGAACTG CAGGCCAACAAGGCTA CCCTCGTGTGCCTGAT CTCCGACTTTTACCCT GGCGCCGTGACCGTGG CTTGGAAGGCTGATAG TTCTCCTGTGAAGGCC GGCGTGGAAACCACCA

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
		AAGACCATCTCCAAGGCCAAGGGCCAGCCTAGG GAACCCCAGGTTTACACCCTGCCACCTAGCCGG GAAGAGATGACCAAGAACCAGGTGTCCCTGTCC TGTGCCGTGAAGGGCTTCTACCCTTCCGATATC GCCGTGGAATGGGAGAGCAATGGCCAGCCTGAG AACAACTACAAGACAACCCCTCCTGTGCTGGAC TCCGACGGCTCATTCTTCCTGGTGTCCAAGCTG ACAGTGGACAAGTCTAGATGGCAGCAGGGCAAC GTGTTCTCCTGCTCCGTGATGCACGAGGCCCTG CACAACAGATACACCCAGAAGTCCCTGTCTCTG AGCCCCGGAAAA	CACCTAGCAAGCAGTC CAACAACAAATACGCC GCCTCCTCCTACCTGT CTCTGACCCCTGAACA GTGGAAGTCCCACCGG TCCTACAGCTGCCAAG TGACCCATGAGGGCTC CACCGTGGAAAAGACA GTGGCCCCTACCGAGT GCTCT
432 **hCD4 D1.22 Fc AAS+S AV+R/ huSP3 4.3.1 3 AAS+W +YTE**	SEQ ID NO: 1001 AAGAAAGTGGTGTACGGCAAAAAGGGCGACACC GTGGAACTGACCTGTACCGCCAGCCAGAAGAAG AACATCCAGTTCCACTGGAAGAACTCCAACCAG ATCAAGATCCTGGGCAACCAGGGCAGCTTCCTG ACCAAGGGACCTTCCAAGCTGAACGACAGAGTG GACTCCAGACGGTCCCTGTGGGACCAGGGCAAC TTTCCACTGATCATCAAGAACCTGAAGCCTGAG GACTCCGACACCTACATCTGCGAGGTGGAAGAT CAGAAAGAAGAGGTGCAGCTGGTCGTCGTCGGA GGATCTGACAAGACCCACACCTGTCCTCCATGT CCTGCTCCAGAAGCTGCTGGCGGCCCTTCCGTG TTTCTGTTCCCTCCAAAGCCTAAGGACACCCTG ATGATCAGCAGAACCCCTGAAGTGACCTGCGTG	SEQ ID NO: 1002 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCC ATGAACTGGGTCCGACAGGCTCCTGGCAAAGGC CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC AACAATTACGCCACCTACTACGCCGACTCCGTG AAGGGCAGATTCACCATCTCTCGGGACGACTCC AAGAACTCCCTGTACCTGCAGATGAACAGCCTG CGGACCGAGGATACCGCCGTGTACTATTGTGTG CGGCACGGCAACTTCGGCCACTCCTATGTGTCT TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC ACAGTTTCTTCCGCTAGCACCAAGGGCCCCTCC GTGTTTCCACTGGCTCCTAGCAGCAAGAGCACA	SEQ ID NO: 1003 CAAGCTGTTGTGACAC AAGAGCCCAGCCTGAC AGTGTCTCCTGGCGGA ACAGTGACACTGACCT GTGGATCTTCTACAGG CGCCGTGACAACCGGC CACTATGCTAATTGGG TGCAGCAGAAACCCGG ACAGGCCCCTAGAGGA CTGATCGGCGGAACAT CTAATAGAGCCCCTGG CGTGCCAGCCAGATTT TCTGCCGAGTATTATT

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules

Ab name	unpaired HC	Fab Arm – HC	Fab Arm – LC
	GTGGTGGATGTGTCCCACGAGGATCCCGAAGTG	AGCGGAGGAACAGCCGCTCTGGGCTGTCTGGTC	GTGCCCTGTGGTACAG
	AAGTTCAATTGGTACGTGGACGGCGTGGAAGTG	AAGGACTACTTTCCCGAGCCTGTGACCGTGTCC	CAACAGATGGGTGTTC
	CACAACGCCAAGACCAAGCCTAGAGAGGAACAG	TGGAATTCTGGCGCTCTGACAAGCGGCGTGCAC	GGCGGAGGCACCAAAC
	TACAACAGCACCTACAGAGTGGTGTCCGTGCTG	ACCTTTCCAGCTGTGCTGCAAAGCAGCGGCCTG	TGACAGTGCTGGGACA
	ACCGTGCTGCACCAGGATTGGCTGAACGGCAAA	TACTCTCTGAGCAGCGTGGTCACAGTGCCAAGC	ACCTAAGGCTGCCCCT
	GAGTACAAGTGCAAGGTGTCCAACAAGGCCCTG	TCTAGCCTGGGCACCCAGACCTACATCTGCAAT	AGCGTGACACTGTTTC
	CCTGCCAGCATCGAGAAAACCATCAGCAAGGCC	GTGAACCACAAGCCTAGCAACACCAAGGTGGAC	CTCCAAGCTCTGAGGA
	AAGGGCCAGCCTAGGGAACCCCAGGTTTACACA	AAGAAGGTGGAACCCAAGAGCTGCGACAAGACC	ACTCCAGGCCAACAAG
	CTGCCTCCAAGCCGGGAAGAGATGACCAAGAAC	CACACCTGTCCTCCATGTCCTGCTCCAGAAGCT	GCCACACTCGTGTGCC
	CAGGTGTCCCTGAGCTGTGCCGTGAAGGGCTTC	GCTGGCGGCCCTTCTGTGTTCCTGTTTCCTCCA	TGATCAGCGATTTTTA
	TACCCTTCCGATATCGCCGTGGAATGGGAGAGC	AAGCCTAAGGACACCCTGTACATCACCCGCGAG	CCCTGGCGCTGTGACA
	AATGGCCAGCCTGAGAACAACTACAAGACAACC	CCTGAAGTGACCTGTGTGGTGGTGGATGTGTCC	GTGGCCTGGAAGGCTG
	CCTCCTGTGCTGGACAGCGACGGCTCATTCTTC	CACGAGGACCCCGAAGTGAAGTTCAATTGGTAC	ATAGCTCTCCTGTGAA
	CTGGTGTCCAAGCTGACAGTGGACAAGTCCAGA	GTGGACGGCGTGGAAGTGCACAACGCCAAGACC	AGCCGGCGTGGAAACC
	TGGCAGCAGGGCAACGTGTTCAGCTGCAGCGTG	AAGCCTAGAGAGGAACAGTACAACAGCACCTAC	ACCACACCTAGCAAGC
	ATGCACGAGGCCCTGCACAACCGGTACACCCAG	AGAGTGGTGTCCGTGCTGACCGTGCTGCACCAG	AGAGCAACAACAAATA
	AAGTCCCTGTCTCTGAGCCCCGGCAAA	GATTGGCTGAACGGCAAAGAGTACAAGTGCAAG	CGCCGCCAGCAGCTAC
		GTGTCCAACAAGGCCCTGCCTGCCAGCATCGAG	CTGAGCCTGACACCTG
		AAAACCATCAGCAAGGCCAAGGGCCAGCCTAGG	AGCAGTGGAAGTCCCA
		GAACCCCAGGTTTACACACTGCCTCCAAGCCGG	CAGATCCTACAGCTGC
		GAAGAGATGACCAAGAACCAGGTGTCCCTGTGG	CAAGTGACCCACGAGG
		TGCCTCGTGAAGGGCTTCTACCCTTCCGATATC	GCAGCACCGTGGAAAA
		GCCGTGGAATGGGAGAGCAATGGCCAGCCTGAG	AACAGTGGCCCCTACC
		AACAACTACAAGACAACCCCTCCTGTGCTGGAC	GAGTGCAGC
		AGCGACGGCTCATTCTTCCTGTACAGCAAGCTG	

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
		ACAGTGGACAAGTCCAGATGGCAGCAGGGCAAC GTGTTCAGCTGCAGCGTGATGCACGAGGCCCTG CACAACCACTACACCCAGAAGTCCCTGAGCCTG TCTCCTGGCAAA	
433 **hCD4 D1.22 Fc AAS+S AV+R/ huSP3 4.3.1 3 AAS+W +YTE**	SEQ ID NO: 1004 AAAAAGGTGGTGTACGGCAAGAAGGGCGACACC GTCGAGCTGACCTGTACCGCCTCTCAGAAGAAG AACATCCAGTTCCACTGGAAGAACTCCAACCAG ATCAAGATCCTGGGCAACCAGGGCAGCTTCCTG ACCAAGGGACCTTCCAAGCTGAACGACAGAGTG GACTCCAGACGGTCCCTGTGGGACCAGGGCAAC TTTCCACTGATCATCAAGAACCTGAAGCCTGAG GACTCCGACACCTACATCTGCGAGGTGGAAGAT CAGAAAGAAGAGGTGCAGCTGGTCGTCGTCGGC GGCTCTGATAAGACCCATACCTGTCCTCCATGT CCTGCTCCAGAAGCTGCTGGCGGCCCTTCCGTG TTTCTGTTCCCTCCAAAGCCTAAGGACACCCTG ATGATCTCTCGGACCCCTGAAGTGACCTGCGTG GTGGTGGATGTGTCTCACGAGGATCCCGAAGTG AAGTTCAATTGGTACGTGGACGGCGTGGAAGTG CACAACGCCAAGACCAAGCCTAGAGAGGAACAG TACAACTCCACCTACAGAGTGGTGTCCGTGCTG ACCGTGCTGCACCAGGATTGGCTGAACGGCAAA GAGTACAAGTGCAAGGTGTCCAACAAGGCCCTG CCTGCCTCCATCGAAAAGACCATCTCCAAGGCC	SEQ ID NO: 1005 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCT ATGAACTGGGTCCGACAGGCCCCTGGCAAAGGA CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC AACAACTACGCCACCTACTACGCCGACTCCGTG AAGGGCAGATTCACCATCTCTCGGGACGACTCC AAGAACTCCCTGTACCTGCAGATGAACAGCCTG CGGACCGAGGATACCGCCGTGTACTATTGTGTG CGGCACGGCAACTTCGGCCACTCCTATGTGTCT TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC ACAGTTTCTTCCGCCTCCACCAAGGGACCCAGC GTTTTCCCTCTGGCTCCATCCTCCAAGTCTACC TCTGGCGGAACATGGAACTCTGGCGCTCTGACA TCTGGCGTGCACACCTTTCCAGCTGTGCTGCAG TCCTCCGGCCTGTACTCTCTGTCCTCTGTCGTG ACCGTGCCTTCCAGCTCTCTGGGAACCCAGACC TACATCTGCAATGTGAACCACAAGCCTTCCAAC ACCAAGGTGGACAAGAAGGTGGAACCCAAGTCC TGCGACAAGACCCACACCTGTCCTCCATGTCCT	SEQ ID NO: 1000 CAGGCCGTGGTCACCC AAGAGCCTAGCCTGAC AGTTTCTCCTGGCGGC ACCGTGACACTGACCT GTGGATCTTCTACCGG CGCTGTGACCACCGGC CACTACGCTAATTGGG TGCAGCAGAAGCCTGG ACAGGCTCCCAGAGGA CTGATCGGCGGCACCT CTAATAGAGCACCTGG CGTGCCAGCCAGATTC TCCGGATCTCTGCTTG GCGGAAAGGCCGCTCT GACAATCTCTGGTGCT CAGCCTGAGGACGAGG CCGAGTACTATTGTGC CCTGTGGTACTCCAAC AGATGGGTGTTCGGCG GAGGCACCAAGCTGAC

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	AAGGGCCAGCCTAGGGAACCCCAGGTTTACACC CTGCCACCTAGCCGGGAAGAGATGACCAAGAAC CAGGTGTCCCTGTCCTGTGCCGTGAAGGGCTTC TACCCTTCCGATATCGCCGTGGAATGGGAGAGC AATGGCCAGCCTGAGAACAACTACAAGACCACA CCTCCTGTGCTGGACAGCGACGGCTCATTCTTC CTGGTGTCTAAGCTGACAGTGGACAAGTCCAGA TGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTG ATGCACGAGGCCCTGCACAACAGATACACCCAG AAGTCCCTGAGCCTGTCTCCTGGCAAA	GCTCCAGAAGCTGCTGGCGGCCCTTCCGTGTTT CTGTTCCCTCCAAAGCCTAAGGACACCCTGTAC ATCACCCGCGAGCCTGAAGTGACCTGCGTGGTG GTGGATGTGTCTCACGAGGACCCCGAAGTGAAG TTCAATTGGTACGTGGACGGCGTGGAAGTGCAC AACGCCAAGACCAAGCCTAGAGAGGAACAGTAC AACTCCACCTACAGAGTGGTGTCCGTGCTGACC GTGCTGCACCAGGATTGGCTGAACGGCAAAGAG TACAAGTGCAAGGTGTCCAACAAGGCCCTGCCT GCCTCCATCGAAAAGACCATCTCCAAGGCCAAG GGCCAGCCTAGGGAACCCCAGGTTTACACCCTG CCACCTAGCCGGGAAGAGATGACCAAGAACCAG GTGTCCCTGTGGTGCCTGGTTAAGGGCTTCTAC CCCTCCGATATCGCCGTGGAATGGGAGTCTAAT GGCCAGCCTGAGAACAACTACAAGACAACCCCT CCTGTGCTGGACTCCGACGGCTCATTCTTCCTG TACTCCAAGCTGACAGTGGACAAGTCCAGATGG CAGCAGGGCAACGTGTTCTCCTGCTCCGTGATG CACGAGGCCCTGCACAATCACTACACCCAGAAG TCCCTGTCTCTGAGCCCTGGCAAG	AGTTCTGGGACAGCCT AAGGCTGCCCCTTCCG TGACTCTGTTCCCTCC ATCCTCTGAGGAACTG CAGGCCAACAAGGCTA CCCTCGTGTGCCTGAT CTCCGACTTTTACCCT GGCGCCGTGACCGTGG CTTGGAAGGCTGATAG TTCTCCTGTGAAGGCC GGCGTGGAAACCACCA CACCTAGCAAGCAGTC CAACAACAAATACGCC GCCTCCTCCTACCTGT CTCTGACCCCTGAACA GTGGAAGTCCCACCGG TCCTACAGCTGCCAAG TGACCCATGAGGGCTC CACCGTGGAAAAGACA GTGGCCCCTACCGAGT GCTCT
434 **hCD4 D1.22 Fc**	SEQ ID NO: 1006 AAGAAAGTGGTGTACGGCAAAAAGGGCGACACC GTGGAACTGACCTGTACCGCCAGCCAGAAGAAG AACATCCAGTTCCACTGGAAGAACTCCAACCAG	SEQ ID NO: 1002 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCC	SEQ ID NO: 997 CAAGCTGTTGTGACAC AAGAGCCCAGCCTGAC AGTGTCTCCTGGCGGA

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
AAS+SAV+YTE/huSP34.3.13 AAS+W+YTE	ATCAAGATCCTGGGCAACCAGGGCAGCTTCCTG	ATGAACTGGGTCCGACAGGCTCCTGGCAAAGGC	ACAGTGACACTGACCT
	ACCAAGGGACCTTCCAAGCTGAACGACAGAGTG	CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC	GTGGATCTTCTACAGG
	GACTCCAGACGGTCCCTGTGGGACCAGGGCAAC	AACAATTACGCCACCTACTACGCCGACTCCGTG	CGCCGTGACAACCGGC
	TTTCCACTGATCATCAAGAACCTGAAGCCTGAG	AAGGGCAGATTCACCATCTCTCGGGACGACTCC	CACTATGCTAATTGGG
	GACTCCGACACCTACATCTGCGAGGTGGAAGAT	AAGAACTCCCTGTACCTGCAGATGAACAGCCTG	TGCAGCAGAAACCCGG
	CAGAAAGAAGAGGTGCAGCTGGTCGTCGTCGGA	CGGACCGAGGATACCGCCGTGTACTATTGTGTG	ACAGGCCCCTAGAGGA
	GGATCTGACAAGACCCACACCTGTCCTCCATGT	CGGCACGGCAACTTCGGCCACTCCTATGTGTCT	CTGATCGGCGGAACAT
	CCTGCTCCAGAAGCTGCTGGCGGCCCTTCCGTG	TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC	CTAATAGAGCCCCTGG
	TTTCTGTTCCCTCCAAAGCCTAAGGACACCCTG	ACAGTTTCTTCCGCTAGCACCAAGGGCCCCTCC	CGTGCCAGCCAGATTT
	TACATCACCCGCGAGCCTGAAGTGACCTGCGTG	GTGTTTCCACTGGCTCCTAGCAGCAAGAGCACA	TCTGGATCTCTGCTCG
	GTGGTGGATGTGTCCCACGAGGATCCCGAAGTG	AGCGGAGGAACAGCCGCTCTGGGCTGTCTGGTC	GAGGCAAGGCCGCTCT
	AAGTTCAATTGGTACGTGGACGGCGTGGAAGTG	AAGGACTACTTTCCCGAGCCTGTGACCGTGTCC	GACAATTTCTGGCGCC
	CACAACGCCAAGACCAAGCCTAGAGAGGAACAG	TGGAATTCTGGCGCTCTGACAAGCGGCGTGCAC	CAGCCAGAGGATGAGG
	TACAACAGCACCTACAGAGTGGTGTCCGTGCTG	ACCTTTCCAGCTGTGCTGCAAAGCAGCGGCCTG	CCGAGTATTATTGTGC
	ACCGTGCTGCACCAGGATTGGCTGAACGGCAAA	TACTCTCTGAGCAGCGTGGTCACAGTGCCAAGC	CCTGTGGTACAGCAAC
	GAGTACAAGTGCAAGGTGTCCAACAAGGCCCTG	TCTAGCCTGGGCACCCAGACCTACATCTGCAAT	AGATGGGTGTTCGGCG
	CCTGCCAGCATCGAGAAAACCATCAGCAAGGCC	GTGAACCACAAGCCTAGCAACACCAAGGTGGAC	GAGGCACCAAACTGAC
	AAGGGCCAGCCTAGGGAACCCCAGGTTTACACA	AAGAAGGTGGAACCCAAGAGCTGCGACAAGACC	AGTGCTGGGACAACCT
	CTGCCTCCAAGCCGGGAAGAGATGACCAAGAAC	CACACCTGTCCTCCATGTCCTGCTCCAGAAGCT	AAGGCTGCCCCTAGCG
	CAGGTGTCCCTGAGCTGTGCCGTGAAGGGCTTC	GCTGGCGGCCCTTCTGTGTTCCTGTTTCCTCCA	TGACACTGTTTCCTCC
	TACCCTTCCGATATCGCCGTGGAATGGGAGAGC	AAGCCTAAGGACACCCTGTACATCACCCGCGAG	AAGCTCTGAGGAACTC
	AATGGCCAGCCTGAGAACAACTACAAGACAACC	CCTGAAGTGACCTGTGTGGTGGTGGATGTGTCC	CAGGCCAACAAGGCCA
	CCTCCTGTGCTGGACAGCGACGGCTCATTCTTC	CACGAGGACCCCGAAGTGAAGTTCAATTGGTAC	CACTCGTGTGCCTGAT
	CTGGTGTCCAAGCTGACAGTGGACAAGTCCAGA	GTGGACGGCGTGGAAGTGCACAACGCCAAGACC	CAGCGATTTTTACCCT
	TGGCAGCAGGGCAACGTGTTCAGCTGCAGCGTG	AAGCCTAGAGAGGAACAGTACAACAGCACCTAC	GGCGCTGTGACAGTGG

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	ATGCACGAGGCCCTGCACAACCACTACACCCAG AAGTCCCTGTCTCTGAGCCCCGGCAAA	AGAGTGGTGTCCGTGCTGACCGTGCTGCACCAG GATTGGCTGAACGGCAAAGAGTACAAGTGCAAG GTGTCCAACAAGGCCCTGCCTGCCAGCATCGAG AAAACCATCAGCAAGGCCAAGGGCCAGCCTAGG GAACCCCAGGTTTACACACTGCCTCCAAGCCGG GAAGAGATGACCAAGAACCAGGTGTCCCTGTGG TGCCTCGTGAAGGGCTTCTACCCTTCCGATATC GCCGTGGAATGGGAGAGCAATGGCCAGCCTGAG AACAACTACAAGACAACCCCTCCTGTGCTGGAC AGCGACGGCTCATTCTTCCTGTACAGCAAGCTG ACAGTGGACAAGTCCAGATGGCAGCAGGGCAAC GTGTTCAGCTGCAGCGTGATGCACGAGGCCCTG CACAACCACTACACCCAGAAGTCCCTGAGCCTG TCTCCTGGCAAA	CCTGGAAGGCTGATAG CTCTCCTGTGAAAGCC GGCGTGGAAACCACCA CACCTAGCAAGCAGAG CAACAACAAATACGCC GCCAGCAGCTACCTGA GCCTGACACCTGAGCA GTGGAAGTCCCACAGA TCCTACAGCTGCCAAG TGACCCACGAGGGCAG CACCGTGGAAAAAACA GTGGCCCCTACCGAGT GCAGC
435 **hCD4 D1.22 Fc AAS+S AV+YT E/huS P34.3 .13 AAS+W +YTE**	SEQ ID NO: 1007 AAAAAGGTGGTGTACGGCAAGAAGGGCGACACC GTCGAGCTGACCTGTACCGCCTCTCAGAAGAAG AACATCCAGTTCCACTGGAAGAACTCCAACCAG ATCAAGATCCTGGGCAACCAGGGCAGCTTCCTG ACCAAGGGACCTTCCAAGCTGAACGACAGAGTG GACTCCAGACGGTCCCTGTGGGACCAGGGCAAC TTTCCACTGATCATCAAGAACCTGAAGCCTGAG GACTCCGACACCTACATCTGCGAGGTGGAAGAT CAGAAAGAAGAGGTGCAGCTGGTCGTCGTCGGC GGCTCTGATAAGACCCATACCTGTCCTCCATGT	SEQ ID NO: 1093 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCT ATGAACTGGGTCCGACAGGCCCCTGGCAAAGGA CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC AACAACTACGCCACCTACTACGCCGACTCCGTG AAGGGCAGATTCACCATCTCTCGGGACGACTCC AAGAACTCCCTGTACCTGCAGATGAACAGCCTG CGGACCGAGGATACCGCCGTGTACTATTGTGTG CGGCACGGCAACTTCGGCCACTCCTATGTGTCT	SEQ ID NO: 1000 CAGGCCGTGGTCACCC AAGAGCCTAGCCTGAC AGTTTCTCCTGGCGGC ACCGTGACACTGACCT GTGGATCTTCTACCGG CGCTGTGACCACCGGC CACTACGCTAATTGGG TGCAGCAGAAGCCTGG ACAGGCTCCCAGAGGA CTGATCGGCGGCACCT

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	CCTGCTCCAGAAGCTGCTGGCGGCCCTTCCGTG	TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC	CTAATAGAGCACCTGG
	TTTCTGTTCCCTCCAAAGCCTAAGGACACCCTG	ACAGTTTCTTCCGCCTCCACCAAGGGACCCAGC	CGTGCCAGCCAGATTC
	TACATCACCCGCGAGCCTGAAGTGACCTGCGTG	GTTTTCCCTCTGGCTCCATCCTCCAAGTCTACC	TCCGGATCTCTGCTTG
	GTGGTGGATGTGTCTCACGAGGACCCCGAAGTG	TCTGGCGGAACAGCTGCTCTGGGCTGCCTGGTC	GCGGAAAGGCCGCTCT
	AAGTTCAATTGGTACGTGGACGGCGTGGAAGTG	AAGGACTACTTTCCTGAGCCTGTGACCGTGTCC	GACAATCTCTGGTGCT
	CACAACGCCAAGACCAAGCCTAGAGAGGAACAG	TGGAACTCTGGCGCTCTGACATCTGGCGTGCAC	CAGCCTGAGGACGAGG
	TACAACTCCACCTACAGAGTGGTGTCCGTGCTG	ACCTTTCCAGCTGTGCTGCAGTCCTCCGGCCTG	CCGAGTACTATTGTGC
	ACCGTGCTGCACCAGGATTGGCTGAACGGCAAA	TACTCTCTGTCCTCTGTCGTGACCGTGCCTTCC	CCTGTGGTACTCCAAC
	GAGTACAAGTGCAAGGTGTCCAACAAGGCCCTG	AGCTCTCTGGGAACCCAGACCTACATCTGCAAT	AGATGGGTGTTCGGCG
	CCTGCCTCCATCGAAAAGACCATCTCCAAGGCC	GTGAACCACAAGCCTTCCAACACCAAGGTGGAC	GAGGCACCAAGCTGAC
	AAGGGCCAGCCTAGGGAACCCCAGGTTTACACC	AAGAAGGTGGAACCCAAGTCCTGCGACAAGACC	AGTTCTGGGACAGCCT
	CTGCCACCTAGCCGGGAAGAGATGACCAAGAAC	CACACCTGTCCTCCATGTCCTGCTCCAGAAGCT	AAGGCTGCCCCTTCCG
	CAGGTGTCCCTGTCCTGTGCCGTGAAGGGCTTC	GCTGGCGGCCCTTCCGTGTTTCTGTTCCCTCCA	TGACTCTGTTCCCTCC
	TACCCTTCCGATATCGCCGTGGAATGGGAGAGC	AAGCCTAAGGACACCCTGTACATCACCCGCGAG	ATCCTCTGAGGAACTG
	AATGGCCAGCCTGAGAACAACTACAAGACCACA	CCTGAAGTGACCTGCGTGGTGGTGGATGTGTCT	CAGGCCAACAAGGCTA
	CCTCCTGTGCTGGACAGCGACGGCTCATTCTTC	CACGAGGACCCCGAAGTGAAGTTCAATTGGTAC	CCCTCGTGTGCCTGAT
	CTGGTGTCTAAGCTGACAGTGGACAAGTCCAGA	GTGGACGGCGTGGAAGTGCACAACGCCAAGACC	CTCCGACTTTTACCCT
	TGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTG	AAGCCTAGAGAGGAACAGTACAACTCCACCTAC	GGCGCCGTGACCGTGG
	ATGCACGAGGCCCTGCACAATCACTACACCCAG	AGAGTGGTGTCCGTGCTGACCGTGCTGCACCAG	CTTGGAAGGCTGATAG
	AAGTCCCTGAGCCTGTCTCCTGGCAAA	GATTGGCTGAACGGCAAAGAGTACAAGTGCAAG	TTCTCCTGTGAAGGCC
		GTGTCCAACAAGGCCCTGCCTGCCTCCATCGAA	GGCGTGGAAACCACCA
		AAGACCATCTCCAAGGCCAAGGGCCAGCCTAGG	CACCTAGCAAGCAGTC
		GAACCCCAGGTTTACACCCTGCCACCTAGCCGG	CAACAACAAATACGCC
		GAAGAGATGACCAAGAACCAGGTGTCCCTGTGG	GCCTCCTCCTACCTGT
		TGCCTGGTTAAGGGCTTCTACCCCTCCGATATC	CTCTGACCCCTGAACA

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
		GCCGTGGAATGGGAGTCTAATGGCCAGCCTGAG AACAACTACAAGACAACCCCTCCTGTGCTGGAC TCCGACGGCTCATTCTTCCTGTACTCCAAGCTG ACAGTGGACAAGTCCAGATGGCAGCAGGGCAAC GTGTTCTCCTGCTCCGTGATGCACGAGGCCCTG CACAATCACTACACCCAGAAGTCCCTGTCTCTG AGCCCTGGCAAG	GTGGAAGTCCCACCGG TCCTACAGCTGCCAAG TGACCCATGAGGGCTC CACCGTGGAAAAGACA GTGGCCCCTACCGAGT GCTCT
436 **hCD4 D1.22 Fc AAS+W +YTE/ huSP3 4.40. 13 AAS+S AV+R**	SEQ ID NO: 998 AAAAAGGTGGTGTACGGCAAGAAGGGCGACACC GTCGAGCTGACCTGTACCGCCTCTCAGAAGAAG AACATCCAGTTCCACTGGAAGAACTCCAACCAG ATCAAGATCCTGGGCAACCAGGGCAGCTTCCTG ACCAAGGGACCTTCCAAGCTGAACGACAGAGTG GACTCCAGACGGTCCCTGTGGGACCAGGGCAAC TTTCCACTGATCATCAAGAACCTGAAGCCTGAG GACTCCGACACCTACATCTGCGAGGTGGAAGAT CAGAAAGAAGAGGTGCAGCTGGTCGTCGTCGGC GGCTCTGATAAGACCCATACCTGTCCTCCATGT CCTGCTCCAGAAGCTGCTGGCGGCCCTTCCGTG TTTCTGTTCCCTCCAAAGCCTAAGGACACCCTG TACATCACCCGCGAGCCTGAAGTGACCTGCGTG GTGGTGGATGTGTCTCACGAGGACCCCGAAGTG AAGTTCAATTGGTACGTGGACGGCGTGGAAGTG CACAACGCCAAGACCAAGCCTAGAGAGGAACAG TACAACTCCACCTACAGAGTGGTGTCCGTGCTG	SEQ ID NO: 1008 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCT ATGAACTGGGTCCGACAGGCCCCTGGCAAAGGA CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC AACAACTACGCCGCCTACTACGCCGACTCCGTG AAGTCCAGATTCACCATCTCTCGGGACGACTCC AAGAACTCCCTGTACCTGCAGATGAACAGCCTG CGGACCGAGGATACCGCCGTGTACTATTGTGTG CGGCACGGCAACTTCGGCCACTCCTATGTGTCT TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC ACAGTTTCTTCCGCCTCCACCAAGGGACCCAGC GTTTTCCCTCTGGCTCCATCCTCCAAGTCTACC TCTGGCGGAACAGCTGCTCTGGGCTGCCTGGTC AAGGACTACTTTCCTGAGCCTGTGACCGTGTCC TGGAACTCTGGCGCTCTGACATCTGGCGTGCAC ACCTTTCCAGCTGTGCTGCAGTCCTCCGGCCTG	SEQ ID NO: 1000 CAGGCCGTGGTCACCC AAGAGCCTAGCCTGAC AGTTTCTCCTGGCGGC ACCGTGACACTGACCT GTGGATCTTCTACCGG CGCTGTGACCACCGGC CACTACGCTAATTGGG TGCAGCAGAAGCCTGG ACAGGCTCCCAGAGGA CTGATCGGCGGCACCT CTAATAGAGCACCTGG CGTGCCAGCCAGATTC TCCGGATCTCTGCTTG GCGGAAAGGCCGCTCT GACAATCTCTGGTGCT CAGCCTGAGGACGAGG CCGAGTACTATTGTGC

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	ACCGTGCTGCACCAGGATTGGCTGAACGGCAAA GAGTACAAGTGCAAGGTGTCCAACAAGGCCCTG CCTGCCTCCATCGAAAAGACCATCTCCAAGGCC AAGGGCCAGCCTAGGGAACCCCAGGTTTACACC CTGCCACCTAGCCGGGAAGAGATGACCAAGAAC CAGGTGTCACTGTGGTGCCTGGTCAAGGGCTTC TACCCCTCTGATATCGCCGTGGAATGGGAGAGC AATGGCCAGCCTGAGAACAACTACAAGACCACA CCTCCTGTGCTGGACAGCGACGGCTCATTCTTC CTGTACAGCAAGCTGACAGTGGACAAGTCCAGA TGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTG ATGCACGAGGCCCTGCACAATCACTACACCCAG AAGTCCCTGTCTCTGTCCCCTGGCAAA	TACTCTCTGTCCTCTGTCGTGACCGTGCCTTCC AGCTCTCTGGGAACCCAGACCTACATCTGCAAT GTGAACCACAAGCCTTCCAACACCAAGGTGGAC AAGAAGGTGGAACCCAAGTCCTGCGACAAGACC CACACCTGTCCTCCATGTCCTGCTCCAGAAGCT GCTGGCGGCCCTTCCGTGTTTCTGTTCCCTCCA AAGCCTAAGGACACCCTGATGATCTCTCGGACC CCTGAAGTGACCTGCGTGGTGGTGGATGTGTCT CACGAGGATCCCGAAGTGAAGTTCAATTGGTAC GTGGACGGCGTGGAAGTGCACAACGCCAAGACC AAGCCTAGAGAGGAACAGTACAACTCCACCTAC AGAGTGGTGTCCGTGCTGACCGTGCTGCACCAG GATTGGCTGAACGGCAAAGAGTACAAGTGCAAG GTGTCCAACAAGGCCCTGCCTGCCTCCATCGAA AAGACCATCTCCAAGGCCAAGGGCCAGCCTAGG GAACCCCAGGTTTACACCCTGCCACCTAGCCGG GAAGAGATGACCAAGAACCAGGTGTCCCTGTCC TGTGCCGTGAAGGGCTTCTACCCTTCCGATATC GCCGTGGAATGGGAGAGCAATGGCCAGCCTGAG AACAACTACAAGACAACCCCTCCTGTGCTGGAC TCCGACGGCTCATTCTTCCTGGTGTCCAAGCTG ACAGTGGACAAGTCCAGGTGGCAGCAGGGCAAC GTGTTCTCCTGCTCTGTGATGCACGAGGCCCTG CACAACCGGTACACCCAGAAGTCTCTGTCTCTG AGCCCTGGCAAG	CCTGTGGTACTCCAAC AGATGGGTGTTCGGCG GAGGCACCAAGCTGAC AGTTCTGGGACAGCCT AAGGCTGCCCCTTCCG TGACTCTGTTCCCTCC ATCCTCTGAGGAACTG CAGGCCAACAAGGCTA CCCTCGTGTGCCTGAT CTCCGACTTTTACCCT GGCGCCGTGACCGTGG CTTGGAAGGCTGATAG TTCTCCTGTGAAGGCC GGCGTGGAAACCACCA CACCTAGCAAGCAGTC CAACAACAAATACGCC GCCTCCTCCTACCTGT CTCTGACCCCTGAACA GTGGAAGTCCCACCGG TCCTACAGCTGCCAAG TGACCCATGAGGGCTC CACCGTGGAAAAGACA GTGGCCCCTACCGAGT GCTCT

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
437 hCD4 D1.22 Fc AAS+W +YTE/ huSP3 4.41. 13 AAS+S AV+R	SEQ ID NO: 998	SEQ ID NO: 1009	SEQ ID NO: 1000
	AAAAAGGTGGTGTACGGCAAGAAGGGCGACACC	GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG	CAGGCCGTGGTCACCC
	GTCGAGCTGACCTGTACCGCCTCTCAGAAGAAG	GTTCAGCCTGGCGGCTCTCTGTCTCTGTCTTGT	AAGAGCCTAGCCTGAC
	AACATCCAGTTCCACTGGAAGAACTCCAACCAG	GCCGCTTCTGGCTTCACCTTCAACACCTACGCT	AGTTTCTCCTGGCGGC
	ATCAAGATCCTGGGCAACCAGGGCAGCTTCCTG	ATGAACTGGGTCCGACAGGCCCCTGGCAAAGGA	ACCGTGACACTGACCT
	ACCAAGGGACCTTCCAAGCTGAACGACAGAGTG	CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC	GTGGATCTTCTACCGG
	GACTCCAGACGGTCCCTGTGGGACCAGGGCAAC	AACAACTACGCCACCTACTACGCCGACTCCGTG	CGCTGTGACCACCGGC
	TTTCCACTGATCATCAAGAACCTGAAGCCTGAG	AAGTCCCGGTTCACCATCTCTCGGGACGACTCC	CACTACGCTAATTGGG
	GACTCCGACACCTACATCTGCGAGGTGGAAGAT	AAGAACTCCCTGTACCTGCAGATGAACAGCCTG	TGCAGCAGAAGCCTGG
	CAGAAAGAAGAGGTGCAGCTGGTCGTCGTCGGC	CGGACCGAGGATACCGCCGTGTACTATTGTGTG	ACAGGCTCCCAGAGGA
	GGCTCTGATAAGACCCATACCTGTCCTCCATGT	CGGCACGGCAACTTCGGCCACTCCTATGTGTCT	CTGATCGGCGGCACCT
	CCTGCTCCAGAAGCTGCTGGCGGCCCTTCCGTG	TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC	CTAATAGAGCACCTGG
	TTTCTGTTCCCTCCAAAGCCTAAGGACACCCTG	ACAGTTTCTTCCGCCTCCACCAAGGGACCCAGC	CGTGCCAGCCAGATTC
	TACATCACCCGCGAGCCTGAAGTGACCTGCGTG	GTTTTCCCTCTGGCTCCATCCTCCAAGTCTACC	TCCGGATCTCTGCTTG
	GTGGTGGATGTGTCTCACGAGGACCCCGAAGTG	TCTGGCGGAACAGCTGCTCTGGGCTGCCTGGTC	GCGGAAAGGCCGCTCT
	AAGTTCAATTGGTACGTGGACGGCGTGGAAGTG	AAGGACTACTTTCCTGAGCCTGTGACCGTGTCC	GACAATCTCTGGTGCT
	CACAACGCCAAGACCAAGCCTAGAGAGGAACAG	TGGAACTCTGGCGCTCTGACATCTGGCGTGCAC	CAGCCTGAGGACGAGG
	TACAACTCCACCTACAGAGTGGTGTCCGTGCTG	ACCTTTCCAGCTGTGCTGCAGTCCTCCGGCCTG	CCGAGTACTATTGTGC
	ACCGTGCTGCACCAGGATTGGCTGAACGGCAAA	TACAGTCTGTCCTCTGTCGTGACCGTGCCTTCC	CCTGTGGTACTCCAAC
	GAGTACAAGTGCAAGGTGTCCAACAAGGCCCTG	AGCTCTCTGGGAACCCAGACCTACATCTGCAAT	AGATGGGTGTTCGGCG
	CCTGCCTCCATCGAAAAGACCATCTCCAAGGCC	GTGAACCACAAGCCTTCCAACACCAAGGTGGAC	GAGGCACCAAGCTGAC
	AAGGGCCAGCCTAGGGAACCCCAGGTTTACACC	AAGAAGGTGGAACCCAAGTCCTGCGACAAGACC	AGTTCTGGGACAGCCT
	CTGCCACCTAGCCGGGAAGAGATGACCAAGAAC	CACACCTGTCCTCCATGTCCTGCTCCAGAAGCT	AAGGCTGCCCCTTCCG
	CAGGTGTCACTGTGGTGCCTGGTCAAGGGCTTC	GCTGGCGGCCCTTCCGTGTTTCTGTTCCCTCCA	TGACTCTGTTCCCTCC
	TACCCCTCTGATATCGCCGTGGAATGGGAGAGC	AAGCCTAAGGACACCCTGATGATCTCTCGGACC	ATCCTCTGAGGAACTG

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	AATGGCCAGCCTGAGAACAACTACAAGACCACA CCTCCTGTGCTGGACAGCGACGGCTCATTCTTC CTGTACAGCAAGCTGACAGTGGACAAGTCCAGA TGGCAGCAGGGCAACGTGTTCTCCTGCTCCGTG ATGCACGAGGCCCTGCACAATCACTACACCCAG AAGTCCCTGTCTCTGTCCCCTGGCAAA	CCTGAAGTGACCTGCGTGGTGGTGGATGTGTCT CACGAGGATCCCGAAGTGAAGTTCAATTGGTAC GTGGACGGCGTGGAAGTGCACAACGCCAAGACC AAGCCTAGAGAGGAACAGTACAACTCCACCTAC AGAGTGGTGTCCGTGCTGACCGTGCTGCACCAG GATTGGCTGAACGGCAAAGAGTACAAGTGCAAG GTGTCCAACAAGGCCCTGCCTGCCTCCATCGAA AAGACCATCTCCAAGGCCAAGGGCCAGCCTAGG GAACCCCAGGTTTACACCCTGCCACCTAGCCGG GAAGAGATGACCAAGAACCAGGTGTCCCTGTCC TGCGCCGTGAAGGGCTTCTACCCTTCTGATATC GCCGTGGAATGGGAGAGCAACGGCCAGCCTGAG AACAACTACAAGACAACCCCTCCTGTGCTGGAC TCCGACGGCTCATTCTTCCTGGTGTCCAAGCTG ACAGTGGACAAGTCTAGATGGCAGCAGGGCAAC GTGTTCTCCTGCTCCGTGATGCACGAGGCCCTG CACAACAGATACACCCAGAAGTCCCTGTCTCTG AGCCCCGGAAAA	CAGGCCAACAAGGCTA CCCTCGTGTGCCTGAT CTCCGACTTTTACCCT GGCGCCGTGACCGTGG CTTGGAAGGCTGATAG TTCTCCTGTGAAGGCC GGCGTGGAAACCACCA CACCTAGCAAGCAGTC CAACAACAAATACGCC GCCTCCTCCTACCTGT CTCTGACCCCTGAACA GTGGAAGTCCCACCGG TCCTACAGCTGCCAAG TGACCCATGAGGGCTC CACCGTGGAAAAGACA GTGGCCCCTACCGAGT GCTCT
438 **h3BNC 117.5 2.64 AAS+ SAV+Y TE/hu**	SEQ ID NO: 1010 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCC ATGAACTGGGTCCGACAGGCTCCTGGCAAAGGC CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC AACAATTACGCCACCTACTACGCCGACTCCGTG	SEQ ID NO: 1011 CAGGTGCAGCTGCTGCAGTCTGGCGCCGCTGTG ACAAAACCAGGCGCTTCTGTGCGGGTGTCCTGC GAGGCCAGCGGCTACAACATCCGGGACTACTTC ATTCACTGGTGGCGCCAGGCCCCTGGACAGGGA CTGCAGTGGGTGGGATGGATCAACCCCAAGACC GGCCAGCCCAACAACCCCAGACAGTTCCAGGGC	SEQ ID NO: 1012 GATATTCAGATGACAC AGAGCCCCAGTAGCCT GAGCGCCAGCGTGGGC GACACCGCAACCATCA CCTGTCAGGCCAACGG CTATCTGAACTGGTAT

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
SP34.3.13 scFv AAS+W +YTE	AAGGGCAGATTCACCATCTCTCGGGACGACTCC	AGAGTGTCCCTGACCAGACACGCCAGCTTCGAC	CAACAGAGGAGGGGCA
	AAGAACTCCCTGTACCTGCAGATGAACAGCCTG	TTCGACACCTTCAGCTTCTACATGGACCTGAAG	AGGCCCCCAAGCTCCT
	CGGACCGAGGATACCGCCGTGTACTATTGTGTG	GCCCTGCGGAGCGACGATACCGCCGTGTACTTC	GATATACGACGGCAGC
	CGGCACGGCAACTTCGGCCACTCCTATGTGTCT	TGCGCCAGACAGAGAAGCGACTACTGGGATTTC	AAGCTGGAGAGGGGCG
	TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC	GACGTGTGGGGCAGCGGCACCCAAGTGACCGTG	TTCCCAGCCGCTTCAG
	ACAGTTTCTTCCGGCGGAGGTGGAAGCGGAGGC	TCATCTGCCTCTACAAAGGGCCCTAGTGTGTTC	CGGCAGGAGGTGGGGC
	GGAGGTAGTGGCGGTGGTGGTTCAGGTGGTGGT	CCTCTGGCTCCCAGCAGCAAGTCTACATCTGGC	CAGGAGTACAACCTTA
	GGATCTCAGGCTGTGGTTACCCAGGAGCCTAGC	GGAACAGCCGCTCTGGGCTGCCTGGTCAAGGAT	CAATCAACAACCTGCA
	CTGACAGTTTCTCCTGGCGGCACCGTGACACTG	TACTTTCCCGAGCCTGTGACCGTGTCCTGGAAT	GCCCGAGGACATCGCC
	ACCTGTGGATCTTCTACCGGCGCTGTGACCACC	TCTGGCGCTCTGACAAGCGGCGTGCACACCTTT	ACCTATTTCTGCCAAG
	GGCCATTACGCTAATTGGGTGCAGCAGAAGCCT	CCAGCTGTGCTGCAAAGCAGCGGCCTGTACTCT	TTTACGAGTTCGTGGT
	GGACAGGCCCCAAGAGGACTGATCGGCGGCACA	CTGAGCAGCGTGGTCACAGTGCCTAGCTCTAGC	GCCCGGCACCAGGCTG
	TCTAACAGAGCCCCTGGCGTCCCAGCCAGATTC	CTGGGCACCCAGACCTACATCTGCAATGTGAAC	GACCTGAAGCGGACCG
	TCTGGATCTCTGCTTGGCGGCAAGGCCGCTCTG	CACAAGCCTAGCAACACCAAGGTGGACAAGAAG	TGGCCGCCCCCAGCGT
	ACAATTTCTGGTGCTCAGCCTGAGGACGAGGCC	GTGGAACCCAAGAGCTGCGACAAGACCCACACC	GTTCATCTTCCCTCCC
	GAGTACTACTGTGCCCTGTGGTACTCCAACAGA	TGTCCTCCATGTCCTGCTCCAGAAGCTGCTGGC	AGCGACGAGCAGCTGA
	TGGGTGTTCGGCGGAGGCACCAAGCTGACAGTG	GGCCCTTCCGTGTTTCTGTTCCCTCCAAAGCCT	AGTCTGGCACCGCCAG
	TTGGAGCCCAAATCTTCAGACAAGACCCACACC	AAGGACACCCTGTACATCACCCGCGAGCCTGAA	CGTGGTGTGCCTGCTG
	TGTCCTCCATGTCCTGCTCCAGAAGCTGCTGGC	GTGACCTGCGTGGTGGTGGATGTGTCCCACGAG	AACAACTTCTACCCCC
	GGCCCTTCTGTGTTCCTGTTTCCTCCAAAGCCT	GATCCCGAAGTGAAGTTCAATTGGTACGTGGAC	GCGAGGCCAAGGTGCA
	AAGGACACCCTGTACATCACCCGCGAGCCTGAA	GGCGTGGAAGTGCACAACGCCAAGACCAAGCCT	GTGGAAGGTGGACAAC
	GTGACCTGTGTGGTGGTGGATGTGTCCCACGAG	AGAGAGGAACAGTACAACAGCACCTACAGAGTG	GCCCTGCAGAGCGGCA
	GACCCCGAAGTGAAGTTCAATTGGTACGTGGAC	GTGTCCGTGCTGACCGTGCTGCACCAGGATTGG	ACAGCCAGGAGAGCGT
	GGCGTGGAAGTGCACAACGCCAAGACCAAGCCT	CTGAACGGCAAAGAGTACAAGTGCAAGGTGTCC	GACCGAGCAGGACTCC
	AGAGAGGAACAGTACAACAGCACCTACAGAGTG	AACAAGGCCCTGCCTGCCAGCATCGAGAAAACC	AAGGACAGCACCTACA

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	GTGTCCGTGCTGACCGTGCTGCACCAGGATTGG CTGAACGGCAAAGAGTACAAGTGCAAGGTGTCC AACAAGGCCCTGCCTGCCAGCATCGAGAAAACC ATCAGCAAGGCCAAGGGCCAGCCTAGGGAACCC CAGGTTTACACACTGCCTCCAAGCCGGGAAGAG ATGACCAAGAACCAGGTGTCCCTGTGGTGCCTC GTGAAGGGCTTCTACCCTTCCGATATCGCCGTG GAATGGGAGAGCAATGGCCAGCCTGAGAACAAC TACAAGACAACCCCTCCTGTGCTGGACAGCGAC GGCTCATTCTTCCTGTACAGCAAGCTGACAGTG GACAAGTCCAGATGGCAGCAGGGCAACGTGTTC AGCTGCAGCGTGATGCACGAGGCCCTGCACAAC CACTACACCCAGAAGTCCCTGAGCCTGTCTCCT GGCAAA	ATCAGCAAGGCCAAGGGCCAGCCTAGGGAACCC CAGGTTTACACACTGCCTCCAAGCCGGGAAGAG ATGACCAAGAACCAGGTGTCCCTGAGCTGTGCC GTGAAGGGCTTCTACCCTTCCGATATCGCCGTG GAATGGGAGAGCAATGGCCAGCCTGAGAACAAC TACAAGACAACCCCTCCTGTGCTGGACAGCGAC GGCTCATTCTTCCTGGTGTCCAAGCTGACAGTG GACAAGTCCAGATGGCAGCAGGGCAACGTGTTC AGCTGCAGCGTGATGCACGAGGCCCTGCACAAC CACTACACCCAGAAGTCCCTGTCTCTGAGCCCC GGCAAA	GCCTGAGCAGCACCCT GACCCTGAGCAAGGCC GACTACGAGAAGCACA AGGTGTACGCCTGCGA GGTGACCCACCAGGGA CTGTCTAGCCCCGTGA CCAAGAGCTTCAACCG GGGCGAGTGC
439 **h3BNC 117.5 2.64 AAS+S AV+YT E/huS P34.3 .13 scFv AAS+W +YTE**	SEQ ID NO: 1013 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCT ATGAACTGGGTCCGACAGGCCCCTGGCAAAGGA CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC AACAACTACGCCACCTACTACGCCGACTCCGTG AAGGGCAGATTCACCATCTCTCGGGACGACTCC AAGAACTCCCTGTACCTGCAGATGAACAGCCTG CGGACCGAGGATACCGCCGTGTACTATTGTGTG CGGCACGGCAACTTCGGCCACTCCTATGTGTCT	SEQ ID NO: 1014 CAGGTGCAGCTGTTGCAATCTGGCGCCGCTGTG ACAAAGCCTGGTGCCTCTGTTAGAGTGTCCTGC GAGGCCTCCGGCTACAACATCCGGGACTACTTC ATCCACTGGTGGCGGCAGGCTCCAGGACAGGGA TTGCAATGGGTCGGATGGATCAACCCCAAGACC GGCCAGCCTAACAACCCTAGACAGTTCCAGGGC AGAGTGTCTCTGACCCGGCACGCCTCTTTCGAC TTCGACACCTTCAGCTTCTACATGGACCTGAAG GCCCTGCGGAGCGACGATACCGCCGTGTACTTT TGCGCCAGACAGAGATCCGACTACTGGGACTTC	SEQ ID NO: 1015 GACATCCAGATGACCC AGTCTCCATCCTCTCT GTCCGCCTCTGTGGGC GATACCGCTACCATTA CCTGTCAGGCCAACGG CTACCTGAACTGGTAT CAGCAGCGGAGAGGCA AGGCCCCTAAGCTGCT GATCTACGACGGCTCC AAGCTGGAAAGAGGCG

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC	GACGTGTGGGGCTCTGGCACCCAAGTGACAGTG	TGCCCTCCAGATTCTC
	ACAGTTTCTAGCGGCGGAGGTGGAAGCGGAGGC	TCCTCCGCTTCCACCAAGGGACCCTCTGTGTTT	CGGCAGAAGATGGGGC
	GGAGGTAGTGGTGGTGGCGGATCTGGTGGCGGT	CCTCTGGCTCCCTCCAGCAAGTCTACCTCTGGT	CAAGAGTACAACCTGA
	GGATCTCAGGCTGTGGTCACCCAAGAGCCTAGC	GGAACAGCTGCTCTGGGCTGCCTGGTCAAGGAT	CCATCAACAACCTGCA
	CTGACAGTTTCTCCTGGCGGCACCGTGACACTG	TACTTCCCTGAGCCTGTGACCGTGTCCTGGAAT	GCCTGAGGATATCGCC
	ACCTGTGGATCTTCTACCGGCGCTGTGACCACC	TCTGGCGCTCTGACATCCGGCGTGCACACCTTT	ACATACTTTTGCCAGG
	GGCCACTACGCTAATTGGGTGCAGCAGAAGCCT	CCAGCTGTGCTGCAATCCTCCGGCCTGTACTCT	TGTACGAGTTCGTGGT
	GGACAGGCTCCCAGAGGACTGATCGGCGGCACC	CTGTCCTCCGTCGTGACCGTGCCTTCTAGCTCT	GCCCGGCACAAGACTG
	TCTAATAGAGCACCTGGCGTGCCAGCCAGATTC	CTGGGCACCCAGACCTACATCTGCAATGTGAAC	GACCTGAAGAGAACAG
	TCTGGATCTCTGCTCGGCGGAAAGGCCGCTCTG	CACAAGCCTTCCAACACCAAGGTGGACAAGAAG	TGGCCGCTCCTTCCGT
	ACAATTTCTGGTGCCCAGCCTGAGGACGAGGCC	GTGGAACCCAAGTCCTGCGACAAGACCCACACC	GTTCATCTTCCCACCT
	GAGTATTATTGTGCCCTGTGGTACTCCAACCGC	TGTCCTCCATGTCCTGCTCCAGAAGCTGCTGGC	TCCGACGAGCAGCTGA
	TGGGTTTTCGGCGGAGGCACCAAGCTGACAGTG	GGCCCATCCGTGTTTCTGTTCCCTCCAAAGCCT	AGTCTGGCACAGCCTC
	CTGGAACCTAAGTCCTCCGACAAGACCCACACC	AAGGACACCCTGTACATCACCCGCGAGCCTGAA	TGTCGTGTGCCTGCTG
	TGTCCTCCATGTCCTGCTCCAGAAGCTGCTGGC	GTGACCTGCGTGGTGGTGGATGTGTCTCACGAG	AACAACTTCTACCCTC
	GGCCCTTCCGTGTTTCTGTTCCCTCCAAAGCCT	GACCCCGAAGTGAAGTTCAATTGGTACGTGGAC	GGGAAGCCAAGGTGCA
	AAGGACACCCTGTACATCACCCGCGAGCCTGAA	GGCGTGGAAGTGCACAACGCCAAGACCAAGCCT	GTGGAAGGTGGACAAT
	GTGACCTGCGTGGTGGTCGATGTGTCTCACGAG	AGAGAGGAACAGTACAACTCCACCTACAGAGTG	GCCCTGCAGTCCGGCA
	GACCCCGAAGTGAAGTTCAATTGGTACGTGGAC	GTGTCCGTGCTGACCGTGCTGCACCAGGATTGG	ACTCCCAAGAGTCTGT
	GGCGTGGAAGTGCACAACGCCAAGACCAAGCCT	CTGAACGGCAAAGAGTACAAGTGCAAGGTGTCC	GACCGAGCAGGACTCC
	AGAGAGGAACAGTACAACTCCACCTACAGAGTG	AACAAGGCTCTGCCCGCCTCCATCGAAAAGACC	AAGGACAGCACCTACA
	GTGTCCGTGCTGACCGTGCTGCACCAGGATTGG	ATCTCCAAGGCTAAGGGCCAGCCTCGGGAACCC	GCCTGTCCTCCACACT
	CTGAACGGCAAAGAGTACAAGTGCAAGGTGTCC	CAGGTTTACACATTGCCTCCAAGCCGGGAAGAG	GACCCTGTCCAAGGCC
	AACAAGGCCCTGCCTGCCTCCATCGAAAAGACC	ATGACCAAGAACCAGGTGTCCCTGAGCTGCGCC	GACTACGAGAAGCACA
	ATCTCCAAGGCCAAGGGCCAGCCTAGGGAACCC	GTGAAGGGCTTCTACCCTTCTGATATCGCCGTG	AGGTGTACGCCTGCGA

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	CAGGTTTACACCCTGCCACCTAGCCGGGAAGAG ATGACCAAGAACCAGGTGTCCCTGTGGTGCCTG GTCAAGGGCTTCTACCCTTCCGATATCGCCGTG GAATGGGAGAGCAACGGACAGCCCGAGAACAAC TACAAGACAACCCCTCCTGTGCTGGACTCCGAC GGCTCATTCTTCCTGTACAGCAAGCTGACTGTG GACAAGTCCAGATGGCAGCAGGGCAACGTGTTC TCCTGCTCCGTGATGCACGAGGCCCTGCACAAT CACTACACCCAGAAGTCCCTGTCTCTGAGCCCT GGCAAG	GAATGGGAGTCCAACGGCCAGCCAGAGAACAAC TACAAGACAACCCCTCCTGTGCTGGACTCCGAC GGCTCATTCTTCCTGGTGTCTAAGCTGACAGTG GACAAGTCCAGATGGCAGCAGGGCAACGTGTTC TCCTGCTCCGTGATGCACGAGGCCCTGCACAAT CACTACACCCAGAAGTCCCTGTCTCTGTCCCCT GGCAAA	AGTGACCCATCAGGGC CTGTCTAGCCCTGTGA CCAAGTCTTTCAACCG GGGCGAGTGT
440 **h3BNC 117.5 2.64 AAS+S AV/hu SP34. 3.13s cFv AAS+W**	SEQ ID NO: 1016 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCC ATGAACTGGGTCCGACAGGCTCCTGGCAAAGGC CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC AACAATTACGCCACCTACTACGCCGACTCCGTG AAGGGCAGATTCACCATCTCTCGGGACGACTCC AAGAACTCCCTGTACCTGCAGATGAACAGCCTG CGGACCGAGGATACCGCCGTGTACTATTGTGTG CGGCACGGCAACTTCGGCCACTCCTATGTGTCT TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC ACAGTTTCTTCCGGCGGAGGTGGAAGCGGAGGC GGAGGTAGTGGCGGTGGTGGTTCAGGTGGTGGT GGATCTCAGGCTGTGGTTACCCAGGAGCCTAGC	SEQ ID NO: 1017 CAGGTGCAGCTGCTGCAGTCTGGCGCCGCTGTG ACAAAACCAGGCGCTTCTGTGCGGGTGTCCTGC GAGGCCAGCGGCTACAACATCCGGGACTACTTC ATTCACTGGTGGCGCCAGGCCCCTGGACAGGGA CTGCAGTGGGTGGGATGGATCAACCCCAAGACC GGCCAGCCCAACAACCCCAGACAGTTCCAGGGC AGAGTGTCCCTGACCAGACACGCCAGCTTCGAC TTCGACACCTTCAGCTTCTACATGGACCTGAAG GCCCTGCGGAGCGACGATACCGCCGTGTACTTC TGCGCCAGACAGAGAAGCGACTACTGGGATTTC GACGTGTGGGGCAGCGGCACCCAAGTGACCGTG TCATCTGCCTCTACAAAGGGCCCTAGTGTGTTC CCTCTGGCTCCCAGCAGCAAGTCTACATCTGGC GGAACAGCCGCTCTGGGCTGCCTGGTCAAGGAT	SEQ ID NO: 1012 GATATTCAGATGACAC AGAGCCCCAGTAGCCT GAGCGCCAGCGTGGGC GACACCGCAACCATCA CCTGTCAGGCCAACGG CTATCTGAACTGGTAT CAACAGAGGAGGGGCA AGGCCCCCAAGCTCCT GATATACGACGGCAGC AAGCTGGAGAGGGGCG TTCCCAGCCGCTTCAG CGGCAGGAGGTGGGGC CAGGAGTACAACCTTA CAATCAACAACCTGCA

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	CTGACAGTTTCTCCTGGCGGCACCGTGACACTG	TACTTTCCCGAGCCTGTGACCGTGTCCTGGAAT	GCCCGAGGACATCGCC
	ACCTGTGGATCTTCTACCGGCGCTGTGACCACC	TCTGGCGCTCTGACAAGCGGCGTGCACACCTTT	ACCTATTTCTGCCAAG
	GGCCATTACGCTAATTGGGTGCAGCAGAAGCCT	CCAGCTGTGCTGCAAAGCAGCGGCCTGTACTCT	TTTACGAGTTCGTGGT
	GGACAGGCCCCAAGAGGACTGATCGGCGGCACA	CTGAGCAGCGTGGTCACAGTGCCTAGCTCTAGC	GCCCGGCACCAGGCTG
	TCTAACAGAGCCCCTGGCGTCCCAGCCAGATTC	CTGGGCACCCAGACCTACATCTGCAATGTGAAC	GACCTGAAGCGGACCG
	TCTGGATCTCTGCTTGGCGGCAAGGCCGCTCTG	CACAAGCCTAGCAACACCAAGGTGGACAAGAAG	TGGCCGCCCCCAGCGT
	ACAATTTCTGGTGCTCAGCCTGAGGACGAGGCC	GTGGAACCCAAGAGCTGCGACAAGACCCACACC	GTTCATCTTCCCTCCC
	GAGTACTACTGTGCCCTGTGGTACTCCAACAGA	TGTCCTCCATGTCCTGCTCCAGAAGCTGCTGGC	AGCGACGAGCAGCTGA
	TGGGTGTTCGGCGGAGGCACCAAGCTGACAGTG	GGCCCTTCCGTGTTTCTGTTCCCTCCAAAGCCT	AGTCTGGCACCGCCAG
	TTGGAGCCCAAATCTTCAGACAAGACCCACACC	AAGGACACCCTGATGATCAGCAGAACCCCTGAA	CGTGGTGTGCCTGCTG
	TGTCCTCCATGTCCTGCTCCAGAAGCTGCTGGC	GTGACCTGCGTGGTGGTGGATGTGTCCCACGAG	AACAACTTCTACCCCC
	GGCCCTTCCGTGTTTCTGTTCCCTCCAAAGCCT	GATCCCGAAGTGAAGTTCAATTGGTACGTGGAC	GCGAGGCCAAGGTGCA
	AAGGACACCCTGATGATCAGCAGAACCCCTGAA	GGCGTGGAAGTGCACAACGCCAAGACCAAGCCT	GTGGAAGGTGGACAAC
	GTGACCTGCGTGGTGGTGGATGTGTCCCACGAG	AGAGAGGAACAGTACAACAGCACCTACAGAGTG	GCCCTGCAGAGCGGCA
	GATCCCGAAGTGAAGTTCAATTGGTACGTGGAC	GTGTCCGTGCTGACCGTGCTGCACCAGGATTGG	ACAGCCAGGAGAGCGT
	GGCGTGGAAGTGCACAACGCCAAGACCAAGCCT	CTGAACGGCAAAGAGTACAAGTGCAAGGTGTCC	GACCGAGCAGGACTCC
	AGAGAGGAACAGTACAACAGCACCTACAGAGTG	AACAAGGCCCTGCCTGCCAGCATCGAGAAAACC	AAGGACAGCACCTACA
	GTGTCCGTGCTGACCGTGCTGCACCAGGATTGG	ATCAGCAAGGCCAAGGGCCAGCCTAGGGAACCC	GCCTGAGCAGCACCCT
	CTGAACGGCAAAGAGTACAAGTGCAAGGTGTCC	CAGGTTTACACACTGCCTCCAAGCCGGGAAGAG	GACCCTGAGCAAGGCC
	AACAAGGCCCTGCCTGCCAGCATCGAGAAAACC	ATGACCAAGAACCAGGTGTCCCTGAGCTGTGCC	GACTACGAGAAGCACA
	ATCAGCAAGGCCAAGGGCCAGCCTAGGGAACCC	GTGAAGGGCTTCTACCCTTCCGATATCGCCGTG	AGGTGTACGCCTGCGA
	CAGGTTTACACCCTGCCTCCAAGCCGGGAAGAG	GAATGGGAGAGCAATGGCCAGCCTGAGAACAAC	GGTGACCCACCAGGGA
	ATGACCAAGAACCAGGTGTCCCTGTGGTGCCTG	TACAAGACAACCCCTCCTGTGCTGGACAGCGAC	CTGTCTAGCCCCGTGA
	GTCAAGGGCTTCTACCCTTCCGATATCGCCGTG	GGCTCATTCTTCCTGGTGTCCAAGCTGACAGTG	CCAAGAGCTTCAACCG
	GAATGGGAGAGCAATGGCCAGCCTGAGAACAAC	GACAAGTCCAGATGGCAGCAGGGCAACGTGTTC	GGGCGAGTGC

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	TACAAGACAACCCCTCCTGTGCTGGACAGCGAC GGCTCATTCTTCCTGTACAGCAAGCTGACAGTG GACAAGAGCAGATGGCAGCAGGGCAACGTGTTC AGCTGCAGCGTGATGCACGAGGCCCTGCACAAC CACTACACCCAGAAGTCCCTGAGCCTGTCTCCT GGCAAA	AGCTGCAGCGTGATGCACGAGGCCCTGCACAAC CACTACACCCAGAAGTCCCTGTCTCTGAGCCCC GGCAAA	
441 **h3BNC 117.5 2.64 AAS+W +YTE/ huSP3 4.39. 13scF v AAS+S AV+R**	SEQ ID NO: 1018 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCC ATGAACTGGGTCCGACAGGCTCCTGGCAAAGGC CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC AACAATTACGCCACCTACTACGCCGACTCCGTG AAGAGCAGATTCACCATCTCTCGGGACGACTCC AAGAACTCCCTGTACCTGGAGATGAACAGCCTG CGGACCGAGGATACCGCCGTGTACTATTGTGTG CGGCACGGCAACTTCGGCCACTCCTATGTGTCT TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC ACAGTTTCTTCCGGCGGAGGTGGAAGCGGAGGC GGAGGTAGTGGCGGTGGTGGTTCAGGTGGTGGT GGATCTCAGGCTGTGGTTACCCAGGAGCCTAGC CTGACAGTTTCTCCTGGCGGCACCGTGACACTG ACCTGTGGATCTTCTACCGGCGCTGTGACCACC GGCCATTACGCTAATTGGGTGCAGCAGAAGCCT GGACAGGCCCCAAGAGGACTGATCGGCGGCACA	SEQ ID NO: 1019 CAGGTGCAGCTGCTGCAGTCTGGCGCCGCTGTG ACAAAACCAGGCGCTTCTGTGCGGGTGTCCTGC GAGGCCAGCGGCTACAACATCCGGGACTACTTC ATTCACTGGTGGCGCCAGGCCCCTGGACAGGGA CTGCAGTGGGTGGGATGGATCAACCCCAAGACC GGCCAGCCCAACAACCCCAGACAGTTCCAGGGC AGAGTGTCCCTGACCAGACACGCCAGCTTCGAC TTCGACACCTTCAGCTTCTACATGGACCTGAAG GCCCTGCGGAGCGACGATACCGCCGTGTACTTC TGCGCCAGACAGAGAAGCGACTACTGGGATTTC GACGTGTGGGGCAGCGGCACCCAAGTGACCGTG TCATCTGCTAGCACCAAGGGCCCCTCCGTGTTT CCACTGGCTCCTAGCAGCAAGAGCACAAGCGGA GGAACAGCCGCTCTGGGCTGTCTGGTCAAGGAC TACTTTCCCGAGCCTGTGACCGTGTCCTGGAAT TCTGGCGCTCTGACAAGCGGCGTGCACACCTTT CCAGCTGTGCTGCAAAGCAGCGGCCTGTACTCT CTGAGCAGCGTGGTCACAGTGCCAAGCTCTAGC	SEQ ID NO: 1012 GATATTCAGATGACAC AGAGCCCCAGTAGCCT GAGCGCCAGCGTGGGC GACACCGCAACCATCA CCTGTCAGGCCAACGG CTATCTGAACTGGTAT CAACAGAGGAGGGGCA AGGCCCCCAAGCTCCT GATATACGACGGCAGC AAGCTGGAGAGGGGCG TTCCCAGCCGCTTCAG CGGCAGGAGGTGGGGC CAGGAGTACAACCTTA CAATCAACAACCTGCA GCCCGAGGACATCGCC ACCTATTTCTGCCAAG TTTACGAGTTCGTGGT GCCCGGCACCAGGCTG

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	TCTAACAGAGCCCCTGGCGTCCCAGCCAGATTC TCTGGATCTCTGCTTGGCGGCAAGGCCGCTCTG ACAATTTCTGGTGCTCAGCCTGAGGACGAGGCC GAGTACTACTGTGCCCTGTGGTACTCCAACAGA TGGGTGTTCGGCGGAGGCACCAAGCTGACAGTG TTGGAGCCCAAATCTTCAGACAAGACCCACACC TGTCCTCCATGTCCTGCTCCAGAAGCTGCTGGC GGCCCTTCCGTGTTTCTGTTCCCTCCAAAGCCT AAGGACACCCTGATGATCAGCAGAACCCCTGAA GTGACCTGCGTGGTGGTGGATGTGTCCCACGAG GATCCCGAAGTGAAGTTCAATTGGTACGTGGAC GGCGTGGAAGTGCACAACGCCAAGACCAAGCCT AGAGAGGAACAGTACAACAGCACCTACAGAGTG GTGTCCGTGCTGACCGTGCTGCACCAGGATTGG CTGAACGGCAAAGAGTACAAGTGCAAGGTGTCC AACAAGGCCCTGCCTGCCAGCATCGAGAAAACC ATCAGCAAGGCCAAGGGCCAGCCTAGGGAACCC CAGGTTTACACACTGCCTCCAAGCCGGGAAGAG ATGACCAAGAACCAGGTGTCCCTGAGCTGTGCC GTGAAGGGCTTCTACCCTTCCGATATCGCCGTG GAATGGGAGAGCAATGGCCAGCCTGAGAACAAC TACAAGACAACCCCTCCTGTGCTGGACAGCGAC GGCTCATTCTTCCTGGTGTCCAAGCTGACAGTG GACAAGTCCAGATGGCAGCAGGGCAACGTGTTC AGCTGCAGCGTGATGCACGAGGCCCTGCACAAC	CTGGGCACCCAGACCTACATCTGCAATGTGAAC CACAAGCCTAGCAACACCAAGGTGGACAAGAAG GTGGAACCCAAGAGCTGCGACAAGACCCACACC TGTCCTCCATGTCCTGCTCCAGAAGCTGCTGGC GGCCCTTCTGTGTTCCTGTTTCCTCCAAAGCCT AAGGACACCCTGTACATCACCCGCGAGCCTGAA GTGACCTGTGTGGTGGTGGATGTGTCCCACGAG GACCCCGAAGTGAAGTTCAATTGGTACGTGGAC GGCGTGGAAGTGCACAACGCCAAGACCAAGCCT AGAGAGGAACAGTACAACAGCACCTACAGAGTG GTGTCCGTGCTGACCGTGCTGCACCAGGATTGG CTGAACGGCAAAGAGTACAAGTGCAAGGTGTCC AACAAGGCCCTGCCTGCCAGCATCGAGAAAACC ATCAGCAAGGCCAAGGGCCAGCCTAGGGAACCC CAGGTTTACACACTGCCTCCAAGCCGGGAAGAG ATGACCAAGAACCAGGTGTCCCTGTGGTGCCTC GTGAAGGGCTTCTACCCTTCCGATATCGCCGTG GAATGGGAGAGCAATGGCCAGCCTGAGAACAAC TACAAGACAACCCCTCCTGTGCTGGACAGCGAC GGCTCATTCTTCCTGTACAGCAAGCTGACAGTG GACAAGTCCAGATGGCAGCAGGGCAACGTGTTC AGCTGCAGCGTGATGCACGAGGCCCTGCACAAC CACTACACCCAGAAGTCCCTGAGCCTGTCTCCT GGCAAA	GACCTGAAGCGGACCG TGGCCGCCCCCAGCGT GTTCATCTTCCCTCCC AGCGACGAGCAGCTGA AGTCTGGCACCGCCAG CGTGGTGTGCCTGCTG AACAACTTCTACCCCC GCGAGGCCAAGGTGCA GTGGAAGGTGGACAAC GCCCTGCAGAGCGGCA ACAGCCAGGAGAGCGT GACCGAGCAGGACTCC AAGGACAGCACCTACA GCCTGAGCAGCACCCT GACCCTGAGCAAGGCC GACTACGAGAAGCACA AGGTGTACGCCTGCGA GGTGACCCACCAGGGA CTGTCTAGCCCCGTGA CCAAGAGCTTCAACCG GGGCGAGTGC

