

**MULTISPECIFIC ANTIBODIES OR ANTIGEN BINDING FRAGMENTS
THEREOF TO B7-H7 AND IMMUNE EFFECTOR CELL ANTIGENS**

BACKGROUND

[0001] Although immunotherapies have been investigated for many diseases and disorders, including cancer, functional limitations have been encountered that still need to be addressed. A network of costimulatory and co-inhibitory ligands and receptors tightly controls the immune system. Immune checkpoints negatively regulate immune response progression based on complex interactions. Currently available immunotherapies can modulate immune responses in some patients, but immune checkpoint expression and interactions with natural binding partners can vary between patients.

[0002] Therefore, a need exists for the development of new and improved therapeutic modalities optimized to target tumor sites, particularly in the tumor microenvironment.

SUMMARY

[0003] The present disclosure, among other things, provides multispecific antibodies or antigen-binding fragments thereof that interact with particular targets and methods of using such multispecific antibodies or antigen-binding fragments thereof. In some embodiments, a multispecific antibody or antigen-binding fragment thereof described herein comprises a first antigen-binding domain that selectively binds to B7-H7. In some embodiments, a multispecific antibody or antigen-binding fragment thereof described herein comprises a second antigen-binding domain that selectively binds an immune effector cell antigen, such as cluster of differentiation 3 (CD3). B7-H7 is a B7 gene family member that is broadly expressed in a variety of tumors and antigen presenting cells, which interacts with both inhibitory and stimulatory receptors to regulate T cell and NK cell functions. CD3 is a protein complex and T cell co-receptor that is involved in T cell activation. Accordingly, the present disclosure provides multispecific antibodies or antigen-binding fragments thereof that are particularly useful for treating a variety of cancers, including solid tumors or hematological tumors, as well as modulating an immune response in a subject.

[0004] In some aspects, the disclosure provides a multispecific antibody or antigen-binding fragment thereof comprising: (i) a first antigen-binding domain that selectively binds

to B7-H7, and (ii) a second antigen-binding domain that selectively binds an immune effector cell antigen.

[0005] In some embodiments, a multispecific antibody or antigen-binding fragment thereof further comprises a third antigen-binding domain that selectively binds to B7-H7 or an immune effector cell antigen. In some embodiments, an immune effector cell antigen comprises or is cluster determinant 3 (CD3) or cluster determinant 137 (4-1BB). In some embodiments, an immune effector cell comprises or is a T-cell or an NK cell.

[0006] In some embodiments, a first antigen-binding domain, second antigen-binding domain, and/or third antigen-binding domain comprises or is an scFv, Fab, Fab', F(ab')₂, nanobody, or camelid antibody. In some embodiments, a multispecific antibody or antigen-binding fragment thereof comprises or is a bispecific antibody or antigen-binding fragment thereof.

[0007] In some embodiments, the first antigen-binding domain that selectively binds to B7-H7 comprises: (a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 43; a VLCDR2 amino acid sequence of SEQ ID NO: 44; and a VLCDR3 amino acid sequence of SEQ ID NO: 45; (b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4; a VHCDR2 amino acid sequence of SEQ ID NO: 5; and a VHCDR3 amino acid sequence of SEQ ID NO: 6; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 46; a VLCDR2 amino acid sequence of SEQ ID NO: 47; and a VLCDR3 amino acid sequence of SEQ ID NO: 48; (c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 7; a VHCDR2 amino acid sequence of SEQ ID NO: 8; and a VHCDR3 amino acid sequence of SEQ ID NO: 9; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 49; a VLCDR2 amino acid sequence of SEQ ID NO: 50; and a VLCDR3 amino acid sequence of SEQ ID NO: 51; (d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 69; a VHCDR2 amino acid sequence of SEQ ID NO: 70; and a VHCDR3 amino acid sequence of SEQ ID NO: 71; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 111; a VLCDR2 amino acid sequence of SEQ ID NO: 112; and a VLCDR3 amino acid sequence of SEQ ID NO: 113; (e) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 72; a VHCDR2 amino

acid sequence of SEQ ID NO: 73; and a VHCDR3 amino acid sequence of SEQ ID NO: 74; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 114; a VLCDR2 amino acid sequence of SEQ ID NO: 115; and a VLCDR3 amino acid sequence of SEQ ID NO: 116; (f) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 75; a VHCDR2 amino acid sequence of SEQ ID NO: 76; and a VHCDR3 amino acid sequence of SEQ ID NO: 77; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 117; a VLCDR2 amino acid sequence of SEQ ID NO: 118; and a VLCDR3 amino acid sequence of SEQ ID NO: 119; (g) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 137; a VHCDR2 amino acid sequence of SEQ ID NO: 138; and a VHCDR3 amino acid sequence of SEQ ID NO: 139; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 179; a VLCDR2 amino acid sequence of SEQ ID NO: 180; and a VLCDR3 amino acid sequence of SEQ ID NO: 181; (h) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 140; a VHCDR2 amino acid sequence of SEQ ID NO: 141; and a VHCDR3 amino acid sequence of SEQ ID NO: 142; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 182; a VLCDR2 amino acid sequence of SEQ ID NO: 183; and a VLCDR3 amino acid sequence of SEQ ID NO: 184; and/or (i) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 143; a VHCDR2 amino acid sequence of SEQ ID NO: 144; and a VHCDR3 amino acid sequence of SEQ ID NO: 145; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 185; a VLCDR2 amino acid sequence of SEQ ID NO: 186; and a VLCDR3 amino acid sequence of SEQ ID NO: 187.

[0008] In some embodiments, the second antigen-binding domain that selectively binds an immune effector cell antigen comprises: (a) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 28; a VHCDR2 amino acid sequence of SEQ ID NO: 29; and a VHCDR3 amino acid sequence of SEQ ID NO: 30; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 56; a VLCDR2 amino acid sequence of SEQ ID NO: 57; and a VLCDR3 amino acid sequence of SEQ ID NO: 58; (b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 31; a VHCDR2 amino acid sequence of SEQ ID NO: 32; and a VHCDR3 amino acid sequence of SEQ ID NO: 33; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 59; a VLCDR2 amino acid sequence of SEQ ID NO: 60; and a VLCDR3 amino acid sequence of SEQ ID NO: 61; (c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 34; a VHCDR2 amino acid sequence of SEQ ID NO: 35; and a VHCDR3 amino acid sequence of SEQ ID NO: 36; and a VL comprising a VLCDR1 amino

acid sequence of SEQ ID NO: 62; a VLCDR2 amino acid sequence of SEQ ID NO: 63; and a VLCDR3 amino acid sequence of SEQ ID NO: 64; (d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 164; a VHCDR2 amino acid sequence of SEQ ID NO: 165; and a VHCDR3 amino acid sequence of SEQ ID NO: 166; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 192; a VLCDR2 amino acid sequence of SEQ ID NO: 193; and a VLCDR3 amino acid sequence of SEQ ID NO: 194; (e) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 167; a VHCDR2 amino acid sequence of SEQ ID NO: 168; and a VHCDR3 amino acid sequence of SEQ ID NO: 169; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 195; a VLCDR2 amino acid sequence of SEQ ID NO: 196; and a VLCDR3 amino acid sequence of SEQ ID NO: 197; (f) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 170; a VHCDR2 amino acid sequence of SEQ ID NO: 171; and a VHCDR3 amino acid sequence of SEQ ID NO: 172; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 198; a VLCDR2 amino acid sequence of SEQ ID NO: 199; and a VLCDR3 amino acid sequence of SEQ ID NO: 200; (g) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 96; a VHCDR2 amino acid sequence of SEQ ID NO: 97; and a VHCDR3 amino acid sequence of SEQ ID NO: 98; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 124; a VLCDR2 amino acid sequence of SEQ ID NO: 125; and a VLCDR3 amino acid sequence of SEQ ID NO: 126; (h) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 99; a VHCDR2 amino acid sequence of SEQ ID NO: 100; and a VHCDR3 amino acid sequence of SEQ ID NO: 101; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 127; a VLCDR2 amino acid sequence of SEQ ID NO: 128; and a VLCDR3 amino acid sequence of SEQ ID NO: 129; and/or (i) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 102; a VHCDR2 amino acid sequence of SEQ ID NO: 103; and a VHCDR3 amino acid sequence of SEQ ID NO: 104; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 130; a VLCDR2 amino acid sequence of SEQ ID NO: 131; and a VLCDR3 amino acid sequence of SEQ ID NO: 132.

[0009] In some embodiments, the third antigen-binding domain that selectively binds to B7-H7 or an immune effector cell antigen comprises: (a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 14; a VHCDR2 amino acid sequence of SEQ ID NO: 15; and a VHCDR3 amino acid sequence of SEQ ID NO: 16; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ

ID NO: 43; a VLCDR2 amino acid sequence of SEQ ID NO: 44; and a VLCDR3 amino acid sequence of SEQ ID NO: 45; (b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 17; a VHCDR2 amino acid sequence of SEQ ID NO: 18; and a VHCDR3 amino acid sequence of SEQ ID NO: 19; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 46; a VLCDR2 amino acid sequence of SEQ ID NO: 47; and a VLCDR3 amino acid sequence of SEQ ID NO: 48; (c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 20; a VHCDR2 amino acid sequence of SEQ ID NO: 21; and a VHCDR3 amino acid sequence of SEQ ID NO: 22; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 49; a VLCDR2 amino acid sequence of SEQ ID NO: 50; and a VLCDR3 amino acid sequence of SEQ ID NO: 51; (d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 82; a VHCDR2 amino acid sequence of SEQ ID NO: 83; and a VHCDR3 amino acid sequence of SEQ ID NO: 84; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 111; a VLCDR2 amino acid sequence of SEQ ID NO: 112; and a VLCDR3 amino acid sequence of SEQ ID NO: 113; (e) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 85; a VHCDR2 amino acid sequence of SEQ ID NO: 86; and a VHCDR3 amino acid sequence of SEQ ID NO: 87; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 114; a VLCDR2 amino acid sequence of SEQ ID NO: 115; and a VLCDR3 amino acid sequence of SEQ ID NO: 116; (f) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 88; a VHCDR2 amino acid sequence of SEQ ID NO: 89; and a VHCDR3 amino acid sequence of SEQ ID NO: 90; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 117; a VLCDR2 amino acid sequence of SEQ ID NO: 118; and a VLCDR3 amino acid sequence of SEQ ID NO: 119; and/or (g) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 150; a VHCDR2 amino acid sequence of SEQ ID NO: 151; and a VHCDR3 amino acid sequence of SEQ ID NO: 152; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 179; a VLCDR2 amino acid sequence of SEQ ID NO: 180; and a VLCDR3 amino acid sequence of SEQ ID NO: 181; (h) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 153; a VHCDR2 amino acid sequence of SEQ ID NO: 154; and a VHCDR3 amino acid sequence of SEQ ID NO: 155; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 182; a VLCDR2 amino acid sequence of SEQ ID NO: 183; and a VLCDR3 amino acid sequence of SEQ ID NO: 184; and/or (i) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 156; a VHCDR2 amino acid sequence of SEQ ID NO: 157; and a VHCDR3 amino acid sequence of SEQ ID NO: 158; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO:

185; a VLCDR2 amino acid sequence of SEQ ID NO: 186; and a VLCDR3 amino acid sequence of SEQ ID NO: 187.

[0010] In some embodiments, the first antigen-binding domain that selectively binds to B7-H7 comprises: (a) a VH comprising an amino acid sequence of SEQ ID NO: 10, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 10; and a VL comprising an amino acid sequence of SEQ ID NO: 52, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 52; (b) a VH comprising an amino acid sequence of SEQ ID NO: 78, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 78; and a VL comprising an amino acid sequence of SEQ ID NO: 120, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 120; and/or (c) a VH comprising an amino acid sequence of SEQ ID NO: 146, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 146; and a VL comprising an amino acid sequence of SEQ ID NO: 188, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 188.

[0011] In some embodiments, the second antigen-binding domain that selectively binds an immune effector cell antigen comprises: (a) a VH comprising an amino acid sequence of SEQ ID NO: 37, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 37; and a VL comprising an amino acid sequence of SEQ ID NO: 65, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 65; (b) a VH comprising an amino acid sequence of SEQ ID NO: 173, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 173; and a VL comprising an amino acid sequence of SEQ ID NO: 201, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 201; and/or (c) a VH comprising an amino acid sequence of SEQ ID NO: 105, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 105; and a VL comprising an amino acid sequence of SEQ ID NO: 133, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 133.

[0012] In some embodiments, the third antigen-binding domain that selectively binds to B7-H7 or an immune effector cell antigen comprises: (a) a VH comprising an amino acid sequence of SEQ ID NO: 23, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 23; and a VL comprising an amino acid sequence of SEQ ID NO: 52, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 52; (b) a VH comprising an amino acid sequence of SEQ ID NO: 91, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 91; and a VL comprising an amino acid sequence of SEQ ID NO: 120, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 120; and/or (c) a VH comprising an amino acid sequence of SEQ ID NO: 159, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 159; and a VL comprising an amino acid sequence of SEQ ID NO: 188, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 188.

[0013] In some embodiments, the multispecific antibody or antigen-binding fragment thereof comprises: (a) a heavy chain comprising an amino acid sequence of SEQ ID NO: 12, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 12; and a light chain comprising an amino acid sequence of SEQ ID NO: 54, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 54; and/or a second heavy chain comprising an amino acid sequence of SEQ ID NO: 39, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 39; and a second light chain comprising an amino acid sequence of SEQ ID NO: 67, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 67; (b) a heavy chain comprising an amino acid sequence of SEQ ID NO: 80, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 80; and a light chain comprising an amino acid sequence of SEQ ID NO: 122, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 122; and/or a second heavy chain comprising an amino acid sequence of SEQ ID NO: 107, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 107; and a second light chain comprising an amino acid sequence of SEQ ID NO: 135, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO:

135; or (c) a heavy chain comprising an amino acid sequence of SEQ ID NO: 148, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 148; and a light chain comprising an amino acid sequence of SEQ ID NO: 190, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 190; and/or a second heavy chain comprising an amino acid sequence of SEQ ID NO: 175, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 175; and a second light chain comprising an amino acid sequence of SEQ ID NO: 203, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 203.

[0014] In some embodiments, a multispecific antibody or antigen-binding fragment thereof comprises: (a) a first heavy chain comprising an amino acid sequence of SEQ ID NO: 12; a light chain comprising an amino acid sequence of SEQ ID NO: 54; and (b) a second heavy chain comprising an amino acid sequence of SEQ ID NO: 39; a light chain comprising an amino acid sequence of SEQ ID NO: 67. In some embodiments, a multispecific antibody or antigen-binding fragment thereof comprises a linker comprising an amino acid sequence of SEQ ID NO: 27.

[0015] In some embodiments, a multispecific antibody or antigen-binding fragment thereof, comprises or is: (i) a chimeric, human, or humanized bispecific antibody or antigen-binding fragment thereof; (ii) a monoclonal bispecific antibody or antigen-binding fragment thereof; and/or (iii) a knob-into-hole bispecific antibody, a 1:1 bispecific antibody, or a 2:1 bispecific antibody. In some embodiments, a multispecific antibody or antigen-binding fragment thereof, comprises: (i) a heavy chain constant region chosen from IgG1, IgG2, IgG3, or IgG4, and/or (ii) a light chain constant region chosen from light chain constant regions of kappa or lambda.

[0016] In some embodiments, a multispecific antibody or antigen-binding fragment thereof, comprises an Fc region with reduced effector function relative to a reference agent. In some embodiments, an Fc region comprises one or more amino acid substitutions of L234A, L235A, and/or P329A numbering according to EU index.

[0017] In another aspect, the disclosure provides pharmaceutical compositions comprising a multispecific antibody or antigen-binding fragment thereof of any aspect or embodiment described herein, and a pharmaceutically acceptable carrier.

[0018] In another aspect, the disclosure provides methods of treating a subject having a disease, disorder, or condition and/or modulating an immune response in a subject comprising administering a therapeutically effective amount of any aspect or embodiment described herein.

[0019] In some embodiments, a subject has or is at risk of developing a cancer. In some embodiments, a subject has a solid tumor or a hematological cancer. In some embodiments, a solid tumor is or comprises one or more of: a renal cancer, a bone cancer, a skin cancer, a breast cancer, a cervical cancer, a colorectal cancer, an endometrial cancer, a lung cancer, an ovarian cancer, a liver cancer, cholangiocarcinoma, a thyroid cancer, a prostate cancer, a bladder cancer, a brain cancer, a retinoblastoma cancer, an esophageal cancer, a gastric cancer, a stomach cancer, a testicular cancer, a head and neck cancer, a metastatic cancer, a neuroblastoma cancer, a pancreatic cancer, or a small intestine cancer.

[0020] In some embodiments, a hematological cancer comprises or is a leukemia or lymphoma. In some embodiments, a leukemia comprises or is acute lymphocytic leukemia, acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, chronic leukemia, or acute leukemia. In some embodiments, a lymphoma comprises or is Hodgkin lymphoma (HL), non-Hodgkin's lymphoma, lymphocytic lymphoma, or diffuse large B cell lymphoma (DLBCL).

[0021] In some embodiments, a pharmaceutical composition is administered in combination with at least one additional agent.

[0022] In another aspect, the disclosure provides a nucleic acid encoding a multispecific antibody or antigen-binding fragment thereof of any aspect or embodiment described herein.

[0023] In another aspect, the disclosure provides an expression vector comprising the nucleic acid of any aspect or embodiment described herein.

[0024] In another aspect, the disclosure provides a host cell comprising or expressing a multispecific antibody or antigen-binding fragment, the nucleic acid, or the expression vector of any aspect or embodiment described herein.

[0025] In another aspect, the disclosure provides a method of making a multispecific antibody or antigen-binding fragment thereof, comprising: (i) culturing a host cell comprising the nucleic acid or the expression vector of any aspect or embodiment described hereinunder conditions suitable for expression of the multispecific antibody or antigen-binding fragment thereof, and (ii) recovering the multispecific antibody or antigen-binding fragment thereof.

[0026] In another aspect, the disclosure provides a kit comprising a multispecific antibody or antigen-binding fragment thereof or pharmaceutical composition of any one of the aspects or embodiments described herein, and instructions for use.

BRIEF DESCRIPTION OF THE DRAWING

[0027] The Figures described below, which together make up the Drawing, are for illustration purposes only, not for limitation.

[0028] **FIGS. 1A-1B** are schematics of a 2+1 knob-in-hole bispecific antibody format showing locations of binding sites/paratopes (**FIG. 1A**) and various heavy and light chains (**FIG. 1B**).

[0029] **FIGS. 2A-2B** are graphs of flow cytometry histograms showing binding of exemplary anti-B7-H7/CD3 bispecific antibodies NPXAB-1, NPXAB-2, and NPXAB-3 to 300.19 cells over-expressing human B7-H7 (**FIG. 2A**) or cynomolgus B7-H7 (**FIG. 2B**) relative to two negative controls (80210 and 80214).

[0030] **FIG. 3A-3B** are a series of graphs of flow cytometry histograms showing binding of exemplary anti-B7-H7/CD3 bispecific antibodies NPXAB-1 and NPXAB-3 to Jurkat cells endogenously expressing human CD3 (**FIG. 3A**), and a graph of NPXAB-2 binding to human CD3 on Jurkat cells (**FIG. 3B**); respective EC₅₀ and maximum mean binding signal are shown in **FIG. 3A**.

[0031] **FIGS. 4A-4B** are graphs of Octet histograms showing binding of exemplary anti-B7-H7/CD3 bispecific antibodies NPXAB-1 and NPXAB-3 to recombinant human B7-H7-Fc (**FIG. 4A**) and cynomolgus B7-H7-Fc (**FIG. 4B**); respective K_D, k_{on}, and k_{off} are shown.

[0032] **FIGS. 5A-5B** are graphs of Octet histograms showing binding of exemplary anti-B7-H7/CD3 bispecific antibodies NPXAB-1 and NPXAB-3 to recombinant human CD3-Fc (**FIG. 5A**) and cynomolgus CD3-Fc (**FIG. 5B**); respective K_D , k_{on} and k_{off} are shown.

[0033] **FIGS. 6A-6C** are a schematic of a reporter TCR/CD3 effector cell assay using transcription factor Nuclear Factor of Activated T cells (NFAT; **FIG. 6A**) and a graph showing that exemplary anti-B7-H7/CD3 bispecific antibodies NPXAB-1, NPXAB-2, and NPXAB-3 modulate activation of reporter TCR/CD3 effector cells (NFAT) via interaction with B7-H7-expressing Raji cells, relative to two negative controls (80210 and 80214; **FIG. 6B**), and a graph showing that NPXAB-1 and NPXAB-2 induce T cell activation in a Jurkat-CD3 reporter assay in a B7-H7 dependent fashion (**FIG. 6C**)

[0034] **FIGS. 7A-7C** are a graph showing that exemplary anti-B7-H7/CD3 bispecific antibodies NPXAB-1, NPXAB-2, and NPXAB-3 mediate killing of B7-H7-expressing A204 cells in the presence of primary human PBMCs, relative to two negative controls, 80210 and 80214 (**FIG. 7A**), a graph showing that exemplary antibodies NPXAB-1, and NPXAB-2 induce killing of Raji-B7-H7 overexpressing cells (**FIG. 7B**) and HT29 cells endogenously expressing B7-H7 (**FIG. 7C**).

[0035] **FIGS. 8A-8B** are graphs showing that exemplary anti-B7-H7/CD3 bispecific antibodies NPXAB-1 and NPXAB-2 induce primary CD4-positive (**FIG. 8A**) and CD8-positive (**FIG. 8B**) T cell activation in vitro.

[0036] **FIGS. 9A-9C** are graphs of tumor volume over time of HT29 tumors in NCG mice humanized with activated human T cells showing anti-tumor efficacy of NPXAB-2 compared to untreated control mice (**FIG. 9A**), and the anti-tumor efficacy of a dose range of NPXAB-2 (**FIG. 9B**) or NPXAB-1 (**FIG. 9C**) compared to untreated control mice. Data represents average tumor volume $\pm$ SD over time of N=6 animals per group.

[0037] **FIGS. 10A-10B** are a graph of PC3M prostate adenocarcinoma tumor volume in mice showing that NPXAB-1 and NPXAB-2 delay the growth of the tumors relative to the PBMC alone control (**FIG. 10A**), and a table summarizing tumor growth inhibition induced by NPXAB-1 and NPXAB-2 in the PC3M tumor model in humanized mice (**FIG. 10B**).

[0038] **FIGS. 11A-11D** are a graph showing that NPXAB-1 and NPXAB-2 induce A204 tumor regression in mice humanized with activated T cells (**FIG. 11A**), and graphs of

individual mouse tumor volumes by a treatment group of a T cell control alone (**FIG. 11B**), NPXAB-1 treatment (**FIG. 11C**) and NPXAB-2 treatment (**FIG. 11D**).

[0039] **FIGS. 12A-12B** are graphs of primate body weight measurements taken 7 days prior to and up to 49 days after intravenous administration of one or two doses of NPXAB-2 or NPXAB-1. Data represents average body weight in kilograms (**FIG. 12A**) or average percent change in body weights from day 0 (**FIG. 12B**) $\pm$ standard error of the mean over time of N=2 animals per group.

[0040] **FIGS. 13A-13B** are graphs of fold change of CD3-positive primate immune cells after one 3 $\mu\text{g/kg}$ or 10 $\mu\text{g/kg}$ dose (**FIG. 13A**) or two (1 + 3) $\mu\text{g/kg}$ doses (**FIG. 13B**) of NPXAB-2 compared to the pre-dose measurement at day 0.

[0041] **FIGS. 14A-14B** are graphs of fold change of CD20-positive primate immune cells after one 3 $\mu\text{g/kg}$ or 10 $\mu\text{g/kg}$ dose (**FIG. 14A**) or two (1 + 3) $\mu\text{g/kg}$ doses (**FIG. 14B**) of NPXAB-2 compared to the pre-dose measurement at day 0.

[0042] **FIGS. 15A-15B** are graphs of fold change of CD3-positive primate immune cells after one 10 $\mu\text{g/kg}$ or 1000 $\mu\text{g/kg}$ dose (**FIG. 15A**) or two (100 + 300) $\mu\text{g/kg}$ doses (**FIG. 15B**) of NPXAB-1 compared to the pre-dose measurement at day 0.

[0043] **FIGS. 16A-16B** are graphs of fold change of CD20-positive primate immune cells after one 10 $\mu\text{g/kg}$ or 1000 $\mu\text{g/kg}$ dose (**FIG. 16A**) or two (100 + 300) $\mu\text{g/kg}$ doses (**FIG. 16B**), of NPXAB-1 compared to the pre-dose measurement at day 0.

[0044] **FIGS. 17A-17F** are graphs of fold change of CD25-positive primate cells as a subset of CD3-positive cells (**FIGS. 17A** and **17B**), CD4-positive cells (**FIGS. 17C** and **17D**), and CD8-positive cells (**FIGS. 17E** and **17F**) after one 3 $\mu\text{g/kg}$ or 10 $\mu\text{g/kg}$ dose (**FIGS. 17A, 17C, and 17E**) or two (1 + 3) $\mu\text{g/kg}$ doses (**FIGS. 17B, 17D, and 17F**) of NPXAB-2 compared to the pre-dose measurement at day 0.

[0045] **FIGS. 18A-18F** are graphs of fold change of CD69-positive primate cells as a subset of CD3-positive cells (**FIGS. 18A** and **18B**), CD4-positive cells (**FIGS. 18C** and **18D**), and CD8-positive cells (**FIGS. 18E** and **18F**) after one 3 $\mu\text{g/kg}$ or 10 $\mu\text{g/kg}$ dose (**FIGS. 18A, 18C, and 18E**) or two (1 + 3) $\mu\text{g/kg}$ doses (**FIGS. 18B, 18D, and 18F**) of NPXAB-2 compared to the pre-dose measurement at day 0.

[0046] **FIGS. 19A-19F** are graphs of fold change of CD25-positive primate cells as a subset of CD3-positive cells (**FIGS. 19A** and **19B**), CD4-positive cells (**FIGS. 19C** and **19D**), and CD8-positive cells (**FIGS. 19E** and **19F**) after one 10 µg/kg or 1000 µg/kg dose (**FIGS. 19A, 19C, and 19E**) or two (100 + 300) µg/kg doses (**FIGS. 19B, 19D, and 19F**) of NPXAB-1 compared to the pre-dose measurement at day 0.

[0047] **FIGS. 20A-20F** are graphs of fold change of CD69-positive primate cells as a subset of CD3-positive cells (**FIGS. 20A** and **20B**), CD4-positive cells (**FIGS. 20C** and **20D**), and CD8-positive cells (**FIGS. 20E** and **20F**) after one 10 µg/kg or 1000 µg/kg dose (**FIGS. 20A, 20C, and 20E**) or two (100 + 300) µg/kg doses (**FIGS. 20B, 20D, and 20F**) of NPXAB-1 compared to the pre-dose measurement at day 0.

[0048] **FIGS. 21A-21L** are graphs of observed concentrations of immune cytokines in the serum of primates after treatment with NPXAB-2. NPXAB-2 was administered as one dose of 3 or 10 µg/kg, or two doses of 1 + 3 µg/kg. Reported are cytokine levels in pg/mL of G-CSF after one (**FIG. 21A**) and two (**FIG. 21B**) doses; IFN-γ after one (**FIG. 21C**) and two (**FIG. 21D**) doses; IL-1RA after one (**FIG. 21E**) and two (**FIG. 21F**) doses; IL-8 after one (**FIG. 21G**) and two (**FIG. 21H**) doses; MCP-1 after one (**FIG. 21I**) and two (**FIG. 21J**) doses; and MIP-1β after one (**FIG. 21K**) and two (**FIG. 21L**) doses of NPXAB-2.

[0049] **FIGS. 22A-22L** are graphs of observed concentrations of immune cytokines in the serum of primates after treatment with NPXAB-1. NPXAB-1 was administered as one dose of 10 or 1000 µg/kg, or two doses of 100 + 300 µg/kg. Reported are cytokine levels in pg/mL of G-CSF after one (**FIG. 22A**) and two (**FIG. 22B**) doses; IFN-γ after one (**FIG. 22C**) and two (**FIG. 22D**) doses; IL-1RA after one (**FIG. 22E**) and two (**FIG. 22F**) doses; IL-8 after one (**FIG. 22G**) and two (**FIG. 22H**) doses; MCP-1 after one (**FIG. 22I**) and two (**FIG. 22J**) doses; and MIP-1β after one (**FIG. 22K**) and two (**FIG. 22L**) doses of NPXAB-1.

[0050] **FIG. 23** is a schematic of TMIGD2 blocking properties of an exemplary anti-B7-H7/CD3 bispecific antibody (NPXAB-1) and TMIGD2 sparing properties of an exemplary anti-B7-H72/CD3 bispecific antibody (NPXAB-2).

[0051] **FIG. 24** is a graph showing recombinant human Fc-conjugated TMIGD2 protein binding to 300.19 cells with increasing concentrations of exemplary anti-B7-H7/CD3

bispecific antibodies NPXAB-1 and NPXAB-2, and antibody 6F10 (IgG4), which is a B7-H7-specific TMIGD2 blocking antibody that was included as a positive control.

[0052] **FIG. 25** is a schematic of a Jurkat/CD3/NFAT/TMIGD2 luciferase reporter assay described herein.

[0053] **FIG. 26** is a graph showing T cell activation, graphed as luminescence, in the Jurkat/CD3/NFAT/TMIGD2 luciferase reporter assay for exemplary anti-B7-H7/CD3 bispecific antibodies NPXAB-1 and NPXAB-2.

[0054] **FIGS. 27A-27B** are graphs showing CD25-associated primary CD4+ (**FIG. 27A**) and CD8+ (**FIG. 27B**) T-cell activation as geometric Mean Fluorescence Intensity (gMFI) with increasing concentrations of exemplary anti-B7-H7/CD3 bispecific NPXAB-1, NPXAB-4, NPXAB-5, or NPXAB-3.

[0055] **FIG. 28** is a graph showing CD69-associated CD8+ T cell activation with exemplary anti-B7-H7/CD3 bispecific antibodies NPXAB-1, NPXAB-4, NPXAB-5, or NPXAB-3 as gMFI with either TMIGD2 blockade with an anti-TMIGD2 monoclonal antibody 17C7 or no TMIGD2 blockade isotype control.

[0056] **FIGS. 29A-29C** are graphs showing IFN γ (**FIG. 29A**), Perforin (**FIG. 29B**) and Granzyme B (**FIG. 29C**) release by T cells co-cultured with A204 wild-type cells (A204-WT), B7-H7-overexpressing A204 cells (A204-B7-H7) or A204 cells with B7-H7 knocked out (A204-KO) incubated with exemplary anti-B7-H7/CD3 bispecific antibody NPXAB-1.

[0057] **FIGS. 30A-30G** are graphs showing A204 tumor volume (in mm³) in individual mice in response to treatment with no antibody (**FIG. 30A**), T cells alone (**FIG. 30B**) and exemplary anti-B7-H7/CD3 bispecific antibody NPXAB-1 administered at doses of 0.01 mg/kg (**FIG. 30C**), 0.1 mg/kg (**FIG. 30D**), 1 mg/kg (**FIG. 30E**) and 10 mg/kg (**FIG. 30F**), and averaged tumor volume values from six mice (**FIG. 30G**) in a model of rhabdomyosarcoma.

DEFINITIONS

[0058] In order for the present disclosure to be more readily understood, certain terms are first defined below. Additional definitions for the following terms and other terms are set forth throughout the specification. The publications and other reference materials referenced herein to describe the background of the disclosure and to provide additional detail regarding its practice are hereby incorporated by reference in their entirety.

[0059] In this application, unless otherwise clear from context, (i) the term “a” may be understood to mean “at least one”; (ii) the term “or” may be understood to mean “and/or”; (iii) the terms “comprising” and “including” may be understood to encompass itemized components or steps whether presented by themselves or together with one or more additional components or steps; and (iv) where ranges are provided, endpoints are included.

[0060] *About:* As used herein, the term “about” as applied to one or more values of interest, refers to a value that is similar to a stated reference value. In some embodiments, the term “about” refers to a range of values that fall within 25%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 11%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1 %, or less in either direction (greater than or less than) of the stated reference value unless otherwise stated or otherwise evident from the context (except where such number would exceed 100% of a possible value).

[0061] *Affinity matured:* As used herein, the term “affinity matured” refers to an antibody with one or more alterations in one or more CDRs thereof, which result in an improvement in affinity of an antibody for an antigen, compared to a parent antibody that does not possess those one or more alterations. In some embodiments, affinity matured antibodies will have nanomolar or even picomolar affinities for a target antigen. Affinity matured antibodies may be produced by any of a variety of procedures known in the art. Affinity maturation by V_H and V_L domain shuffling is described in Marks et al., *BioTechnology* 10:779-783 (1992). Random mutagenesis of CDR and/or framework residues is described in: Barbas et al. *Proc. Nat. Acad. Sci. U.S.A* 91:3809-3813 (1994); Schier et al., *Gene* 169: 147-155 (1995); Yelton et al., *J. Immunol.* 155: 1994-2004 (1995); Jackson et al., *J. Immunol.* 154(7):3310-9 (1995); and Hawkins et al., *J. Mol. Biol.* 226:889-896 (1992).

[0062] *Agent:* As used herein, the term “agent” refers to a form of treatment, for example, a biological, chemical, or other treatment. For example, a biological agent may be or comprise a biological entity and/or compound including, for example, an antibody or antigen-binding fragment thereof, an organic molecule (e.g., a small molecule), a peptide (e.g., a fusion protein), an aptamer, a nucleic acid, a chimeric antigen receptor, a glycoprotein, a saccharide, a lipid, a growth factor, an enzyme, a synthetic molecule, a carbohydrate, a lipid, a hormone, a polymer, or a derivative, variation, complex, or any combination thereof. In appropriate circumstances, as will be clear from context to those skilled in the art, the term may be utilized to refer to an entity that is or comprises a cell or organism, or a fraction, extract, or component thereof. Alternatively, or additionally, as context will make clear, the term may be used to refer to a natural product. In some instances, again as will be clear from context, the term may be used to refer to one or more entities that is man-made in that it is designed, engineered, and/or produced through human action and/or is not found in nature. In some embodiments, an agent may be utilized in isolated or pure form. In some embodiments, an agent may be utilized in crude form. In some embodiments, agents are provided as collections or libraries, which may be screened to identify or characterize active agents within them. An agent may bind any cell moiety, such as a receptor, an antigenic determinant, or other binding site present on a target or target cell. Various agents are useful in the compositions and methods described herein.

[0063] For example, an agent can be or comprise one or more of: a chemotherapeutic agent, a hormone therapy, a cell-based therapy, treatment with hyperthermia, a photodynamic therapy, surgery, radiation, or a transplant. In some embodiments, a chemotherapeutic agent comprises or is one or more anthracyclines, one or more cytoskeletal disruptors (e.g. microtubule targeting agents such as taxanes, maytansine, and analogs thereof), one or more epothilones, one or more histone deacetylase inhibitors (HDACs), one or more topoisomerase inhibitors (e.g., one or more of inhibitors of topoisomerase I or topoisomerase II), one or more kinase inhibitors, one or more nucleotide analogs or nucleotide precursor analogs, one or more peptide antibiotics, one or more platinum-based agents, one or more retinoids, one or more vinca alkaloids, or a combination thereof. In some embodiments, a chemotherapeutic agent comprises or is one or more of: Actinomycin, All-trans retinoic acid, an Auiristatin, Azacitidine, Azathioprine, Bleomycin, Bortezomib, Carboplatin, Capecitabine, Cisplatin, Chlorambucil, Cyclophosphamide, Curcumin, Cytarabine, Daunorubicin, Docetaxel,

Doxifluridine, Doxorubicin, Epirubicin, Epothilone, Etoposide, Fludarabine, Fluorouracil, Gemcitabine, Hydroxyurea, Idarubicin, Imatinib, Irinotecan, Maytansine and/or analogs thereof (e.g. DM1), Mechlorethamine, Mercaptopurine, Methotrexate, Mitoxantrone, a Maytansinoid, Oxaliplatin, Paclitaxel, Pemetrexed, Rituxan, Teniposide, Tioguanine, Topotecan, Valrubicin, Vinblastine, Vincristine, Vindesine, or Vinorelbine. In some embodiments, a chemotherapeutic agent comprises or is an antibody-drug conjugate (ADC). In some embodiments, an ADC comprises or is hLL1-doxorubicin, hRS7-SN-38, hMN-14-SN-38, hLL2-SN-38, hA20-SN-38, hPAM4-SN-38, hLL1-SN-38, hRS7-Pro-2-P-Dox, hMN-14-Pro-2-P-Dox, hLL2-Pro-2-P-Dox, hA20-Pro-2-P-Dox, hPAM4-Pro-2-P-Dox, hLL1-Pro-2-P-Dox, P4/D10-doxorubicin, gemtuzumab ozogamicin, brentuximab vedotin, trastuzumab emtansine, inotuzumab ozogamicin, glembatumomab vedotin, SAR3419, SAR566658, BIIB015, BT062, SGN-75, SGN-CD19A, AMG-172, AMG-595, BAY-94-9343, ASG-5ME, ASG-22ME, ASG-16M8F, MDX-1203, MLN-0264, anti-PSMA ADC, RG-7450, RG-7458, RG-7593, RG-7596, RG-7598, RG-7599, RG-7600, RG-7636, ABT-414, IMGN-853, IMGN-529, vorsetuzumab mafodotin, lorvotuzumab mertansine, or a combination thereof.

