[0034] Despite such advances in identifying the molecules involved in mammalian immune responses, a need remains for improved therapies for treating cancers and infectious diseases. The present invention is directed to this and other goals.

SUMMARY

[0035] The present disclosure is directed to a combination therapy for the treatment of cancer and pathogen-associated diseases, that comprises the administration of: (1) a molecule (*e.g.*, a diabody, an scFv, an antibody, a TandAb, *etc*.) capable of binding PD-1 or a natural ligand of PD-1, and (2) a molecule (*e.g.*, a diabody, a BiTe, a bispecific antibody, a CAR, *etc.*) capable of mediating the redirected killing of a target cell (*e.g.*, a cancer cell or a pathogen-infected cell, *etc*.) expressing a Disease Antigen. The disclosure particularly concerns the example in which the molecule capable of mediating the redirected killing of the target cell is a bispecific binding molecule that comprises a first epitope-binding site capable of immunospecifically binding an epitope of a cell surface molecule of an effector cell and a second epitope-binding site that is capable of immunospecifically binding an epitope of such target cells (*i.e.*, a Disease Antigen such as a Cancer Antigen or a Pathogen-Associated Antigen). The present disclosure is also directed to pharmaceutical compositions that comprise such molecule(s).

[0036] In detail, the disclosure provides a method for the treatment of cancer or a pathogen-associated disease, comprising administering to a subject in need thereof a therapeutically effective amount of:

(1) a molecule capable of binding PD-1 or a natural ligand of PD-1, and

(2) a molecule capable of mediating the redirected killing of a target cell, wherein the target cell is:

  (a) a cancer cell that expresses a Cancer Antigen; or

  (b) a pathogen-infected cell that expresses a Pathogen-Associated Antigen.

[0036a] In an aspect, there is provided a composition comprising a first binding molecule and a second binding molecule for use in the treatment of a cancer, wherein:

(1) the first binding molecule comprises an epitope-binding domain of an antibody capable of immunospecifically binding to a PD-1 that comprises:

the six CDRs of SEQ ID NO:106 and 108, 106 and 109, 106 and 110, 107 and 108, 107 and 109, or 107 and 110; or

the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:110, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:109, or the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:110; and

(2) the second binding molecule is capable of mediating the redirected killing of a cancer cell that expresses a Cancer Antigen and comprises:

(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a cell surface molecule of an effector cell; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to the Cancer Antigen.

[0036b] In another aspect, there is provided use of a first binding molecule and a second binding molecule in the manufacture of a medicament for treating cancer, wherein:

(1) the first binding molecule comprises an epitope-binding domain of an antibody capable of immunospecifically binding to a PD-1 that comprises:

the six CDRs of SEQ ID NO:106 and 108, 106 and 109, 106 and 110, 107 and 108, 107 and 109, or 107 and 110; or

the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:110, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:109, or the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:110; and

(2) the second binding molecule is capable of mediating the redirected killing of a cancer cell that expresses a Cancer Antigen and comprises:

(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a cell surface molecule of an effector cell; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to the Cancer Antigen.

[0036c] In another aspect, there is provided use of a first binding molecule in the manufacture of a medicament for treating a cancer, wherein the medicament is to be administered with a second binding molecule, and wherein:

(1) the first binding molecule comprises an epitope-binding domain of an antibody capable of immunospecifically binding to a PD-1 that comprises:

the six CDRs of SEQ ID NO:106 and 108, 106 and 109, 106 and 110, 107 and 108, 107 and 109, or 107 and 110; or

the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:110, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:109, or the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:110; and

(2) the second binding molecule is capable of mediating the redirected killing of a cancer cell that expresses a Cancer Antigen and comprises:

(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a cell surface molecule of an effector cell; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to the Cancer Antigen.

[0036d] In another aspect, there is provided use of a second binding molecule in the manufacture of a medicament for treating a cancer, wherein the medicament is to be administered with a first binding molecule, and wherein:

(1) the first binding molecule comprises an epitope-binding domain of an antibody capable of immunospecifically binding to a PD-1 that comprises:

the six CDRs of SEQ ID NO:106 and 108, 106 and 109, 106 and 110, 107 and 108, 107 and 109, or 107 and 110; or

the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:110, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:109, or the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:110; and

(2) the second binding molecule is capable of mediating the redirected killing of a cancer cell that expresses a Cancer Antigen and comprises:

(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a cell surface molecule of an effector cell; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to the Cancer Antigen.

[0037] The disclosure particularly concerns the example of such method wherein the molecule capable of binding PD-1 or a natural ligand of PD-1 is capable of inhibiting binding between PD-1 and a natural ligand of PD-1.

[0038] The disclosure further concerns the example of such method, wherein the method comprises administration of two binding molecules that cumulatively comprise three epitope-binding domains, the two binding molecules being:

(A) a binding molecule that comprises an epitope-binding domain of an antibody that is capable of binding PD-1, or an epitope-binding domain of an antibody that is capable of binding a natural ligand of PD-1; and

(B) a binding molecule that comprises:

(1) an epitope-binding domain of an antibody that is capable of binding a cell surface molecule of the effector cell; and

(2) an epitope-binding domain of an antibody that that is capable of binding the Cancer Antigen or the Pathogen Antigen of the target cell;

wherein the epitope-binding domain of the binding molecule (A) is capable of binding PD-1 or a natural ligand of PD-1, and the epitope-binding domains (1) and (2) of the binding molecule (B) are capable of mediating the redirected killing of the target cell.