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	CGGTACACCCAGAAGTCCCTGTCTCTGAGCCCC GGCAAA		
442	SEQ ID NO: 1018	SEQ ID NO: 1020	SEQ ID NO: 1012
h3BNC 117.5 2.64 AAS+W /huSP 34.39 .13sc Fv AAS+S AV+R	GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG	CAGGTGCAGCTGCTGCAGTCTGGCGCCGCTGTG	GATATTCAGATGACAC
	GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT	ACAAAACCAGGCGCTTCTGTGCGGGTGTCCTGC	AGAGCCCCAGTAGCCT
	GCCGCTTCTGGCTTCACCTTCAACACCTACGCC	GAGGCCAGCGGCTACAACATCCGGGACTACTTC	GAGCGCCAGCGTGGGC
	ATGAACTGGGTCCGACAGGCTCCTGGCAAAGGC	ATTCACTGGTGGCGCCAGGCCCCTGGACAGGGA	GACACCGCAACCATCA
	CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC	CTGCAGTGGGTGGGATGGATCAACCCCAAGACC	CCTGTCAGGCCAACGG
	AACAATTACGCCACCTACTACGCCGACTCCGTG	GGCCAGCCCAACAACCCCAGACAGTTCCAGGGC	CTATCTGAACTGGTAT
	AAGAGCAGATTCACCATCTCTCGGGACGACTCC	AGAGTGTCCCTGACCAGACACGCCAGCTTCGAC	CAACAGAGGAGGGGCA
	AAGAACTCCCTGTACCTGGAGATGAACAGCCTG	TTCGACACCTTCAGCTTCTACATGGACCTGAAG	AGGCCCCCAAGCTCCT
	CGGACCGAGGATACCGCCGTGTACTATTGTGTG	GCCCTGCGGAGCGACGATACCGCCGTGTACTTC	GATATACGACGGCAGC
	CGGCACGGCAACTTCGGCCACTCCTATGTGTCT	TGCGCCAGACAGAGAAGCGACTACTGGGATTTC	AAGCTGGAGAGGGGCG
	TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC	GACGTGTGGGGCAGCGGCACCCAAGTGACCGTG	TTCCCAGCCGCTTCAG
	ACAGTTTCTTCCGGCGGAGGTGGAAGCGGAGGC	TCATCTGCTAGCACCAAGGGCCCCTCCGTGTTT	CGGCAGGAGGTGGGGC
	GGAGGTAGTGGCGGTGGTGGTTCAGGTGGTGGT	CCACTGGCTCCTAGCAGCAAGAGCACAAGCGGA	CAGGAGTACAACCTTA
	GGATCTCAGGCTGTGGTTACCCAGGAGCCTAGC	GGAACAGCCGCTCTGGGCTGTCTGGTCAAGGAC	CAATCAACAACCTGCA
	CTGACAGTTTCTCCTGGCGGCACCGTGACACTG	TACTTTCCCGAGCCTGTGACCGTGTCCTGGAAT	GCCCGAGGACATCGCC
	ACCTGTGGATCTTCTACCGGCGCTGTGACCACC	TCTGGCGCTCTGACAAGCGGCGTGCACACCTTT	ACCTATTTCTGCCAAG
	GGCCATTACGCTAATTGGGTGCAGCAGAAGCCT	CCAGCTGTGCTGCAAAGCAGCGGCCTGTACTCT	TTTACGAGTTCGTGGT
	GGACAGGCCCCAAGAGGACTGATCGGCGGCACA	CTGAGCAGCGTGGTCACAGTGCCAAGCTCTAGC	GCCCGGCACCAGGCTG
	TCTAACAGAGCCCCTGGCGTCCCAGCCAGATTC	CTGGGCACCCAGACCTACATCTGCAATGTGAAC	GACCTGAAGCGGACCG
	TCTGGATCTCTGCTTGGCGGCAAGGCCGCTCTG	CACAAGCCTAGCAACACCAAGGTGGACAAGAAG	TGGCCGCCCCCAGCGT
	ACAATTTCTGGTGCTCAGCCTGAGGACGAGGCC	GTGGAACCCAAGAGCTGCGACAAGACCCACACC	GTTCATCTTCCCTCCC
	GAGTACTACTGTGCCCTGTGGTACTCCAACAGA	TGTCCTCCATGTCCTGCTCCAGAAGCTGCTGGC	AGCGACGAGCAGCTGA

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	TGGGTGTTCGGCGGAGGCACCAAGCTGACAGTG TTGGAGCCCAAATCTTCAGACAAGACCCACACC TGTCCTCCATGTCCTGCTCCAGAAGCTGCTGGC GGCCCTTCCGTGTTTCTGTTCCCTCCAAAGCCT AAGGACACCCTGATGATCAGCAGAACCCCTGAA GTGACCTGCGTGGTGGTGGATGTGTCCCACGAG GATCCCGAAGTGAAGTTCAATTGGTACGTGGAC GGCGTGGAAGTGCACAACGCCAAGACCAAGCCT AGAGAGGAACAGTACAACAGCACCTACAGAGTG GTGTCCGTGCTGACCGTGCTGCACCAGGATTGG CTGAACGGCAAAGAGTACAAGTGCAAGGTGTCC AACAAGGCCCTGCCTGCCAGCATCGAGAAAACC ATCAGCAAGGCCAAGGGCCAGCCTAGGGAACCC CAGGTTTACACACTGCCTCCAAGCCGGGAAGAG ATGACCAAGAACCAGGTGTCCCTGAGCTGTGCC GTGAAGGGCTTCTACCCTTCCGATATCGCCGTG GAATGGGAGAGCAATGGCCAGCCTGAGAACAAC TACAAGACAACCCCTCCTGTGCTGGACAGCGAC GGCTCATTCTTCCTGGTGTCCAAGCTGACAGTG GACAAGTCCAGATGGCAGCAGGGCAACGTGTTC AGCTGCAGCGTGATGCACGAGGCCCTGCACAAC CGGTACACCCAGAAGTCCCTGTCTCTGAGCCCC GGCAAA	GGCCCTTCTGTGTTCCTGTTTCCTCCAAAGCCT AAGGACACCCTGATGATCAGCAGAACCCCTGAA GTGACCTGCGTGGTGGTGGATGTGTCCCACGAG GATCCCGAAGTGAAGTTCAATTGGTACGTGGAC GGCGTGGAAGTGCACAACGCCAAGACCAAGCCT AGAGAGGAACAGTACAACAGCACCTACAGAGTG GTGTCCGTGCTGACCGTGCTGCACCAGGATTGG CTGAACGGCAAAGAGTACAAGTGCAAGGTGTCC AACAAGGCCCTGCCTGCCAGCATCGAGAAAACC ATCAGCAAGGCCAAGGGCCAGCCTAGGGAACCC CAGGTTTACACACTGCCTCCAAGCCGGGAAGAG ATGACCAAGAACCAGGTGTCCCTGTGGTGCCTC GTGAAGGGCTTCTACCCTTCCGATATCGCCGTG GAATGGGAGAGCAATGGCCAGCCTGAGAACAAC TACAAGACAACCCCTCCTGTGCTGGACAGCGAC GGCTCATTCTTCCTGTACAGCAAGCTGACAGTG GACAAGTCCAGATGGCAGCAGGGCAACGTGTTC AGCTGCAGCGTGATGCACGAGGCCCTGCACAAC CACTACACCCAGAAGTCCCTGAGCCTGTCTCCT GGCAAA	AGTCTGGCACCGCCAG CGTGGTGTGCCTGCTG AACAACTTCTACCCCC GCGAGGCCAAGGTGCA GTGGAAGGTGGACAAC GCCCTGCAGAGCGGCA ACAGCCAGGAGAGCGT GACCGAGCAGGACTCC AAGGACAGCACCTACA GCCTGAGCAGCACCCT GACCCTGAGCAAGGCC GACTACGAGAAGCACA AGGTGTACGCCTGCGA GGTGACCCACCAGGGA CTGTCTAGCCCCGTGA CCAAGAGCTTCAACCG GGGCGAGTGC

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
443 hPGT121.66 AAS+W/huSP34.3.13scFv AAS+SAV+R	SEQ ID NO: 1021 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCC ATGAACTGGGTCCGACAGGCTCCTGGCAAAGGC CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC AACAATTACGCCACCTACTACGCCGACTCCGTG AAGGGCAGATTCACCATCTCTCGGGACGACTCC AAGAACTCCCTGTACCTGCAGATGAACAGCCTG CGGACCGAGGATACCGCCGTGTACTATTGTGTG CGGCACGGCAACTTCGGCCACTCCTATGTGTCT TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC ACAGTTTCTTCCGGCGGAGGTGGAAGCGGAGGC GGAGGTAGTGGCGGTGGTGGTTCAGGTGGTGGT GGATCTCAGGCTGTGGTTACCCAGGAGCCTAGC CTGACAGTTTCTCCTGGCGGCACCGTGACACTG ACCTGTGGATCTTCTACCGGCGCTGTGACCACC GGCCATTACGCTAATTGGGTGCAGCAGAAGCCT GGACAGGCCCCAAGAGGACTGATCGGCGGCACA TCTAACAGAGCCCCTGGCGTCCCAGCCAGATTC TCTGGATCTCTGCTTGGCGGCAAGGCCGCTCTG ACAATTTCTGGTGCTCAGCCTGAGGACGAGGCC GAGTACTACTGTGCCCTGTGGTACTCCAACAGA TGGGTGTTCGGCGGAGGCACCAAGCTGACAGTG TTGGAGCCCAAATCTTCAGACAAGACCCACACC	SEQ ID NO: 1022 CAGATGCAGCTGCAGGAATCTGGCCCTGGCCTC GTGAAGCCCTCCGAGACACTGTCCCTGACCTGC TCTGTGTCCGGCGCCTCCATCTCCGACTCCTAC TGGTCTTGGATCCGGCGATCCCCTGGCAAGGGC CTGGAATGGATCGGCTACGTGCACAAGTCCGGC GACACCAACTACAATCCCAGCCTGAAGTCCAGA GTGCACCTGTCCCTGGACACCTCCAAGAACCAG GTGTCCCTGTCTCTGACTGGTGTCACCGCTGCT GACTCCGGCAAGTACTACTGCGCCAGAACCCTG CACGGCAGACGGATCTACGGCATCGTGGCCTTC AACGAGTGGTTCACCTACTTCTACATGGACGTG TGGGGCACCGGCACCCAAGTGACCGTGTCCTCT GCCTCTACAAAGGGCCCTAGTGTGTTCCCTCTG GCTCCCAGCAGCAAGTCTACATCTGGCGGAACA GCCGCTCTGGGCTGCCTGGTCAAGGATTACTTT CCCGAGCCTGTGACCGTGTCCTGGAATTCTGGC GCTCTGACAAGCGGCGTGCACACCTTTCCAGCT GTGCTGCAAAGCAGCGGCCTGTACTCTCTGAGC AGCGTGGTCACAGTGCCTAGCTCTAGCCTGGGC ACCCAGACCTACATCTGCAATGTGAACCACAAG CCTAGCAACACCAAGGTGGACAAGAAGGTGGAA CCCAAGAGCTGCGACAAGACCCACACCTGTCCT CCATGTCCTGCTCCAGAAGCTGCTGGCGGCCCT TCCGTGTTTCTGTTCCCTCCAAAGCCTAAGGAC	SEQ ID NO: 1023 AGCGACATCAGCGTGG CCCCAGGCGAGACCGC CAGGATCAGCTGCGGC GAGAAGAGCCTGGGCA GCAGGGCCGTGCAATG GTATCAGCACAGGGCA GGCCAGGCCCCCAGCC TGATCATCTACAACAA CCAGGACAGGCCCAGC GGCATCCCCGAGAGGT TCAGTGGCAGCCCCGA CTTCAGGCCCGGTACC ACAGCCACCCTGACCA TCACCTCAGTGGAGGC CGGTGACGAGGCCGAC TACTACTGCCATATCT GGGACAGCAGAGTTCC CACCAAGTGGGTCTTT GGAGGCGGAACCACCT TGACCGTGCTGGGACA GCCTAAGGCCGCTCCT TCCGTGACCCTGTTCC CTCCATCCTCCGAGGA ACTGCAGGCCAACAAG

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	TGTCCTCCATGTCCTGCTCCAGAAGCTGCTGGC GGCCCTTCCGTGTTTCTGTTCCCTCCAAAGCCT AAGGACACCCTGATGATCAGCAGAACCCCTGAA GTGACCTGCGTGGTGGTGGATGTGTCCCACGAG GATCCCGAAGTGAAGTTCAATTGGTACGTGGAC GGCGTGGAAGTGCACAACGCCAAGACCAAGCCT AGAGAGGAACAGTACAACAGCACCTACAGAGTG GTGTCCGTGCTGACCGTGCTGCACCAGGATTGG CTGAACGGCAAAGAGTACAAGTGCAAGGTGTCC AACAAGGCCCTGCCTGCCAGCATCGAGAAAACC ATCAGCAAGGCCAAGGGCCAGCCTAGGGAACCC CAGGTTTACACACTGCCTCCAAGCCGGGAAGAG ATGACCAAGAACCAGGTGTCCCTGAGCTGTGCC GTGAAGGGCTTCTACCCTTCCGATATCGCCGTG GAATGGGAGAGCAATGGCCAGCCTGAGAACAAC TACAAGACAACCCCTCCTGTGCTGGACAGCGAC GGCTCATTCTTCCTGGTGTCCAAGCTGACAGTG GACAAGTCCAGATGGCAGCAGGGCAACGTGTTC AGCTGCAGCGTGATGCACGAGGCCCTGCACAAC CGGTACACCCAGAAGTCCCTGTCTCTGAGCCCC GGCAAA	ACCCTGATGATCAGCAGAACCCCTGAAGTGACC TGCGTGGTGGTGGATGTGTCCCACGAGGATCCC GAAGTGAAGTTCAATTGGTACGTGGACGGCGTG GAAGTGCACAACGCCAAGACCAAGCCTAGAGAG GAACAGTACAACAGCACCTACAGAGTGGTGTCC GTGCTGACCGTGCTGCACCAGGATTGGCTGAAC GGCAAAGAGTACAAGTGCAAGGTGTCCAACAAG GCCCTGCCTGCCAGCATCGAGAAAACCATCAGC AAGGCCAAGGGCCAGCCTAGGGAACCCCAGGTT TACACACTGCCTCCAAGCCGGGAAGAGATGACC AAGAACCAGGTGTCCCTGTGGTGTCTGGTGAAG GGCTTCTACCCTTCCGATATCGCCGTGGAATGG GAGAGCAATGGCCAGCCTGAGAACAACTACAAG ACAACCCCTCCTGTGCTGGACAGCGACGGCTCA TTCTTCCTGTACTCCAAGCTGACAGTGGACAAG TCCAGATGGCAGCAGGGCAACGTGTTCAGCTGC AGCGTGATGCACGAGGCCCTGCACAACCACTAC ACCCAGAAGTCCCTGTCTCTGAGCCCCGGCAAA	GCCACCCTCGTGTGCC TGATCTCCGACTTCTA CCCTGGCGCCGTGACC GTGGCCTGGAAGGCTG ATAGCTCTCCTGTGAA GGCCGGCGTGGAAACC ACCACCCCTTCCAAGC AGTCCAACAACAAATA CGCCGCCTCCTCCTAC CTGTCCCTGACCCCTG AGCAGTGGAAGTCCCA CCGGTCCTACAGCTGC CAAGTGACCCACGAGG GCTCCACCGTGGAAAA GACCGTGGCTCCTACC GAGTGCTCC
444 **hPGT121.66 AAS+W**	SEQ ID NO: 1024 GAGGTGCAGCTGGTGGAATCTGGCGGAGGATTG GTTCAGCCTGGCGGCTCTCTGAGACTGTCTTGT GCCGCTTCTGGCTTCACCTTCAACACCTACGCC	SEQ ID NO: 1025 CAGATGCAGCTGCAGGAATCTGGCCCTGGCCTC GTGAAGCCCTCCGAGACACTGTCCCTGACCTGC TCTGTGTCCGGCGCCTCCATCTCCGACTCCTAC	SEQ ID NO: 1023 AGCGACATCAGCGTGG CCCCAGGCGAGACCGC CAGGATCAGCTGCGGC

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
/huSP34.39.13 scFv AAS+SAV+R	ATGAACTGGGTCCGACAGGCTCCTGGCAAAGGC	TGGTCTTGGATCCGGCGATCCCCTGGCAAGGGC	GAGAAGAGCCTGGGCA
	CTGGAATGGGTCGGACGGATCCGGTCCAAGTAC	CTGGAATGGATCGGCTACGTGCACAAGTCCGGC	GCAGGGCCGTGCAATG
	AACAATTACGCCACCTACTACGCCGACTCCGTG	GACACCAACTACAATCCCAGCCTGAAGTCCAGA	GTATCAGCACAGGGCA
	AAGAGCAGATTCACCATCTCTCGGGACGACTCC	GTGCACCTGTCCCTGGACACCTCCAAGAACCAG	GGCCAGGCCCCCAGCC
	AAGAACTCCCTGTACCTGGAGATGAACAGCCTG	GTGTCCCTGTCTCTGACTGGTGTCACCGCTGCT	TGATCATCTACAACAA
	CGGACCGAGGATACCGCCGTGTACTATTGTGTG	GACTCCGGCAAGTACTACTGCGCCAGAACCCTG	CCAGGACAGGCCCAGC
	CGGCACGGCAACTTCGGCCACTCCTATGTGTCT	CACGGCAGACGGATCTACGGCATCGTGGCCTTC	GGCATCCCCGAGAGGT
	TGGTTTGCCTACTGGGGCCAGGGCACACTGGTC	AACGAGTGGTTCACCTACTTCTACATGGACGTG	TCAGTGGCAGCCCCGA
	ACAGTTTCTTCCGGCGGAGGTGGAAGCGGAGGC	TGGGGCACCGGCACCCAAGTGACCGTGTCCTCT	CTTCAGGCCCGGTACC
	GGAGGTAGTGGCGGTGGTGGTTCAGGTGGTGGT	GCCTCTACAAAGGGCCCTAGTGTGTTCCCTCTG	ACAGCCACCCTGACCA
	GGATCTCAGGCTGTGGTTACCCAGGAGCCTAGC	GCTCCCAGCAGCAAGTCTACATCTGGCGGAACA	TCACCTCAGTGGAGGC
	CTGACAGTTTCTCCTGGCGGCACCGTGACACTG	GCCGCTCTGGGCTGCCTGGTCAAGGATTACTTT	CGGTGACGAGGCCGAC
	ACCTGTGGATCTTCTACCGGCGCTGTGACCACC	CCCGAGCCTGTGACCGTGTCCTGGAATTCTGGC	TACTACTGCCATATCT
	GGCCATTACGCTAATTGGGTGCAGCAGAAGCCT	GCTCTGACAAGCGGCGTGCACACCTTTCCAGCT	GGGACAGCAGAGTTCC
	GGACAGGCCCCAAGAGGACTGATCGGCGGCACA	GTGCTGCAAAGCAGCGGCCTGTACTCTCTGAGC	CACCAAGTGGGTCTTT
	TCTAACAGAGCCCCTGGCGTCCCAGCCAGATTC	AGCGTGGTCACAGTGCCTAGCTCTAGCCTGGGC	GGAGGCGGAACCACCT
	TCTGGATCTCTGCTTGGCGGCAAGGCCGCTCTG	ACCCAGACCTACATCTGCAATGTGAACCACAAG	TGACCGTGCTGGGACA
	ACAATTTCTGGTGCTCAGCCTGAGGACGAGGCC	CCTAGCAACACCAAGGTGGACAAGAAGGTGGAA	GCCTAAGGCCGCTCCT
	GAGTACTACTGTGCCCTGTGGTACTCCAACAGA	CCCAAGAGCTGCGACAAGACCCACACCTGTCCT	TCCGTGACCCTGTTCC
	TGGGTGTTCGGCGGAGGCACCAAGCTGACAGTG	CCATGTCCTGCTCCAGAAGCTGCTGGCGGCCCT	CTCCATCCTCCGAGGA
	TTGGAGCCCAAATCTTCAGACAAGACCCACACC	TCCGTGTTTCTGTTCCCTCCAAAGCCTAAGGAC	ACTGCAGGCCAACAAG
	TGTCCTCCATGTCCTGCTCCAGAAGCTGCTGGC	ACCCTGATGATCAGCAGAACCCCTGAAGTGACC	GCCACCCTCGTGTGCC
	GGCCCTTCCGTGTTTCTGTTCCCTCCAAAGCCT	TGCGTGGTGGTGGATGTGTCCCACGAGGATCCC	TGATCTCCGACTTCTA
	AAGGACACCCTGATGATCAGCAGAACCCCTGAA	GAAGTGAAGTTCAATTGGTACGTGGACGGCGTG	CCCTGGCGCCGTGACC
	GTGACCTGCGTGGTGGTGGATGTGTCCCACGAG	GAAGTGCACAACGCCAAGACCAAGCCTAGAGAG	GTGGCCTGGAAGGCTG

TABLE J – polynucleotide encoding three chains of illustrative CD3/gp120-targeting bi-specific binding molecules			
Ab name	**unpaired HC**	**Fab Arm – HC**	**Fab Arm – LC**
	GATCCCGAAGTGAAGTTCAATTGGTACGTGGAC GGCGTGGAAGTGCACAACGCCAAGACCAAGCCT AGAGAGGAACAGTACAACAGCACCTACAGAGTG GTGTCCGTGCTGACCGTGCTGCACCAGGATTGG CTGAACGGCAAAGAGTACAAGTGCAAGGTGTCC AACAAGGCCCTGCCTGCCAGCATCGAGAAAACC ATCAGCAAGGCCAAGGGCCAGCCTAGGGAACCC CAGGTTTACACACTGCCTCCAAGCCGGGAAGAG ATGACCAAGAACCAGGTGTCCCTGAGCTGTGCC GTGAAGGGCTTCTACCCTTCCGATATCGCCGTG GAATGGGAGAGCAATGGCCAGCCTGAGAACAAC TACAAGACAACCCCTCCTGTGCTGGACAGCGAC GGCTCATTCTTCCTGGTGTCCAAGCTGACAGTG GACAAGTCCAGATGGCAGCAGGGCAACGTGTTC AGCTGCAGCGTGATGCACGAGGCCCTGCACAAC CGGTACACCCAGAAGTCCCTGTCTCTGAGCCCC GGCAAA	GAACAGTACAACAGCACCTACAGAGTGGTGTCC GTGCTGACCGTGCTGCACCAGGATTGGCTGAAC GGCAAAGAGTACAAGTGCAAGGTGTCCAACAAG GCCCTGCCTGCCAGCATCGAGAAAACCATCAGC AAGGCCAAGGGCCAGCCTAGGGAACCCCAGGTT TACACACTGCCTCCAAGCCGGGAAGAGATGACC AAGAACCAGGTGTCCCTGTGGTGTCTGGTGAAG GGCTTCTACCCTTCCGATATCGCCGTGGAATGG GAGAGCAATGGCCAGCCTGAGAACAACTACAAG ACAACCCCTCCTGTGCTGGACAGCGACGGCTCA TTCTTCCTGTACTCCAAGCTGACAGTGGACAAG TCCAGATGGCAGCAGGGCAACGTGTTCAGCTGC AGCGTGATGCACGAGGCCCTGCACAACCACTAC ACCCAGAAGTCCCTGTCTCTGAGCCCCGGCAAA	ATAGCTCTCCTGTGAA GGCCGGCGTGGAAACC ACCACCCCTTCCAAGC AGTCCAACAACAAATA CGCCGCCTCCTCCTAC CTGTCCCTGACCCCTG AGCAGTGGAAGTCCCA CCGGTCCTACAGCTGC CAAGTGACCCACGAGG GCTCCACCGTGGAAAA GACCGTGGCTCCTACC GAGTGCTCC

[0231] In some embodiments, the one or more polynucleotides encoding the antibodies or antigen-binding fragments, described herein, are formulated or encapsulated in a lipoplex, *e.g.*, a lipid nanoparticle (LNP). As used herein, a "lipoplex" refers to cationic liposomes that are nonviral (synthetic) lipid carriers of DNA. In some embodiments the lipoplex is a lipid nanoparticle (LNP). As used herein, the term "lipid nanoparticle" refers to one or more spherical nanoparticles with an average diameter of between 10 to 1000 nanometers, and which comprise a solid lipid core matrix that can solubilize lipophilic molecules. In certain embodiments, the lipid core is stabilized by surfactants (*e.g.*, emulsifiers), and can comprise one or more of triglycerides (*e.g.*, tristearin), diglycerides (*e.g.*, glycerol bahenate), monoglycerides (*e.g.*, glycerol monostearate), fatty acids (*e.g.*, stearic acid), steroids (*e.g.*, cholesterol), and waxes (*e.g.*, cetyl palmitate), including combinations thereof. Lipid nanoparticles are described, for example, in Petrilli et al., Curr Pharm Biotechnol. 15:847-55, 2014; and U.S. Patent Nos. 6,217,912; 6,881,421; 7,402,573; 7,404,969; 7,550,441; 7,727,969; 8,003,621; 8,691,750; 8,871,509; 9,017,726; 9,173,853; 9,220,779; 9,227,917; and 9,278,130, each of which is incorporated by reference in its entirety. LNP-encapsulated mRNA molecules encoding a broadly neutralizing antibody are described, *e.g.*, in Pardi, *et al.*, *Nat Commun.* (2017) 8:14630. In certain embodiments, the one or more polynucleotides encoding the antibodies or antigen-binding fragments, described herein, are formulated or encapsulated in an LNP comprised of an ionizable cationic lipid/phosphatidylcholine/cholesterol/PEG-lipid, *e.g.*, in molar ratios of about 50:10:38.5:1.5 mol mol^{-1}, respectively.

7. Vectors and Host Cells

[0232] Further provided are vectors comprising one or more polynucleotides encoding one or more of the multi-specific antigen binding molecules, described herein. A vector can be of any type, for example, a recombinant vector such as an expression vector. Vectors include, but are not limited to, plasmids, cosmids, bacterial artificial chromosomes (BAC) and yeast artificial chromosomes (YAC) and vectors derived from bacteriophages or plant or animal (including human) viruses. Vectors can comprise an origin of replication recognized by the proposed host cell (*e.g.*, including prokaryotic and eukaryotic host cells) and in the case of expression vectors, promoter and other regulatory regions recognized by the host cell. In additional embodiments, a vector comprises a polynucleotide encoding an antibody of the disclosure operably linked to a promoter and optionally additional regulatory elements. Certain vectors are capable of autonomous replication in a host into

which they are introduced (*e.g.*, vectors having a bacterial origin of replication can replicate in bacteria). Other vectors can be integrated into the genome of a host upon introduction into the host, and thereby are replicated along with the host genome. Vectors include, but are not limited to, those suitable for recombinant production of the antibodies disclosed herein.

[0233] The choice of the vector is dependent on the recombinant procedures followed and the host used. Introduction of vectors into host cells can be effected by *inter alia* calcium phosphate transfection, virus infection, DEAE-dextran-mediated transfection, lipofectamine transfection or electroporation. Vectors may be autonomously replicating or may replicate together with the chromosome into which they have been integrated. In certain embodiments, the vectors contain one or more selection markers. The choice of the markers may depend on the host cells of choice. These include, but are not limited to, kanamycin, neomycin, puromycin, hygromycin, zeocin, ampicillin (AmpR), thymidine kinase gene from Herpes simplex virus (HSV-TK), mammalian glutamine synthetase (GS) and dihydrofolate reductase gene from mouse (dhfr). Vectors comprising one or more nucleic acid molecules encoding the antibodies described herein, operably linked to one or more nucleic acid molecules encoding proteins or peptides that can be used to isolate the antibodies, are also covered by the disclosure. These proteins or peptides include, but are not limited to, glutathione-S-transferase, maltose binding protein, metal-binding polyhistidine, green fluorescent protein, luciferase and beta-galactosidase. In other embodiments, the vector that is used is or is based on pcDNA™3.1+ (ThermoFisher, MA) or pCGS3. In various embodiments, the vector can have one, two, three, four or five open reading frames or expression cassettes. In various embodiments, the vector can have one, two, three, four or five cistrons. In some embodiments, the first, second and third expression cassettes (*e.g.*, as set forth below) each comprise a promoter of identical or equivalent transcription strength. In varying embodiments, the promoter is a constitutive promoter. In some embodiments, the first, second and third expression cassettes (*e.g.*, as set forth below) comprise one or more promoters of different transcription strength. Illustrative promoters of use include without limitation cytomegalovirus (CMV), SV40, RSV, EF1a, UBC, PGK and CAGG (*see, e.g.*, Qin, *et al.*, *PLoS One*. (2010) 5(5):e10611). In embodiments, the expression vector further comprises a fourth expression cassette positioned 5′ to the first expression cassette comprising a polynucleotide encoding a eukaryotic selection marker protein, *e.g.*, glutamine synthetase (GS). Generally, the promoter driving expression of the polynucleotide encoding a eukaryotic selection marker

protein (fourth expression cassette) has a relatively weaker transcription strength in comparison to the promoters driving expression of the polynucleotide in the first, second and third expression cassettes.

[0234] In some embodiments, the expression vector or expression vectors comprise a plasmid vector or a viral vector. In some embodiments, the expression vector comprises three, four or five expression cassettes or cistrons. In some embodiments, the expression vector comprises, optionally in sequential order from 5′ to 3′: (i) a first expression cassette comprising a first polynucleotide encoding an anti-HIV gp120 VL-light chain constant domain (CL) fusion protein; (ii) a second expression cassette comprising a second polynucleotide encoding an anti-HIV gp120 VH-Fc fusion protein; and (iii) a third expression cassette comprising a third polynucleotide encoding an anti-CD3 scFv-Fc fusion protein. In some embodiments, the anti-HIV gp120 VL-CL fusion protein, the anti-HIV gp120 VH-Fc fusion protein and the anti-CD3 scFv-Fc fusion protein comprise amino acid sequences set forth, respectively, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 802, 801 and 800; SEQ ID NOs: 802, 803 and 800; SEQ ID NOs: 802, 803 and 804; SEQ ID NOs: 802, 805 and 804; SEQ ID NOs: 802, 801 and 806; SEQ ID NOs: 802, 803 and 806; SEQ ID NOs: 802, 803 and 807; SEQ ID NOs: 802, 805 and 807; SEQ ID NOs: 802, 809 and 808; SEQ ID NOs: 802, 810 and 808; SEQ ID NOs: 802, 801 and 811; SEQ ID NOs: 802, 809 and 812; SEQ ID NOs: 802, 810 and 812; SEQ ID NOs: 802, 805 and 813; SEQ ID NOs: 802, 814 and 812; SEQ ID NOs: 802, 801 and 815; SEQ ID NOs: 802, 805 and 816; SEQ ID NOs: 802, 801 and 817; SEQ ID NOs: 802, 805 and 818; SEQ ID NOs: 802, 810 and 819; SEQ ID NOs: 802, 810 and 820; SEQ ID NOs: 823, 822 and 821; SEQ ID NOs: 823, 825 and 824; SEQ ID NOs: 823, 825 and 826; SEQ ID NOs: 823, 827 and 826; SEQ ID NOs: 823, 829 and 828; SEQ ID NOs: 823, 822 and 830; SEQ ID NOs: 823, 825 and 830; SEQ ID NOs: 823, 825 and 831; SEQ ID NOs: 823, 827 and 831; SEQ ID NOs: 823, 833 and 832; SEQ ID NOs: 823, 829 and 832; SEQ ID NOs: 823, 827 and 834; SEQ ID NOs: 823, 829 and 835; SEQ ID NOs: 823, 829 and 836; SEQ ID NOs: 823, 833 and 837; SEQ ID NOs: 823, 838 and 837; SEQ ID NOs: 823, 840 and 839; SEQ ID NOs: 823, 829 and 841; SEQ ID NOs: 823, 829 and 842; SEQ ID NOs: 823, 829 and 843; SEQ ID NOs: 823, 829 and 844; SEQ ID NOs: 823, 829 and 845; SEQ ID NOs: 823, 829 and 846; SEQ ID NOs: 823, 833 and 846; SEQ ID NOs: 823, 838 and 846; SEQ ID NOs: 823, 827 and 847; SEQ ID NOs: 823, 829 and

848; SEQ ID NOs: 823, 829 and 849; SEQ ID NOs: 823, 829 and 850; SEQ ID NOs: 823, 829 and 851; SEQ ID NOs: 823, 829 and 852; SEQ ID NOs: 823, 829 and 853; SEQ ID NOs: 823, 829 and 854; SEQ ID NOs: 823, 829 and 855; SEQ ID NOs: 823, 829 and 856; SEQ ID NOs: 823, 829 and 857; SEQ ID NOs: 823, 829 and 858; SEQ ID NOs: 823, 829 and 859; SEQ ID NOs: 823, 829 and 860; SEQ ID NOs: 863, 862 and 861; SEQ ID NOs: 863, 864 and 861; SEQ ID NOs: 863, 864 and 865; SEQ ID NOs: 863, 866 and 865; SEQ ID NOs: 863, 868 and 867; SEQ ID NOs: 863, 862 and 869; SEQ ID NOs: 863, 864 and 869; SEQ ID NOs: 863, 864 and 870; SEQ ID NOs: 863, 866 and 870; SEQ ID NOs: 863, 872 and 871; SEQ ID NOs: 863, 868 and 871; SEQ ID NOs: 863, 862 and 873; SEQ ID NOs: 863, 866 and 874; SEQ ID NOs: 863, 872 and 875; SEQ ID NOs: 863, 868 and 875; SEQ ID NOs: 863, 876 and 875; SEQ ID NOs: 863, 862 and 877; SEQ ID NOs: 863, 866 and 878; SEQ ID NOs: 863, 862 and 879; SEQ ID NOs: 863, 866 and 880; SEQ ID NOs: 883, 882 and 881; SEQ ID NOs: 883, 884 and 881; SEQ ID NOs: 883, 884 and 885; SEQ ID NOs: 883, 886 and 885; SEQ ID NOs: 883, 888 and 887; SEQ ID NOs: 883, 882 and 889; SEQ ID NOs: 883, 884 and 889; SEQ ID NOs: 883, 884 and 890; SEQ ID NOs: 883, 886 and 890; SEQ ID NOs: 883, 892 and 891; SEQ ID NOs: 883, 888 and 891; SEQ ID NOs: 883, 882 and 883; SEQ ID NOs: 883, 886 and 894; SEQ ID NOs: 883, 892 and 895; SEQ ID NOs: 883, 888 and 895; SEQ ID NOs: 883, 896 and 895; SEQ ID NOs: 883, 882 and 897; SEQ ID NOs: 883, 886 and 898; SEQ ID NOs: 883, 882 and 899; or SEQ ID NOs: 883, 886 and 900.

[0235] In some embodiments, the expression vector comprises, optionally in sequential order from 5′ to 3′: (i) a first expression cassette comprising a first polynucleotide encoding an anti-CD3 VL-CL fusion protein; (ii) a second expression cassette comprising a second polynucleotide encoding an anti-CD3 VH-Fc fusion protein; and (iii) a third expression cassette comprising a third polynucleotide encoding a CD4 extracellular (EC) domain-Fc fusion protein. In some embodiments, the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences set forth, respectively, below, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below: SEQ ID NOs: 753, 752 and 751; SEQ ID NOs: 753, 752 and 754; SEQ ID NOs: 753, 756 and 755; SEQ ID NOs: 753, 757 and 755; SEQ ID NOs: 753, 757 and 758; SEQ ID NOs: 753, 756 and 759; SEQ ID NOs: 761, 760 and 754; SEQ ID NOs: 761, 760 and 762; SEQ ID NOs: 753, 763 and 751; SEQ ID NOs:

753, 752 and 764; SEQ ID NOs: 753, 752 and 765; SEQ ID NOs: 753, 767 and 766; SEQ ID NOs: 753, 768 and 766; SEQ ID NOs: 753, 768 and 769; SEQ ID NOs: 753, 767 and 770; SEQ ID NOs: 761, 771 and 765; SEQ ID NOs: 761, 771 and 772; SEQ ID NOs: 776, 775 and 774; SEQ ID NOs: 776, 778 and 777; SEQ ID NOs: 776, 778 and 779; SEQ ID NOs: 776, 780 and 779; SEQ ID NOs: 776, 781 and 777; SEQ ID NOs: 753, 752 and 782; SEQ ID NOs: 753, 752 and 783; SEQ ID NOs: 753, 785 and 784; SEQ ID NOs: 753, 786 and 784; SEQ ID NOs: 753, 786 and 787; SEQ ID NOs: 753, 785 and 788; SEQ ID NOs: 761, 789 and 783; SEQ ID NOs: 761, 789 and 790; SEQ ID NOs: 794, 793 and 792; SEQ ID NOs: 794, 796 and 795; SEQ ID NOs: 794, 796 and 797; SEQ ID NOs: 794, 798 and 797; or SEQ ID NOs: 794, 799 and 795. In some embodiments, the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 753, 752 and 751. In some embodiments, the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences set forth, respectively: SEQ ID NOs: 753, 752 and 751.

[0236] In some embodiments, the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 753, 752 and 751. In some embodiments, the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 753, 752 and 751. In some embodiments, the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 753, 752 and 751. In some embodiments, the anti-CD3 VL-CL fusion protein comprises an amino acid sequence that is at least 95% (*e.g.*, 99%) identical to the amino acid sequence of SEQ ID NO: 753, the anti-CD3 VH-Fc fusion protein comprises an amino acid sequence that is at least 95% (*e.g.*, 99%) identical to the amino acid sequence of SEQ ID NO: 752, and the CD4 EC domain-Fc fusion protein comprises an amino acid sequence that is at least 95% (*e.g.*, 99%) identical to the amino acid sequence of SEQ ID

NO: 751. In some embodiments, the anti-CD3 VL-CL fusion protein comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 753, the anti-CD3 VH-Fc fusion protein comprises an amino acid sequence of SEQ ID NO: 752, and the CD4 EC domain-Fc fusion protein comprises an amino acid sequence that is at least 95% (*e.g.*, 99%) identical to the amino acid sequence of SEQ ID NO: 751. In some embodiments, the anti-CD3 VL-CL fusion protein comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 753, the anti-CD3 VH-Fc fusion protein comprises an amino acid sequence of SEQ ID NO: 752, and the CD4 EC domain-Fc fusion protein comprises an amino acid sequence that is at least 95% (*e.g.*, 99%) identical to the amino acid sequence of SEQ ID NO: 751. In some embodiments, the anti-CD3 VL-CL fusion protein comprises an amino acid sequence of SEQ ID NO: 753, the anti-CD3 VH-Fc fusion protein comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 752, and the CD4 EC domain-Fc fusion protein comprises an amino acid sequence that is at least 95% (*e.g.*, 99%) identical to the amino acid sequence of SEQ ID NO: 751. In some embodiments, the anti-CD3 VL-CL fusion protein comprises an amino acid sequence of SEQ ID NO: 753, the anti-CD3 VH-Fc fusion protein comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 752, and the CD4 EC domain-Fc fusion protein comprises an amino acid sequence that is at least 95% (*e.g.*, 99%) identical to the amino acid sequence of SEQ ID NO: 751. In some embodiments, the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences set forth, respectively: SEQ ID NOs: 753, 752 and 751.

[0237] The disclosure also provides host cells comprising one or more recombinant polynucleotides or one or more vectors, as described herein. Any of a variety of host cells can be used. In one embodiment, a host cell is a prokaryotic cell, for example, *E. coli*. In another embodiment, a host cell is a eukaryotic cell, for example, a yeast cell, a plant cell, an insect cell, a mammalian cell, such as a Chinese Hamster Ovary (CHO)- based or CHO-origin cell (*e.g.*, CHO-S, CHO DG44, ExpiCHO™, CHOZN® ZFN-modified GS-/- CHO cell line or CHO-K1, CHO-K1a cells), COS cells, BHK cells, NSO cells or Bowes melanoma cells. Examples of human host cells are, *inter alia*, HeLa, 911, AT1080, A549, 293, Expi293™ and HEK293T-cells.

[0238] The terms "polynucleotide" and "nucleic acid molecule" interchangeably refer to a polymeric form of nucleotides and includes both sense and anti-sense strands of

RNA, cDNA, genomic DNA, and synthetic forms and mixed polymers of the above. As used herein, the term nucleic acid molecule may be interchangeable with the term polynucleotide. In some embodiments, a nucleotide refers to a ribonucleotide, deoxynucleotide or a modified form of either type of nucleotide, and combinations thereof. The terms also include, but are not limited to, single- and double-stranded forms of DNA. In addition, a polynucleotide, *e.g.*, a cDNA or mRNA, may include either or both naturally occurring and modified nucleotides linked together by either or both of naturally occurring and non-naturally occurring nucleotide linkages. The nucleic acid molecules may be modified chemically or biochemically or may contain non-natural or derivatized nucleotide bases, as will be readily appreciated by those of skill in the art. Such modifications include, for example, labels, methylation, substitution of one or more of the naturally occurring nucleotides with an analogue, internucleotide modifications such as uncharged linkages (*e.g.*, methyl phosphonates, phosphotriesters, phosphoramidates, carbamates, etc.), charged linkages (*e.g.*, phosphorothioates, phosphorodithioates, etc.), pendent moieties (*e.g.*, polypeptides), intercalators (*e.g.*, acridine, psoralen, etc.), chelators, alkylators, and modified linkages (*e.g.*, alpha anomeric nucleic acids, etc.). The above term is also intended to include any topological conformation, including single-stranded, double-stranded, partially duplexed, triplex, hairpinned, circular and padlocked conformations. A reference to a nucleic acid sequence encompasses its complement unless otherwise specified. Thus, a reference to a nucleic acid molecule having a particular sequence should be understood to encompass its complementary strand, with its complementary sequence. The term also includes codon-biased polynucleotides for improved expression in a desired host cell.

[0239] The term "operably linked" refers to two or more nucleic acid sequence elements that are usually physically linked and are in a functional relationship with each other. For instance, a promoter is operably linked to a coding sequence if the promoter is able to initiate or regulate the transcription or expression of a coding sequence, in which case, the coding sequence should be understood as being "under the control of" the promoter.

[0240] A "substitution," as used herein, denotes the replacement of one or more amino acids or nucleotides by different amino acids or nucleotides, respectively.

[0241] An "isolated" nucleic acid refers to a nucleic acid molecule that has been separated from a component of its natural environment. An isolated nucleic acid includes a

nucleic acid molecule contained in cells that ordinarily contain the nucleic acid molecule, but the nucleic acid molecule is present extrachromosomally or at a chromosomal location that is different from its natural chromosomal location. "Isolated nucleic acid encoding an multi-specific antigen binding domain or fragment thereof" refers to one or more nucleic acid molecules encoding first antigen binding domain, and optionally second antigen binding domain, antibody heavy and light chains (or fragments thereof), including such nucleic acid molecule(s) in a single vector or separate vectors, and such nucleic acid molecule(s) present at one or more locations in a host cell.

[0242] The term "vector," as used herein, refers to a nucleic acid molecule capable of propagating another nucleic acid to which it is linked. The term includes the vector as a self-replicating nucleic acid structure as well as the vector incorporated into the genome of a host cell into which it has been introduced. Some vectors are suitable for delivering the nucleic acid molecule or polynucleotide of the present application. Certain vectors are capable of directing the expression of nucleic acids to which they are operatively linked. Such vectors are referred to herein as expression vectors.

[0243] The terms "host cell," "host cell line," and "host cell culture" are used interchangeably and refer to cells into which exogenous nucleic acid has been introduced, including the progeny of such cells. Host cells include "transformants" and "transformed cells," which include the primary transformed cell and progeny derived therefrom without regard to the number of passages. Progeny may not be completely identical in nucleic acid content to a parent cell, but may contain mutations. Mutant progeny that have the same function or biological activity as screened or selected for in the originally transformed cell are included herein.

[0244] A polynucleotide "variant," as the term is used herein, is a polynucleotide that typically differs from a polynucleotide specifically disclosed herein in one or more substitutions, deletions, additions and insertions. Such variants may be naturally occurring or may be synthetically generated, for example, by modifying one or more of the polynucleotide sequences described herein and evaluating one or more biological activities of the encoded polypeptide as described herein, *e.g.*, using any of a number of techniques well known in the art.

[0245] A polypeptide "variant," as the term is used herein, is a polypeptide that typically differs from a polypeptide specifically disclosed herein in one or more substitutions, deletions, additions and insertions. Such variants may be naturally occurring

or may be synthetically generated, for example, by modifying one or more of the above polypeptide sequences described herein and evaluating one or more biological activities of the polypeptide as described herein, *e.g.*, using any of a number of techniques well known in the art.

[0246] The term "variant" may also refer to any naturally occurring or engineered molecule comprising one or more nucleotide or amino acid mutations. In one embodiment, the multi-specific antigen binding molecule is a bispecific antigen binding molecule. In one embodiment, the multi-specific antigen binding molecule is a bispecific antibody. For example, somatic variants may encompass all related naturally occurring antibodies that are part of or derived from the same B-cell lineage. Engineered variants may encompass all single mutations or combinatorial mutations made to an antibody.

8. Methods of Producing Multi-Specific Antigen Binding Molecules

[0247] Multi-specific and bispecific antigen binding molecules that bind to an HIV antigen (*e.g.*, gp120, gp41) and human CD3 (*e.g.*, human CD3ε or human CD3δ) can be produced by any method known in the art for the synthesis of multi-specific antibodies, for example, by chemical synthesis or by recombinant expression techniques.

[0248] Methods of making monospecific antibodies are known. Methods of making bispecific antibodies are known and described, for example, in PCT Publ. Nos. WO2011/038290; WO2012/158818, WO2012/162067, WO2015/104346, WO2016/086189, WO2016/182751, WO2017/009442, WO2017/125897, WO2017/136659, WO2017/157305, WO2017/201493, WO2018/183139, WO2018/191438, WO2019/034580, WO2019/078697 and WO2019/143636; U.S. Pat. Nos. 5,731,168; 5,807,706; 5,821,333; and U.S. Appl. Publ. Nos. 2003/020734, 2002/0155537, 2014/242079, 2015/133640, 2016/297885 and 2017/037130. Bispecific tetravalent antibodies, and methods of making them are described, *e.g.*, in WO 02/096948 and WO 00/44788, the disclosures of both of which are herein incorporated by reference in its entirety. In addition, other publications relating to making bispecific antibodies include WO 91/00360; WO 92/08802; WO 92/05793, and WO 93/17715; Tutt *et al.*, J. Immunol. 147:60-69 (1991); U.S. Pat. Nos. 4,474,893; 4,714,681; 4,925,648; 5,573,920; 5,601,819, 9,212,230 and 9,701,759; and Kostelny *et al.*, J. Immunol. 148:1547-1553 (1992). Heterodimeric bispecific antibodies having an scFv first antigen binding domain and a Fab second antigen binding domain are described, *e.g.*, in WO 2013/163427 and in U.S. Patent No. 9,701,759.

[0249] One method of making bispecific antibodies and the multi-specific antigen binding molecules described herein employs so-called "knobs-into-holes" technology (Ridgway *et al.*, Protein Eng., 9:617-621 (1996); WO 2006/028936). The mispairing problem of Ig heavy chains that is a chief drawback for making bispecific antibodies is reduced in this technology by mutating selected amino acids forming the interface of the CH3 domains in IgG. At positions within the CH3 domain at which the two heavy chains interact directly, an amino acid with a small side chain (hole) is introduced into the sequence of one heavy chain and an amino acid with a large side chain (knob) into the counterpart interacting residue location on the other heavy chain. In some instances, multi-specific antigen binding molecules described herein have immunoglobulin chains in which the CH3 domains have been modified by mutating selected amino acids that interact at the interface between two polypeptides so as to preferentially form a bispecific antigen binding molecule. In some embodiments, the multi-specific antigen binding molecules can be composed of immunoglobulin chains of the same subclass or different subclasses. In one instance, a multi-specific antigen binding molecule that binds to gp120 and CD3 comprises a T366W (EU numbering) mutation in the "knobs chain" and T366S, L368A, Y407V (EU numbering) mutations in the "hole chain." In certain embodiments, an additional interchain disulfide bridge is introduced between the CH3 domains by, *e.g.*, introducing a Y349C mutation into the "knobs chain" and a E356C mutation or a S354C mutation into the "hole chain." In certain embodiments, R409D, K370E mutations are introduced in the "knobs chain" and D399K, E357K mutations in the "hole chain." In other embodiments, Y349C, T366W mutations are introduced in one of the chains and E356C, T366S, L368A, Y407V mutations in the counterpart chain. In some embodiments. Y349C, T366W mutations are introduced in one chain and S354C, T366S, L368A, Y407V mutations in the counterpart chain. In some embodiments, Y349C, T366W mutations are introduced in one chain and S354C, T366S, L368A, Y407V mutations in the counterpart chain. In yet other embodiments, Y349C, T366W mutations are introduced in one chain and S354C, T366S, L368A, Y407V mutations in the counterpart chain (all EU numbering).

[0250] Another exemplary method of making bispecific antibodies is by using the Bispecific T-cell Engagers (BiTEs®) platform. BiTEs are made by genetically fusing a first scFv (*e.g.*, a scFv that binds gp120) to a second scFv (*e.g.*, a scFv that binds human CD3) via a flexible peptide linker (*e.g.*, GGGGS (SEQ ID NO: 1088)). See, *e.g.*, Staerz *et al.*, Nature, 314:628-631 (1985); Mack *et al.*, PNAS, 92:7021-7025 (1995); Huehls *et al.*, Immunol. Cell Biol., 93:290-296 (2015).

[0251] Another exemplary method of making bispecific antibodies is by using the Dual-Affinity Re-targeting (DART) platform. This technology is based on the diabody format of Holliger *et al.* (PNAS, 90:6444-6448 (1993)) and further improved for stability and optimal pairing of the VH and VL chains (Johnson *et al.*, J Mol. Biol., 399: 436-449 (2010); Sung *et al.*, J Clin Invest., 125(11): 4077-4090 (2015)).

[0252] Yet another exemplary method of making bispecific antibodies is by using the Trifunctional Hybrid Antibodies platform - Triomab®. This platform employs a chimeric construction made up of half of two full-length antibodies of different isotypes, mouse IgG2a and rat IgG2b. This technology relies on species-preferential heavy/light chain pairing associations. *See*, Lindhofer *et al.*, J Immunol., 155:219-225 (1995).

[0253] A further exemplary method of making bispecific antibodies is by using the TandAb® platform. This technology is based on the diabody concept but are designed as a single polypeptide chain VH1-VL2-VH2-VL1 comprising short linkers to prevent intra-chain pairing. Head-to-tail dimerization of this single chain results in the formation of a tetravalent homodimer (Kipriyanov *et al.*, J Mol. Biol., 293: 41-56 (1999)).

[0254] Yet another method for making bispecific antibodies is the CrossMab technology. CrossMab are chimeric antibodies constituted by the halves of two full-length antibodies. For correct chain pairing, it combines two technologies: (i) the knob-into-hole which favors a correct pairing between the two heavy chains; and (ii) an exchange between the heavy and light chains of one of the two Fabs to introduce an asymmetry which avoids light-chain mispairing. See, Ridgway *et al.*, Protein Eng., 9:617-621 (1996); Schaefer *et al.*, PNAS, 108:11187-11192 (2011). CrossMabs can combine two or more antigen binding domains for targeting two or more targets or for introducing bivalency towards one target such as the 2:1 format.

[0255] In various embodiments, the multi-specific antigen binding molecules described herein may be produced in bacterial or eukaryotic cells. The multi-specific antigen binding molecules can also be produced in eukaryotic cells such as transformed cell lines (*e.g.*, CHO, CHO-S, 293E, 293T, Expi293™, COS, NIH3T3). In addition, the multi-specific antigen binding molecules described herein (*e.g.*, Fabs, Fab-scFv, scFv's) can be expressed in a yeast cell such as *Pichia* (see, *e.g.*, Powers *et al.*, J Immunol Methods. 251:123-35 (2001)), *Hanseula*, or *Saccharomyces*. In one embodiment, the bispecific antibodies described herein are produced in a CHO-based or CHO-origin cell line (*e.g.*, CHO-S, CHO DG44, ExpiCHO™, CHOZN® ZFN-modified GS-/- CHO cell line or CHO-

K1, CHO-K1a) or a HEK293 (*e.g.*, Expi293™) cell line. To produce the multi-specific antigen binding molecules of interest, one or more polynucleotides encoding the multi-specific antigen binding molecules is constructed, introduced into an expression vector, and then expressed in one or more suitable host cells. In some embodiments, three polynucleotides encoding an scFv heavy chain comprising the first antigen binding domain, a Fab heavy chain and a Fab light chain comprising the second antigen binding domain are co-expressed in a single host cell. In some embodiments, three polynucleotides encoding a Fab heavy chain and a Fab light chain comprising the first antigen binding domain, and an EC domain comprising the second antigen binding domain are co-expressed in a single host cell. Standard molecular biology techniques are used to prepare the recombinant expression vector, transfect the host cells, select for transformants, culture the host cells, and recover the multi-specific antigen binding molecules.

[0256] In some embodiments, the host cell predominantly sialylates N-linked glycosylation sites within the variable regions of an immunoglobulin antigen binding domain. In some embodiments, the polynucleotides encoding a multi-specific antigen binding molecule, as described herein, are expressed in a host cell that sialylates at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, or more, N-linked glycosylation sites in the variable domains (Fv) of expressed antigen binding molecules. In various embodiments, in multi-specific antigen binding molecules expressed from such host cells, at least 50%, at least 60%, at least 70%, least 80%, at least 85%, at least 90%, or more, N-linked glycosylation sites in at least one of the first VH, the first VL, the second VH and the second VL of the multi-specific antigen binding molecule are sialylated. In various embodiments, in multi-specific antigen binding molecules expressed from such host cells, the N-linked glycosylation sites in at least one of the first VL, the second VH and the second VL have a sialic acid occupancy (*e.g.*, a glycan comprising one or two terminal sialic acid residues) of at least 40%, at least 50%, at least 60%, at least 70%, least 80%, at least 85%, at least 90%, or more. In some embodiments, the sialylated N-linked glycosylation sites in at least one of the first VL, the second VH and the second VL of the multi-specific antigen binding molecule comprise from 1 to 5 sialic acid residues, *e.g.*, from 1 to 4 sialic acid residues, *e.g.*, from 1 to 3 sialic acid residues, *e.g.*, from 1 to 2 sialic acid residues. In some embodiments, at least one of the first VL, the second VH and the second VL are sialylated with N-acetylneuraminic acid (NANA). In some embodiments, the sialic acid residues are present in biantennary structures. In some

embodiments, the sialic acid residues are present in complex N-linked glycan structures. In some embodiments, the sialic acid residues are present in hybrid N-linked glycan structures. In some embodiments, the glycans are terminally sialylated.

[0257] If the multi-specific antigen binding molecules are to be expressed in bacterial cells (*e.g.*, *E. coli*), the expression vector should have characteristics that permit amplification of the vector in the bacterial cells. Additionally, when *E. coli* such as JM109, DH5α, HB101, or XL1-Blue is used as a host, the vector must have a promoter, for example, a lacZ promoter (Ward *et al.*, 341:544-546 (1989), araB promoter (Better *et al.*, Science, 240:1041-1043 (1988)), or T7 promoter that can allow efficient expression in *E. coli*. Examples of such vectors include, for example, M13-series vectors, pUC-series vectors, pBR322, pBluescript, pCR-Script, pGEX-5X-1 (Pharmacia), "QIAexpress system" (QIAGEN), pEGFP, and pET (when this expression vector is used, the host is preferably BL21 expressing T7 RNA polymerase). The expression vector may contain a signal sequence for secretion of the multi-specific antigen binding molecules. For production into the periplasm of *E. coli*, the pelB signal sequence (Lei *et al.*, J. Bacteriol., 169: 4379 (1987)) may be used as the signal sequence for secretion of the multi-specific antigen binding molecules. For bacterial expression, calcium chloride methods or electroporation methods may be used to introduce the expression vector into the bacterial cell.

[0258] If the multi-specific antigen binding molecules are to be expressed in animal cells, *e.g.*, such as CHO-based or CHO-origin cells, COS, and NIH3T3 cells, the expression vector includes a promoter useful for expression in these cells. In various embodiments, the promoter for expression of the multi-specific antigen binding molecules in mammalian cells is a constitutive promoter or an inducible promoter. Illustrative promoters for expression of the multi-specific antigen binding molecules in mammalian cells include without limitation an SV40 promoter (Mulligan *et al.*, Nature, 277:108 (1979)), MMLV-LTR promoter, EF1α promoter (Mizushima *et al.*, Nucleic Acids Res., 18:5322 (1990)), or CMV promoter. In addition to the nucleic acid sequence encoding the immunoglobulin or domain thereof, the recombinant expression vectors may carry additional sequences, such as sequences that regulate replication of the vector in host cells (*e.g.*, origins of replication) and selectable marker genes. The selectable marker gene facilitates selection of host cells into which the vector has been introduced (see *e.g.*, U.S. Pat. Nos. 4,399,216, 4,634,665 and 5,179,017). For example, typically the selectable marker gene confers resistance to drugs, such as G418, hygromycin, or methotrexate, on a host cell into which the vector has been introduced.

Examples of vectors with selectable markers include pMAM, pDR2, pBK-RSV, pBK-CMV, pOPRSV, and pOP13.

[0259] In one embodiment, the multi-specific antigen binding molecules are produced in mammalian cells. Exemplary mammalian host cells for expressing multi-specific antigen binding molecules include Chinese Hamster Ovary (CHO cells) (including dhfr– CHO cells, *e.g.*, described in Urlaub and Chasin (1980) Proc. Natl. Acad. Sci. USA 77: 4216-4220, used with a DHFR selectable marker, *e.g.*, as described in Kaufman and Sharp (1982) Mol. Biol. 159:601 621 and glutamine synthetase (GS)- cells used with a GS selectable marker, *e.g.*, described in Lin, *et al.*, *MAbs*. (2019) 11(5):965-976; and Noh, *et al.*, *Sci Rep*. (2018) 8(1):5361), human embryonic kidney 293 cells (*e.g.*, 293, 293E, 293T, Expi293™), COS cells, NIH3T3 cells, lymphocytic cell lines, *e.g.*, NS0 myeloma cells and SP2 cells, and a cell from a transgenic animal, *e.g.*, a transgenic mammal. For example, the cell is a mammary epithelial cell. CHO and NS0 cell lines for recombinant antibody production are reviewed by Dhara, *et al.*, *BioDrugs*. (2018) 32(6):571-584.

[0260] In an exemplary system for expression of the multi-specific antigen binding molecules, recombinant expression vectors encoding the first and second binding domains (*e.g.*, VH and VL of an anti-CD3 targeting arm and VH and VL of an anti-gp120 targeting arm) are introduced into dhfr– CHO cells by calcium phosphate-mediated transfection. In a specific embodiment, the dhfr– CHO cells are cells of the DG44 cell line, such as DG44i (see, *e.g.*, Derouaz *et al.*, *Biochem Biophys Res Commun*., (2006) 340(4):1069-77). Within the recombinant expression vectors, the immunoglobulin heavy and light chain genes are each operatively linked to enhancer/promoter regulatory elements (*e.g.*, derived from SV40, CMV, adenovirus and the like, such as a CMV enhancer/AdMLP promoter regulatory element or an SV40 enhancer/AdMLP promoter regulatory element) to drive high levels of transcription of the genes. The recombinant expression vectors also carry a DHFR gene, which allows for selection of CHO cells that have been transfected with the vector using methotrexate selection/amplification. The selected transformant host cells are cultured to allow for expression of the immunoglobulin heavy and light chains and the multi-specific antigen binding molecule is recovered from the culture medium. In one embodiment, all three polypeptides of a bi-specific antigen binding molecule, as described herein, are expressed in a single cell. In one embodiment, all three polypeptides of a bi-specific antigen binding molecule, as described herein, are expressed in a single cell from a single vector.

[0261] The multi-specific antigen binding molecules can also be produced by a transgenic animal. For example, U.S. Pat. No. 5,849,992 describes a method of expressing an antibody in the mammary gland of a transgenic mammal. A transgene is constructed that includes a milk-specific promoter and one or more polynucleotides encoding the multi-specific antigen binding molecule of interest and a signal sequence for secretion. The milk produced by females of such transgenic mammals includes, secreted-therein, the multi-specific antigen binding molecule of interest. The multi-specific antigen binding molecule can be purified from the milk, or for some applications, used directly. Animals are also provided comprising one or more of the nucleic acids described herein.

[0262] The multi-specific antigen binding molecules can be isolated from inside or outside (such as medium) of the host cell and purified as substantially pure and homogenous, non-aggregated multi-specific antigen binding molecules (*e.g.,* heterodimeric bispecific antigen binding molecules). As appropriate or desired, the cell or population of cells are cultured in a culture volume of at least 2L, *e.g.*, at least 5L, 10L, 50L, 100L, 150L, 200L, 250L, or more. Methods for isolation and purification commonly used for antibody purification may be used for the isolation and purification of herein described multi-specific antigen binding molecules, and are not limited to any particular method. The multi-specific antigen binding molecules may be isolated and purified by appropriately selecting and combining, for example, column chromatography, filtration, ultrafiltration, salting out, solvent precipitation, solvent extraction, distillation, immunoprecipitation, SDS-polyacrylamide gel electrophoresis, isoelectric focusing, dialysis, and recrystallization. Chromatography includes, for example, affinity chromatography, ion exchange chromatography, hydrophobic chromatography, gel filtration, reverse-phase chromatography, and adsorption chromatography (Strategies for Protein Purification and Characterization: A Laboratory Course Manual. Ed Daniel R. Marshak *et al.*, Cold Spring Harbor Laboratory Press, 1996). Chromatography can be carried out using liquid phase chromatography such as HPLC and FPLC. Columns used for affinity chromatography include Protein A column and protein G column. Examples of columns using Protein A column include Hyper D, POROS, and Sepharose FF (GE Healthcare Biosciences). The present disclosure also includes multi-specific antigen binding molecules that are highly purified using these purification methods. In various embodiments, the isolating or purifying step comprises Protein A chromatography, and at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more, of the multi-specific antigen binding molecules are isolated or purified. In various embodiments, the isolating or purifying step comprises

Protein A chromatography, followed by ion exchange chromatography, and at least 95%, 96%, 97%, 98%, 99%, or more, of the multi-specific antigen binding molecules are isolated or purified. In various embodiments, at least 95%, 96%, 97%, 98%, 99%, or more, of the multi-specific antigen binding molecules isolate or purify as non-aggregated soluble heterodimer as determined using size exclusion chromatography (SEC). In some embodiments, the isolated or purified multi-specific antigen binding molecules have increased homogeneity as assessed by analytical ion exchange chromatography, wherein the integrated area of a main peak representing an unmodified target species is at least 95%, 96%, 97%, 98%, or more, of the sum of all integrated protein peak areas. In some embodiments, the isolated or purified antigen binding molecules have fewer than 35%, 30%, 25%, 20%, 15%, 10%, 9%, 8%, 7%, or fewer, acidic contaminants.

9. Methods of Treating and Preventing HIV

[0263] Provided are methods for treating or preventing an HIV infection or a related disease or disorder in a subject in need thereof (*e.g.*, a human subject), comprising providing to a subject in need thereof an effective amount of one or more of the multi-specific antigen binding molecules (*e.g.*, bispecific antigen binding molecules, bispecific antibodies) described herein, or one or more polynucleotides encoding the multi-specific antigen binding molecules.

[0264] In some embodiments, the methods entail administering a multi-specific antigen binding molecule having a first antigen binding domain that binds to CD3, and a second antigen binding domain that binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises one or more extracellular (EC) domains of CD4, and optionally, an IL-15 receptor agonist. In some embodiments, the one or more EC domains of CD4 comprise a sequence as set forth in SEQ ID NOs: 746-749, or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NOs: 746-749 (e.g., SEQ ID NO:746). In some embodiments, the EC domain of CD4 comprises a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 95% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 99% identical to the sequence of SEQ ID NO: 746. In some

embodiments, the EC domain of CD4 comprises the sequence of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (e.g., SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first

VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (e.g., SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (e.g., at least 99%) identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (e.g., SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (e.g., at least 99%) identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24

and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (e.g., SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (e.g., at least 99%) identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID

NOs: 51 and 56; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (e.g., SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino

acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4

comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence of SEQ ID NO:746.

[0265] The term "treatment" or "treating," to the extent it relates to a disease or condition, includes one or more of preventing the disease or condition from occurring, inhibiting the disease or condition, eliminating the disease or condition, and relieving one or more symptoms of the disease or condition. The terms "treating" and "treatment" as used herein are intended to mean the administration of a compound or composition according to the embodiments disclosed herein to at least one of alleviate or eliminate symptoms of HIV infection and to reduce viral load in a patient. As used herein, the term "effective amount" in the context of the administration of a therapy to a subject refers to the amount of a therapy that achieves a desired prophylactic or therapeutic effect. In various embodiments, the polynucleotide or polynucleotides may be present in a lipid nanoparticle (LNP) or a vector, *e.g.*, a plasmid vector or a viral vector. In some embodiments, the related disease or disorder is caused by infection with HIV. In other embodiments, it is acquired immune deficiency syndrome (AIDS). In certain embodiments, the subject is a virologically suppressed HIV-infected mammal, while in other embodiments, the subject is a treatment-naïve HIV-infected mammal. In certain embodiments, a treatment-naïve subject has a viral load between 10^3 and 10^5 copies/ml, and in certain embodiments, a virologically suppressed subject has a viral load of copies/ml in blood of less than 500, *e.g.*, less than 400, less than 300, less than 200, less than 100, less than 50. In another embodiment, the subject is a mammal, *e.g.*, a human. In certain embodiments, the subject has been diagnosed with an

HIV, *e.g.*, HIV-1 or HIV-2, infection or a related disease or disorder, *e.g.*, AIDS, or is considered at risk for developing an HIV, *e.g.*, HIV-1 or HIV-2, infection or a related disease or disorder, *e.g.*, AIDS. Subjects at risk for HIV-related diseases or disorders include patients who have come into contact with an infected person or who have been exposed to HIV in some other way. Administration of a prophylactic agent can occur prior to the manifestation of symptoms characteristic of HIV-related disease or disorder, such that a disease or disorder is prevented or, alternatively, delayed in its progression.

[0266] Also provided are methods for preventing or inhibiting an increase in HIV virus titer, virus replication, virus proliferation or an amount of an HIV viral DNA, HIV proviral DNA, or HIV viral protein in a subject (*e.g.*, a human subject). In one embodiment, the method comprises providing to the subject in need thereof an amount of one or more multi-specific antigen binding molecules described herein, or one or more polynucleotides encoding the one or more multi-specific antigen binding molecules (or their antigen binding fragments), effective to prevent, reduce or inhibit an increase in HIV titer, virus replication, virus proliferation, or an amount of an HIV protein of one or more HIV strains or isolates in the subject. In certain embodiments, the method further comprises measuring an amount of HIV viral or proviral DNA or protein at one or more time points, *e.g.*, before and after the subject in provided with an antibody or antibodies of the present disclosure. Methods and biomarkers for determining an amount of HIV viral or proviral DNA or protein in a subject are known and available in the art, and described for example, in Siliciano, J.D. *et al.*, Curr Opin. HIV AIDS, 5(6): 491-7 (2010), and Rouzioux, C. *et al.*, Curr Opin HIV AIDS, 8(3):170-5 (2013). In various embodiments, the human subject is an adult, a juvenile or an infant. The subject may be symptomatic (*e.g.*, viremic) or asymptomatic (*e.g.*, acutely infected or ART suppressed). In some embodiments, the human subject is acutely infected or recently infected with HIV. In certain embodiments, the subject has not seroconverted. In some embodiments, the human subject is chronically infected with HIV. The subject many or may not be receiving a regimen of antiretroviral therapy (ART).

[0267] Patients can be categorized into Fiebig stages I–VI, which are based on a sequential gain in positive HIV-1 clinical diagnostic assays (viral RNA measured by PCR, p24 and p31 viral antigens measured by enzyme-linked immunosorbent assay (ELISA). p24 antigen is a viral core protein that transiently appears in the blood during the ramp-up phase once HIV-1 RNA levels rise above 10,000 copies/mL and before the development of

detectable HIV antibodies. In Fiebig stage I, during ramp-up viremia, only HIV-1 RNA in the blood can be detected. Fiebig stage II commences about 7 days later, when results of tests to detect p24 antigen become positive. In Fiebig stage III, within about 5 days after p24 antigen test results become positive, IgM anti-HIV-1 antibodies can be detected with sufficiently sensitive enzyme immunoassays (EIAs) (*e.g.*, third-generation EIAs). Stage III typically occurs 1–2 weeks after the onset of acute retroviral symptoms. Fiebig stage IV represents the development of an indeterminate Western blot test and occurs about 3 days after EIA tests show positive results. Conversion to a clearly positive Western blot test, Fiebig stage V, generally occurs after another 7 days, or about 1 month after initial infection. Fiebig stages of HIV infection are described, *e.g.*, in Fiebig, *et al.*, AIDS. (2003) 17(13):1871-9; Cohen, *et al., J Infect Dis*. (2010) 202 Suppl 2:S270-7; and McMichael, *et al.*, *Nature Reviews Immunology* (2010) 10:11–23, which are hereby incorporated herein by reference in their entireties for all purposes. In some embodiments, the one or more multi-specific antigen binding molecules described herein, or one or more polynucleotides encoding the one or more multi-specific antigen binding molecules (or their antigen binding fragments), is administered to a human subject having an HIV infection of Fiebig stage IV or earlier, *e.g.*, Fiebig stage I, Fiebig stage II, Fiebig stage III or Fiebig stage IV. In some embodiments, the biological sample evaluated is from a human subject having an HIV infection of an HIV infection of Fiebig stage V or Fiebig stage VI.

[0268] In some embodiments, the multi-specific antigen binding molecules comprise a second binding domain, or are co-administered with an antibody or antigen-binding fragment thereof, comprising second VH and VL regions that compete with or comprise VH and VL regions that bind to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and may be used in, for example, methods of inhibiting certain viruses such as HIV isolates described herein, prophylactic inhibiting or preventing infections of certain viruses such as HIV isolates described herein, detection of certain viruses such as HIV isolates described herein in a sample, inhibiting certain viruses such as HIV isolates described herein, or diagnosis of certain viruses such as HIV isolates described herein. Accordingly, in some embodiments, the methods comprise: a) Identifying a human subject who is infected with an HIV expressing a gp120 comprising the following amino acid residues: a glycosylated asparagine at the position corresponding to amino acid residue position 332 (N332glycan), an aspartate at the position corresponding to amino acid residue position 325 (D325), and one or more amino acid residues selected from the group consisting of: a threonine at the position corresponding to amino acid residue position 63

(T63), a leucine at the position corresponding to amino acid residue position 179 (L179), a threonine at the position corresponding to amino acid residue position 320 (T320), and a histidine at the position corresponding to amino acid residue position 330 (H330), wherein the amino acid positions are with reference to SEQ ID NO: 69 (*i.e.*, residues 1-511 of NCBI Ref Seq No. NP_057856.1); and b) Administering to the subject an effective amount of one or more multi-specific antigen binding molecules, a polynucleotide or polynucleotides encoding one or more multi-specific antigen binding molecules, or LNPs or pharmaceutical compositions comprising one or more multi-specific antigen binding molecules or polynucleotide or polynucleotides encoding one or more multi-specific antigen binding molecules, as described above and herein, wherein the second binding domain of at least one multi-specific antigen binding molecule competes with or comprises second VH and VL regions that bind to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan. In some embodiments, the method entails identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues: i. N332glycan, D325 and T63; ii. N332glycan, D325 and L179; iii. N332glycan, D325 and T320; iv. N332glycan, D325 and H330; v. N332glycan, D325, T63 and L179; vi. N332glycan, D325, T63 and T320; vii. N332glycan, D325, T63 and H330; viii. N332glycan, D325, L179 and T320; ix. N332glycan, D325, L179 and H330; x. N332glycan, D325, T320 and H330; xi. N332glycan, D325, T63, T320 and H330; xii. N332glycan, D325, T63, L179 and T320; xiii. N332glycan, D325, T63, L179 and H330; xiv. N332glycan, D325, L179, T320 and H330; or xv. N332glycan, D325, T63, L179, T320 and H330, wherein the amino acid positions are with reference to SEQ ID NO: 69. In some embodiments, the method entails identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues: i. N332glycan, D325 and T63; ii. N332glycan, D325 and L179; iii. N332glycan, D325 and T320; or iv. N332glycan, D325 and H330, wherein the amino acid positions are with reference to SEQ ID NO: 69. In some embodiments, the method entails identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues: i. N332glycan, D325, T63 and L179; ii. N332glycan, D325, T63 and T320; iii. N332glycan, D325, T63 and H330; iv. N332glycan, D325, L179 and T320; v. N332glycan, D325, L179 and H330; or vi. N332glycan, D325, T320 and H330, wherein the amino acid positions are with reference to SEQ ID NO: 69. In some embodiments, the method entails identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues: i. N332glycan, D325, L179, T320 and H330;

ii. N332glycan, D325, T63, T320 and H330; iii. N332glycan, D325, T63, L179 and T320; or iv. N332glycan, D325, T63, L179 and H330, wherein the amino acid positions are with reference to SEQ ID NO: 69. In some embodiments, the method entails identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising at least one of the following amino acid residues: i. N332glycan, D325, T63 and H330; ii. N332glycan, D325, T320 and H330; iii. N332glycan, D325, L179, T320 and H330; or iv. N332glycan, D325, T63, L179, T320 and H330, wherein the amino acid positions are with reference to SEQ ID NO: 69. In some embodiments, the subject is infected with an HIV or a population of HIV expressing a gp120 further comprising one or more of the following amino acid residues: a glycan at amino acid residue 301 (glycan301); a lysine at amino acid residue 677 (K677); an amino acid residue other than tryptophan (*e.g.*, A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V or Y) at position 17 (not_W17); an amino acid residue other than arginine (*e.g.*, A, C, D, E, F, G, H, I, K, L, M, N, P, Q, S, T, V, W or Y) at position 747 (not_R747); an insertion_321.01 (*e.g.*, an insertion of any amino acid (*e.g.*, A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W or Y) between position G321 and K322); a glutamic acid at position 429 (E429); a glutamine at position 442 (Q442); an arginine at position 335 (R335); an isoleucine at position 165 (I165); a serine at position 393 (S393); an isoleucine at position 307 (I307); a glycan at position 295 (295 glycan); and an asparagine at position 300 (N300), wherein the amino acid positions are with reference to SEQ ID NO: 69. In some embodiments, the second antigen binding domain competes with or comprises second VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-9721, GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the second antigen binding domain competes with or comprises second VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-9721, GS-2872, PGT-121.66, PGT-121, PGT-121.414, 10-1074, 10-1074-J and PGT-134. *See*, co-owned and co-pending Intl. Appl. No. PCT/US2020/033470, entitled "METHODS OF IDENTIFYING HIV PATIENTS SENSITIVE TO THERAPY WITH GP120 V3 GLYCAN-DIRECTED ANTIBODIES," published as WO 2020/236753, which is hereby incorporated herein by reference in its entirety for all purposes.