[0064] In some embodiments, a hormone therapy may be or comprise tamoxifen, raloxifene, leuprolide, bicalutamide, granisetron, flutamide, or a combination thereof. In some embodiments, a cell-based therapy comprises or is chimeric antigen receptor T (CAR-T) cells, TCR-transduced T cells, dendritic cells, tumor infiltrating lymphocytes (TILs), natural killer (NK) cells, or a combination thereof. In some embodiments, treatment with hyperthermia comprises or is local hyperthermia (e.g., external, intraluminal, or interstitial hyperthermia), regional hyperthermia (e.g., deep tissue hyperthermia, regional perfusion, or (continuous hyperthermic peritoneal perfusion), or whole-body hyperthermia. In some embodiments, a photodynamic therapy comprises or is administration of photosensitizers, such as hematoporphyrin and its derivatives, Verteporfin (BPD-MA), phthalocyanine, photosensitizer Pc4, demethoxy-hypocrellin A, 2BA-2-DMHA, or a combination thereof. In some embodiments, surgery comprises or is surgery to remove cancerous or precancerous tissue. In some embodiments, a transplant comprises or is a stem cell transplant or an organ transplant.

[0065] *Antibody:* As used herein, the term “antibody” refers to a polypeptide, e.g., an immunoglobulin chain or fragment thereof, including canonical immunoglobulin sequence elements sufficient to confer specific binding to a particular target, e.g., an antigen. As is

known in the art, intact antibodies as produced in nature are approximately 150 kD tetrameric agents comprising two identical heavy chain polypeptides (about 50 kD each) and two identical light chain polypeptides (about 25 kD each) that associate with each other into what is commonly referred to as a “Y-shaped” structure. Each heavy chain comprises at least four domains (each about 110 amino acids long): an amino-terminal variable (V_H) domain followed by three constant domains: CH1, CH2, and a carboxy-terminal CH3 (located at the base of the Y’s stem). A short region, known as a “switch,” connects the heavy chain variable and constant regions. A “hinge” region connects CH2 and CH3 domains to CH1 domain. Two disulfide bonds in this hinge region connect two heavy chain polypeptides to one another in an intact antibody. Each light chain comprises two domains: an amino-terminal variable (V_L) domain, followed by a carboxy-terminal constant (CL) domain, separated from one another by another “switch” region. Naturally produced antibodies are glycosylated, typically on a CH2 domain. Each domain in an antibody has a structure characterized by an “immunoglobulin fold” formed from two beta sheets (e.g., 3-stranded sheets, 4-stranded sheets, or 5-stranded sheets) packed against each other in a compressed antiparallel beta barrel. Each variable domain contains three hypervariable loops known as “complementarity determining regions” (CDR1, CDR2, and CDR3) and four somewhat invariant “framework” regions (FR1, FR2, FR3, and FR4). When natural antibodies fold, FR regions form beta sheets that provide a structural framework for the domains, and CDR loop regions from both heavy and light chains are brought together in three-dimensional space to create a single hypervariable antigen binding site located at the tip of the Y structure. An Fc region of naturally occurring antibodies binds to receptors on effector cells, including, for example, effector cells that mediate cytotoxicity. Affinity and/or other binding attributes of Fc regions for Fc receptors can be modulated through glycosylation or other modification.

[0066] In some embodiments, any polypeptide or complex of polypeptides that includes sufficient immunoglobulin domain sequences can be referred to and/or used as an “antibody,” whether such polypeptide is naturally produced (e.g., generated by an organism reacting to an antigen) or produced by recombinant engineering, chemical synthesis, or other artificial system or methodology. In some embodiments, an antibody is monoclonal. In some embodiments, an antibody is polyclonal. In some embodiments, an antibody has constant region sequences characteristic of mouse, rabbit, primate, or human antibodies. In some embodiments, one or more antibody sequences are humanized, primatized, or chimeric as is known in the art. Moreover, the term “antibody,” can refer to any of the art-known or

developed constructs or formats for utilizing antibody structural and functional features. For example, an antibody can be in a format selected from, but not limited to, intact IgA, IgG, IgE or IgM antibodies including subclasses (e.g., IgG1, IgG2, IgG3, and IgG4), and multispecific (e.g., bispecific) antibodies. An antibody can be an immunoglobulin, heavy chain antibody, light chain antibody, leucine-rich repeat (LRR) based antibody, or other protein scaffold with antibody-like properties. An antibody can be any immunological binding moiety known in the art including, but not limited to, a scFv, Fab, Fab', Fab'₂, Fab₂, Fab₃, F(ab')₂, Fd, Fd', Fv, Feb, diabody, triabody, tetrabody, minibody, maxibody, tandab, DVD, BiTe, TandAb, single domain antibody (e.g., shark single domain antibody, such as IgNAR or fragments thereof), camelid antibody, masked antibody (e.g., Probodyes®), Small Modular ImmunoPharmaceutical (SMIP™), single chain or Tandem diabody (TandAb®), VHH, Anticalin®, Nanobody®, BiTE®, ankyrin repeat protein or DARPIN®, Avimer®, DART, TCR-like antibody, Adnectin®, Affilin®, Trans-body®, Affibody®, TrimerX®, MicroProtein, Fynomer®, Centyrin®, KALBITOR®, or any combination thereof.

[0067] An “antibody” can be or comprise a polypeptide including one or more structural elements recognized by those skilled in the art as a CDR. An antibody can be or comprise a polypeptide including at least one CDR (e.g., at least one V_H CDR and/or at least one V_L CDR) that is substantially identical to a CDR found in a reference antibody. A CDR substantially identical to a reference CDR can be identical or contain between 1-5 amino acid substitutions relative to a reference CDR. In some embodiments a CDR is substantially identical to a reference CDR by at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or greater sequence identity with a reference CDR. In some embodiments, a CDR is substantially identical to a reference CDR in that at least one amino acid (e.g., at least one, at least two, at least three, at least four, or at least five amino acids) is deleted, added, or substituted compared with a reference CDR.

[0068] *Antibody heavy chain:* As used herein, the term “antibody heavy chain” refers to the larger of two types of polypeptide chains present in antibodies in their naturally occurring conformations.

[0069] *Antibody light chain:* As used herein, the term “antibody light chain” refers to the smaller of two types of polypeptide chains present in antibodies in their naturally occurring conformations.

[0070] *Antigen:* As used herein, the terms “antigen” or “Ag” refer to a molecule that is capable of provoking an immune response. This immune response may involve either antibody production, activation of specific immunologically competent cells, or both. A skilled artisan will understand that any macromolecule, including virtually all proteins or peptides, can serve as an antigen. Furthermore, antigens can be derived from recombinant or genomic DNA. A skilled artisan will understand that any DNA that comprises a nucleotide sequence or a partial nucleotide sequence encoding a protein that elicits an immune response encodes an “antigen” as that term is used herein. Furthermore, one skilled in the art will understand that an antigen need not be encoded solely by a full length nucleotide sequence of a gene. It is readily apparent that the present disclosure includes, but is not limited to, the use of partial nucleotide sequences of more than one gene and that these nucleotide sequences are arranged in various combinations to elicit the desired immune response. Moreover, a skilled artisan will understand that an antigen need not be encoded by a “gene” at all. It is readily apparent that an antigen can be generated synthesized or can be derived from a biological sample. Such a biological sample can include, but is not limited to, a tissue sample, a tumor sample, a cell, or a biological fluid.

[0071] *Antigen-binding fragment:* As used herein, the term “antigen-binding fragment” refers to a portion of an intact antibody or recombinant variants thereof that binds a target, e.g., an antigen, to which the intact antibody binds. An antigen-binding fragment refers to the antigen-binding domain, e.g., an antigenic determining variable region of an intact antibody, which is sufficient to confer recognition and specific binding of the antibody fragment to a particular target, e.g., an antigen. An antigen-binding fragment includes any naturally occurring, enzymatically obtainable, synthetic, or genetically engineered polypeptide or glycoprotein that specifically binds an antigen to form a complex. Exemplary antigen-binding fragments include, but are not limited to, Fab, Fab', Fab'-SH, F(ab')₂ and Fv fragments; single-chain antibodies, such as scFv, VHH, or camelid; single domain antibodies, such as sdAb (either V_L or V_H); linear antibodies; or multispecific antibodies formed from antibody fragments, such as a fragment comprising two or more Fab fragments linked by a disulfide bridge at a hinge region. An antigen-binding fragment can be incorporated into single domain antibodies, maxibodies, minibodies, nanobodies, intrabodies, diabodies, triabodies, tetrabodies, v-NAR, or bis-scFv (see, e.g., Hollinger and Hudson, *Nature Biotechnology* 23:1126-1136, 2005). Antigen-binding fragments can be grafted into scaffolds based on polypeptides, such as a fibronectin type III (Fn3) (see, U.S. Patent No.:

6,703,199, which describes fibronectin polypeptide minibodies). As with intact antibodies, antigen-binding fragments may be mono-specific or multispecific (e.g., bispecific). A multispecific antigen-binding fragment can comprise at least two different variable domains that is each capable of specifically binding to a separate antigen or to a different epitope of the same antigen. An antigen-binding fragment may be produced by any means. For example, an antigen-binding fragment can be enzymatically or chemically produced by fragmentation of an intact antibody or antibody agent. Alternatively, an antigen-binding fragment can be recombinantly produced. An antigen-binding fragment can be wholly or partially synthetically produced. An antigen-binding fragment can have a length of at least about 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, or 200 amino acids or more.

[0072] *Antibody-Dependent Cellular Cytotoxicity:* As used herein, the terms “antibody-dependent cellular cytotoxicity” or “ADCC” refer to a phenomenon in which target cells bound by an antibody are killed by immune effector cells. Without wishing to be bound by theory, ADCC is typically understood to involve Fc receptor (FcR)-bearing effector cells recognizing and subsequently killing antibody-coated target cells (e.g., cells that express on their surface specific antigens to which an antibody is bound). Immune effector cells that mediate ADCC include, but are not limited to, NK cells, macrophage, neutrophils, and eosinophils.

[0073] *Associated:* As used herein, two events or entities are “associated” with one another if the presence, level, degree, type and/or form of one event or entity is correlated with that of the other event or entity. For example, a particular entity (e.g., antigen, polypeptide, genetic signature, metabolite, or microbe) is considered to be associated with a particular disease, disorder, or condition, if its presence, level and/or form correlates with incidence of and/or susceptibility to the disease, disorder, or condition (e.g., across a relevant population).

[0074] *B7-H7:* As used herein, the term “B7H7” refers to a member of the B7 family. B7-H7 is also known as HERV-H LTR-associating 2, B7y, HHLA2, or B7H7. B7-H7 and HERV-H LTR-associating 2, B7y, HHLA2, or B7H7 are used herein interchangeably. B7-H7 protein has limited expression in normal human tissues but is widely expressed in human cancers. B7-H7 is a membrane protein with three Ig-like domains (IgV-IgC-IgV), whereas other members of the B7 family generally have only two Ig domains

(IgV-IgC). HHLA2 in normal human tissues is expressed in the epithelium of kidney, gut, gallbladder, and breast as well as placental trophoblast cells. In the immune system, B7-H7 can be up-regulated on human monocytes and macrophages in the tumor microenvironment. B7-H7 regulates human T cell and HK cell functions including, for example, T cell and NK cell proliferation and cytokine production. B7-H7 is expressed in higher levels in a wide range of human cancers including, but not limited to, colorectal, renal, lung, pancreas, ovary, and prostate cancer. B7-H7 is also expressed in human cancers of thyroid, melanoma, liver, bladder, colon, kidney, breast, and esophagus tissue.

[0075] The term “B7-H7” includes fragments, variants (e.g., allelic variants), and derivatives thereof. Representative human B7-H7 cDNA and human B7-H7 protein sequences are publicly available from the National Center for Biotechnology Information (NCBI). Human B7-H7 variants include variant 1 (NM_007072.3 and NP_009003.1, which represents the longest transcript and encodes the longest isoform a), variant 2 (NM_001282556.1 and NP_001269485.1, which includes an alternate promoter and differs in the 5' UTR compared to variant 1), variant 3 (NM_001282557.1 and NP_001269486.1, which includes an alternate promoter and differs in the 5' UTR compared to variant 1), variant 4 (NM_001282558.1 and NP_001269487.1, which encodes isoform b, includes an alternate promoter, differs in the 5' UTR, and lacks an alternate in-frame exon in the 3' coding region compared to variant 1, resulting a shorter isoform than isoform a), and variant 5 (NM_001282559.1 and NP_001269488.1, which encodes isoform c, includes an alternate promoter, has a distinct 5' UTR, and translation initiation starts at an alternate start codon compared to variant 1 resulting in a distinct N-terminus and shorter polypeptide than isoform a).

[0076] *Binding:* As used herein, the term “binding” refers to a non-covalent association between or among two or more entities. “Direct” binding involves physical contact between entities or moieties. Indirect binding involves physical interaction by way of physical contact with one or more intermediate entities. Binding between two or more entities can typically be assessed in any of a variety of contexts – including where interacting entities or moieties are studied in isolation or in a context of more complex systems (e.g., while covalently or otherwise associated with a carrier entity and/or in a biological system or cell).

[0077] *Bispecific antibody*: As used herein, the term “bispecific antibody” refers to an antibody having two distinct binding specificities. Typically, a bispecific binding molecule comprises at least two antigen-binding domains, each of which specifically binds to a different antigen or epitope. A variety of different structures of bispecific antibodies is known in the art. In some embodiments, each antigen-binding domain comprises an antibody or antigen-binding fragment thereof including at least one V_H region and/or at least one V_L region. In some embodiments, V_H regions and/or V_L regions are from a particular monoclonal antibody. In certain embodiments, a bispecific antibody comprises: (i) a first antigen-binding domain that comprises or is an antibody fragment (e.g., scFv, Fab, Fab', F(ab')₂, Fd, Fv, nanobody, or camelid antibody); and (ii) a second antigen-binding domain that comprises or is a full length antibody.

[0078] *Cancer*: As used herein, the terms “cancer,” “malignancy,” “neoplasm,” “tumor,” and “carcinoma,” refer to cells that exhibit relatively abnormal, uncontrolled, and/or autonomous growth, thereby exhibiting an aberrant growth phenotype characterized by a significant loss of control of cell proliferation. Cancer cells can spread locally or through bloodstream and lymphatic system to other body parts. In some embodiments, a tumor is or comprises cells that are precancerous (e.g., benign), malignant, pre-metastatic, metastatic, and/or non-metastatic. In some embodiments, cancer is or comprises a solid tumor. In some embodiments, cancer is or comprises a hematologic tumor. Examples of various cancers are described herein and include, but are not limited to, hematopoietic cancers (e.g., leukemias, lymphomas (Hodgkin’s lymphoma and non-Hodgkin’s lymphoma) myelomas, and myeloproliferative disorders); sarcomas; melanomas; adenomas, carcinomas of solid tissue; squamous cell carcinomas of the mouth, throat, larynx, and lung; liver cancer; genitourinary cancers (e.g., prostate, cervical, bladder, uterine, and endometrial cancer, and renal cell carcinomas); bone cancer; pancreatic cancer; skin cancer; cutaneous or intraocular melanoma; cancer of the endocrine system, thyroid gland, or parathyroid gland; head and neck cancers; breast cancer; gastro-intestinal cancers; nervous system cancers; benign lesions, such as papillomas; or any combination thereof as well as several other types including cancers described elsewhere herein.

[0079] *Carrier*: As used herein, the term “carrier” refers to a diluent, adjuvant, excipient, and/or vehicle with which a composition is administered. In some exemplary embodiments, carriers include sterile liquids, such as, for example, water and oils, including

oils of petroleum, animal, vegetable or synthetic origin, such as, for example, peanut oil, soybean oil, mineral oil, sesame oil, and the like. In some embodiments, carriers are or include one or more solid components.

[0080] *CDR*: As used herein, the terms “complementarity determining region” or “CDR” refer to sequences of amino acids within antibody variable regions that confer antigen specificity and binding affinity. For example, in general, there are three CDRs in each heavy chain variable region (e.g., HCDR1, HCDR2, and HCDR3) and three CDRs in each light chain variable region (LCDR1, LCDR2, and LCDR3). Exact definitional CDR boundaries and lengths are subject to different classification and numbering systems. Certain systems have been established in the art for defining CDR boundaries (e.g., Kabat, IMGT, Chothia, or a combination thereof). CDRs may therefore be referred to by Kabat, Chothia, IMGT, or any other boundary definitions known in the art. For example, in a combined Kabat and Chothia numbering scheme, CDRs correspond to amino acid residues that are part of a Kabat CDR, a Chothia CDR, or both. Despite differing boundaries, each of these systems has some degree of overlap in what constitutes “hypervariable regions” within variable sequences. CDR definitions according to these systems may differ in length and boundary areas with respect to adjacent framework regions (see, e.g., Kabat et al., in “Sequences of Proteins of Immunological Interest,” 5th Edition, U.S. Department of Health and Human Services, 1992; Chothia et al. (1987) J. Mol. Biol. 196, 901; and MacCallum et al., J. Mol. Biol. (1996) 262, 732). Those skilled in the art appreciate differences between and among these systems and are capable of understanding CDR boundaries to an extent required to understand and to practice the claims and disclosure herein.

[0081] *CD3*: As used herein, the terms “CD3 or “cluster of differentiation 3” refer to a T cell co-receptor that can activate both cytotoxic T cells (CD8+ T cells) and helper T cells (CD4+ T cells). Typically, CD3 is a protein complex having multiple protein chains, e.g., CD3 includes a CD3 γ chain, a CD3 δ chain, and two CD3 ϵ chains in mammals. These chains can associate with a T-cell receptor (TCR), in particular, a ζ -chain to generate an activation signal in T cells. A TCR, ζ -chain and CD3 together can be referred to as a TCR complex.

[0082] *Composition*: As used herein, the term “composition” refers to a discrete physical entity that comprises one or more specified components. In general, unless otherwise specified, a composition may be of any form, e.g., gas, gel, liquid, or solid.

[0083] *Comprising:* As used herein, a composition or method described herein as “comprising” one or more named elements or steps is open-ended, meaning that the named element(s) or step(s) are essential, but other elements or steps may be added within the scope of the composition or method. Any composition or method described as “comprising” one or more named elements or steps also describes the corresponding, more limited composition or method “consisting essentially of” the same named elements or steps, meaning that the composition or method includes the named essential elements or steps and may also include additional elements or steps that do not materially affect the basic and novel characteristic(s) of the composition or method. Any composition or method described herein as “comprising” or “consisting essentially of” one or more named elements or steps also describes the corresponding, more limited, and closed-ended composition or method “consisting of” the named elements or steps to the exclusion of any other unnamed element or step. In any composition or method disclosed herein, known or disclosed equivalents of any named essential element or step may be substituted for that element or step.

[0084] *Combination therapy:* As used herein, the term “combination therapy” refers to those situations in which two or more different therapeutic agents (e.g., a multispecific antibody or antigen binding fragment thereof and at least one additional agent) are administered in overlapping regimens so that the subject is simultaneously exposed to both agents. When used in combination therapy, two or more different therapeutic agents may be administered simultaneously or separately. This administration in combination can include simultaneous administration of two or more therapeutic agents in the same dosage form, simultaneous administration in separate dosage forms, and separate administration. That is, two or more therapeutic agents can be formulated together in the same dosage form and administered simultaneously. Alternatively, two or more therapeutic agents can be simultaneously administered in separate formulations. In another alternative, a first therapeutic agent can be administered followed by one or more additional therapeutic agents. In a separate administration protocol, two or more therapeutic agents may be administered a few minutes apart, a few hours apart, a few days apart, or a few weeks apart. In some embodiments, two or more therapeutic agents may be administered within hours (e.g., less than about 1 hour, about 2 hours, about 3 hours, about 4 hours, or about 5 hours) apart.

[0085] *Effective amount:* As used herein, the term “effective amount” refers to a dose that is adequate to prevent or treat at least one sign and/or symptom of a disease, disorder, or condition (e.g., cancer) in an individual. Amounts effective for a therapeutic or prophylactic

use can depend on, for example, stage and severity of a disease, disorder, or condition being treated; age, weight, and general state of health of a patient; and judgment of a prescribing physician. Size of a dose will also be determined by the active ingredient/therapeutic selected; method of administration; timing and frequency of administration; existence, nature, and extent of any adverse side effects that might accompany the administration of a particular active; and desired physiological effect. It will be appreciated by one of skill in the art that various diseases, disorders, or conditions could require prolonged treatment involving multiple administrations. For purposes of the disclosure, an amount or dose of a therapeutic agent (e.g., one or more bispecific antibodies or antigen-binding fragments thereof described herein) administered should be sufficient to affect a therapeutic or prophylactic response in a subject over a reasonable time frame (e.g., reduction or other lessening of severity or duration of at least one sign or symptom). For example, a dose should be sufficient to detect, treat, or prevent cancer in a period of from about 2 hours or longer, e.g., about 12 to about 24 or more hours, from time of administration. In some embodiments, a time period is even longer. Dosing will be determined by efficacy of one or more particular therapeutic agents and condition of a subject (e.g., a human) as well as body weight of a subject (e.g., a human) to be treated.

[0086] *Encoding:* As used herein, the term “encoding” refers to the inherent property of specific sequences of nucleotides in a polynucleotide, such as a gene, a cDNA, or an mRNA, to serve as templates for synthesis of other polymers and macromolecules in biological processes having either a defined sequence of nucleotides (e.g., rRNA, tRNA or mRNA) or a defined sequence of amino acids and biological properties resulting therefrom. Thus, a gene encodes a protein if transcription and translation of mRNA corresponding to that gene produces the protein in a cell or other biological system. Both a coding strand (a nucleotide sequence corresponding to an mRNA sequence and typically provided in sequence listings) and a non-coding strand (used as a template for transcription of a gene or cDNA) can be referred to as encoding a protein or other product of that gene or cDNA.

[0087] *Epitope:* As used herein, the term “epitope” refers to any moiety that is specifically recognized by an immunoglobulin (e.g., antibody or receptor) binding component. In some embodiments, an epitope is comprised of a plurality of chemical atoms or groups on an antigen. In some embodiments, such chemical atoms or groups are surface-exposed when the antigen adopts a relevant three-dimensional conformation. In some

embodiments, such chemical atoms or groups are physically near to each other in space when the antigen adopts such a conformation. In some embodiments, at least some such chemical atoms or groups are physically separated from one another when the antigen adopts an alternative conformation (e.g., is linearized).

[0088] *Expression:* As used herein, the term “expression” of a nucleic acid sequence refers to generation of any gene product from a nucleic acid sequence (e.g., a nucleic acid sequence encoding one or more bispecific antibodies or antigen-binding fragments thereof described herein). In some embodiments, a gene product can be a transcript. In some embodiments, a gene product can be a polypeptide. In some embodiments, expression of a nucleic acid sequence involves one or more of the following: (1) production of an RNA template from a DNA sequence (e.g., by transcription); (2) processing of an RNA transcript (e.g., by splicing, editing, 5' cap formation, and/or 3' end formation); (3) translation of an RNA into a polypeptide or protein; and/or (4) post-translational modification of a polypeptide or protein.

[0089] *Fragment:* As used herein, the term “fragment” refers to a structure that includes a discrete portion of a whole structure, but lacks one or more moieties found in a whole structure. In some embodiments, a fragment consists of such a discrete portion. In some embodiments, a fragment comprises or is a characteristic structural element or moiety found in a whole structure. In some embodiments, a fragment (e.g., an antigen-binding fragment described herein) comprises or is at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 275, 300, 325, 350, 375, 400, 425, 450, 475, 500, or more monomeric units (e.g., amino acids) as found in a whole antibody. In some embodiments, fragment (e.g., an antigen-binding fragment described herein) comprises or consists of at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or more of monomeric units (e.g., residues) found in a whole antibody. In some embodiments, a nucleotide fragment comprises or consists of at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or more of monomeric units (e.g., residues) found in a whole nucleotide.

[0090] *Framework region:* As used herein, the terms “framework region” or “FR” refers to the sequences of a variable region minus CDRs. Because a CDR sequence can be determined by different systems, likewise a framework sequence is subject to

correspondingly different interpretations. Six CDRs divide framework regions on heavy and light chains into four sub-regions (FR1, FR2, FR3, and FR4) on each chain, in which CDR1 is positioned between FR1 and FR2, CDR2 between FR2 and FR3, and CDR3 between FR3 and FR4. Without specifying particular sub-regions as FR1, FR2, FR3 or FR4, a framework region, as referred by others, represents combined FRs within a variable region of a single, naturally occurring immunoglobulin chain. As used herein, a FR represents one of four sub-regions. For example, FR1 represents a first framework region closest to the amino terminal end of a variable region and 5' with respect to CDR1. FRs represents two or more sub-regions constituting a framework region.

[0091] *Host cell:* As used herein, the term “host cell” refers to a cell into which exogenous DNA (recombinant or otherwise) has been introduced. Persons of skill in the art upon reading this disclosure will understand that such terms refer not only to the particular subject cell, but also to progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to a parent cell, but are still included within the scope of the term “host cell” as used herein. In some embodiments, host cells include prokaryotic and eukaryotic cells selected from any Kingdom of life that are suitable for expressing an exogenous DNA (e.g., a recombinant nucleic acid sequence). Exemplary cells include those of prokaryotes and eukaryotes (single-cell or multiple-cell), bacterial cells (e.g., strains of *E. coli*, *Bacillus spp.*, or *Streptomyces spp.*), mycobacteria cells, fungal cells, yeast cells (e.g., *S. cerevisiae*, *S. pombe*, *P. pastoris*, or *P. methanolica*), plant cells, insect cells (e.g., SF-9, SF-21, baculovirus-infected insect cells, or *Trichoplusia ni*), non-human animal cells, human cells, or cell fusions (e.g., hybridomas or quadromas). In some embodiments, a host cell comprises or is a human, monkey, ape, hamster, rat, or mouse cell. In some embodiments, a host cell comprises one or more of: CHO (e.g., CHO K1, DXB-1 1 CHO, Veggie-CHO), COS (e.g., COS-7), retinal cell, Vero, CV1, kidney (e.g., HEK293, 293 EBNA, MSR 293, MDCK, HaK, BHK), HeLa, HepG2, WI38, MRC 5, Colo205, HB 8065, HL-60, (e.g., BHK21), Jurkat, Daudi, A431 (epidermal), CV-1, U937, 3T3, L cell, C127 cell, SP2/0, NS-0, MMT 060562, Sertoli cell, BRL 3 A cell, HT1080 cell, myeloma cell, tumor cell, or a cell line derived from an aforementioned cell. In some embodiments, a host cell comprises one or more viral genes.

[0092] *Human antibody*: As used herein, the term “human antibody” refers to antibodies having variable and constant regions generated (or assembled) from human immunoglobulin sequences. Antibodies or antigen-binding fragments thereof may be considered “human” even though their amino acid sequences include residues or elements not encoded by human germline immunoglobulin sequences (e.g., sequence variations that may have been introduced by random or site-specific mutagenesis *in vitro* or by somatic mutation *in vivo*), such as in one or more CDRs, particularly CDR3.

[0093] *Humanized*: As used herein, the term “humanized” refers to antibodies or antigen-binding fragments thereof whose amino acid sequence includes V_H and/or V_L region sequences from a reference antibody raised in a non-human species (e.g., a mouse), but also includes modifications in those sequences relative to the reference antibody intended to render them more “human-like” or more similar to human germline variable sequences. In some embodiments, a humanized antibody or antigen-binding fragment thereof is one that immunospecifically binds to an antigen of interest and has a FR region with substantially an amino acid sequence of a human antibody and a CDR with substantially an amino acid sequence of a non-human antibody. A humanized antibodies comprises substantially all of at least one, and typically two, variable domains (Fab, Fab', F(ab')₂, FabC, Fv) in which all or substantially all CDR regions correspond to a non-human immunoglobulin (e.g., a donor immunoglobulin) and all or substantially all framework regions correspond to a human immunoglobulin consensus sequence. In some embodiments, a humanized antibody also comprises at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin constant region. In some embodiments, a humanized antibody comprises both light chain as well as at least a variable domain of a heavy chain. An antibody also may include a CH1, hinge, CH2, CH3, and, optionally, a CH4 region of a heavy chain constant region. In some embodiments, a humanized antibody only contains a humanized VL region. In some embodiments, a humanized antibody only contains a humanized VH region. In some certain embodiments, a humanized antibody contains humanized VH and VL regions.

[0094] *Immunoglobulin*: As used herein, the terms “immunoglobulin” or “Ig,” refer to a class of proteins that function as antibodies. Antibodies expressed by B cells may be referred to as a BCR (B cell receptor) or antigen receptor. The five members included in this class of proteins are IgA, IgG, IgM, IgD, and IgE, which further include subclasses (e.g., IgG1, IgG2, IgG3, and IgG4). IgA is the primary antibody that is present in body secretions,

such as saliva, tears, breast milk, gastrointestinal secretions, and mucus secretions of respiratory and genitourinary tracts. IgG is the most common circulating antibody. IgM is the main immunoglobulin produced in the primary immune response in most subjects. It is the most efficient immunoglobulin in agglutination, complement fixation, and other antibody responses, and is important in defense against bacteria and viruses. IgD is an immunoglobulin that has no known antibody function, but may serve as an antigen receptor. IgE is an immunoglobulin that mediates immediate hypersensitivity by causing release of mediators from mast cells and basophils upon exposure to allergen.

[0095] *Identity:* As used herein, the term “identity” refers to subunit sequence identity between two polymeric molecules, particularly between two amino acid molecules, such as between two polypeptide molecules. When two amino acid sequences have the same residues at the same positions; e.g., if a position in each of two polypeptide molecules is occupied by an Arginine, then they are identical at that position. The identity or extent to which two amino acid sequences have the same residues at the same positions in an alignment is often expressed as a percentage. The identity between two amino acid sequences is a direct function of the number of matching or identical positions, e.g., if half of the positions (e.g., five positions in a polymer of 10 amino acids in length) in two sequences are identical, the two sequences are 50% identical; if 90% of the positions (e.g., nine positions in a polymer of 10 amino acids in length) are identical, the two amino acids sequences are 90% identical.

[0096] *Immune effector cell:* As used herein, the term “immune effector cell,” refers to a cell that is involved in an immune response, e.g., promotion of an immune response. Examples of immune effector cells include, but are not limited to, T cells, natural killer (NK) cells, macrophages, monocytes, dendritic cells, neutrophils, eosinophils, mast cells, platelets, large granular lymphocytes, Langerhans' cells, or B-lymphocytes.

[0097] *Immune response:* As used herein the term “immune response” refers to a cellular and/or systemic response to an antigen that occurs when lymphocytes identify antigenic molecules as foreign and induce the formation of antibodies and/or activate lymphocytes to remove the antigen. In some embodiments, an immune cell response can include proliferation of an immune effector cell (e.g., a T cell or a NK cell), cytokine production by an immune effector cell (e.g., a T cell or a NK cell), and/or release of cytotoxic

granules comprising perforin and/or granzymes by an immune effector cell (e.g., a T cell or a NK cell).

[0098] *“Improve,” “increase,” “inhibit” or “reduce”:* As used herein, the terms “improve,” “increase,” “inhibit,” “reduce,” or grammatical equivalents thereof, indicate values that are relative to a baseline or other reference measurement. In some embodiments, an appropriate reference measurement is or comprises a measurement in a particular system (e.g., in a single individual) under otherwise comparable conditions absent presence of (e.g., prior to and/or after) a particular agent or treatment, or in presence of an appropriate comparable reference agent. In some embodiments, an appropriate reference measurement is or comprises a measurement in comparable system known or expected to respond in a particular way, in presence of the relevant agent or treatment.

[0099] *Modulating:* As used herein the term “modulating,” refers to mediating a detectable increase or decrease in a level of a response and/or change in nature of a response in a subject compared with a level and/or nature of a response in a subject without a treatment or an untreated subject. The term encompasses perturbing and/or affecting a native signal or response thereby mediating a beneficial therapeutic response in a subject, preferably, a human.

[0100] *Monoclonal antibody:* As used herein, the terms “monoclonal antibody” or “mAb” refer to an antibody obtained from a population of substantially homogeneous antibodies, such that individual antibodies in the population are substantially identical and/or bind the same epitope, except for possible variant antibodies (e.g., containing naturally occurring mutations or arising during production of a monoclonal), such variants generally being present in minor amounts. In contrast to polyclonal antibody preparations, which typically include different antibodies directed against different determinants (epitopes), each monoclonal antibody in such a preparation is directed against a single determinant on an antigen. Thus, “monoclonal” typically indicates a population of antibodies is not a mixture of discrete antibodies.

[0101] *Nucleic acid molecule:* As used herein, the term “nucleic acid molecule” refers to a polymer of at least three nucleotides. In some embodiments, a nucleic acid molecule comprises DNA. In some embodiments, a nucleic acid molecule comprises RNA. In some embodiments, a nucleic acid molecule is single stranded. In some embodiments, a nucleic acid molecule is double stranded. In some embodiments, a nucleic acid molecule

comprises both single and double stranded portions. In some embodiments, a nucleic acid molecule comprises a backbone that comprises one or more phosphodiester linkages. In some embodiments, a nucleic acid molecule comprises a backbone that comprises both phosphodiester and non-phosphodiester linkages. For example, a nucleic acid molecule may comprise a backbone that comprises one or more phosphorothioate or 5'-N-phosphoramidite linkages and/or one or more peptide bonds, e.g., as in a peptide nucleic acid molecule. In some embodiments, a nucleic acid molecule comprises one or more, or all, natural residues (e.g., adenine, cytosine, deoxyadenosine, deoxycytidine, deoxyguanosine, deoxythymidine, guanine, thymine, and/or uracil). In some embodiments, a nucleic acid molecule comprises one or more, or all, non-natural residues. In some embodiments, a non-natural residue comprises a nucleoside analog (e.g., 2-aminoadenosine, 2-thiothymidine, inosine, pyrrolo-pyrimidine, 3-methyl adenosine, 5-methylcytidine, C-5 propynyl-cytidine, C-5 propynyl-uridine, 2-aminoadenosine, C5-bromouridine, C5-fluorouridine, C5-iodouridine, C5-propynyl-uridine, C5-propynyl-cytidine, C5-methylcytidine, 2-aminoadenosine, 7-deazaadenosine, 7-deazaguanosine, 8-oxoadenosine, 8-oxoguanosine, 0(6)-methylguanine, 2-thiocytidine, methylated bases, intercalated bases, or combinations thereof). In some embodiments, a non-natural residue comprises one or more modified sugars (e.g., 2'-fluororibose, ribose, 2'-deoxyribose, arabinose, hexose, or combinations thereof) as compared to those in natural residues. In some embodiments, a nucleic acid molecule has a nucleotide sequence that encodes a functional gene product, such as an RNA or polypeptide. In some embodiments, a nucleic acid molecule has a nucleotide sequence that comprises one or more introns. In some embodiments, a nucleic acid molecule may be prepared by isolation from a natural source, enzymatic synthesis (e.g., by polymerization based on a complementary template (e.g., *in vivo* or *in vitro*), reproduction in a recombinant cell or system, or chemical synthesis. In some embodiments, a nucleic acid molecule is at least 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 225, 250, 275, 300, 325, 350, 375, 400, 425, 450, 475, 500, 600, 700, 800, 900, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 5000 or more residues long.