[0039] The disclosure further concerns the example of such method, wherein the binding molecule capable of binding PD-1 or a natural ligand of PD-1 comprises a diabody, scFv, antibody or TandAb, and the binding molecule (B) comprises a bispecific diabody, a CAR, a BiTe, or bispecific antibody.

[0040] The disclosure further concerns the example of such methods wherein the binding molecule capable of binding PD-1 or a natural ligand of PD-1 comprises an epitope-binding domain of an antibody that binds to PD-1.

[0041] The disclosure further concerns the example of such methods wherein the binding molecule capable of binding PD-1 or a natural ligand of PD-1 comprises an epitope-binding domain of an antibody that binds to a natural ligand of PD-1.

[0042] The disclosure further concerns the example of such methods wherein the binding molecule capable of binding PD-1 or a natural ligand of PD-1 comprises a second epitope-binding domain capable of binding PD-1, wherein such epitope-binding domains:

(a) compete for binding the same epitope of PD-1; or

(b) do not compete for binding the same epitope of PD-1.

[0043] The disclosure further concerns the example of such methods wherein the PD-1-epitope-binding domains are capable of simultaneous binding to the same PD-1 molecule.

[0044] The disclosure further concerns the example of such methods wherein the binding molecule capable of binding PD-1 or a natural ligand of PD-1 comprises a second epitope-binding domain capable of binding the natural ligand of PD-1, wherein such epitope-binding domains:

(a) compete for binding to the same epitope of such natural ligand of PD-1; or

(b) do not compete for binding to the same epitope of such natural ligand of PD-1.

[0045] The disclosure further concerns the example of such methods wherein the PD-1 ligand-epitope-binding domains are capable of simultaneous binding the same molecule of the natural ligand of PD-1.

[0046] The disclosure further concerns the example of such methods wherein the binding molecule capable of binding PD-1 or a natural ligand of PD-1 comprises a second epitope-binding domain capable of binding an epitope of a molecule that is not PD-1 or a natural ligand of PD-1.

[0047] The disclosure further concerns the example of such methods wherein in the second epitope-binding domain binds an epitope of CD137, LAG-3, OX40, TIGIT, TIM-3, or VISTA.

[0048] The disclosure further concerns the example of such methods wherein the binding molecule capable of mediating the redirected killing of the target cell comprises a third epitope-binding domain capable of binding a cell surface molecule of the effector cell.

[0049] The disclosure further concerns the example of such methods wherein the third epitope-binding-domain of the binding molecule capable of mediating the redirected killing of the target cell is capable of binding a different cell surface molecule of the effector cell, such that the binding molecule capable of mediating the redirected killing is capable of binding two different cell surface molecules of the effector cell.

[0050] The disclosure further concerns the example of such methods wherein the binding molecule capable of mediating the redirected killing of the target cell comprises a third epitope-binding domain capable of binding to a Cancer Antigen or a Pathogen-Associated Antigen of the target cell.

[0051] The disclosure further concerns the example of such methods wherein the third epitope-binding-domain of the binding molecule capable of mediating the redirected killing of the target cell is capable of binding a different Cancer Antigen or a different Pathogen Antigen of the target cell, such that the binding molecule capable of mediating the redirected killing is capable of binding to two different Cancer Antigens or two different Pathogen Antigens of the target cell.

[0052] The disclosure further concerns the example of such methods wherein the cell surface molecule of the effector cell is selected from the group consisting of: CD2, CD3, CD8, CD16, TCR, and NKG2D.

[0053] The disclosure further concerns the example of such methods wherein the Cancer Antigen is selected from the group consisting of the Cancer Antigens: 19.9, 4.2, A33, ADAM-9, AH6, ALCAM, B1, B7-H3, BAGE, beta-catenin, blood group ALe^b/Le^y, Burkitt's lymphoma antigen-38.13, C14, CA125, Carboxypeptidase M, CD5, CD19, CD20, CD22, CD23, CD25, CD27, CD28, CD33, CD36, CD40/CD154, CD45, CD56, CD46, CD52, CD56, CD79a/CD79b, CD103, CD123, CD317, CDK4, CEA, CEACAM5/CEACAM6, CO17-1A, CO-43, CO-514, CTA-1, CTLA-4, Cytokeratin 8, D1.1, $D_1$56-22, DR5, E_1 series, EGFR, an Ephrin receptor, Erb, GAGE, a GD2/GD3/GM2 ganglioside, GICA 19-9, gp100, Gp37, gp75, gpA33, HER2/neu, HMFG, human papillomavirus-E6/human papillomavirus-E7, HMW-MAA, I antigen, IL13Rα2, Integrin β6, JAM-3, KID3, KID31, KS 1/4 pan-carcinoma antigen, L6,L20, LEA, LUCA-2, M1:22:25:8, M18, M39, MAGE, MART, mesothelin, MUC-1, MUM-1, Myl, N-acetylglucosaminyltransferase, neoglycoprotein, NS-10, OFA-1, OFA-2, Oncostatin M, p15, p97, PEM, PEMA, PIPA, PSA, PSMA, prostatic acid phosphate, R_{24}, ROR1, a sphingolipid, SSEA-1, SSEA-3, SSEA-4, sTn, the T cell receptor derived peptide, T_5A_7, TAG-72, TL5, TNF-receptor, TNF-γ receptor, TRA-1-85, a Transferrin Receptor, 5T4, TSTA, VEGF, a VEGF Receptor, VEP8, VEP9, VIM-D5, and Y hapten, Le^y.