[0269] In some embodiments, the multi-specific antigen binding molecules comprise a second binding domain, or are co-administered with an antibody or antigen-binding fragment thereof, comprising second VH and VL regions that compete with or comprise VH and VL regions that bind to theCD4 binding site (CD4bs) and may be used in, for example, methods of inhibiting certain viruses such as HIV isolates described herein, prophylactic inhibiting or preventing infections of certain viruses such as HIV isolates described herein, detection of certain viruses such as HIV isolates described herein in a sample, inhibiting certain viruses such as HIV isolates described herein, or diagnosis of certain viruses such as HIV isolates described herein. Accordingly, in some embodiments, the methods entail (a) Identifying a human subject who is infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues: I201 and one or more of the amino acid residues selected from the group consisting of E102, I108, A281, Y318 and F353, wherein the amino acid positions are with reference to SEQ ID NO: 73; and (b) Administering to the subject an effective amount of an antibody or antigen-binding fragment thereof that competes with or comprises VH and VL regions that bind to an epitope of gp120 comprising the CD4 binding site (CD4bs). In some embodiments, the methods entail identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues: I201 and F353; I201, I108 and F353; I201, I108, A281 and F353; I201, E102, I108, A281 and F353; or I201, E102, I108, A281, Y318 and F353. In some embodiments, the methods entail identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues: I201, I108 and F353; I201, I108, A281 and F353; I201, E102, I108, A281 and F353; or I201, E102, I108, A281, Y318 and F353. In some embodiments, the methods entail identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues: I201, I108, A281 and F353; I201, E102, I108, A281 and F353; or I201, E102, I108, A281, Y318 and F353. In some embodiments, the administered antibody or antigen-binding fragment thereof competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the administered antibody or antigen-binding fragment thereof competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-

9723, GS-5423, 3BNC60, VRC01, VRC07 and VRC07-523. *See,* co-owned and co-pending Provisional Appl. No. 63/112,512, entitled "METHODS OF IDENTIFYING HIV PATIENTS SENSITIVE TO THERAPY WITH gp120 CD4 BINDING SITE-DIRECTED ANTIBODIES," which is hereby incorporated herein by reference in its entirety for all purposes.

[0270] For *in vivo* treatment of mammalian subject, *e.g.*, humans, the subject may be administered or provided a pharmaceutical composition comprising one or more multi-specific antigen binding molecules, described herein, and optionally an additional anti-HIV therapeutic agent (*e.g.*, an anti-HIV a broadly neutralizing antibody (bNAb), a TLR agonist). When used for *in vivo* therapy, an antibody or antibodies described herein are typically administered or provided to the patient in therapeutically effective amounts (*i.e.*, amounts that eliminate or reduce at least one of the patient's viral burden and viral reservoir). In some embodiments, a multi-specific antigen binding molecule is administered at a dose in the range of 0.05 mg to 1000 mg per administration, *e.g.,* from 0.05 mg to 150 mg per administration, *e.g.,* from 0.05 mg to 0.35 mg per administration, *e.g.,* from 25 mg to 50 mg per administration, *e.g.,* from 30 mg to 35 mg per administration, *e.g.,* from 10 mg to 1000 mg per administration, *e.g.,* from 50 mg to 1000 mg per administration, *e.g.,* from 100 mg to 700 mg per administration, *e.g.*, at least 0.05 mg up to 0.1 mg, 0.2 mg, 0.3 mg, 0.35 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg, 0.8 mg, 1.0 mg, 5 mg, 10 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 200 mg, 300 mg, 400 mg, 500 mg, 600 mg, 700 mg, 800 mg, 900 mg, or 1000 mg per administration. In some embodiments, a multi-specific antigen binding molecule is administered at a dose of from 1 μg/kg to 50 mg/kg body weight per administration, *e.g.*, from 1 μg/kg to 5 μg/kg, *e.g.*, from 350 μg/kg to 550 μg/kg, *e.g.*, from 0.3 mg/kg to 30 mg/kg, *e.g.*, from 2 mg/kg to 10 mg/kg, *e.g.*, from 1 μg/kg up to 2 μg/kg, 3 μg/kg, 4 μg/kg, 5 μg/kg, 10 μg/kg, 50 μg/kg, 100 μg/kg, 250 μg/kg, 300 μg/kg, 350 μg/kg, 400 μg/kg, 410 μg/kg, 420 μg/kg, 430 μg/kg, 440 μg/kg, 450 μg/kg, 460 μg/kg, 470 μg/kg, 480 μg/kg, 490 μg/kg, 500 μg/kg, 750 μg/kg, 1 mg/kg, 1.5 mg/kg, 2 mg/kg, 2.5 mg/kg, 3 mg/kg, 3.5 mg/kg, 4 mg/kg, 4.5 mg/kg, 5 mg/kg, 6 mg/kg, 7 mg/kg, 8 mg/kg, 9 mg/kg, 10 mg/kg, 15 mg/kg, 20 mg/kg, 25 mg/kg, 30 mg/kg, 35 mg/kg, 40 mg/kg, 45 mg/kg, or 50 mg/kg, body weight per administration. In some embodiments, dosing of a multi-specific antigen binding molecule can be reduced or decreased when combining with a second therapeutic agent, *e.g.*, at least one of a second antigen binding molecule and a TLR agonist.

[0271] In particular embodiments, a multi-specific antigen binding molecule, described herein, may be provided to a subject in an amount sufficient to achieve a C_{trough} level of ≤ 0.1 μg/mL, ≤ 0.5 μg/ml, ≤ 1 μg/ml, ≤ 10 μg/ml, ≤ 20 μg/ml, ≤ 25 μg/ml, ≤ 30 μg/ml, ≤ 40 μg/ml, ≤ 50 μg/ml, ≤ 75 μg/ml, ≤ 100 μg/ml, *e.g.*, with a dosing regimen in the range of 2-10 mg/kg at 2 week intervals (Q2W). In certain embodiments, a multi-specific antigen binding molecule, described herein, may be provided to a subject in an amount sufficient to achieve a C_{trough} level in the range of 0.0025 μg/ml to 100 μg/ml, *e.g.*, 0.1 μg/ml to 100 μg/ml, *e.g.*, 0.1 μg/ml to 25 μg/ml. In particular embodiments, a multi-specific antigen binding molecule, described herein, may be provided to a subject in an amount sufficient to achieve a C_{max} level in the range of 0.25 μg/ml to 1000 μg/ml, *e.g.*, in the range of 50 μg/ml to 250 μg/ml, *e.g.*, > 0.25 μg/ml, > 0.5 μg/ml, > 0.75 μg/ml, > 1 μg/ml, > 5 μg/ml, > 10 μg/ml, > 50 μg/ml, > 100 μg/ml, > 200 μg/ml, > 300 μg/ml, > 400 μg/ml, > 500 μg/ml, or ≥ 1000 μg/mL. In certain embodiments, a multi-specific antigen binding molecule, described herein, may be provided to a subject in an amount sufficient to achieve a C_{max} level of 1 μg/ml to 1000 μg/ml, *e.g.*, in the range of 50 μg/ml to 250 μg/ml, *e.g.*, with a dosing regimen in the range of 2-10 mg/kg at 2 week intervals (Q2W). Administration of lower doses and/or repeat dosing at less frequent intervals will result in lower C_{trough} levels and lower C_{max} levels. Administration of higher doses and/or repeat dosing at more frequent intervals will result in higher C_{trough} levels and higher C_{max} levels.

[0272] In various embodiments, the multi-specific antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least 3 days, *e.g.*, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, or longer. In various embodiments, the multi-specific antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least at least 5 days, *e.g.*, at least 5.5 days, at least 6 days, at 6.5 days, at least 7 days, at least 7.5 days, at least 8 days, at least 8.5 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, or longer. In some embodiments, the multi-specific antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least 7 days. In various embodiments, the multi-specific antigen binding molecule has a first antigen binding domain that binds to CD3 with a K_D of lower than 10 nM, *e.g.*, lower than 5.0 nM, 4.5 nM, 4.0 nM, 3.5 nM, 3.0 nM, or lower and antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least at least 5 days, *e.g.*, at least 5.5 days, at least 6 days, at least 6.5 days, at least 7 days, at least 7.5 days, at

least 8 days, at least 8.5 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, or longer. In some embodiments, the multi-specific antigen binding molecule has a first antigen binding domain that binds to CD3 with a K_D of lower than 3.0 nM (*e.g.*, 2.5 nM) and antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least 7 days.

[0273] In various embodiments, the one or more multi-specific antigen binding molecules described herein are administered one or multiple times. In embodiments employing multiple administration regimens, as appropriate the one or more multi-specific antigen binding molecules described herein can be administered in once daily, once weekly (*i.e.*, QW), once bi-weekly (*i.e.* once every other week, or once every two weeks or Q2W), once monthly (*i.e.*, QM) or once bi-monthly dosing (*i.e.* once every other month, or once every two months or Q2M) dosing or administration intervals. In some embodiments, the one or more multi-specific antigen binding molecules are administered once daily, once weekly (*i.e.*, QW), once bi-weekly (*i.e.* once every other week, or once every two weeks or Q2W), once monthly (*i.e.*, QM), once bi-monthly (*i.e.* once every other month, or once every two months or Q2M), once every three months (*i.e.*, Q3M), once every four months (*i.e.*, Q4M), once every 5 months (*i.e.*, Q5M), or once every 6 months (*i.e.*, Q6M) dosing. In some embodiments, the one or more multi-specific antigen binding molecules are administered intravenously, subcutaneously or intramuscularly bi-weekly (*i.e.* once every other week, or once every two weeks or Q2W). In some embodiments, the one or more multi-specific antigen binding molecules are administered intravenously, subcutaneously or intramuscularly monthly (*e.g.*, once every four weeks (Q4W) or once monthly (Q1M)). As appropriate, doses administered in multiple administration regimens can be the same or different between the first and subsequent doses of a first multi-specific antigen binding molecule. As appropriate, doses administered in multiple administration regimens can be the same or different between a first multi-specific antigen binding molecule and a second therapeutic agent (*e.g.*, a second antigen binding molecule or an anti-HIV broadly neutralizing antibody (bNAb)).

[0274] The one or more multi-specific antigen binding molecules described herein are administered or provided to a mammalian subject, *e.g.*, a human, in accord with known methods, such as, but not limited to, intravenous administration, *e.g.*, as a bolus or by continuous infusion over a period of time, by intramuscular, subcutaneous, intraperitoneal, intracerebrospinal, intraarticular, intrasynovial, intrathecal, oral, topical, or inhalation

routes. As appropriate, the multi-specific antigen binding molecules may be administered parenterally, when possible, at the target cell site, or intravenously. In one embodiment, administration of the one or more multi-specific antigen binding molecules to the subject is via an intravenous route. In another embodiment, administration of the one or more multi-specific antigen binding molecules to the subject is via a subcutaneous route. In another embodiment, administration of the one or more multi-specific antigen binding molecules to the subject is via an intramuscular route. In various embodiments, polynucleotides encoding the multi-specific antigen binding molecules can be electroporated, *e.g.*, for transdermal delivery. In some embodiments, pharmaceutical compositions of the disclosure are administered to a subject systemically, parenterally, or locally.

[0275] Further provided are methods for treating an HIV infection, comprising administering to a human subject in need thereof a therapeutically effective amount of one or more multi-specific antigen binding molecules, as disclosed herein. In some embodiments, the present disclosure provides a method for preventing an HIV infection, comprising administering to a human subject in need thereof a therapeutically effective amount of one or more multi-specific antigen binding molecules, as disclosed herein.

[0276] In one embodiment, a method for treating an HIV infection in a human subject having or at risk of having the infection is provided, the method comprising administering to the human subject a therapeutically effective amount of one or more multi-specific antigen binding molecules disclosed herein, optionally in combination with a therapeutically effective amount of one or more (*e.g.,* one, two, three, one or two, or one to three) additional therapeutic agents. In some embodiments, after one or more administrations of the one or more multi-specific antigen binding molecules described herein, optionally with one or more additional therapeutic agents, the subject does not exhibit symptoms of HIV or AIDS in the absence of anti-retroviral treatment (ART) for at least 6 months, at least 1 year, at least 2 years, at least 3 years, or more. In some embodiments, after one or more administrations of the one or more multi-specific antigen binding molecules, optionally with one or more additional therapeutic agents, the subject has a viral load of copies/ml blood of less than 500, *e.g.*, less than 400, less than 300, less than 200, less than 100, less than 50, in the absence of anti-retroviral treatment (ART) for at least 6 months, at least 1 year, at least 2 years, at least 3 years, or more.

10. Combination Therapies

[0277] In certain embodiments, this disclosure provides a method for treating or preventing an HIV infection in a human subject having, or at risk of having, the HIV infection. The method comprises administering to the human subject a therapeutically effective amount of one or more multi-specific antigen binding molecules, as disclosed herein, or a pharmaceutical composition thereof, in combination with a therapeutically effective amount of one or more (*e.g.*, one, two, three, one or two, or one to three) additional therapeutic agents. In one embodiment, a method for treating an HIV infection in a human subject having or at risk of having the infection is provided, the method comprising administering to the human subject a therapeutically effective amount of one or more multi-specific antigen binding molecule, or a pharmaceutically acceptable salt thereof, in combination with a therapeutically effective amount of one or more (*e.g.*, one, two, three, one or two, or one to three) additional therapeutic agents.

[0278] In one embodiment, pharmaceutical compositions comprising one or more of the multi-specific antigen binding molecules disclosed herein, or a pharmaceutical composition thereof, in combination with one or more (*e.g.*, one, two, three, one or two, or one to three) additional therapeutic agents, and a pharmaceutically acceptable carrier, diluent, or excipient are provided.

[0279] In certain embodiments, provided are methods for treating an HIV infection, comprising administering to a patient in need thereof a therapeutically effective amount of one or more of the multi-specific antigen binding molecules described herein, or a pharmaceutical composition thereof, in combination with a therapeutically effective amount of one or more additional therapeutic agents which are suitable for treating an HIV infection.

[0280] In certain embodiments, one or more of the multi-specific antigen binding molecules described herein, or a pharmaceutical composition thereof, are combined or co-administered with one, two, three, four, or more additional therapeutic agents. In certain embodiments, one or more of the multi-specific antigen binding molecules described herein, or a pharmaceutical composition thereof, are combined or co-administered with two additional therapeutic agents. In other embodiments, one or more of the multi-specific antigen binding molecules described herein, or a pharmaceutical composition thereof, are combined or co-administered with three additional therapeutic agents. In further embodiments, one or more of the multi-specific antigen binding molecules described herein, or a pharmaceutical composition thereof, is combined or co-administered with four

additional therapeutic agents. The one, two, three, four, or more additional therapeutic agents can be different therapeutic agents selected from the same class of therapeutic agents (*e.g.*, one or more anti-HIV broadly neutralizing antibodies), and/or they can be selected from different classes of therapeutic agents (*e.g.*, one or more anti-HIV broadly neutralizing antibodies and one or more TLR agonists).

Administration of HIV Combination Therapies

[0281] In certain embodiments, one or more of the multi-specific antigen binding molecules described herein are co-administered with one or more additional therapeutic agents. Co-administration of one or more multi-specific antigen binding molecules disclosed herein with one or more additional therapeutic agents generally refers to simultaneous or sequential administration of one or more multi-specific antigen binding molecules disclosed herein and one or more additional therapeutic agents, such that therapeutically effective amounts of the one or more multi-specific antigen binding molecules disclosed herein and the one or more additional therapeutic agents are both present in the body of the patient. When administered sequentially, the combination may be administered in two or more administrations.

[0282] Co-administration includes concurrent administration as well as sequential administration of unit dosages of the one or more of the multi-specific antigen binding molecules described herein before or after administration of unit dosages of one or more additional therapeutic agents. For example, one or more of the multi-specific antigen binding molecules described herein may be administered within seconds, minutes, hours or days of the administration of the one or more additional therapeutic agents. In some embodiments, a unit dose of one or more multi-specific antigen binding molecules disclosed herein is administered first, followed within seconds, minutes, hours or days by administration of a unit dose of one or more additional therapeutic agents. Alternatively, a unit dose of one or more additional therapeutic agents is administered first, followed by administration of a unit dose of one or more multi-specific antigen binding molecules disclosed herein within seconds, minutes, hours or days. In other embodiments, a unit dose of one or more multi-specific antigen binding molecules disclosed herein is administered first, followed, after a period of hours (*e.g.*, 1-12 hours, 1-24 hours, 1-36 hours, 1-48 hours, 1-60 hours, 1-72 hours), by administration of a unit dose of one or more additional therapeutic agents. In yet other embodiments, a unit dose of one or more additional therapeutic agents is administered first, followed, after a period of hours (*e.g.*, 1-12 hours,

1-24 hours, 1-36 hours, 1-48 hours, 1-60 hours, 1-72 hours), by administration of a unit dose of one or more multi-specific antigen binding molecules disclosed herein.

[0283] In certain embodiments, one or more multi-specific antigen binding molecules disclosed herein is combined or co-administered with one or more additional therapeutic agents in a unitary dosage form for simultaneous administration to a patient, for example as a liquid or suspension dosage form, *e.g.*, for intravenous, intramuscular or subcutaneous administration.

[0284] In certain embodiments, the one or more multi-specific antigen binding molecules are formulated as a liquid solution or suspension which may optionally contain one or more other additional therapeutic agents useful for treating HIV. In certain embodiments, the liquid solution or suspension can contain another active ingredient for treating HIV, as another anti-HIV antibody or antigen-binding fragment thereof, a HIV protease inhibitor, a HIV non-nucleoside or non-nucleotide inhibitor of reverse transcriptase, a HIV nucleoside or nucleotide inhibitor of reverse transcriptase, a HIV integrase inhibitor, a HIV non-catalytic site (or allosteric) integrase inhibitor, pharmacokinetic enhancer, and combinations thereof.

[0285] In certain embodiments, the one or more multi-specific antigen binding molecules can be administered in multiple administration regimens, *i.e.,* are administered two or more times at first and subsequent time points. In certain embodiments, such liquid solutions or suspensions are suitable for once daily, once weekly (*i.e.*, QW), once bi-weekly (*i.e.* once every other week, or once every two weeks or Q2W), once monthly (*i.e.*, QM) or once bi-monthly dosing (*i.e.* once every other month, or once every two months or Q2M) dosing or administration intervals. In some embodiments, the one or more multi-specific antigen binding molecules are administered once daily, once weekly (*i.e.*, QW), once bi-weekly (*i.e.* once every other week, or once every two weeks or Q2W), once monthly (*i.e.*, QM), once bi-monthly (*i.e.* once every other month, or once every two months or Q2M), once every three months (*i.e.*, Q3M), once every four months (*i.e.*, Q4M), once every 5 months (*i.e.*, Q5M), or once every 6 months (*i.e.*, Q6M) dosing. In some embodiments, the one or more multi-specific antigen binding molecules are administered intravenously, subcutaneously or intramuscularly bi-weekly (*i.e.* once every other week, or once every two weeks or Q2W). In some embodiments, the one or more multi-specific antigen binding molecules are administered intravenously, subcutaneously or intramuscularly monthly (*e.g.*, once every four weeks (Q4W) or once monthly (Q1M)).

a. Combination Therapies With One or More Additional Broadly Neutralizing Antibodies

[0286] In certain embodiments, a multi-specific antigen binding molecule disclosed herein is combined or co-administered with one or more additional anti-HIV broadly neutralizing antibodies (bNAbs), or fragments thereof. The one or more additional bNAbs can be in any format (*e.g.*, monospecific, multi-specific, IgG, scFv). Generally, the one or more additional bNAbs bind to a different antigen, or region or epitope of HIV that does not compete with the first multi-specific antigen binding molecule. Multiple clinical studies have now shown that treatment of HIV infected individuals with single broadly neutralizing antibodies (bNAbs) leads to temporary suppression of sensitive viruses, followed by rapid outgrowth of resistant viruses – many of which appear to be rare pre-existing viral variants.

[0287] Scheid, *et al.* reported that VRC01 (a V3-glycan binding bNAb) and 3BNC117 (a CD4 binding site binding bNAb) neutralized 96% of 118 cross-clade viruses tested in-vitro (Scheid *et al.*, Science, 333: 1633-1637 (2011)). Further, clinical trials showed that many HIV infected patients receiving the antibody treatment exhibited rare and pre-existing resistant clones, even when their plasma HIV isolates appeared to be sensitive to the antibody (Caskey *et al.*, Nature, 522: 487-491 (2016); Scheid *et al.*, Nature, 535:556-560 (2016)). These results suggested that 3BNC117 may be broad when tested against HIV isolates collected from different patients (inter-patient bread), yet it may not neutralize 100% of viral isolates within individual patients (intra-patient breadth).

[0288] An antibody known as 10-1074, part of the PGT121 lineage and taken from the same donor and with similar neutralizing breadth, has also been tested in clinical trials (Mouquet *et al.*, PNAS, 109:E3268-3277 (2012); Caskey *et al.*, Nature Medicine, 23:185-191 (2017)). 10-1074 was originally shown to neutralize approximately 66% of 60 viruses tested at an IC50 below 50 μg/mL (Mouquet *et al.*, PNAS (supra)). The 10-1074 trials showed that in many patients received 10-1074 therapy, there were resistant clones, even when the plasma HIV isolates appeared to be sensitive to the antibody (Caskey *et al.* Nature Medicine (supra)). This data suggests that most patients may harbor rare pre-existing viral variants that are resistant to 10-1074. These 10-1074 resistance variants showed correlated cross-resistance to PGT121, consistent with close evolutionary relationship between 10-1074 and PGT121. However, nearly all of the resistant viruses isolated during the 10-1074 clinical trial were sensitive to neutralization by 3BNC117 (Caskey *et al.* Nature Medicine (supra)). This data is consistent with the conclusion that combination antibody therapy,

using complementary bNAbs that bind to different regions of gp120, allows for more complete intra-patient viral coverage.

[0289] In certain embodiments, the bNAb combinations can achieve complete intra-patient viral coverage. In some embodiments, the combination therapy includes first and second antigen binding molecules, wherein the first and second antigen binding molecules bind to different first and second epitopes or regions of gp120, or gp120 and gp41. In some embodiments, the combination therapy includes a multi-specific antigen binding molecule and an anti-HIV broadly neutralizing antibody (bNAb), wherein the multi-specific antigen binding molecule and the bNAb bind to different first and second epitopes or regions of gp120, or gp120 and gp41. In some embodiments, the different first and second epitopes or regions of gp120 are selected from the group consisting of: (i) third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan; (ii) second variable loop (V2) (*e.g.*, Env trimer apex); (iii) CD4 binding site (CD4bs); (iv) gp120/gp41 interface; or (v) silent face of gp120. In some embodiments, the combination therapy includes a first multi-specific antigen binding molecule, described herein, and another anti-HIV broadly neutralizing antibody or bNAb (*i.e.*, a neutralizing antibody that neutralizes multiple HIV-1 viral strains). Various bNAbs are known in the art and may be used as one or both of a combining therapeutic agent and in the anti-HIV antigen targeting arm or second antigen binding domain of the herein described multi-specific antigen binding molecules, identified herein. Additional illustrative bNAbs of use include, without limitation, those described in U.S. Patent Nos. 8,673,307; 9,493,549; 9,783,594; and WO 2012/154312; WO2012/158948; WO2013/086533; WO2013/142324; WO2014/063059; WO 2014/089152, WO 2015/048462; WO 2015/103549; WO2015/117008; WO2016/014484; WO 2016/154003; WO 2016/196975; WO2016/149710; WO2017/096221; WO 2017/133639; WO 2017/133640, WO 2018/125813, including antibodies 12A12, 12A21, NIH45-46, bANC131, 8ANC134, IB2530, INC9, 8ANC195, 8ANC196, 10-259, 10-303, 10-410, 10-847, 10-996, 10-1074, 10-1121, 10-1130, 10-1146, 10-1341, 10-1369, 10-1074GM and BG18. Additional examples include those described in Sajadi, *et al.*, Cell. (2018) 173(7):1783-1795; Sajadi, *et al.*, J Infect Dis. (2016) 213(1):156-64; Klein *et al.*, Nature, 492(7427): 118-22 (2012), Horwitz *et al.*, Proc Natl Acad Sci U S A, 110(41): 16538-43 (2013), Scheid, *et al.*, Science, 333 : 1633-1637 (2011), Scheid, *et al.*, Nature, 458:636-640 (2009), Eroshkin *et al*, Nucleic Acids Res., 42 (Database issue):Dl 133-9 (2014), Mascola *et al.*, Immunol Rev., 254(l):225-44 (2013), such as 2F5, 4E10, M66.6, CAP206-CH12, 10E8, 10E8v4, 10E8-5R-100cF, DH511.11P, 7b2, and LN01 (all of

which bind the MPER of gp41); PG9, PG16, CH01-04 (all of which bind V1V2-glycan), 2G12 (which binds to outer domain glycan); b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, 3BNC117, 3BNC60, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25 (all of which bind to the CD4 binding site).

[0290] In some embodiments, the combination therapy includes a multi-specific antigen binding molecule or an antibody that binds to an epitope or region of gp120 in the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and competes with or comprises one or more of CDRs and VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the combination therapy includes a multi-specific antigen binding molecule or an antibody that binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and competes with or comprises one or more of CDRs and VH and VL regions from an antibody selected from the group consisting of b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, 3BNC117, 3BNC60, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the combination therapy comprises co-administering (i) a multi-specific antigen binding molecule targeting CD3 and comprising a soluble extracellular region of CD4 (*e.g.*, domain 1 (D1), D1-D2, D1-D3, D1-D4), as described herein; (ii) an antibody that competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134; and; (iii) an antibody that competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523.

[0291] In some embodiments, the combination therapy includes a multi-specific antigen binding molecule or an antibody that binds to an epitope or region of gp120 in the

second variable loop (V2) (*e.g.*, Env trimer apex) and competes with or comprises one or more of CDRs and VH and VL regions from an antibody selected from the group consisting of PG9, PG16, PGC14, PGG14, PGT-142, PGT-143, PGT-144, PGT-145, CH01, CH59, PGDM1400, CAP256, CAP256-VRC26.08, CAP256-VRC26.09, CAP256-VRC26.25, PCT64-24E and VRC38.01. In some embodiments, the combination therapy includes a multi-specific antigen binding molecule or an antibody that binds to an epitope or region of gp120 in the gp120/gp41 interface and competes with or comprises second VH and VL regions from an antibody selected from the group consisting of PGT-151, CAP248-2B, 35O22, 8ANC195, ACS202, VRC34 and VRC34.01. In some embodiments, the combination therapy includes a multi-specific antigen binding molecule or an antibody that binds to an epitope or region of the gp120 silent face and competes with or comprises second VH and VL regions from an antibody selected from VRC-PG05 and SF12. In some embodiments, the combination therapy includes a multi-specific antigen binding molecule or an antibody that binds to an epitope or region of gp41 in the membrane proximal region (MPER) and competes with or comprises second VH and VL regions from an antibody selected from the group consisting of 10E8, 10E8v4, 10E8-5R-100cF, 4E10, DH511.11P, 2F5, 7b2, and LN01. In some embodiments, the combination therapy includes a multi-specific antigen binding molecule or an antibody that binds to and epitope or region of the gp41 fusion peptide and competes with or comprises second VH and VL regions from an antibody selected from the group consisting of VRC34 and ACS202.

[0292] In certain embodiments, the multi-specific antigen binding molecules and/or bNAbs may be improved to have enhanced drug-like-properties, reduced immunogenicity, enhanced ADCC, and suitable pharmacokinetic properties. Such antibodies were shown to bind to the HIV envelope glycoprotein expressed on the surface of virion or infected cells, and mediating both direct neutralization of the virus as well as potent NK, Monocyte and PBMC killing of these cells. This property allows the antibodies to treat HIV infections by neutralizing the virus, and also kill and eliminate latently HIV infected cells in infected individuals, potentially leading to a sterilizing cure for HIV.

b. Combination Therapies with One or More Additional Anti-HIV Therapeutic Agents

HIV Combination Therapy

[0293] In some embodiments, the additional therapeutic agent is a latency reversing agent (LRA). Example LRAs include IL-15 receptor agonists (*e.g.*, ALT-803; interleukin-

15/Fc fusion protein (*e.g.*, XmAb24306)); recombinant interleukin-15 (*e.g.*, AM0015, NIZ-985); pegylated IL-15 (*e.g.*, NKTR-255)) and agonists of a toll-like receptor (TLR), *e.g.*, an agonist of one or more of TLR1 (NCBI Gene ID: 7096), TLR2 (NCBI Gene ID: 7097), TLR3 (NCBI Gene ID: 7098), TLR4 (NCBI Gene ID: 7099), TLR5 (NCBI Gene ID: 7100), TLR6 (NCBI Gene ID: 10333), TLR7 (NCBI Gene ID: 51284), TLR8 (NCBI Gene ID: 51311), TLR9 (NCBI Gene ID: 54106), and TLR10 (NCBI Gene ID: 81793). In some embodiments, the LRA is a TLR7 agonist. In other embodiments, the additional therapeutic agent is a latency reversing agent (LRA), *e.g.*, a TLR8 agonist. Examples of TLR agonists include but are not limited to vesatolimod. Additional examples include but are not limited to the compounds described in U.S. Patent No. 8,367,670 and the compounds described in U.S. Patent Application Publication No. 2016/0289229. In one embodiment, the antibody described herein may be combined with TLR7 agonist such as vesatolimod. In another embodiment, the antibody described herein may be combined with TLR8 agonist, *e.g.*, selgantolimod (GS-9688). In one embodiment, the additional therapeutic agent is a TLR modulator. TLR modulators may include modulators of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, TLR11, TLR12, and TLR13. Examples of TLR3 modulators include rintatolimod, poly-ICLC, RIBOXXON®, Apoxxim, RIBOXXIM®, IPH-33, MCT-465, MCT-475, and ND-1.1. Examples of TLR7 modulators include GS-9620, GSK-2245035, imiquimod, resiquimod, DSR-6434, DSP-3025, IMO-4200, MCT-465, MEDI-9197, 3M-051, SB-9922, 3M-052, Limtop, TMX-30X, TMX-202, RG-7863, RG-7795, and the compounds disclosed in US20100143301 (Gilead Sciences), US20110098248 (Gilead Sciences), and US20090047249 (Gilead Sciences). Examples of TLR8 modulators include selgantolimod (GS-9688), motolimod, resiquimod, 3M-051, 3M-052, MCT-465, IMO-4200, VTX-763, VTX-1463, and the compounds disclosed in US20140045849 (Janssen), US20140073642 (Janssen), WO2014/056953 (Janssen), WO2014/076221 (Janssen), WO2014/128189 (Janssen), US20140350031 (Janssen), WO2014/023813 (Janssen), US20080234251 (Array Biopharma), US20080306050 (Array Biopharma), US20100029585 (Ventirx Pharma), US20110092485 (Ventirx Pharma), US20110118235 (Ventirx Pharma), US20120082658 (Ventirx Pharma), US20120219615 (Ventirx Pharma), US20140066432 (Ventirx Pharma), US20140088085 (Ventirx Pharma), US20140275167 (Novira Therapeutics), and US20130251673 (Novira Therapeutics). Examples of TLR9 modulators (*e.g.*, agonists) include BB-001, BB-006, CYT-003, IMO-2055, IMO-2125, IMO-3100, IMO-8400, IR-103, IMO-9200, AST-008 (cavrotolimod),

cobitolimod, CMP-001, agatolimod, DIMS-9054, DV-1079, DV-1179, AZD-1419, leftolimod (MGN-1703), litenimod, CYT-003-QbG10, tilsotolimod and PUL-042.

[0294] In some embodiments, the additional therapeutic agent is an agonist of DExD/H-box helicase 58 (DDX58; *a.k.a.*, RIG-I, RIG1, RIGI, RLR-1, SGMRT2; NCBI Gene ID: 23586). An illustrative RIG-I agonist is KIN1148, described by Hemann, et al., JImmunol May 1, 2016, 196 (1 Supplement) 76.1. Additional RIG-I agonists are described, *e.g.*, in Elion, et al., Cancer Res. (2018) 78(21):6183-6195; and Liu, et al., J Virol. (2016) 90(20):9406-19. RIG-I agonists are commercially available, *e.g.*, from Invivogen (invivogen.com).

[0295] In certain embodiments, such formulations are suitable for once daily, once weekly, once bi-weekly, once monthly, once every two months, or once every three months dosing.

[0296] In some embodiments, the additional therapeutic agent may be an anti-HIV agent. In some instances, the additional therapeutic agent can be HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry inhibitors, HIV maturation inhibitors, HIV capsid inhibitors, nucleocapsid protein 7 (NCp7) inhibitors, HIV Tat or Rev inhibitors, inhibitors of Tat-TAR-P-TEFb, immunomodulators (*e.g.*, immunostimulators), immunotherapeutic agents, antibody-drug conjugates, gene modifiers, gene editors (such as CRISPR/Cas9, zinc finger nucleases, homing nucleases, synthetic nucleases, TALENs), cell therapies (such as chimeric antigen receptor T-cell, CAR-T, and engineered T-cell receptors, TCR-T, autologous T-cell therapies, engineered B cells, NK cells), latency reversing agents, compounds that target the HIV capsid, immune-based therapies, phosphatidylinositol 3-kinase (PI3K) inhibitors, HIV antibodies, bispecific antibodies and "antibody-like" therapeutic proteins, HIV p17 matrix protein inhibitors, IL-13 antagonists, peptidyl-prolyl cis-trans isomerase A modulators, protein disulfide isomerase inhibitors, complement C5a receptor antagonists, DNA methyltransferase inhibitor, Fatty acid synthase inhibitor, HIV vif gene modulators, Vif dimerization antagonists, HIV-1 viral infectivity factor inhibitors, HIV-1 Nef modulators, TNF alpha ligand inhibitors, HIV Nef inhibitors, Hck tyrosine kinase modulators, mixed lineage kinase-3 (MLK-3) inhibitors, HIV-1 splicing inhibitors, integrin antagonists, nucleoprotein inhibitors, splicing factor modulators, COMM domain containing protein 1 modulators, HIV ribonuclease H inhibitors, IFN

antagonists, retrocyclin modulators, CD3 antagonists, CDK-4 inhibitors, CDK-6 inhibitors, CDK-9 inhibitors, Cytochrome P450 3 inhibitors, CXCR4 modulators, dendritic ICAM-3 grabbing nonintegrin 1 inhibitors, HIV GAG protein inhibitors, HIV POL protein inhibitors, Complement Factor H modulators, ubiquitin ligase inhibitors, deoxycytidine kinase inhibitors, cyclin dependent kinase inhibitors, HPK1 (MAP4K1) inhibitors, proprotein convertase PC9 stimulators, ATP dependent RNA helicase DDX3X inhibitors, reverse transcriptase priming complex inhibitors, G6PD and NADH-oxidase inhibitors, mTOR complex 1 inhibitors, mTOR complex 2 inhibitors, P-Glycoprotein modulators, RNA polymerase modulators, TAT protein inhibitors, Prolylendopeptidase inhibitors, Phospholipase A2 inhibitors, pharmacokinetic enhancers, HIV gene therapy, HIV vaccines, anti-HIV peptides, and combinations thereof.

[0297] In some embodiments, the additional therapeutic agent is selected from the group consisting of combination drugs for HIV, other drugs for treating HIV, HIV protease inhibitors, HIV reverse transcriptase inhibitors, HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry (fusion) inhibitors, HIV maturation inhibitors, latency reversing agents, capsid inhibitors, immune-based therapies, PI3K inhibitors, HIV antibodies, and bispecific antibodies, and "antibody-like" therapeutic proteins, and combinations thereof.

[0298] In some embodiments, the additional therapeutic agent or agents are selected from HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, HIV capsid inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, Nef inhibitors, latency reversing agents, HIV bNAbs, agonists of TLR7, TLR8, and TLR9, HIV vaccines, cytokines, immune checkpoint inhibitors, FLT3 ligands, T cell and NK cell recruiting bispecific antibodies, chimeric T cell receptors targeting HIV antigens, pharmacokinetic enhancers, and other drugs for treating HIV, and combinations thereof.

[0299] In some embodiments, the additional therapeutic agent or agents are selected from dolutegravir, cabotegravir, islatravir, darunavir, bictegravir, elsulfavirine, rilpivirine, and lenacapavir, and combinations thereof.

[0300] In some embodiments, the additional therapeutic agent or agents are selected from dolutegravir, cabotegravir, islatravir, darunavir, bictegravir, elsulfavirine, rilpivirine, and lenacapavir.

HIV Long Acting Therapies

[0301] In some embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV long-acting anti-HIV regimen. Examples of as long acting regimens that can be combined or co-adminisered include without limitation cabotegravir, rilpivirine, any integrase LA, VM-1500 LAI, maraviroc (LAI), tenofovir implant, islatravir implant, doravirine, raltegravir, and long acting dolutegravir.

HIV Combination Drugs

[0302] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV combination drug. Examples of combination drugs that can be employed with the one or more multi-specific antigen binding molecules described herein include ATRIPLA® (efavirenz, tenofovir disoproxil fumarate, and emtricitabine); COMPLERA® (EVIPLERA®; rilpivirine, tenofovir disoproxil fumarate, and emtricitabine); STRIBILD® (elvitegravir, cobicistat, tenofovir disoproxil fumarate, and emtricitabine); TRUVADA® (tenofovir disoproxil fumarate and emtricitabine; TDF+FTC); DESCOVY® (tenofovir alafenamide and emtricitabine); ODEFSEY® (tenofovir alafenamide, emtricitabine, and rilpivirine); GENVOYA® (tenofovir alafenamide, emtricitabine, cobicistat, and elvitegravir); darunavir, tenofovir alafenamide hemifumarate, emtricitabine, and cobicistat; efavirenz, lamivudine, and tenofovir disoproxil fumarate; lamivudine and tenofovir disoproxil fumarate; tenofovir and lamivudine; tenofovir alafenamide and emtricitabine ;tenofovir alafenamide hemifumarate and emtricitabine; tenofovir alafenamide hemifumarate, emtricitabine, and rilpivirine; tenofovir alafenamide hemifumarate, emtricitabine, cobicistat, and elvitegravir; tenofovir analog; COMBIVIR® (zidovudine and lamivudine; AZT+3TC); EPZICOM® (LIVEXA®; abacavir sulfate and lamivudine; ABC+3TC); KALETRA® (ALUVIA®; lopinavir and ritonavir); TRIUMEQ® (dolutegravir, abacavir, and lamivudine); BIKTARVY® (bictegravir + emtricitabine + tenofovir alafenamide), DOVATO® (dolutegravir + lamivudine), TRIZIVIR® (abacavir sulfate, zidovudine, and lamivudine; ABC+AZT+3TC); atazanavir and cobicistat; atazanavir sulfate and cobicistat; atazanavir sulfate and ritonavir; darunavir and cobicistat; dolutegravir and rilpivirine; dolutegravir and rilpivirine hydrochloride; dolutegravir, abacavir sulfate, and lamivudine; lamivudine, nevirapine, and zidovudine; raltegravir and lamivudine; doravirine, lamivudine, and tenofovir disoproxil fumarate; doravirine, lamivudine, and tenofovir disoproxil;

dolutegravir + lamivudine, lamivudine + abacavir + zidovudine, lamivudine + abacavir, lamivudine + tenofovir disoproxil fumarate, lamivudine + zidovudine + nevirapine, lopinavir + ritonavir, lopinavir + ritonavir + abacavir + lamivudine, lopinavir + ritonavir + zidovudine + lamivudine, tenofovir + lamivudine, and tenofovir disoproxil fumarate + emtricitabine + rilpivirine hydrochloride, lopinavir , ritonavir, zidovudine, lopinavir + ritonavir + abacavir + lamivudine, and lamivudine; cabotegravir + rilpivirine; 3BNC117 + albuvirtide, elpida (elsulfavirine; VM-1500), VM-1500A, lenacapavir + islatravir (oral, injectable), and dual-target HIV-1 reverse transcriptase/nucleocapsid protein 7 inhibitors.

Other HIV Drugs

[0303] Examples of other drugs for treating HIV that can be combined with the one or more multi-specific antigen binding molecules described herein include aspernigrin C, acemannan, alisporivir, BanLec, deferiprone, Gamimune, metenkefalin, naltrexone, Prolastin, REP 9, RPI-MN, VSSP, H1viral, SB-728-T, 1,5-dicaffeoylquinic acid, rHIV7-shl-TAR-CCR5RZ, AAV-eCD4-Ig gene therapy, MazF gene therapy, BlockAide, bevirimat derivatives, ABX-464, AG-1105, APH-0812, bryostatin analogs, BIT-225, BRII-732, BRII-778, CYT-107, CS-TATI-1, fluoro-beta-D-arabinose nucleic acid (FANA)-modified antisense oligonucleotides, FX-101, GILENYA® (fingolimod), griffithsin, HGTV-43, HPH-116, HS-10234, hydroxychloroquine, IMB-10035, IMO-3100, IND-02, JL-18008, LADAVRU, MK-1376, MK-2048, MK-4250, MK-8507, MK-8558, islatravir (MK-8591) (islatravir), NOV-205, OB-002H, ODE-Bn-TFV, PA-1050040 (PA-040), PC-707, PGN-007, QF-036, S-648414, SCY-635, SB-9200, SCB-719, TR-452, TEV-90110, TEV-90112, TEV-90111, TEV-90113, RN-18, DIACC-1010, Fasnall, Immuglo, 2-CLIPS peptide, HRF-4467, thrombospondin analogs, TBL-1004HI, VG-1177, xl-081, AVI-CO-004, rfhSP-D, [18F]-MC-225, URMC-099-C, RES-529, Verdinexor, IMC-M113V, IML-106, antiviral fc conjugate (AVC), VIR-576, nipamovir, Covimro, and ABBV-1882.

HIV Protease Inhibitors

[0304] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV protease inhibitor. Examples of HIV protease inhibitors that can be combined with the one or more multi-specific antigen binding molecules, described herein, include amprenavir, atazanavir, brecanavir, darunavir, fosamprenavir, fosamprenavir calcium, indinavir, indinavir sulfate, lopinavir, nelfinavir, nelfinavir mesylate, ritonavir, saquinavir, saquinavir mesylate, tipranavir, ASC-09 + ritonavir, AEBL-2, DG-17, GS-1156, TMB-657 (PPL-100), T-169,

BL-008, MK-8122, TMB-607, GRL-02031, and TMC-310911. Additional examples of protease inhibitors that can be combined or co-administered are disclosed in U.S. Patent Nos. 10,294,234, US2020030327 and US2019210978.

HIV ribonuclease H inhibitors

[0305] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV ribonuclease H inhibitor. Examples of HIV ribonuclease H inhibitors that can be combined with the one or more multi-specific antigen binding molecules described herein include NSC-727447.

HIV Nef inhibitors

[0306] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV Nef inhibitor. Examples of HIV Nef inhibitors that can be combined with the one or more multi-specific antigen binding molecules described herein include FP-1.

HIV Reverse Transcriptase Inhibitors

[0307] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a non-nucleoside or non-nucleotide inhibitor. Examples of HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase that can be combined with the one or more multi-specific antigen binding molecules, described herein, include dapivirine, delavirdine, delavirdine mesylate, doravirine, efavirenz, etravirine, lentinan, nevirapine, rilpivirine, ACC-007, ACC-008, AIC-292, F-18, KM-023, PC-1005, M1-TFV, M2-TFV, VM-1500A-LAI, PF-3450074, elsulfavirine (sustained release oral, HIV infection), doravirine + islatravir (fixed dose combination/oral tablet formulation, HIV-1 infection), elsulfavirine (long-acting injectable nanosuspension, HIV infection), and elsulfavirine (VM-1500).

[0308] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with long acting anti-HIV regimen. Examples of drugs that are being developed as long acting anti-HIV regimens that can be co-administered include without limitation cabotegravir LA, rilpivirine LA, cabotegravir LA + rilpivirine LA, elvitegravir (extended release), lenacapavir long acting, raltegravir long acting, darunavir long acting, any integrase LA, VM-1500A -LAI, VM-3500, maraviroc (LAI), T-1144, ODE-Bn-TFV, CP-112, S-648414, tenofovir implant, tenofovir long acting, tenofovir prodrug long acting, islatravir (MK-8591) subdermal

implant, long-acting dolutegravir, long acting raltegravir + lamivudine, transdermal devices that can deliver HIV drugs, such as transdermal tenofovir (WO2020092990).

[0309] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV nucleoside or nucleotide inhibitor. Examples of HIV nucleoside or nucleotide inhibitors of reverse transcriptase that can be combined with the one or more multi-specific antigen binding molecules, described herein, include adefovir, adefovir dipivoxil, azvudine, emtricitabine, tenofovir, tenofovir alafenamide, tenofovir alafenamide fumarate, tenofovir alafenamide hemifumarate, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir octadecyloxyethyl ester (AGX-1009), tenofovir disoproxil hemifumarate, VIDEX® and VIDEX EC® (didanosine, ddl), abacavir, abacavir sulfate, alovudine, apricitabine, censavudine, didanosine, elvucitabine, festinavir, fosalvudine tidoxil, CMX-157, dapivirine, doravirine, etravirine, OCR-5753, tenofovir disoproxil orotate, fozivudine tidoxil, lamivudine, phosphazid, stavudine, zalcitabine, zidovudine, rovafovir etalafenamide (GS-9131), GS-9148, MK-8504, islatravir (MK-8591), MK-8583, VM-2500 and KP-1461.

[0310] Additional examples of HIV nucleoside or nucleotide inhibitors of reverse transcriptase include, but are not limited to those described in US patent No. US2007049754, US2016250215, US2016237062, US2016251347; US2002119443, US2013065856, US2013090473, US2014221356; and WO04096286.

HIV Integrase Inhibitors

[0311] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV integrase inhibitor. Examples of HIV integrase inhibitors that can be combined with the one or more multi-specific antigen binding molecules, described herein, include elvitegravir, elvitegravir (extended-release microcapsules), curcumin, derivatives of curcumin, chicoric acid, derivatives of chicoric acid, 3,5-dicaffeoylquinic acid, derivatives of 3,5-dicaffeoylquinic acid, aurintricarboxylic acid, derivatives of aurintricarboxylic acid, caffeic acid phenethyl ester, derivatives of caffeic acid phenethyl ester, tyrphostin, derivatives of tyrphostin, quercetin, derivatives of quercetin, raltegravir, PEGylated raltegravir, dolutegravir, JTK-351, bictegravir, AVX-15567, cabotegravir, cabotegravir (long-acting injectable), diketo quinolin-4-1 derivatives, integrase-LEDGF inhibitor, ledgins, M-522, M-532, MK-0536, NSC-310217, NSC-371056, NSC-48240, NSC-642710, NSC-699171, NSC-699172, NSC-

699173, NSC-699174, stilbenedisulfonic acid, T-169, STP-0404, VM-3500, XVIR-110, and ACC-017.

[0312] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a HIV non-catalytic site, or allosteric, integrase inhibitor (NCINI). Examples of HIV non-catalytic site, or allosteric, integrase inhibitors (NCINI) that can be combined with the one or more multi-specific antigen binding molecules, described herein, include CX-05045, CX-05168, and CX-14442. Additional examples of HIV capsid inhibitors that can be combined or co-administered include without limitation those described in U.S. Patent Nos. US2014221356 and US2016016973.

HIV viral infectivity factor inhibitor

[0313] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV viral infectivity factor inhibitor. Examples of HIV viral infectivity factor inhibitors that can be combined with the one or more multi-specific antigen binding molecules described herein include 2-amino-N-(2-methoxyphenyl)-6-((4-nitrophenyl)thio)benzamide derivatives, and Irino-L.

HIV Entry (Fusion) Inhibitors

[0314] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV entry (fusion) inhibitor. Examples of HIV entry (fusion) inhibitors that can be combined with the one or more multi-specific antigen binding molecules, described herein, include AAR-501, LBT-5001, cenicriviroc, CCR5 inhibitors, gp41 inhibitors, CD4 attachment inhibitors, gp120 inhibitors, gp160 inhibitors, CXCR4 inhibitors and D-peptide HIV entry inhibitors (*e.g.*, cholesterol-PIE12-trimer (CPT31)).

[0315] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a C-C motif chemokine receptor 5 (CCR5; NCBI Gene ID: 1234) inhibitor. Examples of CCR5 inhibitors that can be combined with the one or more multi-specific antigen binding molecules, described herein, include aplaviroc, MK-7690 (vicriviroc), maraviroc, maraviroc (long-acting injectable nanoemulsion), cenicriviroc, leronlimab (PRO-140), adaptavir (RAP-101), nifeviroc (TD-0232), anti-GP120/CD4 or CCR5 bispecific antibodies, B-07, MB-66,

polypeptide C25P, TD-0680, thioraviroc, vMIP (Haimipu), CCR5 / CCR2 dual inhibitors, *e.g.*, cenicriviroc, BMS-813160.

[0316] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a CXCR4 inhibitor. Examples of CXCR4 inhibitors that can be combined with the one or more multi-specific antigen binding molecules, described herein, include plerixafor, ALT-1188, N15 peptide, vMIP (Haimipu), BL-8040, LY2510924, burixafor (TG-0054), X4P-002 and X4P-001-IO.

[0317] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a gp41 inhibitor. Examples of gp41 inhibitors that can be combined with the one or more multi-specific antigen binding molecules, described herein, include albuvirtide, enfuvirtide, griffithsin (gp41/gp120/gp160 inhibitor), BMS-986197, enfuvirtide biobetter, enfuvirtide biosimilar, HIV-1 fusion inhibitors (P26-Bapc), ITV-1, ITV-2, ITV-3, ITV-4, CPT-31, Cl3hmAb, lipuvirtide, PIE-12 trimer and sifuvirtide.

[0318] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a CD4 attachment inhibitor. Examples of CD4 attachment inhibitors that can be combined with the one or more multi-specific antigen binding molecules, described herein, include ibalizumab and CADA analogs.

[0319] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a gp120 inhibitor. Examples of gp120 inhibitors that can be combined with the one or more multi-specific antigen binding molecules, described herein, include anti-HIV microbicide, Radha-108 (receptol) 3B3-PE38, BMS818251, BanLec, bentonite-based nanomedicine, fostemsavir tromethamine, IQP-0831, VVX-004, and BMS-663068.

[0320] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a gp160 inhibitor. Examples of gp160 inhibitors that can be combined with the one or more multi-specific antigen binding molecules described herein include fangchinoline.

HIV Maturation Inhibitors

[0321] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV maturation

inhibitor. Examples of HIV maturation inhibitors that can be combined with the one or more multi-specific antigen binding molecules, described herein, include BMS-955176, GSK-3640254 and GSK-2838232.

Capsid Inhibitors

[0322] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a capsid inhibitor. Examples of capsid inhibitors that can be combined with the one or more multi-specific antigen binding molecules, described herein, include capsid polymerization inhibitors or capsid disrupting compounds, HIV nucleocapsid p7 (NCp7) inhibitors such as azodicarbonamide, HIV p24 capsid protein inhibitors, lenacapavir (GS-6207), GS-CA1, AVI-621, AVI-101, AVI-201, AVI-301, and AVI-CAN1-15 series, PF-3450074, HIV-1 capsid inhibitors (HIV-1 infection, Shandong University), and compounds described in Intl. Patent Publ. No. WO2019/087016. Additional examples of capsid inhibitors that can be combined or co-administered include without limitation those described in U.S. Patent Publ. Nos. US2018051005 and US2016108030.

Cytochrome P450 3 inhibitors

[0323] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a cytochrome P450 3 inhibitor. Examples of Cytochrome P450 3 inhibitors that can be combined or co-administered include without limitation those described in U.S. Patent No. 7,939,553.

RNA polymerase modulators

[0324] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a RNA polymerase modulator (*e.g.*, inhibitor). Examples of RNA polymerase modulators (*e.g.*, inhibitors) include without limitation those described in U.S. Patent Nos. 10,065,958 and 8,008,264.

Latency Reversing Agents

[0325] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV latency reversing agent. Examples of latency reversing agents that can be combined with the one or more multi-specific antigen binding molecules, described herein, include IL-15 receptor agonists (*e.g.*, ALT-803; interleukin-15/Fc fusion protein (*e.g.*, XmAb24306); recombinant interleukin-15 (*e.g.*, AM0015, NIZ-985); pegylated IL-15 (*e.g.*, NKTR-255)); toll-like

receptor (TLR) agonists (including TLR7 agonists, *e.g.*, GS-9620 and TLR8 agonists, *e.g.*, selgantolimod (GS-9688)), TLR9 agonists, *e.g.*, lefitolimod (MGN-1703)), histone deacetylase (HDAC) inhibitors, proteasome inhibitors such as velcade, protein kinase C (PKC) activators, Smyd2 inhibitors, BET-bromodomain 4 (BRD4) inhibitors (such as ZL-0580, apabetalone), ionomycin, IAP antagonists (inhibitor of apoptotis proteins, such as APG-1387, LBW-242), SMAC mimetics (including including ciapavir, BI-891065, TL32711, LCL161, GDC-0917, HGS1029, AT-406, APG-1387, LCL-161 (NVP-LCL161)), Debio-1143), PMA, SAHA (suberanilohydroxamic acid, or suberoyl, anilide, and hydroxamic acid), NIZ-985, IL-15 modulating antibodies (including IL-15, IL-15 fusion proteins and IL-15 receptor agonists, *e.g.*, ALT-803), JQ1, disulfiram, amphotericin B, and ubiquitin inhibitors such as largazole analogs, APH-0812, and GSK-343. Examples of HDAC inhibitors include romidepsin, vorinostat, and panobinostat. Examples of PKC activators include indolactam, prostratin, ingenol B, and DAG-lactones. Additional examples of TLR7 agonists that can be combined or co-administered include without limitation described in U.S. Patent Publ. No. US2010143301. Additional examples of TLR8 agonists that can be combined or co-administered include without limitation described in U.S. Patent Publ. No. US2017071944.

Histone Deacetylase (HDAC) Inhibitors

[0326] In various embodiments, the one or more multi-specific antigen binding molecules as described herein, are combined or co-administered with an inhibitor of a histone deacetylase, *e.g.*, histone deacetylase 1 (HDAC1; NCBI Gene ID: 3065), histone deacetylase 2 (HDAC2; NCBI Gene ID: 3066), histone deacetylase 3 (HDAC3; NCBI Gene ID: 8841), histone deacetylase 4 (HDAC4; NCBI Gene ID: 9759), histone deacetylase 5 (HDAC5; NCBI Gene ID: 10014), histone deacetylase 6 (HDAC6; NCBI Gene ID: 10013), histone deacetylase 7 (HDAC7; NCBI Gene ID: 51564), histone deacetylase 8 (HDAC8; NCBI Gene ID: 55869), histone deacetylase 9 (HDAC9; NCBI Gene ID: 9734), histone deacetylase 11 (HDAC11; NCBI Gene ID: 79885). Examples of HDAC inhibitors that can be combined with the one or more multi-specific antigen binding molecules, described herein, include without limitation, abexinostat, ACY-241, AR-42, BEBT-908, belinostat, CKD-581, CS-055 (HBI-8000), CT-101, CUDC-907 (fimepinostat), entinostat, givinostat, mocetinostat, panobinostat, pracinostat, quisinostat (JNJ-26481585), resminostat, ricolinostat, romidepsin, SHP-141, TMB-ADC, valproic acid (VAL-001), vorinostat, tinostamustine, remetinostat, and entinostat.

Immune-based Therapies

[0327] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an immune-based therapy. Examples of immune-based therapies include agonists or stimulators of a toll-like receptor (TLR) (*e.g.*, one or more of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, and TLR10); programmed cell death protein 1 (PD-1) modulators; programmed death-ligand 1 (PD-L1) modulators; IL-15 receptor agonists (*e.g.*, ALT-803; interleukin-15/Fc fusion protein (*e.g.*, XmAb24306); recombinant interleukin-15 (*e.g.*, AM0015, NIZ-985); pegylated IL-15 (*e.g.*, NKTR-255)); DermaVir; interleukin-7; plaquenil (hydroxychloroquine); proleukin (aldesleukin, IL-2); interferon alfa; interferon alfa-2b; interferon alfa-n3; pegylated interferon alfa; interferon gamma; hydroxyurea; mycophenolate mofetil (MPA) and its ester derivative mycophenolate mofetil (MMF); ribavirin; polymer polyethyleneimine (PEI); gepon; IL-12; WF-10; VGV-1; MOR-22; BMS-936559; CYT-107, normferon, peginterferon alfa-2a, peginterferon alfa-2b, RPI-MN, STING modulators, RIG-I modulators, NOD2 modulators, SB-9200, and IR-103.

Toll-Like Receptor (TLR) Agonists

[0328] In various embodiments, the one or more multi-specific antigen binding molecules as described herein, are combined or co-administered with an agonist of a toll-like receptor (TLR), *e.g.*, an agonist of one or more of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, and TLR10). Example TLR7 agonists that can be co-administered or combined with the one or more multi-specific antigen binding molecules, described herein, include without limitation AL-034, DSP-0509, GS-9620 (vesatolimod), vesatolimod analogs, LHC-165, TMX-101 (imiquimod), GSK-2245035, resiquimod, DSR-6434, DSP-3025, IMO-4200, MCT-465, MEDI-9197, 3M-051, SB-9922, 3M-052, Limtop, TMX-30X, TMX-202, RG-7863, RG-7854, RG-7795, and the compounds disclosed in US20100143301 (Gilead Sciences), US20110098248 (Gilead Sciences), and US20090047249 (Gilead Sciences), US20140045849 (Janssen), US20140073642 (Janssen), WO2014/056953 (Janssen), WO2014/076221 (Janssen), WO2014/128189 (Janssen), US20140350031 (Janssen), WO2014/023813 (Janssen), US20080234251 (Array Biopharma), US20080306050 (Array Biopharma), US20100029585 (Ventirx Pharma), US20110092485 (Ventirx Pharma), US20110118235 (Ventirx Pharma), US20120082658 (Ventirx Pharma), US20120219615 (Ventirx Pharma), US20140066432 (Ventirx Pharma), US20140088085 (Ventirx Pharma), US20140275167 (Novira Therapeutics), and

US20130251673 (Novira Therapeutics). An TLR7/TLR8 agonist that can be co-administered is NKTR-262, telratolimod and BDB-001. Example TLR8 agonists that can be co-administered or combined with the one or more multi-specific antigen binding molecules, described herein, include without limitation E-6887, IMO-4200, IMO-8400, IMO-9200, MCT-465, MEDI-9197, motolimod, resiquimod, selgantolimod (GS-9688), VTX-1463, VTX-763, 3M-051, 3M-052, and the compounds disclosed in US20140045849 (Janssen), US20140073642 (Janssen), WO2014/056953 (Janssen), WO2014/076221 (Janssen), WO2014/128189 (Janssen), US20140350031 (Janssen), WO2014/023813 (Janssen), US20080234251 (Array Biopharma), US20080306050 (Array Biopharma), US20100029585 (Ventirx Pharma), US20110092485 (Ventirx Pharma), US20110118235 (Ventirx Pharma), US20120082658 (Ventirx Pharma), US20120219615 (Ventirx Pharma), US20140066432 (Ventirx Pharma), US20140088085 (Ventirx Pharma), US20140275167 (Novira Therapeutics), and US20130251673 (Novira Therapeutics). Example TLR9 agonists that can be co-administered include without limitation AST-008, cobitolimod, CMP-001, IMO-2055, IMO-2125, S-540956, litenimod, MGN-1601, BB-001, BB-006, IMO-3100, IMO-8400, IR-103, IMO-9200, agatolimod, DIMS-9054, DV-1079, DV-1179, AZD-1419, lefitolimod (MGN-1703), CYT-003, CYT-003-QbG10, tilsotolimod and PUL-042. Examples of TLR3 agonist include rintatolimod, poly-ICLC, RIBOXXON®, Apoxxim, RIBOXXIM®, IPH-33, MCT-465, MCT-475, and ND-1.1. Examples of TLR4 agonist include G-100, and GSK-1795091.

CDK inhibitors or antagonists

[0329] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with inhibitor of cyclin dependent kinase 1 (CDK1, CDC2; CDC28A; P34CDC2; NCBI Gene ID: 983); cyclin dependent kinase 2 (CDK2, CDKN2; p33(CDK2); NCBI Gene ID: 1017); cyclin dependent kinase 3 (CDK3; NCBI Gene ID: 1018); cyclin dependent kinase 4 (CDK4, CMM3; PSK-J3; NCBI Gene ID: 1019); cyclin dependent kinase 6 (CDK6, MCPH12; PLSTIRE; NCBI Gene ID: 1021); cyclin dependent kinase 7 (CDK7, CAK; CAK1; HCAK; MO15; STK1; CDKN7; p39MO15; NCBI Gene ID: 1022); cyclin dependent kinase 9 (CDK9, TAK; C-2k; CTK1; CDC2L4; PITALRE; NCBI Gene ID: 1025). Inhibitors of one or more of CDK 1, 2, 3, 4, 6, 7 and 9 that can be combined or co-administered include without limitation abemaciclib, alvocidib (HMR-1275, flavopiridol), AT-7519, dinaciclib, ibrance, FLX-925, LEE001, palbociclib, ribociclib, rigosertib, selinexor, UCN-01, SY1365, CT-7001, SY-

1365, G1T38, milciclib, trilaciclib, PF-06873600, AZD4573, and TG-02. In some embodiments, the CDK4/CDK6/CDK9 inhibitor or antagonist is selected from the group consisting of VS2-370.

Stimulator of Interferon Genes (STING) agonists

[0330] In some embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an agonist of stimulator of interferon response cGAMP interactor 1 (STING1; NCBI Gene ID: 340061). In some embodiments, the STING receptor agonist or activator is selected from the group consisting of ADU-S100 (MIW-815), SB-11285, MK-1454, SR-8291, AdVCA0848, GSK-532, SYN-STING, MSA-1, SR-8291, STING agonist (latent HIV), GSK3745417, 5,6-dimethylxanthenone-4-acetic acid (DMXAA), cyclic-GAMP (cGAMP) and cyclic-di-AMP.

RIG-I Agonists

[0331] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an agonist of DExD/H-box helicase 58 (DDX58; *a.k.a.*, RIG-I, RIG1, RIGI, RLR-1, SGMRT2; NCBI Gene ID: 23586). In some embodiments, the agents described herein are combined or co-administered with a RIG-I modulator such as RGT-100, or NOD2 modulator, such as SB-9200 (*a.k.a.*, GS 9992; inarigivir soproxil), and IR-103. An illustrative RIG-I agonist is KIN1148, described by Hemann, et al., J Immunol May 1, 2016, 196 (1 Supplement) 76.1. Additional RIG-I agonists are described, *e.g.*, in Elion, et al., Cancer Res. (2018) 78(21):6183-6195; and Liu, et al., J Virol. (2016) 90(20):9406-19. RIG-I agonists are commercially available, *e.g.*, from Invivogen (invivogen.com).

LAG-3 and TIM-3 inhibitors

[0332] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an anti-TIM-3 (*a.k.a.*, hepatitis A virus cellular receptor 2 antibody (HAVCR2; NCBI Gene ID: 84868), such as TSR-022, LY-3321367, MBG-453, INCAGN-2390. In some embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an anti-lymphocyte activating 3 (LAG3, *a.k.a.*, CD223; NCBI Gene ID: 3902) antibody, such as relatlimab (ONO-4482), LAG-525, MK-4280, REGN-3767, INCAGN2385.

Cytokine Receptor Agonists

[0333] In various embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with one or more cytokine receptor or chemokine receptor agonists. Illustrative cytokine or chemokine receptor agonists that can be co-administered include without limitation IL-12, IL-18, gamma chain-dependent cytokines (*e.g.*, IL-2, IL-7, IL-9, IL-15 and IL-21) and fms related tyrosine kinase 3 (FLT3) ligand (FLT3LG).

[0334] Examples of IL-2 receptor agonists that can be combined or co-administered include proleukin (aldesleukin, IL-2); BC-IL (Cel-Sci), pegylated IL-2 (*e.g.*, NKTR-214 (bempegaldesleukin)); modified variants of IL-2 (*e.g.*, THOR-707), AIC-284, ALKS-4230, CUI-101 and Neo-2/15.

[0335] Examples of IL-15 receptor agonists that can be combined or co-administered include without limitation PRGN-3006, ALT-803, NKTR-255, and hetIL-15, interleukin-15/Fc fusion protein (*e.g.*, XmAb24306); recombinant interleukin-15 (*e.g.*, AM0015, NIZ-985); pegylated IL-15 (*e.g.*, NKTR-255, Synthorin), hetIL-15, SO-C101, P-22339, and the IL-15-PD-1 fusion protein N-809.

[0336] Examples of IL-12 receptor agonists that can be combined or co-administered include IL-12A (NCBI Gene ID: 3592) + IL-12B (NCBI Gene ID: 3593) mRNAs, such as MEDI1191; IL-12 gene stimulators, such as EGEN-001, tavokinogene telseplasmid; dendritic cells transduced to express IL-12, such as DC-RTS-IL-12; autologous T-Cells genetically engineered to secrete IL-12 and to target the mucin 16, cell surface associated (MUC16, *a.k.a.*, CA125; NCBI Gene ID: 94025), such as JCAR-020; and mRNA encoding the cytokines interleukin-12 single chain (IL-12sc), interleukin-15 + IL15RA sushi domain (IL-15sushi), interferon alpha (IFNα) and granulocyte-macrophage colony-stimulating factor (GM-CSF), such as SAR441000 (BNT131).

[0337] An illustrative IL-7 receptor agonist that can be co-administered includes CYT-107.

[0338] Illustrative fms related tyrosine kinase 3 (FLT3) ligand (FLT3LG) agonists that can be combined or co-administered include GS-3583 and CDX-301.

Interferon Receptor Ligands

[0339] In various embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with one or more interferon receptor (*e.g.*, interferon alpha and beta receptor subunit 1 (IFNAR1; NCBI Gene ID:

3454); interferon alpha and beta receptor subunit 2(IFNAR2; NCBI Gene ID: 3455); interferon gamma receptor 1(IFNGR1; NCBI Gene ID: 3459); interferon gamma receptor 2 (IFNGR2; NCBI Gene ID: 3460) ligands, which can be one or more of recombinant, PEGylated, fusion proteins and conjugates. Examples of interferon receptor ligands that can be combined or co-administered include an interferon alpha-1b, an interferon alpha-2a, an interferon alpha-2b, an interferon beta-1a, and an interferon gamma. Illustrative interferon alpha-1b that can be combined or co-administered include without limitation, recombinant human interferon alpha-1b, interferon alpha 1b, PEGylated interferon alpha-1b, interferon alpha 1b (HAPGEN®). Illustrative interferon alpha-2a that can be combined or co-administered include without limitation, recombinant human interferon alpha-2a, interferon alfa 2a, PEG-IFN-alpha, pegylated interferon alpha-2a (PEGASYS®), YPEG-interferon alfa-2a (YPEG-rhIFNalpha-2a), interferon alpha-2a biosimilar (Biogenomics), rHSA-IFN alpha-2a (recombinant human serum albumin interferon alpha 2a fusion protein), interferon alfa-2a follow-on biologic (Biosidus)(Inmutag, Inter 2A). Illustrative interferon alpha-2b that can be combined or co-administered include without limitation, recombinant human interferon alpha-2b, alpha-2b (INTRON A®), interferon alfa-2b (from numerous sources, including, *e.g.*, Amega, Axxo, IFN, Laboratorios Bioprofarma, Virchow, Zydus-Cadila, BioGeneric Pharma, Changchun Institute of Biological Products), ropeginterferon alfa-2b (AOP-2014, P-1101, PEG IFN alpha-2b), peginterferon alfa-2b (Amega), Ypeginterferon alfa-2b (YPEG-rhIFNalpha-2b), peginterferon alfa-2b (PEG-INTRON®), rHSA-IFN alpha 2b (recombinant human serum albumin interferon alpha 2b fusion protein), veltuzumab-IFN alpha 2b conjugate, interferon alfa-2b follow-on biologic (Biosidus - Bioferon, Citopheron, Ganapar, Beijing Kawin Technology – Kaferon). Additional illustrative interferon alpha and beta receptor ligands that can be combined or co-administered include without limitation Veldona, Infradure, Roferon-A, Algeron, Alfarona, Ingaron (interferon gamma), rSIFN-co (recombinant super compound interferon), MOR-22, Bioferon, Novaferon, Inmutag (Inferon), MULTIFERON® (Alfanative, Viragen), interferon alfa-n1(HUMOFERON®, SM-10500, Sumiferon), Shaferon, Alfaferone, interferon-alpha 2 (CJ), Laferonum, VIPEG, BLAUFERON-A, BLAUFERON-B, Dynavax (SD-101), Intermax Alpha, Realdiron, Lanstion, Pegaferon, PDferon-B PDferon-B, Pegnano, Feronsure, PegiHep, Optipeg A, Realfa 2B, Reliferon, Reaferon-EC, Roferon-A (Canferon, Ro-25-3036), Proquiferon, Uniferon, Urifron, Anterferon, Shanferon, Layfferon, Shang Sheng Lei Tai, INTEFEN, SINOGEN, Fukangtai, Pegstat, SFR-9216, Interapo (Interapa), GEPON®, NORMFERON™. Illustrative interferon beta-1a that can be

combined or co-administered include without limitation, interferon beta-1a (AVONEX®). Illustrative interferon gamma receptor ligands that can be combined or co-administered include without limitation, interferon gamma (OH-6000, Ogamma 100) and RPI-MN (modified cobratoxin).

Immune Checkpoint Receptor Protein Modulators

[0340] In various embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with one or more blockers or inhibitors of inhibitory immune checkpoint proteins or receptors and/or with one or more stimulators, activators or agonists of one or more stimulatory immune checkpoint proteins or receptors. Blockade or inhibition of inhibitory immune checkpoints can positively regulate T-cell or NK cell activation and prevent immune escape of infected cells. Activation or stimulation of stimulatory immune check points can augment the effect of immune checkpoint inhibitors in infective therapeutics. In various embodiments, the immune checkpoint proteins or receptors regulate T cell responses (*e.g.*, reviewed in Xu, et al., J Exp Clin Cancer Res. (2018) 37:110). In various embodiments, the immune checkpoint proteins or receptors regulate NK cell responses (*e.g.*, reviewed in Davis, et al., Semin Immunol. (2017) 31:64–75 and Chiossone, et al., Nat Rev Immunol. (2018) 18(11):671-688).