[0102] *Pharmaceutically acceptable:* As used herein, the term “pharmaceutically acceptable” refers to compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with tissues of human

beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication and commensurate with a reasonable benefit/risk ratio.

[0103] *Pharmaceutically acceptable carrier:* As used herein, the term “pharmaceutically acceptable carrier” refers to a pharmaceutically acceptable material, composition, or vehicle, such as a liquid or solid filler, diluent, excipient, or solvent encapsulating material, involved in carrying or transporting a subject compound from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be “acceptable” in the sense of being compatible with other ingredients of a formulation and not injurious to a subject. Some exemplary pharmaceutically acceptable carriers include, but are not limited to, sugars, such as lactose, 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; pH buffered solutions; polyesters, polycarbonates or polyanhydrides; or combinations thereof and other non-toxic compatible substances employed in pharmaceutical formulations.

[0104] *Polypeptide:* As used herein, the terms “polypeptide” or “protein” refer to any polymeric chain of residues (e.g., amino acids) that are typically linked by peptide bonds. In some embodiments, a polypeptide has an amino acid sequence that occurs in nature. In some embodiments, a polypeptide has an amino acid sequence that does not occur in nature. In some embodiments, a polypeptide has an amino acid sequence that is engineered in that it is designed and/or produced through action of the hand of humans. A polypeptide may comprise or consist of natural amino acids, non-natural amino acids, or both. A polypeptide may comprise or consist of only natural amino acids or only non-natural amino acids. A polypeptide may comprise D-amino acids, L-amino acids, or both. A polypeptide may include one or more pendant groups or other modifications, e.g., modifying or attached to one or more amino acid side chains at the N-terminus, at the C-terminus, or both. In some embodiments, such pendant groups or modifications are chosen from acetylation, amidation, lipidation, methylation, or pegylation, including combinations thereof. A polypeptide may be

cyclic and/or may comprise a cyclic portion. In some embodiments, a polypeptide is not cyclic and/or does not comprise any cyclic portion. In some embodiments, a polypeptide is linear. A polypeptide may be or comprise a stapled polypeptide. The term “polypeptide” may be appended to a name of a reference polypeptide, activity, or structure; in such instances, it is used herein to refer to polypeptides that share relevant activity or structure and thus can be considered members of a same class or family of polypeptides. For each such class, the present disclosure provides and/or those skilled in the art will be aware of exemplary polypeptides within such class whose amino acid sequences and/or functions are known. In some embodiments, such exemplary polypeptides are reference polypeptides for a polypeptide class or family. In some embodiments, a member of a polypeptide class or family shows significant sequence homology or identity with, shares a common sequence motif (e.g., a characteristic sequence element) with, and/or shares a common activity (in some embodiments at a comparable level or within a designated range) with a reference polypeptide of a class. For example, a member polypeptide may have an overall degree of sequence homology or identity with a reference polypeptide that is at least about 30-40% and is often about 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more and/or includes at least one region (e.g., a conserved region that may be or comprise a characteristic sequence element) that shows very high sequence identity, often greater than 90% or even 95%, 96%, 97%, 98%, or 99%. Such a conserved region usually encompasses at least 3 to 4 and often up to 20 or more amino acids; in some embodiments, a conserved region encompasses at least one stretch of at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or more contiguous amino acids. A useful polypeptide may comprise or consist of a fragment of a parent polypeptide. A useful polypeptide may comprise or consist of a plurality of fragments, each of which is found in a same parent polypeptide in a different spatial arrangement relative to one another than is found in a polypeptide of interest (e.g., fragments that are directly linked in a parent may be spatially separated in a polypeptide of interest or vice versa, and/or fragments may be present in a different order in a polypeptide of interest than in a parent), such that a polypeptide of interest is a derivative of its parent polypeptide.

[0105] *scFv*: As used herein, the term “scFv” refers to a fusion protein comprising at least one antibody fragment comprising a variable region of a light chain and at least one antibody fragment comprising a variable region of a heavy chain, wherein light and heavy chain variable regions are contiguously linked via a short flexible polypeptide linker. A scFv

is capable of being expressed as a single chain polypeptide and retains specificity of an intact antibody from which it is derived. Unless specified, a scFv may have V_L and V_H regions in either order with respect to N-terminal and C-terminal ends of a polypeptide, such that an scFv may comprise V_L-linker-V_H or may comprise V_H-linker-V_L.

[0106] *Subject:* As used herein, the term “subject” refers to an organism, for example, a mammal (e.g., a human, a non-human mammal, a non-human primate, a primate, a laboratory animal, a mouse, a rat, a hamster, a gerbil, a cat, or a dog). In some embodiments, a human subject is an adult, adolescent, or pediatric subject. In some embodiments, a subject is suffering from a disease, disorder or condition, e.g., a disease, disorder, or condition that can be treated as provided herein, e.g., a cancer or a tumor listed herein. In some embodiments, a subject is susceptible to a disease, disorder, or condition. In some embodiments, a susceptible subject is predisposed to and/or shows an increased risk (as compared to an average risk observed in a reference subject or population) of developing a disease, disorder, or condition. In some embodiments, a subject displays one or more symptoms of a disease, disorder, or condition. In some embodiments, a subject does not display a particular symptom (e.g., clinical manifestation of disease) or characteristic of a disease, disorder, or condition. In some embodiments, a subject does not display any symptom or characteristic of a disease, disorder, or condition. In some embodiments, a subject is a patient. In some embodiments, a subject is an individual to whom one or more of diagnosis or therapy has been administered.

[0107] *Substantially:* As used herein, the term “substantially” refers to the qualitative condition of exhibiting total or near-total extent or degree of a characteristic or property of interest. One of ordinary skill in the biological arts will understand that biological and chemical phenomena rarely, if ever, go to completion and/or proceed to completeness or achieve or avoid an absolute result. The term “substantially” is therefore used herein to capture the potential lack of completeness inherent in many biological and chemical phenomena.

[0108] *Substantial identity:* As used herein, the term “substantial identity” refers to a comparison between amino acid or nucleic acid sequences. As will be appreciated by those of ordinary skill in the art, two sequences are generally considered to be “substantially identical” if they contain identical residues in corresponding positions. As is well known in this art, amino acid or nucleic acid sequences may be compared using any of a variety of

algorithms, including those available in commercial computer programs such as BLASTN for nucleotide sequences and BLASTP, gapped BLAST, and PSI-BLAST for amino acid sequences. In some embodiments, two sequences are considered to be substantially identical if at least 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more of their corresponding residues are identical over a relevant stretch of residues. In some embodiments, the relevant stretch is a complete sequence. In some embodiments, the relevant stretch is at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 125, 150, 175, 200, 225, 250, 275, 300, 325, 350, 375, 400, 425, 450, 475, 500 or more residues. In the context of a CDR, reference to “substantial identity” typically refers to a CDR having an amino acid sequence at least 70%, at least 75%, at least 80%, or at least 85% identical to that of a reference CDR.

[0109] *Therapeutic:* As used herein, the term “therapeutic” refers to a treatment and/or prophylaxis. A therapeutic effect is obtained, for example, by suppression, remission, or eradication of a disease state.

[0110] *Therapeutically effective amount:* As used herein, the term “therapeutically effective amount” means an amount of a substance (*e.g.*, a therapeutic agent, composition, and/or formulation) that elicits a desired biological response when administered as part of a therapeutic regimen. In some embodiments, a therapeutically effective amount of a substance is an amount that is sufficient, when administered to a subject suffering from or susceptible to a disease, disorder, and/or condition, to treat, diagnose, prevent, and/or delay the onset of the disease, disorder, and/or condition. As will be appreciated by those of ordinary skill in this art, an effective amount of a substance may vary depending on such factors as the desired biological endpoint, the substance to be delivered, and/or the target cell or tissue. For example, an effective amount of a bispecific antibody or antigen-binding fragment thereof in a formulation to treat a disease, disorder, or condition described herein is the amount that alleviates, ameliorates, relieves, inhibits, prevents, delays onset of, reduces severity of and/or reduces incidence of one or more symptoms or features of the disease, disorder, or condition. In some embodiments, a therapeutically effective amount is administered in a single dose. In some embodiments, multiple unit doses are required to deliver a therapeutically effective amount.

[0111] *Treat:* As used herein, the terms “treat,” “treatment,” or “treating” refer to partial or complete alleviation, amelioration, delay of onset of, inhibition, prevention, relief, and/or reduction in incidence and/or severity of one or more symptoms or features of a disease, disorder, and/or condition described herein. In some embodiments, treatment is administered to a subject who does not exhibit signs or features of a disease, disorder, and/or condition (e.g., may be prophylactic). In some embodiments, treatment is administered to a subject who exhibits early or mild signs or features of a disease, disorder, and/or condition described herein, for example to decrease a risk of developing pathology associated with a disease, disorder, and/or condition described herein. In some embodiments, treatment is administered to a subject who exhibits established, severe, and/or late-stage signs of a disease, disorder, and/or condition described herein. In some embodiments, treating comprises administering one or more bispecific antibodies or antigen-binding fragments thereof described herein to a subject.

[0112] *Tumor:* As used herein, the term “tumor” refers to an abnormal growth of cells or tissue. A tumor may comprise cells that are precancerous (e.g., benign), malignant, pre-metastatic, metastatic, and/or non-metastatic. In some embodiments, a tumor is associated with or is a manifestation of a cancer. In some embodiments, a tumor is a disperse tumor or a liquid tumor. In some embodiments, a tumor is a solid tumor.

[0113] Throughout this disclosure, various aspects can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the disclosure. Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range, such as from 1 to 6, should be considered to have specifically disclosed subranges, such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, and from 3 to 6, as well as individual numbers within that range, for example, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, and 6. This applies regardless of the breadth of the range.

DETAILED DESCRIPTION

[0114] The present disclosure, among other things, provides multispecific antibodies or antigen-binding fragments thereof that can: (i) target cancer cells by binding selectively to B7-H7, and (ii) activate immune effector cells (e.g., T cells (e.g., cytotoxic and/or helper T

cells) and/or NK cells) by binding selectively to one or more immune effector cell antigens. Accordingly, the present disclosure provides several examples of such multispecific antibodies or antigen-binding fragments thereof that are particularly useful for treating a variety of cancers, including solid tumors or hematological tumors, as well as modulating an immune response in a subject.

[0115] Multispecific antibodies and antigen-binding fragments thereof of the present disclosure can have particularly useful immunomodulatory and target cell (e.g., cancer cell) killing properties. The present disclosure encompasses the surprising finding that certain such molecules can cause the formation of a powerful immune synapse, capable of addressing disease. For example, in some embodiments, a multispecific antibody or antigen-binding fragment thereof described herein blocks an interaction of B7-H7 with TMIGD2 on an immune effector cell surface while bringing a desirable immune cell (e.g., via CD3 interaction) into close proximity to tumor cells, which results in activation of a T cell involved in the immune synapse. In some embodiments, a multispecific antibody or antigen-binding fragment thereof described herein spares an interaction of B7-H7 with TMIGD2 on an immune effector cell surface while bringing a desirable immune cell (e.g., via CD3 interaction) into close proximity to tumor cells, which results in increased activation of a T cell involved in the immune synapse compared to activation of a T cell involved in the immune synapse caused by a multispecific antibody or antigen-binding fragment thereof described herein that blocks an interaction of B7-H7 with TMIGD2.

[0116] In some embodiments, a multispecific antibody or antigen-binding fragment thereof described herein that blocks an interaction of B7-H7 with TMIGD2 on an immune effector cell surface results in reduced toxicity in non-target cells (e.g., healthy cells) relative to a multispecific antibody or antigen-binding fragment thereof described herein that spares an interaction of B7-H7 with TMIGD2.

Multispecific (e.g., Bispecific) Antibodies and Antigen-Binding Fragments Thereof

[0117] The present disclosure, among other things, provides multispecific (e.g., bispecific) antibodies or antigen-binding fragments thereof. Multispecific (e.g., Bispecific) antibodies or antigen-binding fragments thereof described herein can have specificity for at least two antigens. Bispecific antibodies or antigen-binding fragments thereof can be

characterized by a first immunoglobulin variable domain sequence that has binding specificity for a first antigen and a second immunoglobulin variable domain sequence that has binding specificity for a second antigen.

[0118] Bispecific antibodies or antigen-binding fragments thereof described herein can comprise: (i) a first antigen-binding domain that selectively binds to B7-H7, and (ii) a second antigen-binding domain that selectively binds an immune effector cell antigen (e.g., cluster of differentiation (CD3)). A first antigen-binding domain of a bispecific antibody or antigen-binding fragment thereof described herein can selectively bind to at least one epitope on B7-H7. A second antigen-binding domain of a bispecific antibody or antigen-binding fragment thereof described herein can selectively bind to at least one epitope of an immune effector cell antigen described herein.

[0119] An antigen binding domain described herein can bind to at least one immune effector cell antigen described herein. Immune effector cells can include, but are not limited to, T cells (e.g., cytotoxic or helper T cells), natural killer (NK) cells, macrophages, monocytes, dendritic cells, neutrophils, eosinophils, mast cells, platelets, large granular lymphocytes, Langerhans' cells, or B-lymphocytes. In certain embodiments, at least one immune effector cell antigen comprises or is a T cell (e.g., cytotoxic or helper T cell) antigen. In certain embodiments, at least one immune effector cell antigen comprises or is a NK cell antigen. In certain embodiments, at least one immune effector cell antigen comprises or is a macrophage antigen. In certain embodiments, at least one immune effector cell antigen comprises or is a dendritic cell antigen. In certain embodiments, at least one immune effector cell antigen comprises or is a neutrophil antigen. In certain embodiments, at least one immune effector cell antigen comprises or is an eosinophil antigen. In certain embodiments, at least one immune effector cell antigen comprises or is a mast cell antigen. In certain embodiments, at least one immune effector cell antigen comprises or is a platelet antigen. In certain embodiments, at least one immune effector cell antigen comprises or is a large granular lymphocyte antigen. In certain embodiments, at least one immune effector cell antigen comprises or is a Langerhans' cell antigen. In certain embodiments, at least one immune effector cell antigen comprises or is a B-lymphocyte cell antigen.

[0120] In some embodiments, binding of a bispecific antibody or antigen-binding fragment thereof described herein to B7-H7 and/or at least one first immune effector cell

antigen affects an interaction with at least one second immune effector cell antigen that is not the first immune effector cell antigen. In some embodiments, binding of a bispecific antibody or antigen-binding fragment thereof described herein to B7-H7 and/or at least one first immune effector cell antigen blocks an interaction with at least one second immune effector cell antigen that is not the first immune effector cell antigen. In some embodiments, binding of a bispecific antibody or antigen-binding fragment thereof described herein to B7-H7 and/or at least one first immune effector cell antigen spares an interaction with at least one second immune effector cell antigen that is not the first immune effector cell antigen.

[0121] In some embodiments, at least one immune effector cell antigen comprises or is CD3, cluster determinant 137 (4-1BB), TMIGD2 (CD28H), KIR3DL3, CD7, B7-1 (CD80), B7-2 (CD86), PD-L1, PD-L2, 4-1BBL, OX40L, inducible costimulatory ligand (ICOS-L), intercellular adhesion molecule (ICAM), CD30L, CD40, CD70, HLA-G, MICB, HVEM, lymphotoxin beta receptor, 3/TR6, ILT3, ILT4, HVEM, a Toll ligand receptor, B7-H3, CD27, CD28, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, or CD83. In certain embodiments, at least one immune effector cell antigen comprises or is CD3. In certain embodiments, at least one immune effector cell antigen comprises or is 4-1BB. In certain embodiments, at least one immune effector cell antigen comprises or is TMIGD2 (CD28H). In certain embodiments, at least one immune effector cell antigen comprises or is KIR3DL3. In certain embodiments, at least one immune effector cell antigen comprises or is CD7. In certain embodiments, at least one immune effector cell antigen comprises or is B7-1 (CD80). In certain embodiments, at least one immune effector cell antigen comprises or is B7-2 (CD86). In certain embodiments, at least one immune effector cell antigen comprises or is PD-L1. In certain embodiments, at least one immune effector cell antigen comprises or is PD-L2. In certain embodiments, at least one immune effector cell antigen comprises or is 4-1BBL. In certain embodiments, at least one immune effector cell antigen comprises or is OX40L. In certain embodiments, at least one immune effector cell antigen comprises or is ICOS-L. In certain embodiments, at least one immune effector cell antigen comprises or is ICAM. In certain embodiments, at least one immune effector cell antigen comprises or is CD30L. In certain embodiments, at least one immune effector cell antigen comprises or is CD40. In certain embodiments, at least one immune effector cell antigen comprises or is CD70. In certain embodiments, at least one immune effector cell antigen comprises or is HLA-G. In certain embodiments, at

least one immune effector cell antigen comprises or is MICB. In certain embodiments, at least one immune effector cell antigen comprises or is HVEM. In certain embodiments, at least one immune effector cell antigen comprises or is lymphotoxin beta receptor. In certain embodiments, at least one immune effector cell antigen comprises or is 3/TR6. In certain embodiments, at least one immune effector cell antigen comprises or is ILT3. In certain embodiments, at least one immune effector cell antigen comprises or is ILT4. In certain embodiments, at least one immune effector cell antigen comprises or is HVEM. In certain embodiments, at least one immune effector cell antigen comprises or is a Toll ligand receptor. In certain embodiments, at least one immune effector cell antigen comprises or is B7-H3. In certain embodiments, at least one immune effector cell antigen comprises or is CD27. In certain embodiments, at least one immune effector cell antigen comprises or is CD28. In certain embodiments, at least one immune effector cell antigen comprises or is OX40. In certain embodiments, at least one immune effector cell antigen comprises or is CD30. In certain embodiments, at least one immune effector cell antigen comprises or is CD40. In certain embodiments, at least one immune effector cell antigen comprises or is PD-1. In certain embodiments, at least one immune effector cell antigen comprises or is ICOS. In certain embodiments, at least one immune effector cell antigen comprises or is LFA-1. In certain embodiments, at least one immune effector cell antigen comprises or is CD2. In certain embodiments, at least one immune effector cell antigen comprises or is CD7. In certain embodiments, at least one immune effector cell antigen comprises or is LIGHT. In certain embodiments, at least one immune effector cell antigen comprises or is NKG2C. In certain embodiments, at least one immune effector cell antigen comprises or is CD83.

[0122] A first antigen-binding domain of a bispecific antibody or antigen-binding fragment thereof described herein can comprise or be an antibody or an antigen-binding fragment thereof. A second antigen-binding domain of a bispecific antibody or antigen-binding fragment thereof described herein can comprise or be an antibody or an antigen-binding fragment thereof. An antibody or antigen-binding fragment thereof can be any immunological binding moiety including, but not limited to, a scFv, Fab, Fab', Fab'₂, Fab₂, Fab₃, F(ab')₂, Fd, Fd', Fv, Feb, diabody, triabody, tetrabody, minibody, maxibody, tandab, DVD, BiTe, TandAb, single domain antibody (e.g., shark single domain antibody, such as IgNAR or fragments thereof), camelid antibody, full length antibody, masked antibody (e.g., Probodyes®), Small Modular ImmunoPharmaceutical (SMIPTM), single chain or Tandem

diabody (TandAb®), VHH, Anticalin®, Nanobody®, BiTE®, ankyrin repeat protein or DARPIN®, Avimer®, DART, TCR-like antibody, Adnectin®, Affilin®, Trans-body®, Affibody®, TrimerX®, MicroProtein, Fynomer®, Centyrin®, KALBITOR®, or any combination thereof.

[0123] In some embodiments, a first antigen-binding domain of a bispecific antibody or antigen-binding fragment thereof described herein comprises or is an antigen-binding fragment. In some embodiments, a second antigen-binding domain of a bispecific antibody or antigen-binding fragment thereof described herein comprises or is an antigen-binding fragment. An antigen-binding fragment can comprise or be any polypeptide or peptide-containing molecule comprising at least a portion of an immunoglobulin including at least one complementarity determining region (CDR) of a V_H or a V_L derived from any antibody, e.g., an antibody described herein. Antigen-binding fragments can be obtained using conventional techniques known to those of skill in the art, and the fragments are screened for utility in the same manner as intact antibodies. Such functional antibody fragments can retain an ability to bind selectively with B7-H7 or at least one immune effector cell antigen described herein.

[0124] Examples of antigen-binding fragments described herein can include, but are not limited to: (i) a Fab fragment, a monovalent fragment comprising V_L, V_H, CL, and CH1 domains; (ii) a F(ab')₂ fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at a hinge region; (iii) a Fd fragment comprising V_H and CH1 domains; (iv) a Fv fragment comprising V_L and V_H domains of a single arm of an antibody, (v) a diabody (dAb) fragment comprising a V_H domain; (vi) a camelid or camelized variable domain; (vii) a scFv, a fusion protein of V_H and V_L regions; (viii) a single domain antibody; or (viii) a heavy chain and a light chain (e.g., a half antibody)).

[0125] A first antigen-binding domain of a bispecific antibody or antigen-binding fragment thereof described herein can comprise or be a full length antibody, e.g., comprising an immunoglobulin Fc region. A second antigen-binding domain of a bispecific antibody or antigen-binding fragment thereof described herein can comprise or be a full length antibody, e.g., comprising an Fc region. In some embodiments, an Fc region has reduced effector function relative to a reference antibody or antigen-binding fragment thereof. In some embodiments, an Fc region comprises a modification to reduce glycosylation of the Fc region. In some embodiments, a modification comprises one or more of the following amino

acid substitutions: N297A, L234A, L235A, C220, C226S, C229S, P238S, C226S, C229S, E3233P, L234V, L235A, L234F, L235E, P331S, P329A or combinations thereof, numbering according to EU index. In some embodiments, a modification comprises one or more amino acid substitutions in the CH2 region at positions 234, 235, 237, or combinations thereof, numbering according to EU index.

[0126] An antibody or antigen-binding fragment thereof of a bispecific antibody or antigen-binding fragment thereof described herein can include a V_H and V_L domain. In some embodiments, an antibody or antigen-binding fragment thereof comprises an immunoglobulin molecule of four polypeptide chains, e.g., two heavy chains and two light chains. A heavy chain can include a V_H domain and a heavy chain constant domain. A heavy chain constant domain can include CH1, hinge, CH2, CH3, and optionally, a CH4 region. A light chain can include a V_L domain and a light chain constant domain. A light chain constant domain can include a CL domain.

[0127] A V_H and/or a V_L can be further subdivided into regions of variability, termed CDRs, interspersed with regions that are more conserved, termed framework regions (FR). Such V_H and/or V_L domains can each include three CDRs and four framework regions, arranged from amino-terminus to carboxyl-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4, one or more of which can be engineered as described herein. In general, there are three CDRs in each V_H region (HCDR1, HCDR2, and HCDR3) and three CDRs in each V_L region (LCDR1, LCDR2, and LCDR3). Framework region and CDRs can be defined using a number of well-known schemes (see, e.g., Kabat, E. A., et al. (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; Chothia, C. et al. (1987) J. Mol. Biol. 196:901-917; and the AbM definition used by Oxford Molecular's AbM antibody modeling software, each of which is hereby incorporated by reference in its entirety).

[0128] An antibody or antigen-binding fragment thereof of a bispecific antibody or antigen-binding fragment thereof described herein can be or comprise: (a) a V_H comprising one, two, or three V_H CDR sequences each with 0, 1, 2, or 3 substitutions relative to a V_H CDR in Table 1; and/or (b) a V_L comprising one, two, or three V_L CDR sequences each with 0, 1, 2, or 3 substitutions relative to a V_L CDR in Table 1.

[0129] An antibody or antigen-binding fragment thereof of a bispecific antibody or antigen-binding fragment thereof described herein can be or comprise: (a) a V_H comprising one, two, or three V_H CDR sequences each with at least about 80%, 85%, 90%, 91%, 92%,

93%, 94%, 95%, 96%, 97%, 98%, 99%, or more identity to a VH CDR in Table 1; and/or (b) a VL comprising one, two, or three VL CDR sequences each with at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more identity to a VL CDR in Table 1. In some embodiments, an antibody or antigen-binding fragment thereof described herein is or comprises: (a) a VH comprising one, two, or three VH CDR sequences each with at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity to a VH CDR of Table 1; and/or (b) a VL comprising one, two, or three VL CDR sequences each with at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity to a VL CDR of Table 1. In some embodiments, an antibody or antigen-binding fragment thereof described herein is or comprises: (a) a VH comprising one, two, or three VH CDR sequences each comprising or consisting of a VH CDR of Table 1; and/or (b) a VL comprising one, two, or three VL CDR sequences each comprising or consisting of a VL CDR of Table 1.

[0130] An antibody or antigen-binding fragment thereof of a bispecific antibody or antigen-binding fragment thereof described herein can be or comprise: (a) a VH with at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more identity to a VH in Table 1; and/or (a) a VL with at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more identity to a VL in Table 1. In some embodiments, an antibody or antigen-binding fragment thereof is or comprises: (a) a VH with at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity to a VH of Table 1; and/or (b) a VL with at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity to a VL of Table 1. In some embodiments, an antibody or antigen-binding fragment thereof is or comprises: (a) a VH comprising or consisting of a VH of Table 1; and/or (b) a VL comprising or consisting of a VL of Table 1.

[0131] An antibody or antigen-binding fragment thereof of a bispecific antibody or antigen-binding fragment thereof described herein can be or comprise: (a) a heavy chain with at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more identity to a heavy chain in Table 1; and/or (a) a light chain with at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more identity to a light chain in Table 1. In some embodiments, an antibody or antigen-binding fragment thereof is or comprises: (a) a heavy chain with at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity to a heavy chain of Table 1; and/or (b) a light chain with at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity to a

light chain of Table 1. In some embodiments, an antibody or antigen-binding fragment thereof is or comprises: (a) a heavy chain comprising or consisting of a heavy chain of Table 1; and/or (b) a light chain comprising or consisting of a light chain of Table 1.

Table 1. Amino acid and nucleotide sequences of exemplary bispecific antibody and antigen-binding fragments thereof.

Clone	Sequences	SEQ ID NO
NPXAB-1	Heavy Chain A	
	HCDR1 (IMGT) GFTFDDNA	SEQ ID NO: 1
	HCDR2 (IMGT) ISWSSNSI	SEQ ID NO: 2
	HCDR3 (IMGT) AKGSIIAGIWLGYFDL	SEQ ID NO: 3
	HCDR1 (Kabat) DNAMH	SEQ ID NO: 4
	HCDR2 (Kabat) GISWSSNSIAYADSVKG	SEQ ID NO: 5
	HCDR3 (Kabat) GSIIAGIWLGYFDL	SEQ ID NO: 6
	HCDR1 (Combined Kabat/IMGT) GFTFDDNAMH	SEQ ID NO: 7
	HCDR2 (Combined Kabat/IMGT) GISWSSNSIAYADSVKG	SEQ ID NO: 8
	HCDR3 (Combined Kabat/IMGT) GSIIAGIWLGYFDL	SEQ ID NO: 9
	VH - Amino acid sequence EVQLVESGGGLVQPGRSLRLSCAASGFTFDDNAMHWVRQAP GKGLEWVSGISWSSNSIAYADSVKGRFTISRDNKNSLYLQMN SLRAEDTAVYYCAKGSIIAGIWLGYFDLWGRGTLVTSS	SEQ ID NO: 10
	VH - DNA sequence	SEQ ID NO: 11

	GAAGTGCAGCTGGTGGAAAGCGGCGGCGCCTGGTGCAGC CGGGCCGCAGCCTGCGCCTG AGCTGCGCGGCGAGCGGCTTTACCTTTGATGATAACGCGAT GCATTGGGTGCGCCAGGCG CCGGGCAAAGGCCTGGAATGGGTGAGCGGCATTAGCTGGA GCAGCAACAGCATTGCGTAT GCGGATAGCGTGAAAGGCCGCTTTACCATTAGCCGCGATAA CGCGAAAAACAGCCTGTAT CTGCAGATGAACAGCCTGCGCGCGGAAGATACCGCGGTGTA TTATTGCGCGAAAGGCAGC ATTATTGCGGGCATTGCTGGGCTATTTTGATCTGTGGGGC CGCGGCACCCTGGTGACC GTGAGCAGC	
	Heavy chain - Amino acid sequence EVQLVESGGGLVQPGRSLRLSCAASGFTFDDNAMHWVRQAP GKGLEWVSGISWSSNSIAYADSVKGRFTISRDNKNSLYLQMN SLRAEDTAVYYCAKGSIIAGIWLGYFDLWGRGTLVTVSSASTK GPSVFPRAPSSKSTSGGTAALGCLVRDYFPEPVTVSWNSGALT SGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSN TKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKT ISKAKQPREPVCTLPSPRDELTKNQVSLSLVKGFPYPSDIAV EWESNGQPENNYKTTTPVLDSDGSFFLGSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPG	SEQ ID NO: 12
	Heavy chain - DNA sequence GAAGTGCAGCTGGTGGAAAGCGGCGGCGCCTGGTGCAGC CGGGCCGCAGCCTGCGCCTG AGCTGCGCGGCGAGCGGCTTTACCTTTGATGATAACGCGAT GCATTGGGTGCGCCAGGCG CCGGGCAAAGGCCTGGAATGGGTGAGCGGCATTAGCTGGA GCAGCAACAGCATTGCGTAT GCGGATAGCGTGAAAGGCCGCTTTACCATTAGCCGCGATAA CGCGAAAAACAGCCTGTAT CTGCAGATGAACAGCCTGCGCGCGGAAGATACCGCGGTGTA TTATTGCGCGAAAGGCAGC ATTATTGCGGGCATTGCTGGGCTATTTTGATCTGTGGGGC CGCGGCACCCTGGTGACC GTGAGCAGCGCGAGCACCAAAGGCCCGAGCGTGTTTCCGCG CGCGCCGAGCAGCAAAAGC ACGAGCGGCGGCACCGCGCGCTGGGCTGCCTGGTGCGCGA TTATTTTCCGGAACCGGTG ACCGTGAGCTGGAACAGCGGCGCGCTGACCAGCGGCGTGC ATACCTTTCCGGCGGTGCTG CAGAGCAGCGGCCTGTATAGCCTGAGCAGCGTGGTGACCGT GCCGAGCAGCAGCCTGGGC	SEQ ID NO: 13

ACCCAGACCTATATTTGCAACGTGAACCATAAACCGAGCAA CACCAAAGTGGATAAAAAA GTGGAACCGAAAAGCTGCGATAAAACCCATACCTGCCCGCC GTGCCCCGGCGCCGGAAGCG GCGGGCGGCCCCGAGCGTGTCTGTTTCCGCCGAAACCGAA AGATACCCTGATGATTAGC CGCACCCCGGAAGTGACCTGCGTGGTGGTGGATGTGAGCCA TGAAGATCCGGAAGTGAAA TTTAACTGGTATGTGGATGGCGTGGAAGTGCATAACGCGAA AACCAAACCGCGCGAAGAA CAGTATAACAGCACCTATCGCGTGGTGAGCGTGCTGACCGT GCTGCATCAGGATTGGCTG AACGGCAAAGAATATAAATGCAAAGTGAGCAACAAAGCGC TGGCGGCGCCGATTGAAAAA ACCATTAGCAAAGCGAAAGGCCAGCCGCGCGAACC GCAGG TGTGCACCCTGCCGCCGAGC CGCGATGAACTGACCAAAAAACCAGGTGAGCCTGAGCTGCCT GGTGAAAGGCTTTTATCCG AGCGATATTGCGGTGGAATGGGAAAGCAACGGCCAGCCGG AAAACAACCTATAAAACCACC CCGCCGGTGCTGGATAGCGATGGCAGCTTTTTTCTGGGCAG CAAACCTGACCGTGGATAAA AGCCGCTGGCAGCAGGGCAACGTGTTTAGCTGCAGCGTGAT GCATGAAGCGCTGCATAAC CATTATACCCAGAAAAGCCTGAGCCTGAGCCCCGGGC	
Heavy Chain B – B7-H7 binding Fab arm	
HCDR1 (IMGT) GFTFDDNA	SEQ ID NO: 14
HCDR2 (IMGT) ISWSSNSI	SEQ ID NO: 15
HCDR3 (IMGT) AKGSIIAGIWLGYFDL	SEQ ID NO: 16
HCDR1 (Kabat) DNAMH	SEQ ID NO: 17
HCDR2 (Kabat) GISWSSNSIAYADSVKG	SEQ ID NO: 18
HCDR3 (Kabat) GSIIAGIWLGYFDL	SEQ ID NO: 19
HCDR1 (Combined Kabat/IMGT) GFTFDDNAMH	SEQ ID NO: 20
HCDR2 (Combined Kabat/IMGT)	SEQ ID NO: 21

GISWSSNSIAYADSVKG	
HCDR3 (Combined Kabat/IMGT)	SEQ ID NO: 22
GSIIAGIWLGYFDL	
VH - Amino acid sequence	SEQ ID NO: 23
EVQLVESGGGLVQPGRSLRLSCAASGFTFDDNAMHWVRQAP GKGLEWVSGISWSSNSIAYADSVKGRFTISRDNKNSLYLQMN SLRAEDTAVYYCAKGSIIAGIWLGYFDLWGRGTLVTVSS	
VH - DNA sequence	SEQ ID NO: 24
GAAGTGCAGCTGGTGGAAAGCGGCGGCGGCCTGGTGCAGC CGGGCCGAGCCTGCGCCTG AGCTGCGCGGCGAGCGGCTTTACCTTTGATGATAACGCGAT GCATTGGGTGCGCCAGGCG CCGGGCAAAGGCCTGGAATGGGTGAGCGGCATTAGCTGGA GCAGCAACAGCATTGCGTAT GCGGATAGCGTGAAAGGCCGCTTTACCATTAGCCGCGATAA CGCGAAAAACAGCCTGTAT CTGCAGATGAACAGCCTGCGCGCGGAAGATACCGCGGTGTA TTATTGCGCGAAAGGCAGC ATTATTGCGGGCATTGCTGGGCTATTTTATCTGTGGGGC CGCGGCACCCTGGTGACC GTGAGCAGC	
Heavy chain (Fab arm) - Amino acid sequence	SEQ ID NO: 25
EVQLVESGGGLVQPGRSLRLSCAASGFTFDDNAMHWVRQAP GKGLEWVSGISWSSNSIAYADSVKGRFTISRDNKNSLYLQMN SLRAEDTAVYYCAKGSIIAGIWLGYFDLWGRGTLVTVSSASTK GPSVFPRAPSSKSTSGGTAALGCLVRDYFPEPVTVSWNSGALT SGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSN TKVDKKVEPKSCD	
Heavy chain (Fab arm) - DNA sequence	SEQ ID NO: 26
GAAGTGCAGCTGGTGGAAAGCGGCGGCGGCCTGGTGCAGC CGGGCCGAGCCTGCGCCTG AGCTGCGCGGCGAGCGGCTTTACCTTTGATGATAACGCGAT GCATTGGGTGCGCCAGGCG CCGGGCAAAGGCCTGGAATGGGTGAGCGGCATTAGCTGGA GCAGCAACAGCATTGCGTAT GCGGATAGCGTGAAAGGCCGCTTTACCATTAGCCGCGATAA CGCGAAAAACAGCCTGTAT CTGCAGATGAACAGCCTGCGCGCGGAAGATACCGCGGTGTA TTATTGCGCGAAAGGCAGC ATTATTGCGGGCATTGCTGGGCTATTTTATCTGTGGGGC CGCGGCACCCTGGTGACC GTGAGCAGCGCGAGCACCAAGGCCCGAGCGTGTTCGCGC CGCGCCGAGCAGCAAAAGC	