[0054] The disclosure further concerns the example of such methods wherein the method comprises the administration of the pharmaceutical composition, and wherein the Pathogen-Associated Antigen is selected from the group consisting of the Pathogen-Associated Antigens: Herpes Simplex Virus infected cell protein (ICP)47, Herpes Simplex Virus gD, Epstein-Barr Virus LMP-1, Epstein-Barr Virus LMP-2A, Epstein-Barr Virus LMP-2B, Human Immunodeficiency Virus gp160, Human Immunodeficiency Virus gp120,

Human Immunodeficiency Virus gp41, *etc*.), Human Papillomavirus E6, Human Papillomavirus E7, human T-cell leukemia virus gp64, human T-cell leukemia virus gp46, and human T-cell leukemia virus gp21.

[0055] The disclosure further provides a pharmaceutical composition that comprises:

(A) therapeutically effective amounts of:

(1) a molecule capable of binding PD-1 or a natural ligand of PD-1, and

(2) a molecule capable of mediating the redirected killing of a target cell expressing a Cancer Antigen or a Pathogen Antigen; and

(B) a pharmaceutically acceptable carrier.

[0055a] In another aspect, there is provided a pharmaceutical composition, comprising:

(A) therapeutically effective amounts of:

(1) a first binding molecule comprising an epitope-binding domain of an antibody capable of immunospecifically binding to a PD-1 that comprises:

the six CDRs of SEQ ID NO:106 and 108, 106 and 109, 106 and 110, 107 and 108, 107 and 109, or 107 and 110; or

the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:110, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:109, or the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:110; and

(2) a second binding molecule capable of mediating the redirected killing of a cancer cell that expresses a Cancer Antigen and comprises:

(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a cell surface molecule of an effector cell; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to the Cancer Antigen;

and

(B) a pharmaceutically acceptable carrier.

[0056] The disclosure further concerns the example of such pharmaceutical composition wherein the pharmaceutical composition comprises two binding molecules that cumulatively comprise three epitope-binding domains, the two binding molecules being:

(A) a binding molecule that comprises an epitope-binding domain of an antibody that is capable of binding PD-1, or an epitope-binding domain of an antibody that is capable of binding a natural ligand of PD-1; and

(B) a binding molecule that comprises:

(1) an epitope-binding domain of an antibody that is capable of binding a cell surface molecule of the effector cell; and

(2) an epitope-binding domain of an antibody that that is capable of binding a Cancer Antigen or a Pathogen-Associated Antigen of the target cell;

wherein the epitope-binding domain of the binding molecule (A) is capable of binding PD-1 or a natural ligand of PD-1, and the epitope-binding domains (1) and (2) of the binding molecule (B) are capable of mediating the redirected killing of the target cell.

[0057] The disclosure further concerns the example of such pharmaceutical compositions wherein the binding molecule (A) comprises a diabody, scFv, antibody, or TandAb, and the binding molecule (B) comprises a diabody, a CAR, a BiTe, or bispecific antibody.

[0058] The disclosure further concerns the example of such pharmaceutical compositions wherein the molecule capable of binding PD-1 or a natural ligand of PD-1 comprises an epitope-binding domain of an antibody that binds to PD-1.

[0059] The disclosure further concerns the example of such pharmaceutical compositions wherein the molecule capable of binding PD-1 or a natural ligand of PD-1 comprises an epitope-binding domain of an antibody that binds to a natural ligand of PD-1.

[0060] The disclosure further concerns the example of such pharmaceutical compositions wherein the molecule capable of binding PD-1 or a natural ligand of PD-1 comprises a second epitope-binding domain capable of binding PD-1, wherein such PD-1-epitope-binding domains:

(a) compete for binding to the same epitope of PD-1; or

(b) do not compete for binding the same epitope of PD-1.

[0061] The disclosure further concerns the example of such pharmaceutical compositions wherein the PD-1-epitope-binding domains are capable of simultaneous binding the same PD-1 molecule.

[0062] The disclosure further concerns the example of such pharmaceutical compositions wherein the binding molecule capable of binding PD-1 or a natural ligand of PD-1 comprises a second epitope-binding domain capable of binding the natural ligand of PD-1, wherein such epitope-binding domains:

(a) compete for binding to the same epitope of such natural ligand of PD-1; or

(b) do not compete for binding to the same epitope of such natural ligand of PD-1.

[0063] The disclosure further concerns the example of such pharmaceutical compositions wherein the PD-1 ligand-epitope-binding domains are capable of simultaneous binding the same molecule of the natural ligand of PD-1.

[0064] The disclosure further concerns the example of such pharmaceutical compositions wherein the binding molecule capable of binding PD-1 or a natural ligand of PD-1 comprises a second epitope-binding domain capable of binding an epitope of a molecule that is not PD-1 or a natural ligand of PD-1.

[0065] The disclosure further concerns the example of such pharmaceutical compositions wherein the second epitope-binding domain binds an epitope of CD137, LAG-3, OX40, TIGIT, TIM-3, or VISTA.

[0066] The disclosure further concerns the example of such pharmaceutical compositions wherein the molecule capable of mediating the redirected killing of the target cell comprises a third epitope-binding domain, wherein such three epitope-binding domains are capable of simultaneous binding, and wherein the third epitope-binding site is capable of binding an epitope of a cell surface molecule of the effector cell.