[0341] Examples of immune checkpoint proteins or receptors that can be combined with the one or more multi-specific antigen binding molecules described herein include without limitation CD27 (NCBI Gene ID: 939); CD70 (NCBI Gene ID: 970); CD40 (NCBI Gene ID: 958); CD40LG (NCBI Gene ID: 959); CD47 (NCBI Gene ID: 961); CD48 (SLAMF2; NCBI Gene ID: 962); transmembrane and immunoglobulin domain containing 2 (TMIGD2, CD28H; NCBI Gene ID: 126259); CD84 (LY9B, SLAMF5; NCBI Gene ID: 8832); CD96 (NCBI Gene ID: 10225); CD160 (NCBI Gene ID: 11126); MS4A1 (CD20; NCBI Gene ID: 931); CD244 (SLAMF4; NCBI Gene ID: 51744); CD276 (B7H3; NCBI Gene ID: 80381); V-set domain containing T cell activation inhibitor 1 (VTCN1, B7H4; NCBI Gene ID: 79679); V-set immunoregulatory receptor (VSIR, B7H5, VISTA; NCBI Gene ID: 64115); immunoglobulin superfamily member 11 (IGSF11, VSIG3; NCBI Gene ID: 152404); natural killer cell cytotoxicity receptor 3 ligand 1 (NCR3LG1, B7H6; NCBI Gene ID: 374383); HERV-H LTR-associating 2 (HHLA2, B7H7; NCBI Gene ID: 11148); inducible T cell co-stimulator (ICOS, CD278; NCBI Gene ID: 29851); inducible T cell co-stimulator ligand (ICOSLG, B7H2; NCBI Gene ID: 23308); TNF receptor superfamily

member 4 (TNFRSF4, OX40; NCBI Gene ID: 7293); TNF superfamily member 4 (TNFSF4, OX40L; NCBI Gene ID: 7292); TNFRSF8 (CD30; NCBI Gene ID: 943); TNFSF8 (CD30L; NCBI Gene ID: 944); TNFRSF10A (CD261, DR4, TRAILR1; NCBI Gene ID: 8797); TNFRSF9 (CD137; NCBI Gene ID: 3604); TNFSF9 (CD137L; NCBI Gene ID: 8744); TNFRSF10B (CD262, DR5, TRAILR2; NCBI Gene ID: 8795); TNFRSF10 (TRAIL; NCBI Gene ID: 8743); TNFRSF14 (HVEM, CD270; NCBI Gene ID: 8764); TNFSF14 (HVEML; NCBI Gene ID: 8740); CD272 (B and T lymphocyte associated (BTLA); NCBI Gene ID: 151888); TNFRSF17 (BCMA, CD269; NCBI Gene ID: 608); TNFSF13B (BAFF; NCBI Gene ID: 10673); TNFRSF18 (GITR; NCBI Gene ID: 8784); TNFSF18 (GITRL; NCBI Gene ID: 8995); MHC class I polypeptide-related sequence A (MICA; NCBI Gene ID: 100507436); MHC class I polypeptide-related sequence B (MICB; NCBI Gene ID: 4277); CD274 (CD274, PDL1, PD-L1; NCBI Gene ID: 29126); programmed cell death 1 (PDCD1, PD1, PD-1; NCBI Gene ID: 5133); cytotoxic T-lymphocyte associated protein 4 (CTLA4, CD152; NCBI Gene ID: 1493); CD80 (B7-1; NCBI Gene ID: 941); CD28 (NCBI Gene ID: 940); nectin cell adhesion molecule 2 (NECTIN2, CD112; NCBI Gene ID: 5819); CD226 (DNAM-1; NCBI Gene ID: 10666); Poliovirus receptor (PVR) cell adhesion molecule (PVR, CD155; NCBI Gene ID: 5817); PVR related immunoglobulin domain containing (PVRIG, CD112R; NCBI Gene ID: 79037); T cell immunoreceptor with Ig and ITIM domains (TIGIT; NCBI Gene ID: 201633); T cell immunoglobulin and mucin domain containing 4 (TIMD4; TIM4; NCBI Gene ID: 91937); hepatitis A virus cellular receptor 2 (HAVCR2, TIMD3, TIM3; TIM-3; NCBI Gene ID: 84868); galectin 9 (LGALS9; NCBI Gene ID: 3965); lymphocyte activating 3 (LAG3, LAG-3; CD223; NCBI Gene ID: 3902); signaling lymphocytic activation molecule family member 1 (SLAMF1, SLAM, CD150; NCBI Gene ID: 6504); lymphocyte antigen 9 (LY9, CD229, sialic acid binding Ig like lectin 7 (SIGLEC7; p75; QA79; AIRM1; CD328; CDw328; D-siglec; SIGLEC-7; SIGLECP2; SIGLEC19P; p75/AIRM1; NCBI Gene ID: 27036); sialic acid binding Ig like lectin 9 (SIGLEC9; CD329; CDw329; FOAP-9; siglec-9; OBBP-LIKE; NCBI Gene ID: 27180); SLAMF3; NCBI Gene ID: 4063); SLAM family member 6 (SLAMF6, CD352; NCBI Gene ID: 114836); SLAM family member 7 (SLAMF7, CD319; NCBI Gene ID: 57823); UL16 binding protein 1 (ULBP1; NCBI Gene ID: 80329); UL16 binding protein 2 (ULBP2; NCBI Gene ID: 80328); UL16 binding protein 3 (ULBP3; NCBI Gene ID: 79465); retinoic acid early transcript 1E (RAET1E; ULBP4; NCBI Gene ID: 135250); retinoic acid early transcript 1G (RAET1G; ULBP5; NCBI Gene ID: 353091); retinoic acid early transcript 1L

(RAET1L; ULBP6; NCBI Gene ID: 154064); killer cell lectin like receptor C1 (KLRC1, NKG2A, CD159A; NCBI Gene ID: 3821); killer cell lectin like receptor K1 (KLRK1, NKG2D, CD314; NCBI Gene ID: 22914); killer cell lectin like receptor C2 (KLRC2, CD159c, NKG2C; NCBI Gene ID: 3822); killer cell lectin like receptor C3 (KLRC3, NKG2E; NCBI Gene ID: 3823); killer cell lectin like receptor C4 (KLRC4, NKG2F; NCBI Gene ID: 8302); killer cell lectin like receptor D1 (KLRD1; NCBI Gene ID: 3824); killer cell lectin like receptor G1 (KLRG1; 2F1; MAFA; MAFA-L; CLEC15A; MAFA-2F1; MAFA-LIKE; NCBI Gene ID: 10219); killer cell immunoglobulin like receptor, two Ig domains and long cytoplasmic tail 1 (KIR2DL1; NCBI Gene ID: 3802); killer cell immunoglobulin like receptor, two Ig domains and long cytoplasmic tail 2 (KIR2DL2; NCBI Gene ID: 3803); killer cell immunoglobulin like receptor, two Ig domains and long cytoplasmic tail 3 (KIR2DL3; NCBI Gene ID: 3804); killer cell immunoglobulin like receptor, three Ig domains and long cytoplasmic tail 1 (KIR3DL1, KIR, CD158E1; NCBI Gene ID: 3811) (*e.g.*, Lirilumab (IPH2102/BMS-986015), IPH-4102) and Hematopoietic Progenitor Kinase 1 (HPK1, MAP4K1).

[0342] In various embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with one or more blockers or inhibitors of one or more T-cell inhibitory immune checkpoint proteins or receptors. Illustrative T-cell inhibitory immune checkpoint proteins or receptors include without limitation CD274 (CD274, PDL1, PD-L1); programmed cell death 1 ligand 2 (PDCD1LG2, PD-L2, CD273); programmed cell death 1 (PDCD1, PD1, PD-1); cytotoxic T-lymphocyte associated protein 4 (CTLA4, CD152); CD276 (B7H3); V-set domain containing T cell activation inhibitor 1 (VTCN1, B7H4); V-set immunoregulatory receptor (VSIR, B7H5, VISTA); immunoglobulin superfamily member 11 (IGSF11, VSIG3); TNFRSF14 (HVEM, CD270), TNFSF14 (HVEML); CD272 (B and T lymphocyte associated (BTLA)); PVR related immunoglobulin domain containing (PVRIG, CD112R); T cell immunoreceptor with Ig and ITIM domains (TIGIT); lymphocyte activating 3 (LAG3, CD223); hepatitis A virus cellular receptor 2 (HAVCR2, TIMD3, TIM3); galectin 9 (LGALS9); killer cell immunoglobulin like receptor, three Ig domains and long cytoplasmic tail 1 (KIR, CD158E1); killer cell immunoglobulin like receptor, two Ig domains and long cytoplasmic tail 1 (KIR2DL1); killer cell immunoglobulin like receptor, two Ig domains and long cytoplasmic tail 2 (KIR2DL2); killer cell immunoglobulin like receptor, two Ig domains and long cytoplasmic tail 3 (KIR2DL3); and killer cell immunoglobulin like receptor, three Ig domains and long cytoplasmic tail 1 (KIR3DL1). In various embodiments, the one or more

multi-specific antigen binding molecules, as described herein, are combined or co-administered with one or more agonist or activators of one or more T-cell stimulatory immune checkpoint proteins or receptors. Illustrative T-cell stimulatory immune checkpoint proteins or receptors include without limitation CD27, CD70; CD40, CD40LG; inducible T cell costimulator (ICOS, CD278); inducible T cell costimulator ligand (ICOSLG, B7H2); TNF receptor superfamily member 4 (TNFRSF4, OX40); TNF superfamily member 4 (TNFSF4, OX40L); TNFRSF9 (CD137), TNFSF9 (CD137L); TNFRSF18 (GITR), TNFSF18 (GITRL); CD80 (B7-1), CD28; nectin cell adhesion molecule 2 (NECTIN2, CD112); CD226 (DNAM-1); CD244 (2B4, SLAMF4), Poliovirus receptor (PVR) cell adhesion molecule (PVR, CD155). See, *e.g.*, Xu, et al., J Exp Clin Cancer Res. (2018) 37:110.

[0343] In various embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with one or more blockers or inhibitors of one or more NK-cell inhibitory immune checkpoint proteins or receptors. Illustrative NK-cell inhibitory immune checkpoint proteins or receptors include without limitation killer cell immunoglobulin like receptor, three Ig domains and long cytoplasmic tail 1 (KIR, CD158E1); killer cell immunoglobulin like receptor, two Ig domains and long cytoplasmic tail 1 (KIR2DL1); killer cell immunoglobulin like receptor, two Ig domains and long cytoplasmic tail 2 (KIR2DL2); killer cell immunoglobulin like receptor, two Ig domains and long cytoplasmic tail 3 (KIR2DL3); killer cell immunoglobulin like receptor, three Ig domains and long cytoplasmic tail 1 (KIR3DL1); killer cell lectin like receptor C1 (KLRC1, NKG2A, CD159A); and killer cell lectin like receptor D1 (KLRD1, CD94). In various embodiments, the one or more multi-specific antigen binding molecules, as described herein, are combined or co-administered with one or more agonist or activators of one or more NK-cell stimulatory immune checkpoint proteins or receptors. Illustrative NK-cell stimulatory immune checkpoint proteins or receptors include without limitation CD16, CD226 (DNAM-1); CD244 (2B4, SLAMF4); killer cell lectin like receptor K1 (KLRK1, NKG2D, CD314); SLAM family member 7 (SLAMF7). See, *e.g.*, Davis, et al., Semin Immunol. (2017) 31:64–75; Fang, et al., Semin Immunol. (2017) 31:37-54; and Chiossone, et al., Nat Rev Immunol. (2018) 18(11):671-688.

[0344] In some embodiments, the one or more immune checkpoint inhibitors comprises a proteinaceous (*e.g.*, antibody or fragment thereof, or antibody mimetic) inhibitor of PD-L1 (CD274), PD-1 (PDCD1) or CTLA4. In some embodiments, the one or

more immune checkpoint inhibitors comprises a small organic molecule inhibitor of PD-L1 (CD274), PD-1 (PDCD1) or CTLA4.

[0345] Examples of inhibitors of CTLA4 that can be co-administered include without limitation ipilimumab, tremelimumab, BMS-986218, AGEN1181, AGEN1884, BMS-986249, MK-1308, REGN-4659, ADU-1604, CS-1002, BCD-145, APL-509, JS-007, BA-3071, ONC-392, AGEN-2041, JHL-1155, KN-044, CG-0161, ATOR-1144, PBI-5D3H5, BPI-002, as well as multi-specific inhibitors FPT-155 (CTLA4/PD-L1/CD28), PF-06936308 (PD-1/ CTLA4), MGD-019 (PD-1/CTLA4), KN-046 (PD-1/CTLA4), MEDI-5752 (CTLA4/PD-1), XmAb-20717 (PD-1/CTLA4), and AK-104 (CTLA4/PD-1).

[0346] Examples of inhibitors of PD-L1 (CD274) or PD-1 (PDCD1) that can be co-administered include without limitation pembrolizumab, nivolumab, cemiplimab, pidilizumab, AMP-224, MEDI0680 (AMP-514), spartalizumab, atezolizumab, avelumab, durvalumab, BMS-936559, CK-301, PF-06801591, BGB-A317 (tislelizumab), GLS-010 (WBP-3055), AK-103 (HX-008), AK-105, CS-1003, HLX-10, MGA-012, BI-754091, AGEN-2034, JS-001 (toripalimab), JNJ-63723283, genolimzumab (CBT-501), LZM-009, BCD-100, LY-3300054, SHR-1201, SHR-1210 (camrelizumab), Sym-021, ABBV-181 (budigalimab), PD1-PIK, BAT-1306, (MSB0010718C), CX-072, CBT-502, TSR-042 (dostarlimab), MSB-2311, JTX-4014, BGB-A333, SHR-1316, CS-1001 (WBP-3155, KN-035, IBI-308 (sintilimab), HLX-20, KL-A167, STI-A1014, STI-A1015 (IMC-001), BCD-135, FAZ-053, TQB-2450, MDX1105-01, GS-4224, GS-4416, INCB086550, MAX10181, as well as multi-specific inhibitors FPT-155 (CTLA4/PD-L1/CD28), PF-06936308 (PD-1/ CTLA4), MGD-013 (PD-1/LAG-3), FS-118 (LAG-3/PD-L1) MGD-019 (PD-1/CTLA4), KN-046 (PD-1/CTLA4), MEDI-5752 (CTLA4/PD-1), RO-7121661 (PD-1/TIM-3), XmAb-20717 (PD-1/CTLA4), AK-104 (CTLA4/PD-1), M7824 (PD-L1/TGFβ-EC domain), CA-170 (PD-L1/VISTA), CDX-527 (CD27/PD-L1), LY-3415244 (TIM3/PDL1), and INBRX-105 (4-1BB/PDL1).

[0347] In some embodiments, the small molecule inhibitor of CD274 or PDCD1 is selected from the group consisting of GS-4224, GS-4416, INCB086550 and MAX10181. In some embodiments, the small molecule inhibitor of CTLA4 comprises BPI-002.

Inhibitors of T cell immunoreceptor with Ig and ITIM domains (TIGIT)

[0348] In various embodiments, the immunogenic polypeptides, polynucleotides encoding such polypeptides, vectors, LNPs and immunogenic compositions comprising such polypeptides or polynucleotides, as described herein, are combined or co-administered with one or more inhibitors of T cell immunoreceptor with Ig and ITIM domains (TIGIT) (NCBI Gene ID: 201633). Example anti-TIGIT antibodies, that can be combined or co-administered include etigilimab, BMS-986207, tiragolumab (*a.k.a.*, MTIG-7192A; RG-6058; RO 7092284), vibostolimab (MK-7684), ociperlimab (BGB-A1217), domvanalimab (AB154), AGEN1307, AGEN1327, AGEN1777, COM-902, IBI-939, AB154, SGN-TGT, MG1131 and EOS884448 (EOS-448).

TNF Receptor Superfamily (TNFRSF) Member Agonists or Activators

[0349] In various embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an agonist of one or more TNF receptor superfamily (TNFRSF) members, *e.g.*, an agonist of one or more of TNFRSF1A (NCBI Gene ID: 7132), TNFRSF1B (NCBI Gene ID: 7133), TNFRSF4 (OX40, CD134; NCBI Gene ID: 7293), TNFRSF5 (CD40; NCBI Gene ID: 958), TNFRSF6 (FAS, NCBI Gene ID: 355), TNFRSF7 (CD27, NCBI Gene ID: 939), TNFRSF8 (CD30, NCBI Gene ID: 943), TNFRSF9 (4-1BB, CD137, NCBI Gene ID: 3604), TNFRSF10A (CD261, DR4, TRAILR1, NCBI Gene ID: 8797), TNFRSF10B (CD262, DR5, TRAILR2, NCBI Gene ID: 8795), TNFRSF10C (CD263, TRAILR3, NCBI Gene ID: 8794), TNFRSF10D (CD264, TRAILR4, NCBI Gene ID: 8793), TNFRSF11A (CD265, RANK, NCBI Gene ID: 8792), TNFRSF11B (NCBI Gene ID: 4982), TNFRSF12A (CD266, NCBI Gene ID: 51330), TNFRSF13B (CD267, NCBI Gene ID: 23495), TNFRSF13C (CD268, NCBI Gene ID: 115650), TNFRSF16 (NGFR, CD271, NCBI Gene ID: 4804), TNFRSF17 (BCMA, CD269, NCBI Gene ID: 608), TNFRSF18 (GITR, CD357, NCBI Gene ID: 8784), TNFRSF19 (NCBI Gene ID: 55504), TNFRSF21 (CD358, DR6, NCBI Gene ID: 27242), and TNFRSF25 (DR3, NCBI Gene ID: 8718).

[0350] Example anti-TNFRSF4 (OX40) antibodies that can be co-administered include without limitation, MEDI6469, MEDI6383, MEDI0562 (tavolixizumab), MOXR0916, PF-04518600, RG-7888, GSK-3174998, INCAGN1949, BMS-986178, GBR-8383, ABBV-368, and those described in WO2016179517, WO2017096179, WO2017096182, WO2017096281, and WO2018089628.

[0351] Example anti-TNFRSF5 (CD40) antibodies that can be co-administered include without limitation RG7876, SEA-CD40, APX-005M and ABBV-428.

[0352] In some embodiments, the anti-TNFRSF7 (CD27) antibody varlilumab (CDX-1127) is co-administered.

[0353] Example anti-TNFRSF9 (4-1BB, CD137) antibodies that can be co-administered include without limitation urelumab, utomilumab (PF-05082566), AGEN2373 and ADG-106.

[0354] Example anti-TNFRSF18 (GITR) antibodies that can be co-administered include without limitation, MEDI1873, FPA-154, INCAGN-1876, TRX-518, BMS-986156, MK-1248, GWN-323, and those described in WO2017096179, WO2017096276, WO2017096189, and WO2018089628. In some embodiments, an antibody, or fragment thereof, co-targeting TNFRSF4 (OX40) and TNFRSF18 (GITR) is co-administered. Such antibodies are described, *e.g.*, in WO2017096179 and WO2018089628.

Bi-and Tri-Specific Natural Killer (NK)-Cell Engagers

[0355] In various embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a bi-specific NK-cell engager (BiKE) or a tri-specific NK-cell engager (TriKE) (*e.g.*, not having an Fc) or bi-specific antibody (*e.g.*, having an Fc) against an NK cell activating receptor, *e.g.*, CD16A, C-type lectin receptors (CD94/NKG2C, NKG2D, NKG2E/H and NKG2F), natural cytotoxicity receptors (NKp30, NKp44 and NKp46), killer cell C-type lectin-like receptor (NKp65, NKp80), Fc receptor FcγR (which mediates antibody-dependent cell cytotoxicity), SLAM family receptors (*e.g.*, 2B4, SLAM6 and SLAM7), killer cell immunoglobulin-like receptors (KIR) (KIR-2DS and KIR-3DS), DNAM-1 and CD137 (4-1BB). Illustrative anti-CD16 bi-specific antibodies, BiKEs or TriKEs that can be co-administered include AFM26 (BCMA/CD16A) and AFM-13 (CD16/CD30). As appropriate, the anti-CD16 binding bi-specific molecules may or may not have an Fc. BiKEs and TriKEs are described, *e.g.*, in Felices, et al., Methods Mol Biol. (2016) 1441:333–346; Fang, et al., Semin Immunol. (2017) 31:37-54. Examples of a trispecific NK cell engager (TRiKE) include OXS-3550, HIV-TriKE, and CD16-IL-15-B7H3 TriKe.

Phosphatidylinositol 3-kinase (PI3K) Inhibitors

[0356] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an inhibitor of at least

one of a phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit, *e.g.*, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3CA, CLAPO, CLOVE, CWS5, MCAP, MCM, MCMTC, PI3K, PI3K-alpha, p110-alpha; NCBI Gene ID: 5290); phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit beta (PIK3CB, P110BETA, PI3K, PI3KBETA, PIK3C1; NCBI Gene ID: 5291); phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit gamma (PIK3CG, PI3CG, PI3K, PI3Kgamma, PIK3, p110gamma, p120-PI3K; Gene ID: 5494); and phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit delta (PIK3CD, APDS, IMD14, P110DELTA, PI3K, p110D, NCBI Gene ID: 5293). In some embodiments, the PI3K inhibitor is a pan-PI3K inhibitor. Examples of PI3K inhibitors that can be combined or co-administered include without limitation, ACP-319, AEZA-129, AMG-319, AS252424, AZD8186, BAY 1082439, BEZ235, bimiralisib (PQR309), buparlisib (BKM120), BYL719 (alpelisib), carboxyamidotriazole orotate (CTO), CH5132799, CLR-457, CLR-1401, copanlisib (BAY 80-6946), DS-7423, duvelisib (IPI-145), fimepinostat (CUDC-907), gedatolisib (PF-05212384), GDC-0032, GDC-0084 (RG7666), GDC-0077, pictilisib (GDC-0941), GDC-0980, GSK2636771, GSK2269577, idelalisib (Zydelig®), INCB040093, INCB50465, IPI-443, IPI-549, KAR4141, LY294002, LY3023414, NERLYNX® (neratinib), nemiralisib (GSK2269557), omipalisib (GSK2126458, GSK458), OXY111A, panulisib (P7170, AK151761), PA799, perifosine (KRX-0401), Pilaralisib (SAR245408; XL147), puquitinib mesylate (XC-302), SAR260301, seletalisib (UCB-5857), serabelisib (INK-1117,MLN-1117,TAK-117), SF1126, sonolisib (PX-866), RG7604, rigosertib sodium (ON-01910 sodium), RP5090, tenalisib (RP6530), RV-1729, SRX3177, taselisib, TG100115, umbralisib (TGR-1202), TGX221, voxtalisib (SAR245409), VS-5584, WX-037, X-339, X-414, XL499, XL756, wortmannin, ZSTK474, and the compounds described in WO 2005/113556 (ICOS), WO 2013/052699 (Gilead Calistoga), WO 2013/116562 (Gilead Calistoga), WO 2014/100765 (Gilead Calistoga), WO 2014/100767 (Gilead Calistoga), and WO 2014/201409 (Gilead Sciences).

alpha-4/beta-7 antagonists

[0357] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an alpha-4/beta-7 antagonist. Examples of Integrin alpha-4/beta-7 antagonists include PTG-100, TRK-170, abrilumab, etrolizumab, carotegrast methyl, and vedolizumab.

HPK1 Inhibitors

[0358] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an inhibitor of mitogen-activated protein kinase kinase kinase kinase 1 (MAP4K1; NCBI Gene ID: 11184; *a.k.a.*, Hematopoietic Progenitor Kinase 1 (HPK1)). Examples of HPK1 inhibitors include, but are not limited to, ZYF-0272, and ZYF-0057.

Pharmacokinetic Enhancers

[0359] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a pharmacokinetic enhancer. Examples of pharmacokinetic enhancers include cobicistat and ritonavir.

Additional Therapeutic Agents

[0360] Examples of additional therapeutic agents include the compounds disclosed in WO 2004/096286 (Gilead Sciences); WO 2006/015261 (Gilead Sciences); WO 2006/110157 (Gilead Sciences); WO 2012/003497 (Gilead Sciences); WO 2012/003498 (Gilead Sciences); WO 2012/145728 (Gilead Sciences); WO 2013/006738 (Gilead Sciences); WO 2013/159064 (Gilead Sciences); WO 2014/100323 (Gilead Sciences), US 2013/0165489 (University of Pennsylvania), US 2014/0221378 (Japan Tobacco), US 2014/0221380 (Japan Tobacco); WO 2009/062285 (Boehringer Ingelheim); WO 2010/130034 (Boehringer Ingelheim); WO 2013/006792 (Pharma Resources), US 20140221356 (Gilead Sciences), US 20100143301 (Gilead Sciences) and WO 2013/091096 (Boehringer Ingelheim).

Long-Acting HIV Inhibitors

[0361] In some embodiments, the one or more multi-specific antigen binding molecules described herein can be co-administered with a long-acting HIV inhibitor. Examples of drugs that are being developed as long acting HIV inhibitors include without limitation: cabotegravir LA, rilpivirine LA, any integrase LA, VM-1500 LAI, maraviroc (LAI), tenofovir implant, islatravir (MK-8591) implant, long-acting dolutegravir.

HIV Vaccines

[0362] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV vaccine. Examples of HIV vaccines that can be combined with an agent of this disclosure include peptide vaccines, recombinant subunit protein vaccines, live vector vaccines, DNA vaccines, HIV MAG DNA vaccine, CD4-derived peptide vaccines, vaccine combinations,

adenoviral vector vaccines (an adenoviral vector such as Ad5, Ad26 or Ad35), simian adenovirus (chimpanzee, gorilla, rhesus, *i.e.*, rhAd), adeno-associated virus vector vaccines, Chimpanzee adenoviral vaccines (*e.g.*, ChAdOX1, ChAd68, ChAd3, ChAd63, ChAd83, ChAd155, ChAd157, Pan5, Pan6, Pan7, Pan9), Coxsackieviruses based vaccines, enteric virus based vaccines, Gorilla adenovirus vaccines, lentiviral vector based vaccine, arenavirus vaccines (such as LCMV, Pichinde), bi-segmented or tri-segmented arenavirus based vaccine, trimer-based HIV-1 vaccine, measles virus based vaccine, flavivirus vector based vaccines, tobacco mosaic virus vector based vaccine, Varicella-zoster virus based vaccine, Human parainfluenza virus 3 (PIV3) based vaccines, poxvirus based vaccine (modified vaccinia virus Ankara (MVA)), orthopoxvirus-derived NYVAC, and avipoxvirus-derived ALVAC (canarypox virus) strains); fowlpox virus based vaccine, rhabdovirus-based vaccines, such as VSV and marabavirus; recombinant human CMV (rhCMV) based vaccine, alphavirus-based vaccines, such as Semliki forest virus, Venezuelan equine encephalitis virus and sindbis virus (*see, e.g.*, Lauer, *et al., Clin Vaccine Immunol* (2017) 24(1):e00298-16); LNP formulated mRNA based therapeutic vaccines; LNP-formulated self-replicating RNA/self-amplifying RNA vaccines.

[0363] Examples of vaccines include: AAVLP-HIV vaccine, anti-CD40.Env-gp140 vaccine, Ad4-EnvC150, BG505 SOSIP.664 gp140 adjuvanted vaccine, BG505 SOSIP.GT1.1 gp140 adjuvanted vaccine, ChAdOx1.tHIVconsv1 vaccine, CMV-MVA triplex vaccine, ChAdOx1.HTI, Chimigen HIV vaccine, ConM SOSIP.v7 gp140, rgp120 (AIDSVAX), ALVAC HIV (vCP1521)/AIDSVAX B/E (gp120) (RV144), monomeric gp120 HIV-1 subtype C vaccine, MPER-656 liposome subunit vaccine, Remune, ITV-1, Contre Vir, Ad5-ENVA-48, DCVax-001 (CDX-2401), Vacc-4x, Vacc-C5, VAC-3S, multiclade DNA recombinant adenovirus-5 (rAd5), rAd5 gag-pol env A/B/C vaccine, Pennvax-G, Pennvax-GP, Pennvax-G/MVA-CMDR, HIV-TriMix-mRNA vaccine, HIV-LAMP-vax, Ad35, Ad35-GRIN, NAcGM3/VSSP ISA-51, poly-ICLC adjuvanted vaccines, TatImmune, GTU-multiHIV (FIT-06), ChAdV63.HIVconsv, gp140[delta]V2.TV1+MF-59, rVSVIN HIV-1 gag vaccine, SeV-EnvF, SeV-Gag vaccine, AT-20, DNK-4, ad35-Grin/ENV, TBC-M4, HIVAX, HIVAX-2, N123-VRC-34.01 inducing epitope-based HIV vaccine, NYVAC-HIV-PT1, NYVAC-HIV-PT4, DNA-HIV-PT123, rAAV1-PG9DP, GOVX-B11, GOVX-B21, GOVX-C55, TVI-HIV-1, Ad-4 (Ad4-env Clade C+Ad4-mGag), Paxvax, EN41-UGR7C, EN41-FPA2, ENOB-HV-11, PreVaxTat, AE-H, MYM-V101, CombiHIVvac, ADVAX, MYM-V201, MVA-CMDR, MagaVax, DNA-Ad5 gag/pol/nef/nev (HVTN505), MVATG-17401, ETV-01, CDX-1401, DNA and Sev vectors

vaccine expressing SCaVII, rcAD26.MOS1.HIV-Env, Ad26.Mod.HIV vaccine, Ad26.Mod.HIV + MVA mosaic vaccine + gp140, AGS-004, AVX-101, AVX-201, PEP-6409, SAV-001, ThV-01, TL-01, TUTI-16, VGX-3300, VIR-1111, IHV-001, and virus-like particle vaccines such as pseudovirion vaccine, CombiVICHvac, LFn-p24 B/C fusion vaccine, GTU-based DNA vaccine, HIV gag/pol/nef/env DNA vaccine, anti-TAT HIV vaccine, conjugate polypeptides vaccine, dendritic-cell vaccines (such as DermaVir), gag-based DNA vaccine, GI-2010, gp41 HIV-1 vaccine, HIV vaccine (PIKA adjuvant), i-key/MHC class II epitope hybrid peptide vaccines, ITV-2, ITV-3, ITV-4, LIPO-5, multiclade Env vaccine, MVA vaccine, Pennvax-GP, pp71-deficient HCMV vector HIV gag vaccine, , rgp160 HIV vaccine, RNActive HIV vaccine, SCB-703, Tat Oyi vaccine, TBC-M4, UBI HIV gp120, Vacc-4x + romidepsin, variant gp120 polypeptide vaccine, rAd5 gag-pol env A/B/C vaccine, DNA.HTI and MVA.HTI, VRC-HIVDNA016-00-VP + VRC-HIVADV014-00-VP, INO-6145, JNJ-9220, gp145 C.6980; eOD-GT8 60mer based vaccine, PD-201401, env (A, B, C, A/E)/gag (C) DNA Vaccine, gp120 (A,B,C,A/E) protein vaccine, PDPHV-201401, Ad4-EnvCN54, EnvSeq-1 Envs HIV-1 vaccine (GLA-SE adjuvanted), HIV p24gag prime-boost plasmid DNA vaccine, HIV-1 iglb12 neutralizing VRC-01 antibody-stimulating anti-CD4 vaccine, arenavirus vector-based vaccines (Vaxwave, TheraT), MVA-BN HIV-1 vaccine regimen, UBI HIV gp120, mRNA based prophylactic vaccines, VPI-211, TBL-1203HI, CH505 TF chTrimer, CD40.HIVRI.Env vaccine, Drep-HIV-PT-1, mRNA-1644, and mRNA-1574.

Birth control (contraceptive) combination therapy

[0364] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a birth control or contraceptive regimen. Therapeutic agents used for birth control (contraceptive) include cyproterone acetate, desogestrel, dienogest, drospirenone, estradiol valerate, ethinyl Estradiol, ethynodiol, etonogestrel, levomefolate, levonorgestrel, lynestrenol, medroxyprogesterone acetate, mestranol, mifepristone, misoprostol, nomegestrol acetate, norelgestromin, norethindrone, noretynodrel, norgestimate, ormeloxifene, segestersone acetate, ulipristal acetate, and any combinations thereof.

Gene Therapy and Cell Therapy

[0365] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a gene or cell therapy regimen. Gene therapy and cell therapy include without limitation the genetic modification

to silence a gene; genetic approaches to directly kill the infected cells; the infusion of immune cells designed to replace most of the patient's own immune system to enhance the immune response to infected cells, or activate the patient's own immune system to kill infected cells, or find and kill the infected cells; genetic approaches to modify cellular activity to further alter endogenous immune responsiveness against the infection. Examples of cell therapy include LB-1903, ENOB-HV-01, ENOB-HV-21, ENOB-HV-31, GOVX-B01, HSPCs overexpressing ALDH1 (LV-800, HIV infection), AGT103-T, and SupT1 cell-based therapy. Examples of dendritic cell therapy include AGS-004. CCR5 gene editing agents include SB-728T. CCR5 gene inhibitors include Cal-1, and lentivirus vector CCR5 shRNA/TRIM5alpha/TAR decoy-transduced autologous CD34-positive hematopoietic progenitor cells (HIV infection/HIV-related lymphoma). In some embodiments, C34-CCR5/C34-CXCR4 expressing CD4-positive T-cells are co-administered with one or more multi-specific antigen binding molecules. In some embodiments, the agents described herein are co-administered with AGT-103-transduced autologous T-cell therapy or AAV-eCD4-Ig gene therapy.

Gene Editors

[0366] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a gene editor, *e.g.*, an HIV targeted gene editor. In various embodiments, the genome editing system can be selected from the group consisting of: a CRISPR/Cas9 complex, a zinc finger nuclease complex, a TALEN complex, a homing endonucleases complex, and a meganuclease complex. An illustrative HIV targeting CRISPR/Cas9 system includes without limitation EBT-101.

CAR-T-cell therapy

[0367] In some embodiments, the one or more multi-specific antigen binding molecules described herein can be co-administered with a population of immune effector cells engineered to express a chimeric antigen receptor (CAR), wherein the CAR comprises an HIV antigen binding domain. The HIV antigen includes an HIV envelope protein or a portion thereof, gp120 or a portion thereof, a CD4 binding site on gp120, the CD4-induced binding site on gp120, N glycan on gp120, the V2 of gp120, the membrane proximal region on gp41. The immune effector cell is a T-cell or an NK cell. In some embodiments, the T-cell is a CD4+ T-cell, a CD8+ T-cell, or a combination thereof. Cells can be autologous or allogeneic. Examples of HIV CAR-T include convertible CAR-T, VC-CAR-T, CMV-N6-

CART, anti-CD4 CART-cell therapy, CD4 CAR+C34-CXCR4+CCR5 ZFN T-cells, dual anti-CD4 CART-T cell therapy (CD4 CAR+C34-CXCR4 T-cells), anti-CD4 MicAbody antibody + anti-MicAbody CAR T-cell therapy (iNKG2D CAR, HIV infection), GP-120 CAR-T therapy, autologous hematopoietic stem cells genetically engineered to express a CD4 CAR and the C46 peptide.

TCR-T-cell therapy

[0368] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a population of TCR-T-cells. TCR-T-cells are engineered to target HIV derived peptides present on the surface of virus-infected cells, for example ImmTAV.

B-cell therapy

[0369] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a population of B cells genetically modified to express broadly neutralizing antibodies, such as 3BNC117 (Hartweger, *et al, J. Exp. Med.* (2019) 1301, Moffett, *et al., Sci. Immunol.* 4, eaax0644 (2019) 17 May 2019).

Illustrative Combination Therapies

[0370] In some embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with one, two, three, four or more additional therapeutic agents selected from ATRIPLA® (efavirenz, tenofovir disoproxil fumarate, and emtricitabine); COMPLERA® (EVIPLERA®; rilpivirine, tenofovir disoproxil fumarate, and emtricitabine); STRIBILD® (elvitegravir, cobicistat, tenofovir disoproxil fumarate, and emtricitabine); TRUVADA® (tenofovir disoproxil fumarate and emtricitabine; TDF +FTC); DESCOVY® (tenofovir alafenamide and emtricitabine); ODEFSEY® (tenofovir alafenamide, emtricitabine, and rilpivirine); GENVOYA® (tenofovir alafenamide, emtricitabine, cobicistat, and elvitegravir); BIKTARVY® (bictegravir + emtricitabine + tenofovir alafenamide), adefovir; adefovir dipivoxil; cobicistat; emtricitabine; tenofovir; tenofovir alafenamide and elvitegravir; tenofovir alafenamide + elvitegravir (rectal formulation, HIV infection); tenofovir disoproxil; tenofovir disoproxil fumarate; tenofovir alafenamide; tenofovir alafenamide hemifumarate; TRIUMEQ® (dolutegravir, abacavir, and lamivudine); dolutegravir, abacavir sulfate, and lamivudine; raltegravir; PEGylated raltegravir; raltegravir and

lamivudine; maraviroc; tenofovir + emtricitabine + maraviroc, enfuvirtide; ALUVIA® (KALETRA®; lopinavir and ritonavir); COMBIVIR® (zidovudine and lamivudine; AZT+3TC); EPZICOM® (LIVEXA®; abacavir sulfate and lamivudine; ABC+3TC); TRIZIVIR® (abacavir sulfate, zidovudine, and lamivudine; ABC+AZT+3TC); rilpivirine; rilpivirine hydrochloride; atazanavir sulfate and cobicistat; atazanavir and cobicistat; darunavir and cobicistat; atazanavir; atazanavir sulfate; dolutegravir; elvitegravir; ritonavir; atazanavir sulfate and ritonavir; darunavir; lamivudine; prolastin; fosamprenavir; fosamprenavir calcium efavirenz; etravirine; nelfinavir; nelfinavir mesylate; interferon; didanosine; stavudine; indinavir; indinavir sulfate; tenofovir and lamivudine; zidovudine; nevirapine; saquinavir; saquinavir mesylate; aldesleukin; zalcitabine; tipranavir; amprenavir; delavirdine; delavirdine mesylate; Radha-108 (receptol); lamivudine and tenofovir disoproxil fumarate; efavirenz, lamivudine, and tenofovir disoproxil fumarate; phosphazid; lamivudine, nevirapine, and zidovudine; abacavir; and abacavir sulfate.

[0371] In some embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with an HIV nucleoside or nucleotide inhibitor of reverse transcriptase and an HIV non-nucleoside inhibitor of reverse transcriptase. In another specific embodiment, the one or more multi-specific antigen binding molecules described herein, or a pharmaceutical composition thereof, is combined or co-administered with an HIV nucleoside or nucleotide inhibitor of reverse transcriptase, and an HIV protease inhibiting compound. In an additional embodiment, the one or more multi-specific antigen binding molecules described herein, or a pharmaceutical composition thereof, is combined or co-administered with an HIV nucleoside or nucleotide inhibitor of reverse transcriptase, an HIV non-nucleoside inhibitor of reverse transcriptase, and a pharmacokinetic enhancer. In certain embodiments, the one or more multi-specific antigen binding molecules described herein, or a pharmaceutical composition thereof, is combined or co-administered with at least one HIV nucleoside inhibitor of reverse transcriptase, an integrase inhibitor, and a pharmacokinetic enhancer. In another embodiment, the one or more multi-specific antigen binding molecules described herein, or a pharmaceutical composition thereof, is combined or co-administered with two HIV nucleoside or nucleotide inhibitors of reverse transcriptase.

[0372] In some embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with abacavir sulfate,

tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, tenofovir alafenamide, or tenofovir alafenamide hemifumarate.

[0373] In some embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir alafenamide, or tenofovir alafenamide hemifumarate.

[0374] In some embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a first additional therapeutic agent selected from the group consisting of abacavir sulfate, tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir alafenamide, and tenofovir alafenamide hemifumarate, and a second additional therapeutic agent selected from the group consisting of emtricitabine and lamivudine.

[0375] In some embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a first additional therapeutic agent selected from the group consisting of tenofovir, tenofovir disoproxil, tenofovir disoproxil fumarate, tenofovir alafenamide, and tenofovir alafenamide hemifumarate, and a second additional therapeutic agent, wherein the second additional therapeutic agent is emtricitabine.

[0376] In some embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a first additional therapeutic agent selected from a first additional therapeutic agent selected from dolutegravir, cabotegravir, islatravir, darunavir, bictegravir, elsulfavirine, rilpivirine, and lenacapavir and a second additional therapeutic agent selected from emtricitabine and lamivudine.

[0377] In some embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with a first additional therapeutic agent (a contraceptive) selected from the group consisting of cyproterone acetate, desogestrel, dienogest, drospirenone, estradiol valerate, ethinyl Estradiol, ethynodiol, etonogestrel, levomefolate, levonorgestrel, lynestrenol , medroxyprogesterone acetate, mestranol, mifepristone , misoprostol, nomegestrol acetate, norelgestromin, norethindrone, noretynodrel, norgestimate, ormeloxifene , segestersone acetate, ulipristal acetate, and any combinations thereof.

[0378] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with one or more additional therapeutic agents in a therapeutically effective dosage in the amount in the range of *e.g.*, in the range of 0.05 mg to 1000 mg per administration, *e.g.,* from 0.05 mg to 150 mg per administration, *e.g.,* from 0.05 mg to 0.35 mg per administration, *e.g.,* from 25 mg to 50 mg per administration, *e.g.,* from 30 mg to 35 mg per administration, *e.g.,* from 10 mg to 1000 mg per administration, *e.g.,* from 50 mg to 1000 mg per administration, *e.g.,* from 100 mg to 700 mg per administration, *e.g.*, at least 0.05 mg up to 0.1 mg, 0.2 mg, 0.3 mg, 0.35 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg, 0.8 mg, 1.0 mg, 5 mg, 10 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 200 mg, 300 mg, 400 mg, 500 mg, 600 mg, 700 mg, 800 mg, 900 mg, or 1000 mg per administration of the multi-specific antigen binding molecule. In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with one or more additional therapeutic agents, the multi-specific antigen binding molecule being administered in a therapeutically effective dosage amount, *e.g.*, in the range of from 1 μg/kg to 5 μg/kg, *e.g.*, from 350 μg/kg to 550 μg/kg, *e.g.*, from 0.3 mg/kg to 30 mg/kg, *e.g.*, from 2 mg/kg to 10 mg/kg, *e.g.*, from 1 μg/kg up to 2 μg/kg, 3 μg/kg, 4 μg/kg, 5 μg/kg, 10 μg/kg, 50 μg/kg, 100 μg/kg, 250 μg/kg, 300 μg/kg, 350 μg/kg, 400 μg/kg, 410 μg/kg, 420 μg/kg, 430 μg/kg, 440 μg/kg, 450 μg/kg, 460 μg/kg, 470 μg/kg, 480 μg/kg, 490 μg/kg, 500 μg/kg, 750 μg/kg, 1 mg/kg, 1.5 mg/kg, 2 mg/kg, 2.5 mg/kg, 3 mg/kg, 3.5 mg/kg, 4 mg/kg, 4.5 mg/kg, 5 mg/kg, 6 mg/kg, 7 mg/kg, 8 mg/kg, 9 mg/kg, 10 mg/kg, 15 mg/kg, 20 mg/kg, 25 mg/kg, 30 mg/kg, 35 mg/kg, 40 mg/kg, 45 mg/kg, or 50 mg/kg, body weight per administration.

[0379] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with 5-30 mg tenofovir alafenamide fumarate, tenofovir alafenamide hemifumarate, or tenofovir alafenamide, and 200 mg emtricitabine. In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with 5-10, 5-15, 5-20, 5-25, 25-30, 20-30, 15-30, or 10-30 mg tenofovir alafenamide fumarate, tenofovir alafenamide hemifumarate, or tenofovir alafenamide, and 200 mg emtricitabine. In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with 10 mg tenofovir alafenamide fumarate, tenofovir alafenamide hemifumarate, or tenofovir alafenamide, and 200 mg emtricitabine. In certain embodiments, the one or more multi-specific antigen binding molecules described herein

are combined or co-administered with 25 mg tenofovir alafenamide fumarate, tenofovir alafenamide hemifumarate, or tenofovir alafenamide, and 200 mg emtricitabine. In some embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with the agents provided herein in any dosage amount of the one or more multi-specific antigen binding molecules (*e.g.*, from 1 mg to 500 mg of the one or more multi-specific antigen binding molecules, as described herein) the same as if each combination of dosages were specifically and individually listed.

[0380] In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with 200-400 mg tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, or tenofovir disoproxil, and 200 mg emtricitabine. In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with 200-250, 200-300, 200-350, 250-350, 250-400, 350-400, 300-400, or 250-400 mg tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, or tenofovir disoproxil, and 200 mg emtricitabine. In certain embodiments, the one or more multi-specific antigen binding molecules described herein are combined or co-administered with 300 mg tenofovir disoproxil fumarate, tenofovir disoproxil hemifumarate, or tenofovir disoproxil, and 200 mg emtricitabine. The one or more multi-specific antigen binding molecules may be combined with the agents provided herein in any dosage amount (*e.g.*, from 1 mg to 500 mg of the one or more multi-specific antigen binding molecules) the same as if each combination of dosages were specifically and individually listed.

11. Pharmaceutical Compositions

[0381] Further provided are pharmaceutical compositions comprising one or more (*e.g.*, one, two or three) multi-specific antigen binding molecules, as described herein, or one or more polynucleotide encoding one or more multi-specific antigen binding molecules, as described herein, and a pharmaceutically acceptable diluent, carrier or excipient. In certain embodiments, the pharmaceutical composition comprises a therapeutically effective amount of one or more unitary doses of one or more multi-specific antigen binding molecules, or one or more polynucleotides encoding the one or more multi-specific antigen binding molecules.

[0382] Various pharmaceutically acceptable diluents, carriers, and excipients, and techniques for the preparation and use of pharmaceutical compositions will be known to those of skill in the art in light of the present disclosure. Illustrative pharmaceutical

compositions and pharmaceutically acceptable diluents, carriers, and excipients are also described, *e.g.*, in Remington: The Science and Practice of Pharmacy 20th Ed. (Lippincott, Williams & Wilkins 2003); Loyd V. Allen Jr (Editor), "Remington: The Science and Practice of Pharmacy," 22nd Edition, 2012, Pharmaceutical Press; Brunton, Knollman and Hilal-Dandan, "Goodman and Gilman's The Pharmacological Basis of Therapeutics," 13th Edition, 2017, McGraw-Hill Education / Medical; McNally and Hastedt (Editors), "Protein Formulation and Delivery, 2nd Edition, 2007, CRC Press; Banga, "Therapeutic Peptides and Proteins: Formulation, Processing, and Delivery Systems," 3rd Edition, 2015, CRC Press; Lars Hovgaard, Frokjaer and van de Weert (Editors), "Pharmaceutical Formulation Development of Peptides and Proteins," 2nd Edition, 2012, CRC Press; Carpenter and Manning (Editors), "Rational Design of Stable Protein Formulations: Theory and Practice," 2002, Springer (Pharmaceutical Biotechnology (Book 13)); Meyer (Editor), "Therapeutic Protein Drug Products: Practical Approaches to Formulation in the Laboratory, Manufacturing, and the Clinic, 2012, Woodhead Publishing; and Shire, "Monoclonal Antibodies: Meeting the Challenges in Manufacturing, Formulation, Delivery and Stability of Final Drug Product, 2015, Woodhead Publishing.

[0383] In some embodiments, each carrier, diluent or excipient is "acceptable" in the sense of being compatible with the other ingredients of the pharmaceutical composition and not injurious to the subject. Often, the pharmaceutically acceptable carrier is an aqueous pH-buffered solution. Some examples of materials which can serve as pharmaceutically-acceptable carriers, diluents or excipients include: water; buffers, *e.g.*, phosphate-buffered saline; sugars, such as lactose, trehalose, glucose and sucrose; starches, such as corn starch and potato starch; cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients, such as cocoa butter and suppository waxes; oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene glycol; polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; esters, such as ethyl oleate and ethyl laurate; agar; buffering agents, such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline; Ringer's solution; ethyl alcohol; phosphate buffer solutions; 2-Amino-2-(hydroxymethyl)propane-1,3-diol (*i.e.*, tris(hydroxymethyl)aminomethane; Tris) buffers, amino acids (*e.g.*, charged amino acids, including without limitation, aspartate, asparagine, glutamate, glutamine, histidine, lysine, arginine); and other non-toxic compatible substances employed in pharmaceutical formulations. Wetting agents, emulsifiers and lubricants, such

as sodium lauryl sulfate, a polysorbate (*e.g.*, polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80) and magnesium stearate, as well as coloring agents, release agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants can also be present in the compositions. In one embodiment, the pharmaceutical composition comprises a physiologically acceptable buffer, pH 5.5 to 8.5, *e.g.*, pH 5.5 to 6.5, sucrose, and polysorbate 80. In one embodiment, the pharmaceutical composition comprises histidine, sucrose, and polysorbate 80. In one embodiment, the pharmaceutical composition comprises sodium phosphate, sucrose, and polysorbate 80. In one embodiment, the pharmaceutical composition comprises a Tris buffer, sucrose, and polysorbate 80. In certain embodiments, pharmaceutical compositions are sterile. In certain embodiments, the pharmaceutical composition has a pH in the range of 4.5 to 8.5, 5.5 to 7.4, 4.5 to 6.5, 6.4 to 7.0, 6.5 to 8.5, 7.2 to 7.8, or a pH of 5.0, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.5, 7.0, 7.5, 8.0 or 8.5. In one embodiment, the pharmaceutical composition has an osmolarity in the range of 240-260 or 250-330 mOsmol/L. In certain embodiments, the pharmaceutical composition is isotonic or near isotonic.

[0384] The formulation of and delivery methods of pharmaceutical compositions will generally be adapted according to the site and the disease to be treated. Exemplary formulations include, but are not limited to, those suitable for parenteral administration, *e.g.*, intravenous, intra-arterial, intramuscular, or subcutaneous administration, including formulations encapsulated in micelles, liposomes or drug-release capsules (active agents incorporated within a biocompatible coating designed for slow-release); ingestible formulations; formulations for topical use, such as creams, ointments and gels; and other formulations such as inhalants, aerosols and sprays.

[0385] In some embodiments, the pharmaceutical compositions are formulated for parenteral, *e.g.*, intravenous, subcutaneous, or intramuscular). In particular embodiments, for parenteral administration, the antibodies or antigen-binding fragments thereof are formulated in a unit dosage injectable form (solution, suspension, emulsion) in association with a pharmaceutically acceptable, parenteral vehicle. Examples of such vehicles include water, saline, Ringer's solution, dextrose solution, and 5% human serum albumin. Nonaqueous vehicles such as fixed oils and ethyl oleate may also be used. Liposomes may be used as carriers. The vehicle may contain minor amounts of additives such as substances that enhance isotonicity and chemical stability, *e.g.*, buffers and preservatives. In certain embodiments, the multi-specific antigen binding molecules are formulated in such vehicles

at concentrations of from 0.10 mg/ml to 150 mg/ml, *e.g.*, from 0.11 mg/ml to 100 mg/ml, *e.g.*, from 1 mg/ml to 100 mg/ml, *e.g.*, from 5 mg/ml to 60 mg/ml, *e.g.*, from 20 mg/ml to 150 mg/ml, *e.g.*, from 10 mg/ml to 50 mg/ml, *e.g.*, 5mg/ml, 10 mg/ml, 15 mg/ml, 20 mg/ml, 25 mg/ml, 30 mg/ml, 35 mg/ml, 40 mg/ml, 45 mg/ml, 50 mg/ml, 60 mg/ml, 70 mg/ml, 80 mg/ml, 90 mg/ml, 100 mg/ml, 125 mg/ml or 150 mg/ml.

[0386] In some embodiments, the pharmaceutical composition comprises a multi-specific antigen binding molecule having a first antigen binding domain that binds to CD3, and a second antigen binding domain that binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises one or more extracellular (EC) domains of CD4, and optionally, an IL-15 receptor agonist. In some embodiments, the one or more EC domains of CD4 comprise a sequence as set forth in SEQ ID NOs: 746-749, or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO:746). In some embodiments, the EC domain of CD4 comprises a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 95% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises the sequence of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid

sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (*e.g.*, at least 99%) identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first

VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (*e.g.*, at least 99%) identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen

binding domain comprises one EC domain of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (*e.g.*, at least 99%) identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (*e.g.*, SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL

comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC

domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively: SEQ ID

NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence of SEQ ID NO:746.

[0387] In some embodiments, the pharmaceutical composition comprises first and second antigen binding molecules. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03, and the second antigen binding molecule or antibody or fragment thereof, competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT121.414, 10-1074, 10-1074-J and PGT-134, and the second antigen binding molecule or antibody or antigen binding fragment thereof competes with or comprises VH and VL regions from 3BNC117, GS-9723, VRC07 or VRC07-523.

[0388] In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25, and the second antigen binding molecule or antibody or fragment thereof, competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8,

354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, VRC07 or VRC07-523, and the second antigen binding molecule or antibody or antigen binding fragment thereof competes with or comprises VH and VL regions from GS-9722 (elipovimab), GS-2872, PGT-121, PGT121.414, 10-1074, 10-1074-J and PGT-134.

[0389] In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT121.414, 10-1074, 10-1074-J and PGT-134, and the second antigen binding molecule comprises a soluble extracellular region of CD4 (*e.g.*, domain 1 (D1), D1-D2, D1-D3, D1-D4). In some embodiments, the first multi-specific antigen binding molecule comprises a soluble extracellular region of CD4 (*e.g.*, domain 1 (D1), D1-D2, D1-D3, D1-D4), and the second antigen binding molecule or antibody or fragment thereof, competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the first multi-specific antigen binding molecule comprises a soluble extracellular region of CD4 (*e.g.*, domain 1 (D1), D1-D2, D1-D3, D1-D4), and the second antigen binding molecule or antibody or antigen binding fragment thereof competes with or comprises VH and VL regions from GS-9722 (elipovimab), GS-2872, PGT-121, PGT121.414, 10-1074, 10-1074-J and PGT-134.

[0390] In some embodiments, the pharmaceutical composition comprises first, second and third antigen binding molecules. In some embodiments, the pharmaceutical composition comprises a first multi-specific antigen binding molecule and second and third multi-specific antigen binding molecules or antibodies or fragments thereof. In some embodiments, the first multi-specific antigen binding molecule comprises a soluble extracellular region of CD4 (*e.g.*, domain 1 (D1), D1-D2, D1-D3, D1-D4); the second antigen binding molecule or antibody or fragment thereof, competes with or comprises VH

and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03; and the third multi-specific antigen binding molecule or antibody or fragment thereof, competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the first multi-specific antigen binding molecule comprises a soluble extracellular region of CD4 (*e.g.*, domain 1 (D1), D1-D2, D1-D3, D1-D4); the second antigen binding molecule or antibody or fragment thereof, competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT121.414, 10-1074, 10-1074-J and PGT-134; and the third multi-specific antigen binding molecule or antibody or antigen binding fragment thereof competes with or comprises VH and VL regions from 3BNC117, GS-9723, VRC07 or VRC07-523.

12. Kits

[0391] Further provided are kits comprising one or more of the multi-specific antigen binding molecules described herein, including polynucleotides, pharmaceutical compositions and conjugates thereof.

[0392] In some embodiments, the kit comprises a multi-specific antigen binding molecule having a first antigen binding domain that binds to CD3, and a second antigen binding domain that binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises one or more extracellular (EC) domains of CD4, and optionally, an IL-15 receptor agonist. In some embodiments, the one or more EC domains of CD4 comprise a sequence as set forth in SEQ ID NOs: 746-749, or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NOs: 746-749 (e.g., SEQ ID NO:746). In some embodiments, the EC domain of CD4 comprises a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at

least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 95% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises a sequence that is at least 99% identical to the sequence of SEQ ID NO: 746. In some embodiments, the EC domain of CD4 comprises the sequence of SEQ ID NO: 746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (e.g., SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first

VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (e.g., SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (e.g., at least 99%) identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (e.g., SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain

comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (e.g., at least 99%) identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (e.g., SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence is at least 95% (e.g., at least 99%) identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one EC domain of CD4 comprising the amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL

comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749 (e.g., SEQ ID NO:746). In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and

the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising the amino acid sequence of SEQ ID NO: 51 and a first VL comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4

comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH comprising an amino acid sequence that is at least 99% identical to the amino acid sequence of SEQ ID NO: 51 and a first VL comprising the amino acid sequence of SEQ ID NO: 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO:746. In some embodiments, the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence of SEQ ID NO:746.

[0393] In some embodiments, the kits comprise one or more containers (*e.g.*, vials, ampules) comprising one or more of the multi-specific antigen binding molecules described herein, polynucleotides encoding such multi-specific antigen binding molecules, LNPs or pharmaceutical compositions containing such multi-specific antigen binding molecules.

[0394] In one embodiment, kits comprise the one or more multi-specific antigen binding molecules described herein in combination with one or more (*e.g.*, one, two, three, one or two, or one to three) additional therapeutic agents. In some embodiments, the kits comprise one or more unitary doses of the one or more multi-specific antigen binding molecules, or the polynucleotide or polynucleotides, in one or more containers. In some embodiments, the kits comprise one or more unitary doses of the one or more multi-specific antigen binding molecules and a second agent for treating an HIV infection in separate containers.

[0395] In some embodiments, the kits further comprise one or more unitary doses of a toll-like receptor (TLR) agonist. In some embodiments, the TLR agonist is a TLR7 agonist or a TLR8 agonist. In some embodiments, the TLR7 agonist is selected from the group consisting of vesatolimod, imiquimod, and resiquimod. In some embodiments, the kits comprise a first multi-specific antigen binding molecule and a second antigen binding molecule or antibody or antigen binding fragment thereof, wherein the first multi-specific antigen binding molecule and a second antigen binding molecule or antibody or antigen binding fragment thereof bind to different first and second epitopes or regions of gp120 selected from the group consisting of: (i) third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan; (ii) second variable loop (V2) (*e.g.*, Env trimer apex); (iii) CD4 binding site (CD4bs); (iv) gp120/gp41 interface; or (v) silent face of gp120. In some embodiments, the first multi-specific antigen binding molecule binds to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and the second antigen binding molecule binds to the CD4 binding site (CD4bs).

[0396] In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03, and the second antigen binding molecule or antibody or fragment thereof, competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT121.414, 10-1074, 10-1074-J and PGT-134, and the second antigen binding molecule or antibody or antigen binding fragment thereof competes with or comprises VH and VL regions from 3BNC117, GS-9723, VRC07 or VRC07-523.

[0397] In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25, and the second antigen binding molecule or antibody or fragment thereof, competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, VRC07 or VRC07-523, and the second antigen binding molecule or antibody or antigen binding fragment thereof competes with or comprises VH and VL regions from GS-9722 (elipovimab), GS-2872, PGT-121, PGT121.414, 10-1074, 10-1074-J and PGT-134.

[0398] In some embodiments, the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT121.414, 10-1074, 10-1074-J and PGT-134, and the second antigen binding molecule comprises a soluble extracellular region of CD4 (*e.g.*, domain 1 (D1), D1-D2, D1-D3, D1-D4). In some embodiments, the first multi-specific antigen binding molecule comprises a soluble extracellular region of CD4 (*e.g.*, domain 1 (D1), D1-D2, D1-D3, D1-D4), and the second antigen binding molecule or antibody or fragment thereof, competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03. In some embodiments, the first multi-specific antigen binding molecule comprises a soluble extracellular region of CD4 (*e.g.*, domain 1 (D1), D1-D2, D1-D3, D1-D4), and the second antigen binding molecule or

antibody or antigen binding fragment thereof competes with or comprises VH and VL regions from GS-9722 (elipovimab), GS-2872, PGT-121, PGT121.414, 10-1074, 10-1074-J and PGT-134.

[0399] In some embodiments, the kits comprise a first multi-specific antigen binding molecule and second and third multi-specific antigen binding molecules or antibodies or fragments thereof. In some embodiments, the first multi-specific antigen binding molecule comprises a soluble extracellular region of CD4 (*e.g.*, domain 1 (D1), D1-D2, D1-D3, D1-D4); the second antigen binding molecule or antibody or fragment thereof, competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03; and the third multi-specific antigen binding molecule or antibody or fragment thereof, competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25. In some embodiments, the first multi-specific antigen binding molecule comprises a soluble extracellular region of CD4 (*e.g.*, domain 1 (D1), D1-D2, D1-D3, D1-D4); the second antigen binding molecule or antibody or fragment thereof, competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT121.414, 10-1074, 10-1074-J and PGT-134; and the third multi-specific antigen binding molecule or antibody or antigen binding fragment thereof competes with or comprises VH and VL regions from 3BNC117, GS-9723, VRC07 or VRC07-523.

[0400] In some embodiments, the kits comprise two or more unitary doses of one or more multi-specific antigen binding molecules, and optionally, one or more anti-HIV bNAbs, wherein the unitary doses are the same. In some embodiments, the kits comprise two or more unitary doses of one or more multi-specific antigen binding molecules, and optionally, one or more anti-HIV bNAbs, wherein the unitary doses are different.

[0401] In one embodiment, the additional therapeutic agent or agents of the kit is an anti-HIV agent, selected from HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry inhibitors, HIV maturation inhibitors, immunomodulators, immunotherapeutic agents, antibody-drug conjugates, gene modifiers, gene editors (such as CRISPR/Cas9, zinc finger nucleases, homing nucleases, synthetic nucleases, TALENs), cell therapies (such as chimeric antigen receptor T-cell, CAR-T, and engineered T cell receptors, TCR-T, autologous T cell therapies), compounds that target the HIV capsid, latency reversing agents, HIV bNAbs, immune-based therapies, phosphatidylinositol 3-kinase (PI3K) inhibitors, HIV antibodies, broadly neutralizing HIV antibodies, bispecific antibodies and "antibody-like" therapeutic proteins, HIV p17 matrix protein inhibitors, IL-13 antagonists, peptidyl-prolyl cis-trans isomerase A modulators, protein disulfide isomerase inhibitors, complement C5a receptor antagonists, DNA methyltransferase inhibitor, HIV vif gene modulators, Vif dimerization antagonists, HIV viral infectivity factor inhibitors, TAT protein inhibitors, HIV Nef modulators, Hck tyrosine kinase modulators, mixed lineage kinase-3 (MLK-3) inhibitors, HIV splicing inhibitors, Rev protein inhibitors, integrin antagonists, nucleoprotein inhibitors, splicing factor modulators, COMM domain containing protein 1 modulators, HIV ribonuclease H inhibitors, retrocyclin modulators, CDK-9 inhibitors, dendritic ICAM-3 grabbing nonintegrin 1 inhibitors, HIV GAG protein inhibitors, HIV POL protein inhibitors, Complement Factor H modulators, ubiquitin ligase inhibitors, deoxycytidine kinase inhibitors, cyclin dependent kinase inhibitors, proprotein convertase PC9 stimulators, ATP dependent RNA helicase DDX3X inhibitors, reverse transcriptase priming complex inhibitors, G6PD and NADH-oxidase inhibitors, pharmacokinetic enhancers, HIV gene therapy, HIV vaccines, and combinations thereof.

[0402] In some embodiments, the additional therapeutic agent or agents of the kit are selected from combination drugs for HIV, other drugs for treating HIV, HIV protease inhibitors, HIV reverse transcriptase inhibitors, HIV integrase inhibitors, HIV non-catalytic site (or allosteric) integrase inhibitors, HIV entry (fusion) inhibitors, HIV maturation inhibitors, latency reversing agents, capsid inhibitors, immune-based therapies, PI3K inhibitors, HIV antibodies, and bispecific antibodies, and "antibody-like" therapeutic proteins, and combinations thereof.

[0403] In a specific embodiment, the kit includes a multi-specific antigen binding molecule, polynucleotide encoding or pharmaceutical composition comprising, and an HIV nucleoside or nucleotide inhibitor of reverse transcriptase. In a specific embodiment, the kit includes a multi-specific antigen binding molecule, polynucleotide encoding or pharmaceutical composition comprising, and an HIV nucleoside or nucleotide inhibitor of reverse transcriptase and an HIV non-nucleoside inhibitor of reverse transcriptase. In another specific embodiment, the kit includes a multi-specific antigen binding molecule, polynucleotide encoding or pharmaceutical composition comprising, and an HIV nucleoside or nucleotide inhibitor of reverse transcriptase, and an HIV protease inhibiting compound. In an additional embodiment, the kit includes a multi-specific antigen binding molecule, polynucleotide encoding or pharmaceutical composition comprising, and an HIV nucleoside or nucleotide inhibitor of reverse transcriptase, an HIV non-nucleoside inhibitor of reverse transcriptase, and a pharmacokinetic enhancer. In certain embodiments, the kit includes a multi-specific antigen binding molecule, polynucleotide encoding or pharmaceutical composition comprising, and at least one HIV nucleoside inhibitor of reverse transcriptase, an integrase inhibitor, and a pharmacokinetic enhancer. In another embodiment, the kit includes a multi-specific antigen binding molecule, polynucleotide encoding or pharmaceutical composition comprising, and two HIV nucleoside or nucleotide inhibitors of reverse transcriptase. In a specific embodiment, the kit includes a multi-specific antigen binding molecule, polynucleotide encoding or pharmaceutical composition comprising, and an HIV nucleoside or nucleotide inhibitor of reverse transcriptase and an HIV capsid inhibitor. In a specific embodiment, the kit includes a multi-specific antigen binding molecule, polynucleotide encoding or pharmaceutical composition comprising, and an HIV nucleoside inhibitor of reverse transcriptase and an HIV capsid inhibitor. In a specific embodiment, the kit includes a multi-specific antigen binding molecule, polynucleotide encoding or pharmaceutical composition comprising, and an HIV capsid inhibitor. In a specific embodiment, the kit includes a multi-specific antigen binding molecule, polynucleotide encoding or pharmaceutical composition comprising, and one, two, three or four HIV bNAbs. In a specific embodiment, the kit includes a multi-specific antigen binding molecule, polynucleotide encoding or pharmaceutical composition comprising, and one, two, three or four HIV bNAbs and an HIV capsid inhibitor. In a specific embodiment, the kit includes a multi-specific antigen binding molecule, polynucleotide encoding or pharmaceutical composition comprising, and one, two, three or four HIV bNAbs, an HIV capsid inhibitor, and an HIV nucleoside inhibitor of reverse transcriptase.

[0404] In one embodiment, the kit comprises one or more pharmaceutical packs comprising one or more containers (*e.g.*, vials, ampules) containing one or more of the ingredients of the pharmaceutical compositions described herein, such as one or more multi-specific (*e.g.*, bispecific antibodies) provided herein. In some instances, the kits contain a pharmaceutical composition described herein. In one embodiment, kits comprising a multi-specific antigen binding molecule disclosed herein, or a pharmaceutical composition thereof, in combination with one or more (*e.g.*, one, two, three, one or two, or one to three) additional therapeutic agents (such as those disclosed above) are provided.

[0405] Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

EXAMPLES

[0406] The following examples are offered to illustrate, but not to limit the claimed invention.

Example 1

Humanization of Mouse SP34 Variable Domains

[0407] Bispecific antibodies, in which one of the antigen binding domains interacts with the human CD3 extracellular domain (referred to as "CD3 bispecific antibodies hereafter") can re-direct CD3+ T-cells to kill target cells expressing a second antigen (*e.g.*, Blinatumomab recruitment of CD3+ T-cells to kill CD19+ B-cells). The anti-CD3 binding domain can be used in a modular fashion to re-direct T-cells to attack cells expressing any target antigen of interest (*e.g.* tumor antigens or viral antigens). In most cases, the anti-CD3 antibody is selected to be cross-reactive to non-human primate (NHP) CD3, thus facilitating animal efficacy and toxicity studies. These animal studies are of critical importance given the potential for toxicity associated with CD3 engaging bispecific antibodies. However, a review of the literature suggests that current generation anti-CD3 bispecific antibodies suffer from numerous challenges in pre-clinical studies.

[0408] A 2017 FDA analysis of investigational new drug (IND) applications for clinical stage CD3 bispecific antibodies found that anti-drug-antibodies (ADA) presented significant pre-clinical challenges for all 10 INDs analyzed (Saber, *et al. Regul. Toxicol. Pharmacol.* (2017) 90:144-152). These high preclinical ADA rates may cause difficulty in conducting and/or interpreting pre-clinical efficacy and toxicity studies. In at least one of the examples analyzed by Saber *et al*, where clinical data was also available, approximately 60% of patients developed ADA. Although this data is far from definitive, and it is generally accepted that high ADA rates in NHP do not correlate with high ADA rates in humans (van Meer, *et al. mAbs* (2013) 5:810-816), these results suggest that prior to the present disclosure, there did not exist anti-CD3 antibodies with low immunogenicity in both NHPs and humans in order to facilitate both the pre-clinical and clinical study of CD3 bispecific antibodies for the treatment of human diseases. This may be particularly important outside of heme malignancies (*e.g.* solid tumors, infectious disease) where elimination of the target cell type (*e.g.* B-cells) can often limit the host immune response and reduce or eliminate the negative impacts of ADA. Further, it is not feasible to implement a high dose strategy in toxicology studies for immune activating biologics in

NHP where ADA is observed, where a high dose overcomes the ADA (*e.g.*, "dosing through" ADA), due to dose-related toxicity.

[0409] The murine SP34 (mSP34) antibody binds human CD3 and cross reacts with many primate CD3 proteins with similar affinity (Pessano, *et al., EMBO J.* (1985) 4:337-344, Conrad, *et al. Cytometry A.* (2007) 71:925-933). For this reason, humanized variants of mSP34 (huSP34) are among the most commonly used anti-CD3 domains in clinical stage bispecific antibodies. To better understand potential sources of immunogenicity, we conducted a primary sequence analysis of mSP34 as well as a panel of six clinical stage huSP34 variants. Sequences were obtained from the WHO Drug Information INN lists (who.int/medicines/publications/druginformation/innlists/en/), and all antibodies with ≤ 2 amino acid mismatches to mSP34 across both CDR H3 and CDR L3 were compiled. The variable heavy (VH) and variable light (VL) sequences of these antibodies along with that of Trastuzumab (anti-HER2) were compared to the closest human germlines using the IMGT domain-gap-align server (imgt.org/3Dstructure-DB/cgi/DomainGapAlign.cgi). The results of this analysis (Table 1) demonstrate that mSP34 and all clinical stage comparators that were analyzed exhibit lower variable (Fv) identity to the human germline ($\leq$ 80% ID) when compared to Trastuzumab (82% ID), a humanized antibody with low clinical ADA rates (Jackisch, *et al., Annals of Oncology* (2015) 26: 320-325).

Table 1 - Similarity of mSP34 Fv and clinical stage huSP34 Fv to the human germline

Name	VH % ID Human Germline	Closest Human VH Germline	VL % ID Human Germline	Closest Human VL Germline	Fv %ID Human Germline
mSP34 Fv	71	IGHV3-73*01 IGHJ4*1	65	IGLV7-46*01 IGLJ3*02	69
Comparator #5 Fv	80	IGHV3-73*01 IGHJ4*01	77	IGLV7-46*01 IGLJ3*02	79
Comparator #1 Fv	80	IGHV3-73*01 IGHJ4*01	78	IGLV7-46*01 IGLJ3*02	79
Comparator #2 Fv	75	IGHV3-73*01 IGHJ4*01	73	IGLV8-61*01 IGLJ3*02	74
Comparator #3 Fv	81	IGHV3-72*01 IGHJ4*01	79	IGLV7-46*01 IGLJ3*02	80
Comparator #4 Fv	80	IGHV3-23*03 IGHJ4*01	80	IGLV7-46*01 IGLJ3*02	80
hu4D5 Fv Trastuzumab	78	IGHV3-66*01 IGHJ4*01	87	IGKV1-39*01 IGKJ1*01	82

[0410] In addition to the primary sequence, post-translational modification to antibodies, such as oxidation, deamidation and aspartate isomerization have also been implicated in the immunogenicity of biotherapeutics (FDA Guidance For Industry "Immunogenicity Assessment for Therapeutic Protein Products," by U.S. Department of Health and Human Services Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), August 2014, Clinical/Medical; available at fda.gov/media/85017/download). The primary sequence of a biotherapeutic contributes to the risk of these modifications, and as such, they are often referred to as "sequence liabilities." Modification of sequence liabilities can also lead to structural and functional heterogeneity in the final purified product that can complicate manufacturing and product stability (Lu, *et al., mAbs* (2019) 11:45-57). To better understand if mSP34 and clinical stage huSP34 variants contained solvent exposed sequence liabilities, we generated mSP34 homology models and conducted a primary sequence analysis of all solvent exposed sequence liabilities in mSP34 and clinical stage comparator Fv domains (Figures 1-2). The results suggest that mSP34 and many huSP34 variants contains several theoretical sequence liabilities that could potentially lead to product heterogeneity, manufacturing difficulties and increased immunogenic risk.