ACCAGCGGCGGCACCGCGGCGCTGGGCTGCCTGGTGCGCGA TTATTTTCCGGAACCGGTG ACCGTGAGCTGGAACAGCGGCGCGCTGACCAGCGGCGTGC ATACCTTCCGCGCGGTGCTG CAGAGCAGCGGCCTGTATAGCCTGAGCAGCGTGGTGACCGT GCCGAGCAGCAGCCTGGGC ACCCAGACCTATATTTGCAACGTGAACCATAAACCGAGCAA CACCAAAGTGGATAAAAAA GTGGAACCGAAAAGCTGCGAT	
Linker	SEQ ID NO: 27
GGGGS	
Heavy Chain B – CD3 binding Fab arm + Fc	
HCDR1 (IMGT)	SEQ ID NO: 28
GFNIKDY	
HCDR2 (IMGT)	SEQ ID NO: 29
IDLENANT	
HCDR3 (IMGT)	SEQ ID NO: 30
ARDAYGRYFYDV	
HCDR1 (Kabat)	SEQ ID NO: 31
DYYMH	
HCDR2 (Kabat)	SEQ ID NO: 32
WIDLENANTIYDAKFQG	
HCDR3 (Kabat)	SEQ ID NO: 33
DAYGRYFYDV	
HCDR1 (Combined Kabat/IMGT)	SEQ ID NO: 34
GFNIKDYMH	
HCDR2 (Combined Kabat/IMGT)	SEQ ID NO: 35
WIDLENANTIYDAKFQG	
HCDR3 (Combined Kabat/IMGT)	SEQ ID NO: 36
DAYGRYFYDV	
VH - Amino acid sequence	SEQ ID NO: 37
QVQLVQSGAEVKKPGASVKVSCKASGFNIKDYMHVVRQAP GQRLEWMGWIDLENANTIYDAKFQGRVTITRDTASTAYMEL SSLRSEDVAVYYCARDAYGRYFYDVWGQGLTVSS	
VH - DNA sequence	SEQ ID NO: 38

	CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTTTAACATTAAAGATTATTATAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCTGGATTGATCTGGA AAACGCGAACACCATTTAT GATGCGAAATTTTCAGGGCCGCGTGACCATTACCCGCGATAC CAGCGCGAGCACC GCGTAT ATGGAAGTGCAGCCTGCGCAGCGAAGATAACCGCGGTGT ATTATTGCGCGCGCGATGCG TATGGCCGCTATTTTTATGATGTGTGGGGCCAGGGCACCT GGTGACCGTGAGCAGC	
	Heavy chain (Fab arm + Fc) - Amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGFNIKDYIMHWVRQAP GQRLEWMGWIDLENANTIYDAKFQGRVTITRDTASTAYMEL SSLRSEDVAVYYCARDAYGRYFYDVWGQGLVTVSSASTKGP SVFPLAPSSKSTSGGTAALGCQVEDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYELSSVTVPSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTIS KAKGQPREPQVYTLPPCRDELTKNQVSLWCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMEALHNHYTQKSLSLSPG	SEQ ID NO: 39
	Heavy chain (Fab arm + Fc) - DNA sequence CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTTTAACATTAAAGATTATTATAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCTGGATTGATCTGGA AAACGCGAACACCATTTAT GATGCGAAATTTTCAGGGCCGCGTGACCATTACCCGCGATAC CAGCGCGAGCACC GCGTAT ATGGAAGTGCAGCCTGCGCAGCGAAGATAACCGCGGTGT ATTATTGCGCGCGCGATGCG TATGGCCGCTATTTTTATGATGTGTGGGGCCAGGGCACCT GGTGACCGTGAGCAGCGCG AGCACCAAAGGCCCGAGCGTGTTTCCGCTGGCGCCGAGCAG CAAAAGCACCAGCGGCGGC ACCGCGCGCTGGGCTGCCAGGTGGAAGATTATTTTCCGGA ACCGGTGACCGTGAGCTGG AACAGCGGCGCGCTGACCAGCGGCGTGATACCTTTCCGGC GGTGCTGCAGAGCAGCGGC CTGTATGAACTGAGCAGCGTGGTGACCGTGCCGAGCAGCAG CCTGGGCACCCAGACCTAT ATTTGCAACGTGAACCATAAACCGAGCAACACCAAAGTGG ATAAAAAAGTGGAACCGAAA	SEQ ID NO: 40

	AGCTGCGATAAAACCCATACCTGCCCCCGGTGCCCCGGCGCC GGAAGCGGCGGGCGGCCCG AGCGTGTTTCTGTTTCCGCCGAAACCGAAAGATACCCTGAT GATTAGCCGCACCCCGGAA GTGACCTGCGTGGTGGTGGATGTGAGCCATGAAGATCCGGA AGTGAAATTTAACTGGTAT GTGGATGGCGTGGAAGTGCATAACGCGAAAACCAAACCGC GCGAAGAACAGTATAACAGC ACCTATCGCGTGGTGAAGCGTGCTGACCGTGCTGCATCAGGA TTGGCTGAACGGCAAAGAA TATAAATGCAAAGTGAGCAACAAAGCGCTGGCGGGCGCCGA TTGAAAAAACCATTAGCAAA GCGAAAGGCCAGCCGCGCGAACCGCAGGTGTATACCCTGCC GCCGTGCCGCGATGAACTG ACCAAAAACCAAGGTGAGCCTGTGGTGCCTGGTGAAAGGCTT TTATCCGAGCGATATTGCG GTGGAATGGGAAAGCAACGGCCAGCCGAAAAACAACATA AAACCACCCCGCCGGTGCTG GATAGCGATGGCAGCTTTTTTCTGTATAGCAAACCTGACCGT GGATAAAAGCCGCTGGCAG CAGGGCAACGTGTTTAGCTGCAGCGTGATGCATGAAGCGCT GCATAACCATTATACCCAG AAAAGCCTGAGCCTGAGCCCGGGC	
	Heavy chain (Full chain) - Amino acid sequence EVQLVESGGGLVQPGRSLRLSCAASGFTFDDNAMHWVRQAP GKGLEWVSGISWSSNSIAYADSVKGRFTISRDNKNSLYLQMN SLRAEDTAVYYCAKGSIIAGIWLGYFDLWGRGTLVTVSSASTK GPSVFPRAPSSKSTSGGTAALGCLVRDYFPEPVTVSWNSGALT SGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHNKPSN TKVDKKVEPKSCDGGGSGGGGSQVQLVQSGAEVKKPGASV KVSKASGFNIKDYMHWRQAPGQRLEWMGWIDLENANTI YDAKFQGRVTITRDTASTAYMELSSLRSEDVAVYYCARDAY GRYFYDVWGQGTTLVTVSSASTKGPSVFPLAPSSKSTSGGTAAL GCQVEDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYELSSV VTVPSSSLGTQTYICNVNHNKPSNTKVDKKVEPKSCDKTHTCPP CPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPCR DELTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTPPV LDSGDSFELYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQK SLSLSPG	SEQ ID NO: 41
	Heavy chain (Full chain) - DNA sequence GAAGTGCAGCTGGTGGAAAGCGGCGGCGGCCTGGTGCAGC CGGGCCGCAGCCTGCGCCTG AGCTGCGCGGCGAGCGGCTTTACCTTTGATGATAACGCGAT GCATTGGGTGCGCCAGGCG	SEQ ID NO: 42

CCGGGCAAAGGCCTGGAATGGGTGAGCGGCATTAGCTGGA GCAGCAACAGCATTGCGTAT GCGGATAGCGTGAAAGGCCGCTTTACCATTAGCCGCGATAA CGCGAAAAACAGCCTGTAT CTGCAGATGAACAGCCTGCGCGCGGAAGATACCGCGGTGTA TTATTGCGCGAAAGGCAGC ATTATTGCGGGCATTGCTGGGCTATTTTGATCTGTGGGGC CGCGGCACCCTGGTGACC GTGAGCAGCGCGAGCACCAAAGGCCCGAGCGTGTTCCGCG CGCGCCGAGCAGCAAAAGC ACCAGCGGCGGCACCGCGGCGCTGGGCTGCCTGGTGCGCGA TTATTTTCCGGAACCGGTG ACCGTGAGCTGGAACAGCGGCGCGCTGACCAGCGGCGTGC ATACCTTTCCGGCGGTGCTG CAGAGCAGCGGCTGTATAGCCTGAGCAGCGTGGTGACCGT GCCGAGCAGCAGCCTGGGC ACCCAGACCTATATTTGCAACGTGAACCATAAACCGAGCAA CACCAAAGTGGATAAAAAA GTGGAACCGAAAAGCTGCGATGGCGGCGGCGGCAGCGGCG GCGGCGGCAGCCAGGTGCAG CTGGTGAGAGCGGCGCGGAAGTGAAAAAACCGGGCGCGA GCGTGAAAGTGAGCTGCAAA GCGAGCGGCTTTAACATTAAAGATTATTATATGCATTGGGT GCGCCAGGCGCCGGGCCAG CGCCTGGAATGGATGGGCTGGATTGATCTGGAAAACGCGAA CACCATTTATGATGCGAAA TTTCAGGGCCGCGTGACCATTACCCGCGATACCAGCGCGAG CACCGCGTATATGGAAGT AGCAGCCTGCGCAGCGAAGATACCGCGGTGTATTATTGCGC GCGCGATGCGTATGGCCGC TATTTTATGATGTGTGGGGCCAGGGCACCTGGTGACCGT GAGCAGCGCGAGCACCAA GGCCCGAGCGTGTTCCGCTGGCGCCGAGCAGCAAAAGCAC CAGCGGCGGCACCGCGGCG CTGGGCTGCCAGGTGGAAGATTATTTCCGGAACCGGTGAC CGTGAGCTGGAACAGCGGC GCGCTGACCAGCGGCGTGCATACCTTTCCGGCGGTGCTGCA GAGCAGCGGCCTGTATGAA CTGAGCAGCGTGGTGACCGTGCCGAGCAGCAGCCTGGGCAC CCAGACCTATATTTGCAAC GTGAACCATAAACCGAGCAACACCAAAGTGGATAAAAAAG TGGAACCGAAAAGCTGCGAT AAAACCCATACCTGCCC GCCGTGCCCGGCGCCGGAAGCGGC GGGCGGCCCCGAGCGTGTTT CTGTTTCCGCCGAAACCGAAAGATACCCTGATGATTAGCCG CACCCCGGAAGTGACCTGC GTGGTGGTGGATGTGAGCCATGAAGATCCGGAAGTGAAATT TAACTGGTATGTGGATGGC	
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GTGGAAGTGCATAACGCGAAAAACCAACCGCGCGAAGAAC AGTATAACAGCACCTATCGC GTGGTGAGCGTGCTGACCGTGCTGCATCAGGATTGGCTGAA CGGCAAAGAATATAAATGC AAAGTGAGCAACAAAGCGCTGGCGGCGCCGATTGAAAAA CCATTAGCAAAGCGAAAGGC CAGCCGCGCGAACCGCAGGTGTATACCCTGCCGCGTGCCG CGATGAACTGACCAAAAAC CAGGTGAGCCTGTGGTGCCTGGTGAAAGGCTTTTATCCGAG CGATATTGCGGTGGAATGG GAAAGCAACGGCCAGCCGGAACAACACTATAAAACCACCC CGCCGGTGCTGGATAGCGAT GGCAGCTTTTTTCTGTATAGCAAACCTGACCGTGGATAAAAG CCGCTGGCAGCAGGGCAAC GTGTTTAGCTGCAGCGTGATGCATGAAGCGCTGCATAACCA TTATACCCAGAAAAGCCTG AGCCTGAGCCCGGGC	
Light Chain A	
LCDR1 (IMGT) QSVSSY	SEQ ID NO: 43
LCDR2 (IMGT) DA	SEQ ID NO: 44
LCDR3 (IMGT) QQVSISPPWT	SEQ ID NO: 45
LCDR1 (Kabat) RASQSVSSYLA	SEQ ID NO: 46
LCDR2 (Kabat) DASNRAT	SEQ ID NO: 47
LCDR3 (Kabat) QQVSISPPWT	SEQ ID NO: 48
LCDR1 (Combined Kabat/IMGT) RASQSVSSYLA	SEQ ID NO: 49
LCDR2 (Combined Kabat/IMGT) DASNRAT	SEQ ID NO: 50
LCDR3 (Combined Kabat/IMGT) QQVSISPPWT	SEQ ID NO: 51
VL - Amino acid sequence	SEQ ID NO: 52

	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAP RLLIYDASNRATGIPARFSGSGSGTDFTLTISSELPEDFAVYYCQ QVSISPPWTFGGGTKVEIK	
	VL - DNA sequence GAAATTGTGCTGACCCAGAGCCCGGCGACCCTGAGCCTGAG CCCGGGCGAACGCGCGACC CTGAGCTGCCGCGCGAGCCAGAGCGTGAGCAGCTATCTGGC GTGGTATCAGCAGAAACCG GGCCAGGCGCCGCGCCTGCTGATTTATGATGCGAGCAACCG CGCGACCGGCATTCCGGCG CGCTTTAGCGGCAGCGGCAGCGGCACCGATTTTACCCTGAC CATTAGCAGCCTGGAACCG GAAGATTTTGCAGGTGTATTATTGCCAGCAGGTGAGCATTAG CCCGCCGTGGACCTTTGGC GGCGGCACCAAAGTGGAATTTAAA	SEQ ID NO: 53
	Light chain - Amino acid sequence EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAP RLLIYDASNRATGIPARFSGSGSGTDFTLTISSELPEDFAVYYCQ QVSISPPWTFGGGTKVEIKRTVAAPSVFIFPPSDEELKSGTASVQ CLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLS SSELTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 54
	Light chain - DNA sequence GAAATTGTGCTGACCCAGAGCCCGGCGACCCTGAGCCTGAG CCCGGGCGAACGCGCGACC CTGAGCTGCCGCGCGAGCCAGAGCGTGAGCAGCTATCTGGC GTGGTATCAGCAGAAACCG GGCCAGGCGCCGCGCCTGCTGATTTATGATGCGAGCAACCG CGCGACCGGCATTCCGGCG CGCTTTAGCGGCAGCGGCAGCGGCACCGATTTTACCCTGAC CATTAGCAGCCTGGAACCG GAAGATTTTGCAGGTGTATTATTGCCAGCAGGTGAGCATTAG CCCGCCGTGGACCTTTGGC GGCGGCACCAAAGTGGAATTTAAACGCACCGTGCGGCGC CGAGCGTGTTTATTTTCCG CCGAGCGATGAAGAACTGAAAAGCGGCACCGCGAGCGTGC AGTGCCTGCTGAACAACTTT TATCCGCGCGAAGCGAAAGTGCAAGTGGAAGTGGAACG CGCTGCAGAGCGGCAACAGC CAGGAAAGCGTGACCGAACAGGATAGCAAAGATAGCACCT ATAGCCTGAGCAGCGAACTG ACCCTGAGCAAAGCGGATTATGAAAAACATAAAGTGATGC GTGCGAAGTGACCCATCAG GGCCTGAGCAGCCCGGTGACCAAAGCTTTAACCGCGGCGA ATGC	SEQ ID NO: 55
	Light Chain B	

LCDR1 (IMGT)	SEQ ID NO: 56
QSLLNARTGKNY	
LCDR2 (IMGT)	SEQ ID NO: 57
WA	
LCDR3 (IMGT)	SEQ ID NO: 58
KQSYSRRT	
LCDR1 (Kabat)	SEQ ID NO: 59
KSSQSLLNARTGKNYLA	
LCDR2 (Kabat)	SEQ ID NO: 60
WASTRES	
LCDR3 (Kabat)	SEQ ID NO: 61
KQSYSRRT	
LCDR1 (Combined Kabat/IMGT)	SEQ ID NO: 62
KSSQSLLNARTGKNYLA	
LCDR2 (Combined Kabat/IMGT)	SEQ ID NO: 63
WASTRES	
LCDR3 (Combined Kabat/IMGT)	SEQ ID NO: 64
KQSYSRRT	
VL - Amino acid sequence	SEQ ID NO: 65
DIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKNYLAWYQ QKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAE DVAVYYCKQSYSRRTFGGGTKVEIK	
VL - DNA sequence	SEQ ID NO: 66
GATATTGTGATGACCCAGAGCCCGGATAGCCTGGCGGTGAG CCTGGGCGAACGCGCGACC ATTAAGTGCAAAAGCAGCCAGAGCCTGCTGAACGCGCGCAC CGGCAAAAACCTATCTGGCG TGGTATCAGCAGAAACCGGGCCAGCCGCCGAAACTGCTGAT TTATTGGGCGAGCACCCGC GAAAGCGGCGTGCCGGATCGCTTTAGCGGCAGCGGCAGCG GCACCGATTTTACCCTGACC ATTAGCAGCCTGCAGGCGGAAGATGTGGCGGTGTATTATTG CAAACAGAGCTATAGCCGC CGCACCTTTGGCGGCGGCACCAAAGTGGAATTAAA	
Light chain - Amino acid sequence	SEQ ID NO: 67
DIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKNYLAWYQ QKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAE	

	DVAVYYCKQSYSRRFTGGGKVEIKRTVAAPSVFIFPPSDEQLKSGRASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSSRLQLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	
	Light chain - DNA sequence GATATTGTGATGACCCAGAGCCCGGATAGCCTGGCGGTGAGCCTGGGCGAACGCGCGACC ATTAAGTGCAGAAAGCAGCCAGAGCCTGCTGAACGCGCGCACCGGCAAAAACCTATCTGGCG TGGTATCAGCAGAAACCGGGCCAGCCGCCGAAACTGCTGATTATTGGGCGAGCACCCGC GAAAGCGGCGTGCCGGATCGCTTTAGCGGCAGCGGCAGCGGCACCGATTTTACCCTGACC ATTAGCAGCCTGCAGGCGGAAGATGTGGCGGTGTATTATTGCAACAGAGCTATAGCCGC CGCACCTTTGGCGGCGGCACCAAAGTGGAATTAAACGCACCGTGCGGCGCCGAGCGTG TTTATTTTCCGCCGAGCGATGAACAGCTGAAAAGCGGCCGCGAGCGTGGTGTGCCTG CTGAACAACCTTTATCCGCGCGAAGCGAAAGTGCAGTGGAAGTGATAACGCGCTGCAG AGCGGCAACAGCCAGGAAAGCGTGACCGAACAGGATAGCAAGATAGCACCTATAGCCTG AGCAGCCGCTGCAGCTGAGCAAAGCGGATTATGAAAAACATAAAGTGTATGCGTGCGAA GTGACCCATCAGGGCCTGAGCAGCCCGGTGACCAAAAGCTTAACCGCGGCGAATGC	SEQ ID NO: 68
Clone	Sequences	SEQ ID NO
NPXAB-2	Heavy Chain A	
	HCDR1 (IMGT)	SEQ ID NO: 69
	GYTFEQYA	
	HCDR2 (IMGT)	SEQ ID NO: 70
	IPAGTGNT	
	HCDR3 (IMGT)	SEQ ID NO: 71
	ARDRGGYWYDSWDD	
	HCDR1 (Kabat)	SEQ ID NO: 72
	QYAMH	
	HCDR2 (Kabat)	SEQ ID NO: 73
	FIPAGTGNTKYSQKFQG	
	HCDR3 (Kabat)	SEQ ID NO: 74
	DRGGYWYDSWDD	

HCDR1 (Combined Kabat/IMGT)	SEQ ID NO: 75
GYTFEQYAMH	
HCDR2 (Combined Kabat/IMGT)	SEQ ID NO: 76
FIPAGTGNTKYSQKFQG	
HCDR3 (Combined Kabat/IMGT)	SEQ ID NO: 77
DRGGYWYDSWDD	
VH - Amino acid sequence	SEQ ID NO: 78
QVQLVQSGAEVKKPGASVKVSCKASGYTFEQYAMHWVRQAP GQRLEWMGFIPAGTGNTKYSQKFQGRVTITRDTSASTAYMEL SSLRSEDVAVYYCARDRGGYWYDSWDDWGQGLTVTVSS	
VH - DNA sequence	SEQ ID NO: 79
CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTATACCTTTGAACAGTATGCGAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCTTTATCCGGCGGG CACCGGCAACACCAAATAT AGCCAGAAATTTACGGGCGCGTGACCATTACCCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGAAGCAGCCTGCGCAGCGAAGATACCGCGGTGT ATTATTGCGCGCGCGATCGC GGCGGCTATTGGTATGATAGCTGGGATGATTGGGGCCAGGG CACCTGGTGACCGTGAGC AGC	
Heavy chain - Amino acid sequence	SEQ ID NO: 80
QVQLVQSGAEVKKPGASVKVSCKASGYTFEQYAMHWVRQAP GQRLEWMGFIPAGTGNTKYSQKFQGRVTITRDTSASTAYMEL SSLRSEDVAVYYCARDRGGYWYDSWDDWGQGLTVTVSSAST KGPSVFPRAPSSKSTSGGTAALGCLVRDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEK TISKAKGQPREPQVCTLPSSRDELTKNQVSLVKGFPYPSDIA VEWESNGQPENNYKTTTPVLDSDGSFFLGSKLTVDKSRWQQG NVFSCSVMEALHNHYTQKSLSLSPG	

	Heavy chain - DNA sequence CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTATACCTTTGAACAGTATGCGAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCTTTATTCCGGCGGG CACCGGCAACACCAAATAT AGCCAGAAATTTTCAGGGCCGCGTGACCATTACCCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGCAGCCTGCGCAGCGAAGATACCGCGGTGT ATTATTGCGCGCGCGATCGC GGCGGCTATTGGTATGATAGCTGGGATGATTGGGGCCAGGG CACCTTGGTGACCGTGAGC AGCGCGAGCACCAAAGGCCCGAGCGTGTTCGCGCGCGCC GAGCAGCAAAAGCACACG GGCGGCACCGCGGCGCTGGGCTGCCTGGTGCGCGATTATTT TCCGGAACCGGTGACCGTG AGCTGGAACAGCGGCGCGCTGACCAGCGGCGTGACATACCTT TCCGGCGGTGCTGCAGAGC AGCGGCCTGTATAGCCTGAGCAGCGTGGTGACCGTGCCGAG CAGCAGCCTGGGCACCCAG ACCTATATTTGCAACGTGAACCATAAACCGAGCAACACCAA AGTGGATAAAAAAGTGGA CCGAAAAGCTGCGATAAAACCCATACCTGCCCCGCGTGCCC GGCGCCGGAAGCGGCGGGC GGCCCGAGCGTGTCTGTCTTCGCGGAAACCGAAAGATAC CCTGATGATTAGCCGCACC CCGGAAGTGACCTGCGTGGTGGTGGATGTGAGCCATGAAGA TCCGGAAGTGAAATTTAAC TGGTATGTGGATGGCGTGGAAGTGCATAACGCGAAAACCA AACCGCGCAAGAACAGTAT AACAGCACCTATCGCGTGGTGAGCGTGCTGACCGTGCTGCA TCAGGATTGGCTGAACGGC AAAGAATATAAATGCAAAGTGAGCAACAAAGCGCTGGCGG CGCCGATTGAAAAAACCAT AGCAAAGCGAAAGGCCAGCCGCGGAACCGCAGGTGTGCA CCCTGCCGCCGAGCCGCGAT GAACTGACCAAAAACAGGTGAGCCTGAGCTGCCTGGTGA AAGGCTTTTATCCGAGCGAT ATTGCGGTGGAATGGGAAAGCAACGGCCAGCCGGAAAACA ACTATAAAACCAACCCCGCCG GTGCTGGATAGCGATGGCAGCTTTTTCTGGGCAGCAAAC GACCGTGGATAAAAGCCGC TGGCAGCAGGGCAACGTGTTTAGCTGCAGCGTGATGCATGA AGCGCTGCATAACCATAT ACCCAGAAAAGCCTGAGCCTGAGCCCGGGC	SEQ ID NO: 81
	Heavy Chain B – B7-H7 binding Fab arm	

HCDR1 (IMGT)	SEQ ID NO: 82
GYTFEQYA	
HCDR2 (IMGT)	SEQ ID NO: 83
IPAGTGNT	
HCDR3 (IMGT)	SEQ ID NO: 84
ARDRGGYWYDSWDD	
HCDR1 (Kabat)	SEQ ID NO: 85
QYAMH	
HCDR2 (Kabat)	SEQ ID NO: 86
FIPAGTGNTKYSQKFQG	
HCDR3 (Kabat)	SEQ ID NO: 87
DRGGYWYDSWDD	
HCDR1 (Combined Kabat/IMGT)	SEQ ID NO: 88
GYTFEQYAMH	
HCDR2 (Combined Kabat/IMGT)	SEQ ID NO: 89
FIPAGTGNTKYSQKFQG	
HCDR3 (Combined Kabat/IMGT)	SEQ ID NO: 90
DRGGYWYDSWDD	
VH - Amino acid sequence	SEQ ID NO: 91
QVQLVQSGAEVKKPGASVKVSCKASGYTFEQYAMHWVRQAP GQRLEWMGFIPAGTGNTKYSQKFQGRVTITRDTSASTAYMEL SSLRSEDTAVYYCARDRGYWYDSWDDWGQGLTVTVSS	
VH - DNA sequence	SEQ ID NO: 92
CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTATACCTTTGAACAGTATGCGAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCTTTATCCGGCGGG CACCGGCAACACCAAATAT AGCCAGAAATTCAGGGCCGCGTGACCATTACCCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGCAGCCTGCGCAGCGAAGATACCGCGGTGT ATTATTGCGCGCGCGATCGC GGCGGCTATTGGTATGATAGCTGGGATGATTGGGGCCAGGG CACCTGGTGACCGTGAGC AGC	
Heavy chain (Fab arm) - Amino acid sequence	SEQ ID NO: 93

QVQLVQSGAEVKKPGASVKVSCKASGYTFEQYAMHWVRQAP GQRLEWMGFIPAGTGNTKYSQKFQGRVTITRDTASTAYMEL SSLRSEDVAVYYCARDRGGYWYDSWDDWGQGLTVTVSSAST KGPSVFPAPSSKSTSGGTAALGCLVRDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKVEPKSCD	
Heavy chain (Fab arm) - DNA sequence CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTATACCTTTGAACAGTATGCGAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCTTTATTCGGGCGGG CACCGGCAACACCAAATAT AGCCAGAAATTTAGGGCCGCGTGACCATTACCCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGAAGCAGCCTGCGCAGCGAAGATACCGCGGTGT ATTATTGCGCGCGCGATCGC GGCGGCTATTGGTATGATAGCTGGGATGATTGGGGCCAGGG CACCTGGTGACCGTGAGC AGCGCGAGCACCAAAGGCCCGAGCGTGTTCGCGCGCGCC GAGCAGCAAAAGCACCAAGC GGCGGCACCGCGGCGCTGGGCTGCCTGGTGCGCGATTATTT TCCGGAACCGGTGACCGTG AGCTGGAACAGCGGCGCGCTGACCAGCGGCGTGATACCTT TCCGGCGGTGCTGCAGAGC AGCGGCCTGTATAGCCTGAGCAGCGTGGTGACCGTGCCGAG CAGCAGCCTGGGCACCCAG ACCTATATTTGCAACGTGAACCATAAACCGAGCAACACCAA AGTGGATAAAAAAGTGGA CCGAAAAGCTGCGAT	SEQ ID NO: 94
Linker GGGSGGGGS	SEQ ID NO: 95
Heavy Chain B – CD3 binding Fab arm + Fc	
HCDR1 (IMGT) GFNIKDY	SEQ ID NO: 96
HCDR2 (IMGT) IDLENANT	SEQ ID NO: 97
HCDR3 (IMGT) ARDAYGRYFYDV	SEQ ID NO: 98
HCDR1 (Kabat) DYMH	SEQ ID NO: 99
HCDR2 (Kabat)	SEQ ID NO: 100

WIDLENANTIYDAKFQG	
HCDR3 (Kabat) DAYGRYFYDV	SEQ ID NO: 101
HCDR1 (Combined Kabat/IMGT) GFNIKDYMH	SEQ ID NO: 102
HCDR2 (Combined Kabat/IMGT) WIDLENANTIYDAKFQG	SEQ ID NO: 103
HCDR3 (Combined Kabat/IMGT) DAYGRYFYDV	SEQ ID NO: 104
VH - Amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGFNIKDYMHWRQAP GQRLEWMGWIDLENANTIYDAKFQGRVTITRDTSASTAYMEL SSLRSEDVAVYYCARDAYGRYFYDVWGQGTLLTVSS	SEQ ID NO: 105
VH - DNA sequence CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTTTAACATTAAAGATTATTATAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCTGGATTGATCTGGA AAACGCGAACACCATTTAT GATGCGAAATTTTCAGGGCCGCGTGACCATTACCCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGAAGCAGCCTGCGCAGCGAAGATACCGCGGTGT ATTATTGCGCGCGCGATGCG TATGGCCGCTATTTTATGATGTGTGGGGCCAGGGCACCCCT GGTGACCGTGAGCAGC	SEQ ID NO: 106
Heavy chain (Fab arm + Fc) - Amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGFNIKDYMHWRQAP GQRLEWMGWIDLENANTIYDAKFQGRVTITRDTSASTAYMEL SSLRSEDVAVYYCARDAYGRYFYDVWGQGTLLTVSSASTKGP SVFPLAPSSKSTSGGTAALGCQVEDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYELSSVVTVPSSSLGTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTIS KAKGQPREPQVYTLPPCRDELTKNQVSLWCLVKGFYPSDIAVE WESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPG	SEQ ID NO: 107
Heavy chain (Fab arm + Fc) - DNA sequence CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG	SEQ ID NO: 108

AGCTGCAAAGCGAGCGGCTTTAACATTAAAGATTATTATAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCTGGATTGATCTGGA AAACGCGAACACCATTAT GATGCGAAATTTTCAGGGCCGCGTGACCATTAACCCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGAAGCAGCCTGCGCAGCGAAGATACCGCGGTGT ATTATTGCGCGCGCGATGCG TATGGCCGCTATTTTTATGATGTGTGGGGCCAGGGCACCT GGTGACCGTGAGCAGCGCG AGCACCAAAGGCCCGAGCGTGTTTCCGCTGGCGCCGAGCAG CAAAAGCACCGCGCGCGC ACCGCGGCGCTGGGCTGCCAGGTGGAAGATTATTTTCCGGA ACCGGTGACCGTGAGCTGG AACAGCGGCGCGCTGACCAGCGGCGTGATACCTTTCCGGC GGTGCTGCAGAGCAGCGCG CTGTATGAACTGAGCAGCGTGGTGACCGTGCCGAGCAGCAG CCTGGGCACCCAGACCTAT ATTTGCAACGTGAACCATAAACCGAGCAACACCAAAGTGG ATAAAAAAGTGGAACCGAAA AGCTGCGATAAAACCCATACCTGCCCGCCGTGCCCGGCGCC GGAAGCGGCGGGCGGCCCCG AGCGTGTTTCTGTTTCCGCCGAAACCGAAAGATACCTGAT GATTAGCCGCACCCCGGAA GTGACCTGCGTGGTGGTGGATGTGAGCCATGAAGATCCGGA AGTGAAATTTAACTGGTAT GTGGATGGCGTGGAAGTGCATAACGCGAAAACCAAACCGC GCGAAGAACAGTATAACAGC ACCTATCGCGTGGTGAGCGTGCTGACCGTGCTGCATCAGGA TTGGCTGAACGGCAAAGAA TATAAATGCAAAGTGAGCAACAAAGCGCTGGCGGCGCCGA TTGAAAAAACCATTAGCAAA GCGAAAGGCCAGCCGCGCGAACCGCAGGTGTATACCCTGCC GCCGTGCCGCGATGAACTG ACCAAAAACCAGGTGAGCCTGTGGTGCCTGGTGAAAGGCTT TTATCCGAGCGATATTGCG GTGGAATGGGAAAGCAACGGCCAGCCGGAACAACACTATA AAACCACCCCGCCGGTGCTG GATAGCGATGGCAGCTTTTTTCTGTATAGCAAAGTACCCTG GGATAAAAGCCGCTGGCAG CAGGGCAACGTGTTTAGCTGCAGCGTGATGCATGAAGCGCT GCATAACCATTATACCCAG AAAAGCCTGAGCCTGAGCCCGGGC	
Heavy chain (Full chain) - Amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGYTFEQYAMHWVRQAP GQRLEWMGFIPAGTGNTKYSQKFQGRVTITRDTSASTAYMEL SSLRSEDVAVYYCARDGGYWDYDSWDDWGQGLTVTVSSAST KGPSVFPAPSSKSTSGGTAALGLVIRDYFPEPVTVSWNSGAL	SEQ ID NO: 109

	TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS NTKVDKKVEPKSCDGGGGSGGGGSQVQLVQSGAEVKKPGAS VKVSCKASGFNIKDYMHWRQAPGQRLEWMGWIDLENAN TIYDAKFQGRVTITRDTASTAYMELSSLRSEDATAVYYCARD YGRYFYDVWGQGLVTVSSASTKGPSVFPLAPSSKSTSGGTAA LGCQVEDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYELSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP PCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPCR DELTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPV LDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQK SLSLSPG	
	Heavy chain (Full chain) - DNA sequence CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTATACCTTTGAACAGTATGCGAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCTTTATTCCGGCGGG CACCGGCAACACCAAATAT AGCCAGAAATTTACAGGGCCGCGTGACCATTACCCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGCAGCCTGCGCAGCGAAGATACCGCGGTGT ATTATTGCGCGCGCGATCGC GGCGGCTATTGGTATGATAGCTGGGATGATTGGGGCCAGGG CACCTGGTGACCGTGAGC AGCGCGAGCACCAAAGGCCCGAGCGTGTTCGCGCGCGCC GAGCAGCAAAAGCACCGC GGCGGCACCGCGGCGCTGGGCTGCCTGGTGCGCGATTATTT TCCGGAACCGGTGACCGTG AGCTGGAACAGCGGCGCGCTGACCAGCGGCGTGACATACCTT TCCGGCGGTGCTGCAGAGC AGCGGCCTGTATAGCCTGAGCAGCGTGGTGACCGTGCCGAG CAGCAGCCTGGGCACCCAG ACCTATATTTGCAACGTGAACCATAAACCGAGCAACACCAA AGTGGATAAAAAAGTGGA CCGAAAAGCTGCGATGGCGGCGGCGGCAGCGGCGGCGGCG GCAGCCAGGTGCAGCTGGTG CAGAGCGGCGCGGAAGTGAAAAAACCGGCGCGAGCGTGA AAGTGAGCTGCAAAGCGAGC GGCTTTAACATTAAAGATTATTATATGCATTGGGTGCGCCA GGCGCCGGGCCAGCGCCTG GAATGGATGGGCTGGATTGATCTGGAAAACGCGAACACCAT TTATGATGCGAAATTTTACG GGCCGCGTGACCATACCCGCGATACCAGCGCGAGCACCGC GTATATGGAAGTGCAGCAGC CTGCGCAGCGAAGATACCGCGGTGTATTATTGCGCGCGCGA TGCGTATGGCCGCTATTTT	SEQ ID NO: 110

TATGATGTGTGGGGCCAGGGCACCTGGTGACCGTGAGCAG CGCGAGCACCAAAGGCCCG AGCGTGTTTCCGCTGGCGCCGAGCAGCAAAAGCACCAGCGG CGGCACCGCGGCGCTGGGC TGCCAGGTGGAAGATTATTTTCCGGAACCGGTGACCGTGAG CTGGAACAGCGGCGCGCTG ACCAGCGGCGTGCATACCTTTCCGGCGGTGCTGCAGAGCAG CGGCCTGTATGAACTGAGC AGCGTGGTGACCGTGCCGAGCAGCAGCCTGGGCACCCAGA CCTATATTTGCAACGTGAAC CATAAACCGAGCAACACCAAAGTGGATAAAAAAGTGGAAC CGAAAAGCTGCGATAAAACC CATACCTGCCCCGCGTGCCCCGGCGCCGGAAGCGGCGGGCGG CCCGAGCGTGTTTCTGTTT CCGCCGAAACCGAAAGATACCCTGATGATTAGCCGCACCCC GGAAGTGACCTGCGTGGTG GTGGATGTGAGCCATGAAGATCCGGAAGTGAAATTTAACTG GTATGTGGATGGCGTGGA GTGCATAACGCGAAAACCAAACCGCGCGAAGAACAGTATA ACAGCACCTATCGCGTGGTG AGCGTGCTGACCGTGCTGCATCAGGATTGGCTGAACGGCAA AGAATATAAATGCAAAGTG AGCAACAAAGCGCTGGCGGCGCCGATTGAAAAAACCATTA GCAAAGCGAAAGGCCAGCCG CGCGAACCGCAGGTGTATACCCTGCCGCCGTGCCGCGATGA ACTGACCAAAAACCGGTG AGCCTGTGGTGCCTGGTGAAAGGCTTTTATCCGAGCGATAT TGCGGTGGAATGGGAAAGC AACGGCCAGCCGGAACAACTATAAAACCAACCCCGCCGG TGCTGGATAGCGATGGCAGC TTTTTTCTGTATAGCAAACCTGACCGTGGATAAAAGCCGCTG GCAGCAGGGCAACGTGTTT AGCTGCAGCGTGATGCATGAAGCGCTGCATAACCATTATAC CCAGAAAAGCCTGAGCCTG AGCCCGGGC	
Light Chain A	
LCDR1 (IMGT) QSISSY	SEQ ID NO: 111
LCDR2 (IMGT) GA	SEQ ID NO: 112
LCDR3 (IMGT) QQVVFPTPT	SEQ ID NO: 113
LCDR1 (Kabat) RASQSISSYLN	SEQ ID NO: 114