[0067] The disclosure further concerns the example of such pharmaceutical compositions wherein the third epitope-binding-domain of the binding molecule capable of mediating the redirected killing of the target cell is capable of binding a different cell surface molecule of the effector cell, such that the binding molecule capable of mediating the redirected killing is capable of binding two different cell surface molecules of the effector cell.

[0068] The disclosure further concerns the example of such pharmaceutical compositions wherein the binding molecule capable of mediating the redirected killing of the target cell comprises a third epitope-binding domain capable of binding to a Cancer Antigen or a Pathogen-Associated Antigen of the target cell.

[0069] The disclosure further concerns the example of such pharmaceutical compositions wherein the third epitope-binding-domain of the binding molecule capable of mediating the redirected killing of the target cell is capable of binding a different Cancer Antigen or a different Pathogen-Associated Antigen of the target cell, such that the binding molecule capable of mediating the redirected killing is capable of binding to two different Cancer Antigens or two different Pathogen-Associated Antigens of the target cell.

[0070] The disclosure further concerns the example of such pharmaceutical compositions wherein the cell surface molecule of the effector cell is selected from the group consisting of: CD2, CD3, CD8, CD16, TCR, and NKG2D.

[0071] The disclosure further concerns the example of such pharmaceutical compositions wherein the Cancer Antigen is selected from the group consisting of the Cancer Antigens: 19.9, 4.2, A33, ADAM-9, AH6, ALCAM, B1, B7-H3, BAGE, beta-

catenin, blood group ALe^b/Le^y, Burkitt's lymphoma antigen-38.13, C14, CA125, Carboxypeptidase M, CD5, CD19, CD20, CD22, CD23, CD25, CD27, CD28, CD33, CD36, CD40/CD154, CD45, CD56, CD46, CD52, CD56, CD79a/CD79b, CD103, CD123, CD317, CDK4, CEA, CEACAM5/CEACAM6, CO17-1A, CO-43, CO-514, CTA-1, CTLA-4, Cytokeratin 8, D1.1, $D_1$56-22, DR5, E_1 series, EGFR, an Ephrin receptor, Erb, GAGE, a GD2/GD3/GM2 ganglioside, GICA 19-9, gp100, Gp37, gp75, gpA33, HER2/neu, HMFG, human papillomavirus-E6/human papillomavirus-E7, HMW-MAA, I antigen, IL13Rα2, Integrin β6, JAM-3, KID3, KID31, KS 1/4 pan-carcinoma antigen, L6,L20, LEA, LUCA-2, M1:22:25:8, M18, M39, MAGE, MART, mesothelin, MUC-1, MUM-1, Myl, N-acetylglucosaminyltransferase, neoglycoprotein, NS-10, OFA-1, OFA-2, Oncostatin M, p15, p97, PEM, PEMA, PIPA, PSA, PSMA, prostatic acid phosphate, R_{24}, ROR1, a sphingolipid, SSEA-1, SSEA-3, SSEA-4, sTn, the T cell receptor derived peptide, T_5A_7, TAG-72, TL5, TNF-receptor, TNF-γ receptor, TRA-1-85, a Transferrin Receptor, 5T4, TSTA, VEGF, a VEGF Receptor, VEP8, VEP9, VIM-D5, and Y hapten, Le^y.

[0072] The disclosure further concerns the example of such pharmaceutical compositions wherein the Pathogen-Associated Antigen is selected from the group consisting of the Pathogen Antigens: Herpes Simplex Virus infected cell protein (ICP)47, Herpes Simplex Virus gD, Epstein-Barr Virus LMP-1, Epstein-Barr Virus LMP-2A, Epstein-Barr Virus LMP-2B, Human Immunodeficiency Virus gp160, Human Immunodeficiency Virus gp120, Human Immunodeficiency Virus gp41, *etc*.), Human Papillomavirus E6, Human Papillomavirus E7, human T-cell leukemia virus gp64, human T-cell leukemia virus gp46, and human T-cell leukemia virus gp21.

[0073] In another aspect, there is provided a kit comprising any of the above-described pharmaceutical compositions, wherein the binding molecules thereof are compartmentalized in one or more containers.

BRIEF DESCRIPTION OF THE DRAWINGS:

[0074] **Figure 1** provides a schematic of a representative covalently bonded diabody having two epitope-binding domains composed of two polypeptide chains, each having an E-coil or K-coil Heterodimer-Promoting Domain (alternative Heterodimer-Promoting Domains are provided below). A cysteine residue may be present in a linker and/or in the Heterodimer-Promoting Domain as shown in **Figure 3B**. VL and VH Domains that recognize the same epitope are shown using the same shading or fill pattern.

WHAT IS CLAIMED IS:

Claim 1. A composition comprising a first binding molecule and a second binding molecule for use in the treatment of a cancer, wherein:

(1) the first binding molecule comprises an epitope-binding domain of an antibody capable of immunospecifically binding to a PD-1 that comprises:

the six CDRs of SEQ ID NO:106 and 108, 106 and 109, 106 and 110, 107 and 108, 107 and 109, or 107 and 110; or

the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:110, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:109, or the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:110; and

(2) the second binding molecule is capable of mediating the redirected killing of a cancer cell that expresses a Cancer Antigen and comprises:

(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a cell surface molecule of an effector cell; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to the Cancer Antigen.