[0411] Aggregation propensity has also been associated with the immunogenicity of biotherapeutics (Rosenberg, *AAPS J.* (2006) 8:E501-507, Seidl, *et al. Pharm Res.* (2012) 29:1454-1467). Engineering of antibodies including humanization and conversion to scFv formats can lead to unintended increases in aggregation propensity (Glockshuber, *et al., Biochemistry* (1990) 29: 1362-1367, Wörn and Plückthun. *J. Mol. Biol.* (2001) 305: 989-1010). It is not known if humanization of mSP34 or other anti-CD3 binding domains can influence the aggregation propensity and/or immunogenic risk of CD3 engaging bispecific antibodies.

[0412] The affinity of anti-CD3 antibodies has been reported to impact both targeted cell-killing potency as well as pharmacokinetics (PK) (Ellerman, *Methods* (2019) 154:102-117). In animal models containing cross-reactive CD3 antigens, anti-CD3 antibodies with higher affinities (< 10 nM) are associated with reduced antibody half-life, while anti-CD3 antibodies with lower affinities (> 10 nM) are associated with improved antibody half-life similar to that observed in the same animal model without a cross-reactive CD3 antigen (Leong, *et al., Blood* (2017) 129:609-618). This suggests that CD3 target mediated drug

disposition (TMDD) may play a role in limiting the PK half-life of high affinity anti-CD3 mAbs. However, antibody polyspecificity or polyreactivity can also influence the PK half-life of antibodies (Hötzel, *et al.*, *mAbs* (2012) 4:753-760) and mutations that increase antibody affinity are sometimes associated with reductions in antibody specificity (Rabia *et al., Biochem Eng. J.* (2018) 137:365-374). It is not clear if it is possible to identify an anti-CD3 antibody with both high CD3 affinity and corresponding high targeted killing potency with the PK characteristics of a typical IgG.

[0413] Based on these challenges and considerations, we sought to develop an anti-CD3 antibody variable domain with (i) a high affinity for human and non-human primate (NHP) (*e.g.*, to facilitate pre-clinical toxicity studies) CD3, (ii) a high sequence similarity to the human germline (*e.g.*, to reduce or eliminate risk of immunogenicity and ADA reactions in human patients), (iii) IgG-like PK properties with no evidence of ADA in non-human primates (*e.g.*, to facilitate pre-clinical efficacy and toxicity studies), (iv) reduced product heterogeneity via removal of sequence liabilities (*e.g.*, deamidation, aspartate isomerization) to improve ease of manufacturing, (v) high thermodynamic stability (to ensure product stability), (vi) low aggregate content (to reduce risk of immunogenicity) and (vii) low polyspecificity (to reduce the risk of immunogenicity and improve PK properties). We also sought to develop such an anti-CD3 antibody with (viii) a heavy chain variable region (VH) with low or no binding to Protein A affinity chromatography resin in order to facilitate purification of bispecific antibody heterodimers. Finally, we sought to develop an anti-CD3 antibody variable domain that possessed all these properties as an scFv or Fab, such that it could be incorporated into a variety of bispecific antibody formats containing three or fewer polypeptide chains to limit light chain miss-pairing or other sources of bispecific antibody product heterogeneity (Example 2).

[0414] We selected the murine SP34 antibody as a starting point for humanization because it binds human CD3 and cross-reacts with many primate CD3 proteins (Pessano, *et al. EMBO J.* (1985) 4:337-344, Conrad, *et al., Cytometry A* (2007) 71:925-933).

[0415] The sequences of the murine SP34 (mSP34) variable heavy (VH) and variable light (VL) domains are shown below.

mSP34 VH

EVKLLESGGGLVQPKGSLKLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKDRFTISRDDSQSILYLQMNNLKTEDTAMYYCVRHGNFGNSYVSWFAYWGQGTLVT VSA (SEQ ID NO: 713)

mSP34 VL

QAVVTQESALTTSPGETVTLTCRSSTGAVTTSNYANWVQEKPDHLFTGLIGGTNKRAPGVP ARFSGSLIGDKAALTITGAQTEDEAIYFCALWYSNLWVFGGGTKLTVLG (SEQ ID NO: 714)

[0416] The mSP34 VH and VL sequences were compared to the IMGT database (imgt.org) to identify suitable target human germlines for humanization. The closest heavy chain variable (V) and joining (J) segment matches identified were IGHV3-72 and IGHJ6 respectively. The closest light chain variable (V) and joining (J) segment matches identified were IGLV7-46 and IGLJ3 respectively. Next, we used the default homology modeling protocol in Discovery Studio 2017r2 (Biovia) to generate a structure model of mSP34, using a dual-affinity re-targeting (DART®) bispecific molecule as a template for homology modeling (Root, *et al.*, *Antibodies* (Basel) (2016) 5(1):6; RCSB Protein Data Bank (PDB) ID: 5FCS; rcsb.org/structure/5FCS). We further used the default antibody modeling cascade protocol in Discovery Studio 2017r2 to generate structural models of the target human germline antibodies. By superposing these two homology models (Figure 3), we identified CDR graft points as well as framework residues from mSP34 to retain in huSP34. Consistent with the goals outlined above, we also explored whether mSP34 CDR residues could be mutated to human germline residues in order to increase identity to the human germline and further reduce the risk of immunogenicity, whether germline consensus residues and structure guided salt-bridges could be used to stabilize and/or improve structural or functional properties, and also mutated residues involved in putative sequence liabilities to assess their role in product heterogeneity.

[0417] The initial round of structure-based humanization for mSP34 led to the design of 6 VL and 10 VH variants. The sequences of these variants are shown aligned to mSP34 and the human germline target VH and VL sequences in Figures 4A-4B. The human germline identity of all 60 possible huSP34 combinations are shown in Table 2. The amino acid sequences of the variable region sequences of HC1-HC10 are provided in Table 3. The amino acid sequences of the variable region sequences of LC1-LC6 are provided in Table 4.

Table 2

First round huSP34 Fv variant percentage identify to the human germline

	HC1	HC2	HC3	HC4	HC5	HC6	HC7	HC8	HC9	HC10
LC1	80	80	79.6	80	79.1	78.7	81.3	81.3	81.7	81.7
LC2	82.1	82.1	81.7	82.1	81.3	80.9	83.4	83.4	83.8	83.8
LC3	82.1	82.1	81.7	82.1	81.3	80.9	83.4	83.4	83.8	83.8
LC4	82.6	82.6	82.1	82.6	81.7	81.3	83.8	83.8	84.3	84.3
LC5	83.8	83.8	83.4	83.8	83	82.6	85.1	85.1	85.5	85.5
LC6	81.7	81.7	81.3	81.7	80.9	80.4	83	83	83.4	83.4

Table 3

Amino Acid Sequences of the Variable Region Sequences of HC1-HC10

Name	SEQ ID NO:	Amino acid sequence
HC1	53	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLE WVGRIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTED TAMYYCVRHGNFGNSYVSWFAYWGQGTLVTVSS
HC2	715	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLE WVGRIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTED TAMYYCVRHGNFGNSYVSWFAVWGQGTLVTVSS
HC3	50	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLE WVGRIRSKYNNYATYYADSVKGRFTISRDDSKNSLYLQMNSLRTED TAVYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS
HC4	716	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLE WVGRIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLRTED TAVYYCVRHGNFGHSYVSWFAVWGQGTLVTVSS
HC5	717	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLE WVGRIRSKYNNYATYYADSVKGRFTISRDNSKNTLYLQMNSLRAED TAVYYCVRHGNFGHSYVSWFAVWGQGTLVTVSS
HC6	718	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLE WVGRIRSKYNNYATYYADSVKGRFTISRDNSKNTLYLQMNSLRAED TAMYYCVRHGNFGNSYVSWFAVWGQGTLVTVSS
HC7	719	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYAMNWVRQAPGKGLE WVGRTRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTED TAVYYCVRHGNFGNSYVSWFAVWGQGTLVTVSS
HC8	720	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYAMNWVRQAPGKGLE WVGRTRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTED TAVYYCVRHGNFGHSYVSWFAVWGQGTLVTVSS

Name	SEQ ID NO:	Amino acid sequence
HC9	721	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYAMNWVRQAPGKGLE WVGRTRSKYNSYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTED TAVYYCVRHGNFGNSYVSWFAVWGQGTLVTVSS
HC10	722	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYAMNWVRQAPGKGLE WVGRTRSKYNSYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTED TAVYYCVRHGNFGHSYVSWFAVWGQGTLVTVSS

Table 4

Amino Acid Sequences of the Variable Region Sequences of LC1-LC6

Name	SEQ ID NO:	Amino acid sequence
LC1	723	QAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYANWVQQKPGQAP RGLIGGTNKRAPWTPARFSGSLIGDKAALTLSGAQPEDEAEYYCAL WYSNLWVFGGGTKLTVL
LC2	724	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWVQQKPGQAP RGLIGGTSNRAPWTPARFSGSLLGGKAALTLSGAQPEDEAEYYCAL WYSNLWVFGGGTKLTVL
LC3	57	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGAQPEDEAEYYCAL WYSNLWVFGGGTKLTVL
LC4	725	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSHYANWVQQKPGQAP RGLIGGTSKRAPWTPARFSGSLLGGKAALTLSGAQPEDEAEYYCAL WYSALWVFGGGTKLTVL
LC5	726	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTSNRAPWTPARFSGSLLGGKAALTLSGAQPEDEAEYYCAL WYSARWVFGGGTKLTVL
LC6	727	QAVVTQPPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTSNRAPGVPARFSGSLSGGKAALTISGAQPEDEAEYYCAL WYSARWVFGGGTKLTVL

[0418] All 60 possible combinations of huSP34 heavy chain and light chain variants (the 1st round huSP34 variants), as well as the mSP34 parent antibody and a comparator huSP34 molecule (Comparator #6), were then expressed in HEK293 cells as Fabs incorporating a human CH1 domain and a human lambda light chain constant domain. The heavy chain Fab polypeptide incorporated a C-terminal His8-Flag tag (His8 or HHHHHHHH disclosed as SEQ ID NO: 1041) to facilitate purification using standard nickel affinity chromatography methods (Porath, *et al., Nature* (1975) 258: 598–599). The

resulting Fabs were subjected to analysis using the following methods: expression titer assessment, analytical size exclusion chromatography (SEC) to assess structural heterogeneity, analytical CX-1 ion exchange chromatography to assess charge heterogeneity, thermal denaturation to determine melting temperature (Tm) and aggregation temperature (Tagg), competition flow cytometry binding to primary T-cells to assess relative T-cell binding compared to mSP34, affinity analysis using Octet in order to assess relative binding kinetics (k_{on} and k_{off}) and dissociation constants (K_D), and competition flow cytometry assays to assess relative binding affinity to human T-cells as outlined in Examples 4, 5, 7 and 8.

[0419] The resulting data revealed several unexpected observations. The majority of humanized Fab variants from round 1 had significantly higher melting temperatures than the chimeric mSP34 Fab containing mSP34 variable regions fused to human constant domains. This suggested that the structure-guided humanization improved the thermodynamic stability of this molecule (Example 4). However, both the competition flow cytometry and Octet biolayer interferometry (BLI) assays suggested that the round 1 huSP34 variants had reduced CD3 binding affinity compared to the mSP34 chimeric Fab (Examples 5 and 8). Furthermore, the majority of purified round 1 huSP34 Fab variants demonstrated more charge-based heterogeneity when analyzed using strong cation exchange chromatography, and an increase in aggregate levels as measured by size exclusion chromatography when compared to mSP34 chimeric Fab (Example 4). By analyzing the relationship between the sequences of the huSP34 variants and their functional and biophysical properties (sequence-activity relationships or SAR) we identified multiple amino acids associated with improved properties (Examples 4 and 5). This allowed for the rational design of new variants (the second round huSP34 variants) incorporating mutations designed to optimize the various functional and biophysical properties assayed (Examples 4, 5, 7 and 8). The sequences of the heavy chain and light chain variable domains used in the second round huSP34 variants are shown in Figures 5A-5B.

[0420] All 16 possible combinations of the second round huSP34 heavy chain and light chain variants were expressed in HEK293 cells as Fabs incorporating a human CH1 domain and a human lambda light chain constant domain. The human germline identities of the second round huSP34 variants are shown in Table 5. The amino acid sequences of the variable region sequences of HC11-HC13 are provided in Table 6. The amino acid sequences of the variable region sequences of LC7-LC10 are provided in Table 7. The

heavy chain Fab polypeptide incorporated a C-terminal His8-Flag tag (His8 or HHHHHHHH disclosed as SEQ ID NO: 1041) to facilitate purification using standard nickel affinity chromatography methods (Porath, *et al.*, *supra*). After purification, the resulting Fabs were subjected to analysis using the following methods: analytical size exclusion chromatography (SEC), analytical CX-1 ion exchange chromatography, affinity analysis using Octet, and competition flow cytometry on human T-cells as outlined in Examples 4, 5, and 8. The results of the analysis revealed that our SAR guided approach was successful, as many of the second round huSP34 variants had improved affinity, improved CX-1 profiles (*e.g.* reduced heterogeneity) and improved SEC profiles (*e.g.* reduced aggregate levels) all while maintaining a high match to the human germline when compared to the first-round variants, the mSP34 chimeric Fab and comparator molecules (Figure 6).

Table 5

Second round huSP34 Fv variant percentage identify to the human germline

	HC3	**HC11**	**HC12**	**HC13**
LC7	80	80.9	80.4	81.3
LC8	80.9	81.7	81.3	82.1
LC9	79.6	80.4	80	80.9
LC10	80	80.9	80.4	81.3

Table 6

Amino Acid Sequences of the Variable Region Sequences of HC11-HC13

Name	**SEQ ID NO:**	**Amino acid sequence**
HC11	728	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLE WVGRIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLRTED TAVYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS
HC12	729	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLE WVARIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLRTED TAVYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS
HC13	730	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLE WVGRIRSKYNNYATYYAASVKGRFTISRDDSKNTLYLQMNSLRTED TAVYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS

Table 7

Amino Acid Sequences of the Variable Region Sequences of LC7-LC10

Name	SEQ ID NO:	Amino acid sequence
LC7	731	QAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTGHYANWVQQKPGQAP RGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAEYYCAL WYSNLWVFGGGTKLTVL
LC8	58	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAEYYCAL WYSNRWVFGGGTKLTVL
LC9	732	QAVVTQPPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTNKRAPGVPARFSGSLSGGKAALTISGAQPEDEAEYYCAL WYSNLWVFGGGTKLTVL
LC10	733	QAVVTQPPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTNKRAPGVPARFSGSLSGGKAALTISGAQPEDEAEYYCAL WYSNRWVFGGGTKLTVL

[0421] Selected first and second round huSP34 Fab variants were next reformatted as anti-HIV gp120 bispecific antibodies (Example 2). These antibodies were assessed in vitro in T-cell binding (Example 9) and T-cell mediated killing assays targeting HIV infected cells (Examples 10-11). The results demonstrated that the bispecific antibodies incorporating the huSP34 anti-CD3 binding arms potently killed HIV infected cells, and also showed the killing potency was directly correlated with anti-CD3 affinity.

[0422] Selected bispecific antibodies containing first and second round huSP34 variants were next tested in non-human primate PK assays (Example 13). Antibodies were tested in the presence and absence of Fc mutations, each made in only one of the two Fc domains, known to impact Protein A binding as well as enhance FcRn binding. Surprisingly, bispecific antibodies incorporating the lower affinity first round huSP34.1.3 scFv showed ideal IgG-like PK properties and no evidence of ADAs, consistent with our design goals, while bispecific antibodies incorporating the higher affinity second round huSP34.13.10 scFv demonstrated increased clearance, reduced half-life and high apparent rates of ADA induction. While mutations that eliminated Protein A binding (*e.g.* H435R, H435R+Y436F, Jendeberg, *et al., J. Immunol. Methods* (1997) 201:25–34) did not appear to significantly impact PK, certain mutations that improved pH dependent FcRn binding (YTE) did appear to mitigate some of the undesirable PK properties introduced by the high affinity huSP34.13.8 variant. Unfortunately, these FcRn binding mutations did not appear to eliminate the apparent high ADA rates observed for bispecific antibodies incorporating

higher affinity second round huSP34 scFv domains. The huSP34.1.3 variant did not show the highest potency in our killing assays, and it also contained the N100 residue in CDR H3 that appeared to be associated with increased product heterogeneity. We thus set out to conduct a third round of humanization seeking to identify a high affinity huSP34 variant containing the N100H mutation in CDRH3 and demonstrating ideal IgG-like PK properties and no evidence of ADA induction in non-human primates.

[0423] Although CD3 affinity has been directly implicated in the PK properties of bispecific antibodies (Ellerman, *Methods* (2019) 154:102-117), antibody polyspecificity can also influence PK (Hötzel, *et al., mAbs* (2012) 4:753-760) and was not tested during the first and second rounds of humanization. We thus generated a panel of the highest affinity huSP34 variants from rounds one and two as human IgG1 antibodies, thus enabling additional biophysical assessment (Example 4) including polyspecificity analysis using baculoviral particle (BVP) assays (Example 7). The BVP results revealed significant differences in polyspecificity within the huSP34 IgG1 panel. Selected bispecific antibodies, including those containing the huSP34.1.3 and huSP34.13.10 scFv were also tested in the BVP assay and revealed a direct correlation between moderate to high BVP scores and poor PK parameters.

[0424] We next used the BVP data to guide the selection of three distinct huSP34 variants to be used as starting points for the third round of humanization. The huSP34.1.3 variant was selected based on its low BVP score and ideal PK properties. The huSP34.3.8 variant was selected based on its low BVP score, high affinity and excellent results across all biophysical screening assays. The huSP34.1.10 variant had not yet been produced or tested in any form, but was selected based on the observation of SAR around HC1 and LC10 – both of which were associated with the lowest BVP scores. To determine if polyspecificity or affinity attributes contributed to the *in vivo* PK properties of the huSP34 containing bispecific antibodies, we generated variants with a range of affinities using SAR data from the first and second rounds of humanization. We further incorporated the N100H mutation into all tested variants (where not already present in any of the three lead variants) to eliminate the HC CDR H3 deamidation motif and reduce product heterogeneity as observed in the analytical CX-1 analysis. The identity of the third round huSP34 variants compared to the human germline is shown in Table 8. The amino acid sequences of the variable region sequences of HC34-HC38 are provided in Table 9. The amino acid sequences of the variable region sequences of LC11-LC20 are provided in Table 10.

Table 8

Third round huSP34 Fv variant percentage identify to the human germline

Heavy Chain Variant	Light Chain Variant	%ID human Germline
34	10	80.4
34	14	81.3
34	15	80.9
34	12	81.3
34	6	81.7
35	10	81.3
34	16	82.1
35	14	82.1
34	17	81.7
35	15	81.7
34	18	82.6
35	12	82.1
35	6	82.6
36	10	80.9
37	10	80.9
3	13	81.7
3	19	81.3
38	13	82.6
34	3	82.1
34	11	81.3

Table 9

Amino Acid Sequences of the Variable Region Sequences of HC34-HC38

Name	SEQ ID NO:	Amino acid sequence
HC34	52	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLE WVGRIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTED TAMYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS

Name	SEQ ID NO:	Amino acid sequence
HC35	734	EVQLVESGGGLVQPGGSLRLSCAASGFTFNDYAMNWVRQAPGKGLE WVGRTRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTED TAMYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS
HC36	735	EVQLVESGGGLVQPGGSLRLSCAASGFTFNDYAMNWVRQAPGKGLE WVGRIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTED TAMYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS
HC37	736	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLE WVGRTRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTED TAMYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS
HC38	737	EVQLVESGGGLVQPGGSLRLSCAASGFTFNDYAMNWVRQAPGKGLE WVGRTRSKYNNYATYYADSVKGRFTISRDDSKNSLYLQMNSLRTED TAVYYCVRHGNFGHSYVSWFAYWGQGTLVTVSS

Table 10

Amino Acid Sequences of the Variable Region Sequences of LC11-LC20

Name	SEQ ID NO:	Amino acid sequence
LC11	738	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTNKRAPGVPARFSGSLLGGKAALTLSGAQPEDEAEYYCAL WYSNLWVFGGGTKLTVL
LC12	739	QAVVTQPPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTNKRAPWTPARFSGSLSGGKAALTISGAQPEDEAEYYCAL WYSNRWVFGGGTKLTVL
LC13	56	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTSNRAPGVPARFSGSLLGGKAALTISGAQPEDEAEYYCAL WYSNRWVFGGGTKLTVL
LC14	740	QAVVTQPPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTSNRAPGVPARFSGSLSGGKAALTISGAQPEDEAEYYCAL WYSNRWVFGGGTKLTVL
LC15	741	QAVVTQPPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTNKRAPGVPARFSGSLSGGKAALTISGAQPEDEAEYYCAL WYSARWVFGGGTKLTVL
LC16	742	QAVVTQPPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTSNRAPWTPARFSGSLSGGKAALTISGAQPEDEAEYYCAL WYSNRWVFGGGTKLTVL
LC17	743	QAVVTQPPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTNKRAPWTPARFSGSLSGGKAALTISGAQPEDEAEYYCAL WYSARWVFGGGTKLTVL

Name	SEQ ID NO:	Amino acid sequence
LC18	744	QAVVTQPPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTSNRAPWTPARFSGSLSGGKAALTISGAQPEDEAEYYCAL WYSARWVFGGGTKLTVL
LC19	745	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTGHYANWVQQKPGQAP RGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEAEYYCAL WYSARWVFGGGTKLTVL

[0425] The third round huSP34 variants were next generated as Fabs or incorporated into anti-HIV gp120 targeting bispecific antibodies. These molecules were then characterized in BLI (Example 5) and SPR (Example 6) affinity assays, BVP polyspecificity assays (Example 7), T-cell binding assays (Example 9) and non-human primate PK analysis (Example 13). The T-cell binding assays confirmed that binding to human and NHP T-cells was nearly identical among all variants tested (Example 9). Surprisingly, and in contrast to previous literature reports (Leong, *et al., Blood* (2017) 129:609-618), the results presented here demonstrate no relationship between CD3 affinity and antibody clearance. More specifically, huSP34.3.8 and its variant huSP34.3.13 had both the highest anti-CD3 affinities (Example 6) and longest serum half-life among all molecules tested (Example 13). The huSP34.3.13 variant had both the lowest polyspecificity risk and the lowest clearance, suggesting that the BVP score may be a better predictor of anti-CD3 bispecific mAb PK properties than anti-CD3 affinity.

Example 2

Design, Expression and Purification of Anti-HIV-gp120 Bispecific Antibodies and Fc Fusion Proteins Containing huSP34 Anti-CD3 Binding Domains.

[0426] Many different bispecific antibody formats have been described, with many of these being used to develop therapeutic molecules (reviewed in Spiess and Carter, *Mol. Immunol.*, (2015) 67: 95-106, Labrijn, *et al., Nat. Rev. Drug Disc.* (2019) 18, 585-608). While early generation fragment-based formats built around one or two polypeptide chains and lacking an IgG Fc can be readily manufactured, they suffer from poor PK. Short half-life can increase the C_{max} driven toxicity of CD3 directed bispecific antibodies and necessitates complex dosing (*e.g.* continuous infusion with Blinatumomab). While many technologies have been developed to facilitate heterodimerization of the Fc domain, no robust technologies exist to facilitate unique pairing of the heavy chain and light chain, thus necessitating the use of common light chain antibodies (Shiraiwa, *et al., Methods* (2019)

154:10-20) or the generation of multiple stable cell lines followed by either complex redox chemistry, or co-culturing methods to produce bispecific antibodies without light chain miss-pairing (Gramer, *et al., mAbs* (2013) 5:962-973, Spiess, *et al., Nat. Biotechnol.* (2013) 31:753-758, Shatz, *et al., mAbs* (2016) 8:1487-1497). Finally, even if Fc heterodimerization and appropriate light chain pairing can be achieved, homodimeric contaminants can be challenging to remove during manufacturing, reducing final yields and/or presenting safety risks. We therefore sought to design and produce a bispecific antibody with IgG-like manufacturing properties, IgG-like PK properties and incorporating technologies to simplify purification. Examples of bispecific antibody designs that may address these challenges are illustrated in Figures 7A-7D. The technologies that may be incorporated into these designs are described below.

[0427] In bispecific antibodies incorporating two antigen targeting antibody variable domains, the use of a single chain fragment variable (scFv) domain can directly eliminate mispairing of light chains by removing one light chain polypeptide from the construct. scFv fragments represent a minimal antibody-derived antigen binding unit and are generated by direct fusion of a variable heavy and variable light domain via a flexible polypeptide linker (Huston *et al., Proc Natl Acad Sci U S A* (1988) 85(16):5879-83). The sequence of this linker can contain 3 or preferably 4 repeats of a GGGGS motif (SEQ ID NO: 712) (Desplancq, *et al., Protein Engineering* (1994) 7:1027-1033). The G44C mutation (variable heavy domain) and the G100C mutation (variable light domain) may also be used to generate a covalent disulfide bond between the VH and VL domains of the scFv if additional thermodynamic stability is required (Brinkmann, *et al., Proc Natl Acad Sci U S A* (1993) 90(16):7538-42).

[0428] To maximize heterodimerization of the two different heavy chain-containing species, so-called 'knobs-into-holes' mutations can be introduced into the Fc regions (Atwell, *et al., J Mol Biol* (1997) 270(1):26-35). The 'hole' mutations (T366S, L368A and Y407V) are incorporated into one Fc-containing chain, while the T366W 'knob' mutation is used in the other chain (Atwell, *et al., supra*). These mutations will also be referred to as "SAV" and "W" respectively herein. In addition, the C220S mutation is incorporated into the IgG1 hinge region of the scFv-containing arm to eliminate a free cysteine (in the context of a native IgG, this cysteine is responsible for forming a disulfide bond with a corresponding cysteine in the light chain). Co-transfection of such constructs leads to preferential formation of a heterodimeric Fc, with low levels of homodimer contaminants.

The S354C (made in the Fc containing the 'knob' mutations) and Y349C (made in the Fc containing the 'hole' mutations) mutations may optionally be used to generate a covalent bond between the two halves of the heterodimeric Fc if additional thermodynamic stability is required (Merchant, *et al., Nat. Biotechnol.* (1998) 16: 677-81).

[0429] To facilitate purification of the heterodimeric molecule away from contaminating homodimeric products, the H435R or H435R+Y436F mutations found in IgG3 allotypes may be introduced in either of the Fc-containing chains (Jendeberg, *et al., supra*). These mutations, which will be referred to as "R" or "RF" respectively, eliminate Protein A and FcRn binding when introduced in to the IgG1 Fc. When incorporated into only a single Fc domain in the context of a bispecific antibody construct, these mutations can eliminate Protein A binding of any homodimer contaminant containing these mutations, and greatly simplifies purification of the desired heterodimer away from the single remaining homodimer contaminant via additional chromatography steps (*e.g.* ion exchange). If one of the antibody variable domains is a VH3 family member (known to bind Protein A in addition to the Fc), additional engineering can be conducted to remove residual VH3 Protein A binding (Example 3).

[0430] Technologies to enhance PK half-life of IgG antibodies can be introduced into bispecific antibodies including Fc mutations such as M428L + N434S (LS) or M252Y + S254T + T256E (YTE) that improve pH dependent binding to FcRn and have been shown to significantly improve antibody half-life (Zalevsky, *et al., Nat. Biotechnol.* (2010) 28:157-159; Dall'Acqua, *et al., J. Biol. Chem.* (2006) 281:23514-23524). In the context of a bispecific antibody, and in particular a bispecific antibody containing mutations to knock out Fc Protein A binding (which also reduce FcRn binding), the LS or YTE mutations may only be introduced into the Fc polypeptide lacking the Protein A binding knockout mutations.

[0431] Many applications of bispecific antibodies require that the Fc domain is devoid of effector function (ADCC, ADCP, CDC). In these contexts, the L234A and L235A mutations to reduce or eliminate FcγR binding (Chappel, *et al., Proc Natl Acad Sci U S A* (1991) 88(20):9036-40), and the P331S mutations to reduce or eliminate C1q binding (Xu, *et al., J Biol Chem.* (1994) 269:3469-74) may be used. This set of mutations will be referred to as "AAS" herein.

[0432] To express the anti-HIV gp120 bispecific antibodies described herein (Figure 7A), the VH coding sequences of anti-HIV gp120 broadly neutralizing antibody variants

were codon-biased for improved *Homo sapiens* expression and cloned into pcDNA3.1 vector containing immunoglobulin Fc (CH1-CH3) with AAS, SAV, W, R or RF mutations in various combinations (HC1). Broadly neutralizing antibody variable domains used include PGT121.66 and PGT121.42 (described in WO2018237148) and 3BNC117 1.52.64-1 (described in WO2020010107). Codon-biased VL sequences were cloned into pcDNA3.1 vector containing human light chain constant region (LC). The VH and VL coding sequences of various huSP34 variants connected by four repeats of G4S linker $(GGGGS)_4$ (SEQ ID NO: 750) were cloned into pcDNA3.1 vector containing the immunoglobulin Fc (CH2-CH3) containing AAS, SAV, W, R or RF mutations in various combinations (HC2). Transfection of Expi293 cells was conducted according to manufacturer's protocol. One microgram total DNA was used per ml transfection. The plasmids were combined in a ratio of 25% HC1 : 50% LC : 25% HC2 (w/w) when co-transfecting into Expi293 cells. Four days post-transfection, the cell-free culture media was harvested. Expression titer was determined by using PhyTips® harboring 20 µl of MabSelect™ SuRe™ resin using 200 µl of clarified supernatant. Formation of heterodimer was monitored by size fractionation on SDS/polyacrylamide gel electrophoresis.

[0433] Extracellular domains 1 and 2 (D1D2) of the human CD4 protein bind HIV gp120, and when fused to Fc domains or incorporated into engineered T-cells, also have the ability to neutralize HIV and/or kill HIV infected cells (*see, e.g.*, Capon, *et al., Nature* (1989) 337(6207):525-31; Zhen, *et al., PLoS Pathog* (2017) 13(12):e1006753: Leibman, *et al., PLoS Pathog.* (2017) 13(10):e1006613; Carillo, *et al, Transl Res.* (2017) 187:83-92; Kamata, *et al., Biochem Biophys Res Commun.* (2015) 463(3):216-21; Liu, *et al., J Virol.* (2015) 89(13):6685-94; Sahu, *et al., Virology.* (2013) 446(1-2):268-75; Scholler, *et al., Sci Transl Med.* (2012) 4(132):132ra53). Derivatives of CD4 have demonstrated broad antiviral activity. For example, PRO542 is a tetravalent CD4-IgG2 fusion that contains extracellular domains 1 and 2 of CD4. PRO542 exhibited potent, broad antiviral activity across different HIV clades (A-F) *in vitro* (Trkola, *et al., J Virol.* (1998) 72(3):1876-85; Trkola, *et al., J Virol.* (1995) 69(11):6609-17) and demonstrated antiviral activity in the clinic (Jacobson JM, 2000). However, protein therapeutics incorporating CD4 D1D2 have also demonstrated poor PK properties, hypothesized to be a result of either MHCII binding or polyspecificity (Chen, *et al., J Virol.* (2014) 88(2):1125-39). Recent work has identified an engineered CD4 domain known as CD4 D1.22 that has been improved for higher gp120 binding affinity and reduced polyspecificity (Chen, *et al., J Virol* (2011) 85(18):9395-405; Chen, *et al., J Virol.* (2014) 88(2):1125-39; Myszka, *et al., Proc Natl Acad Sci U S A* (2000)

97(16):9026-31). A greater than 10-fold increase in HIV gp120 binding affinity was reported for CD4 D1.22 compared to wild-type 2 domain CD4 (D1D2) (Chen, *et al.*, *J Virol* (2011) *supra*). In addition, CD4 D1.22 exhibited reduced non-specific binding to an MHC class II expressing B-cells compared to wild-type CD4 (D1D2) (Chen, *et al.*, *J Virol.* (2014) *supra*). To understand if CD4 D1D2 or CD4 D1.22 could serve as an HIV targeting domain, we next designed, expressed and purified a panel of bispecific fusion proteins incorporating huSP34 scFv or Fab variants fused to a first Fc domain and CD4 D1D2 or CD4 D1.22 extracellular domains (ECDs) fused to a second Fc domain. Versions with monovalent, bivalent and tandem CD4 ECD domains (Figures 7B-7D) were screened in CD3 binding assays (Example 6), infected T cell killing and binding assays (Examples 10 and 11) and their PK were assessed in NHPs (Example 13).

[0434] To express the anti-HIV-gp120 ECD-Fc bispecific fusion constructs described herein (Figures 7B-7D), the CD4 D1.22 or CD4 D1-D2 coding sequence was cloned into pcDNA3.1 expression vector carrying an immunoglobulin Fc (CH2-CH3) with AAS, SAV, W, R or RF mutations in various combinations (HC1). The VH coding sequences of humanized SP34 variants were codon-biased for *Homo sapiens* expression and cloned into pcDNA3.1 containing an immunoglobulin Fc (CH1-CH3) with AAS, SAV, W, R or RF mutations in various combinations (HC2). Codon-biased of humanized SP34 variant VL sequences were cloned into pcDNA3.1 vector containing human lambda light chain (LC). In some cases, the VH and VL coding sequence connected by four repeats of G4S linker $(GGGGS)_4$ (SEQ ID NO: 750) was cloned into pcDNA3.1 vector containing the immunoglobulin CH2-CH3 Fc with AAS, SAV, W, R or RF mutations (HC2'). Transfection of Expi293 cells was conducted according to manufacturer's protocol. One microgram total DNA was used per ml transfection. The plasmids were combined in a ratio of 25% HC1 : 50% LC : 25% HC2 (w/w) or 50% HC1 : 50% HC2' (w/w) when co-transfecting into Expi293 cells. Four days post-transfection, the cell-free culture media was harvested. Expression titer was determined by using PhyTips® harboring 20 µl of MabSelect™ SuRe™ resin using 200 µl of clarified supernatant. Formation of heterodimer is monitored by size fractionation on SDS/polyacrylamide gel electrophoresis.

[0435] To purify the bispecific antibody and protein fusion constructs described herein, culture supernatant was subjected to MabSelect™ SuRe™ affinity purification followed by ion exchange chromatography to isolate pure heterodimers using an ÄKTA FPLC (Cytiva Life Sciences) enclosed within a 4.0°C chromatography chamber. Cell

culture media was loaded onto a MabSelect™ SuRe™ (Cytiva Life Sciences) column. The column was washed with a low salt buffer of 25mM Tris HCl pH 7.5, 25mM NaCl for 10 column volumes (CV), then with a high salt buffer of 25mM Tris HCl pH 7.5, 500mM NaCl for 5CV to remove non-specific binding, and finally with a low salt wash of 25mM Tris HCl pH 7.5, 25mM NaCl for 10CV. To elute the antibody, an isocratic elution step of 100mM Sodium Acetate pH 3.7 (used with Protein A knockout mutation in huSP34 VH and Fc) or 100mM Glycine pH 2.8 (used when no Protein A knockout mutations are present in huSP34 VH and Fc) was used. The eluted pool was neutralized to pH 6.0 with 1M Tris HCl pH 9.0, and subjected to a cation ion purification, HiTrap® SP HP (Cytiva Life Sciences) to further remove impurities. The cation captured protein was washed with 10mM Sodium Phosphate pH 7.0 for 10CV, then eluted in 0-30% gradient of 10mM Sodium Phosphate pH 7.0, 1M NaCl for 50CV to separate the desired bispecific antibody or fusion protein Fc heterodimer from Fc homodimer or other contaminants with low isoelectric points (pI). Then the cation captured protein was subjected to gradient elution from 30-100% of 10mM Sodium Phosphate pH 7.0, 1M NaCl for 10CV to separate the desired bispecific antibody or fusion protein Fc heterodimer from Fc homodimer contaminants with high isoelectric points (pI) or from aggregates. Fractions representing the desired antibody heterodimer were then pooled and dialyzed in 20mM Histidine pH 5.8, supplemented with sucrose/tween-80, sterile filtered, and stored at 4°C. Concentration of the formulated protein was determined using UV absorbance at 280 nM (A280). Purity was assessed by analytical size-exclusion chromatography and SDS-PAGE electrophoresis. Identity of the bispecific antibody was confirmed by Mass Spec (MS).

[0436] Examples of HiTrap® SP HP (Cytiva Life Sciences) cation exchange chromatography profiles and SDS-PAGE purity analysis for anti-gp120 bispecific antibodies and anti-gp120 bispecific Fc fusion proteins are shown in Figures 8A-8B. These results demonstrate that pure bispecific antibodies and Fc fusion proteins can be expressed and purified using the designs and methods described herein (*e.g.*, HiTrap® SP HP (Cytiva Life Sciences) where cation exchange chromatography successfully isolated the desired bispecific antibody or fusion protein Fc heterodimer from Fc homodimer or other contaminants with low isoelectric points (pI) using a gradient of 0-30% 1M NaCl in 20 mM sodium phosphate pH 7.0).

Example 3

Engineering Humanized SP34 Antibody Variable Domains that do not Bind Protein A

[0437] Protein A affinity chromatography is commonly used to purify human IgGs for both research and therapeutic applications (Shukla, *et al., J, Chromatogr. B Analyt. Technol. Biomed. Life Sci.* (2007) 848:29-39). This method takes advantage of Staphylococcus aureus Protein A, which binds with high affinity to IgG1 Fc domains at neutral pH but not at acidic pH, thus allowing capture of IgGs from cellular supernatants, and elution of purified IgG using acidic buffers. In addition to its interaction with the Fc domain of IgGs, Protein A can bind to a subset of VH3 derived human variable domains. In some cases, VH3 derived antibodies may require harsher and more acidic elution buffers to be eluted from Protein A, which may destabilize the structure of the antibody, lead to aggregation and/or precipitation and reductions in overall yield. While engineered variants of Protein A, such as those used in MabSelect™ Sure™ resin, have reduced affinity to VH3 domains, some VH3 domains are still capable of binding this resin (Bach, *et al., Journal of Chromatography A.* (2015) 1409:60-69).

[0438] In certain embodiments of the bispecific antigen binding molecules described herein, the H435R (R) or the H435R+Y436F (RF) mutation is incorporated into the CH3 domain of one heavy chain, but not the other. As a result, the bispecific heterodimer retains binding to Protein A, while one of the two possible homodimeric contaminants does not bind Protein A, and is thus eliminated during purification. However, residual Protein A binding, present in a VH3 domain fused to an H435R containing CH3 domain, could cause such a homodimeric contaminant to bind Protein A, and obviate the utility of the H435R mutation.

[0439] To minimize or eliminate residual binding of the humanized anti-CD3 VH3 domain to Protein A, we used structural modeling to design a series of single- and double-point mutants predicted to reduce or eliminate Protein A binding. A homology model of huSP34.13.18 (made using the default antibody homology modeling protocols in Discovery Studio 2017r2), a structure of Protein A bound to a VH3 domain (PDB: 1DEE), as well as the sequence of the engineered Protein A Z domain found in MabSelect™ Sure™ (Nilsson, *et al., Protein Engineering* (1987) 1:107-113) were used to generate a model of huSP34.13.8 bound to the Protein A Z domain. Next, we examined the interface between the Z domain and huSP34.13.8 in order to identify residues potentially contributing to Protein A binding. Based on this analysis, we selected residues S17, R19, T57, Y59, G65,

T68, S70, Q81, N82a and S82b for further analysis. A variety of mutations at each position were initially tested for their ability to disrupt binding to Protein A in-silico using default protocols in Discovery Studio 2017r2. Mutations selected for further experimental analysis were predicted to increase the binding free energy between the Z-domain and huSP34.13.8 Fv.

[0440] We next conducted small scale Protein A purifications on huSP34.13.8 and the designed variants, all fused to an Fc containing the H435R mutation. 5 µg of the DNA encoding the scFv-Fc constructs was transfected into 5 ml of Expi293 cells according to manufacturer's protocol. Clarified supernatant of each transfection was collected 4 days post-transfection. 15 µl of supernatant was saved for gel loading. scFv-Fc protein was purified from 200 µl of supernatant using 20 µl Protein A resin in PhyTips® over Bravo Liquid Handling platform. Captured proteins on PhyTips® were washed 3x with 1x PBS prior to elution using 60 µl of 100mM sodium acetate pH 3.7. 30 µl of each elution was fractionated over a 12-well 4-20% Criterion TGX Stain-free gel well and imaged. Relative intensity of the homodimer band of various scFv-Fc variants was quantified using Bio-Rad Image Lab™ 6.0 software. Relative binding of each variant to Protein A was normalized to the band intensity of the parental scFv (huSP34.13.8 scFv-AAS+SAV+R) and is shown in Table 11.

Table 11

Relative Protein A Binding of First Round huSP34.13.8scFv-Fc Variants

Name	Amino Acid Substitutions	% normalized binding to ProA resin
huSP34.14.8 scFv AAS+SAV+R	R19S	0.8
huSP34.15.8 scFv AAS+SAV+R	T57A	10.9
huSP34.16.8 scFv AAS+SAV+R	T57E	0.4
huSP34.17.8 scFv AAS+SAV+R	G65S	7.9
huSP34.18.8 scFv AAS+SAV+R	G65T	6.3
huSP34.19.8 scFv AAS+SAV+R	Q81E	1.4
huSP34.20.8 scFv AAS+SAV+R	Q81T	10.5
huSP34.21.8 scFv AAS+SAV+R	N82aS	19.4
huSP34.22.8 scFv AAS+SAV+R	N82aR	1.6
huSP34.23.8 scFv AAS+SAV+R	R19K, Q81E	1.3

Name	Amino Acid Substitutions	% normalized binding to ProA resin
huSP34.24.8 scFv AAS+SAV+R	Q81E, N82aS	1.1
huSP34.25.8 scFv AAS+SAV+R	T57A, G65S	0.3
huSP34.13.8 scFv AAS+SAV+R	**parent**	**100**

[0441] All variants demonstrated reduced binding to Protein A, although some were much more effective and led to near complete loss of retention during Protein A chromatography. Based on these data, a series of double mutants, *e.g.*, R19S and T57A; R19S and T57E; R19S and G65S; R19S and Q81E; T57A and Q81E; T57E and G65S; T57E and Q81E; and G65S and Q81E, were generated to further reduce or eliminate binding of the anti-CD3 binding VH domain to Protein A. Results are provided in Table 12.

Table 12

Protein A Binding of Second Round huSP34.13.8scFv-Fc Homodimer Variants

Name	Amino Acid Substitutions	% normalized binding to ProA resin
huSP34.26.8 scFv AAS+SAV+R	R19S, T57A	0.41
huSP34.27.8 scFv AAS+SAV+R	R19S, T57E	0.29
huSP34.28.8 scFv AAS+SAV+R	R19S, G65S	0.38
huSP34.29.8 scFv AAS+SAV+R	R19S, Q81E	1.55
huSP34.30.8 scFv AAS+SAV+R	T57A, Q81E	1.75
huSP34.31.8 scFv AAS+SAV+R	T57E, G65S	1.57
huSP34.32.8 scFv AAS+SAV+R	T57E, Q81E	2.91
huSP34.33.8 scFv AAS+SAV+R	G65S, Q81E	0.31
huSP34.25.8 scFv AAS+SAV+R	T57A, G65S	0.45
huSP34.13.8 scFv AAS+SAV+R	**Parent**	**100**

[0442] Next, a selection of variant huSP34 scFv-Fc fusion proteins containing one or two VH region mutations along with the unmutated control were expressed at larger scale to increase the relative loading concentration on the Protein A resin and thus increase the

stringency of the Protein A knockout screen. 500 ml of Expi293 cells were transfected with 0.5 mg DNA encoding selected huSP34 scFv-Fc Protein A knockout variants according to manufacturer's protocol. Four days post transfection, the cell-free clarified supernatant was collected and loaded to a MabSelect™ SuRe™ (Cytiva Life Sciences) column. Afterwards the column was washed with a low salt buffer of 25 mM Tris HCl pH 7.5, 25 mM NaCl for 10 column volumes (CV), then high salt wash of 25 mM Tris HCl pH 7.5, 500 mM NaCl for 5CV to remove non-specific binding, and finally washed with a low salt wash of 25 mM Tris HCl pH 7.5, 25 mM NaCl for 10CV. To elute the antibody, an isocratic elution step of 100 mM sodium acetate pH 3.7 was performed. The eluted pool was neutralized to pH 6.0 with 1 M Tris HCl pH 9.0, and subjected to a cation ion purification, HiTrap SP HP (Cytiva Life Sciences) to further remove impurities. The cation captured protein was washed with 10mM sodium phosphate pH 7.0 for 10CV, then eluted in 0-30% gradient of 10 mM sodium phosphate pH 7.0, 1M NaCl for 50CV to separate the desired two targeting arm antibody (heterodimer) from the one targeted arm antibody (homodimer). Followed with gradient elution from 30-100% of 10 mM sodium phosphate pH 7.0, 1 M NaCl for 10CV to remove aggregation or homodimer in higher isoelectric point (pI). All proteins were formulated into 20 mM histidine pH 5.8 by dialysis, added additive of sucrose/tween-80, sterile filtered, and stored at 4°C. Concentration of the formulated protein was measured by A280. Purity was assessed as percent monodispersed by analytical size-exclusion chromatography. Identity of the bispecific antibody was determined by Mass Spec (MS). The three VH-region variants with the lowest residual Protein A binding, along with the parental construct were further scaled up as anti-gp120 bispecific antibodies and final yield was assessed. The results of this work are shown in Table 13.

Table 13

Protein A Binding of huSP34.13.8scFv-Fc Protein A Knockout Homodimer Variants

Name	Mutant	scFv-Fc Homodimer Yield Relative to WT (*e.g.* Protein A binding)	PGT121.66 Bispecific Antibody Yield
huSP34.13.8 scFv AAS+SAV+R	Parent	100%	178 mg/L
huSP34.14.8 scFv AAS+SAV+R	R19S	21%	n.d.*
huSP34.19.8 scFv AAS+SAV+R	Q81E	86%	n.d.
huSP34.25.8 scFv AAS+SAV+R	T57A + G65S	1%	165 mg/L
huSP34.26.8 scFv AAS+SAV+R	R19S + T57A	8%	n.d.

Name	Mutant	scFv-Fc Homodimer Yield Relative to WT (*e.g.* Protein A binding)	PGT121.66 Bispecific Antibody Yield
huSP34.27.8 scFv AAS+SAV+R	R19S + T57E	8%	n.d.
huSP34.28.8 scFv AAS+SAV+R	R19S + G65S	1.50%	151 mg/L
huSP34.33.8 scFv AAS+SAV+R	G65S + Q81E	0.70%	122 mg/L

*n.d. – not determined

[0443] The top three mutants were incorporated into the background of anti-gp120 bispecific antibodies and CD4 ECD-Fc fusions built around the huSP34.3.13 variant. BLI and SPR analysis confirmed that these mutations did not impact anti-CD3 affinity (Examples 6), however BVP (Example 7) and PK analysis revealed distinct differences among the various bispecific antibodies tested (Example 13).

Example 4

Expression, Purification and Biophysical Assessment of huSP34 Fab and IgG Variants

[0444] For Fab production, the VH coding sequences of mSP34, huSP34 variants and comparator molecules were codon-optimized for Homo sapiens expression and cloned into pcDNA3.1 vector containing CH1 domain of human IgG1 followed by a C-terminal His8-FLAG tag (His8 or HHHHHHHH disclosed as SEQ ID NO: 1041). Codon-optimized VL sequences were cloned into pcDNA3.1 vector with CL domain of human lambda light chain. Expi293 cells transfection was conducted according to manufacturer's protocol. One microgram total DNA was used per ml of transfection. Expression vectors encoding the heavy and light chain were mixed in a DNA ratio of 2:3 (w:w) respectively before addition to diluted Expifectamine reagent. After incubation at room temperature for 20 minutes, the DNA transfection complex was added to Expi293 cells at 3 million per ml. Four days post-transfection, the clarified supernatant was harvested. Fabs were purified using Ni-IMAC PhyTips® on Hamilton Star Liquid Handling platform. Fabs bound were eluted from Ni-IMAC resin with 250 mM imidazole-containing 25 mM Tris, pH 8 and 300 mM NaCl and quantified by absorbance measurement at A280 using Nanodrop after blanking with elution buffer. Concentration of each Fab recovered was determined by dividing the A280 reading with the respective extinction coefficient. Expression titer (mg/L) was calculated as follows: [(Concentration (mg/ml) x volume of eluate (ml) *1000]/30 ml. The expression titers of mSP34 and comparator #6 were 58 mg/L and 128 mg/L respectively, while the value for the first round of huSP34 Fabs is shown in Table 14. Heavy chains 6 and 8 were associated with huSP34 variants that had the highest levels of expression.

Table 14

Expression Titer of First Round huSP34 Fabs in mg/L

	HC1	HC2	HC3	HC4	HC5	HC6	HC7	HC8	HC9	HC10
LC1	114	102	60	85	94	179	97	168	95	15
LC2	92	147	67	78	47	154	101	165	115	85
LC3	82	93	90	87	96	113	97	208	115	122
LC4	97	97	92	88	73	108	43	141	69	100
LC5	91	105	85	74	76	140	80	104	66	81
LC6	97	105	87	92	79	97	88	82	76	87

[0445] Based in part on these results, a second round of humanized SP34 variants was designed. The expression titers of comparator #1 and comparator #5 Fabs were 80 mg/mL and 184 mg/mL respectively, while the values for the second round of huSP34 Fabs is shown in Table 15. Heavy chains 12 and 13 were associated with the highest expression titers, while heavy chain 3 was associated with the lowest expression titers.

Table 15

Expression Titer of Second Round huSP34 Fabs in mg/L

	HC3	HC11	HC12	HC13
LC7	105	124	137	137
LC8	87	107	133	118
LC9	95	116	143	154
LC10	78	96	112	108

[0446] For production of huSP34 variants as human IgG1 antibodies, the VH and VL coding sequences of humanized SP34 variants were cloned into pcDNA3.1 vector containing immunoglobulin isotype 1 Fc and human lambda constant region sequence respectively. Transfection of Expi293 cells was performed according to manufacturer's protocol. One (1) microgram total DNA was used per ml of transfection. The DNA was combined in a ratio of 60% LC to 40% HC with diluted Expifectamine® reagent before addition to cells. Four days post-transfection, the cell-free culture media was purified using MabSelect™ SuRe™ resin embedded PhyTips® on Hamilton Star Liquid Handling

platform. Bound IgG was eluted from the tips using 100mM sodium acetate pH 3.7 and neutralized by the addition of 1/10th volume of 1M Tris pH 9.0. Eluted IgG was quantified by absorbance measurement at A280 using Nanodrop after blanking with elution buffer. Concentration of each IgG recovered was determined by dividing the A280 reading with the respective extinction coefficient. Expression titer (mg/L) was calculated as follows: [(Concentration (mg/ml) x volume of eluate (ml) *1000]/30 ml (transfected volume).

[0447] The expression titer of huSP34 IgG1 variants (n=1) is shown in Table 16. All huSP34 IgG1 variants show reduced expression titer relative to comparator #1 (121 mg/L, n=2).

Table 16

Expression Titer of huSP34 IgGs in mg/L

	HC1	HC2	HC4	HC3	HC11	HC12	HC13
LC1	72	74	117	125	n.d.*	n.d.	n.d.
LC3	100	168	147	103	n.d.	n.d.	n.d.
LC6	93	134	125	115	n.d.	n.d.	n.d.
LC7	n.d.	n.d.	n.d.	135	69	126	143
LC8	n.d.	n.d.	n.d.	47	103	87	108
LC9	n.d.	n.d.	n.d.	100	140	108	156
LC10	n.d.	n.d.	n.d.	98	74	58	69

*n.d. not determined

[0448] Purified huSP34 variant samples were analyzed via analytical size exclusion chromatography (SEC) to determine aggregate levels. All analyses were run on an Agilent 1200 HPLC system using a Shodex LW-803, 8 x 300mm, 3-micron column. The resin within the column has spherical beads containing pores of a specific size distribution. Separation occurs when molecules of different sizes are included or excluded from the pores within the matrix. The mobile phase was 200mM KPO_4, 25 mM KCl, pH 6.0, and the column was run at a 0.5 mL/min flow rate. Protein detection was accomplished via OD280 detection, and a calibration run was performed using Bio-Rad SEC standards to ensure correct separation of proteins with different molecular weights. A nominal injection amount was set at 20µg of test protein and the total area of each eluted protein-containing peak was calculated. From these data, the SEC purity of each sample was defined as the percentage of monomeric Fab material, this calculated by dividing the area of the monomer-containing

peak by the combined area of this peak plus any earlier-eluting aggregate-containing peaks (no later eluting peaks containing protein were observed).

[0449] The average (n=2) SEC purity for mSP34 and comparator #6 were 81% and 84% respectively, while the value (n=1) for each huSP34 Fab is shown in Table 17. The SEC purity of the first round huSP34 Fabs ranged from 75% to 92%. Heavy chains 1, 2, 4, 5 and 8 were associated with the lowest levels of aggregation, while light chain 6 was associated with the highest levels of aggregation. Interestingly, heavy chain 2 (HC2) was associated with the lowest levels of aggregation when paired with all light chain variants tested.

Table 17

SEC Purity (%) of First Round huSP34 Fabs.

	HC1	HC2	HC3	HC4	HC5	HC6	HC7	HC8	HC9	HC10
LC1	89	89	78	86	87	83	84	90	80	n.d
LC2	90	92	85	87	87	86	87	89	86	80
LC3	83	85	81	84	85	83	85	87	86	83
LC4	83	85	82	81	82	82	77	82	79	83
LC5	84	89	85	84	75	84	77	85	75	82
LC6	79	85	79	83	78	84	81	79	82	81

*n.d. = not determined

[0450] The SEC results for the second round of huSP34 Fabs are shown in Table 18. All second round huSP34 Fabs show improved % monodispersion values when compared to the first round huSP34 Fabs and were similar to the comparator #5 (97.4%) Fab.

Table 18

SEC Purity (%) of Second Round huSP34 Fabs.

	HC3	HC11	HC12	HC13
LC7	98.1	97.1	97.7	97.2
LC8	97.7	97.7	97.5	97.1
LC9	97.3	97.6	98	97.2
LC10	97.4	96.9	96.8	96.9

[0451] The SEC results for the huSP34 IgG1 molecules are shown in Table 19. All of the huSP34 IgG1 antibodies displayed a high degree of purify with aggregation levels <6%. Heavy chain 3 (HC3) is associated with the lowest levels of aggregation.

Table 19

SEC Purity (%) of huSP34 IgGs

	HC1	HC2	HC4	HC3	HC11	HC12	HC13
LC1	96.0	94.5	94.8	96.6	n.d.*	n.d.	n.d.
LC3	95.7	95.0	94.4	96.6	n.d.	n.d.	n.d.
LC6	94.6	95.2	93.5	95.3	n.d.	n.d.	n.d.
LC7	n.d.	n.d.	n.d.	97.3	n.d	96.2	95.3
LC8	n.d.	n.d.	n.d.	95.8	96.4	95.8	96.1
LC9	n.d.	n.d.	n.d.	96.1	97.4	95.1	96.5
LC10	n.d.	n.d.	n.d.	96.9	96.5	94.4	96.1

*n.d. = not determined

[0452] To determine the charge heterogeneity of purified huSP34 Fabs and identify any mutations associated with potential sequence liabilities, we conducted strong cation exchange chromatography. All analysis was run on an Agilent 1200 HPLC system using a MabPac™ SCX 4x50mm, 5µm strong cation exchange column (Thermo Scientific) at 30°C. A short analytical scale CX-1 method was run according to the manufacture's guidelines using their proprietary mobile phase known as "CX-1 pH gradient buffer" which is designed to generate a linear pH. The buffers were provided as a 10x concentrate and diluted at the time of use with deionized sterile water. Buffer A is pH 5.6; Buffer B is pH 10.2. A nominal injection amount was set at 20µg of test protein.

[0453] The following gradient was used: 0-1min at 0.5ml/min 0% B, 1-16min 0-100% B, 18.7-19.5min 0%B, 23min 0%B. When the resulting OD280 vs volume chromatograph has a correctly drawn baseline, the protein peaks can be correctly annotated. From the chromatographic profile for each sample, the total area of each peak was calculated and the percentage of the main peak relative to total (% main peak) was determined. Impurities in humanized SP34 samples were predominantly earlier eluting than the main peak and were thus considered acidic in nature.

[0454] The percent main peak of each huSP34 Fab obtained from the analytical CX-1 analysis is presented in Table 20. The values for the first round huSP34 Fabs ranged from

66.8% to 90.6%, while the mSP34 Fab gave a value of 90.9% and comparator #6 gave a value of 83.1%. Fabs having heavy chain 6 (HC6) had substantially lower percent main peak than the other heavy chains, while Fabs containing heavy chain 4 (HC4) had the highest percent main peak. To identify mutations associated with reduced acidic species (higher percentage in the main peak), we next compared the dataset in Table 20, with the heavy chain variable domain sequences shown in Figure 4B. Pairwise comparisons, sequence liability analysis and structural analysis were used to identify mutations that play a role in huSP34 charge heterogeneity. Heavy chain residues showing strong associations with higher percent main peak values include S30, D73, V89 and H100, while N30, N73, M89 and N100 were associated with reduced main peak values and an increase in acidic variants. Among these residues, H100 appeared most strongly associated with reduced levels of acidic variants (Figure 9), consistent with the prediction that it removes a solvent exposed deamidation motif at the tip of heavy chain CDR3 (Figures 1-2). Based on this analysis, D73 and H100 were held constant during the second round of humanization.

Table 20

Percent Main Peak, CX-1 Ion Exchange Analysis of First Round huSP34 Fab.

	HC1	HC2	HC3	HC4	HC5	HC6	HC7	HC8	HC9	HC10
LC1	74.6	79.5	83.6	86.0	84.8	70.6	84.5	71.7	85.2	n.d.*
LC2	80.9	85.5	89.6	90.6	88.7	73.6	82.8	87.8	75.3	70.0
LC3	73.5	77.1	80.9	85.7	84.9	72.2	84.8	86.2	79.8	85.2
LC4	72.1	77.2	81.4	86.6	83.5	69.5	77.7	78.6	77.4	85.2
LC5	77.1	84.1	85.5	89.1	78.8	70.2	72.6	88.4	72.4	82.3
LC6	82.0	77.1	85.3	86.5	78.7	66.8	79.3	85.1	79.6	82.2

*n.d. = not determined

[0455] The analytical scale CX-1 results for the second round of huSP34 Fabs are shown in Table 21. Many of the second round huSP34 Fabs show improved % main peak values when compared to the first round huSP34 Fabs and were more similar to the comparator #5 (99.3%) Fab. Heavy chain 3 was associated with the highest percent main peak values, with the exception of the HC3 + LC7 pair which was among the lowest.

Table 21

Percent Main Peak, CX-1 Ion Exchange Analysis of Second Round huSP34 Fabs

	HC3	HC11	HC12	HC13
LC7	89.9	92.7	91.3	90.6
LC8	92.4	90.4	90.8	90.8
LC9	93.4	90.8	91.1	90.1
LC10	92.2	90.3	91.1	91.1

[0456] The huSP34 IgG molecules were also analyzed using analytical scale CX-1 ion exchange, and the results are shown in Table 22. The results align with those of the huSP34 Fabs, demonstrating that variants from the second round of humanization (HC3, HC11-13 and LC7-10) demonstrate significant improvements in product homogeneity when compared to variants from the first round of humanization (HC1-4 and LC1-6).

Table 22

Percent Main Peak, CX-1 Ion Exchange Analysis of huSP34 IgGs

	HC1	HC2	HC4	HC3	HC11	HC12	HC13
LC1	76.3	84.6	82.3	79.9	n.d.*	n.d.	n.d.
LC3	78.2	82.1	85.2	80.1	n.d.	n.d.	n.d.
LC6	89.9	80.1	79.7	88.2	n.d.	n.d.	n.d.
LC7	n.d.	n.d.	n.d.	86.8	93.4	88.2	89.2
LC8	n.d.	n.d.	n.d.	89.9	86.5	86.6	86.1
LC9	n.d.	n.d.	n.d.	90.4	87.1	86.2	85.8
LC10	n.d.	n.d.	n.d.	87.7	82.3	83.6	86.3

*n.d. = not determined

[0457] To characterize the thermodynamic stability of huSP34 variants we assessed the experimental thermal melting point and the onset of aggregation of the purified Fabs using the UNcle system (Unchained Labs) in a single analytical process. A 9 µl protein sample was prepared in triplicate in formulation buffer (95 mM NaAcetate 50 mM Tris, pH 6.0) at a concentration between 0.1-150 mg/ml. The protocol used for this analysis has a thermal ramp set to 0.4°C/min. The determination of Tm is achieved through fluorescent detection and Tagg is achieved through static light scatter detection. The resulting chromatograph of unfolding fluorescence shift and static light scatter versus the change in

temperature is defined by algorithmic analysis and yield the Tm inflection point and the onset of aggregation is the Tagg.

[0458] The results of the Tm analysis for the first round huSP34 Fab variants are shown in Table 23. All first round Fabs showed improved thermodynamic stability compared to the mSP34 Fab (60.1 °C) and comparator #6 (58.8 °C), suggesting that the structure-guided humanization approach led to significant improvements in thermodynamic stability for the huSP34 variants tested herein.

Table 23

Melting Temperature (Tm) in °C Determined for the First Round huSP34 Fabs

	HC1	HC2	HC3	HC4	HC5	HC6	HC7	HC8	HC9	HC10
LC1	67.5	67.6	68.1	68.4	67.6	67.0	67.0	66.1	65.7	n.d.*
LC2	67.4	67.2	67.7	67.6	67.0	67.6	66.9	66.4	65.6	65.1
LC3	68.1	67.8	67.9	67.9	67.0	67.8	73.4	66.0	65.3	65.5
LC4	67.0	67.5	67.6	67.5	67.1	67.1	65.0	65.5	64.6	65.2
LC5	66.8	66.4	67.5	66.3	65.5	66.5	64.8	64.9	64.3	64.8
LC6	62.2	67.2	64.0	65.1	65.5	65.6	64.4	64.2	63.3	63.8

*n.d. = not determined

[0459] The results of the Tagg analysis for the first round huSP34 Fab variants are shown in Table 24. Many of the first round huSP34 Fabs showed reduce aggregation propensity compared to the mSP34 Fab (57.7 °C) and comparator #6 (54.3 °C), suggesting that the structure-guided humanization approach led to improvements in thermodynamic stability for the huSP34 variants tested herein. Surprisingly, HC3, which showed relatively high levels of aggregate content in the SEC analysis (Table 17), showed the lowest aggregation propensity in the Tagg analysis presented in Table 24.

Table 24

Aggregation Temperature (Tagg) in °C Determined for the First Round huSP34 Fabs

	HC1	HC2	HC3	HC4	HC5	HC6	HC7	HC8	HC9	HC10
LC1	61.8	61.9	63.5	62.0	61.4	61.4	61.9	60.7	59.4	43.2
LC2	61.8	61.6	62.4	62.4	62.5	62.0	62.6	61.4	60.5	60.1
LC3	62.3	62.0	61.9	61.9	60.7	61.8	62.0	61.2	60.0	58.9
LC4	61.6	61.5	61.7	60.9	61.0	61.6	62.6	59.8	60.0	59.3

LC5	61.3	60.9	62.0	60.4	59.8	60.8	61.0	59.9	59.5	59.8
LC6	57.4	61.6	58.4	59.6	59.0	61.4	61.0	58.3	58.2	49.4

Example 5

CD3 Affinity Screening Using Biolayer Interferometry (BLI)

[0460] The CD3 binding kinetics of the purified huSP34 Fabs were determined using OctetRed384 (Pall ForteBio, CA) biolayer interferometry (BLI). Samples or buffer were dispensed into polypropylene 384-well black flat bottom plates (Greiner, Germany 781209) at a volume of 100 µl per well and all measurements were performed at 30 °C with agitation at 1000 rpm. Streptavidin (SA) coated biosensors tips (Pall ForteBio, CA) were used to capture biotinylated CD3 epsilon: delta heterodimer and typical immobilization levels captured on the SA sensors were 1 nm which approximately translates to 300ng/ml of captured protein. For kinetic measurements biosensors were first pre-wetted with assay buffer for 10 minutes to remove protective sucrose coating followed by the recommended regeneration conditions for standardization of the biosensor surface for the experiment. In order to load the biosensors with antigen, 300 ng/ml of biotinylated CD3 epsilon: delta heterodimer protein (Amsbio AMS.CDD-H52WO) was immobilized on the SA sensor for 900 seconds. The CD3 loaded biosensors were then blocked with 20ug/ml biocytin (sigma) for 200 seconds and then dipped into assay buffer containing wells for 200 seconds to remove any non-specific protein or unbound CD3 heterodimer.

[0461] CD3 loaded and biocytin blocked biosensors were then transferred into fresh assay buffer for 200 seconds to collect a baseline read. Kinetic measurements for anti-CD3 Fab and bispecific antibody binding were performed by dipping the CD3-coated biosensors into wells containing multiple concentrations of Fab or Ab (0-300nM) for 100 seconds followed by a 300 second dissociation time by transferring the biosensors into assay buffer containing wells. The CD3 loaded sensors were then regenerated for the next kinetic measurement. Biosensors were generated by removing bound Fabs or Ab from immobilized CD3 on SA biosensors. Regeneration conditions used consisted of 3 cycles of 5 seconds of dipping the biosensors in Regeneration Buffer (10mM Glycine HCl pH 1.5) followed by Assay Buffer (10mM sodium phosphate pH 7.4, 140mM Sodium Chloride, 0.005% Tween20 with 0.2% BSA).

[0462] All sensorgrams were referenced for buffer effects and fitted to an one-site binding model using Octet Data Analysis Software V.11 (Pall ForteBio, CA) generating

affinity values for association (k_{on}), dissociation (k_{off}) rate constants and the equilibrium dissociation constant (K_D).

[0463] The results for the first round huSP34 Fabs and relevant comparators are shown in Table 25. All first round huSP34 Fabs shows reduced affinity relative to the mSP34 Fab and comparator #6. However, comparing this dataset with the sequences shown in Figure 3 revealed numerous SAR relationships, including residues predicted to improve the affinity of huSP34 as well as human residues that could be incorporated in or directly adjacent to the mSP34 CDRs without negatively impacting functional properties. Heavy chain residues T31, I51, D73, and Y102 were all associated with variants that had higher affinity. Heavy chain residues S30 (CDR1) and G49 (adjacent to CDR2) appeared to have no impact on affinity when incorporated in huSP34 variants, but both increased the match of huSP34 variants to the human germline. Residue S30 was also associated with improvements to the analytical CX-1 percent main peak values. Surprisingly, heavy chain residues H100, which was strongly associated with improved charge heterogeneity (Figure 9), did not have a negative impact on CD3 affinity despite being in the center of CDR H3 (Figure 1). Light chain residues had the most pronounced impact on affinity, with N52, K53, G57, V58 and N94 being associated with huSP34 variants that had improved affinity.

Table 25

Humanization of mSP34 – Round 1: Affinity Determined by BLI (Octet)

Ab Name	K_D (nM)	k_{on} (M^{-1} s^{-1})	k_{off} (s^{-1})
Comparator #6 Fab-HF	7.1	3.49E+05	2.44E-03
mSP34 Fab-HF	9.6	2.62E+05	2.50E-03
huSP34.1.1 Fab-HF	13.1	2.29E+05	3.01E-03
huSP34.1.2 Fab-HF	24.9	3.11E+05	7.62E-03
huSP34.1.3 Fab-HF	12.9	3.08E+05	3.98E-03
huSP34.1.4 Fab-HF	59.7	4.82E+05	2.86E-02
huSP34.1.5 Fab-HF	80.7	2.47E+05	1.98E-02
huSP34.1.6 Fab-HF	15.5	2.30E+05	3.53E-03
huSP34.2.1 Fab-HF	24.6	2.46E+05	5.96E-03
huSP34.2.2 Fab-HF	26.4	6.09E+05	1.41E-02
huSP34.2.3 Fab-HF	16.9	4.34E+05	7.30E-03
huSP34.2.4 Fab-HF	99.4	3.98E+05	3.35E-02

Ab Name	K_D (nM)	k_{on} (M^{-1} s^{-1})	k_{off} (s^{-1})
huSP34.2.5 Fab-HF	162	2.51E+05	4.08E-02
huSP34.2.6 Fab-HF	30.6	3.51E+05	1.07E-02
huSP34.3.1 Fab-HF	14.7	2.52E+05	3.66E-03
huSP34.3.2 Fab-HF	25.4	3.81E+05	9.52E-03
huSP34.3.3 Fab-HF	16.4	2.66E+05	4.37E-03
huSP34.3.4 Fab-HF	85.8	2.87E+05	2.46E-02
huSP34.3.5 Fab-HF	68.5	2.60E+05	1.77E-02
huSP34.3.6 Fab-HF	18.9	2.66E+05	4.82E-03
huSP34.4.1 Fab-HF	19.8	3.96E+05	7.23E-03
huSP34.4.2 Fab-HF	45.2	3.21E+05	1.44E-02
huSP34.4.3 Fab-HF	29.6	2.96E+05	8.68E-03
huSP34.4.4 Fab-HF	159	2.74E+05	4.36E-02
huSP34.4.5 Fab-HF	211	2.41E+05	5.06E-02
huSP34.4.6 Fab-HF	22.7	4.51E+05	1.01E-02
huSP34.5.1 Fab-HF	123	3.11E+05	3.65E-02
huSP34.5.2 Fab-HF	1200	9.08E+04	1.09E-01
huSP34.5.3 Fab-HF	539	1.35E+05	7.29E-02
huSP34.5.4 Fab-HF	497	4.29E+05	2.13E-01
huSP34.5.5 Fab-HF	666	2.77E+05	1.85E-01
huSP34.5.6 Fab-HF	268	2.80E+05	7.46E-02
huSP34.6.1 Fab-HF	53.9	4.78E+05	1.99E-02
huSP34.6.2 Fab-HF	351	1.44E+05	4.99E-02
huSP34.6.3 Fab-HF	150	1.89E+05	2.72E-02
huSP34.6.4 Fab-HF	570	3.59E+05	2.02E-01
huSP34.6.5 Fab-HF	353	2.73E+05	9.63E-02
huSP34.6.6 Fab-HF	75.0	4.64E+05	2.92E-02
huSP34.7.1 Fab-HF	372	2.35E+05	8.55E-02
huSP34.7.2 Fab-HF	498	3.18E+05	1.55E-01
huSP34.7.3 Fab-HF	365	2.40E+05	7.43E-02
huSP34.7.4 Fab-HF	4180	2.65E+05	4.24E-01
huSP34.7.5 Fab-HF	1460	3.07E+05	8.48E-01
huSP34.7.6 Fab-HF	425	4.03E+05	1.70E-01

Ab Name	K_D (nM)	k_{on} (M^{-1} s^{-1})	k_{off} (s^{-1})
huSP34.8.1 Fab-HF	443	1.86E+05	8.23E-02
huSP34.8.2 Fab-HF	3440	1.72E+05	9.82E-02
huSP34.8.3 Fab-HF	285	2.80E+05	7.99E-02
huSP34.8.4 Fab-HF	305	5.61E+05	1.63E-01
huSP34.8.5 Fab-HF	234	9.58E+05	2.19E-01
huSP34.8.6 Fab-HF	375	3.67E+05	1.38E-01
huSP34.9.1 Fab-HF	417	1.87E+05	7.79E-02
huSP34.9.2 Fab-HF	761	1.92E+05	1.45E-01
huSP34.9.3 Fab-HF	349	1.87E+05	6.51E-02
huSP34.9.4 Fab-HF	6120	4.09E+04	2.50E-01
huSP34.9.5 Fab-HF	NBD**	NBD	NBD
huSP34.9.6 Fab-HF	289	5.82E+05	1.69E-01
huSP34.10.1 Fab-HF	NBD	NBD	NBD
huSP34.10.2 Fab-HF	307	2.25E+05	6.64E-02
huSP34.10.3 Fab-HF	264	2.40E+05	6.33E-02
huSP34.10.4 Fab-HF	NBD	NBD	NBD
huSP34.10.5 Fab-HF	222	2.22E-07	8.27E-02
huSP34.10.6 Fab-HF	314	3.14E-07	1.57E-01

*Results represent the average of two independent runs

**NBD=no binding detected.

[0464] The results for the second round huSP34 Fabs and relevant comparators are shown in Table 26. Many of the second round huSP34 Fabs show improved affinity relative to the first round huSP34 Fabs and comparator molecules. Heavy chain 13 (HC13) and light chain 10 (LC10) were associated with the highest affinity second round huSP34 variants.