LCDR2 (Kabat)	SEQ ID NO: 115
GASSLQS	
LCDR3 (Kabat)	SEQ ID NO: 116
QQVVFTPPT	
LCDR1 (Combined Kabat/IMGT)	SEQ ID NO: 117
RASQSISSYLN	
LCDR2 (Combined Kabat/IMGT)	SEQ ID NO: 118
GASSLQS	
LCDR3 (Combined Kabat/IMGT)	SEQ ID NO: 119
QQVVFTPPT	
VL - Amino acid sequence	SEQ ID NO: 120
DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAP KLLIYGASSLQSGVPSRFRSGSGSGTDFTLTISLQPEDFATYYCQ QVVFTPPTFGGGTKVEIK	
VL - DNA sequence	SEQ ID NO: 121
GATATTCAGATGACCCAGAGCCCGAGCAGCCTGAGCGCGA GCGTGGGCGATCGCGTGACC ATTACCTGCCGCGCGAGCCAGAGCATTAGCAGCTATCTGAA CTGGTATCAGCAGAAACCG GGCAAAGCGCCGAAACTGCTGATTTATGGCGCGAGCAGCCT GCAGAGCGGCGTGCCGAGC CGCTTTAGCGGCAGCGGCAGCGGCACCGATTTTACCCTGAC CATTAGCAGCCTGCAGCCG GAAGATTTTGCGACCTATTATTGCCAGCAGGTGGTGTGTTTACC CCGCCGACCTTTGGCGGC GGCACCAAAGTGGAATTAATA	
Light chain - Amino acid sequence	SEQ ID NO: 122
DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAP KLLIYGASSLQSGVPSRFRSGSGSGTDFTLTISLQPEDFATYYCQ QVVFTPPTFGGGTKVEIKRTVAAPSVFIFPPSDEELKSGTASVQ CLLNFPYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSL SSELTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	
Light chain - DNA sequence	SEQ ID NO: 123
GATATTCAGATGACCCAGAGCCCGAGCAGCCTGAGCGCGA GCGTGGGCGATCGCGTGACC ATTACCTGCCGCGCGAGCCAGAGCATTAGCAGCTATCTGAA CTGGTATCAGCAGAAACCG GGCAAAGCGCCGAAACTGCTGATTTATGGCGCGAGCAGCCT GCAGAGCGGCGTGCCGAGC	

CGCTTTAGCGGCAGCGGCAGCGGCACCGATTTTACCCTGAC CATTAGCAGCCTGCAGCCG GAAGATTTTGCACCTATTATTGCCAGCAGGTGGTGTTCACC CCGCCGACCTTTGGCGGC GGCACCAAAGTGGAAATTAAACGCACCGTGGCGGCGCCGA GCGTGTTCATTTTCCGCCG AGCGATGAAGAACTGAAAAGCGGCACCGCGAGCGTGCAGT GCCTGCTGAACAACCTTTAT CCGCGCGAAGCGAAAGTGCAGTGGAAAGTGGATAACGCGC TGCAGAGCGGCAACAGCCAG GAAAGCGTGACCGAACAGGATAGCAAAGATAGCACCTATA GCCTGAGCAGCGAACTGACC CTGAGCAAAGCGGATTATGAAAAACATAAAGTGTATGCGTG CGAAGTGACCCATCAGGGC CTGAGCAGCCCGGTGACCAAAAGCTTTAACCGCGGCGAATG C	
Light Chain B	
LCDR1 (IMGT) QSLLNARTGKNY	SEQ ID NO: 124
LCDR2 (IMGT) WA	SEQ ID NO: 125
LCDR3 (IMGT) KQSYSLRT	SEQ ID NO: 126
LCDR1 (Kabat) KSSQSLLNARTGKNYLA	SEQ ID NO: 127
LCDR2 (Kabat) WASTRES	SEQ ID NO: 128
LCDR3 (Kabat) KQSYSLRT	SEQ ID NO: 129
LCDR1 (Combined Kabat/IMGT) KSSQSLLNARTGKNYLA	SEQ ID NO: 130
LCDR2 (Combined Kabat/IMGT) WASTRES	SEQ ID NO: 131
LCDR3 (Combined Kabat/IMGT) KQSYSLRT	SEQ ID NO: 132
VL - Amino acid sequence	SEQ ID NO: 133

	DIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKNYLAWYQ QKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAE DVAVYYCKQSYSLRTFGGGTKVEIK	
	VL - DNA sequence GATATTGTGATGACCCAGAGCCCGGATAGCCTGGCGGTGAG CCTGGGCGAACGCGCGACC ATTAAGTGCAGAAAGCAGCCAGAGCCTGCTGAACGCGCGCAC CGGCAAAACTATCTGGCG TGGTATCAGCAGAAACCGGGCCAGCCGCCGAACTGCTGAT TTATTGGGCGAGCACCCGC GAAAGCGGCGTGCCGGATCGCTTTAGCGGCAGCGGCAGCG GCACCGATTTTACCCTGACC ATTAGCAGCCTGCAGGCGGAAGATGTGGCGGTGTATTATTG CAAACAGAGCTATAGCCTG CGCACCTTTGGCGGCGGCACCAAAGTGGAATTTAA	SEQ ID NO: 134
	Light chain - Amino acid sequence DIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKNYLAWYQ QKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAE DVAVYYCKQSYSLRTFGGGTKVEIKRTVAAPSVFIFPPSDEQL KSGRASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ DSKDSTYLSRLQLSKADYEKHKVYACEVTHQGLSSPVTKSF NRGEC	SEQ ID NO: 135
	Light chain - DNA sequence GATATTGTGATGACCCAGAGCCCGGATAGCCTGGCGGTGAG CCTGGGCGAACGCGCGACC ATTAAGTGCAGAAAGCAGCCAGAGCCTGCTGAACGCGCGCAC CGGCAAAACTATCTGGCG TGGTATCAGCAGAAACCGGGCCAGCCGCCGAACTGCTGAT TTATTGGGCGAGCACCCGC GAAAGCGGCGTGCCGGATCGCTTTAGCGGCAGCGGCAGCG GCACCGATTTTACCCTGACC ATTAGCAGCCTGCAGGCGGAAGATGTGGCGGTGTATTATTG CAAACAGAGCTATAGCCTG CGCACCTTTGGCGGCGGCACCAAAGTGGAATTTAAACGCAC CGTGGCGGCGCCGAGCGTG TTTATTTTCCGCCGAGCGATGAACAGCTGAAAAGCGGCCG CGCGAGCGTGGTGTGCCTG CTGAACAACCTTTATCCGCGCGAAGCGAAAGTGCAAGTGAA AGTGGATAACGCGCTGCAG AGCGGCAACAGCCAGGAAAGCGTGACCGAACAGGATAGCA AAGATAGCACCTATAGCCTG AGCAGCCGCTGCAGCTGAGCAAAGCGGATTATGAAAAAC ATAAAGTGTATGCGTGCGAA GTGACCCATCAGGGCCTGAGCAGCCCGGTGACCAAAGCTT TAACCGCGCGAATGC	SEQ ID NO: 136

Clone	Sequences	SEQ ID NO
NPXAB-3	Heavy Chain A	
	HCDR1 (IMGT) GYTFASYK	SEQ ID NO: 137
	HCDR2 (IMGT) IPAGTGNT	SEQ ID NO: 138
	HCDR3 (IMGT) ARDRGGYYYDSWDD	SEQ ID NO: 139
	HCDR1 (Kabat) SYKMH	SEQ ID NO: 140
	HCDR2 (Kabat) DIPAGTGNTTHYSQKFQG	SEQ ID NO: 141
	HCDR3 (Kabat) DRGGYYYDSWDD	SEQ ID NO: 142
	HCDR1 (Combined Kabat/IMGT) GYTFASYKMH	SEQ ID NO: 143
	HCDR2 (Combined Kabat/IMGT) DIPAGTGNTTHYSQKFQG	SEQ ID NO: 144
	HCDR3 (Combined Kabat/IMGT) DRGGYYYDSWDD	SEQ ID NO: 145
	VH - Amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGYTFASYKMHWVRQAP GQRLEWMGDIPAGTGNTTHYSQKFQGRVTITRDTSASTAYMEL SSLRSEDTA VYYCARDRGGYYYDSWDDWGQGLTVTVSS	SEQ ID NO: 146
	VH - DNA sequence CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTATACCTTTGCGAGCTATAAAAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCGATATTCCGGCGGG CACCGGCAACACCCATTAT AGCCAGAAATTTTCAGGGCCGCGTGACCATTACCCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGAAGCAGCCTGCGCAGCGAAGATAACCGCGGTGT ATTATTGCGCGCGCGATCGC	SEQ ID NO: 147

	GGCGGCTATTATTATGATAGCTGGGATGATTGGGGCCAGGG CACCTGGTGACCGTGAGC AGC	
	Heavy chain - Amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGYTFASYKMHWRQAP GQRLEWMGDIPAGTGNTHYSQKFQGRVTITRDTASTAYMEL SSLRSEDTAVYYCARDGGYYYSWDDWGQGLVTVSSAST KGPSVFPAPSSKSTSGGTAALGCLVRDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDT LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR EEQYNSTYRVVSVLTVHLQDNLNGKEYCKVSNKALAAPIEK TISKAKGQPREPQVCTLPSSRDELTKNQVSLSLVKGFPYSDIA VEWESNGQPENNYKTPPVLDSDGSFFLGSKLTVDKSRWQQG NVFSCSVMEALHNHYTQKSLSLSPG	SEQ ID NO: 148
	Heavy chain - DNA sequence CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTATACCTTTGCGAGCTATAAAAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCGATATTCCGGCGGG CACCGGCAACACCCATTAT AGCCAGAAATTCAGGGCCGCGTGACCATTACCCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGAAGCAGCCTGCGCAGCGAAGATACCGCGGTGT ATTATTGCGCGCGCGATCGC GGCGGCTATTATTATGATAGCTGGGATGATTGGGGCCAGGG CACCTGGTGACCGTGAGC AGCGCGAGCACCAAGGCCGAGCGTGTTCGCGCGCGCC GAGCAGCAAAAGCACCAAGC GGCGGCACCGCGGCGCTGGGCTGCCTGGTGCGCGATTATTT TCCGGAACCGGTGACCGTG AGCTGGAACAGCGGCGCGCTGACCAGCGGCGTGATACCTT TCCGGCGGTGCTGCAGAGC AGCGGCCTGTATAGCCTGAGCAGCGTGGTGACCGTGCCGAG CAGCAGCCTGGGCACCCAG ACCTATATTTGCAACGTGAACCATAAACCAGCAACACCAA AGTGGATAAAAAAGTGGA CCGAAAAGCTGCGATAAAACCCATACCTGCCCCGCGTGCCC GCGCCGGAAGCGGCGGC GGCCCGAGCGTGTCTGTTTCCGCCGAAACCGAAAGATAC CCTGATGATTAGCCGCACC CCGGAAGTGACCTGCGTGGTGGTGGATGTGAGCCATGAAGA TCCGGAAGTGAAATTTAAC TGGTATGTGGATGGCGTGGAAGTGCATAACGCGAAAACCA AACCGCGCAAGAACAGTAT	SEQ ID NO: 149

AACAGCACCTATCGCGTGGTGAGCGTGCTGACCGTGCTGCA TCAGGATTGGCTGAACGGC AAAGAATATAAATGCAAAGTGAGCAACAAAGCGCTGGCGG CGCCGATTGAAAAAACCAT AGCAAAGCGAAAGGCCAGCCGCGCGAACCAGGAGGTGTGCA CCCTGCCGCCGAGCCGCGAT GAACTGACCAAAAACCAGGTGAGCCTGAGCTGCCTGGTGA AAGGCTTTTATCCGAGCGAT ATTGCGGTGGAATGGGAAAGCAACGGCCAGCCGAAAACA ACTATAAAACCACCCCGCCG GTGCTGGATAGCGATGGCAGCTTTTTTCTGGGCAGCAAAC GACCGTGGATAAAAGCCGC TGGCAGCAGGGCAACGTGTTTAGCTGCAGCGTGATGCATGA AGCGCTGCATAACCATTAT ACCCAGAAAAGCCTGAGCCTGAGCCCGGGC	
Heavy Chain B – B7-H7 binding Fab arm	
HCDR1 (IMGT) GYTFASYK	SEQ ID NO: 150
HCDR2 (IMGT) IPAGTGNT	SEQ ID NO: 151
HCDR3 (IMGT) ARDRGGYYYDSWDD	SEQ ID NO: 152
HCDR1 (Kabat) SYKMH	SEQ ID NO: 153
HCDR2 (Kabat) DIPAGTGNTTHYSQKFQG	SEQ ID NO: 154
HCDR3 (Kabat) DRGGYYYDSWDD	SEQ ID NO: 155
HCDR1 (Combined Kabat/IMGT) GYTFASYKMH	SEQ ID NO: 156
HCDR2 (Combined Kabat/IMGT) DIPAGTGNTTHYSQKFQG	SEQ ID NO: 157

HCDR3 (Combined Kabat/IMGT)	SEQ ID NO: 158
DRGGYYYSWDD	
VH - Amino acid sequence	SEQ ID NO: 159
QVQLVQSGAEVKKPGASVKVSCKASGYTFASYKMHWRQAP GQRLEWMGDIPAGTGNTHTYSQKFQGRVTITRDTASTAYMEL SSLRSEDTAVYYCARDRGYYYSWDDWGQGLVTVSS	
VH - DNA sequence	SEQ ID NO: 160
CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTATACCTTTGCGAGCTATAAAAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCGATATTCCGGCGGG CACCGGCAACACCCATTAT AGCCAGAAATTCAGGGCCGCGTGACCATTACCCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGAAGCAGCCTGCGCAGCGAAGATACCGCGGTGT ATTATTGCGCGCGCGATCGC GGCGGCTATTATTATGATAGCTGGGATGATTGGGGCCAGGG CACCTGGTGACCGTGAGC AGC	
Heavy chain (Fab arm) - Amino acid sequence	SEQ ID NO: 161
QVQLVQSGAEVKKPGASVKVSCKASGYTFASYKMHWRQAP GQRLEWMGDIPAGTGNTHTYSQKFQGRVTITRDTASTAYMEL SSLRSEDTAVYYCARDRGYYYSWDDWGQGLVTVSSAST KGPSVFPAPSSKSTSGGTAAALGCLVRDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKVEPKSCD	
Heavy chain (Fab arm) - DNA sequence	SEQ ID NO: 162
CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTATACCTTTGCGAGCTATAAAAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCGATATTCCGGCGGG CACCGGCAACACCCATTAT AGCCAGAAATTCAGGGCCGCGTGACCATTACCCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGAAGCAGCCTGCGCAGCGAAGATACCGCGGTGT ATTATTGCGCGCGCGATCGC GGCGGCTATTATTATGATAGCTGGGATGATTGGGGCCAGGG CACCTGGTGACCGTGAGC AGCGCGAGCACCAAGGCCCGAGCGTGTTCGCGCGCGGCC GAGCAGCAAAAGCACCAGC GGCGGCACCGCGGCGCTGGGCTGCCTGGTGCGCGATTATTT TCCGGAACCGGTGACCGTG	

AGCTGGAACAGCGGCGCGCTGACCAGCGGCGTGCATACCTT TCCGGCGGTGCTGCAGAGC AGCGGCCTGTATAGCCTGAGCAGCGTGGTGACCGTGCCGAG CAGCAGCCTGGGCACCCAG ACCTATATTTGCAACGTGAACCATAAACCGAGCAACACCAA AGTGGATAAAAAAGTGGA CCGAAAAGCTGCGAT	
Linker GGGSGGGGS	SEQ ID NO: 163
Heavy Chain B – CD3 binding Fab arm + Fc	
HCDR1 (IMGT) GFNIKDY	SEQ ID NO: 164
HCDR2 (IMGT) IDLENANT	SEQ ID NO: 165
HCDR3 (IMGT) ARDA YGRYFYDV	SEQ ID NO: 166
HCDR1 (Kabat) DYMH	SEQ ID NO: 167
HCDR2 (Kabat) WIDLENANTIYDAKFQG	SEQ ID NO: 168
HCDR3 (Kabat) DAYGRYFYDV	SEQ ID NO: 169
HCDR1 (Combined Kabat/IMGT) GFNIKDYMH	SEQ ID NO: 170
HCDR2 (Combined Kabat/IMGT) WIDLENANTIYDAKFQG	SEQ ID NO: 171
HCDR3 (Combined Kabat/IMGT) DAYGRYFYDV	SEQ ID NO: 172
VH - Amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGFNIKDYMHWRQAP GQRLEWMGWIDLENANTIYDAKFQGRVTITRDTASTAYMEL SSLRSED TAVYYCARDAYGRYFYDVWGQGLTVSS	SEQ ID NO: 173
VH - DNA sequence CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAC CGGGCGCGAGCGTGAAAGTG	SEQ ID NO: 174

	AGCTGCAAAGCGAGCGGCTTTAACATTAAAGATTATTATAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCTGGATTGATCTGGA AAACGCGAACACCATTAT GATGCGAAATTTAGGGCCGCGTGACCATTAACCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGAAGCAGCCTGCGCAGCGAAGATACCGCGGTGT ATTATTGCGCGCGCGATGCG TATGGCCGCTATTTTTATGATGTGTGGGGCCAGGGCACCT GGTGACCGTGAGCAGC	
	Heavy chain (Fab arm + Fc) - Amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGFNIKDYIMHWVRQAP GQRLEWMGWIDLENANTIYDAKFQGRVTITRDTASTAYMEL SSLRSEDVAVYYCARDAYGRYFYDVWGQGLTVTVSSASTKGP SVFPLAPSSKSTSGGTAALGCQVEDYFPEPVTVSWNSGALTSG VHTFPAVLQSSGLYELSSVTVPSSSLGTQTYICNVNHPKPSNTK VDKKVEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTIS KAKGQPREPQVYTLPPCRDELTKNQVSLWCLVKGFYPSDIAVE WESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCVMHEALHNHYTQKSLSLSPG	SEQ ID NO: 175
	Heavy chain (Fab arm + Fc) - DNA sequence CAGGTGCAGCTGGTGCAGAGCGGCGCGGAAGTGAAAAAAC CGGGCGCGAGCGTGAAAGTG AGCTGCAAAGCGAGCGGCTTTAACATTAAAGATTATTATAT GCATTGGGTGCGCCAGGCG CCGGGCCAGCGCCTGGAATGGATGGGCTGGATTGATCTGGA AAACGCGAACACCATTAT GATGCGAAATTTAGGGCCGCGTGACCATTAACCGCGATAC CAGCGCGAGCACCGCGTAT ATGGAAGTGAAGCAGCCTGCGCAGCGAAGATACCGCGGTGT ATTATTGCGCGCGCGATGCG TATGGCCGCTATTTTTATGATGTGTGGGGCCAGGGCACCT GGTGACCGTGAGCAGCGCG AGCACCAAAGGCCCGAGCGTGTTTCCGCTGGCGCCGAGCAG CAAAAGCACCAGCGGCGGC ACCGCGGCGCTGGGCTGCCAGGTGGAAGATTATTTTCCGGA ACCGGTGACCGTGAGCTGG AACAGCGGCGCGCTGACCAGCGGCGTGCATACCTTTCCGGC GGTGCTGCAGAGCAGCGGC CTGTATGAACTGAGCAGCGTGGTGACCGTGCCGAGCAGCAG CCTGGGCACCCAGACCTAT ATTTGCAACGTGAACCATAAACCGAGCAACACCAAAGTGG ATAAAAAAGTGGAACCGAAA AGCTGCGATAAAACCCATACCTGCCCGCCGTGCCCGGCGCC GGAAGCGGCGGGCGGCCCCG	SEQ ID NO: 176

	AGCGTGTTTCTGTTTCCGCCGAAACCGAAAGATACCCTGAT GATTAGCCGCACCCCGGAA GTGACCTGCGTGGTGGTGGATGTGAGCCATGAAGATCCGGA AGTGAAATTTAACTGGTAT GTGGATGGCGTGGAAGTGCATAACCGGAAAACCAAACCGC GCGAAGAACAGTATAACAGC ACCTATCGCGTGGTGAGCGTGCTGACCGTGCTGCATCAGGA TTGGCTGAACGGCAAAGAA TATAAATGCAAAGTGAGCAACAAAGCGCTGGCGGCGCCGA TTGAAAAAACCATTAGCAAA GCGAAAGGCCAGCCGCGCGAACCGCAGGTGTATACCCTGCC GCCGTGCCGCGATGAACTG ACCAAAAACCAGGTGAGCCTGTGGTGCCTGGTGAAAGGCTT TTATCCGAGCGATATTGCG GTGGAATGGGAAAGCAACGGCCAGCCGGAACAACACTATA AAACCACCCCGCCGGTGCTG GATAGCGATGGCAGCTTTTTTCTGTATAGCAAACTGACCGT GGATAAAAGCCGCTGGCAG CAGGGCAACGTGTTTAGCTGCAGCGTGATGCATGAAGCGCT GCATAACCATTATACCCAG AAAAGCCTGAGCCTGAGCCCGGGC	
	Heavy chain (Full chain) - Amino acid sequence QVQLVQSGAEVKKPGASVKVSCKASGYTFASYKMHWVRQAP GQRLEWMGDIPAGTGNTHYSQKFQGRVTITRDTASTAYMEL SSLRSEDNAVYYCARDRGYYYSWDDWGQGLVTVSSAST KGPSVFPRAPSSKSTSGGTAALGCLVRDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKVEPKSCDGGGSGGGGSQVQLVQSGAEVKKPGAS VKVSCKASGFNIKDYMHWVRQAPGQRLEWMGWIDLENAN TIYDAKFQGRVTITRDTASTAYMELSSLRSEDNAVYYCARDA YGRYFYDVWGQGLVTVSSASTKGPSVFPLAPSSKSTSGGTA LGCQVEDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYELSS VTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCP PCPAPEAAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNQKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPCR DELTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTPPV LDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQK SLSLSPG	SEQ ID NO: 177
	Heavy chain (Full chain) DNA sequence caggtgcagctggtgcagagcggcgcggaagtgaacaaaccggcgcgagcgtgaaagtg agctgcaaacgagcggctatacctttgcagctataaaatgcattgggtgcgagcggcg ccgggccagcgcctggaatggatggcgatattccggcgggcaccggcaacacccattat agccagaaatttcaggcgccgctgaccattaccgcgataccagcgcgagcaccgcgtat atggaactgagcagcctgcgcagcgaagatacccggtgtattattgcgcgcgcatcgc ggcggtattattatgatagctgggatattggggccaggccaccctggtgaccgtgagc agcgcgagcaccaaaaggcccgagcgtgttccgcgcgcgagcagcaaaagcaccagc	SEQ ID NO: 178

ggcgccaccgcggcgctgggctgcctggtgcgcgattatttccggaaccggtgaccgtg agctgggaacagcggcgctgaccagcggcgctgcataccttccggcggtgctgcagagc agcggcctgtatagcctgagcagcgtggtgaccgtgccgagcagcagcctgggcacccag acctatatttgcacgtgaaccataaaccgagcaacaccaaagtggataaaaaagtggaa ccgaaaaagctgcgatggcgcgcgcgagcggcgcgcgcgagccagggtgcagctggtg cagagcggcgcggaagtgaaaaaaccggcgcgagcgtgaaagtgcagctgcaaacgcgagc ggcttaacattaagattattatgcatgggtgcgccaggcgccggccagcgcctg gaatggtgaggctggattgatctgaaaacgcgaacaccatttatgatgcgaaattcag ggcgcgctgaccattaccgcgataccagcgcgagcaccgcgtatatggaactgagcagc ctgcgcagcgaagataccgcgggtgtattattgcgcgcgcatgctatggccgctattt tatgatgtgtgggcccagggcacccctggtgaccgtgagcagcgcgagcaccgaaaggccc agcgtgttccgctggcgccgagcagcaaaagcaccagcggcgccgacccgcgctggg tgccagggtggaagattatttccggaaccggtgaccgtgagctggaacagcggcgcgctg accagcggcgctgcataccttccggcggtgctgcagagcagcggcctgtatgaactgagc agcgtggtgaccgtgccgagcagcagcctgggcacccagacctatattgcaacgtgaac cataaaccgagcaacaccaaagtggataaaaaagtggaaaccgaaaagctgcgataaaac catacctgcccggcgctgcccggcgccggaagcggcgggcgcccagcgtgttctgttt ccgccgaaaccgaaagataccctgatgattagccgcaccccggaagtgcctgcgtgtg gtgatgtgagccatgaagatccggaagtgaatttaactggtatgtggtggcgtggaa gtgcataacgcgaaaacaaaccgcgcgaagaacagtataacagcacctatcgcgtgtg agcgtgctgaccgtgctgcatcaggattgctgaacggcaagaataataatgcaaaagt agcaacaaagcgtgctggcgccgattgaaaaaccattagcaaaagcgaaggccagccg cggaaccgcaggtgtataccctgccgccgtgccgcgatgaactgacaaaaaccaggtg agcctgtggtgcctggtgaaaggctttatccgagcgtatgctggtggaatgggaaagc aacggccagccggaaaacaactataaaaccaccccgccggtgctggtatgcatgagcgc ttttctgtatgcaaaactgaccgtgataaaagccgtggcagcagggaacgtgtt agctgcagcgtgatgcatgaagcgtgcataaccattataccagaaaagcctgagcctg agccccgggc	
Light Chain A	
LCDR1 (IMGT)	SEQ ID NO: 179
QSISSY	
LCDR2 (IMGT)	SEQ ID NO: 180
GA	
LCDR3 (IMGT)	SEQ ID NO: 181
QQVPFEPPT	
LCDR1 (Kabat)	SEQ ID NO: 182
RASQSISSYLN	
LCDR2 (Kabat)	SEQ ID NO: 183
GASSLQS	
LCDR3 (Kabat)	SEQ ID NO: 184
QQVPFEPPT	
LCDR1 (Combined Kabat/IMGT)	SEQ ID NO: 185

RASQSISSYLN	
LCDR2 (Combined Kabat/IMGT) GASSLQS	SEQ ID NO: 186
LCDR3 (Combined Kabat/IMGT) QQVPFEPPT	SEQ ID NO: 187
VL - Amino acid sequence DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAP KLLIYGASSLQSGVPSRFRSGSGTDFTLTISSLQPEDFATYYCQ QVPFEPPTFGGGTKVEIK	SEQ ID NO: 188
VL - DNA sequence GATATTCAGATGACCCAGAGCCCGAGCAGCCTGAGCGCGA GCGTGGGCGATCGCGTGACC ATTACCTGCCGCGAGCCAGAGCATTAGCAGCTATCTGAA CTGGTATCAGCAGAAACCG GGCAAAGCGCCGAAACTGCTGATTTATGGCGCGAGCAGCCT GCAGAGCGGCGTGCCGAGC CGCTTTAGCGGCAGCGGCAGCGCACCGATTTTACCCTGAC CATTAGCAGCCTGCAGCCG GAAGATTTTGCAGCCTATTATTGCCAGCAGGTGCCGTTTGA ACCGCCGACCTTTGGCGGC GGCACCAAAGTGGAATTAATAA	SEQ ID NO: 189
Light chain - Amino acid sequence DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAP KLLIYGASSLQSGVPSRFRSGSGTDFTLTISSLQPEDFATYYCQ QVPFEPPTFGGGTKVEIKRTVAAPSVFIFPPSDEELKSGTASVQC LLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSL SELTLKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC	SEQ ID NO: 190
Light chain - DNA sequence GATATTCAGATGACCCAGAGCCCGAGCAGCCTGAGCGCGA GCGTGGGCGATCGCGTGACC ATTACCTGCCGCGAGCCAGAGCATTAGCAGCTATCTGAA CTGGTATCAGCAGAAACCG GGCAAAGCGCCGAAACTGCTGATTTATGGCGCGAGCAGCCT GCAGAGCGGCGTGCCGAGC CGCTTTAGCGGCAGCGGCAGCGCACCGATTTTACCCTGAC CATTAGCAGCCTGCAGCCG GAAGATTTTGCAGCCTATTATTGCCAGCAGGTGCCGTTTGA ACCGCCGACCTTTGGCGGC GGCACCAAAGTGGAATTAATAACGCACCGTGGCGGCGCCGA GCGTGTTTATTTTCCGCCG AGCGATGAAGAACTGAAAAGCGGCACCGCGAGCGTGCAGT GCCTGCTGAACAACCTTTTAT	SEQ ID NO: 191

CCGCGCGAAGCGAAAGTGCAGTGGAAAGTGGATAACGCGC TGCAGAGCGGCAACAGCCAG GAAAGCGTGACCGAACAGGATAGCAAAGATAGCACCTATA GCCTGAGCAGCGAACTGACC CTGAGCAAAGCGGATTATGAAAAACATAAAGTGTATGCGTG CGAAGTGACCCATCAGGGC CTGAGCAGCCCGGTGACCAAAAGCTTTAACCGCGGCGAATG C	
Light Chain B	
LCDR1 (IMGT) QSLLNARTGKNY	SEQ ID NO: 192
LCDR2 (IMGT) WA	SEQ ID NO: 193
LCDR3 (IMGT) KQSYSLRT	SEQ ID NO: 194
LCDR1 (Kabat) KSSQSLLNARTGKNYLA	SEQ ID NO: 195
LCDR2 (Kabat) WASTRES	SEQ ID NO: 196
LCDR3 (Kabat) KQSYSLRT	SEQ ID NO: 197
LCDR1 (Combined Kabat/IMGT) KSSQSLLNARTGKNYLA	SEQ ID NO: 198
LCDR2 (Combined Kabat/IMGT) WASTRES	SEQ ID NO: 199
LCDR3 (Combined Kabat/IMGT) KQSYSLRT	SEQ ID NO: 200
VL - Amino acid sequence DIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKNYLA WYQ QKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLT ISSLAQAE DVAVYYCKQSYSLRTFGGGTKVEIK	SEQ ID NO: 201
VL - DNA sequence GATATTGTGATGACCCAGAGCCCGGATAGCCTGGCGGTGAG CCTGGGCGAACGCGCGACC ATTAAGTGCAAAAGCAGCCAGAGCCTGCTGAACGCGCGCAC CGGCAAAACTATCTGGCG	SEQ ID NO: 202

	TGGTATCAGCAGAAACCGGGCCAGCCGCCGAAACTGCTGAT TTATTGGGCGAGCACCCGC GAAAGCGGCGTGCCGGATCGCTTTAGCGGCAGCGGCAGCG GCACCGATTTTACCCTGACC ATTAGCAGCCTGCAGGCGGAAGATGTGGCGGTGTATTATTG CAAACAGAGCTATAGCCTG CGCACCTTTGGCGGCGGCACCAAAGTGGAATTTAAA	
	Light chain - Amino acid sequence DIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKKNYLAWYQ QKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFLTITSLQAE DVAVYYCKQSYSLRTFGGKVEIKRTVAAPSVFIFPPSDEQL KSGRASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ DSKDSTYLSRLQLSKADYEKHKVYACEVTHQGLSSPVTKSF NRGEC	SEQ ID NO: 203
	Light chain - DNA sequence GATATTGTGATGACCCAGAGCCCGGATAGCCTGGCGGTGAG CCTGGGCGAACGCGCGACC ATTAAGTCAAAAAGCAGCCAGAGCCTGCTGAACGCGCGCAC CGCAAAAACCTATCTGGCG TGGTATCAGCAGAAACCGGGCCAGCCGCCGAAACTGCTGAT TTATTGGGCGAGCACCCGC GAAAGCGGCGTGCCGGATCGCTTTAGCGGCAGCGGCAGCG GCACCGATTTTACCCTGACC ATTAGCAGCCTGCAGGCGGAAGATGTGGCGGTGTATTATTG CAAACAGAGCTATAGCCTG CGCACCTTTGGCGGCGGCACCAAAGTGGAATTTAAACGCAC CGTGGCGGCGCCGAGCGTG TTTATTTTCCGCCGAGCGATGAACAGCTGAAAAGCGGCCG CGCGAGCGTGGTGTGCCTG CTGAACAACCTTTATCCGCGCGAAGCGAAAGTGCAAGTGAA AGTGGATAACGCGCTGCAG AGCGGCAACAGCCAGGAAAGCGTGACCGAACAGGATAGCA AAGATAGCACCTATAGCCTG AGCAGCCGCTGCAGCTGAGCAAAGCGGATTATGAAAAAC ATAAAGTGTATGCGTGCGAA GTGACCCATCAGGGCCTGAGCAGCCCGGTGACCAAAAGCTT TAACCGCGGCGAATGC	SEQ ID NO: 204

[0132] An antibody or antigen-binding fragment thereof of a bispecific antibody or antigen-binding fragment thereof described herein can be from any class of antibodies including, but not limited to, IgG, IgA, IgM, IgD, and IgE, and from any subclass (e.g., IgG1, IgG2, IgG3, and IgG4) of antibodies. An antibody or antigen-binding fragment thereof described herein can be or comprise a human, humanized, CDR-grafted, or *in vitro* generated antibody. An antibody or antigen-binding fragment thereof described herein can have or

comprise a heavy chain constant region chosen from, e.g., IgG1, IgG2, IgG3, or IgG4. An antibody or antigen-binding fragment thereof described herein can have or comprise a light chain chosen from, e.g., kappa or lambda.

[0133] An antibody or antigen-binding fragment thereof of a bispecific antibody or antigen-binding fragment thereof described herein can be or comprise a monoclonal antibody. In some embodiments, monoclonal antibodies directed to a particular epitope are derived from a single cell line (e.g., a B cell line).

[0134] In some embodiments, an antibody or antigen-binding fragment thereof of a bispecific antibody or antigen-binding fragment thereof described herein is or comprises a polyclonal antibody. In contrast to monoclonal antibodies, polyclonal antibodies are typically obtained from a population of heterogeneous antibodies, such that antibodies in a particular population include structural variation, for example, affinity for different epitopes on a particular target (e.g., B7-H7 or an immune effector cell antigen described herein). Several methods of producing polyclonal antibodies are known and include, for example, use of multiple subcutaneous and/or intraperitoneal injections of a relevant antigen into an animal, optionally including co-administration of one or more adjuvants.

[0135] Many multispecific antibody constructs are known in the art, and the bispecific antibodies or antigen-binding fragments thereof provided herein may be provided in the form of any suitable multispecific construct. In some embodiments, bispecific antibodies or antigen-binding fragments thereof provided herein are multispecific antibodies or antigen-binding fragments thereof. In some embodiments, a multispecific antibody or antigen-binding fragment thereof described herein binds more than one antigen, e.g., at least two antigens, at least three antigens, at least four antigens, or at least five antigens. In some embodiments, a multispecific antibody or antigen-binding fragment thereof described herein binds more than one epitope on B7-H7, e.g., at least two or at least three epitopes on B7-H7. In some embodiments, a multispecific antibody or antigen-binding fragment thereof described herein binds more than one epitope on an immune effector cell antigen described herein (e.g., CD3), e.g., at least two or at least three epitopes on an immune effector cell antigen described herein (e.g., CD3). In some embodiments, a multispecific antibody or antigen-binding fragment thereof described herein binds two or more immune effector cell antigens.