Claim 2. Use of a first binding molecule and a second binding molecule in the manufacture of a medicament for treating a cancer, wherein:

(1) the first binding molecule comprises an epitope-binding domain of an antibody capable of immunospecifically binding to a PD-1 that comprises:

the six CDRs of SEQ ID NO:106 and 108, 106 and 109, 106 and 110, 107 and 108, 107 and 109, or 107 and 110; or

the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109, the VH Domain of SEQ ID NO:106 and the VL Domain of

SEQ ID NO:110, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:109, or the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:110; and

(2) the second binding molecule is capable of mediating the redirected killing of a cancer cell that expresses a Cancer Antigen and comprises:

(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a cell surface molecule of an effector cell; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to the Cancer Antigen.

Claim 3. Use of a first binding molecule in the manufacture of a medicament for treating a cancer, wherein the medicament is to be administered with a second binding molecule, and wherein:

(1) the first binding molecule comprises an epitope-binding domain of an antibody capable of immunospecifically binding to a PD-1 that comprises:

the six CDRs of SEQ ID NO:106 and 108, 106 and 109, 106 and 110, 107 and 108, 107 and 109, or 107 and 110; or

the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:110, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:109, or the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:110; and

(2) the second binding molecule is capable of mediating the redirected killing of a cancer cell that expresses a Cancer Antigen and comprises:

(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a cell surface molecule of an effector cell; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to the Cancer Antigen.

Claim 4. Use of a second binding molecule in the manufacture of a medicament for treating a cancer, wherein the medicament is to be administered with a first binding molecule, and wherein:

(1) the first binding molecule comprises an epitope-binding domain of an antibody capable of immunospecifically binding to a PD-1 that comprises:

the six CDRs of SEQ ID NO:106 and 108, 106 and 109, 106 and 110, 107 and 108, 107 and 109, or 107 and 110; or

the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:110, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:109, or the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:110; and

(2) the second binding molecule is capable of mediating the redirected killing of a cancer cell that expresses a Cancer Antigen and comprises:

(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a cell surface molecule of an effector cell; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to the Cancer Antigen.

Claim 5. The composition of claim 1 or use of any one of claims 2-4, wherein:

the second binding molecule comprises a bispecific diabody, a CAR, a BiTe, or bispecific antibody; and

the diabody optionally consists of two polypeptide chains, three polypeptide chains, four polypeptide chains or five polypeptide chains.

Claim 6. The composition or use of claim 5, wherein:

the first binding molecule, and/or the second binding molecule, comprises a CH2-CH3 Domain and optionally comprises one or more of a Hinge Domain, CL Domain or CH1 Domain;

the CH2-CH3 Domain, Hinge Domain, CL Domain or CH1 Domain optionally are from an IgG1, IgG2, IgG3 or IgG4 antibody;
the CH2-CH3 Domain optionally comprises one or more amino acid substitutions selected from: L234A, L235A, D265A, N297Q, and N297G;
the CH2-CH3 Domain optionally comprises two or more amino acid substitutions selected from: T250Q, M252Y, S254T, T256E, K288D, T307Q, V308P, A378V, M428L, N434A, H435K, and Y436I;
the CH2-CH3 Domain optionally comprises a T366W amino acid substitution or T366S, L368A and Y407V amino acid substitutions; and/or
the Hinge Domain optionally comprises a S228P amino acid substitution.

Claim 7. The composition of any one of claims 1, 5 and 6, or use of any one of claims 2-6, wherein the epitope-binding domain of the antibody capable of immunospecifically binding to PD-1 comprises the six CDRs of SEQ ID NO:106 and 109; or the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109.

Claim 8. The composition or use of claim 7, wherein the first binding molecule is an antibody comprising a Heavy Chain of SEQ ID NO:186 and a Light Chain of SEQ ID NO:187.

Claim 9. The composition of any one of claims 1 and 5-8 or the use of any one of claims 2-8, wherein the second binding molecule comprises:
an epitope-binding domain of an antibody capable of immunospecifically binding to the epitope of a Cancer Antigen, and
the Cancer Antigen is selected from the group consisting of: B7-H3, CD123, EphA2, gpA33, IL13Rα2, ROR1 and 5T4.

Claim 10. The composition or use of claim 9, wherein:
the Cancer Antigen is selected from the group consisting of: B7-H3, CD123, gpA33, 5T4 and IL13Rα2, and
the epitope-binding domain capable of immunospecifically binding to the epitope of a Cancer Antigen comprises:
the six CDRs of SEQ ID NO:213 and 214, 215 and 217, 215 and 218, 216 and 217, 216 and 218, 219 and 220, 221 and 225, 221 and 226, 221 and

227, 221 and 228, 221 and 229, 221 and 230, 222 and 225, 222 and 226, 222 and 227, 222 and 228, 222 and 229, 222 and 230, 223 and 225, 223 and 226, 223 and 227, 223 and 228, 223 and 229, 223 and 230, 224 and 225, 224 and 226, 224 and 227, 224 and 228, 224 and 229, 224 and 230, 231 and 232, 247 and 248, 263 and 264, 257 and 258, 259 and 260, or 261 and 262; or

the VH Domain of SEQ ID NO:213 and the VL Domain of SEQ ID NO:214,
the VH Domain of SEQ ID NO:215 and the VL Domain of SEQ ID NO:217,
the VH Domain of SEQ ID NO:215 and the VL Domain of SEQ ID NO:218,
the VH Domain of SEQ ID NO:216 and the VL Domain of SEQ ID NO:217,
the VH Domain of SEQ ID NO:216 and the VL Domain of SEQ ID NO:218,
the VH Domain of SEQ ID NO:219 and the VL Domain of SEQ ID NO:220,
the VH Domain of SEQ ID NO:221 and the VL Domain of SEQ ID NO:225,
the VH Domain of SEQ ID NO:221 and the VL Domain of SEQ ID NO:226,
the VH Domain of SEQ ID NO:221 and the VL Domain of SEQ ID NO:227,
the VH Domain of SEQ ID NO:221 and the VL Domain of SEQ ID NO:228,
the VH Domain of SEQ ID NO:221 and the VL Domain of SEQ ID NO:229,
the VH Domain of SEQ ID NO:221 and the VL Domain of SEQ ID NO:230,
the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:225,