Table 26

Humanization of mSP34 – Round 2: Affinity Determined by BLI (Octet)

Name	K_D (nM)	k_{on} (M^{-1} s^{-1})	k_{off} (s^{-1})
huSP34.3.7 Fab-HF	5.6	3.23E+05	1.68E-03
huSP34.3.8 Fab-HF	4.4	2.55E+05	1.13E-03
huSP34.3.9 Fab-HF	3.5	6.32E+05	2.21E-03

Name	K_D (nM)	k_{on} (M^{-1} s^{-1})	k_{off} (s^{-1})
huSP34.3.10 Fab-HF	2.0	6.83E+05	1.37E-03
huSP34.11.7 Fab-HF	3.6	6.13E+05	2.12E-03
huSP34.11.8 Fab-HF	2.8	6.10E+05	1.65E-03
huSP34.11.9 Fab-HF	3.4	8.98E+05	2.84E-03
huSP34.11.10 Fab-HF	2.8	6.97E+05	1.92E-03
huSP34.12.7 Fab-HF	2.7	9.66E+05	2.44E-03
huSP34.12.8 Fab-HF	3.4	4.93E+05	1.66E-03
huSP34.12.9 Fab-HF	3.2	1.04E+06	3.35E-03
huSP34.12.10 Fab-HF	4.2	5.01E+05	2.05E-03
huSP34.13.7 Fab-HF	2.8	1.01E+06	2.75E-03
huSP34.13.8 Fab-HF	2.5	9.33E+05	2.16E-03
huSP34.13.9 Fab-HF	2.7	1.38E+06	3.61E-03
huSP34.13.10 Fab-HF	1.7	1.36E+06	2.04E-03
huSP34.1.3 Fab-HF	4.3	1.36E+06	4.97E-03
mSP34 Fab-HF v2	5.2	5.32E+05	2.66E-03
Comparator #5 Fab-HF	4.7	4.91E+05	2.31E-03
huSP34.8.5 Fab-HF	NBD**	NBD	NBD

*Results represent the average of two independent runs

**NBD=no binding detected.

[0465] The results for the third round huSP34 Fabs and relevant comparators are shown in Table 27. A range of affinity variants were explored.

Table 27

Humanization of mSP34 – Round 3: CD3 Affinity Determined by BLI (Octet)

Ab Name	K_D(nM)	k_{on} (M^{-1} s^{-1})	k_{off} (s^{-1})
huSP34.1.3 Fab-HF	3.8	6.03E+05	2.30E-03
huSP34.3.8 Fab-HF	1.9	1.31E+05	2.40E-04
huSP34.3.10 Fab-HF	2.3	1.42E+05	2.35E-04
huSP34.34.10 Fab-HF	4.0	1.55E+05	3.03E-04
huSP34.34.14 Fab-HF	3.9	3.45E+05	1.26E-03
huSP34.34.15 Fab-HF	14.7	1.09E+05	1.50E-03

Ab Name	KD(nM)	k_{on} (M^{-1} s^{-1})	k_{off} (s^{-1})
huSP34.34.12 Fab-HF	8.1	1.89E+05	1.40E-03
huSP34.34.6 Fab-HF	8.0	4.49E+05	3.57E-03
huSP34.35.10 Fab-HF	224	3.39E+05	7.59E-02
huSP34.34.16 Fab-HF	28.8	2.08E+05	5.99E-03
huSP34.35.14 Fab-HF	162	3.97E+07	1.16E-01
huSP34.34.17 Fab-HF	29.9	2.73E+05	8.16E-03
huSP34.35.15 Fab-HF	303	5.60E+05	1.70E-01
huSP34.34.18 Fab-H	87.1	2.57E+05	2.24E-02
huSP34.35.12 Fab-H	125	2.08E+06	1.03E-01
huSP34.35.6 Fab-HF	178	1.55E+06	1.87E-01
huSP34.36.10 Fab-HF	5.8	1.60E+06	9.29E-03
huSP34.37.10 Fab-HF	16.1	1.71E+05	2.67E-03
huSP34.3.13 Fab-HF	6.2	2.18E+05	1.29E-03
huSP34.3.19 Fab-HF	9.9	1.93E+05	1.64E-03
huSP34.34.3 Fab-HF	18.3	2.44E+05	4.10E-03
huSP34.34.11 Fab-HF	10.8	1.43E+05	1.18E-03

*Results represent the average of two independent runs

[0466] Selected huSP34 Fabs were next reformatted into bispecific antibodies (Example 2) and their CD3 affinities assessed by Octet are shown in Table 28.

Table 28

Anti-CD3 Affinity of Selected Bispecific Antibodies*

Ab	Features	KD(nM)	k_{on}(M^{-1} s^{-1})	k_{off}(s^{-1})
257	hPGT121.66 AAS+W/huSP34.34.3 scFv AAS+SAV+R	10.3	6.20E+05	6.19E-03
274	hPGT121.66 AAS+W/huSP34.34.11 scFv AAS+SAV+R	16.0	1.16E+05	1.72E-03
273	hPGT121.66 AAS+W/huSP34.34.10 scFv AAS+SAV+R	8.4	1.20E+05	8.30E-04
275	hPGT121.66 AAS+W/huSP34.34.12 scFv AAS+SAV+R	9.9	4.33E+05	4.31E-03
256	hPGT121.66 AAS+W/huSP34.3.8 scFv AAS+SAV+R	7.1	6.66E+04	4.75E-04
243	hPGT121.66 AAS+W/huSP34.3.13 scFv AAS+SAV+R	16.8	1.06E+05	1.71E-03
261	hPGT121.66 AAS+W/huSP34.13.8 scFv AAS+SAV+R	20.8	4.85E+04	9.47E-04

*Results represent the average of two independent runs

[0467] In order to facilitate purification of bispecific antibodies, A series of huSP34 variants were designed that incorporated mutations designed to reduce or ablate Protein A binding to the huSP34 VH3 domain. The Protein A knockouts were generated in the background of the huSP34.13.8 variant. The CD3 affinities (Octet) of bispecific antibodies incorporating these huSP34 Protein A knockout variants as well as the huSP34.13.8 variant are shown in Table 29. The results suggest that the Protein A knockout mutations had minimal impact on CD3 binding affinity.

Table 29

Protein A Knockouts in Bispecific Format Octet Data*

Ab	Features	K_D(nM)	k_{on}(M^{-1} s^1)	k_{off}(s^{-1})
266	hPGT121.66 AAS+W/huSP34.14.8scFv AAS+SAV+R	24.3	3.90E+04	9.32E-04
267	hPGT121.66 AAS+W/huSP34.19.8scFv AAS+SAV+R	14.7	7.22E+04	1.04E-03
268	hPGT121.66 AAS+W/huSP34.25.8scFv AAS+SAV+R	10.6	8.76E+04	9.28E-04
269	hPGT121.66 AAS+W/huSP34.26.8scFv AAS+SAV+R	9.3	5.59E+04	5.04E-04
270	hPGT121.66 AAS+W/huSP34.27.8 scFv AAS+SAV+R	13.2	7.63E+04	1.00E-03
271	hPGT121.66 AAS+W/huSP34.28.8 scFv AAS+SAV+R	15.8	8.46E+04	1.34E-03
272	hPGT121.66 AAS+W/huSP34.33.8 scFv AAS+SAV+R	15.3	7.74E+04	1.18E-03

*Results represent the average of two independent runs

Example 6

CD3 Affinity Screening Using Surface Plasmon Resonance

[0468] To determine the CD3 binding kinetics of selected Fabs or bispecific antibodies, we next conducted surface plasmon resonance biosensor studies. Experiments were performed on a Biacore 4000 instrument. Streptavidin was chemically immobilized on a C1 chip. Biotinylated CD3 (Acro Biosystems, biotinylated Human CD3E and CD3D Cat CDD-H82W1, lot BVG51-93TF1-NY) was captured at various densities. Various bispecific fusions proteins containing huSP34 anti-CD3 scFv or Fab domains were then injected at various concentrations over the CD3 surfaces. Kinetic data was then fit to a simple kinetic model yielding rate constants k_{on} and k_{off} for the association and dissociation phases, and the equilibrium dissociation constant, K_D. Figure 10 shows an example of data obtained from this study. Shown is the response obtained from the interaction of hPGT121.66 AAS W/huSP34.39.13 scFv AAS+SAV+R, injected at various concentrations all for a contact time of 120 seconds over CD3 surfaces, and then monitored for various

dissociation times. Data was fit to a simple kinetic model. In this example, black lines denote data, and grey lines, the fit to the data. Values for k_{on}, k_{off} and KD have been tabulated in Table 30.

Table 30

CD3 Binding Kinetic Parameters of Selected Bispecific Antibodies

Ab	Features	K_D(nM)	k_{on}(M^{-1} s^{-1})	k_{off}(s^{-1})
243	hPGT121.66 AAS+W/huSP34.3.13 scFv AAS+SAV+R	2.4	3.60E+06	8.40E-03
257	hPGT121.66 AAS+W/huSP34.34.3 scFv AAS+SAV+R	43	3.90E+05	1.70E-02
274	hPGT121.66 AAS+W/huSP34.34.11 scFv AAS+SAV+R	3.9	3.30E+06	1.29E-02
273	hPGT121.66 AAS+W/huSP34.34.10 scFv AAS+SAV+R	3.9	2.60E+06	1.02E-02
275	hPGT121.66 AAS+W/huSP34.34.12 scFv AAS+SAV+R	32	3.70E+05	1.19E-02
256	hPGT121.66 AAS+W/huSP34.3.8 scFv AAS+SAV+R	2.5	2.80E+06	7.10E-03
249	hPGT121.66 AAS W/huSP34.39.13 scFv AAS+SAV+R	2.6	3.40E+06	9.00E-03
276	hPGT121.66 AAS+W/huSP34.40.13 scFv AAS+SAV+R	1.8	3.60E+06	6.30E-03
277	hPGT121.66 AAS+W/huSP34.41.13 scFv AAS+SAV+R	2.8	3.00E+06	8.50E-03
218	h3BNC117.52.64 AAS+SAV+YTE / huSP34.3.13 scFv AAS+W+YTE	2.7	3.30E+06	8.70E-03
180	hCD4 D1.22 Fc AAS+W+YTE / huSP34.39.13 AAS+SAV+R	2.5	2.00E+06	4.90E-03
188	hCD4 D1.22 Fc AAS+W+YTE / huSP34.40.13 AAS+SAV+R	1.6	2.20E+06	3.60E-03
189	hCD4 D1.22 Fc AAS+W+YTE / huSP34.41.13 AAS+SAV+R	2.0	2.40E+06	4.70E-03

Example 7

Polyspecificity Assessment of huSP34 Variant Antibodies

[0469] Polyspecificity of therapeutic antibodies may adversely affect PK properties and present potential safety concerns. In this example, we evaluated the polyspecificity risk of antibodies in an anti-baculoviral particle (BVP) ELISA assay (Hötzel, *et al.*, *mAbs* (2012) 4:753-760). Test articles were assayed at 75 µg/mL concentration in duplicate in each experiment, and the BVP score was calculated as a ratio of OD450 to no mAb background. The risk for polyspecificity of bivalent IgG was then determined by comparison of the BVP

score to thresholds set by four benchmark antibodies for no, low, medium and high risk of polyspecificity (Jain, *et al.*, *Proc. Natl. Acad. Sci. USA* (2017) 114:944-949).

[0470] To compare the polyspecificity of huSP34 variants with different anti-CD3 affinities, a panel of 28 IgG1s was tested in the BVP assay. The results of the BVP assays, including calculated BVP score and polyspecificity risk categorized based on thresholds determined by benchmark controls, are shown in Table 31. Significant differences in polyspecificity risk were observed among variants tested.

Table 31

Polyspecificity Assessment of SP34 IgG1 Variants in BVP assay.

Name	BVP Score (mean)	BVP Score (stdv)	N
huSP34.2.1/hG1/hLam	2.9	0.4	3
huSP34.3.8/hG1/hLam	3.1	0.6	3
huSP34.1.1/hG1/hLam	3.3	0.7	3
huSP34.1.6/hG1/hLam	4.5	0.7	3
huSP34.11.7/hG1/hLam	4.7	1.0	3
huSP34.1.3/hG1/hLam	5.3	1.8	8
huSP34.12.10/hG1/hLam	5.8	1.2	3
huSP34.3.9/hG1/hLam	7.5	0.8	3
huSP34.13.10/hG1/hLam	7.5	2.1	8
huSP34.2.3/hG1/hLam	7.5	11.5	3
huSP34.2.6/hG1/hLam	7.2	0.7	3
huSP34.11.10/hG1/hLam	7.2	2.0	3
huSP34.3.1/hG1/hLam	8.1	2.1	3
huSP34.4.1/hG1/hLam	8.5	1.3	3
huSP34.3.10/hG1/hLam	9.0	1.0	3
huSP34.12.8/hG1/hLam	9.2	0.8	3
huSP34.3.6/hG1/hLam	9.2	3.5	8
huSP34.3.3/hG1/hLam	10.2	2.0	3
huSP34.4.3/hG1/hLam	11.4	3.1	3
huSP34.3.7/hG1/hLam	12.1	3.0	3
huSP34.12.9/hG1/hLam	13.2	1.6	3
huSP34.4.6/hG1/hLam	13.8	3.0	3

Name	BVP Score (mean)	BVP Score (stdv)	N
huSP34.11.8/hG1/hLam	13.4	2.9	3
huSP34.13.8/hG1/hLam	14.3	4.0	8
huSP34.12.7/hG1/hLam	15.5	3.8	3
huSP34.13.9/hG1/hLam	18.0	5.6	3
huSP34.11.9/hG1/hLam	18.1	4.8	3
huSP34.13.7/hG1/hLam	18.2	4.5	3

[0471] In order to further evaluate polyspecificity risk of selected anti-CD3 SP34 variants in various bispecific antibody formats, selected huSP34 heavy chain and light chain variant pairs were selected to produce anti-HIV gp120 bispecific antibodies and tested alongside a number of related human IgG1 and effector enhanced human IgG1 antibodies. The results of this BVP analysis are shown in Table 32. The results suggest that the PGT121.66 anti-gp120 binding arm used for these studies has a low BVP score when formatted as an effector functional enhanced human IgG1. The results also suggest that huSP34 variants with low BVP scores as an IgG1, also have low BVP scores when formatted as bispecific antibodies. Finally, the results suggest that the H435R+Y436F Fc mutation introduced to eliminate Protein A binding in the "hole" Fc domain has no impact on polyspecificity.

Table 32

Polyspecificity Assessment of huSP34 and PGT121 Variants Formatted as IgG1, Effector Enhanced IgG1 or Bispecific Antibodies

Ab	Features	Avg. BVP	stdev	N
	huSP34.13.8/hG1/hLam	14.2	4.1	8
	huSP34.13.10/hG1/hLam	7.1	2.0	8
	huSP34.1.3/hG1/hLam	5.3	1.6	8
	huSP34.3.6/hG1/hLam	9.2	2.9	8
250	hPGT121.66 AAS+SAV/huSP34.1.3 scFv AAS+W	5.5	1.1	5
251	hPGT121.66 AAS+W/huSP34.1.3 scFv AAS+SAV+RF	5.4	2.1	5
265	hPGT121.66 AAS+W/huSP34.13.10 scFv AAS+SAV+RF	12.6	4.4	5
258	hPGT121.66 AAS+W/huSP34.3.4 scFv AAS+SAV+RF	9.3	3.3	5
260	hPGT121.66 AAS+W/huSP34.8.3 scFv AAS+SAV+RF	4.8	1.6	5

	PGT121.66 hIgG1/hLambda	4.0	1.2	5

[0472] In order to assess the role of both anti-CD3 affinity and anti-CD3 Protein A knockout mutations (*see*, Example 3) made in the variable domain of huSP34, we produced a panel of HIV anti-gp120 bispecific antibodies with different anti-CD3 huSP34 variant arms, but containing the same PGT121.66 targeting arm and identical knob-in-hole bispecific Fc domains incorporating the H435R Fc Protein A knockout mutation. The results of the BVP analysis conducted on these antibodies is shown in Table 33. The results suggest that the Protein A knockout variants show only small increases in polyspecificity compared to huSP34.13.8 and further identify the huSP34.3.13 variant as the molecule with the lowest polyspecificity.

Table 33

Polyspecificity assessment of huSP34 scFv Affinity Variants and huSP34 scFv Protein A Knockout Variants Formatted as Anti-HIV gp120 Bispecific Antibodies

Ab	Features	Avg. BVP	stdev	N
261	hPGT121.66 AAS+W/huSP34.13.8scFv AAS+SAV+R	15.1	1.7	3
266	hPGT121.66 AAS+W/huSP34.14.8scFv AAS+SAV+R	15.7	3.7	3
267	hPGT121.66 AAS+W/huSP34.19.8scFv AAS+SAV+R	18.2	2.2	3
268	hPGT121.66 AAS+W/huSP34.25.8scFv AAS+SAV+R	20.0	2.1	3
269	hPGT121.66 AAS+W/huSP34.26.8scFv AAS+SAV+R	20.8	2.1	3
270	hPGT121.66 AAS+W/huSP34.27.8scFv AAS+SAV+R	22.0	1.2	3
271	hPGT121.66 AAS+W/huSP34.28.8scFv AAS+SAV+R	21.7	1.4	3
272	hPGT121.66 AAS+W/huSP34.33.8scFv AAS+SAV+R	21.2	2.0	3
257	hPGT121.66 AAS+W/huSP34.34.3scFv AAS+SAV+R	11.6	3.1	3
274	hPGT121.66 AAS+W/huSP34.34.11scFv AAS+SAV+R	14.8	3.6	3
273	hPGT121.66 AAS+W/huSP34.34.10scFv AAS+SAV+R	18.5	4.2	7
275	hPGT121.66 AAS+W/huSP34.34.12scFv AAS+SAV+R	15.3	3.6	3
256	hPGT121.66 AAS+W/huSP34.3.8scFv AAS+SAV+R	13.9	2.8	5
243	hPGT121.66 AAS+W/huSP34.3.13scFv AAS+SAV+R	8.6	2.5	7

[0473] We next conducted BVP assays on a panel of anti-HIV-gp120 bispecific antibodies containing the three most effective Protein A knockout variants in the huSP34.3.13 scFv background alongside relevant controls. The results of this assessment are shown in Table 34 and demonstrate that huSP34 Protein A knockout variants huSP34.39.13 has a very similar polyspecificity risk as huSP34.3.13. In contrast, huSP34.40.13 and huSP34.41.13 exhibit high BVP scores more like huSP34.34.10.

Table 34

Polyspecificity Assessment of huSP34 scFv Protein A Knockout Variants and Controls Formatted as Anti-HIV gp120 Bispecific Antibodies

Ab	Features	Avg. BVP	stdev	N
243	hPGT121.66 AAS+W/huSP34.3.13scFv AAS+SAV+R	8.6	2.5	7
273	hPGT121.66 AAS+W/huSP34.34.10scFv AAS+SAV+R	18.5	4.2	7
249	hPGT121.66 AAS W/huSP34.39.13scFv AAS SAV R	9.3	1.7	4
276	hPGT121.66 AAS+W/huSP34.40.13scFv AAS+SAV+R	14.2	3.0	4
277	hPGT121.66 AAS+W/huSP34.41.13scFv AAS+SAV+R	13.6	3.0	4

Example 8

T-cell Binding Characterization of huSP34 Variant Fabs and Anti-HIV gp120 Bispecific Antibodies by Flow Cytometry

[0474] Binding of humanized SP34 Fab variants to CD3 expressed on cell-surface of primary human T cells was evaluated in a flow cytometry-based competition assay. Different concentrations of huSP34 Fab variants as well as mSP34, were incubated with $1x10^5$ T-cells in RPMI containing 0.2 µL of murine SP34-Alexa Fluor 488 (BD Pharmingen Cat#557705), 0.5 µL anti-CD4-BV711 mAb (BD Biosciences Cat#563028) and 0.5 µL anti-CD8-APC/Cy7 mAb (BD Biosciences Cat#560179) for 1 hour at room temperature. Cells were then washed, fixed, and murine SP34-AF488 binding to cell-surface CD3 was measured on a flow cytometer (BD LSRFortessa). The concentration of each huSP34 Fab variant or control that resulted in 50% inhibition (IC50) of murine SP34-AF488 binding to cell-surface CD3 was calculated using GraphPad Prism.

Round 1 huSP34 variants

[0475] As summarized in Table 35, all of the first round huSP34 Fab variants tested exhibited mean IC50 values that ranged from 1.3 µg/mL to greater than 20 µg/mL and were higher (*i.e.*, less potent binding) than that of mSP34 (0.70 µg/mL).

Table 35

IC50 values of first round SP34 humanization Fab variants

huSP34 Fab	FACs IC50 (µg/ml) n=1	FACs IC50 (µg/ml) n=2	Average (µg/ml)
huSP34.1.3 Fab-HF	1.53	1.13	1.33
huSP34.1.6 Fab-HF	1.67	1.12	1.39
huSP34.1.1 Fab-HF	1.72	1.27	1.49
huSP34.3.3 Fab-HF	2.95	1.99	2.47
huSP34.3.1 Fab-HF	3.56	2.22	2.89
huSP34.3.6 Fab-HF	8.48	1.03	4.75
huSP34.2.3 Fab-HF	4.24	3.15	3.70
huSP34.2.6 Fab-HF	4.68	3.40	4.04
huSP34.2.1 Fab-HF	6.17	3.68	4.92
huSP34.4.3 Fab-HF	7.94	5.11	6.53
huSP34.1.2 Fab-HF	8.21	5.29	6.75
huSP34.4.1 Fab-HF	9.57	5.90	7.74
huSP34.3.2 Fab-HF	11.93	6.44	9.19
huSP34.4.6 Fab-HF	18.52	4.20	11.36
huSP34.3.5 Fab-HF	12.88	10.00	11.44
huSP34.1.4 Fab-HF	15.03	11.80	13.41
huSP34.1.5 Fab-HF	17.34	12.46	14.90
huSP34.2.2 Fab-HF	>20	16.59	16.59
huSP34.3.4 Fab-HF	>20	17.34	17.34
huSP34.5.1 Fab-HF	>20	>20	>20
huSP34.4.2 Fab-HF	>20	>20	>20
huSP34.5.2 Fab-HF	>20	>20	>20
huSP34.5.3 Fab-HF	>20	>20	>20
huSP34.2.4 Fab-HF	>20	>20	>20

huSP34 Fab	FACs IC50 (µg/ml) n=1	FACs IC50 (µg/ml) n=2	Average (µg/ml)
huSP34.4.4 Fab-HF	>20	>20	>20
huSP34.5.4 Fab-HF	>20	>20	>20
huSP34.2.5 Fab-HF	>20	>20	>20
huSP34.4.5 Fab-HF	>20	>20	>20
huSP34.5.5 Fab-HF	>20	>20	>20
huSP34.5.6 Fab-HF	>20	>20	>20
huSP34.6.1 Fab-HF	>20		>20
huSP34.6.2 Fab-HF	>20		>20
huSP34.6.3 Fab-HF	>20		>20
huSP34.6.4 Fab-HF	>20		>20
huSP34.6.5 Fab-HF	>20		>20
huSP34.6.6 Fab-HF	>20		>20
huSP34.7.1 Fab-HF	>20		>20
huSP34.7.3 Fab-HF	>20		>20
huSP34.7.6 Fab-HF	>20		>20
huSP34.8.1 Fab-HF	>20		>20
huSP34.8.2 Fab-HF	>20		>20
huSP34.8.3 Fab-HF	>20		>20
huSP34.8.4 Fab-HF	>20		>20
huSP34.8.5 Fab-HF	>20		>20
huSP34.8.6 Fab-HF	>20		>20
huSP34.9.1 Fab-HF	>20		>20
huSP34.9.2 Fab-HF	>20		>20
huSP34.9.3 Fab-HF	>20		>20
huSP34.9.4 Fab-HF	>20		>20
huSP34.9.5 Fab-HF	>20		>20
huSP34.9.6 Fab-HF	>20		>20
huSP34.10.1 Fab-HF	>20		>20
huSP34.10.2 Fab-HF	>20		>20
huSP34.10.3 Fab-HF	>20		>20
huSP34.10.4 Fab-HF	>20		>20

huSP34 Fab	FACs IC50 (µg/ml) n=1	FACs IC50 (µg/ml) n=2	Average (µg/ml)
huSP34.10.5 Fab-HF	>20		>20
huSP34.10.6 Fab-HF	>20		>20
mSP34 Fab HF			0.70

Round 2 huSP34 variants

[0476] A second round of huSP34 Fab variants were characterized using the same flow cytometry-based competition assay as described above. As summarized in Table 36, all variants from this round exhibited geometric mean IC50 values that ranged from 0.15-0.73 µg/mL, many of which were improved relative to mSP34 (IC50 0.68 µg/mL).

Table 36

IC50 Values of Second Round SP34 Humanization Fab Variants

huSP34 Fab	FACs IC50 (µg/ml) n=1	FACs IC50 (µg/ml) n=2	Average (µg/ml)
huSP34.3.10 Fab-HF	0.20	0.09	0.15
huSP34.3.8 Fab-HF	0.20	0.10	0.15
huSP34.11.8 Fab-HF	0.30	0.13	0.22
huSP34.3.7 Fab-HF	0.30	0.15	0.23
huSP34.13.8 Fab-HF	0.36	0.14	0.25
huSP34.11.10 Fab-HF	0.35	0.15	0.25
huSP34.13.10 Fab-HF	0.35	0.16	0.25
huSP34.3.9 Fab-HF	0.39	0.17	0.28
huSP34.13.7 Fab-HF	0.43	0.18	0.31
huSP34.11.7 Fab-HF	0.45	0.18	0.32
huSP34.13.9 Fab-HF	0.48	0.25	0.36
huSP34.11.9 Fab-HF	0.57	0.22	0.40
huSP34.12.8 Fab-HF	0.57	0.29	0.43
huSP34.12.10 Fab-HF	0.69	0.33	0.51
huSP34.12.7 Fab-HF	0.77	0.39	0.58
huSP34.12.9 Fab-HF	0.97	0.49	0.73
mSP34 Fab HF			0.68

Example 9

Characterization of HIV x CD3 Bispecific Molecules in T Cell Binding Assay

[0477] We characterized the T cell binding activity of a panel of five HIV x CD3 bispecific molecules that harbor a common a-HIV envelope binding arm, PGT121.66 paired with huSP34 variants (in scFv format) selected to cover a range of CD3-binding affinities as previously determined by bio-layer interferometry (BLI) and flow cytometry-based competition assays. Briefly, peripheral blood mononuclear cells (PBMCs) were incubated with different concentrations of HIV x CD3 bispecific molecules for 1 hour at RT. Cells were then washed and stained with α-huIgG-APC (Jackson ImmunoResearch Cat#109-136-098), α-CD4-BV711 (BD Biosciences Cat# 563028), and α-CD8-APC-Cy7 (BD Biosciences Cat# 560179) for 20 minutes at RT. Cells were then washed, fixed/permeabilized, and analyzed using BD LSRFortessa according to the manufacturer's protocol. The percentage of α-huIgG-APC-positive CD4+ and CD8+ T cells and the mean fluorescence intensity of the α-huIgG-APC of CD4+ and CD8+ cells were collected, and data analyzed using GraphPad Prism.

[0478] Binding experiments were performed using PBMCs from two healthy human donors. Overall, the EC_{50} ranking for this panel of HIV x CD3 bispecific molecules compared well with K_D ranking previously determined by BLI for huSP34 variants in Fab format, and this was observed in both CD4+ and CD8+ T cell populations. The data is depicted in Figures 11 and 12, and summarized in Table 37.

Table 37

EC_{50} Values Derived from Concentration-Response Curves of PGT121.66 x huSP34 Bispecifics Binding to PBMCs and Compared with KD Previously Determined by BLI for huSP34 Variants in Fab Format.

Ab #	Features	huSP34 Fab K_D (nM)	EC_{50} (g/mL)			
			Donor 3761		Donor 4574	
			CD4+ cells	CD8+ cells	CD4+ cells	CD8+ cells
265	hPGT121.66 AAS+W/huSP34.13.10scFv AAS+SAV+RF	1.8	0.045	0.095	0.037	0.062
251	hPGT121.66 AAS+W/huSP34.1.3scFv AAS+SAV+RF	13	0.32	0.36	0.33	0.35
259	hPGT121.66 AAS+W/huSP34.3.6scFv AAS+SAV+RF	19	0.65	0.48	1.4	1.1
258	hPGT121.66 AAS+W/huSP34.3.4scFv AAS+SAV+RF	86	5.1	1.3	5.7	4.8
260	hPGT121.66 AAS+W/huSP34.8.3scFv AAS+SAV+RF	284	>100	31.190	>100	>100

[0479] To assess whether humanized SP34 variants cross react to non-human primate CD3 with similar affinity, we characterized the human and rhesus monkey T cell binding activity of a panel of eight HIV x CD3 bispecific molecules that harbor a common α-HIV envelope binding arm, PGT121.66, or CD4 D1.22 domain, paired with huSP34 variants (in scFv or Fab formats) covering a range of CD3-binding affinities as previously determined by BLI or flow cytometry-based competition assays. Briefly, PBMCs from healthy human donors and healthy rhesus or cynomolgus monkey donors were incubated with different concentrations of HIV x CD3 bispecific molecules for 1 hour at RT. Cells were then washed and stained with α-huIgG-APC (Jackson ImmunoResearch Cat#109-136-098), α-CD4-BV711 (BD Biosciences Cat# 563028), and α-CD8-APC-Cy7 (BD Biosciences Cat# 560179) for 20 minutes at RT. Cells were then washed, fixed/permeabilized, and analyzed on BD LSRFortessa. The percentage of α-huIgG-APC-positive CD4+ and CD8+ T cells and the mFI of the α-huIgG-APC of CD4+ and CD8+ cells were collected, and data analyzed using GraphPad Prism.

[0480] Figure 13-18 depict representative binding concentration-response curves. For all eight bispecific molecules tested in this panel, the EC_{50} values determined for human and rhesus monkey T cell binding were within 2-fold of each other, suggesting huSP34 variant arm bound to human and monkey T cell with similar affinity. The data are summarized in Tables 38-39). This was observed in both CD4+ and CD8+ T cell populations.

Table 38

EC_{50} Values of Binding Concentration-Response Curve of PGT121.66 x huSP34 and CD4 x huSP34 Bispecifics to Human and Monkey CD4+ PBMCs

EC_{50} (μg/mL) of % α-hu+ CD4+ PBMCs									
Donor	Bispecific Antibody Name								
	257	274	273	275	256	243	251	261	180
hu 151	1.41	0.08	0.06	0.51	0.03	0.07	0.41	0.06	-
hu 340	1.64	0.09	0.06	0.57	0.05	0.10	0.42	0.07	-
hu 711	-	-	-	-	-	-	-	-	0.54
hu 921	-	-	-	-	-	-	-	-	0.09
rh 3563	1.48	0.07	0.05	0.68	0.02	0.08	0.40	0.07	-
rh 3483	0.93	0.06	0.03	0.46	0.02	0.06	0.33	0.07	-
cy 2177	-	-	-	-	-	-	-	-	0.50

Table 39

EC_{50} Values of Binding Concentration-Response Curve of PGT121.66 x huSP34 and CD4 x huSP34 Bispecifics to Human and Monkey CD8+ PBMCs

EC_{50} (μg/mL) of % α-hu+ CD8+ cells									
Donor	Bispecific Antibody Name								
	257	274	273	275	256	243	251	261	180
hu 151	1.62	0.10	0.07	0.85	0.04	0.09	0.44	0.08	-
hu 340	1.21	0.13	0.08	0.88	0.06	0.14	0.68	0.10	-
hu 711	-	-	-	-	-	-	-	-	1.10
hu 921	-	-	-	-	-	-	-	-	0.08
rh 3563	3.52	0.22	0.16	1.24	0.08	0.21	1.02	0.20	-
rh 3483	2.35	0.11	0.10	0.93	0.04	0.11	0.55	0.13	-
cy 2177	-	-	-	-	-	-	-	-	1.09

Example 10

In Vitro Killing of HIV-Infected CEM-NKr-CCr5-LucR+ CD4+ T Cells

[0481] The influence of CD3 affinity on CD3-bispecifics killing activity was assessed using HIV x CD3 bispecific molecules created using PGT121.66 as the Env-targeting arm and huSP34 (in scFv format) with a range of CD3 affinities as previously determined by BLI. The equilibrium dissociation constant (KD) of the CD3 Fabs used for creating the HIV x CD3 molecules are presented in Table 40.

Table 40

PGT121.66 x CD3 Bispecific Panel and CD3 Binding Affinity for Corresponding huSP34 Fab Variants

Ab	Features	huSP34 Fab – K_D (nM)
265	hPGT121.66 AAS+W/huSP34.13.10scFv AAS+SAV+RF	1.8
251	hPGT121.66 AAS+W/huSP34.1.3scFv AAS+SAV+RF	13
259	hPGT121.66 AAS+W/huSP34.3.6scFv AAS+SAV+RF	19
258	hPGT121.66 AAS+W/huSP34.3.4scFv AAS+SAV+RF	86
260	hPGT121.66 AAS+W/huSP34.8.3scFv AAS+SAV+RF	284

[0482] The HIV-infected cell killing activity was evaluated using the CEM-NKr-CCR5-LucR+ lymphoblastoid reporter cell line infected with 5 different HIV-1 primary isolates or molecular clones as target cells and PBMCs or isolated T cells from two healthy donors as effector cells. CEM-NKr-CCR5-LucR+ cells were infected for 3 days, washed and co-cultured with PGT121.66 x CD3 bispecific molecules and PBMCs (25:1 effector: target cell ratio) or isolated T cells (20:1 effector: target cell ratio) for 2 days and expression of tat-driven luciferase was quantified using One-Glo luciferase reagent (Promega). The percent infected cell killing was calculated using the following equation:

[0483] 100 – ((RLU of HIV-infected target cells in treated wells/RLU HIV-infected target cells in untreated wells) * 100).

[0484] For concentration-response curves that had an apparent E_{max} < 20%, the E_{max} values were reported as < 20% and the EC_{50} values reported as > 100 µg/mL (maximum concentration tested).

[0485] The results are displayed in Tables 41-42. Figure 19 depicts a representative killing concentration-response curve (BaL-infected CEM-NKr-CCR5-LucR+ cells, PBMC effector cells, Donor 4408). Higher CD3 affinity was significantly correlated with lower (*i.e.*, more potent) killing EC_{50} values using either whole PBMCs (Figure 20; r^2=0.8403, P=0.0285) or isolated T cells (Figure 21; r^2=0.9618, P=0.0032) as effector cells. Thus, increasing CD3 affinity resulted in increased HIV x CD3 bispecific molecule-mediated killing potency.

Table 41

Killing EC_{50} Values (µg/mL) of HIV-Infected CEM-NKr-CCR5-LucR Reporter Cells Using PBMC Effector Cells

EC_{50}s - PBMCs (µg/ml)										
Donor	**4560**	**4408**	**4560**	**4408**	**4560**	**4408**	**4560**	**4408**	**4560**	**4408**
Ab | Isolate	**7552**		**8398**		**Bal**		**1489**		**727**	
265	0.269	0.002	0.063	0.009	0.080	0.008	0.085	0.019	0.197	0.039
251	0.098	0.027	0.248	0.028	0.072	0.026	0.176	0.015	0.207	0.072
259	0.611	0.074	0.500	0.105	0.317	0.064	0.563	0.106	1.268	0.355
258	0.371	0.529	1.796	0.325	1.598	0.164	1.469	0.778	6.220	0.465
260	0.373	0.113	14.950	9.168	0.003	1.308	17.060	2.216	0.005	1.874

Table 42

Killing EC_{50} Values (µg/mL) of HIV-Infected CEM-NKr-CCR5-LucR Reporter Cells Using Isolated T cell Effector Cells.

EC_{50}s - T Cells (µg/ml)										
Donor	**4560**	**4408**	**4560**	**4408**	**4560**	**4408**	**4560**	**4408**	**4560**	**4408**
Ab | Isolate	**7552**		**8398**		**Bal**		**1489**		**727**	
265	0.014	0.001	0.008	0.002	0.005	0.001	0.016	0.007	0.015	0.004
251	0.123	0.004	0.018	0.011	0.010	0.005	0.033	0.042	0.032	0.011
259	0.158	0.064	0.081	0.032	0.043	0.013	0.110	0.141	0.082	0.039
258	0.512	0.774	0.467	0.328	0.349	0.167	0.797	1.082	1.096	0.633
260	1.125	1.508	4.234	4.026	1.023	0.496	3.581	7.090	1.009	20.730

[0486] The influence of CD3 affinity on CD3-bispecifics killing activity was assessed using HIV x CD3 bispecific molecules created using h3BNC117.52.64 as the Env-targeting arm and huSP34 (in scFv format) with a range of CD3 affinities as previously determined by BLI. The equilibrium dissociation constant (KD) of the CD3 Fabs used for creating the HIV x CD3 molecules are presented in Table 43.

Table 43

3BNC117 x CD3 Bispecific Panel and CD3 Binding Affinity for Corresponding huSP34 Fab Variant

Ab Name	huSP34 Fab - K_D (nM)
237	2.49
230	13
238	45.3

[0487] The HIV-infected cell killing activity was evaluated using the CEM-NKr-CCR5-LucR+ lymphoblastoid reporter cell line infected with 5 different HIV-1 primary isolates as target cells and PBMCs from two healthy donors as effector cells. CEM-NKr-CCR5-LucR+ cells were infected for 3 days, washed and co-cultured with 3BNC117 x CD3 bispecific molecules and PBMCs (25:1 effector: target cell ratio) for 2 days and expression

of tat-driven luciferase was quantified using One-Glo luciferase reagent (Promega). The percent infected cell killing was calculated using the following equation:

[0488] 100 – ((RLU of HIV-infected target cells in treated wells/RLU HIV-infected target cells in untreated wells) * 100).

[0489] For concentration-response curves that had an apparent E_{max} < 20%, the E_{max} values were reported as < 20% and the EC_{50} values reported as > 100 µg/mL (maximum concentration tested).

[0490] The results are displayed in Table 44. Figure 22 depicts a representative killing concentration-response curve (PV_12-infected cells, Donor 4622). Higher CD3 affinity was significantly correlated with lower killing EC_{50} values (Figure 23; r^2=0.9968, P=0.0362). Thus, increasing CD3 affinity resulted in increased HIV x CD3 bispecific molecule-mediated killing potency.

Table 44

Killing EC_{50} Values (µg/mL) of HIV-Infected CEM-NKr-CCR5-LucR Reporter Cells.

EC_{50}s - (µg/ml)										
Donor	4622	4359	4622	4359	4622	4359	4622	4359	4622	4359
Ab | Isolate	PV_E1		PV_E3		PV_12		PV_13		PV_19	
237	1.34	0.01	0.22	0.67	0.02	0.33		0.09	0.49	0.01
230	3.21	0.06	1.57	4.32	0.10	2.00	0.02	0.44	2.74	0.04
238	>100	0.18	6.93	23.40	0.31	0.16	0.08	1.91	20.48	0.15

Example 11

In Vitro Killing of HIV-Infected Primary Cells or CEM cells

[0491] PBMCs were isolated by ficoll separation from leukopaks from healthy donors (HIV-/HBV-/HCV-) and rested overnight. CD4+ T cells were isolated using the Stemcells EasySep Human CD4+ T Cell Enrichment Kit (Cat#19052). Isolated CD4+ T cells were spinfected with HIV isolates at 1200xg for 2 hrs and then cultured for 5 days to allow for de novo expression. Target cells were washed and 200,000 cells/well were plated and co-cultured with CD3-bsAb and 600,000 FITC membraned stained (Sigma Aldrich Cat# PKH67GL) PBMCs/well and incubated for 2 day. Cells were washed and stained with live/dead membrane stain (Thermo Fisher Cat# L34966) and a-CD4-BV711 (BD

Biosciences Cat# 563028). Cells were then fixed/permeabilized and stained with a-p24-PE (Beckman Coulter Cat# 6604667) and read on a flow cytometer (BD LSRFortessa). The percent reduction in p24+CD4- live target cells was measured and quantified using the following equation:

[0492] 100 – ((%p24+CD4- live target cells in treated wells/%p24+CD- live target cells in untreated wells) * 100).

[0493] A panel of bispecific molecules was generated with a-CD3 SP34 derived sequences that had a range of affinities measured by SPR and the competition FACs assays and a common a-HIV envelope sequence. To determine if there was a correlation between the initially derived affinities of the α-CD3 SP34 derived sequences and the antibody mediated cytotoxicity, the bispecific molecules were run in the primary cell killing assay with CD4 cells infected with 2 different HIV isolates and autologous PBMCs obtained from a single donor. The results are depicted in Figures 24 and 25, and summarized in Table 45.

PGT121.66 x CD3 bispecific antibodies – CD3 affinity correlation to primary killing

Table 45

EC_{50}s values (µg/ml) of Primary HIV-infected CD4+ Cells by PGT121.66 x huSP34 Bispecific Antibodies Using PBMC Effector Cells.

EC_{50} (µg/ml)		
Ab | Isolate	**657**	**7552**
265	0.275	0.011
251	1.610	0.107
259	2.368	0.123

CD4 ECD x CD3 bispecific molecule evaluation- Killing of HIV-infected CEM-NKr-CCr5-LucR+ CD4+ T cells *in vitro*.

[0494] To identify the CD4 x α-CD3 bispecific formats that confer optimal redirected killing activity, we generated a panel of molecules with CD4 arm varying in domain composition or valency, paired with huSP34 in scFv or Fab format (Table 46, Figures 7B-7D).

Table 46

A Panel of CD4 ECD x α-CD3 Bispecific Molecules Format Evaluation.

Ab name	CD4 arm		huSP34 arm
	domain	valency	format
212	D1D2	1	ScFv
211	D1D2	1	Fab
213	D1D2	2 (bivalent)	ScFv
198	D1.22	2 (tandem)	ScFv
187	D1.22	1	Fab
199	D1.22	2 (bivalent)	ScFv
186	D1.22	1	Fab

[0495] The HIV-infected cell killing activity was evaluated using the CEM-NKr-CCR5-LucR+ lymphoblastoid reporter cell line infected with 3 different HIV-1 primary isolates as target cells and PBMCs from two healthy donors as effector cells. CEM-NKr-CCR5-LucR+ cells were infected for 3 days, washed and co-cultured with CD4 x α-CD3 bispecific molecules and PBMCs (25:1 effector: target cell ratio) for 2 days and expression of tat-driven luciferase was quantified using One-Glo luciferase reagent (Promega). The percent infected cell killing was calculated using the following equation:

[0496] 100 – ((RLU of HIV-infected target cells in treated wells/RLU HIV-infected target cells in untreated wells) * 100).

[0497] For concentration-response curves that had an apparent $E_{max} < 20\%$, the E_{max} values were reported as < 20% and the EC_{50} values reported as > 100 µg/mL (maximum concentration tested).

[0498] Table 47 and Figure 26 summarize the EC50 values calculated from the killing curves for each bispecific test article against all three virus isolates by two donor PBMCs. Mean EC50 values for this panel range from 0.026 to 0.684 µg/ml. When different CD4 targeting domains were employed in otherwise identical molecules, namely D1.22 vs. D1D2 (*e.g.*, 187 vs. 211, 199 vs. 213), EC_{50} values were about 4-5-fold lower for D1.22-containing molecules, suggesting D1.22 is a more effective targeting arm for HIV-infected cells than their two-domain counterpart. The EC_{50} value of 212 was ~3-fold higher

than that of 211; these two molecules employed identical CD4 targeting arm but varied in their huSP34 domain format (scFv vs. Fab), indicating huSP34 conferred more potent killing activity in scFv format than in Fab format in the context of these two molecules. When comparing EC_{50} values of molecules harboring CD4 domains varying in valency and spatial arrangement, the result suggested that bivalent CD4 domain is more effective in targeting HIV-infected cells than their monovalent counterpart (*e.g.*, 213 vs. 212), and that for molecules with two copies of CD4 domain, the "bivalent" configuration confers more potent killing activity than the "tandem" configuration (*e.g.*, 199 vs. 198) (defined in Figure 7D; Example 2).

Table 47

Killing EC_{50} Values (µg/mL) of HIV-Infected CEM-NKr-CCR5-LucR Reporter Cells.

EC_{50}s (µg/ml)							
Donor	151	340	151	340	151	340	Geomean
Ab | Isolate	302076		7015		7576		(all donors/viruses)
212	3.514	0.330	0.878	0.294	2.032	0.169	0.684
211	0.404	0.063	0.485	0.236	0.353	0.110	0.220
213	0.214	0.043	0.095	0.059	0.382	0.038	0.095
198	0.263	0.057	0.402	0.072	0.398	0.085	0.156
187	0.147	0.038	0.130	0.052	0.033	0.007	0.045
199	0.063	0.012	0.014	0.021	0.138	0.011	0.026
186	0.115	0.019	0.095	0.052	0.056	0.042	0.054

CD4 ECD x CD3 bispecific molecule-mediated killing of primary CD4+ T cells infected with different HIV isolates

[0499] Killing of HIV infected cells by bispecific molecule 180 was evaluated and demonstrated in primary cell killing assays using primary CD4+ T cells that were infected with a panel of HIV isolates and autologous PBMCs as effector cells. Bispecific molecule 180 was tested alone or in combination with the bNAbs PGT121.42 (described in WO2017/106346) or h3BNC117.52.64 (described in WO2020/010107). To perform the assays, PBMCs were isolated by ficoll separation from leukopaks from healthy donors (HIV-/HBV-/HCV-) and rested overnight. CD4 cells were then isolated using the Stemcells EasySep Human CD4+ T Cell Enrichment Kit (Cat#19052). Isolated CD4 cells were

spinfected with HIV isolates at 1200xg for 2 hrs and then cultured for 5 days to allow for *de novo* expression. Target cells were washed and 200,000 cells/well were plated and co-cultured in the presence or absence of different concentrations of the indicated antibodies with 600,000 FITC membraned stained (Sigma Aldrich Cat# PKH67GL) PBMCs/well for 2 days. Cells were washed and stained with live/dead membrane stain (Thermo Fisher Cat# L34966) and anti-CD4-BV711 (BD Biosciences Cat# 563028). Cells were then fixed/permeabilized and stained with anti-p24-PE (Beckman Coulter Cat# 6604667) and analyzed on a flow cytometer (BD LSRFortessa). p24+CD4- live target cells were quantified for each condition and the percent reduction in p24+CD4- live target cells relative to the control (no antibody) was determined using the following equation:

[0500] 100 – ((%p24+CD4- live target cells in treated wells/%p24+CD- live target cells in untreated wells) * 100).

[0501] These results were used to determine killing EC_{50} values for each antibody or antibody combination. Effective killing was defined as an EC_{50} value of less than 50 µg/mL. As shown in Figure 27 and Table 48, PGT121.42 and h3BNC117.52.64 mediated killing of CD4+ T cells infected with 23/32 and 26/32 of the HIV isolates tested, respectively, with median EC_{50} values of 0.21 and 0.41 µg/mL, respectively. Bispecific molecule 180 mediated killing of CD4+ T cells infected with 29/32 of the HIV isolates tested with a median EC_{50} value of 0.12 µg/mL. Combining the bNAbs PGT121.42 and h3BNC117.52.64 in the assay mediated killing of CD4+ T cells infected with 28/32 of the HIV isolates tested with a median EC_{50} value of 0.14 µg/mL. When all three bispecific molecules were combined in the assay, PGT121.42, h3BNC117.52.64 and bispecific 180 mediated killing of CD4+ T cells infected with all 32 of the HIV isolates tested with a median EC_{50} value of 0.069 µg/mL (Figure 27, Table 48). Based on these data, the triple combination was the most effective regimen tested in the *in vitro* killing assay as demonstrated by improved HIV isolate coverage and killing potency.

Table 48

Antibody- / Bispecific-Mediated Killing of Primary CD4+ T cells Infected with Different HIV Isolates Using Autologous PBMCs as Effector Cells.

	EC_{50} (µg/mL)				
Virus	PGT121.42	h3BNC117.52.64	180	h3BNC117.52.64 + PGT121.42	h3BNC117.52.64 + PGT121.42 + 180
1003	0.945	0.277	0.192	0.563	0.141
1413	100	0.317	0.624	0.905	0.070
7007	0.063	0.020	0.052	0.334	0.150
7015	0.096	0.579	0.265	0.111	0.129
7046	0.036	100	0.100	0.034	0.067
7103	0.003	0.318	0.384	0.045	0.038
7141	0.070	0.434	0.133	0.041	0.040
7467	0.030	0.021	0.041	0.022	0.027
7576	0.081	0.167	0.066	0.061	0.030
7595	0.705	1.435	0.013	0.160	0.012
7714	100	100	0.140	100	0.168
8084	11.290	1.984	100	1.294	0.140
8089	0.077	0.260	100	0.025	0.011
8106	0.047	0.507	0.026	0.012	0.005
8110	0.256	2.297	0.177	0.302	0.264
8134	0.119	0.079	0.051	0.047	0.038
8176	0.031	0.171	0.993	0.031	0.056
8320	1.334	0.335	0.494	0.679	0.109
8331	0.172	0.269	0.133	0.127	0.120
8339	100	0.393	0.075	0.570	0.074
302076	100	1.799	1.771	1.520	1.502
BaL	0.048	0.055	0.050	0.039	0.031
PV10	100	100	0.052	100	0.036
PV57	0.023	0.312	0.969	0.050	0.020
PV58	100	0.799	0.096	0.520	0.103
PV59	100	1.912	0.111	1.960	0.113
PV61	0.241	100	0.032	0.389	0.093

EC_{50} (µg/mL)					
Virus	PGT121.42	h3BNC117.52.64	180	h3BNC117.52.64 + PGT121.42	h3BNC117.52.64 + PGT121.42 + 180
PV63	0.036	0.107	0.570	0.026	0.037
PV65	0.088	0.547	100	0.082	0.106
PV70	100	100	0.022	100	0.097
PV72	100	100	0.113	100	0.029
PVE2	5.557	0.041	0.043	0.065	0.040

Example 12

Characterization of Infected CEM Cell Binding *In Vitro*

[0502] We evaluated the binding of three HIV x α-CD3 bispecific molecules harboring different Env-targeting specificities to surface expressed Env on HIV-infected cells (Table 49).

Table 49

Bispecific Molecules Evaluated in this Example.

Bispecific Name	Features
186	hCD4 D1.22 Fc AAS+W/huSP34.1.3 AAS+SAV+R
255	hPGT121.66 W/huSP34.1.3scFv SAV+R
230	h3BNC117.52.64 AAS+W/huSP34.1.3scFv AAS+SAV+R

[0503] The HIV-infected cell binding activity was evaluated using the CEM-NKr-CCR5-LucR+ lymphoblastoid reporter cell line infected with 24 different HIV-1 primary isolates. CEM-NKr-CCR5-LucR+ cells were infected for 3 days, washed and co-incubated with different concentrations of HIV x α-CD3 bispecific molecules for 1 hour. Cells were then washed and stained with α-huIgG-APC (Jackson ImmunoResearch Cat#109-136-098), α-CD4-BV711 (BD Biosciences Cat# 563028), and a-CD8-APC-Cy7 (BD Biosciences Cat# 560179). Cells were then washed, fixed/permeabilized and analyzed using a BD LSRFortessa instrument. The percentage of cells that were α-huIgG-APC positive as well as the mean fluorescence intensity (mFI) values of α-huIgG-APC of all samples were collected. Binding curves were generated and EC_{50} values analyzed using GraphPad Prism.

[0504] As summarized in Figure 28 and Table 50, bispecific molecules 186 and 180, bearing the CD4 D1.22 Env-targeting arm, exhibited the highest binding potency against HIV-1-infected CEM-NKr-CCR5-LucR+ cells with a geometric mean of the EC_{50} values of all isolates tested of 7.2 nM and 21.39, respectively, while the geometric means of the EC_{50} values for bispecific molecules 255 and 230 were 68.8 nM and 99.1 nM, respectively. This result demonstrated that all four Env-binding specificities bind to HIV Env expressing cells and that the CD4 D1.22 domain exhibits the most potent binding affinity when evaluating this panel of HIV isolates.

Table 50

EC_{50} Values of Binding Curves for 24 Virus Isolate-Infected Cells of Four Bispecific Molecules Tested.

EC_{50} (mFI) of α-huIgG+ (nM)				
Ab | Isolate	**186**	**255**	**230**	**180**
PVE4	7.54	58.10	115.60	65.11
PV72	8.16	89.13	196.30	66.86
PV71	2.35	89.07	78.43	14.97
PV23	4.62	47.12	102.30	15.40
302076	2.78	108.90	16.04	17.87
8339	66.90	132.80	29.05	n/d*
8331	83.55	100.30	60.32	n/d
8320	11.10	154.20	165.00	10.74
PV59	9.99	477.50	139.80	7.31
7015	7.63	158.80	82.41	n/d
7141	2.50	11.41	194.70	12.82
7467	7.98	31.51	12.70	43.64
8318	17.35	115.50	142.30	5.60
PV58	10.30	564.30	350.70	21.26
7015	2.86	1426.00	103.10	n/d
8110	5.28	75.48	64.44	11.30
7007	5.40	40.42	1156.00	62.13
7576	8.43	64.50	177.90	46.74
7103	6.65	6.92	41.88	30.87

EC_{50} (mFI) of α-huIgG+ (nM)				
Ab | Isolate	**186**	**255**	**230**	**180**
8176	7.62	8.24	20.29	45.61
PV62	2.77	100.00	67.05	15.16
PV64	4.39	20.22	3509.00	10.73
PV63	2.32	13.65	26.27	40.34
PV66	13.11	32.62	92.99	14.13
Geomean	7.22	68.75	99.08	21.39

*n/d = not determined

Example 13

Pharmacokinetics of HIV-Targeted CD3 Bispecific Molecules

[0505] Selected anti-gp120 and CD4 D1.22 targeted anti-CD3 bispecific antibodies were administered by intravenous (IV) bolus injection to naïve male cynomolgus or rhesus macaque monkeys (Covance, TX) to characterize their PK and ADA profiles after single or repeat dosing. Serum samples collected from monkeys were analyzed using a selective bioanalytical method of sufficient sensitivity to determine serum concentration-time profiles and mean serum PK parameters by non-compartmental analysis (NCA). The bioanalytical method utilized clade B gp120 antigen (Immune-tech, CA) as a capture reagent and biotin conjugated goat anti-human IgG antibody (Southern Biotech, AL) as a secondary reagent, with SULFOTAG labeled Streptavidin (MesoScale Discovery, MD) for electrochemical detection on a Mesoscale Discovery Quickplex SQ 120 plate reader. The serum concentration time profiles for anti-gp120 x CD3 bispecific molecules are shown in Figures 29-32. CD4 D1.22 x CD3 bispecific molecules serum concentration time profiles are shown in Figure 33. Aberrant declines in exposure to levels below the limit of quantification was attributed to the formation of ADA and in certain instances aberrant concentration time points were removed from the PK analysis. The calculated NCA PK parameters for anti-gp120 and CD4 D1.22 targeted CD3 bispecific antibodies are presented in Tables 51 and 52, respectively.

[0506] The anti-gp120 antibody, PGT121.66, was evaluated in the context of a comparator bispecific platform containing the comparator #6 huSP34 variable domain (comparator 6 bispecific antibody). The comparator #6 bispecific antibody was found to have IgG-like PK (Cl ≈ 12.5 mL/day/kg) in cynomolgus monkeys, but also a high rate of ADA in nearly every animal and context tested. The high rate of ADA was not mitigated

by various common strategies such as repeat loading (up to 30 mg/kg), concomitant subcutaneous administration with the immunosuppressant methotrexate, or by chimerization with a simian IgG1 Fc, and the ADA was observed in both cynomolgus and rhesus monkeys. Introduction of FcRn enhancing mutations (LS and YTE) also did not reduce the ADA incidence or improve the exposure. Such a high rate of NHP ADA can limit the nonclinical pharmacological assessment and introduce unwanted immunogenicity related toxicities which may or may not be predictive of the clinical outcome thus complicating the development path.

[0507] Selected PGT121 scFv-Fc/Fab-Fc bispecific antibodies from the first and second round of huSP34 engineering were evaluated for PK and ADA in cynomolgus monkeys (Table 51). In all cases, the anti-gp120 binding domain was formatted as a Fab, while the huSP34 anti-CD3 epsilon binding domain was formatted as an scFv. In contrast to the representative Comparator 6 bispecific generated using an identical PGT121.66 anti-gp120 binding domain, and where all animals developed ADA (Figure 29), the huSP34.1.3 scFv bispecifics 250, 252, and 251 were found to have comparable IgG-like PK and no incidence of ADA. The Cl for 250 (10.4 mL/day/kg) was slightly improved over 252 (14.1 mL/day/kg) and 251 (18.1 mL/day/kg) which have Fc mutations which remove Fc Protein A binding, but none of the huSP34.1.3 treated animals (n=9) had observable ADA. Modifications to increase the potency (Figure 30) were found in some instances to increase the ADA incidence and reduce the exposure (264, 265, and 261). While Fc mutations to improve the PK such as LS had no impact (263), or a modest 2-fold improvement in the case of YTE (262), the higher potency variants generally had lower exposure and a higher rate of ADA. Bispecifics selected based on CD3 affinity and BVP ELISA results from the third round of huSP34 optimization were next evaluated in cynomolgus monkeys (Figure 31). In contrast to previous literature reports (Leong et. al, 2017), there was no relationship of CD3 affinity and antibody clearance since the lowest potency bispecific 257 (Cl = 10.5 mL/day/kg) had comparable clearance to the two highest CD3 affinity bispecifics 256 (10.7 mL/day/kg) and 243 (Cl = 8.23 mL/day/kg). It was observed that the best correlate of PK outcome was with BVP score (Example 7).

[0508] The huSP34 variant 3.13 with the longest serum half-life and no detectable ADA (243) was further engineered to remove Protein A binding in the CD3 variable domain and scFv-Fc/Fab-Fc bispecific antibodies containing these variants were next evaluated in cynomolgus monkey (Figure 32). Of the Protein A knockout bispecific

variants evaluated 249 had the longest serum half-life (Cl = 34.4 mL/day/kg), but reduced exposure (~4-fold) relative to 243. To confirm the excellent PK properties of the huSP34.3.13 variant it was evaluated in the context of a second anti-gp120 targeting bNAb (185). The bispecific 185 as was found to retain the excellent IgG-like PK properties (Cl = 8.7 mL/day/kg).

Table 51

Non-Compartmental Analysis (NCA) of Anti-Gp120 X Anti-CD3 Bispecific Antibodies After IV Bolus Administration to Naïve Male Cynomolgus.

Bispecific Name	Dose (mg/kg)	N	Cl (mL/day/kg)	Vz (mL/kg)	Half-life (day)	ADA
Comparator #6	30[a]	5	12.5 ± 1.1*	84.4 ± 7.40*	4.70 ± 0.70*	5
250	1	3	10.4 ± 1.78	133 ± 10.7	9.07 ± 1.56	0
252	1	3	14.1 ± 2.52	146 ± 17.0	7.26 ± 0.526	0
251	1	3	18.2 ± 2.84	203 ± 36.8	7.68 ± 0.273	0
265	1	3	21.6 ± 2.23*	172 ± 53.0*	5.46 ± 1.22*	3
264	1	3	21.7 ± 1.97*	178 ±40.2*	5.75 ± 1.58*	3
261	1	3	18.4 ± 1.98	158 ± 43.8	5.89 ± 0.999	1
262	1	3	10.2 ± 2.42*	100 ± 25.2*	7.37 ± 3.49*	3
263	1	3	17.8 ± 3.68*	146 ± 93.7*	5.41 ± 2.47*	3
257	1	2	10.5	97.7	6.41	0
274	1	2	23.3	152	4.57	0
273	1	2	43.6	280	4.45	0
275	1	2	45.2	395	6.14	0
256	1	2	10.7	84.1	5.47	1
243	1	2	8.23	71.2	5.98	0
249	1	2	34.4	216	6.41	0
276	1	2	58.7	376	4.35	0
277	1	2	59.7	314	4.47	0
218	1	3	8.73 ± 2.27	129 ± 45.5	11.0 ± 6.12	1

a Dosed on day 0 and day 7

* PK analysis impacted by evidence of ADA

[0509] Next, ECD-Fc/Fab-Fc bispecific antibodies incorporating the CD4 D1.22 ECD and huSP34 variant Fabs were tested in NHP PK studies. These molecules were generated with and without Fc mutations designed to enhance pH dependent FcRn binding and with huSP34.1.3 or huSP34.3.13 anti-CD3 binding arms, or variants thereof containing variable domain Protein A knockout mutations (Table 52 and Figure 33). Variants with (187) or without (186) FcRn mutations had comparable IgG-like PK, with Cl of 12.0 and 13.3 mL/day/kg, respectively. In contrast to the results obtained with the scFv-Fc/Fab-Fc bispecific antibodies incorporating the PGT121 derived anti-gp120 targeting domain, ECD-Fc/Fab-Fc variants with (180) or without (185) huSP34 variable domain Protein A knockout mutations showed comparable IgG-like PK with Cl of 14.4 and 17.0 mL/day/kg, respectively.

Table 52

NCA of CD4 x Anti-CD3 Bispecific Antibodies After 1 mg/kg IV Bolus Administration to Naïve Male Cynomolgus Monkeys.

Bispecific Name	Dose (mg/kg)	N	Cl (mL/day/kg)	Vz (mL/kg)	Half-life (day)	ADA
186	1	3	13.3 ± 3.62	89.5 ± 23.6	4.72 ± 0.184	2
187	1[a]	3	12.0 ± 2.82	87.9 ± 17.2	5.14 ± 0.871	1
180	1	3	14.4 ± 0.508	162 ± 18.5	7.80 ± 0.718	2
182	1	3	24.8 ± 4.22*	162 ± 54.5*	4.78 ± 2.35*	3
185	1	3	17.0 ± 3.49*	99.3 ± 23.1*	4.03 ± 0.148*	3

a Dosed on day 0 and day 14
* PK analysis impacted by evidence of ADA

Example 14

Expression Vector Organization for the Production of Asymmetrical Bispecific Molecules Having Three Polypeptide Chains

[0510] *Bispecific molecule having anti-HIV gp120 Fab and anti-CD3 scFv.* A bispecific molecule binding to CD3 and HIV gp120 and having three polypeptide chains, namely a heavy chain (HC) and a light chain (LC) of a Fab that binds to gp120 and a single-chain variable fragment (scFv) that binds to CD3, as described herein, was expressed from a single tricistronic plasmid vector (including two additional cistrons for expressing a eukaryotic selection marker and a prokaryotic selection marker). The expression of each

polypeptide was driven by its own promotor, each promoter of equal transcription strength (*e.g.*, a cytomegalovirus (CMV) promoter). The vector organization is illustrated in Figure 34. The cistrons or expression cassettes are arranged 5′ to 3′ from the replication origin as: (1) a prokaryotic selection marker translated on the reverse or negative strand; and translated on the forward or positive strand (2) a eukaryotic selection marker (*e.g.*, glutamine synthetase (GS); (3) a Fab light chain; (4) a Fab heavy chain; and (5) an scFv-Fc fusion protein. The expression vector was introduced into a Chinese Hamster Ovary (CHO) mammalian cell line, where the endogenous glutamine synthetase (GS) gene was eliminated. Expression of glutamine synthetase from the introduced vector was utilized as a selection marker when culturing the cells using the media without L-glutamine. The expression of bispecific molecules was measured by Protein A (ProA) Biosensors, while the desired format (*i.e.*, assembly of the Fab heavy and light chains and the scFv-Fc fusion protein) of bispecific molecules was further selected using size separation. As shown in Figure 35, various clones were propagated for 30 days (aged population, D30) and fed-batch production expression performance was evaluated and compared with the parental clones (D0). The results demonstrate that this platform enabled stable and high expression (specific titer > 1 g/L, as calculated by the amount of total bispecific molecule detected via ProA Biosensors and then multiplied by the heterotrimer %) of this molecule.

[0511] *Bispecific molecule having anti-CD3 Fab and CD4 extracellular (EC) domain-Fc fusion protein.* A bispecific molecule binding to CD3 and HIV gp120 and having three polypeptide chains, namely a heavy chain (HC) and a light chain (LC) of a Fab that binds to CD3 and a CD4 extracellular domain-Fc fusion protein, described herein, was expressed from a single tricistronic plasmid vector (including two additional cistrons for expressing a eukaryotic selection marker and a prokaryotic selection marker). The expression of each polypeptide was driven by its own promotor, each promoter of equal transcription strength (*e.g.*, a CMV promoter). The vector organization is illustrated in Figure 36. The cistrons or expression cassettes are arranged 5′ to 3′ from the replication origin as: (1) a prokaryotic selection marker translated on the reverse or negative strand; and translated on the forward or positive strand (2) a eukaryotic selection marker (*e.g.*, GS; (3) a Fab light chain; (4) a Fab heavy chain; and (5) a CD4 EC domain-Fc fusion protein. The expression vector was introduced into a CHO mammalian cell line, where the endogenous GS gene was eliminated. Expression of glutamine synthetase from the introduced vector was utilized as a selection marker when culturing the cells using the media without L-glutamine. The expression of bispecific molecules was measured by ProA Biosensors,

while the desired format (*i.e.*, assembly of the Fab heavy and light chains and the CD4 EC-Fc fusion protein) of bispecific molecules was further selected using size separation. As shown in Figure 37, various clones were evaluated, and the results demonstrate high expression (specific titer > 1 g/L) of this molecule.

Example 15

Bispecific Antibody and TLR7 Agonist Combination Can Prevent Viral Rebound in Chronically SHIV-Infected Monkeys

[0512] Viral replication can be efficiently suppressed by ART in HIV-1 infected individuals, however, a viral reservoir in latently infected CD4+ T lymphocytes is formed very early during infection (Colb, *et al.*, *Nat Med* (2018) 24(7):923-6; Finzi, *et al.*, *Science* (1997) 278(5341):1295-300; Siliciano, *et al.*, *Nat Med* (2003) 9(6):727-8; and Wong, *et al.*, Science (1997) 278(5341):1291-5). This viral reservoir represents a challenge for the development of a cure to HIV-1 and various strategies to target the viral reservoir are being investigated including pairing anti-HIV antibodies and immune modulators (Barouch, *et al.*, Science (2014) 345(6193):169-74; Deeks, *et al.*, *Nat Med* 2016;22 (8):839-50). A combination of vesatolimod (VES) and the HIV-1 bNAb PGT121 has been shown to delay or prevent viral rebound in SHIV-infected rhesus macaques following ART discontinuation {Borducchi, *et al.*, *Nature* (2018) 563(7731):360-4; Tsa, *et al.*, *J Virol* (2017) 91(8):e02166-16; and Walker, *et al.*, *Nature* (2011) 477 (7365):466-70).

[0513] A bispecific PGT121/anti-CD3 generated in the DUOBODY® platform (Labrijn, *et al.*, Proc Natl Acad Sci U S A. (2013) 110(13):5145-50) that contained a PGT121 Fv (for SHIV envelope recognition), an anti-CD3 Fv (for T-cell effector cell recruitment) and a rhesus Fc domain was dosed in combination with VES in SHIV-infected rhesus macaques (Macaca mulatta) on ART. Prior to dosing, the rhesus macaques were infected for 1 year followed by 2.5 years of ART. Animals received 2 biweekly doses of a CD3-inactive bispecific PGT121/anti-CD3KO (intravenous infusions of 5 mg/kg) followed by 10 biweekly doses of bispecific PGT121/anti-CD3 (intravenous infusions of 5 mg/kg). VES (oral administrations of 0.15 mg/kg) was given simultaneously for 10 doses with the first administration on the day of the first bispecific PGT121/anti-CD3 administration. The bispecific PGT121/anti-CD3KO was included to tolerize the animals to the bispecific antibody as previously described (Somerfield, *et al.*, *J Immunol* (2010) Jul 1;185(1):763-8). A sham group (saline placebo administrations) of 7 ART suppressed SHIV-infected rhesus macaques was included as controls.

[0514] Despite the administration of the bispecific PGT121/anti-CD3KO antibody, animals developed extensive anti-drug antibodies (ADAs) during the planned dosing period. Due to loss of exposure dosing was prematurely halted in three animals after the fourth, fifth and sixth dose of the bispecific PGT121/anti-CD3 antibody. Prior to the emergence of ADA, antibody serum concentrations had reached between 70 and 180 μg/mL 30 minutes post dosing and declined to between 1.7 and 11 μg/mL two weeks post dosing (Figure 38). Two weeks following the last bispecific PGT121/anti-CD3 dose, all animals had serum concentrations below 1 μg/mL except one animal with a serum concentration of 2.3 μg/mL.

[0515] Twenty weeks after the final antibody dosing, ART was discontinued and animals were monitored for 24 weeks (168 days) to assess for viral rebound (Figure 39). In the sham group, 7 of 7 animals rebounded and remained viremic in the 24 weeks monitoring. In contrast, in the bispecific-PGT121/anti-CD3/VES group, 1 of 9 animals did not rebound and three animals that initially rebounded re-suppressed. CD8+ T and NK cell depletion (intravenous infusion of an anti-CD8α CDR-grafted rhesus IgG1 antibody) did not identify any residual replication competent virus as the bispecific-PGT121/anti-CD3/VES treated animal that did not rebound following ART discontinuation remained aviremic (Figure 40). In contrast, CD8+ T and NK cell depletion in 4 of the animals that rebounded following ART discontinuation resulted in plasma virus spikes in all animals, including 3 animals that were aviremic at the time of depletion demonstrating that in these animals, viral control was $CD8^+$ T or NK cell mediated (Figure 40).

[0516] The results are consistent with the conclusion that treatment of SHIV infected animals initiating ART during chronic infection with a bispecific-PGT121/anti-CD3 antibody in combination with the immune modulator VES resulted in suppression of viral rebound and/or virus control in a subset of animals following discontinuation of ART.