[0136] A bispecific antibody or antigen-binding fragment thereof described herein can comprise or be a first antibody or fragment thereof attached to a N-terminus or C-terminus of a heavy or light chain of a second antibody (see, e.g., Coloma and Morrison, *Nature Biotechnol.*, 1997, 15:159-163; incorporated by reference in its entirety). In some embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprises or is a tetravalent bispecific antibody. In some embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprises or is a scFv attached to a C-terminus of a heavy chain of a full-length antibody (e.g., an IgG). In some embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprises or is a hybrid immunoglobulin comprising at least two different heavy chain variable regions and at least two different light chain variable regions (see, e.g., Milstein and Cuello, *Nature*, 1983, 305:537-540; and Staerz and Bevan, *Proc. Natl. Acad. Sci. USA*, 1986, 83:1453-1457; each of which is incorporated by reference in its entirety).

[0137] In some embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprises or is one or more immunoglobulin chains with alterations to reduce formation of side products that do not have multispecificity. In some embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprise one or more “knobs-into-holes” modifications (see, e.g., U.S. Pat. No. 5,731,168; U.S. Pat. No. 11,542,330; hereby incorporated by reference in its entirety).

[0138] In some embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprises or is two half antibodies comprising a first half antibody having binding specificity for a first epitope and a second half antibody having binding specificity for a second epitope. In some embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprises or is two scFvs comprising a first scFv have binding specificity for a first epitope and a second scFv have binding specificity for a second epitope. In some embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprises or is a bispecific single chain molecule (see, e.g., Traunecker et al., *EMBO J.*, 1991, 10:3655-3659; and Gruber et al., *J. Immunol.*, 1994, 152:5368-5374; each of which is incorporated by reference in its entirety).

[0139] A bispecific antibody or antigen-binding fragment thereof described herein can comprise a linker connecting a first antigen-binding domain and a second antigen-binding

domain. In some embodiments, a linker comprises or is at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100 or more amino acids in length. Typically, a linker is characterized in that it tends not to adopt a rigid three-dimensional structure, but rather provides flexibility to a polypeptide (e.g., a bispecific antibody or antigen-binding fragment thereof described herein). A linker can be employed in a bispecific antibody or antigen-binding fragment thereof described herein based on specific properties imparted to the bispecific antibody or antigen-binding fragment thereof, such as, for example, a reduction in aggregation and/or an increase in stability. In some embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprises one or more G4S linkers. In some embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprises one or more (G4S)_n linkers, wherein n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or more. In certain embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprises one or more (G4S)₂ linkers. In certain embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprises one or more (G4S)₃ linkers. In certain embodiments, a bispecific antibody or antigen-binding fragment thereof described herein comprises one or more (G4S)₄ linkers.

Methods of Making

[0140] The present disclosure, among other things, provides methods of making multispecific antibodies or antigen-binding fragments thereof described herein. In some embodiments, an antibody or antigen-binding fragment thereof of a multispecific antibody or antigen-binding fragment thereof described herein is identified using a display technology, such as yeast display, phage display, or ribosome display. In some embodiments, an antibody or antigen-binding fragment thereof of a multispecific antibody or antigen-binding fragment thereof described herein is identified using a hybridoma library (e.g., a mammalian hybridoma library, e.g., a mouse hybridoma library), followed by supernatant screening.

[0141] Combinatorial methods for generating antibodies are known in the art (as described in, e.g., Ladner et al. U.S. Patent No. 5,223,409; Kang et al. International Publication No. WO 92/18619; Dower et al. International Publication No. WO 91/17271; Winter et al. International Publication WO 92/20791; Markland et al. International Publication No. WO 92/15679; Breitling et al. International Publication WO 93/01288;

McCafferty et al. International Publication No. WO 92/01047; Garrard et al. International Publication No. WO 92/09690; Ladner et al. International Publication No. WO 90/02809; Fuchs et al. (1991) *Bio/Technology* 9:1370-1372; Hay et al. (1992) *Hum Antibody Hybridomas* 3:81-85; Huse et al. (1989) *Science* 246:1275-1281; Griffiths et al. (1993) *EMBO J* 12:725-734; Hawkins et al. (1992) *J Mol Biol* 226:889-896; Clackson et al. (1991) *Nature* 352:624-628; Gram et al. (1992) *PNAS* 89:3576-3580; Garrad et al. (1991) *Bio/Technology* 9:1373-1377; Hoogenboom et al. (1991) *Nuc Acid Res* 19:4133-4137; and Barbas et al. (1991) *PNAS* 88:7978-7982, each of which is hereby incorporated by reference in its entirety).

[0142] An antibody or antigen-binding fragment thereof of a multispecific antibody or antigen-binding fragment thereof described herein can be derived from other species. A humanized antibody is an antibody produced by recombinant DNA technology, in which some or all amino acids of a human immunoglobulin light chain or heavy chain that are not required for antigen binding (e.g., constant regions and/or framework regions of variable domains) are used to substitute for the corresponding amino acids from light chain or heavy chain of the cognate, nonhuman antibody. By way of example, a humanized version of a murine antibody to a given antigen has on both heavy and light chains: (1) constant regions of a human antibody; (2) FRs from the variable domains of a human antibody; and (3) CDRs from the murine antibody. Human FRs may be selected based on their highest sequence homology to mouse FR sequence. When necessary, one or more residues in human FRs can be changed to residues at corresponding positions in a murine antibody so as to preserve binding affinity of the humanized antibody to a target. This change is sometimes called "back mutation." Similarly, forward mutations may be made to revert back to murine sequence for a desired reason, e.g., stability or affinity to a target. Humanized antibodies generally are generally less likely to elicit an immune response in humans as compared to chimeric human antibodies because the former contain considerably fewer non-human components.

[0143] Methods for humanizing non-human antibodies are well known in the art. Suitable methods for making humanized antibodies in accordance with the present disclosure are described in, e.g., Winter EP 0 239 400; Jones et al., *Nature* 321:522-525 (1986); Riechmann et al., *Nature* 332:323-327 (1988); Verhoeyen et al., *Science* 239: 1534-1536 (1988); Queen et al., *Proc. Nat. Acad. Sci. USA* 86:10029 (1989); U.S. Patent 6,180,370; and Orlandi et al., *Proc. Natl. Acad. Sci. USA* 86:3833 (1989); the disclosures of each of which

are incorporated herein by reference in their entireties. Generally, transplantation of non-human (e.g., murine) CDRs onto a human antibody is achieved as follows. cDNAs encoding VH and VL are isolated from a hybridoma, and nucleic acid sequences encoding VH and VL including CDRs are determined by sequencing. Nucleic acid sequences encoding CDRs are inserted into corresponding regions of a human antibody VH or VL coding sequences and attached to human constant region gene segments of a desired isotype (e.g., $\gamma 1$ for CH and κ for CL). Humanized heavy and light chain genes are co-expressed in mammalian host cells (e.g., CHO or NSO cells) to produce soluble humanized antibody. To facilitate large-scale production of antibodies, it is often desirable to select for a high expressor using, for example, a DHFR gene or GS gene in the producer line.

[0144] An antibody or antigen-binding fragment thereof of a multispecific antibody or antigen-binding fragment thereof described herein can be or comprise a human antibody or antigen-binding fragment thereof. Completely human antibodies may be particularly desirable for therapeutic treatment of human subjects. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody libraries derived from human immunoglobulin sequences (see, e.g., U.S. Pat. Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645, WO 98/60433, WO 98/24893, WO 98/16664, WO 96/34096, WO 96/33735, and WO 91/10741; each of which is incorporated herein by reference in its entirety). Techniques are also available for the preparation of human monoclonal antibodies in, e.g., Cole et al., *Monoclonal Antibodies and Cancer Therapy*, Alan R. Riss, (1985); and Boerner et al., *J. Immunol.*, 147(1):86-95, (1991), each of which is incorporated herein by reference in its entirety.

[0145] An antibody or antigen-binding fragment thereof of a multispecific antibody or antigen-binding fragment thereof described herein can be or comprise a chimeric antibody or antigen-binding fragment thereof. Illustrative methods of making chimeric antibodies are described, for example, in U.S. Pat. No. 4,816,567; and Morrison et al., *Proc. Natl. Acad. Sci. USA*, 1984, 81:6851-6855; each of which is incorporated by reference in its entirety. In some embodiments, a chimeric antibody is made by using recombinant techniques to combine a non-human variable region (e.g., a variable region derived from a mouse, rat, hamster, rabbit, or non-human primate, such as a monkey) with a human constant region.

[0146] Any suitable method can be used to introduce variability into one or more polynucleotide sequences encoding a multispecific antibody or antigen-binding fragment thereof described herein, including error-prone PCR, chain shuffling, and oligonucleotide-directed mutagenesis such as trinucleotide-directed mutagenesis (TRIM). In some embodiments, several CDR residues (e.g., 4-6 residues at a time) are randomized. CDR residues involved in antigen binding may be specifically identified, for example, using alanine scanning mutagenesis or modeling. CDR-H3 and CDR-L3 in particular are often targeted for mutation. Introduction of diversity into variable regions and/or CDRs can be used to produce a secondary library. A secondary library is then screened to identify antibody variants with improved affinity. Affinity maturation by constructing and reselecting from secondary libraries has been described, for example, in Hoogenboom et al., *Methods in Molecular Biology*, 2001, 178:1-37, incorporated by reference in its entirety.

Nucleic Acids

[0147] The present disclosure, among other things, provides nucleic acids encoding multispecific antibodies or antigen-binding fragments thereof described herein. The present disclosure includes nucleic acids encoding one or more heavy chains, VH domains, heavy chain FRs, heavy chain CDRs, heavy chain constant domains, light chains, VL domains, light chain FRs, light chain CDRs, light chain constant domains, or other immunoglobulin-like sequences, antibodies, or antigen-binding fragments thereof disclosed herein. Such nucleic acids may be present in a vector. Such nucleic acids may be present in the genome of a cell, e.g., a cell of a subject in need of treatment or a cell for production of an antibody or antigen-binding fragment thereof, e.g., a mammalian cell for production of at least one multispecific antibody or antigen-binding fragment thereof described herein.

[0148] Nucleic acids encoding multispecific antibodies or antigen-binding fragment thereof described herein may be modified to include codons that are optimized for expression in a particular cell type or organism. Codon optimized sequences are synthetic sequences, and preferably encode an identical polypeptide (or biologically active fragment of a full-length polypeptide which has substantially the same activity as the full-length polypeptide) encoded by a non-codon optimized parent polynucleotide. In some embodiments, a coding region of a nucleic acid encoding a multispecific antibody or antigen-binding fragment thereof described herein, in whole or in part, may include an altered sequence to optimize

codon usage for a particular cell type (e.g., a eukaryotic or prokaryotic cell). For example, a coding sequence for a humanized heavy (or light) chain variable region as described herein may be optimized for expression in bacterial cells. Alternatively, the coding sequence may be optimized for expression in a mammalian cell (e.g., a CHO cell). Such a sequence may be described as a codon-optimized sequence.

[0149] Nucleic acid constructs of the present disclosure may be inserted into an expression vector by methods known in the art, and nucleic acids may be operably linked to an expression control sequence. As used herein, the term “operably linked” refers to functional linkage between, for example, a regulatory sequence and a heterologous nucleic acid sequence resulting in expression of the latter. For example, a first nucleic acid sequence is operably linked with a second nucleic acid sequence when the first nucleic acid sequence is placed in a functional relationship with the second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Generally, operably linked DNA sequences are contiguous and, where necessary to join two protein coding regions, in the same reading frame.

[0150] A vector comprising any nucleic acids or fragments thereof described herein is further provided by the present disclosure. Any nucleic acids or fragments thereof described herein can be cloned into any suitable vector and can be used to transform or transfect any suitable host. Selection of vectors and methods to construct them are commonly known to persons of ordinary skill in the art (see, e.g., “Recombinant DNA Part D,” *Methods in Enzymology*, Vol. 153, Wu and Grossman, eds., Academic Press (1987)).

[0151] Conventionally used techniques including, for example, electrophoresis, calcium phosphate precipitation, DEAE-dextran transfection, or lipofection, may be used to introduce a foreign nucleic acid (e.g., DNA or RNA) into a prokaryotic or eukaryotic host cell. Desirably, a vector may include regulatory sequences, such as transcription and/or translation initiation and/or termination codons, which are specific to the type of host (e.g., bacterium, fungus, plant, or animal) into which a vector is to be introduced, as appropriate and taking into consideration whether a vector is DNA or RNA. In some embodiments, a vector comprises regulatory sequences that are specific to a genus of a host cell. In some embodiments, a vector comprises regulatory sequences that are specific to a species of a host.

[0152] In addition to a replication system and an inserted nucleic acid, a nucleic acid construct can include one or more marker genes, which allow for selection of transformed or

transfected hosts. Exemplary marker genes include, e.g., biocide resistance (e.g., resistance to antibiotics or heavy metals) or complementation in an auxotrophic host to provide prototrophy.

[0153] An expression vector can comprise a native or nonnative promoter operably linked to an isolated or purified nucleic acid as described above. Selection of promoters, e.g., strong, weak, inducible, tissue-specific, and/or developmental-specific, is within the skill of one in the art. Similarly, combining a nucleic acid as described above with a promoter is also within the skill of one in the art.

[0154] Suitable vectors include those designed for propagation and expansion and/or for expression. For example, a cloning vector may be selected from the pUC series, the pBluescript series (Stratagene, LaJolla, Calif.), the pET series (Novagen, Madison, Wis.), the pGEX series (Pharmacia Biotech, Uppsala, Sweden), or the pEX series (Clontech, Palo Alto, Calif.). Bacteriophage vectors, such as λ GT10, λ GT11, λ ZapII (Stratagene), λ EMBL4, and λ NM1149, may be used. Examples of plant expression vectors that can be used include pBI110, pBI101.2, pBI101.3, pBI121, or pBIN19 (Clontech). Examples of animal expression vectors that can be used include pEUK-C1, pMAM, or pMAMneo (Clontech). The TOPO cloning system (Invitrogen, Carlsbad, Calif.) also can be used in accordance with the manufacturer's recommendations.

[0155] Additional sequences can be added to such cloning and/or expression sequences to optimize their function in cloning and/or expression, to aid in isolation of a nucleic acid encoding a multispecific antibody or antigen-binding fragment thereof described herein, or to improve introduction of a nucleic acid into a cell. Use of cloning vectors, expression vectors, adapters, and linkers is well known in the art (see, e.g., Sambrook et al., *Molecular Cloning, a Laboratory Manual*, 2d edition, Cold Spring Harbor Press, Cold Spring Harbor, N.Y. (1989); and Ausubel et al., *Current Protocols in Molecular Biology*, Greene Publishing Associates and John Wiley & Sons, New York, N.Y. (1994), each of which is hereby incorporated by reference in its entirety).

[0156] In some embodiments, nucleic acids and vectors described herein are isolated and/or purified. Isolated nucleic acids and vectors may be prepared using standard techniques known in the art including, for example, alkali/SDS treatment, CsCl binding, column chromatography, and/or agarose gel electrophoresis. The composition can comprise other components as described further herein.

[0157] Any method known to one skilled in the art for insertion of nucleic acids into a vector may be used to construct expression vectors encoding a multispecific antibody or antigen-binding fragment thereof described herein under control of transcriptional and/or translational control signals. These methods may include *in vitro* recombinant DNA and synthetic techniques and *in vivo* recombination (see, e.g., Ausubel, *supra*; or Sambrook, *supra*).

Antibodies That Bind to the Same Epitope

[0158] Multispecific antibodies or antigen-binding fragments thereof described herein include antibodies and antibody fragments that bind to one or more of the same epitopes as the antibodies or fragments thereof shown in Table 1. As used herein, the term “epitope” refers to any moiety that is specifically recognized by an immunoglobulin (e.g., antibody or receptor) binding component. In some embodiments, an epitope is comprised of a plurality of chemical atoms or groups on an antigen. In some embodiments, such chemical atoms or groups are surface-exposed when an antigen adopts a relevant three-dimensional conformation. In some embodiments, such chemical atoms or groups are physically near each other in space when the antigen adopts such a conformation. In some embodiments, at least some such chemical atoms or groups are physically separated from one another when an antigen adopts an alternative conformation (e.g., is linearized).

[0159] Additional antibodies or antigen-binding fragments can be identified based on their ability to cross-compete (e.g., to competitively inhibit binding of, in a statistically significant manner) with multispecific antibodies or antigen-binding fragments thereof described herein in B7-H7 binding assays and/or an immune effector cell antigen (e.g., CD3) binding assays. The ability of a test antibody or antigen-binding fragment to inhibit binding of a multispecific antibody or antigen-binding fragment thereof described herein to B7-H7 demonstrates that such a test antibody or antigen-binding fragment can compete with that multispecific antibody or antigen-binding fragment for binding to B7-H7. Accordingly, such an antibody or antigen-binding fragment may bind to the same or a related epitope on B7-H7 as a multispecific antibody or antigen-binding fragment thereof described herein. The ability of a test antibody or antigen-binding fragment to inhibit binding of a multispecific antibody or antigen-binding fragment thereof described herein to an immune effector cell antigen (e.g., CD3) demonstrates that such a test antibody or antigen-binding fragment can compete with that multispecific antibody or antigen-binding fragment for binding to an immune effector

cell antigen (e.g., CD3). Accordingly, such an antibody or antigen-binding fragment may bind to the same or a related epitope on an immune effector cell antigen (e.g., CD3) as a multispecific antibody or antigen-binding fragment thereof described herein.

Additional Agents

[0160] The present disclosure, among other things, provides one or more additional agents (e.g., 2, 3, 4, 5, or more additional agents) that can be administered with multispecific antibodies or antigen-binding fragments thereof described herein in a combination therapy. As used herein, an additional agent may be or comprise any known treatment for a particular disease, disorder, or condition (e.g., a cancer). For example, an additional agent can be or comprise one or more of: a chemotherapeutic agent, a hormone therapy, a cell-based therapy, treatment with hyperthermia, a photodynamic therapy, surgery, radiation, or a transplant. In some embodiments, an additional agent binds to a co-stimulatory molecule (e.g., TMIGD2) on an immune effector cell surface. In some embodiments, an additional agent comprises or is a TMIGD2 agonist. In some embodiments, an additional agent comprises or is an antibody or antigen-binding fragment thereof, an organic molecule (e.g., a small molecule), a peptide (e.g., a fusion protein), an aptamer, a nucleic acid, a chimeric antigen receptor, a glycoprotein, a saccharide, a lipid, a growth factor, an enzyme, a synthetic molecule, a carbohydrate, a lipid, a hormone, a polymer, or any combination thereof that selectively binds to TMIGD2. In some embodiments, an additional agent comprises or is an antibody or antigen-binding fragment thereof that selectively binds to TMIGD2. In some embodiments, an additional agent can cause the formation of a powerful immune synapse, capable of addressing disease.

[0161] In some embodiments, a chemotherapeutic agent comprises or is one or more anthracyclines, one or more cytoskeletal disruptors (e.g. microtubule targeting agents such as taxanes, maytansine, and analogs thereof), one or more epothilones, one or more histone deacetylase inhibitors (HDACs), one or more topoisomerase inhibitors (e.g., one or more of inhibitors of topoisomerase I or topoisomerase II), one or more kinase inhibitors, one or more nucleotide analogs or nucleotide precursor analogs, one or more peptide antibiotics, one or more platinum-based agents, one or more retinoids, one or more vinca alkaloids, or a combination thereof.

[0162] In some embodiments, a chemotherapeutic agent comprises or is one or more of: Actinomycin, All-trans retinoic acid, an Auiristatin, Azacitidine, Azathioprine,

Bleomycin, Bortezomib, Carboplatin, Capecitabine, Cisplatin, Chlorambucil, Cyclophosphamide, Curcumin, Cytarabine, Daunorubicin, Docetaxel, Doxifluridine, Doxorubicin, Epirubicin, Epothilone, Etoposide, Fludarabine, Fluorouracil, Gemcitabine, Hydroxyurea, Idarubicin, Imatinib, Irinotecan, Maytansine and/or analogs thereof (e.g. DM1), Mechlorethamine, Mercaptopurine, Methotrexate, Mitoxantrone, a Maytansinoid, Oxaliplatin, Paclitaxel, Pemetrexed, Rituxan, Teniposide, Tioguanine, Topotecan, Valrubicin, Vinblastine, Vincristine, Vindesine, or Vinorelbine. In some embodiments, a chemotherapeutic agent comprises or is an antibody-drug conjugate (ADC). In some embodiments, an ADC comprises or is hLL1-doxorubicin, hRS7-SN-38, hMN-14-SN-38, hLL2-SN-38, hA20-SN-38, hPAM4-SN-38, hLL1-SN-38, hRS7-Pro-2-P-Dox, hMN-14-Pro-2-P-Dox, hLL2-Pro-2-P-Dox, hA20-Pro-2-P-Dox, hPAM4-Pro-2-P-Dox, hLL1-Pro-2-P-Dox, P4/D10-doxorubicin, gemtuzumab ozogamicin, brentuximab vedotin, trastuzumab emtansine, inotuzumab ozogamicin, glembatumomab vedotin, SAR3419, SAR566658, BIIB015, BT062, SGN-75, SGN-CD19A, AMG-172, AMG-595, BAY-94-9343, ASG-5ME, ASG-22ME, ASG-16M8F, MDX-1203, MLN-0264, anti-PSMA ADC, RG-7450, RG-7458, RG-7593, RG-7596, RG-7598, RG-7599, RG-7600, RG-7636, ABT-414, IMGN-853, IMGN-529, vorsetuzumab mafodotin, lorvotuzumab mertansine, or a combination thereof.

[0163] In some embodiments, a hormone therapy may be or comprise tamoxifen, raloxifene, leuprolide, bicalutamide, granisetron, flutamide, or a combination thereof. In some embodiments, a cell-based therapy comprises or is chimeric antigen receptor T (CAR-T) cells, CAR-NK cells, TCR-transduced T cells, dendritic cells, tumor infiltrating lymphocytes (TILs), natural killer (NK) cells, or a combination thereof. In some embodiments, treatment with hyperthermia comprises or is local hyperthermia (e.g., external, intraluminal, or interstitial hyperthermia), regional hyperthermia (e.g., deep tissue hyperthermia, regional perfusion, or (continuous hyperthermic peritoneal perfusion), or whole-body hyperthermia. In some embodiments, a photodynamic therapy comprises or is administration of photosensitizers, such as hematoporphyrin and its derivatives, Verteporfin (BPD-MA), phthalocyanine, photosensitizer Pc4, demethoxy-hypocrellin A, 2BA-2-DMHA, or a combination thereof. In some embodiments, surgery comprises or is surgery to remove cancerous or precancerous tissue. In some embodiments, a transplant comprises or is a stem cell transplant or an organ transplant.

[0164] In some embodiments, an additional agent is administered prior to, substantially simultaneously with, or subsequent to administration of a multispecific antibody

or antigen-binding fragment thereof described herein. In some embodiments, administration of a multispecific antibody or antigen-binding fragment thereof described herein and an additional agent result in an improvement in a disease, disorder, or condition (e.g., cancer) to an extent that is greater than an improvement produced by either the multispecific antibody or antigen-binding fragment thereof described herein or the additional agent alone. The difference between the combined effect and the effect of each agent alone can be a statistically significant difference. In some embodiments, the combined effect can be a synergistic effect. In some embodiments, combined administration of a multispecific antibody or antigen-binding fragment thereof described herein and an additional agent allows administration of the additional agent at a reduced dose, a reduced number of doses, and/or a reduced frequency of dosage compared to a standard dosing regimen, e.g., an approved dosing regimen for the additional agent.

Conjugates to Therapeutic Agents

[0165] The present disclosure, among other things, provides multispecific antibodies or antigen-binding fragments thereof conjugated to one or more therapeutic agents. In some embodiments, a therapeutic agent comprises or is a cytotoxic agent, a drug, and/or a radioisotope. In some embodiments, a therapeutic agent comprises or is a cytotoxic agent. In some embodiments, a therapeutic agent comprises or is a drug. In some embodiments, a therapeutic agent comprises or is a radioisotope. When conjugated to a cytotoxic agent, such conjugates can be referred to as “immunotoxins.” A cytotoxic agent includes any agent that is detrimental to (e.g., can kill) cells. Examples of cytotoxic agents include, but are not limited to, taxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, teniposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs of any of the foregoing.

[0166] Multispecific antibodies or antigen-binding fragments thereof described herein can be conjugated to one or more therapeutic agents (e.g., one or more drugs) including, but are not limited to, antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, and/or 5-fluorouracil decarbazine), alkylating agents (e.g., mechlorethamine, thiotepa chlorambucil, melphalan, carmustine (BSNU), lomustine (CCNU), cyclophosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and/or cis-

dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and/or doxorubicin), antibiotics (e.g., dactinomycin, bleomycin, mithramycin, and/or anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine and/or vinblastine). Multippecific antibodies or antigen-binding fragments thereof described herein can be conjugated to one or more radioisotopes (e.g., radioactive iodine) to generate cytotoxic radiopharmaceuticals for treating diseases, disorders, or conditions described herein, such as cancers described herein.

Pharmaceutical Compositions

[0167] The present disclosure, among other things, provides pharmaceutical compositions comprising one or more multispecific antibodies or antigen-binding fragments described herein in combination with one or more pharmaceutically or physiologically acceptable carriers, diluents, or excipients.

[0168] When “a therapeutically effective amount” is indicated, a precise amount of a pharmaceutical composition comprising at least one multispecific antibody or antigen-binding fragment thereof described herein can be determined by a physician with consideration of individual differences in age, weight, immune response, and condition of a subject.

[0169] Pharmaceutical compositions described herein may comprise buffers including, but not limited to, neutral buffered saline or phosphate buffered saline (PBS); carbohydrates, such as glucose, mannose, sucrose, dextrans, or mannitol; proteins, polypeptides, or amino acids (e.g., glycine); antioxidants; chelating agents, such as EDTA or glutathione; adjuvants (e.g., aluminum hydroxide); and preservatives. In some embodiments, a pharmaceutical composition is substantially free of contaminants, e.g., there are no detectable levels of at least one contaminant (e.g., an endotoxin).

[0170] Pharmaceutical compositions described herein may be administered in any manner appropriate to the disease, disorder, or condition to be treated or prevented. Quantity and frequency of administration will be determined by such factors as condition of a patient, and type and severity of a patient's disease, disorder, or condition, although appropriate dosages may be determined by clinical trials.

[0171] Pharmaceutical compositions described herein may be in a variety of forms. These include, for example, liquid, semi-solid, and solid dosage forms, such as liquid solutions (e.g., injectable and infusible solutions), dispersions or suspensions, liposomes, and

suppositories. Preferred compositions may be injectable or infusible solutions.

Pharmaceutical compositions described herein can be formulated for administration intravenously, subcutaneously, intradermally, intratumorally, intranodally, intramedullary, intramuscularly, transarterially, or intraperitoneally.

[0172] In some embodiments, a pharmaceutical composition described herein is formulated for parenteral (e.g., intravenous, subcutaneous, intraperitoneal, or intramuscular) administration. In some embodiments, a pharmaceutical composition described herein is formulated for subcutaneous, intravenous, intramuscular, or intrasternal injection or infusion. In preferred embodiments, a pharmaceutical composition described herein is formulated for subcutaneous or intravenous injection or infusion. Pharmaceutical compositions described herein can be formulated for administered by using infusion techniques that are commonly known in immunotherapy (see, e.g., Rosenberg et al., New Eng. J. of Med. 319:1676, 1988, which is hereby incorporated by reference in its entirety).

[0173] As used herein, the terms “parenteral administration” and “administered parenterally” refer to modes of administration other than enteral and topical administration, usually by injection or infusion, and include, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal, epidural, intratumoral, and intrasternal injection and infusion.

[0174] In some embodiments, pharmaceutical compositions described herein are administered in combination with (e.g., before, substantially simultaneously, or following) one or more additional agents. In some embodiments, an additional agent may be or comprise bone marrow transplantation or lymphocyte ablative therapy using one more chemotherapeutic agent (e.g., Actinomycin, All-trans retinoic acid, an Auiristatin, Azacitidine, Azathioprine, Bleomycin, Bortezomib, Carboplatin, Capecitabine, Cisplatin, Chlorambucil, Cyclophosphamide, Curcumin, Cytarabine, Daunorubicin, Docetaxel, Doxifluridine, Doxorubicin, Epirubicin, Epothilone, Etoposide, Fludarabine, Fluorouracil, Gemcitabine, Hydroxyurea, Idarubicin, Imatinib, Irinotecan, Maytansine and/or analogs thereof (e.g. DM1), Mechlorethamine, Mercaptopurine, Methotrexate, Mitoxantrone, a Maytansinoid, Oxaliplatin, Paclitaxel, Pemetrexed, Rituxan, Teniposide, Tioguanine, Topotecan, Valrubicin, Vinblastine, Vincristine, Vindesine, Vinorelbine, or combinations thereof). In certain embodiments, subjects undergo standard treatment with high dose chemotherapy followed by peripheral blood stem cell transplantation. In certain

embodiments, following transplant, subjects receive one or more pharmaceutical compositions described herein. In some embodiments, pharmaceutical compositions described herein are administered before or following surgery.

[0175] A dosage of any aforementioned therapy to be administered to a subject will vary with a disease, disorder, or condition being treated and based on a specific subject. Scaling of dosages for human administration can be performed according to art-accepted practices.

[0176] The present disclosure, among other things, provides pharmaceutical compositions comprising one or more multispecific antibodies or antigen-binding fragments thereof described herein and immune effector cells (e.g., T cells (e.g., naïve and/or effector T cells) and/or NK cells). In some embodiments, immune effector cells described herein are loaded with one or more multispecific antibodies or antigen-binding fragments thereof described herein. In some embodiments, immune effector cells described herein are pre-loaded with one or more multispecific antibodies or antigen-binding fragments thereof described herein prior to cryopreservation. In some embodiments, immune effector cells described herein are cryopreserved prior to loading with one or more multispecific antibodies or antigen-binding fragments thereof described herein. Pharmaceutical compositions comprising immune effector cells pre-loaded with one or more multispecific antibodies or antigen-binding fragments thereof, as described herein, may be administered to a patient suffering from a disease, disorder, or condition described herein. In some embodiments, immune effector cells comprise or are T cells (e.g., naïve and/or effector T cells). In some embodiments, immune effector cells comprise or are NK cells. In some embodiments, immune effector cells described herein are derived from a patient suffering from a disease, disorder, or condition described herein. In some embodiments, immune effector cells described herein are isolated from umbilical cord tissue, placental tissue, induced pluripotent stem cells (iPSCs), or peripheral blood mononuclear cells (PBMCs).

Methods of Treatment

[0177] The present disclosure, among other things, provides methods of treating a disease, disorder or condition described herein in a subject comprising administering a pharmaceutical composition comprising one or more multispecific antibodies or antigen-binding fragments described herein. In some embodiments, a therapeutically effective

amount of at least one pharmaceutical composition described herein is administered to a subject having a disease, disorder, or condition.

[0178] In some embodiments, the disclosure provides one or more multispecific antibodies or antigen-binding fragments described herein comprising amino acid sequences found in Table 1 for use as a medicament. In some embodiments, the disclosure provides one or more multispecific antibodies or antigen-binding fragments described herein comprising amino acid sequences found in Table 1 for use in the treatment of a disease, disorder, or condition described herein. In some embodiments, the disclosure provides use of one or more multispecific antibodies or antigen-binding fragments described herein comprising amino acid sequences found in Table 1 for the manufacture of a medicament for the treatment of a disease, disorder, or condition described herein.

[0179] Pharmaceutical compositions comprising one or more multispecific antibodies or antigen-binding fragments described herein (e.g., in Table 1) can be for use in the manufacture of a medicament for treating a disease, disorder, or condition in a subject. Pharmaceutical compositions comprising one or more multispecific antibodies or antigen-binding fragments described herein can be for use in the manufacture of a medicament for modulating an immune response in a subject. Pharmaceutical compositions comprising one or more multispecific antibodies or antigen-binding fragments described herein can be administered to a subject in accordance with a dosage regimen described herein, alone or in combination with (e.g., before, substantially simultaneously, or following) one or more additional agents which may be or comprise one or more of therapeutic agents, procedures, or modalities.

[0180] A subject to be treated with methods described herein can be a mammal (e.g., a primate, mouse, humanized mouse, rat, non-human mammal, domestic animal, such as a dog, cat, cow, or horse), and is preferably a human (e.g., a patient having, or at risk of having, a disease, disorder or condition described herein). A subject can be an animal model of cancer, such as a xenograft animal model of a human-derived cancer. In some embodiments, a subject has not undergone treatment, such as chemotherapy, radiation therapy, targeted therapy, and/or immune checkpoint therapy. In another embodiment, a subject has undergone treatment, such as chemotherapy, radiation therapy, targeted therapy, and/or immune checkpoint therapy. In certain embodiments, a subject has had surgery to remove cancerous or precancerous tissue. In other embodiments, a cancerous tissue has not been

removed, e.g., the cancerous tissue may be located in an inoperable region of the body, such as in a tissue that is essential for life or in a region where a surgical procedure would cause considerable risk of harm to a subject.

[0181] A method of treating (e.g., one or more of reducing, inhibiting, or delaying progression of) a cancer or a tumor in a subject with a pharmaceutical composition comprising one or more multispecific antibodies or antigen-binding fragments described herein is provided. A subject can have an adult or pediatric form of cancer. A cancer may be at an early, intermediate, or late stage, or a metastatic cancer.

[0182] Methods of treating (e.g., one or more of reducing, inhibiting, or delaying progression of) at least one sign or symptom of cancer in a subject with a pharmaceutical composition comprising one or more multispecific antibodies or antigen-binding fragments described herein are provided. In some embodiments, pharmaceutical compositions described herein are useful to delay the onset of, slow the progression of, or ameliorate one or more signs or symptoms of cancer. In some embodiments, a physiological sign or symptom of cancer comprises or is one or more of: an increase in tumor volume, an increase in number of cancer cells, an increase in number of metastases, a decrease in life expectancy, an increase in cancer cell proliferation, or an increase in cancer cell survival. In some embodiments, a physical sign or symptom of cancer comprises or is one or more of: a skin lesion (e.g., a lump or mole), weight loss, digestive problems, discomfort, fatigue, pain, trouble swallowing, cough, unusual bleeding and/or discharge, changes in bowel and/or bladder habits, or mental confusion.

[0183] A cancer can include, but is not limited to, a solid tumor, a hematological cancer (e.g., leukemia, lymphoma, or myeloma, e.g., multiple myeloma), a metastatic lesion, or a combination thereof. Examples of solid tumors include, but are not limited to, malignancies e.g., sarcomas and carcinomas, e.g., adenocarcinomas of the various organ systems, such as those affecting lungs, breast, ovaries, lymph nodes, genitals, gastrointestinal (e.g., colon) and genitourinary tracts (e.g., renal, urothelial, bladder cells, or prostate), pharynx, CNS (e.g., brain, neural, or glial cells), head and neck, skin (e.g., melanoma, e.g., a cutaneous melanoma), pancreas, and bones (e.g., a chordoma).

[0184] In some embodiments, a cancer comprises or is a lung cancer (e.g., a non-small cell lung cancer (NSCLC) (e.g., a non-small cell lung cancer (NSCLC) with squamous and/or non-squamous histology or a NSCLC adenocarcinoma) or a small cell lung cancer (SCLC)), a skin cancer (e.g., a Merkel cell carcinoma or a melanoma (e.g., an advanced

melanoma)), an ovarian cancer, a mesothelioma, a bladder cancer, a soft tissue sarcoma (e.g., a hemangiopericytoma (HPC)), a bone cancer (a bone sarcoma), a kidney cancer (e.g., a renal cancer (e.g., a renal cell carcinoma)), a liver cancer (e.g., a hepatocellular carcinoma), a cholangiocarcinoma, a sarcoma, a myelodysplastic syndrome (MDS), a prostate cancer, a breast cancer (e.g., a breast cancer that does not express one, two or all of estrogen receptor, progesterone receptor, or Her2/neu, e.g., a triple negative breast cancer (TNBC)), a colorectal cancer (e.g., a relapsed colorectal cancer or a metastatic colorectal cancer, e.g., a microsatellite unstable colorectal cancer, a microsatellite stable colorectal cancer, a mismatch repair proficient colorectal cancer, or a mismatch repair deficient colorectal cancer), a nasopharyngeal cancer, a duodenal cancer, an endometrial cancer, a pancreatic cancer, a head and neck cancer (e.g., head and neck squamous cell carcinoma (HNSCC)), an anal cancer, a gastro-esophageal cancer, a thyroid cancer (e.g., anaplastic thyroid carcinoma), a cervical cancer (e.g., a squamous cell carcinoma of the cervix), a neuroendocrine tumor (e.g., an atypical pulmonary carcinoid tumor), a lymphoproliferative disease (e.g., a post-transplant lymphoproliferative disease), a lymphoma (e.g., T-cell lymphoma, B-cell lymphoma, or a non-Hodgkin lymphoma), a myeloma (e.g., a multiple myeloma), a leukemia (e.g., a myeloid leukemia or a lymphoid leukemia), or a combination thereof.