the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:226,
the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:227,
the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:228,
the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:229,
the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:230,
the VH Domain of SEQ ID NO:223 and the VL Domain of SEQ ID NO:225,
the VH Domain of SEQ ID NO:223 and the VL Domain of SEQ ID NO:226,
the VH Domain of SEQ ID NO:223 and the VL Domain of SEQ ID NO:227,
the VH Domain of SEQ ID NO:223 and the VL Domain of SEQ ID NO:228,
the VH Domain of SEQ ID NO:223 and the VL Domain of SEQ ID NO:229,
the VH Domain of SEQ ID NO:223 and the VL Domain of SEQ ID NO:230,
the VH Domain of SEQ ID NO:224 and the VL Domain of SEQ ID NO:225,
the VH Domain of SEQ ID NO:224 and the VL Domain of SEQ ID NO:226,
the VH Domain of SEQ ID NO:224 and the VL Domain of SEQ ID NO:227,
the VH Domain of SEQ ID NO:224 and the VL Domain of SEQ ID NO:228,
the VH Domain of SEQ ID NO:224 and the VL Domain of SEQ ID NO:229,
the VH Domain of SEQ ID NO:224 and the VL Domain of SEQ ID NO:230,

the VH Domain of SEQ ID NO:231 and the VL Domain of SEQ ID NO:232,
the VH Domain of SEQ ID NO:247 and the VL Domain of SEQ ID NO:248,
the VH Domain of SEQ ID NO:263 and the VL Domain of SEQ ID NO:264,
the VH Domain of SEQ ID NO:257 and the VL Domain of SEQ ID NO:258,
the VH Domain of SEQ ID NO:259 and the VL Domain of SEQ ID NO:260, or
the VH Domain of SEQ ID NO:261 and the VL Domain of SEQ ID NO:262.

Claim 11. The composition of any one of claims 1 and 5-9 or the use of any one of claims 2-9, wherein the second binding molecule comprises an epitope-binding domain of an antibody capable of immunospecifically binding to the epitope of an EphA2 Cancer Antigen comprising the six CDRs of SEQ ID NO:241 and 242, 243 and 244, or 245 and 246.

Claim 12. The composition of any one of claims 1 and 5-11 or the use of any one of claims 2-11, wherein:
the second binding molecule comprises an epitope-binding domain of an antibody capable of immunospecifically binding to the epitope of a cell surface molecule of an effector cell; and
the cell surface molecule of the effector cell is selected from the group consisting of: CD2, CD3, CD8, CD16, TCR, and NKG2D.

Claim 13. The composition or use of claim 12, wherein the cell surface molecule is CD3 and the epitope-binding domain comprises:
the six CDRs of SEQ ID NO:192 and 193, or 194 and 193; or
the VH Domain of SEQ ID NO:192 and the VL Domain of SEQ ID NO:193, or
the VH Domain of SEQ ID NO:194 and the VL Domain of SEQ ID NO:193.

Claim 14. The composition of any one of claims 1 and 5-13 or the use of any one of claims 2-13, wherein the second binding molecule is a bispecific diabody.

Claim 15. The composition of any one of claims 1 and 5-14 or the use of any one of claims 2-14, wherein:

(A) the first binding molecule is an antibody comprising the six CDRs of SEQ ID NO:106 and 109, or the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109; and

(B) the second binding molecule is a bispecific diabody comprising:

(1)(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a B7-H3 Cancer Antigen and comprising the six CDRs of SEQ ID NO:222 and 226, or the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:226; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to a CD3 and comprising the six CDRs of SEQ ID NO:192 and 193, or 194 and 193, or the VH Domain of SEQ ID NO:192 and the VL Domain of SEQ ID NO:193, or the VH Domain of SEQ ID NO:194 and the VL Domain of SEQ ID NO:193: or

(2)(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a CD123 Cancer Antigen and comprising the six CDRs of SEQ ID NO:263 and 264, or the VH Domain of SEQ ID NO:263 and the VL Domain of SEQ ID NO:264; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to a CD3 and comprising the six CDRs of SEQ ID NO:192 and 193, or 194 and 193, or the VH Domain of SEQ ID NO:192 and the VL Domain of SEQ ID NO:193, or the VH Domain of SEQ ID NO:194 and the VL Domain of SEQ ID NO:193; or

(3)(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a gpA33 Cancer Antigen and comprising the six CDRs of SEQ ID NO:247 and 248, or the VH Domain of SEQ ID NO:247 and the VL Domain of SEQ ID NO:248; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to a CD3 and comprising the six CDRs of SEQ

ID NO:192 and 193, or 194 and 193, or the VH Domain of SEQ ID NO:192 and the VL Domain of SEQ ID NO:193, or the VH Domain of SEQ ID NO:194 and the VL Domain of SEQ ID NO:193.

Claim 16. The composition or use of claim 15, wherein the first binding molecule is an antibody comprising a Heavy Chain of SEQ ID NO:186 and a Light Chain of SEQ ID NO:187.