Table 53 – Summary of Bispecific CD3 x gp120 Antigen Binding Molecules

Bispecific Name	Features	SEQ ID NO: unpaired HC	SEQ ID NO: Fab arm - HC	SEQ ID NO: Fab arm - LC
180	hCD4 D1.22 Fc AAS+W+YTE/huSP34.39.13 AAS+SAV+R	751	752	753
181	hCD4 D1.22 Fc AAS+W/huSP34.39.13 AAS+SAV+R	754	752	753
182	hCD4 D1.22 Fc AAS+SAV+R/huSP34.3.13 AAS+W+YTE	755	756	753
183	hCD4 D1.22 Fc AAS+SAV+R/huSP34.3.13 AAS+W	755	757	753
184	hCD4 D1.22 Fc AAS+SAV/huSP34.3.13 AAS+W	758	757	753
185	hCD4 D1.22 Fc AAS+SAV+YTE/huSP34.3.13 AAS+W+YTE	759	756	753
186	hCD4 D1.22 Fc AAS+W/huSP34.1.3 AAS+SAV+R	754	760	761
187	hCD4 D1.22 Fc AAS+W+LS/huSP34.1.3 AAS+SAV+R	762	760	761
188	hCD4 D1.22 Fc AAS+W+YTE/huSP34.40.13 AAS+SAV+R	751	763	753
189	hCD4 D1.22 Fc AAS+W+YTE/huSP34.41.13 AAS+SAV+R	751	901	753
190	hCD4 D1.22(tandem) Fc AAS+W+YTE/huSP34.39.13 AAS+SAV+R	764	752	753
191	hCD4 D1.22(tandem) Fc AAS+W/huSP34.39.13 AAS+SAV+R	765	752	753
192	hCD4 D1.22(tandem) Fc AAS+SAV+R/huSP34.3.13 AAS+W+YTE	766	767	753
193	hCD4 D1.22(tandem) Fc AAS+SAV+R/huSP34.3.13 AAS+W	766	768	753
194	hCD4 D1.22(tandem) Fc AAS+SAV/huSP34.3.13 AAS+W	769	768	753
195	hCD4 D1.22(tandem) Fc AAS+SAV+YTE/huSP34.3.13 AAS+W+YTE	770	767	753

Table 53 – Summary of Bispecific CD3 x gp120 Antigen Binding Molecules

Bispecific Name	Features	SEQ ID NO: unpaired HC	SEQ ID NO: Fab arm - HC	SEQ ID NO: Fab arm - LC
196	hCD4 D1.22(tandem) Fc AAS+W/huSP34.1.3+SAV+R	765	771	761
197	hCD4 D1.22(tandem) Fc AAS+W+LS/huSP34.1.3 AAS+SAV+R	772	771	761
198	hCD4-D1.22(tandem) Fc AAS+W+LS/huSP34.1.3scFv AAS+SAV+R	772	773	
199	hCD4-D1.2(bivalent) AAS+W+LS/huSP34.1.3scFv AAS+SAV+R	774	775	776
200	hCD4 D1.22(bivalent) AAS+SAV+R/huSP34.3.13scFv AAS+W+YTE	777	778	776
201	hCD4 D1.22(bivalent) AAS+SAV+R/huSP34.3.13scFv AAS+W	779	778	776
202	hCD4 D1.22(bivalent) AAS+SAV/huSP34.3.13scFv AAS+W	779	780	776
203	hCD4 D1.22(bivalent) AAS+SAV+YTE/huSP34.3.13scFv AAS+W+YTE	777	781	776
204	hCD4 D1D2 Fc AAS+W+YTE/huSP34.39.13 AAS+SAV+R	782	752	753
205	hCD4 D1D2 Fc AAS+W/huSP34.39.13 AAS+SAV+R	783	752	753
206	hCD4 D1D2 Fc AAS+SAV+R/huSP34.3.13 AAS+W+YTE	784	785	753
207	hCD4 D1D2 Fc AAS+SAV+R/huSP34.3.13 AAS+W	784	786	753
208	hCD4 D1D2 Fc AAS+SAV/huSP34.3.13 AAS+W	787	786	753
209	hCD4 D1D2 Fc AAS+SAV+YTE/huSP34.3.13 AAS+W+YTE	788	785	753
210	hCD4 D1D2 Fc AAS+W/huSP34.1.3 AAS+SAV+R	783	789	761
211	hCD4-D1D2 Fc AAS+W+LS/huSP34.1.3 AAS+SAV+R	790	789	761
212	hCD4-D1D2 Fc AAS+W+LS/huSP34.1.3scFv AAS+SAV+R	790	791	
213	hCD4-D1D2(bivalent) AAS+W+LS/huSP34.1.3scFv AAS+SAV+R	792	793	794

Table 53 – Summary of Bispecific CD3 x gp120 Antigen Binding Molecules

Bispecific Name	Features	SEQ ID NO: unpaired HC	SEQ ID NO: Fab arm - HC	SEQ ID NO: Fab arm - LC
214	hCD4-D1D2(bivalent) AAS+SAV+R/huSP34.3.13scFv AAS+W+YTE	795	796	794
215	hCD4-D1D2(bivalent) AAS+SAV+R/huSP34.3.13scFv AAS+W	797	796	794
216	hCD4-D1D2(bivalent) AAS+SAV/huSP34.3.13scFv AAS+W	797	798	794
217	hCD4-D1D2(bivalent) AAS+SAV+YTE/huSP34.3.13scFv AAS+W+YTE	795	799	794
218	h3BNC117.52.64 AAS+SAV+YTE/huSP34.3.13 scFv AAS+W+YTE	800	801	802
219	h3BNC117.52.64 AAS+SAV+R/huSP34.3.13scFv AAS+W+YTE	800	803	802
220	h3BNC117.52.64 AAS+SAV+R/huSP34.3.13scFv AAS+W	804	803	802
221	h3BNC117.52.64 AAS+SAV/huSP34.3.13scFv AAS+W	804	805	802
222	h3BNC117.52.64 AAS+SAV+YTE/huSP34.39.13 scFv AAS+W+YTE	806	801	802
223	h3BNC117.52.64 AAS+SAV+R/huSP34.39.13scFv AAS+W+YTE	806	803	802
224	h3BNC117.52.64 AAS+SAV+R/huSP34.39.13scFv AAS+W	807	803	802
225	h3BNC117.52.64 AAS+SAV/huSP34.39.13scFv AAS+W	807	805	802
226	h3BNC117.52.64 AAS+W+YTE/huSP34.39.13scFv AAS+SAV+R	808	809	802
227	h3BNC117.52.64 AAS+W/huSP34.39.13scFv AAS+SAV+R	808	810	802
228	h3BNC117.52.64 AAS+SAV+YTE/huSP34.1.3scFv AAS+W+YTE	811	801	802
229	h3BNC117.52.64 AAS+W+YTE/huSP34.1.3 scFv AAS+SAV+R	812	809	802
230	h3BNC117.52.64 AAS+W/huSP34.1.3scFv AAS+SAV+R	812	810	802
231	h3BNC117.52.64 AAS+SAV/huSP34.1.3scFv AAS+W	813	805	802

Table 53 – Summary of Bispecific CD3 x gp120 Antigen Binding Molecules

Bispecific Name	Features	SEQ ID NO: unpaired HC	SEQ ID NO: Fab arm - HC	SEQ ID NO: Fab arm - LC
232	h3BNC117.52.64 AAS+W+LS/huSP34.1.3 scFv AAS+SAV+R	812	814	802
233	h3BNC117.52.64 AAS+SAV+YTE/huSP34.3.8scFv AAS+W+YTE	815	801	802
234	h3BNC117.52.64 AAS+SAV/huSP34.3.8scFv AAS+W	816	805	802
235	h3BNC117.52.64 AAS+SAV+YTE/huSP34.34.3scFv AAS+W+YTE	817	801	802
236	h3BNC117.52.64 AAS+SAV/huSP34.34.3scFv AAS+W	818	805	802
237	h3BNC117.52.64 AAS+W/huSP34.13.8scFv AAS+SAV+R	819	810	802
238	h3BNC117.52.64 AAS+W/huSP34.4.2scFv AAS+SAV+R	820	810	802
239	hPGT121.66 AAS+SAV+YTE/huSP34.3.13scFv AAS+W+YTE	821	822	823
240	hPGT121.66 AAS+SAV+R/huSP34.3.13scFv AAS+W+YTE	824	825	823
241	hPGT121.66 AAS+SAV+R/huSP34.3.13scFv AAS+W	826	825	823
242	hPGT121.66 AAS+SAV/huSP34.3.13scFv AAS+W	826	827	823
243	hPGT121.66 AAS+W/huSP34.3.13scFv AAS+SAV+R	828	829	823
244	hPGT121.66 AAS+SAV+YTE/huSP34.39.13scFv AAS+W+YTE	830	822	823
245	hPGT121.66 AAS+SAV+R/huSP34.39.13scFv AAS+W+YTE	830	825	823
246	hPGT121.66 AAS+SAV+R/huSP34.39.13scFv AAS+W	831	825	823
247	hPGT121.66 AAS+SAV/huSP34.39.13scFv AAS+W	831	827	823
248	hPGT121.66 AAS+W+YTE/huSP34.39.13scFv AAS+SAV+R	832	833	823
249	hPGT121.66 AAS W/huSP34.39.13 scFv AAS+SAV+R	832	829	823

Table 53 – Summary of Bispecific CD3 x gp120 Antigen Binding Molecules

Bispecific Name	Features	SEQ ID NO: unpaired HC	SEQ ID NO: Fab arm - HC	SEQ ID NO: Fab arm - LC
250	hPGT121.66 AAS+SAV/huSP34.1.3 scFv AAS+W	834	827	823
251	hPGT121.66 AAS+W/huSP34.1.3 scFv AAS+SAV+RF	835	829	823
252	hPGT121.66 AAS+W/huSP34.1.3 scFv AAS+SAV+R	836	829	823
253	hPGT121.66 AAS+W+YTE/huSP34.1.3 scFv AAS+SAV+R	837	833	823
254	hPGT121.66 AAS+W+LS/huSP34.1.3 scFv AAS+SAV+R	837	838	823
255	hPGT121.66 W/huSP34.1.3scFv SAV+R	839	840	823
256	hPGT121.66 AAS+W/huSP34.3.8 scFv AAS+SAV+R	841	829	823
257	hPGT121.66 AAS+W/huSP34.34.3 scFv AAS+SAV+R	842	829	823
258	hPGT121.66 AAS+W/huSP34.3.4 scFv AAS+SAV+RF	843	829	823
259	hPGT121.66 AAS+W/huSP34.3.6scFv AAS+SAV+RF	844	829	823
260	hPGT121.66 AAS+W/huSP34.8.3 scFv AAS+SAV+RF	845	829	823
261	hPGT121.66 AAS+W/huSP34.13.8 scFv AAS+SAV+R	846	829	823
262	hPGT121.66 AAS+W+YTE/huSP34.13.8 scFv AAS+SAV+R	846	833	823
263	hPGT121.66 AAS+W+LS/huSP34.13.8 scFv AAS+SAV+R	846	838	823
264	hPGT121.66 AAS+SAV/huSP34.13.10scFv AAS+W	847	827	823
265	hPGT121.66 AAS+W/huSP34.13.10 scFv AAS+SAV+RF	848	829	823
266	hPGT121.66 AAS+W/huSP34.14.8scFv AAS+SAV+R	849	829	823
267	hPGT121.66 AAS+W/huSP34.19.8scFv AAS+SAV+R	850	829	823

Table 53 – Summary of Bispecific CD3 x gp120 Antigen Binding Molecules

Bispecific Name	Features	SEQ ID NO: unpaired HC	SEQ ID NO: Fab arm - HC	SEQ ID NO: Fab arm - LC
268	hPGT121.66 AAS+W/huSP34.25.8scFv AAS+SAV+R	851	829	823
269	hPGT121.66 AAS+W/huSP34.26.8scFv AAS+SAV+R	852	829	823
270	hPGT121.66 AAS+W/huSP34.27.8 scFv AAS+SAV+R	853	829	823
271	hPGT121.66 AAS+W/huSP34.28.8scFv AAS+SAV+R	854	829	823
272	hPGT121.66 AAS+W/huSP34.33.8 scFv AAS+SAV+R	855	829	823
273	hPGT121.66 AAS+W/huSP34.34.10 scFv AAS+SAV+R	856	829	823
274	hPGT121.66 AAS+W/huSP34.34.11scFv AAS+SAV+R	857	829	823
275	hPGT121.66 AAS+W/huSP34.34.12scFv AAS+SAV+R	858	829	823
276	hPGT121.66 AAS+W/huSP34.40.13 scFv AAS+SAV+R	859	829	823
277	hPGT121.66 AAS+W/huSP34.41.13 scFv AAS+SAV+R	860	829	823
278	10-1074 AAS+SAV+YTE/huSP34.3.13scFv AAS+W+YTE	861	862	863
279	10-1074 AAS+SAV+R/huSP34.3.13scFv AAS+W+YTE	861	864	863
280	10-1074 AAS+SAV+R/huSP34.3.13scFv AAS+W	865	864	863
281	10-1074 AAS+SAV/huSP34.3.13scFv AAS+W	865	866	863
282	10-1074 AAS+W/huSP34.3.13scFv AAS+SAV+R	867	868	863
283	10-1074 AAS+SAV+YTE/huSP34.39.13scFv AAS+W+YTE	869	862	863
284	10-1074 AAS+SAV+R/huSP34.39.13scFv AAS+W+YTE	869	864	863
285	10-1074 AAS+SAV+R/huSP34.39.13scFv AAS+W	870	864	863

Table 53 – Summary of Bispecific CD3 x gp120 Antigen Binding Molecules

Bispecific Name	Features	SEQ ID NO: unpaired HC	SEQ ID NO: Fab arm - HC	SEQ ID NO: Fab arm - LC
286	10-1074 AAS+SAV/huSP34.39.13scFv AAS+W	870	866	863
287	10-1074 AAS+W+YTE/huSP34.39.13scFv AAS+SAV+R	871	872	863
288	10-1074 AAS+W/huSP34.39.13scFv AAS+SAV+R	871	868	863
289	10-1074 AAS+SAV+YTE/huSP34.1.3scFv AAS+W+YTE	873	862	863
290	10-1074 AAS+SAV/huSP34.1.3scFv AAS+W	874	866	863
291	10-1074 AAS+W+YTE/huSP34.1.3 scFv AAS+SAV+R	875	872	863
292	10-1074 AAS+W/huSP34.1.3scFv AAS+SAV+R	875	868	863
293	10-1074 AAS+W+LS/huSP34.1.3 scFv AAS+SAV+R	875	876	863
294	10-1074 AAS+SAV+YTE/huSP34.3.8scFv AAS+W+YTE	877	862	863
295	10-1074 AAS+SAV/huSP34.3.8scFv AAS+W	878	866	863
296	10-1074 AAS+SAV+YTE/huSP34.34.3scFv AAS+W+YTE	879	862	863
297	10-1074 AAS+SAV/huSP34.34.3scFv AAS+W	880	866	863
298	PGT-134 AAS+SAV+YTE/huSP34.3.13scFv AAS+W+YTE	881	882	883
299	PGT-134 AAS+SAV+R/huSP34.3.13scFv AAS+W+YTE	881	884	883
300	PGT-134 AAS+SAV+R/huSP34.3.13scFv AAS+W	885	884	883
301	PGT-134 AAS+SAV/huSP34.3.13scFv AAS+W	885	886	883
302	PGT-134 AAS+W/huSP34.3.13scFv AAS+SAV+R	887	888	883
303	PGT-134 AAS+SAV+YTE/huSP34.39.13scFv AAS+W+YTE	889	882	883

Table 53 – Summary of Bispecific CD3 x gp120 Antigen Binding Molecules

Bispecific Name	Features	SEQ ID NO: unpaired HC	SEQ ID NO: Fab arm - HC	SEQ ID NO: Fab arm - LC
304	PGT-134 AAS+SAV+R/huSP34.39.13scFv AAS+W+YTE	889	884	883
305	PGT-134 AAS+SAV+R/huSP34.39.13scFv AAS+W	890	884	883
306	PGT-134 AAS+SAV/huSP34.39.13scFv AAS+W	890	886	883
307	PGT-134 AAS+W+YTE/huSP34.39.13scFv AAS+SAV+R	891	892	883
308	PGT-134 AAS+W/huSP34.39.13scFv AAS+SAV+R	891	888	883
309	PGT-134 AAS+SAV+YTE/huSP34.1.3scFv AAS+W+YTE	893	882	883
310	PGT-134 AAS+SAV/huSP34.1.3scFv AAS+W	894	886	883
311	PGT-134 AAS+W+YTE/huSP34.1.3 scFv AAS+SAV+R	895	892	883
312	PGT-134 AAS+W/huSP34.1.3scFv AAS+SAV+R	895	888	883
313	PGT-134 AAS+W+LS/huSP34.1.3 scFv AAS+SAV+R	895	896	883
314	PGT-134 AAS+SAV+YTE/huSP34.3.8scFv AAS+W+YTE	897	882	883
315	PGT-134 AAS+SAV/huSP34.3.8scFv AAS+W	898	886	883
316	PGT-134 AAS+SAV+YTE/huSP34.34.3scFv AAS+W+YTE	899	882	883
317	PGT-134 AAS+SAV/huSP34.34.3scFv AAS+W	900	886	883

[0517] It is understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and scope of the appended claims. All publications, patents, and patent applications cited herein are hereby incorporated by reference in their entirety for all purposes.

CLAIMS

What is claimed is:

1. A multi-specific antigen binding molecule that binds to human CD3 and an HIV antigen, wherein the antigen binding molecule comprises:

(a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises:

(i) a first VH-complementarity determining region (CDR) 1 comprising the amino acid sequence of TYAMN (SEQ ID NO:1);

(ii) a first VH-CDR2 comprising the amino acid sequence of RIRSKYNNYATYYAX$_1$SVKX$_2$, wherein X$_1$ is A or D and X$_2$ is G or S (SEQ ID NO:2);

(iii) a first VH-CDR3 comprising the amino acid sequence of HGNFGX$_3$SYVSWFAY, wherein X$_3$ is H or N (SEQ ID NO:3);

(iv) a first VL-CDR1 comprising the amino acid sequence of GSSTGAVTTGHYAN (SEQ ID NO: 4);

(v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$X$_5$RAP, wherein X$_4$X$_5$ is SN or NK (SEQ ID NO:5); and

(vi) a first VL-CDR3 comprising the amino acid sequence of ALWYSNX$_6$WV, wherein X$_6$ is L or R (SEQ ID NO:6), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Kabat; and

(b) a second antigen binding domain that binds to an HIV antigen.

2. A multi-specific antigen binding molecule that binds to human CD3 and a second antigen, wherein the antigen binding molecule comprises:

(a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises:

(i) a first VH-complementarity determining region (CDR) 1 comprising the amino acid sequence of TYAMN (SEQ ID NO:1);

(ii) a first VH-CDR2 comprising the amino acid sequence of RIRSKYNNYATYYAX$_1$SVKX$_2$, wherein X$_1$ is A or D and X$_2$ is G or S (SEQ ID NO:2);

(iii) a first VH-CDR3 comprising the amino acid sequence of HGNFGX$_3$SYVSWFAY, wherein X$_3$ is H or N (SEQ ID NO:3);

(iv) a first VL-CDR1 comprising the amino acid sequence of GSSTGAVTTGHYAN (SEQ ID NO: 4);

(v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$X$_5$RAP, wherein X$_4$X$_5$ is SN or NK (SEQ ID NO:5); and

(vi) a first VL-CDR3 comprising the amino acid sequence of ALWYSNX$_6$WV, wherein X$_6$ is L or R (SEQ ID NO:6), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Kabat; and

(b) a second antigen binding domain that binds to a second antigen.

3. The multi-specific antigen binding molecule of any one of claims 1 to 2, wherein:

(i) the first VH-complementarity determining region (CDR) 1 comprises the amino acid sequence of TYAMN (SEQ ID NO:1);

(ii) the first VH-CDR2 comprises the amino acid sequence of RIRSKYNNYATYYADSVKX$_2$, wherein X$_2$ is G or S (SEQ ID NO:7);

(iii) the first VH-CDR3 comprises the amino acid sequence of HGNFGHSYVSWFAY (SEQ ID NO:8);

(iv) the first VL-CDR1 comprises the amino acid sequence of GSSTGAVTTGHYAN (SEQ ID NO: 4);

(v) the first VL-CDR2 comprises the amino acid sequence of GTSNRAP (SEQ ID NO:9); and

(vi) the first VL-CDR3 comprises the amino acid sequence of ALWYSNRWV (SEQ ID NO:10).

4. The multi-specific antigen binding molecule of any one of claims 1 to 3, wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively:

(i) SEQ ID NOs: 1, 11, 8, 4, 5 and 10;

(ii) SEQ ID NOs: 1, 11, 8, 4, 9 and 10;

(iii) SEQ ID NOs: 1, 12, 8, 4, 9 and 10;

(iv) SEQ ID NOs: 1, 13, 8, 4, 14 and 15;

(v) SEQ ID NOs: 1, 13, 16, 4, 14 and 15; or

(vi) SEQ ID NOs: 1, 11, 8, 4, 14 and 10.

5. The multi-specific antigen binding molecule of any one of claims 1 to 4, wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively:

(i) SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or

(ii) SEQ ID NOs: 1, 12, 8, 4, 9 and 10.

6. The multi-specific antigen binding molecule of any one of claims 1 to 5, wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 1, 11, 8, 4, 9 and 10.

7. The multi-specific antigen binding molecule of any one of claims 1 to 5, wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 1, 12, 8, 4, 9 and 10.

8. A multi-specific antigen binding molecule that binds to human CD3 and an HIV antigen, wherein the antigen binding molecule comprises:

(a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises:

(i) a first VH-CDR1 comprising the amino acid sequence of GFTFNTY (SEQ ID NO:17);

(ii) a first VH-CDR2 comprising the amino acid sequence of SKYNNY (SEQ ID NO:18);

(iii) a first VH-CDR3 comprising the amino acid sequence of GNFGX$_3$SYVSWFA, wherein X$_3$ is H or N (SEQ ID NO:19);

(iv) a first VL-CDR1 comprising the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 20);

(v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$, wherein X$_4$ is N or S (SEQ ID NO:21); and

(vi) a first VL-CDR3 comprising the amino acid sequence of $WYSNX_6W$, wherein X_6 is L or R (SEQ ID NO:22), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Chothia; and

(b) a second antigen binding domain that binds to an HIV antigen.

9. A multi-specific antigen binding molecule that binds to human CD3 and a second antigen, wherein the antigen binding molecule comprises:

(a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises:

(i) a first VH-CDR1 comprising the amino acid sequence of GFTFNTY (SEQ ID NO:17);

(ii) a first VH-CDR2 comprising the amino acid sequence of SKYNNY (SEQ ID NO:18);

(iii) a first VH-CDR3 comprising the amino acid sequence of $GNFGX_3SYVSWFA$, wherein X_3 is H or N (SEQ ID NO:19);

(iv) a first VL-CDR1 comprising the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 20);

(v) a first VL-CDR2 comprising the amino acid sequence of GTX_4, wherein X_4 is N or S (SEQ ID NO:21); and

(vi) a first VL-CDR3 comprising the amino acid sequence of $WYSNX_6W$, wherein X_6 is L or R (SEQ ID NO:22), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Chothia; and

(b) a second antigen binding domain that binds to a second antigen.

10. The multi-specific antigen binding molecule of any one of claims 8 to 9, wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively:

(i) SEQ ID NOs: 17, 18, 23, 20, 21 and 25;

(ii) SEQ ID NOs: 17, 18, 23, 20, 24 and 25;

(iii) SEQ ID NOs: 17, 18, 23, 20, 26 and 27;

(iv) SEQ ID NOs: 17, 18, 75, 20, 26 and 27; or

(v) SEQ ID NOs: 17, 18, 23, 20, 26 and 25.

11. The multi-specific antigen binding molecule of any one of claims 8 to 10, wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 17, 18, 23, 20, 24 and 25.

12. A multi-specific antigen binding molecule that binds to human CD3 and an HIV antigen, wherein the antigen binding molecule comprises:

(a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises:

(i) a first VH-CDR1 comprising the amino acid sequence of GFTFNTYA (SEQ ID NO:28);

(ii) a first VH-CDR2 comprising the amino acid sequence of IRSKYNNYAT (SEQ ID NO:29);

(iii) a first VH-CDR3 comprising the amino acid sequence of VRHGNFGX3SYVSWFAY, wherein X3 is H or N (SEQ ID NO:30);

(iv) a first VL-CDR1 comprising the amino acid sequence of TGAVTTGHY (SEQ ID NO:31);

(v) a first VL-CDR2 comprising the amino acid sequence of GTX_4, wherein X_4 is N or S (SEQ ID NO:21); and

(vi) a first VL-CDR3 comprising the amino acid sequence of ALWYSNX6WV, wherein X_6 is L or R (SEQ ID NO:6), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to IMGT; and

(b) a second antigen binding domain that binds to an HIV antigen.

13. A multi-specific antigen binding molecule that binds to human CD3 and a second antigen, wherein the antigen binding molecule comprises:

(a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises:

(i) a first VH-CDR1 comprising the amino acid sequence of GFTFNTYA (SEQ ID NO:28);

(ii) a first VH-CDR2 comprising the amino acid sequence of IRSKYNNYAT (SEQ ID NO:29);

(iii) a first VH-CDR3 comprising the amino acid sequence of VRHGNFGX3SYVSWFAY, wherein X3 is H or N (SEQ ID NO:30);

(iv) a first VL-CDR1 comprising the amino acid sequence of TGAVTTGHY (SEQ ID NO:31);

(v) a first VL-CDR2 comprising the amino acid sequence of GTX_4, wherein X_4 is N or S (SEQ ID NO:21); and

(vi) a first VL-CDR3 comprising the amino acid sequence of ALWYSNX6WV, wherein X_6 is L or R (SEQ ID NO:6), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to IMGT; and

(b) a second antigen binding domain that binds to a second antigen.

14. The multi-specific antigen binding molecule according to any one of claims 12 to 13, wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively:

(i) SEQ ID NOs: 28, 29, 32, 31, 21 and 10;

(ii) SEQ ID NOs: 28, 29, 32, 31, 24 and 10;

(iii) SEQ ID NOs: 28, 29, 32, 31, 26 and 15;

(iv) SEQ ID NOs: 28, 29, 33, 31, 26 and 15; or

(v) SEQ ID NOs: 28, 29, 32, 31, 26 and 10.

15. The multi-specific antigen binding molecule according to any one of claims 12 to 14, wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 28, 29, 32, 31, 24 and 10.

16. A multi-specific antigen binding molecule that binds to human CD3 and an HIV antigen, wherein the antigen binding molecule comprises:

(a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises:

(i) a first VH-CDR1 comprising the amino acid sequence of ASGFTFNTYA (SEQ ID NO:34);

(ii) a first VH-CDR2 comprising the amino acid sequence of IRSKYNNYATYYAX$_1$SVKX$_2$R, wherein X$_1$ is A or D and X$_2$ is G or S (SEQ ID NO:35);

(iii) a first VH-CDR3 comprising the amino acid sequence of HGNFGX$_3$SYVSWFA, X$_3$ is H or N (SEQ ID NO:36);

(iv) a first VL-CDR1 comprising the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 37);

(v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$NRAPX$_7$VPAR, wherein X$_4$ is N or S and X$_7$ is G or W (SEQ ID NO:38); and

(vi) a first VL-CDR3 comprising the amino acid sequence of WYSNX$_6$W, wherein X$_6$ is L or R (SEQ ID NO:22), wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Honegger; and

(b) a second antigen binding domain that binds to an HIV antigen.

17. A multi-specific antigen binding molecule that binds to human CD3 and a second antigen, wherein the antigen binding molecule comprises:

(a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3 and comprises:

(i) a first VH-CDR1 comprising the amino acid sequence of ASGFTFNTYA (SEQ ID NO:34);

(ii) a first VH-CDR2 comprising the amino acid sequence of IRSKYNNYATYYAX$_1$SVKX$_2$R, wherein X$_1$ is A or D and X$_2$ is G or S (SEQ ID NO:35);

(iii) a first VH-CDR3 comprising the amino acid sequence of HGNFGX$_3$SYVSWFA, X$_3$ is H or N (SEQ ID NO:36);

(iv) a first VL-CDR1 comprising the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 37);

(v) a first VL-CDR2 comprising the amino acid sequence of GTX$_4$NRAPX$_7$VPAR, wherein X$_4$ is N or S and X$_7$ is G or W (SEQ ID NO:38); and

(vi) a first VL-CDR3 comprising the amino acid sequence of WYSNX$_6$W, wherein X$_6$ is L or R (SEQ ID NO:22), wherein the first VH-CDR1, the first

VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2, and the first VH-CDR3 are according to Honegger; and

(b) a second antigen binding domain that binds to a second antigen.

18. The multi-specific antigen binding molecule of any one of claims 16 to 17, wherein:

(i) the first VH-CDR1 comprises the amino acid sequence of ASGFTFNTYA (SEQ ID NO:34);

(ii) the first VH-CDR2 comprises the amino acid sequence of IRSKYNNYATYYADSVKX$_2$R, wherein X$_2$ is G or S (SEQ ID NO:39);

(iii) the first VH-CDR3 comprises the amino acid sequence of HGNFGHSYVSWFA (SEQ ID NO:40);

(iv) the first VL-CDR1 comprises the amino acid sequence of SSTGAVTTGHY (SEQ ID NO: 37);

(v) the first VL-CDR2 comprises the amino acid sequence of GTSNRAPGVPAR (SEQ ID NO:41); and

(vi) the first VL-CDR3 comprises the amino acid sequence of WYSNRW (SEQ ID NO:25).

19. The multi-specific antigen binding molecule of any one of claims 16 to 18, wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively:

(i) SEQ ID NOs: 34, 39, 40, 37, 41 and 25;

(ii) SEQ ID NOs: 34, 42, 40, 37, 41 and 25;

(iii) SEQ ID NOs: 34, 43, 40, 37, 41 and 25;

(iv) SEQ ID NOs: 34, 44, 40, 37, 45 and 27;

(v) SEQ ID NOs: 34, 44, 46, 37, 45 and 27; or

(vi) SEQ ID NOs: 34, 42, 40, 37, 47 and 25.

20. The multi-specific antigen binding molecule of any one of claims 16 to 19, wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively:

(i) SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or

(ii) SEQ ID NOs: 34, 43, 40, 37, 41 and 25.

21. The multi-specific antigen binding molecule of any one of claims 16 to 20, wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 34, 42, 40, 37, 41 and 25.

22. The multi-specific antigen binding molecule of any one of claims 16 to 20, wherein the first VH-CDR1, the first VH-CDR2, the first VH-CDR3, the first VL-CDR1, the first VL-CDR2 and the first VL-CDR3 comprise the following amino acid sequences, respectively: SEQ ID NOs: 34, 43, 40, 37, 41 and 25.

23. The multi-specific antigen binding molecule of any one of claims 1 to 22, comprising one or more of the following amino acid substitutions (numbering according to Kabat):

(i) position 81 of the first VH is Q or E;

(ii) position 83 of the first VH is K or R;

(iii) position 89 of the first VH is M or V;

(iv) position 100 of the first VH is H;

(v) position 57 of the first VL is G or W; and/or

(vi) position 75 of the first VL is I or L.

24. The multi-specific antigen binding molecule of claim 23, wherein position 81 of the first VH (numbering according to Kabat) is E.

25. The multi-specific antigen binding molecule of claim 23, wherein position 81 of the first VH (numbering according to Kabat) is Q.

26. The multi-specific antigen binding molecule of claim 23, comprising one or more of the following amino acid substitutions (numbering according to Kabat):

(i) position 81 of the first VH is Q or E;

(ii) position 83 of the first VH is R;

(iii) position 89 of the first VH is V;

(iv) position 100 of the first VH is H;

(v) position 57 of the first VL is G; and/or

(vi) position 75 of the first VL is I.

27. The multi-specific antigen binding molecule of any one of claims 1 to 25, wherein the first VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 48-53, or comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 48-53.

28. The multi-specific antigen binding molecule of any one of claims 1 to 27, wherein the first VH comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NO: 50.

29. The multi-specific antigen binding molecule of any one of claims 1 to 28, wherein the first VH comprises an amino acid sequence that is at least 95% identical to an amino acid sequence of SEQ ID NO: 50.

30. The multi-specific antigen binding molecule of any one of claims 1 to 29, wherein the first VH comprises an amino acid sequence that is at least 99% identical to an amino acid sequence of SEQ ID NO: 50.

31. The multi-specific antigen binding molecule of any one of claims 1 to 30, wherein the first VH comprises an amino acid sequence of SEQ ID NO: 50.

32. The multi-specific antigen binding molecule of any one of claims 1 to 27, wherein the first VH comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NO: 51.

33. The multi-specific antigen binding molecule of any one of claims 1 to 32, wherein the first VH comprises an amino acid sequence that is at least 95% identical to an amino acid sequence of SEQ ID NO: 51.

34. The multi-specific antigen binding molecule of any one of claims 1 to 33, wherein the first VH comprises an amino acid sequence that is at least 99% identical to an amino acid sequence of SEQ ID NO: 51.

35. The multi-specific antigen binding molecule of any one of claims 1 to 34, wherein the first VH comprises an amino acid sequence of SEQ ID NO: 51.

36. The multi-specific antigen binding molecule of claims 1 to 35, wherein the first VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 54-58, or comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 54-58.

37. The multi-specific antigen binding molecule of claims 1 to 36, wherein the first VL comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NO: 56.

38. The multi-specific antigen binding molecule of claims 1 to 37, wherein the first VL comprises an amino acid sequence that is at least 95% identical to an amino acid sequence of SEQ ID NO: 56.

39. The multi-specific antigen binding molecule of claims 1 to 38, wherein the first VL comprises an amino acid sequence that is at least 99% identical to an amino acid sequence of SEQ ID NO: 56.

40. The multi-specific antigen binding molecule of claims 1 to 39, wherein the first VL comprises an amino acid sequence of SEQ ID NO: 56.

41. The multi-specific antigen binding molecule of any one of claims 1 to 40, wherein the first VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 48-53, or comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 48-53 and wherein the first VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 54-58, or comprises an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least

97%, at least 98%, or at least 99% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 54-58.

42. The multi-specific antigen binding molecule of any one of claims 1 to 41, wherein the first VH and the first VL comprise the amino acid sequences set forth, respectively, below, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

i. SEQ ID NOs: 48 and 54;
ii. SEQ ID NOs: 49 and 55;
iii. SEQ ID NOs: 50 and 55;
iv. SEQ ID NOs: 50 and 56;
v. SEQ ID NOs: 51 and 55;
vi. SEQ ID NOs: 51 and 56;
vii. SEQ ID NOs: 52 and 56;
viii. SEQ ID NOs: 53 and 57; or
ix. SEQ ID NOs: 50 and 58.

43. The multi-specific antigen binding molecule of any one of claims 1 to 42, wherein the first VH and the first VL comprise the amino acid sequences set forth, respectively, below, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

i. SEQ ID NOs: 49 and 55;
ii. SEQ ID NOs: 50 and 55;
iii. SEQ ID NOs: 50 and 56;
iv. SEQ ID NOs: 51 and 55; or
v. SEQ ID NOs: 51 and 56.

44. The multi-specific antigen binding molecule of any one of claims 1 to 43, wherein the first VH and the first VL comprise the amino acid sequences set forth, respectively, below, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%,

at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56.

45. The multi-specific antigen binding molecule of any one of claims 1 to 44, wherein the first VH and the first VL comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56.

46. The multi-specific antigen binding molecule of any one of claims 1 to 45, wherein the first VH and the first VL comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56.

47. The multi-specific antigen binding molecule of any one of claims 1 to 46, wherein the first VH and the first VL comprise the amino acid sequences set forth, respectively: SEQ ID NOs: 50 and 56.

48. The multi-specific antigen binding molecule of any one of claims 1 to 43, wherein the first VH and the first VL comprise the amino acid sequences set forth, respectively, below, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56.

49. The multi-specific antigen binding molecule of any one of claims 1 to 48, wherein the first VH and the first VL comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56.

50. The multi-specific antigen binding molecule of any one of claims 1 to 49, wherein the first VH and the first VL comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56.

51. The multi-specific antigen binding molecule of any one of claims 1 to 50, wherein the first VH and the first VL comprise the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56.

52. The multi-specific antigen binding molecule of any one of claims 23 to 51, wherein the amino acid residue at position 100 of the first VH (numbering according to Kabat) is H.

53. The multi-specific antigen binding molecule of any one of claims 1 to 52, wherein at least one of the first antigen binding domain and the second antigen binding domain independently comprise a Fab, an $F(ab)_2$, Fv, a scFv, a $sc(Fv)_2$, or a diabody.

54. The multi-specific antigen binding molecule of any one of claims 1 to 53, wherein:

i. the first antigen binding domain comprises a scFv and the second antigen binding domain comprises a Fab;
ii. the first antigen binding domain comprises a Fab and the second antigen binding domain comprises a scFv;
iii. the first antigen binding domain comprises a Fab and the second antigen binding domain comprises a Fab; or
iv. the first antigen binding domain comprises a scFv and the second antigen binding domain comprises a scFv.

55. The multi-specific antigen binding molecule of any one of claims 1 to 54, wherein the first antigen binding domain comprises a scFv and the second antigen binding domain comprises a Fab.

56. The multi-specific antigen binding molecule of any one of claims 1 to 53, wherein:

i. the first antigen binding domain comprises a Fab and the second antigen binding domain comprises an extracellular domain of CD4; or
ii. the first antigen binding domain comprises a scFv and the second antigen binding domain comprises an extracellular domain of CD4.

57. The multi-specific antigen binding molecule of any one of claims 1 to 53, wherein the first antigen binding domain comprises a Fab and the second antigen binding domain comprises an extracellular domain of CD4.

58. The multi-specific antigen binding molecule of any one of claims 56 to 57, comprising the following amino acid substitutions (numbering according to Kabat):

i. a cysteine (C) at position 44 in the scFv variable heavy domain; and
ii. a cysteine (C) at position 100 in the scFv variable light domain.

59. The multi-specific antigen binding molecule of any one of claims 1 to 56 and 58, wherein the first antigen binding domain is a scFv comprising a VH and a VL, the scFv comprising an amino acid sequence selected from SEQ ID NOs: 59-66, or comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from SEQ ID NOs: 59-66.

60. The multi-specific antigen binding molecule of any one of claims 1 to 56 and 58 to 59, wherein the first antigen binding domain is a scFv comprising a VH and a VL, the scFv comprising an amino acid sequence selected from SEQ ID NOs: 59-63, or comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from SEQ ID NOs: 59-63.

61. The multi-specific antigen binding molecule of any one of claims 1 to 56 and 58 to 59, wherein the first antigen binding domain is a scFv comprising a VH and a VL, the scFv comprising an amino acid sequence selected from SEQ ID NOs: 62-63, or comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence selected from SEQ ID NOs: 62-63.

62. The multi-specific antigen binding molecule of claim 61, wherein the first antigen binding domain is a scFv comprising a VH and a VL, the scFv comprising an amino acid sequence selected from SEQ ID NO: 62, or comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NO: 62.

63. The multi-specific antigen binding molecule of claim 61, wherein the first antigen binding domain is a scFv comprising a VH and a VL, the scFv comprising an amino acid sequence selected from SEQ ID NO: 63, or comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at

least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to an amino acid sequence of SEQ ID NO: 63.

64. The multi-specific antigen binding molecule of any one of claims 1 to 54 and 58 to 61, wherein the second antigen binding domain binds to an HIV envelope protein selected from the group consisting of gp120 and gp41.

65. The multi-specific antigen binding molecule of any one of claims 1 to 64, wherein the second antigen binding domain competes with or comprises VH and VL variable domains of a broadly neutralizing antibody (bNAb) against HIV.

66. The multi-specific antigen binding molecule of any one of claims 1 to 54 and 58 to 65, wherein the second antigen binding domain binds to an epitope or region of gp120 selected from the group consisting of:

i. third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan;
ii. second variable loop (V2) (*e.g.*, Env trimer apex);
iii. CD4 binding site (CD4bs);
iv. gp120/gp41 interface; or
v. silent face of gp120.

67. The multi-specific antigen binding molecule of any one of claims 1 to 54 and 58 to 66, wherein the second antigen binding domain binds to an epitope or region of gp120 in the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03.

68. The multi-specific antigen binding molecule of any one of claims 1 to 54 and 58 to 66, wherein the second antigen binding domain binds to an epitope or region of gp120 in the second variable loop (V2) (*e.g.*, Env trimer apex) and competes with or comprises VH and VL regions from an antibody selected from the group consisting of PG9,

PG16, PGC14, PGG14, PGT-142, PGT-143, PGT-144, PGT-145, CH01, CH59, PGDM1400, CAP256, CAP256-VRC26.08, CAP256-VRC26.09, CAP256-VRC26.25, PCT64-24E and VRC38.01.

69. The multi-specific antigen binding molecule of any one of claims 1 to 54 and 58 to 66, wherein the second antigen binding domain binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25.

70. The multi-specific antigen binding molecule of any one of claims 1 to 64 and 66, wherein the second antigen binding domain binds to an epitope or region of gp120 in the CD4 binding site (CD4bs) and comprises one or more extracellular (EC) domains of CD4.

71. The multi-specific antigen binding molecule of claim 70, wherein the one or more EC domains of CD4 comprise a sequence as set forth below, or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from the group consisting of:

(i) KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRV DSRRSLWDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVG (SEQ ID NO: 746);

(ii) KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRV DSRRSLWDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVGGGGSGKKVVYG KKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRVDSRRSL WDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVG (SEQ ID NO: 747);

(iii) KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRA DSRRSLWDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFG (SEQ ID NO: 748); or

(iv) KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRA DSRRSLWDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFGGGGSGKKVVLG KKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRRSL WDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFG(SEQ ID NO: 749).

72. The multi-specific antigen binding molecule of claim 71, wherein the EC domain of CD4 comprises a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence of SEQ ID NO: 746.

73. The multi-specific antigen binding molecule of any one of claims 71 to 72, wherein the EC domain of CD4 comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 746.

74. The multi-specific antigen binding molecule of any one of claims 71 to 73, wherein the EC domain of CD4 comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 746.

75. The multi-specific antigen binding molecule of any one of claims 71 to 74, wherein the EC domain of CD4 comprises a sequence of SEQ ID NO: 746.

76. The multi-specific antigen binding molecule of any one of claims 71 to 75, wherein the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 11, 8, 4, 9 and 10; or SEQ ID NOs: 1, 12, 8, 4, 9 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749.

77. The multi-specific antigen binding molecule of claim 76, wherein the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Kabat): SEQ ID NOs: 1, 12, 8, 4, 9 and

10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NO: 746.

78. The multi-specific antigen binding molecule of any one of claims 71 to 75, wherein the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749.

79. The multi-specific antigen binding molecule of claim 78, wherein the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Chothia): SEQ ID NOs: 17, 18, 23, 20, 24 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NO: 746.

80. The multi-specific antigen binding molecule of any one of claims 71 to 75, wherein the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749.

81. The multi-specific antigen binding molecule of claim 80, wherein the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to IMGT): SEQ ID NOs: 28, 29, 32, 31, 24 and 10; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NO: 746.

82. The multi-specific antigen binding molecule of any one of claims 71 to 75, wherein the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 42, 40, 37, 41 and 25; or SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749.

83. The multi-specific antigen binding molecule of claim 82, wherein the first antigen binding domain comprises a first VH-CDR1, a first VH-CDR2, a first VH-CDR3, a first VL-CDR1, a first VL-CDR2 and a first VL-CDR3 comprising the following amino acid sequences, respectively (according to Honegger): SEQ ID NOs: 34, 43, 40, 37, 41 and 25; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NO: 746.

84. The multi-specific antigen binding molecule of any one of claims 71 to 75, wherein the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at

least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 49 and 55; SEQ ID NOs: 50 and 55; SEQ ID NOs: 50 and 56; SEQ ID NOs: 51 and 55; or SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one or more EC domains of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain selected from the group consisting of SEQ ID NOs: 746-749.

85. The multi-specific antigen binding molecule of any one of claims 71 to 84, wherein the first antigen binding domain comprises a first VH and a first VL comprising the amino acid sequences set forth, respectively, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that comprises or is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99%, identical to a CD4 EC domain of SEQ ID NO: 746.

86. The multi-specific antigen binding molecule of claim 85, wherein the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 95% identical to a CD4 EC domain of SEQ ID NO: 746.

87. The multi-specific antigen binding molecule of claim 86, wherein the first antigen binding domain comprises a first VH and a first VL comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence that is at least 99% identical to a CD4 EC domain of SEQ ID NO: 746.

88. The multi-specific antigen binding molecule of claim 87, wherein the first antigen binding domain comprises a first VH and a first VL comprising the amino acid

sequences set forth, respectively: SEQ ID NOs: 51 and 56; and the second antigen binding domain comprises one EC domain of CD4 comprising an amino acid sequence of SEQ ID NO: 746.

89. The multi-specific antigen binding molecule of any one of claims 1 to 54 and 58 to 69, wherein the second antigen binding domain binds to an epitope or region of gp120 in the gp120/gp41 interface and competes with or comprises VH and VL regions from an antibody selected from the group consisting of PGT-151, CAP248-2B, 35O22, 8ANC195, ACS202, VRC34 and VRC34.01.

90. The multi-specific antigen binding molecule of any one of claims 1 to 54 and 58 to 69, wherein the second antigen binding domain binds to an epitope or region of the gp120 silent face and competes with or comprises VH and VL regions from an antibody selected from VRC-PG05 and SF12.

91. The multi-specific antigen binding molecule of any one of claims 1 to 54 and 58 to 69, wherein the second antigen binding domain binds to an epitope or region of gp41 in the membrane proximal region (MPER).

92. The multi-specific antigen binding molecule of claim 91, wherein the second antigen binding domain binds to an epitope or region of gp41 in the membrane proximal region (MPER) and competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10E8, 10E8v4, 10E8-5R-100cF, 4E10, DH511.11P, 2F5, 7b2, and LN01.

93. The multi-specific antigen binding molecule of any one of claims 1 to 54 and 58 to 66, wherein the second antigen binding domain binds to an epitope or region of the gp41 fusion peptide and competes with or comprises VH and VL regions from an antibody selected from the group consisting of VRC34 and ACS202.

94. The multi-specific antigen binding molecule of any one of claims 1 to 54, 58 to 69 and 89 to 93, wherein the second antigen binding domain comprises a second VH comprising a second VH-CDR1, a second VH-CDR2, and a second VH-CDR3; and a second VL comprising a second VL-CDR1, a second VL-CDR2, and a second VH-CDR3; comprising the amino acid sequences (according to Kabat) set forth, respectively, in:

a) SEQ ID NOs: 76, 77, 78, 79, 80 and 81;

b) SEQ ID NOs: 76, 82, 78, 79, 80 and 81;
c) SEQ ID NOs: 83, 84, 85, 86, 80 and 87;
d) SEQ ID NOs: 83, 88, 85, 86, 80 and 87;
e) SEQ ID NOs: 90, 91, 92, 93, 94 and 95;
f) SEQ ID NOs: 90, 91, 96, 93, 94 and 95;
g) SEQ ID NOs: 97, 98, 99, 100, 101 and 102;
h) SEQ ID NOs: 103, 104, 105, 106, 94 and 107;
i) SEQ ID NOs: 108, 109, 110, 111, 112 and 113;
j) SEQ ID NOs: 114, 115, 116, 117, 118 and 119;
k) SEQ ID NOs: 114, 120, 121, 122, 118 and 123;
l) SEQ ID NOs: 124, 125, 126, 127, 128 and 113;
m) SEQ ID NOs: 129, 115, 131, 127, 118 and 113;
n) SEQ ID NOs: 132, 133, 134, 135, 136 and 137;
o) SEQ ID NOs: 138, 139, 140, 141, 142 and 143;
p) SEQ ID NOs: 144, 145, 146, 147, 148 and 143;
q) SEQ ID NOs: 149, 150, 151, 152, 153 and 143;
r) SEQ ID NOs: 154, 155, 156, 157, 158 and 159;
s) SEQ ID NOs: 160, 161, 162, 163, 164 and 165;
t) SEQ ID NOs: 166, 161, 167, 163, 164 and 165;
u) SEQ ID NOs: 168, 169, 170, 171, 172 and 173;
v) SEQ ID NOs: 168, 174, 170, 171, 172 and 173;
w) SEQ ID NOs: 175, 176, 177, 171, 172 and 173;
x) SEQ ID NOs: 178, 179, 180, 181, 182 and 183;
y) SEQ ID NOs: 184, 185, 186, 187, 188 and 189;
z) SEQ ID NOs: 190, 191, 192, 193, 194 and 195;
aa) SEQ ID NOs: 196, 197, 198, 199, 200 and 201;
bb) SEQ ID NOs: 202, 203, 204, 205, 206 and 207;
cc) SEQ ID NOs: 208, 209, 210, 211, 212 and 213;
dd) SEQ ID NOs: 214, 215, 216, 217, 218 and 219;
ee) SEQ ID NOs: 214, 220, 216, 221, 218 and 219;
ff) SEQ ID NOs: 214, 220, 222, 221, 218 and 219;
gg) SEQ ID NOs: 223, 224, 225, 226, 227 and 228;
hh) SEQ ID NOs: 229, 230, 231, 232, 233 and 234;
ii) SEQ ID NOs: 902, 903, 904, 905, 906 and 907;

jj) SEQ ID NOs: 908, 909, 910, 911, 912 and 913;

kk) SEQ ID NOs: 914, 915, 916, 917, 918 and 919; or

ll) SEQ ID NOs: 920, 921, 922, 923, 924 and 925.

95. The multi-specific antigen binding molecule of any one of claims 1 to 54, 58 to 69 and 89 to 94, wherein the second antigen binding domain comprises a second VH comprising a second VH-CDR1, a second VH-CDR2, and a second VH-CDR3; and a second VL comprising a second VL-CDR1, a second VL-CDR2, and a second VH-CDR3; comprising the amino acid sequences (according to Chothia) set forth, respectively, in:

a) SEQ ID NOs: 235, 236, 237, 238, 239 and 240;

b) SEQ ID NOs: 241, 242, 243, 244, 239 and 245;

c) SEQ ID NOs: 246, 242, 247, 244, 239 and 245;

d) SEQ ID NOs: 248, 249, 250, 251, 239 and 252;

e) SEQ ID NOs: 248, 249, 253, 251, 239 and 252;

f) SEQ ID NOs: 254, 255, 256, 257, 258 and 259;

g) SEQ ID NOs: 260, 261, 262, 263, 239 and 264;

h) SEQ ID NOs: 265, 266, 267, 268, 269 and 270;

i) SEQ ID NOs: 271, 272, 273, 274, 275 and 270;

j) SEQ ID NOs: 271, 276, 277, 278, 275 and 279;

k) SEQ ID NOs: 280, 281, 282, 283, 284 and 270;

l) SEQ ID NOs: 285, 272, 286, 283, 275 and 270;

m) SEQ ID NOs: 287, 288, 289, 290, 291 and 292;

n) SEQ ID NOs: 293, 294, 295, 296, 297 and 298;

o) SEQ ID NOs: 299, 300, 301, 302, 303 and 298;

p) SEQ ID NOs: 304, 300, 305, 406, 307 and 298;

q) SEQ ID NOs: 308, 309, 310, 311, 312 and 313;

r) SEQ ID NOs: 314, 315, 316, 317, 318 and 165;

s) SEQ ID NOs: 320, 315, 321, 317, 318 and 165;

t) SEQ ID NOs: 322, 323, 324, 325, 326 and 327;

u) SEQ ID NOs: 322, 328, 324, 325, 326 and 327;

v) SEQ ID NOs: 329, 323, 330, 325, 326 and 327;

w) SEQ ID NOs: 331, 332, 333, 334, 335 and 336;

x) SEQ ID NOs: 337, 338, 339, 340, 341 and 342;

y) SEQ ID NOs: 343, 344, 345, 346, 341 and 347;

z) SEQ ID NOs:348, 349, 350, 351, 352 and 353;
aa) SEQ ID NOs: 354, 355, 356, 357, 358 and 359;
bb) SEQ ID NOs: 360, 361, 362, 363, 364 and 365;
cc) SEQ ID NOs: 366, 367, 368, 369, 370 and 371;
dd) SEQ ID NOs: 366, 361, 368, 369, 370 and 371;
ee) SEQ ID NOs: 372, 361, 373, 369, 370 and 371;
ff) SEQ ID NOs: 374, 375, 376, 377, 378 and 379;
gg) SEQ ID NOs: 380, 381, 382, 383, 384 and 385;
hh) SEQ ID NOs: 926, 927, 928, 929, 930 and 931;
ii) SEQ ID NOs: 932, 933, 934, 935, 936 and 937;
jj) SEQ ID NOs: 938, 939, 940, 941, 942 and 943; or
kk) SEQ ID NOs: 944, 945, 946, 947, 948 and 949.

96. The multi-specific antigen binding molecule of any one of claims 1 to 54, 58 to 69 and 89 to 95, wherein the second antigen binding domain comprises a second VH comprising a second VH-CDR1, a second VH-CDR2, and a second VH-CDR3; and a second VL comprising a second VL-CDR1, a second VL-CDR2, and a second VH-CDR3; comprising the amino acid sequences (according to IMGT) set forth, respectively, in:

a) SEQ ID NOs: 386, 387, 388, 389, 239 and 81;
b) SEQ ID NOs: 390, 391, 392, 393, 239 and 87;
c) SEQ ID NOs: 390, 391, 394, 393, 239 and 87;
d) SEQ ID NOs: 395, 396, 397, 393, 239 and 87;
e) SEQ ID NOs: 398, 399, 400, 401, 239 and 95;
f) SEQ ID NOs: 398, 399, 402, 401, 239 and 95;
g) SEQ ID NOs: 403, 404, 405, 406, 258 and 102;
h) SEQ ID NOs: 407, 408, 409, 410, 239 and 107;
i) SEQ ID NOs: 411, 412, 413, 414, 269 and 113;
j) SEQ ID NOs: 415, 416, 417, 418, 275 and 119;
k) SEQ ID NOs: 415, 419, 420, 421, 275 and 123;
l) SEQ ID NOs: 422, 423, 424, 425, 275 and 113;
m) SEQ ID NOs: 426, 416, 427, 425, 275 and 113;
n) SEQ ID NOs: 428, 429, 430, 431, 291 and 137;
o) SEQ ID NOs: 432, 433, 434, 435, 297 and 143;
p) SEQ ID NOs: 436, 437, 438, 439, 303 and 143;

q) SEQ ID NOs: 440, 437, 441, 442, 307 and 143;
r) SEQ ID NOs: 443, 444, 445, 446, 312 and 159;
s) SEQ ID NOs: 447, 448, 449, 450, 318 and 165;
t) SEQ ID NOs: 451, 448, 452, 450, 318 and 165;
u) SEQ ID NOs: 453, 454, 455, 456, 326 and 173;
v) SEQ ID NOs: 453, 457, 455, 456, 326 and 173;
w) SEQ ID NOs: 458, 459, 460, 456, 326 and 173;
x) SEQ ID NOs: 461, 462, 463, 464, 335 and 183;
y) SEQ ID NOs: 465, 466, 467, 468, 341 and 189;
z) SEQ ID NOs: 469, 470, 471, 472, 341 and 195;
aa) SEQ ID NOs: 473, 474, 475, 476, 352 and 201;
bb) SEQ ID NOs: 477, 478, 479, 480, 358 and 207;
cc) SEQ ID NOs: 481, 482, 483, 484, 364 and 213;
dd) SEQ ID NOs: 485, 486, 487, 488, 370 and 219;
ee) SEQ ID NOs: 485, 482, 487, 488, 370 and 219;
ff) SEQ ID NOs: 489, 482, 490, 488, 370 and 219;
gg) SEQ ID NOs: 491, 492, 493, 494, 378 and 228;
hh) SEQ ID NOs: 495, 496, 497, 498, 384 and 234;
ii) SEQ ID NOs: 950, 951, 952, 953, 930 and 907;
jj) SEQ ID NOs: 954, 955, 956, 957, 936 and 913;
kk) SEQ ID NOs: 958, 959, 960, 961, 942 and 919; or
ll) SEQ ID NOs: 962, 963, 964, 965, 948 and 925.

97. The multi-specific antigen binding molecule of any one of claims 1 to 54, 58 to 69 and 89 to 96, wherein the second antigen binding domain comprises a second VH comprising a second VH-CDR1, a second VH-CDR2, and a second VH-CDR3; and a second VL comprising a second VL-CDR1, a second VL-CDR2, and a second VH-CDR3; comprising the amino acid sequences (according to Honegger) set forth, respectively, in:

a) SEQ ID NOs: 499, 500, 501, 238, 502 and 240;
b) SEQ ID NOs: 499, 503, 501, 238, 502 and 240;
c) SEQ ID NOs: 505, 506, 507, 244, 502 and 245;
d) SEQ ID NOs: 508, 509, 510, 244, 502 and 245;
e) SEQ ID NOs: 511, 512, 513, 251, 514 and 252;
f) SEQ ID NOs: 511, 512, 515, 251, 514 and 252;

g) SEQ ID NOs: 516, 517, 518, 257, 519 and 259;

h) SEQ ID NOs: 520, 521, 522, 264, 523 and 264;

i) SEQ ID NOs: 524, 525, 526, 268, 527 and 270;

j) SEQ ID NOs: 528, 529, 530, 274, 531 and 270;

k) SEQ ID NOs: 528, 532, 533, 278, 531 and 279;

l) SEQ ID NOs: 534, 535, 536, 283, 537 and 270;

m) SEQ ID NOs: 1090, 529, 538, 283, 531 and 270;

n) SEQ ID NOs: 539, 540, 541, 290, 542 and 292;

o) SEQ ID NOs: 543, 544, 545, 546, 547 and 298;

p) SEQ ID NOs: 548, 549, 550, 1091, 551 and 298;

q) SEQ ID NOs: 552, 553, 554, 555, 556 and 298;

r) SEQ ID NOs: 557, 558, 559, 311, 560 and 313;

s) SEQ ID NOs: 561, 562, 563, 564, 565 and 165;

t) SEQ ID NOs: 566, 562, 1092, 564, 567 and 165;

u) SEQ ID NOs: 568, 569, 570, 571, 572 and 327;

v) SEQ ID NOs: 568, 573, 570, 571, 572 and 327;

w) SEQ ID NOs: 574, 575, 576, 571, 572 and 327;

x) SEQ ID NOs: 577, 578, 579, 580, 581 and 336;

y) SEQ ID NOs: 582, 583, 584, 340, 585 and 342;

z) SEQ ID NOs: 586, 587, 588, 346, 589 and 347;

aa) SEQ ID NOs: 590, 591, 592, 351, 593 and 353;

bb) SEQ ID NOs: 594, 595, 596, 597, 598 and 359;

cc) SEQ ID NOs: 599, 600, 601, 602, 603 and 365;

dd) SEQ ID NOs: 604, 605, 606, 607, 608 and 371;

ee) SEQ ID NOs: 604, 609, 606, 607, 608 and 371;

ff) SEQ ID NOs: 610, 609, 611, 607, 608 and 371;

gg) SEQ ID NOs: 612, 613, 614, 615, 616 and 379;

hh) SEQ ID NOs: 617, 618, 619, 620, 621 and 385;

ii) SEQ ID NOs: 966, 967, 968, 969, 970 and 931;

jj) SEQ ID NOs: 971, 972, 973, 974, 975 and 937;

kk) SEQ ID NOs: 976, 977, 978, 941, 979 and 943; or

ll) SEQ ID NOs: 980, 981, 982, 983, 984 and 949.

98. The multi-specific antigen binding molecule of any one of claims 1 to 54, 58 to 69 and 89 to 97, wherein the second VH and the second VL comprise the amino acid sequences set forth, respectively, below, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

a) SEQ ID NOs: 622 and 623;
b) SEQ ID NOs: 624 and 625;
c) SEQ ID NOs: 624 and 626;
d) SEQ ID NOs: 627 and 628;
e) SEQ ID NOs: 629 and 630;
f) SEQ ID NOs: 631 and 632;
g) SEQ ID NOs: 633 and 634;
h) SEQ ID NOs: 635 and 636;
i) SEQ ID NOs: 637 and 638;
j) SEQ ID NOs: 639 and 640;
k) SEQ ID NOs: 641 and 642;
l) SEQ ID NOs: 643 and 644;
m) SEQ ID NOs: 645 and 646;
n) SEQ ID NOs: 647 and 648;
o) SEQ ID NOs: 649 and 650;
p) SEQ ID NOs: 651 and 652;
q) SEQ ID NOs: 653 and 654;
r) SEQ ID NOs: 655 and 656;
s) SEQ ID NOs: 657 and 658;
t) SEQ ID NOs: 659 and 660;
u) SEQ ID NOs: 661 and 662;
v) SEQ ID NOs: 663 and 664;
w) SEQ ID NOs: 665 and 666;
x) SEQ ID NOs: 667 and 668;
y) SEQ ID NOs: 669 and 670;
z) SEQ ID NOs:671 and 672;
aa) SEQ ID NOs:673 and 670;
bb) SEQ ID NOs: 674 and 675;

cc) SEQ ID NOs: 676 and 677;
dd) SEQ ID NOs: 678 and 679;
ee) SEQ ID NOs: 680 and 681;
ff) SEQ ID NOs: 682 and 683;
gg) SEQ ID NOs: 684 and 685;
hh) SEQ ID NOs: 686 and 687;
ii) SEQ ID NOs: 688 and 689;
jj) SEQ ID NOs: 690 and 691;
kk) SEQ ID NOs: 692 and 693;
ll) SEQ ID NOs: 694 and 695;
mm) SEQ ID NOs: 985 and 986;
nn) SEQ ID NOs: 987 and 988;
oo) SEQ ID NOs: 989 and 990; or
pp) SEQ ID NOs: 991 and 992.

99. The multi-specific antigen binding molecule of any one of claims 1 to 54, 58 to 69 and 89 to 98, wherein the second VH and the second VL comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth below, respectively, and comprising the following amino acids at the indicated positions (position numbering according to Kabat):

(i) SEQ ID NOs: 622, 624 or 627, comprising one or more of: Ser-Ser-Val (SSV) or Thr-Gly-Val (TGV) at positions 82a-82c, Gln (Q) at position 39, Asn (N) at position 60, His (H) at position 68, any one of Lys (K), His (H) or Thr (T) at position 105, Leu (L) at position 2, Ala (A) at position 32, and Ala (A) at position 95; and SEQ ID NOs: 623, 625, 626 or 628, comprising one or more of: Gly (G) at position 67, Tyr (Y), Phe (F) or Thr (T) at position 67a, Arg (R) at position 67b, Pro (P) at position 67c, and Lys (K) at position 103; or

(ii) SEQ ID NOs: 663, 665 or 667, comprising one or more of: His (H) at position 3, Ser (S) or Val (V) at position 5, Glu (E) at position 10, Lys (K) at position 12, Lys (K) at position 23, Asn (N) at position 28, Arg (R) at position 30, Tyr (Y) at position 32, Thr (T) at position 68, Met (M) at position 69, Gln (Q) or His (H) at position 72, Tyr (Y), Phe (F) at position 74a, Phe (F) or Ser (S) at position 76, Ser (S) at position 77, Ala (A) at position 78, Ser (S) at position 82a, Arg (R) at position 82b, Val (V) at position 82c, Ile

(I) or Thr (T) at position 89, Phe (F) at position 98, Tyr (Y) or Gly (G) at position 99, Gln (Q) at position 105, Met (M) at position 108, Phe-Asp-Phe-Asp (FDFD) (SEQ ID NO: 1040) at positions 74a, 74b, 74c, and 74d and Trp-Asp-Phe-Asp (WDFD) (SEQ ID NO: 1042) at positions 74a, 74b, 74c, and 74d; and SEQ ID NOs: 664, 666 or 668, comprising one or more of Arg (R) at position 14, Arg (R) at position 18, Ala (A) at position 19, Lys (L) at position 39, Pro (P) at position 40, Thr (T) at position 56, Ala (A) at position 60, Ser (S) at position 65, Thr (T) or His (H) at position 72, Lys (K) at position 74, Ser (S) at position 76, Ser (S) at position 77, Val (V) at position 83, Ile (I) or Phe (F) at position 98, Thr (T) or Gly (G) at position 99, Asn (N) at position 103, and Ile (I) at position 106.

100. The multi-specific antigen binding molecule of any one of claims 1 to 54, 58 to 69 and 89 to 99, wherein the second VH and the second VL comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth below, respectively, and comprising the following amino acids at the indicated positions (position numbering according to Kabat):

(i) SEQ ID NOs: 622, 624 or 627, comprising one or more of: Thr-Gly-Val (TGV) at positions 82a-82c, Asn (N) at position 60, His (H) at position 68, any one of Lys (K), His (H) and Thr (T) at position 105; and SEQ ID NOs: 623, 625, 626 or 628, comprising one or more of: Gly (G) at position 67, Tyr (Y), Phe (F) or Thr (T) at position 67a, Arg (R) at position 67b, Pro (P) at position 67c; or

(ii) SEQ ID NOs: 663, 665 or 667, comprising Phe (F) at position 74a; and SEQ ID NOs: 664, 666 or 668, comprising Ala (A) at position 19.

101. The multi-specific antigen binding molecule of any one of claims 1 to 100, comprising a heterodimeric human IgG1 or IgG4, comprising a first Fc region and a second Fc region.

102. The multi-specific antigen binding molecule of claim 101, wherein the first Fc region and the second Fc region are derived from IgG1m17.

103. The multi-specific antigen binding molecule of any one of claims 1 to 102, comprising a heterodimeric human IgG1 or IgG4, comprising a first Fc region and a second Fc region, wherein one or both of the first and second Fc regions comprise one or more of the following amino acids at the indicated positions (EU numbering):

(i) Alanine at position 234

(ii) Alanine at position 235; and

(iii) Serine at position 331.

104. The multi-specific antigen binding molecule of any one of claims 1 to 103, comprising a heterodimeric human IgG1 or IgG4, comprising a first Fc region and a second Fc region, wherein one or both of the first and second Fc regions comprise the following amino acids at the indicated positions (EU numbering):

(i) Tyrosine at position 252, threonine at position 254 and glutamic acid at position 256 (YTE); or

(ii) Leucine at position 428 and serine at position 434 (LS).

105. The multi-specific antigen binding molecule of any one of claims 1 to 104, comprising a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, wherein both of the first and second Fc regions comprise the following amino acids at the indicated positions (EU numbering): Tyrosine at position 252, threonine at position 254 and glutamic acid at position 256 (YTE).

106. The multi-specific antigen binding molecule of any one of claims 1 to 105, comprising a heterodimeric human IgG1 or IgG4, comprising a first Fc region and a second Fc region, comprising the following amino acids at the indicated positions (EU numbering):

(i) the first Fc region comprises a tryptophan at position 366 (T366W); and the second Fc region comprises a serine at position 366 (T366S), an alanine at position 368 (L368A) and a valine at position 407 (Y407V);

(ii) the first Fc region comprises a serine at position 366 (T366S), an alanine at position 368 (L368A) and a valine at position 407 (Y407V); and the second Fc region comprises a tryptophan at position 366 (T366W);

(iii) the first Fc region comprises a cysteine at position 354 (S354C), a tryptophan at position 366 (T366W); and the second Fc region comprises a cysteine at position 349 (Y349C), a serine at position 366 (T366S), an alanine at position 368 (L368A) and a valine at position 407 (Y407V);

(iv) the first Fc region comprises cysteine at position 349 (Y349C), a serine at position 366 (T366S), an alanine at position 368 (L368A) and a valine at position 407 (Y407V); and the second Fc region comprises a cysteine at position 354 (S354C), a tryptophan at position 366 (T366W).

107. The multi-specific antigen binding molecule of any one of claims 1 to 106, comprising a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising the following amino acids at the indicated positions (EU numbering): the first Fc region comprises a serine at position 366 (T366S), an alanine at position 368 (L368A) and a valine at position 407 (Y407V); and the second Fc region comprises a tryptophan at position 366 (T366W).

108. The multi-specific antigen binding molecule of any one of claims 1 to 107, comprising a heterodimeric human IgG1 or IgG4, comprising a first hinge region and a second hinge region, wherein one or both of the first and second hinge regions comprise a serine at position 220 (C220S) (EU numbering).

109. The multi-specific antigen binding molecule of any one of claims 1 to 108, comprising a heterodimeric human IgG1 or IgG4, comprising a first Fc region and a second Fc region, wherein one of the first Fc region or the second Fc region comprise the following amino acids at the indicated positions (EU numbering):

(i) arginine at position 435 (H435R); or

(ii) arginine at position 435 (H435R) and phenylalanine at position 436 (Y436F).

110. The multi-specific antigen binding molecule of any one of claims 1 to 109, comprising a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, wherein the first Fc region comprises the following amino acids at the indicated positions (EU numbering): arginine at position 435 (H435R).

111. The multi-specific antigen binding molecule of any one of claims 1 to 110, comprising a heterodimeric human IgG1 or IgG4, comprising a first Fc region and a second Fc region, comprising the following amino acids at the indicated positions (EU numbering):

(i) the first Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S) and a tryptophan at position 366 (T366W); and the second Fc region comprises an alanine a position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a serine at position 366 (T366S), an alanine at position 368 (L368A), a valine at position 407 (Y407V), and an arginine at position 435 (H435R);

(ii) the first Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S) and a tryptophan at position 366 (T366W); and the second Fc region comprises an alanine a position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a serine at position 366 (T366S), an alanine at position 368 (L368A), a valine at position 407 (Y407V), an arginine at position 435 (H435R) and a phenylalanine at position 436 (Y436F);

(iii) the first Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a serine at position 366 (T366S), an alanine at position 368 (L368A), and a valine at position 407 (Y407V); and the second Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S) and a tryptophan at position 366 (T366W);

(iv) the first Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a tryptophan at position 366 (T366W), a leucine at position 428 (M428L) and a serine at position 434 (N434S); and the second Fc region comprises an alanine a position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a serine at position 366 (T366S), an alanine at position 368 (L368A), a valine at position 407 (Y407V), and an arginine at position 435 (H435R); or

(v) the first Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a tryptophan at position 366 (T366W), a tyrosine at position 252 (M252Y), a threonine at position 254 (S254T) and a glutamic acid at position 256 (T256E); and the second Fc region comprises an alanine a position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a serine at position 366 (T366S), an alanine at position 368 (L368A), a valine at position 407 (Y407V), and an arginine at position 435 (H435R).

112. The multi-specific antigen binding molecule of any one of claims 1 to 111, comprising a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising the following amino acids at the indicated positions (EU numbering): the first Fc region comprises an alanine a position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a serine at position 366 (T366S), an alanine at position 368 (L368A), a valine at position 407 (Y407V), and an arginine at position 435 (H435R); and the second Fc region comprises an alanine at position 234 (L234), an alanine at position 235 (L235A), a serine at position 331 (P331S), a tryptophan at position 366

(T366W), a tyrosine at position 252 (M252Y), a threonine at position 254 (S254T) and a glutamic acid at position 256 (T256E).

113. The multi-specific antigen binding molecule of any one of claims 1 to 112, comprising a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising amino acid sequences set forth, respectively, below, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

a) SEQ ID NOs.: 696 and 697;
b) SEQ ID NOs.: 697 and 696;
c) SEQ ID NOs.: 696 and 698;
d) SEQ ID NOs.: 698 and 696;
e) SEQ ID NOs.: 699 and 700;
f) SEQ ID NOs.: 700 and 699;
g) SEQ ID NOs.: 701 and 698;
h) SEQ ID NOs.: 698 and 701;
i) SEQ ID NOs.: 702 and 703;
j) SEQ ID NOs.: 703 and 702;
k) SEQ ID NOs.: 704 and 698;
l) SEQ ID NOs.: 698 and 704;
m) SEQ ID NOs.: 705 and 703;
n) SEQ ID NOs.: 703 and 705;
o) SEQ ID NOs.: 706 and 704;
p) SEQ ID NOs.: 704 and 706;
q) SEQ ID NOs.: 707 and 703;
r) SEQ ID NOs.: 703 and 707;
s) SEQ ID NOs.: 708 and 704;
t) SEQ ID NOs.: 704 and 708;
u) SEQ ID NOs.: 709 and 710; or
v) SEQ ID NOs.: 710 and 709.

114. The multi-specific antigen binding molecule of any one of claims 1 to 113, comprising a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at

least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705.

115. The multi-specific antigen binding molecule of any one of claims 1 to 114, comprising a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705.

116. The multi-specific antigen binding molecule of any one of claims 1 to 115, comprising a heterodimeric human IgG1, comprising a first Fc region and a second Fc region, comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705.

117. The multi-specific antigen binding molecule of any one of claims 1 to 116, comprising a heterodimeric human IgG1, comprising amino acid sequences set forth, respectively: SEQ ID NOs.: 703 and 705.