[0185] In some embodiments, a cancer comprises or is a brain tumor, e.g., a glioblastoma, a gliosarcoma, or a recurrent brain tumor. In some embodiments, a cancer comprises or is a pancreatic cancer, e.g., an advanced pancreatic cancer. In some embodiments, a cancer comprises or is a skin cancer, e.g., a melanoma (e.g., a stage II-IV melanoma, an HLA-A2 positive melanoma, an unresectable melanoma, or a metastatic melanoma), or a Merkel cell carcinoma. In some embodiments, a cancer comprises or is a renal cancer, e.g., a renal cell carcinoma (RCC) (e.g., a metastatic renal cell carcinoma). In some embodiments, a cancer comprises or is a breast cancer, e.g., a metastatic breast carcinoma or a stage IV breast carcinoma, e.g., a TNBC. In some embodiments, a cancer comprises or is a virus-associated cancer. In some embodiments, a cancer comprises or is an anal canal cancer (e.g., a squamous cell carcinoma of an anal canal). In some embodiments, a cancer comprises or is a cervical cancer (e.g., a squamous cell carcinoma of the cervix). In some embodiments, a cancer comprises or is a gastric cancer (e.g., an Epstein Barr Virus (EBV) positive gastric cancer or a gastric or gastro-esophageal junction carcinoma). In some embodiments, a cancer comprises or is a head and neck cancer (e.g., an HPV-positive or negative squamous cell cancer of the head and neck (SCCHN)). In some embodiments, a

cancer comprises or is a nasopharyngeal cancer (NPC). In some embodiments, a cancer comprises or is a colorectal cancer, e.g., a relapsed colorectal cancer, a metastatic colorectal cancer, e.g., a microsatellite unstable colorectal cancer, a microsatellite stable colorectal cancer, a mismatch repair proficient colorectal cancer, or a mismatch repair deficient colorectal cancer.

[0186] In some embodiments, a cancer comprises or is a hematological cancer. In some embodiments, a cancer comprises or is a leukemia, e.g., acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, chronic leukemia, or acute leukemia. In some embodiments, a cancer comprises or is a lymphoma, e.g., Hodgkin lymphoma (HL), non-Hodgkin's lymphoma, lymphocytic lymphoma, or DLBCL (e.g., a relapsed or refractory HL or DLBCL). In some embodiments, a cancer comprises or is a myeloma, e.g., multiple myeloma.

[0187] Administration of pharmaceutical compositions comprising one or more multispecific antibodies or antigen-binding fragments described herein may be carried out in any medically appropriate manner (e.g., injection, ingestion, transfusion, inhalation, implantation, or transplantation). In some embodiments, a pharmaceutical compositions described herein is administered by injection or infusion. Pharmaceutical compositions described herein may be administered to a patient transarterially, subcutaneously, intravenously, intradermally, intratumorally, intranodally, intramedullary, intramuscularly, or intraperitoneally. In some embodiments, a pharmaceutical composition described herein is administered parenterally (e.g., intravenously, subcutaneously, intraperitoneally, or intramuscularly). In some embodiments, a pharmaceutical composition described herein is administered by subcutaneous, intravenous, intramuscular, or intrasternal infusion or injection. In some embodiments, a pharmaceutical composition described herein is administered by intramuscular or subcutaneous injection. Pharmaceutical compositions described herein may be injected directly into a site of inflammation, a local disease site, a lymph node, an organ, a tumor, or site of infection in a subject.

[0188] In some embodiments, one or more multispecific antibodies or antigen-binding fragments described herein is administered in combination with one or more other therapeutic agents or modalities. In some embodiments, one or more additional agents (e.g., therapeutic agents or modalities) comprises or is an anti-cancer agent or modality. In some embodiments, such a combination therapy shows a synergistic effect in treating cancer. Known additional agents (e.g., compounds or treatments that show therapeutic efficacy in

treating cancer) may include, for example, one or more chemotherapeutic agents, alkylating agents, anti-metabolites, anti-microtubule agents, topoisomerase inhibitors, cytotoxic antibiotics, angiogenesis inhibitors, immunomodulators, vaccines, cell-based therapies (e.g., allogeneic or autologous stem cell transplantation), organ transplantation, radiation therapy, or surgery.

[0189] In some embodiments, a chemotherapeutic agent may be or comprise one or more anthracyclines, one or more cytoskeletal disruptors (e.g. microtubule targeting agents such as taxanes, maytansine, and analogs thereof), one or more epothilones, one or more histone deacetylase inhibitors (HDACs), one or more topoisomerase inhibitors (e.g., one or more of inhibitors of topoisomerase I or topoisomerase II), one or more kinase inhibitors, one or more nucleotide analogs or nucleotide precursor analogs, one or more peptide antibiotics, one or more platinum-based agents, one or more retinoids, one or more vinca alkaloids, or a combination thereof. In some embodiments, a chemotherapeutic agent may be or comprise one or more of: Actinomycin, All-trans retinoic acid, an Auiristatin, Azacitidine, Azathioprine, Bleomycin, Bortezomib, Carboplatin, Capecitabine, Cisplatin, Chlorambucil, Cyclophosphamide, Curcumin, Cytarabine, Daunorubicin, Docetaxel, Doxifluridine, Doxorubicin, Epirubicin, Epothilone, Etoposide, Fludarabine, Fluorouracil, Gemcitabine, Hydroxyurea, Idarubicin, Imatinib, Irinotecan, Maytansine and/or analogs thereof (e.g. DM1), Mechlorethamine, Mercaptopurine, Methotrexate, Mitoxantrone, a Maytansinoid, Oxaliplatin, Paclitaxel, Pemetrexed, Rituxan, Teniposide, Tioguanine, Topotecan, Valrubicin, Vinblastine, Vincristine, Vindesine, or Vinorelbine. In some embodiments, a chemotherapeutic agent may be an antibody-drug conjugate (ADC). In some embodiments, an ADC comprises or is hLL1-doxorubicin, hRS7-SN-38, hMN-14-SN-38, hLL2-SN-38, hA20-SN-38, hPAM4-SN-38, hLL1-SN-38, hRS7-Pro-2-P-Dox, hMN-14-Pro-2-P-Dox, hLL2-Pro-2-P-Dox, hA20-Pro-2-P-Dox, hPAM4-Pro-2-P-Dox, hLL1-Pro-2-P-Dox, P4/D10-doxorubicin, gemtuzumab ozogamicin, brentuximab vedotin, trastuzumab emtansine, inotuzumab ozogamicin, glembatumomab vedotin, SAR3419, SAR566658, BIIB015, BT062, SGN-75, SGN-CD19A, AMG-172, AMG-595, BAY-94-9343, ASG-5ME, ASG-22ME, ASG-16M8F, MDX-1203, MLN-0264, anti-PSMA ADC, RG-7450, RG-7458, RG-7593, RG-7596, RG-7598, RG-7599, RG-7600, RG-7636, ABT-414, IMGN-853, IMGN-529, vorsetuzumab mafodotin, lorvotuzumab mertansine, or a combination thereof.

[0190] In some embodiments, administration of one or more multispecific antibodies or antigen-binding fragments thereof described herein results in a change in activity of one or

more types of immune cells. In some embodiments, administration of one or more multispecific antibodies or antigen-binding fragments thereof described herein results in a change in peripheral blood lymphocytes. In some embodiments, administration of one or more multispecific antibodies or antigen-binding fragments thereof described herein results in an increase in peripheral blood lymphocytes. In some embodiments, administration of one or more multispecific antibodies or antigen-binding fragments thereof described herein results in a decrease in peripheral blood lymphocytes. In some embodiments, increased or decreased peripheral blood lymphocytes, as a result of administration of one or more multispecific antibodies or antigen-binding fragments thereof described herein, include but are not limited to: CD3-positive cells, CD20-positive cells, CD4-positive T cells, CD8-positive T cells, CD25-positive T cells, CD69-positive T cells or combinations thereof.

[0191] In some embodiments, administration of one or more multispecific antibodies or antigen-binding fragments thereof described herein results in increased production of immunomodulatory molecules. In some embodiments, administration of one or more multispecific antibodies or antigen-binding fragments thereof described herein results in increased production of immunomodulatory molecules about 4 or more hours after the administration of the antibody or the antigen-binding fragment thereof. In some embodiments, administration of one or more multispecific antibodies or antigen-binding fragments thereof described herein results in increased production of immunomodulatory molecules from about 4 hours to about 14 days after the administration of the antibody or the antigen-binding fragment thereof. In some embodiments, administration of a second dose of one or more multispecific antibodies or antigen-binding fragments thereof described herein about 4 or more hours after administration of a first dose thereof results in a further increased production of immunomodulatory molecules. In some embodiments, administration of a second dose of one or more multispecific antibodies or antigen-binding fragments thereof described herein from about 4 hours to about 7 days after the administration of the second dose results in a further increased production of immunomodulatory molecules. In some embodiments, administration of one or more multispecific antibodies or antigen-binding fragments thereof described herein results in increased production of one or more of the following immunomodulatory molecules: Granzyme B, Perforin, tumor necrosis factor alpha (TNF α), granulocyte colony stimulating factor (G-CSF), interferon-gamma (IFN- γ), interleukin 1 receptor antagonist (IL-1RA), interleukin 8 (IL-8), monocyte chemoattractant protein 1 (MCP-1), and macrophage inflammatory protein 1 beta (MIP-1 β).

[0192] In some embodiments, pharmaceutical compositions comprising one or more multispecific antibodies or antigen-binding fragments described herein can be administered to a subject (e.g., a primate) in accordance with a dosage regimen described herein. In some embodiments, the dosage regimen comprises administration of the pharmaceutical compositions comprising one or more multispecific antibodies or antigen-binding fragments described herein at a dose of at least about 1 $\mu\text{g/kg}$, 3 $\mu\text{g/kg}$, 10 $\mu\text{g/kg}$, 100 $\mu\text{g/kg}$, 300 $\mu\text{g/kg}$, 1000 $\mu\text{g/kg}$ or more. In some embodiments, the dosage regimen comprises administration of the pharmaceutical compositions at a dose of at least about 1 $\mu\text{g/kg}$. In some embodiments, the dosage regimen comprises administration of the pharmaceutical compositions at a dose of at least about 3 $\mu\text{g/kg}$. In some embodiments, the dosage regimen comprises administration of the pharmaceutical compositions at a dose of at least about 10 $\mu\text{g/kg}$. In some embodiments, the dosage regimen comprises administration of the pharmaceutical compositions at a dose of at least about 100 $\mu\text{g/kg}$. In some embodiments, the dosage regimen comprises administration of the pharmaceutical compositions at a dose of at least about 300 $\mu\text{g/kg}$. In some embodiments, the dosage regimen comprises administration of the pharmaceutical compositions at a dose of at least about 1000 $\mu\text{g/kg}$. In some embodiments, the dosage regimen comprises administration of the pharmaceutical compositions comprising one or more multispecific antibodies or antigen-binding fragments described herein at least once or at least twice during the course of treatment of the subject.. In some embodiments, the dosage regimen comprises administration of the pharmaceutical compositions comprising one or more multispecific antibodies or antigen-binding fragments described herein at least once during the course of treatment of a subject. In some embodiments, the dosage regimen comprises administration of the pharmaceutical compositions comprising one or more multispecific antibodies or antigen-binding fragments described herein at least twice during the course of treatment of a subject. a

Kits

[0193] The present disclosure, among other things, provides kits comprising one or more multispecific antibodies or antigen-binding fragments described herein, and instructions for use and/or administration. In some embodiments, a kit comprises one or more multispecific antibodies or antigen-binding fragments described herein and a pharmaceutically acceptable carrier, and instructions for use and/or administration.

[0194] In some embodiments, a kit comprises instructions for use in any method described herein. Instructions can comprise a description of administration of a first

pharmaceutical composition and second composition (e.g., and additional agent) to a subject to achieve an intended activity in a subject. The kit may further comprise a description of selecting a subject suitable for treatment based on identifying whether a subject is in need of treatment. In some embodiments, instructions comprise a description of administering a first pharmaceutical composition and second pharmaceutical composition to a subject who is in need of treatment.

[0195] Instructions relating to a first pharmaceutical composition and second composition (e.g., an additional agent) described herein generally include information as to dosage, dosing schedule, and route of administration for the intended treatment. Containers may be unit doses, bulk packages (e.g., multi-dose packages), or sub-unit doses. Instructions supplied in kits described herein are typically written instructions on a label or package insert. A label or package insert indicates that one or more pharmaceutical compositions are used for treating, delaying onset, and/or alleviating a disease, disorder or condition in a subject.

[0196] Kits provided herein are in suitable packaging. Suitable packaging includes, but is not limited to, vials, bottles, jars, and/or flexible packaging. Also contemplated are packages for use in combination with a specific device, such as an infusion device. A kit may have a sterile access port (for example, a container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). A container may also have a sterile access port.

[0197] Kits optionally may provide additional components, such as buffers and/or interpretive information. Normally, a kit comprises a container and a label or package insert(s) on or associated with a container. In some embodiment, the disclosure provides articles of manufacture comprising contents of kits described above.

INCORPORATION BY REFERENCE

[0198] All publications, patent applications, patents, and other references mentioned herein, including GenBank Accession Numbers, are incorporated by reference in their entirety. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting. 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 disclosure belongs. Although methods and materials similar or equivalent to those

described herein can be used in the practice or testing of the present disclosure, suitable methods and materials are described herein.

[0199] The disclosure is further illustrated by the following Examples. Examples are provided for illustrative purposes only. It is not to be construed as limiting the scope or content of the disclosure in any way.

EXAMPLES

[0200] The following Examples are provided so as to describe to the skilled artisan how to make and use methods and compositions described herein and are not intended to limit the scope of the present disclosure.

Example 1: Characterization of Certain B7-H7-CD3 Bispecific Antibodies.

[0201] The present Example demonstrates methods for characterizing bispecific antibodies or antigen-binding fragments thereof, specifically anti-B7-H7 and anti-immune effector cell antigen (e.g., CD3) bispecific antibodies or antigen-binding fragments thereof described herein. The present Example further provides various methods for determining and/or characterizing relevant functional activity of bispecific antibodies or antigen-binding fragments thereof described herein. An exemplary anti-B7-H7/CD3 bispecific antibody format is shown in **FIGS. 1A-1B**.

[0202] On-cell binding affinity (avid) of anti-B7-H7/CD3 bispecific antibodies was assessed using flow cytometry on human B7-H7 and cynomolgus B7-H7 expressing cells. The ability of NPXAB-1, NPXAB-2 and NPXAB-3 bispecific antibodies to bind 300.19 mouse pre-B leukemic cells engineered to express human B7-H7 (**FIG. 2A**) or cynomolgus B7-H7 (**FIG. 2B**) was investigated. First, 300.19-human or cynomolgus B7-H7 cells were incubated with 15µg/ml of each antibody for 30 minutes on ice, followed by a 1:10 dilution of a PE-conjugated anti-human secondary antibody. Flow cytometry analysis demonstrated the ability of NPXAB-1, NPXAB-2 and NPXAB-3 to bind to 300.19 cells over-expressing human and cynomolgus B7-H7 (**FIGS. 2A-2B**). Data are shown as mean fluorescent intensity (MFI). Comparable FACS analysis was carried out to characterize the binding of NPXAB-1, NPXAB-2 and/or NPXAB-3 to human CD3 expressed at the surface of Jurkat cells (**FIGS.**

3A-3B). This analysis demonstrated that NPXAB-1, NPXAB-2 and NPXAB-3 bound to CD3.

[0203] The avid affinity of the exemplary anti-B7-H7/ CD3 bispecific antibodies for recombinant B7-H7-Fc was investigated. The Octet system from ForteBio was used to measure avid affinity of the anti-B7-H7/ CD3 bispecific antibodies for recombinant human or cynomolgus B7-H7-Fc. Avid affinity was determined by capturing each antibody on an AHC sensor, followed by transfer to wells with 100 nM B7-H7-Fc antigen in solution. Avid affinities for exemplary anti-B7-H7/ CD3 antibodies NPXAB-1 and NPXAB-3 showed single digit nanomolar avid affinities or better to recombinant human or cynomolgus B7-H7 (**FIGS. 4A-4B**). Comparable analyses were carried out to evaluate the avid affinity of the B7-H7-CD3 antibodies for recombinant human or cynomolgus CD3-Fc using the Octet system using the conditions described above (**FIGS. 5A-5B**). Below is a summary of data characterizing NPXAB-1, NPXAB-2 and NPXAB-3 (**Table 2**). The cell killing IC₅₀ values were < 1pM. The experiments for measuring avid affinity of NPXAB-1 and NPXAB-2 antibodies to B7-H7 and CD3 were repeated using the Octet system under the conditions described above (**Tables 3-4**).

Table 2. Summary of data characterizing exemplary anti-B7-H7/CD3 bispecific antibodies NPXAB-1, NPXAB-2, and NPXAB-3.

Anti-body	B7-H7 Fab Arm	CD3 Fab arm	Octet				On-Cell Binding			Signaling
			Human B7-H7-Fc K _D (M) Avid	Cyno B7-H7-Fc K _D (M) Avid	Human CD3-Fc K _D (M) Monovalent	Cyno CD3-Fc K _D (M) Monovalent	Cell Binding EC50 (M) Human B7-H7 300.19	Cell Binding EC50 (M) Cyno B7-H7 300.19	Cell Binding EC50 (M) Human CD3 Jurkat	Jurkat Assay NFAT Reporter Induction EC50 (M)
NPXAB-1	65872	26906	1.52E-10	5.53E-10	4.76E-09	4.22E-09	1.47E-09	5.29E-10	8.77E-09	5.20E-12
NPXAB-2	65887	26919	9.57E-09	3.20E-08	4.85E-08	4.18E-08	3.26E-09	1.30E-09	ND	9.85E-12
NPXAB-3	65889	26919	1.66E-10	1.97E-09	1.08E-08	1.02E-08	1.85E-09	1.30E-09	2.71E-08	9.78E-12

Table 3: NPXAB-1 and NPXAB-2 bind to recombinant human and cynomolgus B7-H7.

	Human B7-H7			Cyno B7-H7		
	kon (1/Ms)	koff (1/s)	K _D (M)	kon (1/Ms)	koff (1/s)	K _D (M)
NPXAB-1	6.16E+05	2.05E-03	3.33E-09	6.95E+05	1.07E-03	1.53E-09
NPXAB-2	4.97E+05	4.75E-03	9.57E-09	2.65E+05	8.47E-03	3.20E-08

Table 4: NPXAB-1 and NPXAB-2 bind to recombinant human and cynomolgus CD3.

	Human CD3			Cyno CD3		
	kon (1/Ms)	koff (1/s)	K _D (M)	kon (1/Ms)	koff (1/s)	K _D (M)
NPXAB-1	2.59E+05	1.23E-03	4.76E-09	2.78E+05	1.17E-03	4.22E-09
NPXAB-2	3.24E+05	1.57E-02	4.85E-08	3.43E+05	1.43E-02	4.18E-08

[0204] The ability of the anti-B7-H7/CD3 bispecific antibodies to induce signaling of CD3-expressing Jurkat NFAT luciferase reporter cells in the presence of B7-H7-expressing Raji cells was evaluated (**FIG. 6A**). Promega TCR/CD3 Jurkat effector cells (NFAT) were mixed with Raji-B7-H7 cells in a 5:1 ratio in the presence of increasing dose of NPXAB-1, NPXAB-2 and NPXAB-3. CD3-mediated signaling was measured by quantifying luminescence using the Bio-Glo luciferase assay system from Promega. Each of NPXAB-1, NPXAB-2 and NPXAB-3 induced relatively strong CD3 signaling in this assay (**FIG. 6B**). Additionally, the ability of NPXAB-1 and NPXAB-2 to crosslink B7-H7 on tumor cells with CD3 on T cells to induce T cell activation was measured in a CD3 Jurkat reporter assay. To identify the specific effect of crosslinking B7-H7 on tumor cells with CD3 of T-cells on T-cell activation, the above assay was performed with NPXAB-1 and NPXAB-2 antibodies, with either only Jurkat cells present, or with Jurkat and Raji cells. CD3-mediated signaling activation of Jurkat cells required the presence of B7-H7-positive target cells with both NPXAB-1 and NPXAB-2 (**FIG. 6C**). Furthermore, greater potency of CD3-mediated signaling was achieved with NPXAB-1 than with NPXAB-2, which correlates with the higher CD3 binding affinity of NPXAB-1 compared to NPXAB-2 (**FIG. 6C** and **Table 3**).

[0205] Potency of NPXAB-1, NPXAB-2 and NPXAB-3 in a cell killing assay was evaluated in a PBMC co-culture assay. Briefly, cell trace violet-labeled (CTV) A204 cells and HT29 cells endogenously expressing B7-H7 were plated in a 96-well flat bottom tissue culture plate and incubated at 37°C overnight to adhere. CTV labeled Raji lymphoma cells engineered to express B7-H7 were plated in 96-well flat bottom tissue culture plates the day

of treatment. NPXAB-1, NPXAB-2, NPXAB-3, or isotype control bispecific antibodies were added to the plated cells and incubated at 37°C for 30 minutes. PBMCs were subsequently added to the tissue culture plate at a 10:1 immune effector (PBMC) to target (A204) cell ratio and incubated overnight at 37°C. Raji and HT29 cells were treated with either the NPXAB-1 or NPXAB-2 antibodies, and subsequently co-cultured with PBMCs at a 5:1 effector to target ratio. The cells then stained with the Near IR Live/Dead fixable viability stain for 30 minutes at 4°C and then analyzed by flow cytometry to evaluate the frequency of dead tumor cells (CTV+Live/Dead stain+) remaining. Each of NPXAB-1, NPXAB-2 and NPXAB-3 resulted in relatively strong cytotoxic activity of immune effector cells for target A204 cells (**FIG. 7A**). NPXAB-1 and NPXAB-2 also induced potent cell killing in Raji and HT29 cells, although NPXAB-2-treated cells exhibited greater cytotoxicity than NPXAB-1-treated cells (**FIGS. 7B-7C**).

[0206] The ability of NPXAB-1 and NPXAB-2 to induce primary T cell activation was tested in vitro. Primary human peripheral blood mononuclear cells (PBMCs) were co-cultured overnight with Raji-B7-H7 cells at an effector to target cell ratio of 5:1 in the presence of NPXAB-1 and NPXAB-2 at concentrations ranging from 0.0051 ng/mL to 10 µg/mL. Cells were stained with fluorescently conjugated antibodies to CD4, CD8, and CD25. T cell activation was assessed by measuring CD25 upregulation on CD4-positive and CD8-positive T cells by flow cytometry. NPXAB-1 induced CD4-positive and CD8-positive T cell activation with EC50s of 0.010 µg/mL and 0.0016 µg/mL respectively (**FIGS. 8A and 8B**). NPXAB-2 induced CD4-positive and CD8-positive T cell activation with EC50s of 0.010 µg/mL and 0.0015 µg/mL, respectively (**FIGS. 8A and 8B**). No activity was observed for either antibody in the absence of Raji-B7-H7 cells (**FIGS. 8A and 8B**).

[0207] The in vivo activity of NPXAB-2 was assessed in the B7-H7-expressing HT29 colon carcinoma tumor model in NCG mice humanized with activated human T cells. Briefly, female NCG mice were injected with HT29 tumor cells (5×10^6) subcutaneously (sc) in the right flank. When tumors reached an average volume of 80-120 mm³, animals were sorted into groups and injected intraperitoneally (ip) with activated human T cells (2×10^7). One day after T cell injection, mice were then treated with NPXAB-2 (10 mg/kg) intravenously (iv) weekly for a total of 4 injections. Control animals were untreated. Tumor growth was measured over time. NPXAB-2 treatment significantly delayed the growth of HT29 tumors in T cell humanized mice compared to controls (**FIG. 9A**). NPXAB-2 resulted

in tumor growth inhibition of 40%, 57%, 60%, and 63% relative to the control group on study days 12, 15, 20, and 24, respectively.

[0208] The experiment was repeated with minor modification. Briefly, one day after T cell injection, mice were treated with NPXAB-2 and NPXAB-1 at different concentrations of 0.1 mg/kg, 1 mg/kg, and 10 mg/kg iv weekly for a total of 4 injections. NPXAB-2 treatment significantly delayed the growth of HT29 tumors in T cell humanized mice compared to controls (**FIG. 9B**). Administration of NPXAB-2 at 10 mg/kg resulted in significant tumor growth inhibition of 66.2%, 63.1%, 63.1%, 63.1%, 61.2%, and 57.7% on study days 12, 15, 19, 22, 26, and 28, respectively. Administration of NPXAB-2 at 1 mg/kg resulted in significant tumor growth inhibition of 65.6%, 59.7%, 56.8%, 53.3%, and 52.8% on study days 15, 19, 22, 26, and 28, respectively. Administration of NPXAB-2 at 0.1 mg/kg resulted in significant tumor growth inhibition of 44.1%, 35.9%, 35.1%, 45.9%, and 46.5% on study days 15, 19, 22, 26, and 28, respectively. Administration of NPXAB-1 in T cell humanized mice showed a trend toward tumor growth reduction, albeit not statistically significant compared to negative controls (**FIG. 9C**). Below is a summary of the in vivo data characterizing NPXAB-1 and NPXAB-2 (**Table 5**). In all cases, percent (%) tumor growth inhibition (TGI) was calculated using the formula $\%TGI = (1 - (\text{change in tumor volume of treated group})/(\text{change in tumor volume of control group})) \times 100$.

Table 5. Summary of Percent (%) Tumor Growth Inhibition (TGI) of exemplary anti-B7-H7/CD3 bispecific antibodies NPXAB-1 and NPXAB-2.

Anti-body	Dose (mg/kg)	Study Day											
		12		15		19		22		26		28	
		% TGI	P Value	% TGI	P Value	% TGI	P Value	% TGI	P Value	% TGI	P Value	% TGI	P Value
NPXAB-2	0.1	28.2	NS	44.1	0.0291	35.9	0.0205	35.1	0.0375	45.9	0.0016	46.5	0.0021
NPXAB-2	1	48.9	NS	65.6	0.0005	59.7	<0.0001	56.8	0.003	53.3	0.0002	52.8	0.0004
NPXAB-2	10	66.2	0.0224	63.1	0.0008	63.1	<0.0001	63.1	<0.0001	61.2	<0.0001	57.7	0.0001
NPXAB-1	0.1	-7.4	NS	15.9	NS	16.4	NS	12.3	NS	23.6	NS	24.2	NS
NPXAB-1	1	-0.6	NS	22.4	NS	24.3	NS	22.6	NS	20.5	NS	15.1	NS

NPXAB-1	10	18.4	NS	25.5	NS	27.8	NS	27.8	NS	23.2	NS	12.8	NS
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[0209] The *in vivo* activity of NPXAB-1 and NPXAB-2 was assessed in the PC3M prostate adenocarcinoma tumor model in NCG mice mixed with human PBMCs. Briefly, 5×10^6 cells were mixed with 2.5×10^6 PBMCs and injected subcutaneously in the right flank. Seven days after tumor/PBMC implantation mice were dosed with NPXAB-1 or NPXAB-2 (10 mg/kg) intravenously. Antibody injections were delivered weekly for a total of three injections. Tumor volume was measured with calipers. Data from 2 separate PBMC donors was averaged. Both NPXAB-1 and NPXAB-2 significantly inhibited the growth of B7-H7-positive PC3M tumors in a PBMC admixed humanized mouse model (**FIGS. 10A-10B**).

[0210] The effect of NPXAB-1 and NPXAB-2 treatment on A204 tumors in mice humanized with activated T cells was assessed. Female NCG mice were implanted with 1×10^7 cells A204 rhabdomyosarcoma cells subcutaneously in the right flank. After seven days when tumors reached the volume of 60 mm^3 , mice were injected with 2×10^7 cells activated T cells intraperitoneally from two separate human donors. One day after T cell injection, mice were treated with 10 mg/kg NPXAB-1 or NPXAB-2 intravenously. Antibody treatments were continued weekly for a total of four doses. Tumor growth was measured, and data from 2 donors was averaged. Both NPXAB-1 and NPXAB-2 induce tumor regression in A204 tumors grown in mice humanized with activated T cells (**FIGS 11A-D**). NPXAB-1 treatment resulted in complete regression of tumors in 9 of 12 mice (**FIG. 11C**) and NPXAB-2 induced complete regression in 10 of 12 mice (**FIG. 11D**).

Example 2. Safety and efficacy of certain B7-H7-CD3 bispecific antibodies *in vivo*.

[0211] The present Example demonstrates methods for assessing safety and efficacy of certain anti-B7-H7 and anti-CD3 bispecific antibodies or antigen fragments thereof administered *in vivo*. The present example further demonstrates methods for assessing the immune response in a subject after the administration of bispecific antibodies or antigen-binding fragments thereof described herein. The present example also provides evidence that administration of bispecific antibodies or antigen-binding fragments thereof described herein results in immune cell activation and generation of immunomodulatory molecules in primates.

[0212] To evaluate the safety of exemplary B7-H7/CD3-bispecific antibodies NPXAB-1 and NPXAB-2 at different dosages, 14 primates were selected for a study and randomized into seven treatment groups, as summarized in **Table 6**. All primates were Cynomolgus monkeys, male, aged 3-4 years, and of initial body weight of 2.5-4.0 kg. All animals were administered an antibody in a vehicle (a formulation buffer) with the following contents: 20 mM His buffer, 140 mM sodium chloride (NaCl), 0.01% (weight/volume) polysorbate 80 (pH = 6) to a total dose volume of 5 mL/kg and injected intravenously via a saphenous vein as a bolus.

Table 6. Study Design and Animal Grouping

Group	Animal ID – Animal number	Test article	N	Dose (µg/kg)	Dosing Timepoint	Scheduled Endpoint (Necropsy)
1	Y2002039 – 1M001 Y2006043 – 1M002	NPXAB-2	2	10	Day 0	Day 28
2	Y2004033 – 2M001 Y2004019 – 2M002	NPXAB-2	2	1 3	Day 7 Day 21	Day 49
3	Y2004021 – 3M001 Y2004071 – 3M002	NPXAB-2	2	3	Day 14	Day 42
4	Y2004015 – 4M001 Y2006015 – 4M0012	NPXAB-1	2	10	Day 0	Day 28
5	Y2005095 – 5M001 Y2006073 – 5M002	NPXAB-1	2	100 300	Day 7 Day 21	Day 49
6	Y2006013 – 6M001 Y2005001 – 6M002	NPXAB-1	2	1,000	Day 14	Day 42
7	Y2005031 – 7M001 Y2003003 – 7M002	NPXAB-2	2	10	Day 0	Day 28

[0213] All NHPs were checked for health and wellness twice daily during the study period. Cage-side observations for general health and appearance (including stool consistency and diarrhea observations) were conducted twice daily, in the morning and in the afternoon,

during the study period for each group, including 1-hour post-dose and at least 6 hours later on each dosing day. Food consumption was qualitatively assessed once daily from 7 days before the first dosing for each group until the end of the study. Body temperature and respiratory rate were measured once pre-treatment and then at 1, 4, and 24 hours post-each dose for each group. Unscheduled measurement of body temperature was executed when necessary.

[0214] Animal 7M001 of Group 7 (NPXAB-2, 10 µg/kg) was euthanized and necropsied one day (D1) after receiving NPXAB-2. Loose/watery stool was observed around 6h after dosing on the day of NPXAB-2 administration (D0), and due to continued reduced activity, prostration, hypothermia and severe diarrhea-related dehydration through D1, the animal reached the euthanasia criteria. All other animals treated with NPXAB-2 experienced loose watery stool and/or yellow like vomitus. However, only animals treated with the highest dose of NPXAB-1 (1000 µg/kg, Group 6) experienced transient loose watery stool. Additionally, light to medium decrease in food consumption could be seen in all groups within one week post NPXAB-2 or NPXAB-1 dosing, which was considered to be related to test article administration. Furthermore, the animals in Group 6 were measured hypothermic at 48 hours after the single dose of NPXAB-1 at 1000 µg/kg on Day 14, and this symptom lasted until 120 hours in animal 6M001 and until 96 hours in animal 6M002, which was considered to be test article-related, and the animals recovered after that. No other obvious abnormalities of body temperature and/or respiratory rate were found in other animals. Finally, a slight decrease in body weight was observed in all animals for the first 2 weeks after the administration of the first dose, but the animals recovered thereafter without any special care (**FIGS. 12A-12B**).

[0215] To evaluate the effects of NPXAB-2 and NPXAB-1 treatment on immune cell composition and activation, approximately 1 mL of whole blood anticoagulated in potassium-ethylenediaminetetraacetic acid (EDTA) was collected before dosing; and 4 hours, 24 hours, 72 hours, 168 hours, 336 hours and 672 hours after dosing for Groups 1, 3, 4, 6 and 7; and 4 hours, 24 hours, 72 hours, 168 hours and 336 hours after the first dose and 4 hours, 24 hours, 72 hours, 168 hours, 336 hours and 672 hours after the second dose for Groups 2 and 5. The collected whole blood was then processed to lyse red blood cells, centrifuged, and washed with Dulbecco Phosphate Buffered Saline (DPBS, Adamas Life, C8024) twice. The isolated white blood cells were then counted and adjusted to 2×10^6 cells/sample, stained with a

Live/Dead stain Zombie NIR (Biolegend, 423106) for 10 minutes, washed with DPBS, blocked with an FC-chain block for 10 minutes, and stained with the following antibodies for 30 minutes: FITC-conjugated anti-CD45 (Beckton-Dickinson, 557803), BV711-conjugated anti-CD20 (Biolegend, 302342), Pacific Blue™-conjugated anti-CD3 (Beckton-Dickinson, 558124), BV605-conjugated anti-CD4 (Biolegend, 317438), BV510-CD8 (Biolegend, 344732), APC-conjugated anti-CD16 (Biolegend, 302012), BV650-conjugated CD56 (Biolegend, 318344), PE/Cy7-conjugated anti-CD25 (Biolegend, 302612), and PE-conjugated anti-CD69 (Biolegend, 310906). The samples were washed and analyzed with either a Cytex® NL-CLC or a BD LSRFortessa™.

[0216] First, the data were analyzed to evaluate the proportion of CD3-positive T-cells and CD20-positive B cells in all leukocytes (CD45-positive cells). The treatment of animals with a single dose of NPXAB-2 resulted in a significant decrease in the expression of CD3 and CD20 (**FIGS. 13A** and **14A**, respectively). After a two-dose treatment with NPXAB-2 (Group 2), however, 2M001 exhibited a slight increase in a CD3-positive cell population after both the first and the second dose administration, but 2M002 displayed a decrease in CD3-positive cells (**FIG. 13B**). CD20-positive cells, on the other hand, decreased in both animals after both the first and the second doses of NPXAB-2 being administered in Group 2 but recovered by D17 post-first dose (**FIG. 14B**). NPXAB-1 administration resulted in a decrease in CD3-positive cells, with a dose-dependent effect on recovery of the CD3-positive cell population to baseline (**FIG. 15A** and **15B**). Similarly, an immediate decrease in CD20-positive cells was observed in animals that received a single dose of the antibody (**FIG. 16A**) and after the first- and the second-dose administration of NPXAB-1, with a recovery at the subsequent measurement (**FIG. 16B**).

[0217] Next, T-cell activation was assessed by evaluating the proportion of CD25-positive and CD69-positive T-cells (CD3), helper T-cells (CD4), and killer T-cells (CD8). At 4 hours post-single dose administration of NPXAB-2, CD25, a middle/late marker of T-cell activation, surprisingly increased rapidly in all evaluated T-cell populations (**FIGS. 17A, 17C, and 17E**), whereas CD69, an early T-cell activation marker, increased only in CD4-positive cells (**FIG. 18C**) and decreased in CD3-positive and CD8-positive T-cells (**FIGS 18A and 18E**). A two-dose treatment with NPXAB-2 resulted in an increase in all CD25-positive T-cell populations, with a much more pronounced increase after the second dose compared to the first dose (**FIGS. 17B, 17D, and 17F**). On the contrary, a decrease in all

CD69-positive cells was observed immediately after both the first and the second doses of NPXAB-2 (FIGS. 18B, 18D, and 18F).