Claim 17. The composition or use of claim 15 or claim 16, wherein the second binding molecule comprises a first polypeptide chain comprising the polypeptide of SEQ ID NO:271, a second polypeptide chain comprising the polypeptide of SEQ ID NO:272, and a third polypeptide chain comprising the polypeptide of SEQ ID NO:273.

Claim 18. A pharmaceutical composition, comprising:

(A) therapeutically effective amounts of:

(1) a first binding molecule comprising an epitope-binding domain of an antibody capable of immunospecifically binding to a PD-1 that comprises:

the six CDRs of SEQ ID NO:106 and 108, 106 and 109, 106 and 110, 107 and 108, 107 and 109, or 107 and 110; or

the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109, the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:110, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:108, the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:109, or the VH Domain of SEQ ID NO:107 and the VL Domain of SEQ ID NO:110; and

(2) a second binding molecule capable of mediating the redirected killing of a cancer cell that expresses a Cancer Antigen and comprises:

(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a cell surface molecule of an effector cell; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to the Cancer Antigen;

and

(B) a pharmaceutically acceptable carrier.

Claim 19. The pharmaceutical composition of claim 18, wherein:
the second binding molecule comprises a bispecific diabody, a CAR, a BiTe, or bispecific antibody; and
the diabody optionally consists of two polypeptide chains, three polypeptide chains, four polypeptide chains or five polypeptide chains.

Claim 20. The pharmaceutical composition of claim 19, wherein:

the first binding molecule, and/or the second binding molecule, comprises a CH2-CH3 Domain and optionally comprises one or more of a Hinge Domain, CL Domain or CH1 Domain;

the CH2-CH3 Domain, Hinge Domain, CL Domain or CH1 Domain optionally are from an IgG1, IgG2, IgG3 or IgG4 antibody;

the CH2-CH3 Domain optionally comprises one or more amino acid substitutions selected from: L234A, L235A, D265A, N297Q, and N297G;

the CH2-CH3 Domain optionally comprises two or more amino acid substitutions selected from: T250Q, M252Y, S254T, T256E, K288D, T307Q, V308P, A378V, M428L, N434A, H435K, and Y436I;

the CH2-CH3 Domain optionally comprises a T366W amino acid substitution or T366S, L368A and Y407V amino acid substitutions; and/or
the Hinge Domain optionally comprises a S228P amino acid substitution.

Claim 21. The pharmaceutical composition of any one of claims 18-20, wherein the epitope-binding domain of the antibody capable of immunospecifically binding to PD-1 comprises the six CDRs of SEQ ID NO:106 and 109; or the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109.

Claim 22. The pharmaceutical composition of claim 21, wherein the first binding molecule is an antibody comprising a Heavy Chain of SEQ ID NO:186 and a Light Chain of SEQ ID NO:187.

Claim 23. The pharmaceutical composition of any one of claims 18-22, wherein the second binding molecule comprises:

an epitope-binding domain of an antibody capable of immunospecifically binding to the epitope of a Cancer Antigen, and

the Cancer Antigen is selected from the group consisting of: B7-H3, CD123, EphA2, gpA33, IL13Rα2, ROR1 and 5T4.

Claim 24. The pharmaceutical composition of claim 23, wherein:

the Cancer Antigen is selected from the group consisting of: B7-H3, CD123, gpA33, 5T4 and IL13Rα2, and

the epitope-binding domain capable of immunospecifically binding to the epitope of a Cancer Antigen comprises:

the six CDRs of SEQ ID NO:213 and 214, 215 and 217, 215 and 218, 216 and 217, 216 and 218, 219 and 220, 221 and 225, 221 and 226, 221 and 227, 221 and 228, 221 and 229, 221 and 230, 222 and 225, 222 and 226, 222 and 227, 222 and 228, 222 and 229, 222 and 230, 223 and 225, 223 and 226, 223 and 227, 223 and 228, 223 and 229, 223 and 230, 224 and 225, 224 and 226, 224 and 227, 224 and 228, 224 and 229, 224 and 230, 231 and 232, 247 and 248, 263 and 264, 257 and 258, 259 and 260, or 261 and 262; or