118. The multi-specific antigen binding molecule of any one of claims 1 to 117, wherein the first antigen binding domain is a scFv and the second antigen binding domain is a Fab, wherein the first antigen binding domain comprises a first heavy chain (HC), and the second antigen binding domain comprises a second HC and a light chain (LC), the first HC, the second HC and the LC comprising the amino acid sequences set forth, respectively, below, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

1) SEQ ID NOs: 800, 801 and 802;
2) SEQ ID NOs: 800, 803 and 802;
3) SEQ ID NOs: 804, 803 and 802;
4) SEQ ID NOs: 804, 805 and 802;
5) SEQ ID NOs: 806, 801 and 802;
6) SEQ ID NOs: 806, 803 and 802;
7) SEQ ID NOs: 807, 803 and 802;
8) SEQ ID NOs: 807, 805 and 802;
9) SEQ ID NOs: 808, 809 and 802;

10) SEQ ID NOs: 808, 810 and 802;
11) SEQ ID NOs: 811, 801 and 802;
12) SEQ ID NOs: 812, 809 and 802;
13) SEQ ID NOs: 812, 810 and 802;
14) SEQ ID NOs: 813, 805 and 802;
15) SEQ ID NOs: 812, 814 and 802;
16) SEQ ID NOs: 815, 801 and 802;
17) SEQ ID NOs: 816, 805 and 802;
18) SEQ ID NOs: 817, 801 and 802;
19) SEQ ID NOs: 818, 805 and 802;
20) SEQ ID NOs: 819, 810 and 802;
21) SEQ ID NOs: 820, 810 and 802;
22) SEQ ID NOs: 821, 822 and 823;
23) SEQ ID NOs: 824, 825 and 823;
24) SEQ ID NOs: 826, 825 and 823;
25) SEQ ID NOs: 826, 827 and 823;
26) SEQ ID NOs: 828, 829 and 823;
27) SEQ ID NOs: 830, 822 and 823;
28) SEQ ID NOs: 830, 825 and 823;
29) SEQ ID NOs: 831, 825 and 823;
30) SEQ ID NOs: 831, 827 and 823;
31) SEQ ID NOs: 832, 833 and 823;
32) SEQ ID NOs: 832, 829 and 823;
33) SEQ ID NOs: 834, 827 and 823;
34) SEQ ID NOs: 835, 829 and 823;
35) SEQ ID NOs: 836, 829 and 823;
36) SEQ ID NOs: 837, 833 and 823;
37) SEQ ID NOs: 837, 838 and 823;
38) SEQ ID NOs: 839, 840 and 823;
39) SEQ ID NOs: 841, 829 and 823;
40) SEQ ID NOs: 842, 829 and 823;
41) SEQ ID NOs: 843, 829 and 823;
42) SEQ ID NOs: 844, 829 and 823;
43) SEQ ID NOs: 845, 829 and 823;

44) SEQ ID NOs: 846, 829 and 823;
45) SEQ ID NOs: 846, 833 and 823;
46) SEQ ID NOs: 846, 838 and 823;
47) SEQ ID NOs: 847, 827 and 823;
48) SEQ ID NOs: 848, 829 and 823;
49) SEQ ID NOs: 849, 829 and 823;
50) SEQ ID NOs: 850, 829 and 823;
51) SEQ ID NOs: 851, 829 and 823;
52) SEQ ID NOs: 852, 829 and 823;
53) SEQ ID NOs: 853, 829 and 823;
54) SEQ ID NOs: 854, 829 and 823;
55) SEQ ID NOs: 855, 829 and 823;
56) SEQ ID NOs: 856, 829 and 823;
57) SEQ ID NOs: 857, 829 and 823;
58) SEQ ID NOs: 858, 829 and 823;
59) SEQ ID NOs: 859, 829 and 823;
60) SEQ ID NOs: 860, 829 and 823;
61) SEQ ID NOs: 861, 862 and 863;
62) SEQ ID NOs: 861, 864 and 863;
63) SEQ ID NOs: 865, 864 and 863;
64) SEQ ID NOs: 865, 866 and 863;
65) SEQ ID NOs: 867, 868 and 863;
66) SEQ ID NOs: 869, 862 and 863;
67) SEQ ID NOs: 869, 864 and 863;
68) SEQ ID NOs: 870, 864 and 863;
69) SEQ ID NOs: 870, 866 and 863;
70) SEQ ID NOs: 871, 872 and 863;
71) SEQ ID NOs: 871, 868 and 863;
72) SEQ ID NOs: 873, 862 and 863;
73) SEQ ID NOs: 874, 866 and 863;
74) SEQ ID NOs: 875, 872 and 863;
75) SEQ ID NOs: 875, 868 and 863;
76) SEQ ID NOs: 875, 876 and 863;
77) SEQ ID NOs: 877, 862 and 863;

78) SEQ ID NOs: 878, 866 and 863;
79) SEQ ID NOs: 879, 862 and 863;
80) SEQ ID NOs: 880, 866 and 863;
81) SEQ ID NOs: 881, 882 and 883;
82) SEQ ID NOs: 881, 884 and 883;
83) SEQ ID NOs: 885, 884 and 883;
84) SEQ ID NOs: 885, 886 and 883;
85) SEQ ID NOs: 887, 888 and 883;
86) SEQ ID NOs: 889, 882 and 883;
87) SEQ ID NOs: 889, 884 and 883;
88) SEQ ID NOs: 890, 884 and 883;
89) SEQ ID NOs: 890, 886 and 883;
90) SEQ ID NOs: 891, 892 and 883;
91) SEQ ID NOs: 891, 888 and 883;
92) SEQ ID NOs: 893, 882 and 883;
93) SEQ ID NOs: 894, 886 and 883;
94) SEQ ID NOs: 895, 892 and 883;
95) SEQ ID NOs: 895, 888 and 883;
96) SEQ ID NOs: 895, 896 and 883;
97) SEQ ID NOs: 897, 882 and 883;
98) SEQ ID NOs: 898, 886 and 883;
99) SEQ ID NOs: 899, 882 and 883; or
100) SEQ ID NOs: 900, 886 and 883.

119. The multi-specific antigen binding molecule of any one of claims 1 to 118, wherein the first antigen binding domain is a scFv and the second antigen binding domain is a Fab, wherein the first antigen binding domain comprises a first heavy chain (HC), and the second antigen binding domain comprises a second HC and a light chain (LC), the first HC, the second HC and the LC comprising the amino acid sequences set forth, respectively, below, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

1) SEQ ID NOs: 800, 801 and 802;

2) SEQ ID NOs: 800, 803 and 802;
3) SEQ ID NOs: 804, 803 and 802;
4) SEQ ID NOs: 804, 805 and 802;
5) SEQ ID NOs: 806, 801 and 802;
6) SEQ ID NOs: 806, 803 and 802;
7) SEQ ID NOs: 807, 803 and 802;
8) SEQ ID NOs: 807, 805 and 802;
9) SEQ ID NOs: 808, 809 and 802;
10) SEQ ID NOs: 808, 810 and 802;
11) SEQ ID NOs: 821, 822 and 823;
12) SEQ ID NOs: 824, 825 and 823;
13) SEQ ID NOs: 826, 825 and 823;
14) SEQ ID NOs: 826, 827 and 823;
15) SEQ ID NOs: 828, 829 and 823;
16) SEQ ID NOs: 830, 822 and 823;
17) SEQ ID NOs: 830, 825 and 823;
18) SEQ ID NOs: 831, 825 and 823;
19) SEQ ID NOs: 831, 827 and 823;
20) SEQ ID NOs: 832, 833 and 823;
21) SEQ ID NOs: 832, 829 and 823;
22) SEQ ID NOs: 861, 862 and 863;
23) SEQ ID NOs: 861, 864 and 863;
24) SEQ ID NOs: 865, 864 and 863;
25) SEQ ID NOs: 865, 866 and 863;
26) SEQ ID NOs: 867, 868 and 863;
27) SEQ ID NOs: 869, 862 and 863;
28) SEQ ID NOs: 869, 864 and 863;
29) SEQ ID NOs: 870, 864 and 863;
30) SEQ ID NOs: 870, 866 and 863;
31) SEQ ID NOs: 871, 872 and 863;
32) SEQ ID NOs: 871, 868 and 863;
33) SEQ ID NOs: 881, 882 and 883;
34) SEQ ID NOs: 881, 884 and 883;
35) SEQ ID NOs: 885, 884 and 883;

36) SEQ ID NOs: 885, 886 and 883;
37) SEQ ID NOs: 887, 888 and 883;
38) SEQ ID NOs: 889, 882 and 883;
39) SEQ ID NOs: 889, 884 and 883;
40) SEQ ID NOs: 890, 884 and 883;
41) SEQ ID NOs: 890, 886 and 883;
42) SEQ ID NOs: 891, 892 and 883; or
43) SEQ ID NOs: 891, 888 and 883.

120. The multi-specific antigen binding molecule of any one of claims 1 to 119, wherein the first antigen binding domain is a scFv and the second antigen binding domain is a Fab, wherein the first antigen binding domain comprises a first heavy chain (HC), and the second antigen binding domain comprises a second HC and a light chain (LC), the first HC, the second HC and the LC comprising the amino acid sequences set forth, respectively, below, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

1) SEQ ID NOs: 800, 801 and 802;
2) SEQ ID NOs: 800, 803 and 802;
3) SEQ ID NOs: 804, 803 and 802;
4) SEQ ID NOs: 804, 805 and 802;
5) SEQ ID NOs: 821, 822 and 823;
6) SEQ ID NOs: 824, 825 and 823;
7) SEQ ID NOs: 826, 825 and 823;
8) SEQ ID NOs: 826, 827 and 823;
9) SEQ ID NOs: 828, 829 and 823;
10) SEQ ID NOs: 861, 862 and 863;
11) SEQ ID NOs: 861, 864 and 863;
12) SEQ ID NOs: 865, 864 and 863;
13) SEQ ID NOs: 865, 866 and 863;
14) SEQ ID NOs: 867, 868 and 863;
15) SEQ ID NOs: 881, 882 and 883;
16) SEQ ID NOs: 881, 884 and 883;

17) SEQ ID NOs: 885, 884 and 883;

18) SEQ ID NOs: 885, 886 and 883; or

19) SEQ ID NOs: 887, 888 and 883.

121. The multi-specific antigen binding molecule of any one of claims 1 to 120, wherein the first antigen binding domain is a scFv and the second antigen binding domain is a Fab, wherein the first antigen binding domain comprises a first heavy chain (HC), and the second antigen binding domain comprises a second HC and a light chain (LC), the first HC, the second HC and the LC comprising the amino acid sequences set forth, respectively, below, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

1) SEQ ID NOs: 800, 801 and 802;

2) SEQ ID NOs: 800, 803 and 802;

3) SEQ ID NOs: 804, 803 and 802;

4) SEQ ID NOs: 804, 805 and 802;

5) SEQ ID NOs: 821, 822 and 823;

6) SEQ ID NOs: 824, 825 and 823;

7) SEQ ID NOs: 826, 825 and 823;

8) SEQ ID NOs: 826, 827 and 823;

9) SEQ ID NOs: 828, 829 and 823;

10) SEQ ID NOs: 861, 862 and 863;

11) SEQ ID NOs: 861, 864 and 863;

12) SEQ ID NOs: 865, 864 and 863;

13) SEQ ID NOs: 865, 866 and 863; or

14) SEQ ID NOs: 867, 868 and 863.

122. A multi-specific antigen binding molecule that binds to human CD3 and HIV gp120, wherein the antigen binding molecule comprises:

(a) a first antigen binding domain that comprises a first heavy chain variable domain (VH) and a first light chain variable domain (VL), wherein the first antigen binding domain binds to CD3; and

(b) a second antigen binding domain that binds to HIV gp120 comprising one or more extracellular (EC) domain of CD4, wherein the one or more EC domains of

CD4 comprise a sequence as set forth below, or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a sequence selected from the group consisting of:

(i) KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRV DSRRSLWDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVG (SEQ ID NO: 746);

(ii) KKVVYGKKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRV DSRRSLWDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVGGGGSGKKVVYG KKGDTVELTCTASQKKNIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRVDSRRSL WDQGNFPLIIKNLKPEDSDTYICEVEDQKEEVQLVVVG (SEQ ID NO: 747);

(iii) KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRA DSRRSLWDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFG (SEQ ID NO: 748); or

(iv) KKVVLGKKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRA DSRRSLWDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFGGGGSGKKVVLG KKGDTVELTCTASQKKSIQFHWKNSNQIKILGNQGSFLTKGPSKLNDRADSRRSL WDQGNFPLIIKNLKIEDSDTYICEVEDQKEEVQLLVFG(SEQ ID NO: 749).

123. The multi-specific antigen binding molecule of claim 122, wherein the one or more EC domains of CD4 comprise a sequence as set forth below, or a sequence that is at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the sequence of SEQ ID NO: 746.

124. The multi-specific antigen binding molecule of any one of claims 1 to 88, 101 to 117 and 122 to 123, wherein the first antigen binding domain is a Fab and the second antigen binding domain is a scFv or an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, below, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%,

at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

1) SEQ ID NOs: 751, 752 and 753;
2) SEQ ID NOs: 754, 752 and 753;
3) SEQ ID NOs: 755, 756 and 753;
4) SEQ ID NOs: 755, 757 and 753;
5) SEQ ID NOs: 758, 757 and 753;
6) SEQ ID NOs: 759, 756 and 753;
7) SEQ ID NOs: 754, 760 and 761;
8) SEQ ID NOs: 762, 760 and 761;
9) SEQ ID NOs: 751, 763 and 753;
10) SEQ ID NOs: 764, 752 and 753;
11) SEQ ID NOs: 765, 752 and 753;
12) SEQ ID NOs: 766, 767 and 753;
13) SEQ ID NOs: 766, 768 and 753;
14) SEQ ID NOs: 769, 768 and 753;
15) SEQ ID NOs: 770, 767 and 753;
16) SEQ ID NOs: 765, 771 and 761;
17) SEQ ID NOs: 772, 771 and 761;
18) SEQ ID NOs: 774, 775 and 776;
19) SEQ ID NOs: 777, 778 and 776;
20) SEQ ID NOs: 779, 778 and 776;
21) SEQ ID NOs: 779, 780 and 776;
22) SEQ ID NOs: 777, 781 and 776;
23) SEQ ID NOs: 782, 752 and 753;
24) SEQ ID NOs: 783, 752 and 753;
25) SEQ ID NOs: 784, 785 and 753;
26) SEQ ID NOs: 784, 786 and 753;
27) SEQ ID NOs: 787, 786 and 753;
28) SEQ ID NOs: 788, 785 and 753;
29) SEQ ID NOs: 783, 789 and 761;
30) SEQ ID NOs: 790, 789 and 761;
31) SEQ ID NOs: 792, 793 and 794;
32) SEQ ID NOs: 795, 796 and 794;

33) SEQ ID NOs: 797, 796 and 794;

34) SEQ ID NOs: 797, 798 and 794; or

35) SEQ ID NOs: 795, 799 and 794.

125. The multi-specific antigen binding molecule of any one of claims 1 to 88, 101 to 117 and 122 to 124, wherein the first antigen binding domain is a Fab and the second antigen binding domain is a scFv or an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, below, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

1) SEQ ID NOs: 751, 752 and 753;

2) SEQ ID NOs: 754, 752 and 753;

3) SEQ ID NOs: 755, 756 and 753;

4) SEQ ID NOs: 755, 757 and 753;

5) SEQ ID NOs: 758, 757 and 753;

6) SEQ ID NOs: 759, 756 and 753;

7) SEQ ID NOs: 764, 752 and 753;

8) SEQ ID NOs: 765, 752 and 753;

9) SEQ ID NOs: 766, 767 and 753;

10) SEQ ID NOs: 766, 768 and 753;

11) SEQ ID NOs: 769, 768 and 753;

12) SEQ ID NOs: 770, 767 and 753;

13) SEQ ID NOs: 777, 778 and 776;

14) SEQ ID NOs: 779, 778 and 776;

15) SEQ ID NOs: 779, 780 and 776;

16) SEQ ID NOs: 777, 781 and 776;

17) SEQ ID NOs: 782, 752 and 753;

18) SEQ ID NOs: 783, 752 and 753;

19) SEQ ID NOs: 784, 785 and 753;

20) SEQ ID NOs: 784, 786 and 753;

21) SEQ ID NOs: 787, 786 and 753;

22) SEQ ID NOs: 788, 785 and 753;
23) SEQ ID NOs: 795, 796 and 794;
24) SEQ ID NOs: 797, 796 and 794;
25) SEQ ID NOs: 797, 798 and 794; or
26) SEQ ID NOs: 795, 799 and 794.

126. The multi-specific antigen binding molecule of any one of claims 1 to 88, 101 to 117 and 122 to 125, wherein the first antigen binding domain is a Fab and the second antigen binding domain is a scFv or an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, below, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

1) SEQ ID NOs: 751, 752 and 753;
2) SEQ ID NOs: 754, 752 and 753;
3) SEQ ID NOs: 755, 756 and 753;
4) SEQ ID NOs: 755, 757 and 753;
5) SEQ ID NOs: 758, 757 and 753; or
6) SEQ ID NOs: 759, 756 and 753.

127. The multi-specific antigen binding molecule of any one of claims 1 to 88, 101 to 117 and 122 to 126, wherein the first antigen binding domain is a Fab and the second antigen binding domain is a scFv or an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively, below, or comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

1) SEQ ID NOs: 751, 752 and 753; or
2) SEQ ID NOs: 755, 756 and 753.

128. The multi-specific antigen binding molecule of any one of claims 1 to 88, 101 to 117 and 122 to 127, wherein the first antigen binding domain is a Fab and the second antigen binding domain is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753.

129. The multi-specific antigen binding molecule of any one of claims 1 to 88, 101 to 117 and 122 to 128 , wherein the first antigen binding domain is a Fab and the second antigen binding domain is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753.

130. The multi-specific antigen binding molecule of any one of claims 1 to 88, 101 to 117 and 122 to 129, wherein the first antigen binding domain is a Fab and the second antigen binding domain is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753.

131. The multi-specific antigen binding molecule of any one of claims 1 to 88, 101 to 117 and 122 to 130, wherein the first antigen binding domain is a Fab and the second antigen binding domain is an EC domain of CD4 wherein the first antigen binding domain comprises a first HC and a LC, and the second antigen binding domain comprises a second HC, the second HC, the first HC and the LC comprising the amino acid sequences set forth, respectively: SEQ ID NOs: 751, 752 and 753.

132. The multi-specific antigen binding molecule of any one of claims 1 to 131, wherein the multi-specific antigen binding molecule is a bispecific antigen binding molecule.

133. The multi-specific antigen binding molecule of claim 132, binding to or targeting human CD3 and HIV gp120.

134. The multi-specific antigen binding molecule of any one of claims 1 to 133, wherein the first VH and the first VL have at least 80%, 81%, 82%, 83%, 84%, 85%, or more, sequence similarity to a human germline VH and a human germline VL, respectively.

135. The multi-specific antigen binding molecule of any one of claims 1 to 134, wherein the first antigen binding domain has reduced or insignificant or substantially no binding to Protein A, or does not detectably bind to Protein A.

136. The multi-specific antigen binding molecule of any one of claims 1 to 134, wherein the first antigen binding domain binds to Protein A with a K_D of greater than 10^{-6} M.

137. The multi-specific antigen binding molecule of any one of claims 1 to 136, wherein the first antigen binding domain binds to CD3 with a K_D of lower than 10 nM, *e.g.*, lower than 9.5 nM, 9.0 nM, 8.5 nM, 8.0 nM, 7.5 nM, 7.0 nM, 6.5 nM, 6.0 nM, 5.5 nM, 5.0 nM, 4.5 nM, 4.0 nM, 3.5 nM, 3.0 nM, or lower.

138. The multi-specific antigen binding molecule of claim 137, wherein the first antigen binding domain binds to CD3 with a KD of lower than 3.0 nM (*e.g.*, 2.5 nM).

139. The multi-specific antigen binding molecule of any one of claims 1 to 137, wherein the antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least 3 days, *e.g.*, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, or longer.

140. The multi-specific antigen binding molecule of any one of claims 1 to 139, wherein the antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least 7 days.

141. The multi-specific antigen binding molecule of any one of claims 1 to 139, wherein the first antigen binding domain binds to CD3 with a K_D of lower than

7.0 nM, *e.g.*, lower than 6.5 nM, 6.0 nM, 5.5 nM, 5.0 nM, 4.5 nM, 4.0 nM, 3.5 nM, 3.0 nM, or lower, and the antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least at least 5 days, *e.g.*, at least 5.5 days, at least 6 days, at least 6.5 days, at least 7 days, at least 7.5 days, at least 8 days, at least 8.5 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, or longer.

142. The multi-specific antigen binding molecule of any one of claims 1 to 141, wherein the first antigen binding domain binds to CD3 with a KD of lower 3.0 nM (*e.g.*, 2.5 nM), and the antigen binding molecule has a serum half-life in a human or cynomolgus monkey of at least 7 days.

143. The multi-specific antigen binding molecule of any one of claims 1 to 142, wherein at least 50%, at least 60%, at least 70%, least 80%, at least 85%, at least 90%, or more, N-linked glycosylation sites in at least one of the first VH, the first VL, the second VH and the second VL are sialylated.

144. The multi-specific antigen binding molecule of any one of claims 1 to 143, wherein the N-linked glycosylation sites in at least one of the first VH, the first VL, the second VH and the second VL have a sialic acid occupancy (*e.g.*, a glycan comprising one or two terminal sialic acid residues) of at least 40%, at least 50%, at least 60%, at least 70%, least 80%, at least 85%, at least 90%, or more.

145. The multi-specific antigen binding molecule of any one of claims 143 to 144, wherein the sialylated N-linked glycosylation sites in at least one of the first VH, the first VL, the second VH and the second VL comprise from 1 to 5 sialic acid residues, *e.g.*, from 1 to 4 sialic acid residues, *e.g.*, from 1 to 3 sialic acid residues, *e.g.*, from 1 to 2 sialic acid residues.

146. The multi-specific antigen binding molecule of any one of claims 143 to 145, wherein at least one of the first VH, the first VL, the second VH and the second VL are sialylated with N-acetylneuraminic acid (NANA).

147. The multi-specific antigen binding molecule of any one of claims 143 to 146, wherein the sialic acid residues are present in biantennary structures.

148. The multi-specific antigen binding molecule of any one of claims 143 to 147, wherein the sialic acid residues are present in complex N-linked glycan structures.

149. The multi-specific antigen binding molecule of any one of claims 143 to 147, wherein the sialic acid residues are present in hybrid N-linked glycan structures.

150. The multi-specific antigen binding molecule of any one of claims 143 to 147, wherein the glycans are terminally sialylated.

151. A polynucleotide or multiple polynucleotides encoding the first VH and the first VL of the multi-specific antigen binding molecule claimed in any one of claims 1 to 124.

152. The polynucleotide or polynucleotides of claim 151, further comprising a polynucleotide or multiple polynucleotides encoding the second VH and the second VL of the multi-specific antigen binding molecule claimed in any one of claims 64 to 132.

153. The polynucleotide or polynucleotides of any one of claims 151 to 152, comprising a polynucleotide or multiple polynucleotides encoding the HC of the first antigen binding domain that is an scFv, and the HC and LC of the second antigen binding domain that is a Fab, of the multi-specific antigen binding molecule of any one of claims 64 to 121.

154. The polynucleotide or polynucleotides of any one of claims 151 to 152, comprising a polynucleotide or multiple polynucleotides encoding the HC and LC of the first antigen binding domain that is a Fab, and the HC of the second antigen binding domain that is an scFv or an EC domain of CD4, of the multi-specific antigen binding molecule of any one of claims 64 to 132.

155. The polynucleotide or polynucleotides of any one of claims 151 to 154, encoding a multi-specific antigen binding molecule of any one of claims 122 to 132, comprising the following polynucleotide sequences, or polynucleotide sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the polynucleotide sequences set forth, respectively, below:

i. SEQ ID NOs: 995, 996 and 997;

ii. SEQ ID NOs: 998, 999 and 1000;

iii. SEQ ID NOs: 1001, 1002 and 1003;

iv. SEQ ID NOs: 1004, 1005 and 1000;
v. SEQ ID NOs: 1006, 1002 and 997;
vi. SEQ ID NOs: 1007, 1093 and 1000;
vii. SEQ ID NOs: 998, 1008 and 1000;
viii. SEQ ID NOs: 998, 1009 and 1000;
ix. SEQ ID NOs: 1010, 1011 and 1012;
x. SEQ ID NOs: 1013, 1014 and 1015;
xi. SEQ ID NOs: 1016, 1017 and 1012;
xii. SEQ ID NOs: 1018, 1019 and 1012;
xiii. SEQ ID NOs: 1018, 1020 and 1012;
xiv. SEQ ID NOs: 1021, 1022 and 1023; or
xv. SEQ ID NOs: 1024, 1025 and 1023.

156. The polynucleotide or polynucleotides of any one of claims 151 to 155, encoding a multi-specific antigen binding molecule of any one of claims 122 to 132, comprising the following polynucleotide sequences, or polynucleotide sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the polynucleotide sequences set forth, respectively: SEQ ID NOs: 995, 996 and 997.

157. The polynucleotide or polynucleotides of claim 156, comprising polynucleotide sequences that are at least 95% identical to the polynucleotide sequences set forth, respectively: SEQ ID NOs: 995, 996 and 997.

158. The polynucleotide or polynucleotides of any one of claims 156 to 157, comprising polynucleotide sequences that are at least 99% identical to the polynucleotide sequences set forth, respectively: SEQ ID NOs: 995, 996 and 997.

159. The polynucleotide or polynucleotides of any one of claims 156 to 158, comprising the following polynucleotide sequences, respectively: SEQ ID NOs: 995, 996 and 997.

160. The polynucleotide or polynucleotides of any one of claims 151 to 155, encoding a multi-specific antigen binding molecule of any one of claims 122 to 132, comprising the following polynucleotide sequences, or polynucleotide sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%,

at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the polynucleotide sequences set forth, respectively: SEQ ID NOs: 998, 999 and 1000.

161. The polynucleotide or polynucleotides of claim 156, comprising polynucleotide sequences that are at least 95% identical to the polynucleotide sequences set forth, respectively: SEQ ID NOs: 998, 999 and 1000.

162. The polynucleotide or polynucleotides of any one of claims 156 to 157, comprising polynucleotide sequences that are at least 99% identical to the polynucleotide sequences set forth, respectively: SEQ ID NOs: 998, 999 and 1000.

163. The polynucleotide or polynucleotides of any one of claims 156 to 158, comprising the following polynucleotide sequences, respectively: SEQ ID NOs: 998, 999 and 1000.

164. The polynucleotide or polynucleotides of any one of claims 151 to 163, wherein the polynucleotide or polynucleotides are comprised of DNA or RNA.

165. The polynucleotide or polynucleotides of any one of claims 151 to 164, wherein the polynucleotide or polynucleotides are comprised of mRNA.

166. The polynucleotide or polynucleotides of any one of claims 151 to 165, comprising codon bias for efficient expression in a human cell.

167. A lipoplex, *e.g.*, a lipid nanoparticle (LNP), comprising the polynucleotide or polynucleotides of any one of claims 151 to 166.

168. An expression cassette or multiple expression cassettes comprising one or more regulatory sequences operably linked to the polynucleotide or polynucleotides of any one of claims 151 to 166.

169. An expression vector or multiple expression vectors comprising one or more regulatory sequences operably linked to the polynucleotide or polynucleotides of any one of claims 151 to 166, or the expression cassette or expression cassettes of claim 168.

170. The expression vector or expression vectors of claim 169, wherein the expression vector or expression vectors comprise a plasmid vector or a viral vector.

171. The expression vector of any one of claims 169 to 170, wherein the expression vector comprises:

(i) a first expression cassette comprising a first polynucleotide encoding an anti-HIV gp120 VL-CL fusion protein;

(ii) a second expression cassette comprising a second polynucleotide encoding an anti-HIV gp120 VH-Fc fusion protein; and

(iii) a third expression cassette comprising a third polynucleotide encoding an anti-CD3 scFv-Fc fusion protein.

172. The expression vector of any one of claims 169 to 170, wherein the expression vector comprises in sequential order from 5′ to 3′:

(i) a first expression cassette comprising a first polynucleotide encoding an anti-HIV gp120 VL-CL fusion protein;

(ii) a second expression cassette comprising a second polynucleotide encoding an anti-HIV gp120 VH-Fc fusion protein; and

(iii) a third expression cassette comprising a third polynucleotide encoding an anti-CD3 scFv-Fc fusion protein.

173. The expression vector of any one of claims 171 to 172, wherein the anti-HIV gp120 VL-CL fusion protein, the anti-HIV gp120 VH-Fc fusion protein and the anti-CD3 scFv-Fc fusion protein comprise amino acid sequences set forth, respectively, below, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

1) SEQ ID NOs: 802, 801 and 800;
2) SEQ ID NOs: 802, 803 and 800;
3) SEQ ID NOs: 802, 803 and 804;
4) SEQ ID NOs: 802, 805 and 804;
5) SEQ ID NOs: 802, 801 and 806;
6) SEQ ID NOs: 802, 803 and 806;
7) SEQ ID NOs: 802, 803 and 807;
8) SEQ ID NOs: 802, 805 and 807;
9) SEQ ID NOs: 802, 809 and 808;
10) SEQ ID NOs: 802, 810 and 808;

11) SEQ ID NOs: 802, 801 and 811;
12) SEQ ID NOs: 802, 809 and 812;
13) SEQ ID NOs: 802, 810 and 812;
14) SEQ ID NOs: 802, 805 and 813;
15) SEQ ID NOs: 802, 814 and 812;
16) SEQ ID NOs: 802, 801 and 815;
17) SEQ ID NOs: 802, 805 and 816;
18) SEQ ID NOs: 802, 801 and 817;
19) SEQ ID NOs: 802, 805 and 818;
20) SEQ ID NOs: 802, 810 and 819;
21) SEQ ID NOs: 802, 810 and 820;
22) SEQ ID NOs: 823, 822 and 821;
23) SEQ ID NOs: 823, 825 and 824;
24) SEQ ID NOs: 823, 825 and 826;
25) SEQ ID NOs: 823, 827 and 826;
26) SEQ ID NOs: 823, 829 and 828;
27) SEQ ID NOs: 823, 822 and 830;
28) SEQ ID NOs: 823, 825 and 830;
29) SEQ ID NOs: 823, 825 and 831;
30) SEQ ID NOs: 823, 827 and 831;
31) SEQ ID NOs: 823, 833 and 832;
32) SEQ ID NOs: 823, 829 and 832;
33) SEQ ID NOs: 823, 827 and 834;
34) SEQ ID NOs: 823, 829 and 835;
35) SEQ ID NOs: 823, 829 and 836;
36) SEQ ID NOs: 823, 833 and 837;
37) SEQ ID NOs: 823, 838 and 837;
38) SEQ ID NOs: 823, 840 and 839;
39) SEQ ID NOs: 823, 829 and 841;
40) SEQ ID NOs: 823, 829 and 842;
41) SEQ ID NOs: 823, 829 and 843;
42) SEQ ID NOs: 823, 829 and 844;
43) SEQ ID NOs: 823, 829 and 845;
44) SEQ ID NOs: 823, 829 and 846;

45) SEQ ID NOs: 823, 833 and 846;
46) SEQ ID NOs: 823, 838 and 846;
47) SEQ ID NOs: 823, 827 and 847;
48) SEQ ID NOs: 823, 829 and 848;
49) SEQ ID NOs: 823, 829 and 849;
50) SEQ ID NOs: 823, 829 and 850;
51) SEQ ID NOs: 823, 829 and 851;
52) SEQ ID NOs: 823, 829 and 852;
53) SEQ ID NOs: 823, 829 and 853;
54) SEQ ID NOs: 823, 829 and 854;
55) SEQ ID NOs: 823, 829 and 855;
56) SEQ ID NOs: 823, 829 and 856;
57) SEQ ID NOs: 823, 829 and 857;
58) SEQ ID NOs: 823, 829 and 858;
59) SEQ ID NOs: 823, 829 and 859;
60) SEQ ID NOs: 823, 829 and 860;
61) SEQ ID NOs: 863, 862 and 861;
62) SEQ ID NOs: 863, 864 and 861;
63) SEQ ID NOs: 863, 864 and 865;
64) SEQ ID NOs: 863, 866 and 865;
65) SEQ ID NOs: 863, 868 and 867;
66) SEQ ID NOs: 863, 862 and 869;
67) SEQ ID NOs: 863, 864 and 869;
68) SEQ ID NOs: 863, 864 and 870;
69) SEQ ID NOs: 863, 866 and 870;
70) SEQ ID NOs: 863, 872 and 871;
71) SEQ ID NOs: 863, 868 and 871;
72) SEQ ID NOs: 863, 862 and 873;
73) SEQ ID NOs: 863, 866 and 874;
74) SEQ ID NOs: 863, 872 and 875;
75) SEQ ID NOs: 863, 868 and 875;
76) SEQ ID NOs: 863, 876 and 875;
77) SEQ ID NOs: 863, 862 and 877;
78) SEQ ID NOs: 863, 866 and 878;

79) SEQ ID NOs: 863, 862 and 879;
80) SEQ ID NOs: 863, 866 and 880;
81) SEQ ID NOs: 883, 882 and 881;
82) SEQ ID NOs: 883, 884 and 881;
83) SEQ ID NOs: 883, 884 and 885;
84) SEQ ID NOs: 883, 886 and 885;
85) SEQ ID NOs: 883, 888 and 887;
86) SEQ ID NOs: 883, 882 and 889;
87) SEQ ID NOs: 883, 884 and 889;
88) SEQ ID NOs: 883, 884 and 890;
89) SEQ ID NOs: 883, 886 and 890;
90) SEQ ID NOs: 883, 892 and 891;
91) SEQ ID NOs: 883, 888 and 891;
92) SEQ ID NOs: 883, 882 and 883;
93) SEQ ID NOs: 883, 886 and 894;
94) SEQ ID NOs: 883, 892 and 895;
95) SEQ ID NOs: 883, 888 and 895;
96) SEQ ID NOs: 883, 896 and 895;
97) SEQ ID NOs: 883, 882 and 897;
98) SEQ ID NOs: 883, 886 and 898;
99) SEQ ID NOs: 883, 882 and 899; or
100) SEQ ID NOs: 883, 886 and 900.

174. The expression vector of any one of claims 169 to 170, wherein the expression vector comprises:

(i) a first expression cassette comprising a first polynucleotide encoding an anti-CD3 VL-CL fusion protein;
(ii) a second expression cassette comprising a second polynucleotide encoding an anti-CD3 VH-Fc fusion protein; and
(iii) a third expression cassette comprising a third polynucleotide encoding a CD4 extracellular (EC) domain-Fc fusion protein.

175. The expression vector of any one of claims 169 to 170, wherein the expression vector comprises in sequential order from 5′ to 3′:

(i) a first expression cassette comprising a first polynucleotide encoding an anti-CD3 VL-CL fusion protein;

(ii) a second expression cassette comprising a second polynucleotide encoding an anti-CD3 VH-Fc fusion protein; and

(iii) a third expression cassette comprising a third polynucleotide encoding a CD4 EC domain-Fc fusion protein.

176. The expression vector of any one of claims 174 to 175, wherein the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences set forth, respectively, below, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively, below:

1) SEQ ID NOs: 753, 752 and 751;
2) SEQ ID NOs: 753, 752 and 754;
3) SEQ ID NOs: 753, 756 and 755;
4) SEQ ID NOs: 753, 757 and 755;
5) SEQ ID NOs: 753, 757 and 758;
6) SEQ ID NOs: 753, 756 and 759;
7) SEQ ID NOs: 761, 760 and 754;
8) SEQ ID NOs: 761, 760 and 762;
9) SEQ ID NOs: 753, 763 and 751;
10) SEQ ID NOs: 753, 752 and 764;
11) SEQ ID NOs: 753, 752 and 765;
12) SEQ ID NOs: 753, 767 and 766;
13) SEQ ID NOs: 753, 768 and 766;
14) SEQ ID NOs: 753, 768 and 769;
15) SEQ ID NOs: 753, 767 and 770;
16) SEQ ID NOs: 761, 771 and 765;
17) SEQ ID NOs: 761, 771 and 772;
18) SEQ ID NOs: 776, 775 and 774;
19) SEQ ID NOs: 776, 778 and 777;
20) SEQ ID NOs: 776, 778 and 779;

21) SEQ ID NOs: 776, 780 and 779;
22) SEQ ID NOs: 776, 781 and 777;
23) SEQ ID NOs: 753, 752 and 782;
24) SEQ ID NOs: 753, 752 and 783;
25) SEQ ID NOs: 753, 785 and 784;
26) SEQ ID NOs: 753, 786 and 784;
27) SEQ ID NOs: 753, 786 and 787;
28) SEQ ID NOs: 753, 785 and 788;
29) SEQ ID NOs: 761, 789 and 783;
30) SEQ ID NOs: 761, 789 and 790;
31) SEQ ID NOs: 794, 793 and 792;
32) SEQ ID NOs: 794, 796 and 795;
33) SEQ ID NOs: 794, 796 and 797;
34) SEQ ID NOs: 794, 798 and 797; or
35) SEQ ID NOs: 794, 799 and 795.

177. The expression vector of claim 176, wherein the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences set forth, respectively, or comprise amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 753, 752 and 751.

178. The expression vector of claim 177, wherein the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences that are at least 95% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 753, 752 and 751.

179. The expression vector of claim 178, wherein the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion protein comprise amino acid sequences that are at least 99% identical to the amino acid sequences set forth, respectively: SEQ ID NOs: 753, 752 and 751.

180. The expression vector of claim 179, wherein the anti-CD3 VL-CL fusion protein, the anti-CD3 VH-Fc fusion protein and the CD4 EC domain-Fc fusion

protein comprise amino acid sequences set forth, respectively: SEQ ID NOs: 753, 752 and 751.

181. The expression vector of any one of claims 169 to 180, wherein the first, second and third expression cassettes each comprise a promoter of equivalent transcription strength, *e.g.*, a constitutive promoter, *e.g.*, a promoter selected from cytomegalovirus (CMV), SV40, RSV, EF1a, UBC, PGK and CAGG.

182. The expression vector of any one of claims 169 to 180, further comprising a fourth expression cassette positioned 5′ to the first expression cassette comprising a polynucleotide encoding a eukaryotic selection marker protein, *e.g.*, glutamine synthetase (GS).

183. A cell or population of cells, comprising the polynucleotide or polynucleotides of any one of claims 151 to 166, the expression cassette or multiple expression cassettes of claim 168, or the expression vector or expression vectors of any one of claims 169 to 182.

184. The cell or population of cells of claim 183, wherein the cell or population of cells comprises a eukaryotic cell.

185. The cell or population of cells of any one of claims 183 to 184, wherein the cell or population of cells comprises a mammalian cell, an insect cell, a plant cell or a yeast cell.

186. The cell or population of cells of any one of claims 183 to 185, wherein the mammalian cell is a Chinese Hamster Ovary (CHO) cell.

187. The cell or population of cells of any one of claims 183 to 185, wherein the mammalian cell is a human cell.

188. The cell or population of cells of claim 187, wherein the cell is a human embryonic kidney cell.

189. The cell or population of cells of any one of claims 183 to 188, wherein the cell predominantly sialylates N-linked glycosylation sites in the variable domains (Fv) of expressed antigen binding molecules.

190. The cell or population of cells of claim 189, wherein at least 50%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, or more, N-linked glycosylation sites in the variable domains (Fv) of expressed antigen binding molecules are sialylated.

191. A pharmaceutical composition comprising one or more multi-specific antigen binding molecules claimed in any one of claims 1 to 149, and a pharmaceutically acceptable carrier.

192. A pharmaceutical composition comprising one or more polynucleotides of any one of claims 151 to 166 encoding one or more multi-specific antigen binding molecules of any one of claims 1 to 149, or the lipoplex (*e.g.*, LNP) of claim 167, and a pharmaceutically acceptable carrier.

193. The pharmaceutical composition of any one of claims 191 to 192, wherein the composition comprises an aqueous formulation.

194. The pharmaceutical composition of claim 193, comprising one or more multi-specific antigen binding molecules claimed in any one of claims 1 to 149 at a concentration of from 0.1 mg/ml to 150 mg/ml, *e.g.*, 0.1 mg/ml to 100 mg/ml, *e.g.*, 1 mg/ml to 100 mg/ml, *e.g.*, from 5 mg/ml to 60 mg/ml, *e.g.*, from 20 mg/ml to 150 mg/ml, or from 10 mg/ml to 50 mg/ml.

195. The pharmaceutical composition of any one of claims 191 to 192, wherein the composition is lyophilized.

196. The pharmaceutical composition of any one of claims 191 to 195, further comprising a second agent for treating an HIV infection.

197. The pharmaceutical composition of claim 196, further comprising a toll-like receptor (TLR) agonist or an IL-15 receptor agonist.

198. The pharmaceutical composition of claim 197, comprising a multi-specific antigen binding molecule of any one of claims 70 to 84 and an IL-15 receptor agonist.

199. The pharmaceutical composition of claim 197, wherein the TLR agonist is a TLR2 agonist, a TLR3 agonist, a TLR7 agonist, a TLR8 agonist or a TLR9 agonist.

200. The pharmaceutical composition of claim 199, wherein the TLR7 agonist is selected from the group consisting of vesatolimod, imiquimod, and resiquimod.

201. The pharmaceutical composition of claim 199, wherein the TLR8 agonist is selected from the group consisting of selgantolimod (GS-9688), motolimod and resiquimod.

202. The pharmaceutical composition of claim 199, wherein the TLR9 agonist is selected from the group consisting of cavrotolimod, cobitolimod, agatolimod, leftolimod, litenimod and tilsotolimod.

203. The pharmaceutical composition of any one of claims 191 to 202, comprising a first multi-specific antigen binding molecule and second or additional antigen binding molecules, wherein the first multi-specific antigen binding molecule and the second or additional antigen binding molecules bind to different epitopes or regions of gp120 selected from the group consisting of:

(i) third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan;

(ii) second variable loop (V2) (*e.g.*, Env trimer apex);

(iii) CD4 binding site (CD4bs);

(iv) gp120/gp41 interface; or

(v) silent face of gp120.

204. The pharmaceutical composition of claim 203, wherein the first multi-specific antigen binding molecule binds to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and the second antigen binding molecule binds to the CD4 binding site (CD4bs).

205. The pharmaceutical composition of any one of claims 203 to 204, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-

124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25.

206. The pharmaceutical composition of any one of claims 203 to 205, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523.

207. The pharmaceutical composition of any one of claims 203 to 205, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second antigen binding molecule comprises an EC domain of CD4.

208. The pharmaceutical composition of claim 203, wherein the first multi-specific antigen binding molecule binds to the CD4 binding site (CD4bs) and the second antigen binding molecule binds to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan.

209. The pharmaceutical composition of claim 208, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11,

N49P9 and N60P25, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03.

210. The pharmaceutical composition of any one of claims 208 to 209, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134.

211. The pharmaceutical composition of claim 208, wherein the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03.

212. The pharmaceutical composition of any one of claims 208 and 211, wherein the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134.

213. The pharmaceutical composition of any one of claims 208 and 211 to 212, further comprising second antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06,

VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25.

214. The pharmaceutical composition of any one of claims 208 and 211 to 213, further comprising second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523.

215. The pharmaceutical composition of any one of claims 208, 211 to 214, comprising:

(i) a multi-specific antigen binding molecule comprising an EC domain of CD4 of any one of claims 122 to 127;

(ii) an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134; and

(iii) an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523.

216. The pharmaceutical composition of any one of claims 191 to 215, comprising an additional multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody that binds to the gp120 second variable loop (V2) (*e.g.*, Env trimer apex).

217. The pharmaceutical composition of any one of claims 191 to 216, comprising an additional multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of PG9, PG16, PGC14, PGG14, PGT-142, PGT-143, PGT-144, PGT-145, CH01, CH59, PGDM1400, CAP256, CAP256-VRC26.08, CAP256-VRC26.09, CAP256-VRC26.25, PCT64-24E and VRC38.01.

218. The pharmaceutical composition of any one of claims 191 to 217, comprising an additional multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody that binds to the gp120/gp41 interface.

219. The pharmaceutical composition of any one of claims 191 to 218, comprising an additional multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of PGT-151, CAP248-2B, 35O22, 8ANC195, ACS202, VRC34 and VRC34.01.

220. The pharmaceutical composition of any one of claims 191 to 219, comprising an additional multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody that binds to an epitope or region of gp41 in the membrane proximal region (MPER).

221. The pharmaceutical composition of any one of claims 191 to 220, comprising an additional multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10E8, 10E8v4, 10E8-5R-100cF, 4E10, DH511.11P, 2F5, 7b2, and LN01.

222. The pharmaceutical composition of any one of claims 191 to 221, comprising an additional antigen binding molecule or antigen binding fragment thereof that at least one of binds, inhibits, and neutralizes HIV, or a polynucleotide encoding the additional antigen binding molecule or antigen binding fragment thereof, wherein the additional antigen binding molecule or antigen binding fragment does not compete for binding to gp120 with the one or more multi-specific antigen binding molecules.

223. The pharmaceutical composition of any one of claims 191 to 222, formulated for intravenous, intramuscular or subcutaneous administration.

224. A kit comprising one or more containers comprising one or more of the multi-specific antigen binding molecules claimed in any one of claims 1 to 149, the polynucleotide or polynucleotides of any one of claims 151 to 166 or the lipoplex (*e.g.*, LNP) of claim 167, the expression vector or expression vectors of any one of claims 169 to 182, or the pharmaceutical composition of any one of claims 191 to 223.

225. The kit of claim 224, comprising one or more unitary doses of the one or more multi-specific antigen binding molecules, or the polynucleotide or polynucleotides, in one or more containers.

226. The kit of any one of claims 224 to 225, comprising one or more unitary doses of the one or more multi-specific antigen binding molecules and a second agent for treating an HIV infection in separate containers.

227. The kit of claim 226, further comprising at least one of a toll-like receptor (TLR) agonist and an IL-15 receptor agonist.

228. The kit of claim 227, comprising a multi-specific antigen binding molecule of any one of claims 70 to 84 and an IL-15 receptor agonist.

229. The kit of claim 227, wherein the TLR agonist is a TLR2 agonist, a TLR3 agonist, a TLR7 agonist, a TLR8 agonist or a TLR9 agonist.

230. The kit of claim 229, wherein the TLR7 agonist is selected from the group consisting of vesatolimod, imiquimod, and resiquimod.

231. The kit of any one of claims 224 to 230, comprising a first multi-specific antigen binding molecule and second or additional antigen binding molecules, wherein the first multi-specific antigen binding molecule and the second or additional antigen binding molecules bind to different epitopes or regions of gp120 selected from the group consisting of:

(i) third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan;

(ii) second variable loop (V2) (*e.g.*, Env trimer apex);

(iii) CD4 binding site (CD4bs);

(iv) gp120/gp41 interface; or

(v) silent face of gp120.

232. The kit of claim 231, wherein the first multi-specific antigen binding molecule binds to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and the second or additional antigen binding molecules bind to the CD4 binding site (CD4bs).

233. The kit of any one of claims 231 to 232, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04), PGV04; CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25.

234. The kit of any one of claims 231 to 233, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523.

235. The kit of any one of claims 231 to 234, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 and PGT-121, and the second or additional antigen binding molecules comprise an EC domain of CD4.

236. The kit of claim 231, wherein the first multi-specific antigen binding molecule binds to the CD4 binding site (CD4bs) and the second or additional antigen binding molecules bind to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan.

237. The kit of claim 236, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04

(*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03.

238. The kit of any one of claims 236 to 237, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134.

239. The kit of claim 236, wherein the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03.

240. The kit of any one of claims 236 and 239, wherein the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134.

241. The kit of any one of claims 236 and 239 to 240, further comprising second or additional antigen binding molecules compete with or comprise VH and VL

regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25.

242. The kit of any one of claims 236 and 239 to 241, further comprising second or additional antigen binding molecules compete with or comprise VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523.

243. The kit of any one of claims 236 and 239 to 242, comprising:

(i) a multi-specific antigen binding molecule comprising an EC domain of CD4 of any one of claims 122 to 127;

(ii) an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134; and

(iii) an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523.

244. The kit of any one of claims 224 to 243, comprising two or more unitary doses, wherein the unitary doses are the same.

245. The kit of any one of claims 224 to 243, comprising two or more unitary doses, wherein the unitary doses are different.

246. A method of producing a multi-specific antigen binding molecule, the method comprising:

a) culturing a cell or population of cells of any one of claims 183 to 190 transformed with the polynucleotide or polynucleotides of any one of claims 151 to 166, or the expression cassette or multiple expression cassettes of claim 168 in a cell culture under conditions sufficient to express the multi-specific antigen binding molecules; and

b) isolating or purifying the antigen binding molecules from the cell culture.

247. The method of claim 246, wherein the first antigen binding domain is a scFv and the second antigen binding domain is a Fab.

248. The method of claim 246, wherein the first antigen binding domain is a Fab and the second antigen binding domain is a Fab or an EC domain of CD4.

249. The method of claim 248, wherein the first antigen binding domain is a Fab and the second antigen binding domain is an EC domain of CD4.

250. The method of any one of claims 247 to 249, wherein the polypeptide comprising the first antigen binding domain and the polypeptide comprising the second antigen binding domain are expressed and assembled in the same cell.

251. The method of any one of claims 246 to 250, wherein the isolating or purifying step comprises Protein A chromatography.

252. The method of any one of claim 251, wherein at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more, of the multi-specific antigen binding molecules are isolated or purified.

253. The method of any one of any one of claims 251 to 252, wherein the isolating or purifying step further comprises ion exchange chromatography.

254. The method of any one of claims 246 to 253, wherein at least 95%, 96%, 97%, 98%, 99%, or more, of the multi-specific antigen binding molecules are isolated or purified.

255. The method of any one of claims 246 to 254, wherein at least 95%, 96%, 97%, 98%, 99%, or more, of the multi-specific antigen binding molecules isolate or purify as non-aggregated soluble heterodimer as determined using size exclusion chromatography (SEC).

256. The method of any one of claims 246 to 255, wherein the isolated or purified multi-specific antigen binding molecules have increased homogeneity as assessed by analytical ion exchange chromatography, wherein the integrated area of a main peak

representing an unmodified target species is at least 95%, 96%, 97%, 98%, or more, of the sum of all integrated protein peak areas.

257. The method of any one of claims 246 to 256, wherein the isolated or purified antigen binding molecules have fewer than 35%, 30%, 25%, 20%, 15%, 10%, 9%, 8%, 7%, or fewer, acidic contaminants.

258. The method of any one of claims 246 to 257, wherein the cell or population of cells are cultured in a culture volume of at least 2L, *e.g.*, at least 5L, 10L, 50L, 100L, 150L, 200L, 250L, or more.

259. The method of any one of claims 246 to 258, further comprising formulating the antigen binding molecule into a sterile pharmaceutical composition suitable for administration to a human subject.

260. A method of treating or preventing HIV in a human subject in need thereof, the method comprising administering to the subject an effective amount of one or more multi-specific antigen binding molecules of any one of claims 1 to 149, one or more polynucleotides of any one of claims 151 to 166 the lipoplex (*e.g.*, LNP) of claim 167, or the pharmaceutical composition of any one of claims 191 to 223.

261. A method of preventing or treating an HIV infection or an HIV-related disease comprising the steps of: identifying a patient in need of such prevention or treatment, and administering to said patient a first therapeutic agent comprising a therapeutically effective amount of one or more multi-specific antigen binding molecules of any one of claims 1 to 149, one or more polynucleotides of any one of claims 151 to 166 the lipoplex (*e.g.*, LNP) of claim 167, or the pharmaceutical composition of any one of claims 191 to 223.

262. The method of any one of claims 260 to 261, further comprising administering to the subject a second agent for treating an HIV infection.

263. The method of any one of claims 260 to 262, wherein the subject is not receiving antiretroviral therapy (ART) or ART is discontinued prior to administration of the one or more multi-specific antigen binding molecules.

264. The method of any one of claims 260 to 262, wherein ART is discontinued after one or more administrations of the one or more multi-specific antigen binding molecules.

265. The method of any one of claims 260 to 262, further comprising administering one or more antiretroviral therapy (ART) agents to the subject.

266. The method of any one of claims 260 to 265, further comprising administering to the subject at least one of a TLR agonist and an IL-15 receptor agonist.

267. The method of claim 266, comprising administering a multi-specific antigen binding molecule of any one of claims 70 to 84 and an IL-15 receptor agonist.

268. The method of claim 266, wherein the TLR agonist is a TLR2 agonist, a TLR3 agonist, a TLR7 agonist, a TLR8 agonist or a TLR9 agonist.

269. The method of claim 268, wherein the TLR7 agonist is selected from the group consisting of vesatolimod, imiquimod, and resiquimod.

270. The method of claim 268, wherein the TLR8 agonist is selected from the group consisting of selgantolimod, motolimod and resiquimod.

271. The method of claim 268, wherein the TLR9 agonist is selected from the group consisting of cavrotolimod, cobitolimod, agatolimod, leftolimod, litenimod and tilsotolimod.

272. The method of any one of claims 260 to 269, comprising administering a first multi-specific antigen binding molecule and second or additional antigen binding molecules, wherein the first multi-specific antigen binding molecule and the second or additional antigen binding molecules bind to different epitopes or regions of gp120 selected from the group consisting of:

(i) third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan;

(ii) second variable loop (V2) (*e.g.*, Env trimer apex);

(iii) CD4 binding site (CD4bs);

(iv) gp120/gp41 interface; or

(v) silent face of gp120.

273. The method of claim 272, wherein the first multi-specific antigen binding molecule binds to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan and the second antigen binding molecule binds to the CD4 binding site (CD4bs).

274. The method of any one of claims 272 to 273, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25.

275. The method of any one of claims 272 to 274, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second antigen binding molecule competes with or comprises VH and VL regions from GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523.

276. The method of any one of claims 272 to 275, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second antigen binding molecule comprises an EC domain of CD4.

277. The method of claim 272, wherein the first multi-specific antigen binding molecule binds to the CD4 binding site (CD4bs) and the second antigen binding molecule binds to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan.

278. The method of any one of claims 272 to 273, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03.

279. The method of claim 278, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523, and the second antigen binding molecule competes with or comprises VH and VL regions from 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134.

280. The method of claim 277, wherein the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03.

281. The method of any one of claims 277 and 280, wherein the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second antigen binding molecules competes with or comprises VH and VL regions

from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134.

282. The method of any one of claims 277 and 280 to 281, further comprising an additional antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25.

283. The method of any one of claims 277 and 280 to 282, further comprising an additional antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523.

284. The method of any one of claims 277 and 280 to 283, comprising co-administering:

(i) a multi-specific antigen binding molecule comprising an EC domain of CD4 of any one of claims 122 to 127;

(ii) an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134; and

(iii) an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523.

285. The method of any one of claims 260 to 284, further comprising administering to the human subject an additional antigen binding molecule or antigen binding fragment thereof that at least one of binds, inhibits, and neutralizes HIV or a polynucleotide encoding the additional antigen binding molecule or antigen binding fragment thereof.

286. The method of any one of claims 260 to 285, comprising administering an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions that bind to the gp120 third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan, and wherein the human subject is infected with an HIV expressing a gp120 comprising the following amino acid residues, wherein the positions and residues are with reference to SEQ ID NO:69:

(i) N332glycan, D325 and T63;
(ii) N332glycan, D325 and L179;
(iii) N332glycan, D325 and T320;
(iv) N332glycan, D325 and H330;
(v) N332glycan, D325, T63 and L179;
(vi) N332glycan, D325, T63 and T320;
(vii) N332glycan, D325, T63 and H330;
(viii) N332glycan, D325, L179 and T320;
(ix) N332glycan, D325, L179 and H330;
(x) N332glycan, D325, T320 and H330;
(xi) N332glycan, D325, T63, T320 and H330;
(xii) N332glycan, D325, T63, L179 and T320;
(xiii) N332glycan, D325, T63, L179 and H330;
(xiv) N332glycan, D325, L179, T320 and H330; or
(xv) N332glycan, D325, T63, L179, T320 and H330.

287. The method of any one of claims 260 to 286, comprising administering an antibody or multi-specific antigen binding molecule that competes with or comprises VH and VL regions that bind to the gp120 CD4 binding site, and wherein the human subject is infected with an HIV expressing a gp120 comprising the following amino acid residues, wherein the positions and residues are with reference to SEQ ID NO:73:

(i) I201 and F353;
(ii) I201, I108 and F353;
(iii) I201, I108, A281 and F353;
(iv) I201, E102, I108, A281 and F353; or
(v) I201, E102, I108, A281, Y318 and F353.

288. The method of any one of claims 260 to 287, comprising multiple administrations of the one or more multi-specific antigen binding molecules, optionally with a TLR agonist or an IL-15 receptor agonist, at predetermined intervals.

289. The method of claim 288, comprising multiple administrations of a multi-specific antigen binding molecule of any one of claims 70 to 84 and an IL-15 receptor agonist, wherein the multi-specific antigen binding molecule and the IL-15 receptor agonist are independently administered at predetermined intervals.

290. The method or use of any one of claims 260 to 269, wherein the subject is chronically infected with HIV.

291. The method or use of any one of claims 260 to 290, wherein the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition are administered systemically or locally.

292. The method or use of any one of claims 260 to 291, wherein the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition is administered via a route selected from intravenous, subcutaneous, intramuscular, intradermal and mucosal (*e.g.* buccal, intranasal, intrarectal, intravaginal).

293. The method or use of any one of claims 262 to 292, wherein the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition and the one or more additional therapeutic agents are administered by the same routes of administration.

294. The method or use of any one of claims 262 to 292, wherein the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition and the one or more additional therapeutic agents are administered by different routes of administration.

295. The method or use of any one of claims 262 to 294, wherein the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition and the one or more additional therapeutic agents are co-administered according to the same schedule (*e.g.*, co-administered at the same time intervals).

296. The method or use of any one of claims 262 to 294, wherein the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition and the one or more additional therapeutic agents are co-administered according to different schedules (*e.g.*, co-administered at different time intervals).

297. The method or use of any one of any one of claims 260 to 296, wherein the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition is administered at a dose in the range of from 1 μg/kg to 5 μg/kg, *e.g.*, from 350 μg/kg to 550 μg/kg, *e.g.*, from 0.3 mg/kg to 30 mg/kg, *e.g.*, from 2 mg/kg to 10 mg/kg, *e.g.*, from 1 μg/kg up to 2 μg/kg, 3 μg/kg, 4 μg/kg, 5 μg/kg, 10 μg/kg, 50 μg/kg, 100 μg/kg, 250 μg/kg, 300 μg/kg, 350 μg/kg, 400 μg/kg, 410 μg/kg, 420 μg/kg, 430 μg/kg, 440 μg/kg, 450 μg/kg, 460 μg/kg, 470 μg/kg, 480 μg/kg, 490 μg/kg, 500 μg/kg, 750 μg/kg, 1 mg/kg, 1.5 mg/kg, 2 mg/kg, 2.5 mg/kg, 3 mg/kg, 3.5 mg/kg, 4 mg/kg, 4.5 mg/kg, 5 mg/kg, 6 mg/kg, 7 mg/kg, 8 mg/kg, 9 mg/kg, 10 mg/kg, 15 mg/kg, 20 mg/kg, 25 mg/kg, 30 mg/kg, 35 mg/kg, 40 mg/kg, 45 mg/kg, or 50 mg/kg, body weight per administration.

298. The method or use of any one of claims 260 to 296, wherein the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition is administered at a dose in the range of 0.05 mg to 1000 mg per administration, *e.g.,* from 0.05 mg to 150 mg per administration, *e.g.,* from 0.05 mg to 0.35 mg per administration, *e.g.,* from 25 mg to 50 mg per administration, *e.g.,* from 30 mg to 35 mg per administration, *e.g.,* from 10 mg to 1000 mg per administration, *e.g.,* from 50 mg to 1000 mg per administration, *e.g.,* from 100 mg to 700 mg per administration, *e.g.*, at least 0.05 mg up to 0.1 mg, 0.2 mg, 0.3 mg, 0.35 mg, 0.4 mg, 0.5 mg, 0.6 mg, 0.7 mg, 0.8 mg, 1.0 mg, 5 mg, 10 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 200 mg, 300 mg, 400 mg, 500 mg, 600 mg, 700 mg, 800 mg, 900 mg, or 1000 mg per administration.

299. The method or use of any one of claims 260 to 298, comprising multiple administrations of the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition, optionally with one or more additional therapeutic agents, at predetermined intervals.

300. The method or use of any one of claims 260 to 299, comprising administering over a time period of at least about 2 weeks, 3 weeks, 1 month, 6, weeks, 2 months, 10 weeks, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months, 13 months, 14 months, 15 months, 16 months, 17 months, 18 months, 19 months, 20 months, 21 months, 22 months, 23 months, 24 months, or longer.

301. The method or use of any one of claims 260 to 300, comprising administering one or more times at predetermined intervals spaced at least 1 week and up to at least 2 weeks, 3 weeks, 1 month, 2 months, 3 months, 4 months, 5 months or 6 months apart.

302. The method or use of any one of claims 260 to 301, wherein the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition is administered once weekly (*i.e.*, QW), once bi-weekly (*i.e.* once every other week, or once every two weeks or Q2W), once thrice-weekly (*i.e.* once every three weeks or Q3W), once monthly (*i.e.*, QM) or once bi-monthly dosing (*i.e.* once every other month, or once every two months or Q2M), once every three months (Q3M), once every four months (Q4M), once every five months (Q5M), once every six months (Q6M), or less often.

303. The method or use of any one of claims 260 to 302, wherein the one or more multi-specific antigen binding molecules, the polynucleotide, the vector, the LNP and/or the pharmaceutical composition is administered two, three, four, five, or more, times intravenously or subcutaneously at an interval or at intervals between once bi-weekly (*i.e.* once every other week, or once every two weeks or Q2W) to once thrice-weekly (*i.e.* once every three weeks or Q3W).

304. The method or use of any one of claims 260 to 303, wherein the one or more multi-specific antigen binding molecules have a serum half-life in a human of at least 3 days, *e.g.*, at least 4 days, at least 5 days, at least 6 days, at least 7 days, at least 8 days, at least 9 days, at least 10 days, at least 11 days, at least 12 days, at least 13 days, at least 14 days, at least 15 days, at least 16 days, or longer.

305. The method or use of any one of claims 260 to 304, wherein the subject or the mammal is a human.

306. The method of any one of claims 260 to 288, wherein the subject does not exhibit symptoms of HIV or AIDS in the absence of anti-retroviral treatment (ART) for at least 6 months, at least 1 year, at least 2 years, at least 3 years, or more.

307. The method of any one of claims 260 to 306, wherein the subject has a viral load of copies/ml blood of less than 500, *e.g.*, less than 400, less than 300, less than 200, less than 100, less than 50, in the absence of anti-retroviral treatment (ART) for at least 6 months, at least 1 year, at least 2 years, at least 3 years, or more.

308. A method of treating or preventing HIV in a human subject in need thereof, the method comprising:

a) Identifying a human subject who is infected with an HIV expressing a gp120 comprising the following amino acid residues, wherein the positions and residues are with reference to SEQ ID NO:69:

(i) N332glycan, D325 and T63;

(ii) N332glycan, D325 and L179;

(iii) N332glycan, D325 and T320;

(iv) N332glycan, D325 and H330;

(v) N332glycan, D325, T63 and L179;

(vi) N332glycan, D325, T63 and T320;

(vii) N332glycan, D325, T63 and H330;

(viii) N332glycan, D325, L179 and T320;

(ix) N332glycan, D325, L179 and H330;

(x) N332glycan, D325, T320 and H330;

(xi) N332glycan, D325, T63, T320 and H330;

(xii) N332glycan, D325, T63, L179 and T320;

(xiii) N332glycan, D325, T63, L179 and H330;

(xiv) N332glycan, D325, L179, T320 and H330; or

(xv) N332glycan, D325, T63, L179, T320 and H330; and

b) Administering to the subject an effective amount of the multi-specific antigen binding molecule of any one of claims 1 to 149, or the pharmaceutical composition of any one of claims 191 to 223, wherein the second binding domain competes with or comprises VH and VL regions that bind to the gp120 third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan.

309. The method of claim 308, comprising identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues:

(i) N332glycan, D325 and T63;

(ii) N332glycan, D325 and L179;

(iii) N332glycan, D325 and T320; or

(iv) N332glycan, D325 and H330.

310. The method of any one of claims 308 to 309, comprising identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues:

(i) N332glycan, D325, T63 and L179;

(ii) N332glycan, D325, T63 and T320;

(iii) N332glycan, D325, T63 and H330;

(iv) N332glycan, D325, L179 and T320;

(v) N332glycan, D325, L179 and H330; or

(vi) N332glycan, D325, T320 and H330.

311. The method of any one of claims 308 to 310, comprising identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues:

(i) N332glycan, D325, L179, T320 and H330;

(ii) N332glycan, D325, T63, T320 and H330;

(iii) N332glycan, D325, T63, L179 and T320; or

(iv) N332glycan, D325, T63, L179 and H330.

312. The method of any one of claims 308 to 311, comprising identifying a subject infected with an HIV or a population of HIV expressing a gp120 comprising the following amino acid residues:

(i) N332glycan, D325, T63 and H330;

(ii) N332glycan, D325, T320 and H330;

(iii) N332glycan, D325, L179, T320 and H330; or

(iv) N332glycan, D325, T63, L179, T320 and H330.

313. The method of any one of claims 308 to 312, wherein the second antigen binding domain competes with or comprises VH and VL regions from an antibody

selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-9721, GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03.

314. The method of any one of claims 308 to 313, wherein the second antigen binding domain competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-9721, GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134.

315. A method of treating or preventing HIV in a human subject in need thereof, the method comprising:

a) Identifying a human subject who is infected with an HIV expressing a gp120 comprising the following amino acid residues, wherein the positions and residues are with reference to SEQ ID NO: 73:

(i) I201 and F353;

(ii) I201, I108 and F353;

(iii) I201, I108, A281 and F353;

(iv) I201, E102, I108, A281 and F353; or

(v) I201, E102, I108, A281, Y318 and F353; and

b) Administering to the subject an effective amount of the multi-specific antigen binding molecule of any one of claims 1 to 149, or the pharmaceutical composition of any one of claims 191 to 223, wherein the second binding domain competes with or comprises VH and VL regions that bind to the gp120 CD4 binding site (CD4bs).

316. The method of claim 315, wherein the second antigen binding domain competes with or comprises VH and VL regions from an antibody selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25.

317. The method of any one of claims 315 to 316, wherein the second antigen binding domain competes with or comprises VH and VL regions from an antibody

selected from the group consisting of 3BNC117, GS-9723, GS-5423, 3BNC60, VRC01, VRC07 and VRC07-523.

318. The method of any one of claims 308 to 317, further comprising administering to the subject a second agent for treating an HIV infection.

319. The method of any one of claims 308 to 318, wherein the subject is not receiving antiretroviral therapy (ART) or ART is discontinued prior to administration of the one or more multi-specific antigen binding molecules.

320. The method of any one of claims 308 to 318, wherein ART is discontinued after one or more administrations of the one or more multi-specific antigen binding molecules.

321. The method of any one of claims 308 to 318, further comprising administering one or more antiretroviral therapy (ART) agents to the subject.

322. The method of any one of claims 308 to 321, further comprising administering to the subject at least one of a TLR agonist and an IL-15 receptor agonist.

323. The method of claim 322, comprising administering a multi-specific antigen binding molecule of any one of claims 70 to 84 and an IL-15 receptor agonist.

324. The method of claim 322, wherein the TLR agonist is a TLR2 agonist, a TLR3 agonist, a TLR7 agonist, a TLR8 agonist or a TLR9 agonist.

325. The method of claim 324, wherein the TLR7 agonist is selected from the group consisting of vesatolimod, imiquimod, and resiquimod.

326. The method of any one of claims 308 to 325, comprising multiple administrations of the one or more multi-specific antigen binding molecules, optionally with the TLR agonist, at predetermined intervals.

327. The method of any one of claims 308 to 326, wherein the subject does not exhibit symptoms of HIV or AIDS in the absence of anti-retroviral treatment (ART) for at least 6 months, at least 1 year, at least 2 years, at least 3 years, or more.

328. The method of any one of claims 308 to 327, wherein the subject has a viral load copies/ml blood of less than 500, *e.g.*, less than 400, less than 300, less than 200, less than 100, less than 50, in the absence of anti-retroviral treatment (ART) for at least 6 months, at least 1 year, at least 2 years, at least 3 years, or more.

329. Use of the multi-specific antigen binding molecule or antigen binding fragment thereof of any one of claims 1 to 149, or the pharmaceutical composition of any one of claims 191 to 223 in a method of at least one of treating, preventing and inhibiting HIV in a human subject in need thereof.

330. The use of claim 329, further comprising administering to the subject a second agent for treating an HIV infection.

331. The use of any one of claims 329 to 330, further comprising administering to the subject at least one of a TLR agonist and an IL-15 receptor agonist.

332. The use of claim 331, comprising administering a multi-specific antigen binding molecule of any one of claims 70 to 84 and an IL-15 receptor agonist.

333. The use of claim 331, wherein the TLR agonist is a TLR2 agonist, a TLR3 agonist, a TLR7 agonist, a TLR8 agonist or a TLR9 agonist.

334. The use of claim 333, wherein the TLR7 agonist is selected from the group consisting of vesatolimod, imiquimod, and resiquimod.

335. The use of any one of claims 329 to 334, comprising administering a first multi-specific antigen binding molecule and second or additional antigen binding molecules, wherein the first multi-specific antigen binding molecule and the second or additional antigen binding molecules bind to different first and second epitopes or regions of gp120 selected from the group consisting of:

(i) third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan;

(ii) second variable loop (V2) (*e.g.*, Env trimer apex);

(iii) CD4 binding site (CD4bs);

(iv) gp120/gp41 interface; or

(v) silent face of gp120.

336. The use of claim 335, wherein the first multi-specific antigen binding molecule binds to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan, and the second antigen binding molecule binds to the CD4 binding site (CD4bs).

337. The use of any one of claims 335 to 336, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, 3BNC117, 3BNC60, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25.

338. The use of any one of claims 335 to 337, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second antigen binding molecule competes with or comprises VH and VL regions from 3BNC117, GS-9723, VRC07 or VRC07-523.

339. The use of any one of claims 335 to 338, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134, and the second antigen binding molecule comprises an EC domain of CD4.

340. The use of claim 335, wherein the first multi-specific antigen binding molecule binds to the CD4 binding site (CD4bs) and the second antigen binding molecule binds to the third variable loop (V3) (*e.g.*, high mannose patch) comprising a N332 oligomannose glycan.

341. The use of claim 335 or 340, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03.

342. The use of any one of claims 335, 340 and 341, wherein the first multi-specific antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523, and the second antigen binding molecule competes with or comprises VH and VL regions from 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134.

343. The use of claim 335 or 340, wherein the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414, PGT-122, PGT-123, PGT-124, PGT-125, PGT-126, PGT-128, PGT-130, PGT-133, PGT-134, PGT-135, PGT-136, PGT-137, PGT-138, PGT-139, 10-1074, 10-1074-J, VRC24, 2G12, BG18, 354BG8, 354BG18, 354BG42, 354BG33, 354BG129, 354BG188, 354BG411, 354BG426, DH270.1, DH270.6, PGDM12, VRC41.01, PGDM21, PCDN-33A, BF520.1 and VRC29.03.

344. The use of any one of claims 335, 340 and 343, wherein the first multi-specific antigen binding molecule competes with or comprises an EC domain of CD4, and the second antigen binding molecule competes with or comprises VH and VL regions

from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134.

345. The use of any one of claims 335, 340 and 343 to 344, further comprising second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, 3BNC60, b12, F105, VRC01, VRC07, VRC07-523, VRC03, VRC06, VRC06b01 VRC08, VRC0801, NIH45-46, PGV04 (*a.k.a.*, VRC-PG04); CH103, 44-VRC13.01, 1NC9, 12A12, N6, 1-18, N49-P7, NC-Cow1, IOMA, CH235 and CH235.12, N49P6, N49P7, N49P11, N49P9 and N60P25.

346. The use of any one of claims 335, 340 and 343 to 345, further comprising second antigen binding molecule competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523.

347. The use of any one of claims 335, 340 and 343 to 346, comprising co-administering:

(i) a multi-specific antigen binding molecule of any one of claims 122 to 127;

(ii) an antibody that competes with or comprises VH and VL regions from an antibody selected from the group consisting of 10-1074, 10-1074-J, GS-9722 (elipovimab), GS-2872, PGT-121, PGT-121.66, PGT-121.414 and PGT-134; and

(iii) an antibody that competes with or comprises VH and VL regions from an antibody selected from the group consisting of GS-9723, GS-5423, 3BNC117, VRC07 and VRC07-523.

348. The use of any one of claims 335 to 347, further comprising administering to the human subject an additional antigen binding molecule or antigen binding fragment thereof that at least one of binds, inhibits, and neutralizes HIV or a polynucleotide encoding the additional antigen binding molecule or antigen binding fragment thereof.

349. The use of any one of claims 329 to 348, where the human subject is infected with an HIV expressing a gp120 comprising the following amino acid residues:

(i) N332/D325;

(ii) N332/D325/H330;

(iii) N332/D325/H330/T320;

(iv) N332/D325/H330/T63;

(v) N332/D325/H330/T63/T320; or

(vi) N332/D325/H330/T63/T320/L179.