the VH Domain of SEQ ID NO:213 and the VL Domain of SEQ ID NO:214,

the VH Domain of SEQ ID NO:215 and the VL Domain of SEQ ID NO:217,

the VH Domain of SEQ ID NO:215 and the VL Domain of SEQ ID NO:218,

the VH Domain of SEQ ID NO:216 and the VL Domain of SEQ ID NO:217,

the VH Domain of SEQ ID NO:216 and the VL Domain of SEQ ID NO:218,

the VH Domain of SEQ ID NO:219 and the VL Domain of SEQ ID NO:220,

the VH Domain of SEQ ID NO:221 and the VL Domain of SEQ ID NO:225,

the VH Domain of SEQ ID NO:221 and the VL Domain of SEQ ID NO:226,

the VH Domain of SEQ ID NO:221 and the VL Domain of SEQ ID NO:227,

the VH Domain of SEQ ID NO:221 and the VL Domain of SEQ ID NO:228,

the VH Domain of SEQ ID NO:221 and the VL Domain of SEQ ID NO:229,

the VH Domain of SEQ ID NO:221 and the VL Domain of SEQ ID NO:230,

the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:225,

the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:226,

the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:227,

the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:228,

the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:229,

the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:230,

the VH Domain of SEQ ID NO:223 and the VL Domain of SEQ ID NO:225,

the VH Domain of SEQ ID NO:223 and the VL Domain of SEQ ID NO:226,

the VH Domain of SEQ ID NO:223 and the VL Domain of SEQ ID NO:227,

the VH Domain of SEQ ID NO:223 and the VL Domain of SEQ ID NO:228,

the VH Domain of SEQ ID NO:223 and the VL Domain of SEQ ID NO:229,

the VH Domain of SEQ ID NO:223 and the VL Domain of SEQ ID NO:230,

the VH Domain of SEQ ID NO:224 and the VL Domain of SEQ ID NO:225,

the VH Domain of SEQ ID NO:224 and the VL Domain of SEQ ID NO:226,

the VH Domain of SEQ ID NO:224 and the VL Domain of SEQ ID NO:227,

the VH Domain of SEQ ID NO:224 and the VL Domain of SEQ ID NO:228,

the VH Domain of SEQ ID NO:224 and the VL Domain of SEQ ID NO:229,

the VH Domain of SEQ ID NO:224 and the VL Domain of SEQ ID NO:230,

the VH Domain of SEQ ID NO:231 and the VL Domain of SEQ ID NO:232,

the VH Domain of SEQ ID NO:247 and the VL Domain of SEQ ID NO:248,

the VH Domain of SEQ ID NO:263 and the VL Domain of SEQ ID NO:264,

the VH Domain of SEQ ID NO:257 and the VL Domain of SEQ ID NO:258,

the VH Domain of SEQ ID NO:259 and the VL Domain of SEQ ID NO:260, or

the VH Domain of SEQ ID NO:261 and the VL Domain of SEQ ID NO:262.

Claim 25. The pharmaceutical composition of any one of claims 18-22, wherein the second binding molecule comprises an epitope-binding domain of an antibody capable of immunospecifically binding to the epitope of an EphA2 Cancer Antigen comprising the six CDRs of SEQ ID NO:241 and 242, 243 and 244, or 245 and 246.

Claim 26. The pharmaceutical composition of any one of claims 18-25, wherein:

the second binding molecule comprises an epitope-binding domain of an antibody capable of immunospecifically binding to the epitope of a cell surface molecule of an effector cell; and

the cell surface molecule of the effector cell is selected from the group consisting of: CD2, CD3, CD8, CD16, TCR, and NKG2D.

Claim 27. The pharmaceutical composition of claim 26, wherein the cell surface molecule is CD3 and the epitope-binding domain comprises:

the six CDRs of SEQ ID NO:192 and 193, or 194 and 193; or

the VH Domain of SEQ ID NO:192 and the VL Domain of SEQ ID NO:193, or

the VH Domain of SEQ ID NO:194 and the VL Domain of SEQ ID NO:193.

Claim 28. The pharmaceutical composition of any one of claims 18-27, wherein the second binding molecule is a bispecific diabody.

Claim 29. The pharmaceutical composition of any one of claims 18-28, wherein:

(A) the first binding molecule is an antibody comprising the six CDRs of SEQ ID NO:106 and 109, or the VH Domain of SEQ ID NO:106 and the VL Domain of SEQ ID NO:109; and

(B) the second binding molecule is a bispecific diabody comprising:

(1)(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a B7-H3 Cancer Antigen and comprising the six CDRs of SEQ ID NO:222 and 226, or the VH Domain of SEQ ID NO:222 and the VL Domain of SEQ ID NO:226; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to a CD3 and comprising the six CDRs of SEQ ID NO:192 and 193, or 194 and 193, or the VH Domain of SEQ ID NO:192 and the VL Domain of SEQ ID NO:193, or the VH Domain of SEQ ID NO:194 and the VL Domain of SEQ ID NO:193: or

(2)(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a CD123 Cancer Antigen and comprising the six CDRs of SEQ ID NO:263 and 264, or the VH Domain of SEQ ID NO:263 and the VL Domain of SEQ ID NO:264; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to a CD3 and comprising the six CDRs of SEQ ID NO:192 and 193, or 194 and 193, or the VH Domain of SEQ ID NO:192 and the VL Domain of SEQ ID NO:193, or the VH Domain of SEQ ID NO:194 and the VL Domain of SEQ ID NO:193; or

(3)(a) an epitope-binding domain of an antibody capable of immunospecifically binding to a gpA33 Cancer Antigen and comprising the six CDRs of SEQ ID NO:247 and 248, or the VH Domain of SEQ ID NO:247 and the VL Domain of SEQ ID NO:248; and

(b) an epitope-binding domain of an antibody capable of immunospecifically binding to a CD3 and comprising the six CDRs of SEQ ID NO:192 and 193, or 194 and 193, or the VH Domain of SEQ ID NO:192 and the VL Domain of SEQ ID NO:193, or the VH Domain of SEQ ID NO:194 and the VL Domain of SEQ ID NO:193.

Claim 30. The pharmaceutical composition of claim 29, wherein the first binding molecule is

an antibody comprising a Heavy Chain of SEQ ID NO:186 and a Light Chain of SEQ ID NO:187.

Claim 31. The pharmaceutical composition of claim 29 or claim 30, wherein the second binding molecule comprises a first polypeptide chain comprising the polypeptide of SEQ ID NO:271, a second polypeptide chain comprising the polypeptide of SEQ ID NO:272, and a third polypeptide chain comprising the polypeptide of SEQ ID NO:273.

Claim 32. A kit comprising the pharmaceutical composition of any one of claims 18-31, wherein the binding molecules are compartmentalized in one or more containers.