[0218] The NPXAB-1 treatment effect on T-cell activation was similar to the effect of the NPXAB-2 treatment – all T-cell populations had an increase in the CD25-positive cells 4 hours after the treatment (FIGS. 19A, 19C, and 19E). The observed increase in CD25-positive cells was also greater in Primates that had been administered the high (1000 µg/kg) dose of NPXAB-1 compared to the low dose of 10 µg/kg (FIGS. 19A, 19C, and 19E). NPXAB-1-treated primates exhibited a peak increase in CD69-positive cells at or around D3 post-treatment, but, contrary to the NPXAB-2 findings, no decrease in CD69-positive cells was observed at 4 hours post-treatment (FIGS. 20A, 20C, and 20E). In two-dose NPXAB-1-treated Primates, increase in all CD25-positive T-cells was observed after the first dose, but CD8-positive T-cells exhibited the largest degree of activation compared to CD3-positive or CD4-positive T-cells after the second dose (FIGS. 19B, 19D, and 19F). No consistent trend in early (4-hour) T-cell activation was observed with a CD69 marker, but peak activation was observed 24 hours after the NPXAB-1 administration, followed by a lack of consistent T-cell activation after the second dose (FIGS. 20B, 20D, and 20F).

[0219] To evaluate cytokine release by immune cells following the NPXAB-2 and NPXAB-1 treatments, 2 samples of 0.25 mL of blood from primates was collected at the same timepoints as for the flow cytometry analysis disclosed previously. Blood samples were placed on ice for 30 minutes until processed for serum. Serum was then stored at -80°C, thawed on the day of analysis on ice, and centrifuged at 10,000g to remove particulate. Samples were then prepared according to the ProcartaPlex™ Multiplex Immunoassay User Guide. The samples were analyzed with a Bio-Plex Suspension Chip System (BIO-RAD, Bio-Plex™ 200 System).

[0220] In the single NPXAB-2 dose experimental group, the serum concentration of G-CSF (FIG. 21A), IL-1RA (FIG. 21E), MCP-1 (FIG. 21I) and MIP-1 β (FIG. 21K) increased in Primates 4h after the administration of the antibody, and the expression of IL-8 began to increase after 4h of administration, which continued for up to 14 days post-treatment (FIG. 21G). IFN-γ increased in the group treated with the high 10 µg/kg dose of NPXAB-2 (FIG. 21C). In the experimental group that was administered two doses of NPXAB-2, only one animal had a significant change in cytokines, with elevated expression of G-CSF (FIG.

21B), IL-1RA (FIG. 21F), MCP-1 (FIG. 21J) and MIP-1 β (FIG. 21L) 4 hours after treatment, and this effect was more pronounced after the second dose was administered.

[0221] The treatment of Primates with NPXAB-1 resulted in similar serum cytokine profiles as the treatment with NPXAB-2. Transient increase in G-CSF, IL-1RA, MCP-1, MIP-1 β and IL-8 was observed, as illustrated in FIGS. 22A, 22E, 22I, 22K and 22G, respectively. The concentrations of G-CSF and IL-1RA after one dose (FIGS. 22A and 22E, respectively) and two doses (FIGS. 22B and 22F, respectively) increased with higher doses. A moderate increase in IFN- γ was observed in animal 6M002 treated with the high 10 μ g/kg dose of NPXAB-1. These findings indicate that systemic inflammatory responses to either the NPXAB-2 or NPXAB-1 antibody are not different.

[0222] Finally, gross and microscopic evaluations were done on all animals after euthanasia. All animals except for 7M001 reached their respective study points, were sedated and subsequently euthanized. Necropsy procedures were performed by qualified personnel with appropriate training and experience in animal anatomy and gross pathology. The tissues were grossly examined, collected, preserved, and processed for formalin-fixed paraffin-embedded preparation and subsequent hematoxylin and eosin staining.

[0223] Gross examination of animal organs and tissues post-necropsy did not yield any notable findings. Microscopic observations in Group 7, dosed with 10 μ g/kg of the NPXAB-2 antibody, revealed mild to moderate mixed cell inflammation in the duodenum, jejunum, ileum, and rectum. The inflammation consisted of mostly lymphocytes and macrophages with fewer neutrophils. Often, in areas of inflammation, there was evidence of cellular loss and/or destruction (necrosis or apoptosis). In animal 7M001, euthanized due to its poor physical condition, there was mild to moderate mixed cell inflammation in the gastrointestinal tract. The inflammation was likely responsible for the clinically observed diarrhea and led to the animal being euthanized. Incidence of selected microscopic findings is summarized in Table 7. No NPXAB-1-related microscopic findings were observed.

Table 7. Incidence of Selected Microscopic Findings in animals treated with NPXAB-2.

Test article	NPXAB-2			
Sex	Male			
Group No.	3	1	7	2
Dose ($\mu\text{g/kg}$)	3	10	10	1+3
Number of Animals	2	2	2	2
Duodenum				
Inflammation, mixed cell				
Moderate	0	0	1	0
Not Remarkable	2	2	1	2
Jejunum				
Inflammation, mixed cell				
Moderate	0	0	1	0
Not Remarkable	2	2	1	2
Ileum				
Inflammation, mixed cell				
Mild	0	0	1	0
Not Remarkable	2	2	1	2
Lymphangiectasis				
Mild	0	0	1	0
Not Remarkable	2	2	1	2
Rectum				
Inflammation, mixed cell				
Mild	0	0	1	0
Not Remarkable	2	2	1	2

[0224] The present disclosure provides evidence that NPXAB-2 and NPXAB-1 have dose-dependent effects on gastrointestinal tract inflammation. The present Example demonstrates that NPXAB-2 induces gastrointestinal (GI) inflammation in vivo at a dose of 10 $\mu\text{g/kg}$, whereas NPXAB-1 does not induce GI inflammation at a 100 $\times$ dose (e.g., 1000 $\mu\text{g/kg}$). The proposed mechanism that likely accounts for the observed differences in GI toxicity is demonstrated in **FIG. 23** and may be based on the TMIGD2-sparing properties of NPXAB-2 and TMIGD2-blocking properties of NPXAB-1. The present Example demonstrates that exemplary B7-H7/CD3 bispecific antibodies described herein may be safe to be administered as a therapy to a subject.

Example 3. NPXAB-1 blocks TMIGD2 binding to B7-H7 whereas NPXAB-2 spares TMIGD2 binding to B7-H7.

[0225] The present Example demonstrates methods for assessing TMIGD2 binding to B7-H7 after anti-B7-H7 and anti-CD3 bispecific antibodies or antigen fragments thereof are administered.

[0226] The B7-H7 axis incorporates two distinct interactions that can regulate T cell activity, an inhibitory signal when bound to KIR3DL3 and a stimulatory signal when bound to TMIGD2. Both KIR3DL3 and TMIGD2 are expressed on the surface of T cells and bind B7-H7 through distinct epitopes. CD3 T cell engagers (e.g., exemplary anti-B7-H7-CD3 bispecific antibodies) were developed to target B7-H7 as a tumor antigen and to block the inhibitory signal from B7-H7.

[0227] The ability of the B7-H7-CD3 bispecific antibodies NPXAB-1 and NPXAB-2 to block the B7-H7-TMIGD2 interaction was evaluated in an on-cell binding assay in vitro. 300.19 cells engineered to express human B7-H7 were incubated with NPXAB-1 or NPXAB-2 in vitro at concentrations ranging from 0.001 µg/mL to 20 µg/mL. Fluorescently labeled recombinant human Fc-conjugated TMIGD2 protein was then added to the cells and 300.19-B7-H7 cell bound TMIGD2 protein was analyzed by flow cytometry. Data are shown as percentage cell surface bound TMIGD2. This analysis demonstrated that NPXAB-1 blocked TMIGD2 binding to B7-H7 while NPXAB-2 spared TMIGD2 binding to B7-H7 (**FIG. 24**).

Example 4. NPXAB-2 spares B7-H7 induced TMIGD2 co-stimulation in a CD3 Jurkat reporter assay.

[0228] The present Example demonstrates methods for assessing if the TMIGD2 sparing B7-H7-CD3 bispecific antibody NPXAB-2 could induce enhanced T cell activation via B7-H7-TMIGD2 costimulatory signaling.

[0229] Human TMIGD2 was overexpressed in the Jurkat/CD3/NFAT luciferase reporter cell line. In these TMIGD2 overexpressing Jurkat/CD3/NFAT reporter cells, B7-H7-TMIGD2 co-stimulation enhanced the CD3 induced activation signal resulting in enhanced luciferase reporter activity. For example, **FIG. 25** depicts a schematic of the Jurkat/CD3/NFAT/TMIGD2 reporter assay. Jurkat/CD3/NFAT/TMIGD2 reporter cells were incubated with Raji tumor cells engineered to express B7-H7 in the presence of NPXAB-1 and NPXAB-2 at concentrations ranging from 0.0051 ng/mL to 10µg/mL for six hours. Data are shown as luminescence as a surrogate for T cell activation. The analysis demonstrated that both NPXAB-1 and NPXAB-2 induced dose dependent T cell activation in the Jurkat/CD3/NFAT/TMIGD2 luciferase reporter assay with EC₅₀ values of 0.0010 µg/mL and 0.00027 µg/mL respectively (**FIG. 26**). The TMIGD2 sparing B7-H7-CD3 bispecific

antibody NPXAB-2 demonstrated enhanced potency compared to the TMIGD2 blocking B7-H7-CD3 bispecific antibody NPXAB-1.

Example 5. NPXAB-2 spares B7-H7 induced TMIGD2 co-stimulation in a CD3 Jurkat reporter assay.

[0230] The present Example demonstrates methods for assessing the effect of TMIGD2 signaling in T cell activation induced by exemplary B7-H7-CD3 bispecific antibodies.

[0231] A series of TMIGD2 blocking and sparing B7-H7-CD3 bispecific antibodies were generated with matched high and low affinity CD3 binding arms. NPXAB-1 and NPXAB-3 are described in previous Examples. Amino acid sequences of exemplary bispecific NPXAB-4 are shown in **Table 8**. NPXAB-5 comprises a high-affinity CD3 binding arm of NPXAB-1 and a TMIGD2-sparing, B7-H7 binding arm of NPXAB-3. The binding characteristics of these bispecific antibodies are summarized in **Table 9**.

Table 8. Amino acid sequences of exemplary bispecific antibody and antigen-binding fragments thereof.

Antibody	Sequence	SEQ ID NO
NPXAB-4	Heavy Chain A - B7H7 binding arm	
	HCDR1 (IMGT) GFTFDDNA	SEQ ID NO: 205
	HCDR2 (IMGT) ISWSSNSI	SEQ ID NO: 206
	HCDR3 (IMGT) AKGSIIAGIWLGYFDL	SEQ ID NO: 207
	HCDR1 (Kabat) DNAMH	SEQ ID NO: 208

	HCDR2 (Kabat) GISWSSNSIAYADSVKG	SEQ ID NO: 209
	HCDR3 (Kabat) GSIIAGIWLGYFDL	SEQ ID NO: 210
	HCDR1 (Combined Kabat/IMGT) GFTFDDNAMH	SEQ ID NO: 211
	HCDR2 (Combined Kabat/IMGT) GISWSSNSIAYADSVKG	SEQ ID NO: 212
	HCDR3 (Combined Kabat/IMGT) GSIIAGIWLGYFDL	SEQ ID NO: 213
	VH EVQLVESGGGLVQPGRSLRLSCAASGFTFDDNAMHWVRQ APGKGLEWVSGISWSSNSIAYADSVKGRFTISRDNANKNSL YLQMNSLRAEDTAVYYCAKGSIIAGIWLGYFDLWGRGTL VTVSS	SEQ ID NO: 214
	Heavy Chain EVQLVESGGGLVQPGRSLRLSCAASGFTFDDNAMHWVRQ APGKGLEWVSGISWSSNSIAYADSVKGRFTISRDNANKNSL YLQMNSLRAEDTAVYYCAKGSIIAGIWLGYFDLWGRGTL VTVSSASTKGPSVFPRAPSSKSTSGGTAALGCLVRDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSL GTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPE AAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ DWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVCTL PPSRDELTKNQVSLVKGFPYPSDIAVEWESNGQPENNY KTTTPVLDSGDSFFLGSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPG	SEQ ID NO: 215
	Heavy Chain B - B7H7 binding Fab arm	
	HCDR1 (IMGT) GFTFDDNA	SEQ ID NO: 216

	HCDR2 (IMGT) ISWSSNSI	SEQ ID NO: 217
	HCDR3 (IMGT) AKGSIIAGIWLGYFDL	SEQ ID NO: 218
	HCDR1 (Kabat) DNAMH	SEQ ID NO: 219
	HCDR2 (Kabat) GISWSSNSIAYADSVKG	SEQ ID NO: 220
	HCDR3 (Kabat) GSIIAGIWLGYFDL	SEQ ID NO: 221
	HCDR1 (Combined Kabat/IMGT) GFTFDDNAMH	SEQ ID NO: 222
	HCDR2 (Combined Kabat/IMGT) GISWSSNSIAYADSVKG	SEQ ID NO: 223
	HCDR3 (Combined Kabat/IMGT) GSIIAGIWLGYFDL	SEQ ID NO: 224
	VH EVQLVESGGGLVQPGRSLRLSCAASGFTFDDNAMHWVRQ APGKGLEWVSGISWSSNSIAYADSVKGRFTISRDNKNSL YLQMNSLRAEDTAVYYCAKGSIIAGIWLGYFDLWGRGTL VTVSS	SEQ ID NO: 225
	Heavy Chain (Fab arm) EVQLVESGGGLVQPGRSLRLSCAASGFTFDDNAMHWVRQ APGKGLEWVSGISWSSNSIAYADSVKGRFTISRDNKNSL YLQMNSLRAEDTAVYYCAKGSIIAGIWLGYFDLWGRGTL VTVSSASTKGPSVFPRAPSSKSTSGGTAALGCLVRDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSL GTQTYICNVNHKPSNTKVDKKVEPKSCD	SEQ ID NO: 226

	Linker GGGGS GGGGS	SEQ ID NO: 227
	Heavy Chain B - CD3 binding arm (Fab + Fc)	
	HCDR1 (IMGT) GFNIKDY Y	SEQ ID NO: 228
	HCDR2 (IMGT) IDLENANT	SEQ ID NO: 229
	HCDR3 (IMGT) AR DAYGRYFYDV	SEQ ID NO: 230
	HCDR1 (Kabat) DY YMH	SEQ ID NO: 231
	HCDR2 (Kabat) WIDLENANTIYDAKFQG	SEQ ID NO: 232
	HCDR3 (Kabat) DAYGRYFYDV	SEQ ID NO: 233
	HCDR1 (Combined Kabat/IMGT) GFNIKDY YMH	SEQ ID NO: 234
	HCDR2 (Combined Kabat/IMGT) WIDLENANTIYDAKFQG	SEQ ID NO: 235
	HCDR3 (Combined Kabat/IMGT) DAYGRYFYDV	SEQ ID NO: 236
	VH QVQLVQSGAEVKKPGASVKVSCKASGFNIKDY YMHWVR QAPGQRLEWMGWIDLENANTIYDAKFQGRVTITRDT SAS TAYMELSSLRSEDTAVYYCARDAYGRYFYDVWGQGLV TVSS	SEQ ID NO: 237

	Heavy Chain (Fab + Fc) QVQLVQSGAEVKKPGASVKVSCKASGFNIKDYMHVVR QAPGQRLEWMGWIDLENANTIYDAKFQGRVTITRDTAS TAYMELSSLRSEDTAVYYCARDAYGRYFYDVWGQGT TVSSASTKGPSVFPLAPSSKSTSGGTAALGCQVEDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYELSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAA GGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPC RDELTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPG	SEQ ID NO: 238
	Heavy Chain (Full chain B7H7 + CD3 binding arm) EVQLVESGGGLVQPGRSLRLSCAASGFTFDDNAMHWVRQ APGKGLEWVSGISWSSNSIAYADSVKGRFTISRDNKNSL YLQMNSLR AEDTAVYYCAKGSIIAGIWLGYFDLWGRGTL VTVSSASTKGPSVFPRAPSSKSTSGGTAALGCLVRDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL GTQTYICNVNHKPSNTKVDKKVEPKSCDGGGGSGGGGSQ VQLVQSGAEVKKPGASVKVSCKASGFNIKDYMHVVRQ APGQRLEWMGWIDLENANTIYDAKFQGRVTITRDTAST AYMELSSLRSEDTAVYYCARDAYGRYFYDVWGQGT VSSASTKGPSVFPLAPSSKSTSGGTAALGCQVEDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYELSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAA GGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPC RDELTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPG	SEQ ID NO: 239
	Linker GGGGSGGGGS	SEQ ID NO: 240
	Light Chain A and/or B - B7H7 binding arm	
	LCDR1 (IMGT) QSVSSY	SEQ ID NO: 241
	LCDR2 (IMGT) DA	SEQ ID NO: 242

	LCDR3 (IMGT) QQVSISPPWT	SEQ ID NO: 243
	LCDR1 (Kabat) RASQSVSSYLA	SEQ ID NO: 244
	LCDR2 (Kabat) DASNRAT	SEQ ID NO: 245
	LCDR3 (Kabat) QQVSISPPWT	SEQ ID NO: 246
	LCDR1 (Combined Kabat/IMGT) RASQSVSSYLA	SEQ ID NO: 247
	LCDR2 (Combined Kabat/IMGT) DASNRAT	SEQ ID NO: 248
	LCDR3 (Combined Kabat/IMGT) QQVSISPPWT	SEQ ID NO: 249
	VL EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPG QAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSELPEDF AVYYCQQVSISPPWTFGGGTKVEIK	SEQ ID NO: 250
	Light Chain EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPG QAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSELPEDF AVYYCQQVSISPPWTFGGGTKVEIKRTVAAPSVFIFPPSDE ELKSGTASVQCLLNRFYPREAKVQWKVDNALQSGNSQES VTEQDSKDYSLSELTLISKADYEKHKVYACEVTHQGLS SPVTKSFNRGEC	SEQ ID NO: 251
	Light Chain B - CD3 binding arm	
	LCDR1 (IMGT) QSLLNARTGKNY	SEQ ID NO: 252

	LCDR2 (IMGT) WA	SEQ ID NO: 253
	LCDR3 (IMGT) KQSYSLRT	SEQ ID NO: 254
	LCDR1 (Kabat) KSSQSLLNARTGKNYLA	SEQ ID NO: 255
	LCDR2 (Kabat) WASTRES	SEQ ID NO: 256
	LCDR3 (Kabat) KQSYSLRT	SEQ ID NO: 257
	LCDR1 (Combined Kabat/IMGT) KSSQSLLNARTGKNYLA	SEQ ID NO: 258
	LCDR2 (Combined Kabat/IMGT) WASTRES	SEQ ID NO: 259
	LCDR3 (Combined Kabat/IMGT) KQSYSLRT	SEQ ID NO: 260
	VL DIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKNYLA WYQQKPGQPPKLLIWASTRESGVPDRFSGSGSGTDFTLTI SSLQAEDVAVYYCKQSYSLRTFGGGTKVEIK	SEQ ID NO: 261
	Light Chain DIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKNYLA WYQQKPGQPPKLLIWASTRESGVPDRFSGSGSGTDFTLTI IFPPSDEQLKSGRASVCLLNFFYPREAKVQWKVDNALQS GNSQESVTEQDSKDSTYLSRLQLSKADYEKHKVYACEV THQGLSPVTKSFNRGEC	SEQ ID NO: 262

Table 9. TMIGD2 blocking and sparing B7-H7-CD3 T cell engager binding characteristics.

Antibody	TMIGD2 Blocking/Sparing	B7-H7 Avidity (nM)	CD3 Affinity (nM)
NPXAB-1	Blocking	0.15	4.8
NPXAB-4	Blocking	0.16	11.9
NPXAB-5	Sparing	0.14	4.6
NPXAB-3	Sparing	0.17	10.8

[0232] Primary human PBMCs were cocultured overnight with Raji-B7-H7 cells at an effector to target cell ratio of 5:1 in the presence of NPXAB-1, NPXAB-4, NPXAB-5, or NPXAB-3 bispecific antibodies at concentrations ranging from 0.0051 ng/mL to 1 µg/mL. Cells were stained with fluorescently conjugated antibodies to CD4, CD8, and CD25. T cell activation was assessed by measuring CD25 upregulation on CD4+ (**FIG. 27A**) and CD8+ (**FIG. 27B**) T cells by flow cytometry. Data are shown as geometric mean fluorescent intensity (gMFI; y-axis) plotted against log absorbance (ug/ml; x-axis) and T cell activation EC₅₀ values summarized in **Table 10**.

Table 10. TMIGD2 blocking and sparing B7-H7-CD3 T cell engager T cell activation EC₅₀ values.

Antibody	CD4+ EC ₅₀ (ng/ml)	CD8+ EC ₅₀ (ng/ml)
NPXAB-1	2.6	1.6
NPXAB-4	11.0	9.5
NPXAB-5	0.1	0.4
NPXAB-3	0.8	0.9

[0233] This analysis demonstrated that TMIGD2 sparing B7-H7-CD3 bispecific antibodies induce enhanced CD4+ and CD8+ T cell activation more than TMIGD2 blocking B7-H7-CD3 T cell engagers with matched CD3 binding affinities. NPXAB-3, which spares TMIGD2 binding, had similar CD4+ and CD8+ T cell activating potency to the TMIGD2 blocking engager NPXAB-1 even though NPXAB-3 had a weaker CD3 affinity than NPXAB-1. These results suggest that TMIGD2 co-stimulation can enhance the activity of B7-H7 bispecific antibodies.

[0234] The present Example further demonstrates methods for assessing T cell activation by the TMIGD2 sparing B7-H7-CD3 T bispecific antibody NPXAB-2.

[0235] TMIGD2 blockade significantly inhibited T cell activation induced by the TMIGD2 sparing B7-H7-CD3 bispecific antibodies NPXAB-5 and NPXAB-3, but had no effect on T cell activation induced by the TMIGD2 blocking B7-H7-CD3 bispecific antibodies NPXAB-1 and NPXAB-4 (**FIG. 28**). Data are shown as CD69 activation values following treatment with NPXAB-1, NPXAB-4, NPXAB-5, or NPXAB-3 and an anti-TMIGD2 monoclonal antibody 17C7 as geometric mean fluorescent intensities (gMFI) compared to isotype control. This analysis demonstrated that antibody blockade of TMIGD2 abrogated T cell activation induced by TMIGD2 sparing bispecific antibodies.

Example 6. NPXAB-1 induces tumor cell killing in vitro and tumor regression in vivo.

[0236] The present Example demonstrates methods for assessing the immunomodulatory and target cell (e.g., cancer cell) killing effects of administering exemplary B7-H7-CD3 bispecific antibodies disclosed herein in vitro and in vivo.

[0237] A204 cells, which endogenously express B7-H7 (A204-WT), were engineered to further overexpress B7-H7 (A204-B7-H7) or with B7-H7 knocked out (A204-KO). NPXAB-1 was incubated at a concentration of 1 μ g/mL for 24 hours with a co-culture of A204 cells and PBMCs from a healthy donor. Cytokine production (e.g., release of IFN γ) and granulocyte particle production (e.g., release of Granzyme B and Perforin) were measured by collecting supernatant from the co-culture. Data were analyzed using the U-PLEX CAR-T Cell Combo 1 (Mesoscale Discovery, #K15338K) for IFN γ , Granzyme B and Perforin.

[0238] Concentrations of IFN γ , Perforin and Granzyme B were dependent on the level of B7-H7 expression. T cells co-cultured with B7-H7-overexpressing A204 cells released the most IFN γ (**FIG. 29A**), Perforin (**FIG. 29B**), and Granzyme B (**FIG. 29C**) compared to T cells co-cultured with A204 cells with B7-H7 knocked out. Co-cultured T cells not treated with an antibody (e.g., cells only) released substantially lower amounts of IFN γ , Perforin and Granzyme B compared to NPXAB-1-treated cells (**FIGS. 29A-29C**).

[0239] In an additional experiment, the in vivo activity of NPXAB-1 was assessed in the B7-H7-expressing A204 tumor model in NCG mice humanized with activated human T cells. Briefly, NCG mice were injected with A204 tumor cells (1×10^7) subcutaneously in the right flank. When tumors reached an average volume of 80-120 mm³, animals were sorted into groups and injected intraperitoneally with activated human T cells (2×10^7). One day after

the T cell injection, mice were then treated with NPXAB-1 antibody at 0.01 mg/kg, 0.1 mg/kg, 1 mg/kg and 10 mg/kg doses intravenously weekly for a total of 4 injections. Control animals were untreated or treated with T cells only. Tumor growth was measured over time with calipers. NPXAB-1 treatment at all dose levels induced complete tumor regression in all mice at all dose levels by the end of the study (**FIGS. 30C-30G**), whereas no treatment or T cell treatment alone resulted in substantial tumor growth by the end of the study (**FIGS. 30A, 30B and 30G**).

[0240] These data demonstrate that NPXAB-1 is a promising immunomodulatory therapeutic agent that increases T cell activation and induces tumor regression when administered to a subject at various therapeutically useful dose levels (e.g., at low dose levels).

[0241] The present Examples demonstrate that anti-B7-H7-CD3 bispecific antibodies disclosed herein may be safe (e.g., produce no substantial toxicity) and effective (e.g., elicit immunomodulatory and/or target cell (e.g., cancer cell) killing responses) for treating a subject having a disease, disorder, or condition and/or modulating an immune response in a subject.

EQUIVALENTS

[0242] It is to be appreciated by those skilled in the art that various alterations, modifications, and improvements to the present disclosure will readily occur to those skilled in the art. Such alterations, modifications, and improvements are intended to be part of the present disclosure, and are intended to be within the spirit and scope of the disclosure. Accordingly, the foregoing description and drawing are by way of example only and any invention described in the present disclosure if further described in detail by the claims that follow.

[0243] Those skilled in the art will appreciate typical standards of deviation or error attributable to values obtained in assays or other processes described herein. The publications, websites and other reference materials referenced herein to describe the background of the disclosure and to provide additional detail regarding its practice are hereby incorporated by reference in their entireties.

CLAIMS

1. A multispecific antibody or antigen-binding fragment thereof comprising:
 - (i) a first antigen-binding domain that selectively binds to B7-H7, and
 - (ii) a second antigen-binding domain that selectively binds an immune effector cell antigen.
2. The multispecific antibody or antigen-binding fragment thereof of claim 1, further comprising a third antigen-binding domain that selectively binds to B7-H7 or an immune effector cell antigen.
3. The multispecific antibody or antigen-binding fragment thereof of claim 1 or 2, wherein the immune effector cell antigen comprises or is cluster determinant 3 (CD3) or cluster determinant 137 (4-1BB).
4. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-3, wherein the immune effector cell comprises or is a T-cell or an NK cell.
5. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-4, wherein the first antigen-binding domain, second antigen-binding domain, and/or third antigen-binding domain comprises or is an scFv, Fab, Fab', F(ab')₂, nanobody, or camelid antibody.
6. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-5, wherein the multispecific antibody or antigen-binding fragment thereof comprises or is a bispecific antibody or antigen-binding fragment thereof.
7. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-6, wherein the first antigen-binding domain that selectively binds to B7-H7 comprises:
 - (a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 1; a VHCDR2 amino acid sequence of SEQ ID NO: 2; and a VHCDR3 amino acid sequence of SEQ ID NO: 3; and

a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 43; a VLCDR2 amino acid sequence of SEQ ID NO: 44; and a VLCDR3 amino acid sequence of SEQ ID NO: 45;

(b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 4; a VHCDR2 amino acid sequence of SEQ ID NO: 5; and a VHCDR3 amino acid sequence of SEQ ID NO: 6; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 46; a VLCDR2 amino acid sequence of SEQ ID NO: 47; and a VLCDR3 amino acid sequence of SEQ ID NO: 48;

(c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 7; a VHCDR2 amino acid sequence of SEQ ID NO: 8; and a VHCDR3 amino acid sequence of SEQ ID NO: 9; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 49; a VLCDR2 amino acid sequence of SEQ ID NO: 50; and a VLCDR3 amino acid sequence of SEQ ID NO: 51;

(d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 69; a VHCDR2 amino acid sequence of SEQ ID NO: 70; and a VHCDR3 amino acid sequence of SEQ ID NO: 71; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 111; a VLCDR2 amino acid sequence of SEQ ID NO: 112; and a VLCDR3 amino acid sequence of SEQ ID NO: 113;

(e) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 72; a VHCDR2 amino acid sequence of SEQ ID NO: 73; and a VHCDR3 amino acid sequence of SEQ ID NO: 74; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 114; a VLCDR2 amino acid sequence of SEQ ID NO: 115; and a VLCDR3 amino acid sequence of SEQ ID NO: 116;

(f) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 75; a VHCDR2 amino acid sequence of SEQ ID NO: 76; and a VHCDR3 amino acid sequence of SEQ ID NO: 77; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 117; a VLCDR2 amino acid sequence of SEQ ID NO: 118; and a VLCDR3 amino acid sequence of SEQ ID NO: 119;

(g) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 137; a VHCDR2 amino acid sequence of SEQ ID NO: 138; and a VHCDR3 amino acid sequence of SEQ ID NO: 139; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 179; a VLCDR2 amino acid sequence of SEQ ID NO: 180; and a VLCDR3 amino acid sequence of SEQ ID NO: 181;

(h) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 140; a VHCDR2 amino acid sequence of SEQ ID NO: 141; and a VHCDR3 amino acid sequence of SEQ ID NO: 142; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 182; a VLCDR2 amino acid sequence of SEQ ID NO: 183; and a VLCDR3 amino acid sequence of SEQ ID NO: 184; and/or

(i) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 143; a VHCDR2 amino acid sequence of SEQ ID NO: 144; and a VHCDR3 amino acid sequence of SEQ ID NO: 145; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 185; a VLCDR2 amino acid sequence of SEQ ID NO: 186; and a VLCDR3 amino acid sequence of SEQ ID NO: 187.

8. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein the second antigen-binding domain that selectively binds an immune effector cell antigen comprises:

(a) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 28; a VHCDR2 amino acid sequence of SEQ ID NO: 29; and a VHCDR3 amino acid sequence of SEQ ID NO: 30; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 56; a VLCDR2 amino acid sequence of SEQ ID NO: 57; and a VLCDR3 amino acid sequence of SEQ ID NO: 58;

(b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 31; a VHCDR2 amino acid sequence of SEQ ID NO: 32; and a VHCDR3 amino acid sequence of SEQ ID NO: 33; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 59; a VLCDR2 amino acid sequence of SEQ ID NO: 60; and a VLCDR3 amino acid sequence of SEQ ID NO: 61;

(c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 34; a VHCDR2 amino acid sequence of SEQ ID NO: 35; and a VHCDR3 amino acid sequence of SEQ ID NO: 36; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 62; a VLCDR2 amino acid sequence of SEQ ID NO: 63; and a VLCDR3 amino acid sequence of SEQ ID NO: 64;

(d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 164; a VHCDR2 amino acid sequence of SEQ ID NO: 165; and a VHCDR3 amino acid sequence of SEQ ID NO: 166; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 192; a VLCDR2 amino acid sequence of SEQ ID NO: 193; and a VLCDR3 amino acid sequence of SEQ ID NO: 194;

(e) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 167; a VHCDR2 amino acid sequence of SEQ ID NO: 168; and a VHCDR3 amino acid sequence of SEQ ID NO: 169; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 195; a VLCDR2 amino acid sequence of SEQ ID NO: 196; and a VLCDR3 amino acid sequence of SEQ ID NO: 197;

(f) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 170; a VHCDR2 amino acid sequence of SEQ ID NO: 171; and a VHCDR3 amino acid sequence of SEQ ID NO: 172; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 198; a VLCDR2 amino acid sequence of SEQ ID NO: 199; and a VLCDR3 amino acid sequence of SEQ ID NO: 200;

(g) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 96; a VHCDR2 amino acid sequence of SEQ ID NO: 97; and a VHCDR3 amino acid sequence of SEQ ID NO: 98; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 124; a VLCDR2 amino acid sequence of SEQ ID NO: 125; and a VLCDR3 amino acid sequence of SEQ ID NO: 126;

(h) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 99; a VHCDR2 amino acid sequence of SEQ ID NO: 100; and a VHCDR3 amino acid sequence of SEQ ID NO: 101; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 127; a VLCDR2 amino acid sequence of SEQ ID NO: 128; and a VLCDR3 amino acid sequence of SEQ ID NO: 129; and/or

(i) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 102; a VHCDR2 amino acid sequence of SEQ ID NO: 103; and a VHCDR3 amino acid sequence of SEQ ID NO: 104; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 130; a VLCDR2 amino acid sequence of SEQ ID NO: 131; and a VLCDR3 amino acid sequence of SEQ ID NO: 132.

9. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-8, wherein the third antigen-binding domain that selectively binds to B7-H7 or an immune effector cell antigen comprises:

(a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 14; a VHCDR2 amino acid sequence of SEQ ID NO: 15; and a VHCDR3 amino acid sequence of SEQ ID NO: 16; and

a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 43; a VLCDR2 amino acid sequence of SEQ ID NO: 44; and a VLCDR3 amino acid sequence of SEQ ID NO: 45;

(b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 17; a VHCDR2 amino acid sequence of SEQ ID NO: 18; and a VHCDR3 amino acid sequence of SEQ ID NO: 19; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 46; a VLCDR2 amino acid sequence of SEQ ID NO: 47; and a VLCDR3 amino acid sequence of SEQ ID NO: 48;

(c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 20; a VHCDR2 amino acid sequence of SEQ ID NO: 21; and a VHCDR3 amino acid sequence of SEQ ID NO: 22; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 49; a VLCDR2 amino acid sequence of SEQ ID NO: 50; and a VLCDR3 amino acid sequence of SEQ ID NO: 51;

(d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 82; a VHCDR2 amino acid sequence of SEQ ID NO: 83; and a VHCDR3 amino acid sequence of SEQ ID NO: 84; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 111; a VLCDR2 amino acid sequence of SEQ ID NO: 112; and a VLCDR3 amino acid sequence of SEQ ID NO: 113;

(e) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 85; a VHCDR2 amino acid sequence of SEQ ID NO: 86; and a VHCDR3 amino acid sequence of SEQ ID NO: 87; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 114; a VLCDR2 amino acid sequence of SEQ ID NO: 115; and a VLCDR3 amino acid sequence of SEQ ID NO: 116;

(f) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 88; a VHCDR2 amino acid sequence of SEQ ID NO: 89; and a VHCDR3 amino acid sequence of SEQ ID NO: 90; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 117; a VLCDR2 amino acid sequence of SEQ ID NO: 118; and a VLCDR3 amino acid sequence of SEQ ID NO: 119; and/or

(g) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 150; a VHCDR2 amino acid sequence of SEQ ID NO: 151; and a VHCDR3 amino acid sequence of SEQ ID NO: 152; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 179; a VLCDR2 amino acid sequence of SEQ ID NO: 180; and a VLCDR3 amino acid sequence of SEQ ID NO: 181;

(h) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 153; a VHCDR2 amino acid sequence of SEQ ID NO: 154; and a VHCDR3 amino acid sequence of SEQ ID NO: 155; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 182; a VLCDR2 amino acid sequence of SEQ ID NO: 183; and a VLCDR3 amino acid sequence of SEQ ID NO: 184; and/or

(i) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 156; a VHCDR2 amino acid sequence of SEQ ID NO: 157; and a VHCDR3 amino acid sequence of SEQ ID NO: 158; and

a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 185; a VLCDR2 amino acid sequence of SEQ ID NO: 186; and a VLCDR3 amino acid sequence of SEQ ID NO: 187.

10. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-9, wherein the first antigen-binding domain that selectively binds to B7-H7 comprises:

(a) a VH comprising an amino acid sequence of SEQ ID NO: 10, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 10; and

a VL comprising an amino acid sequence of SEQ ID NO: 52, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 52;

(b) a VH comprising an amino acid sequence of SEQ ID NO: 78, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 78; and

a VL comprising an amino acid sequence of SEQ ID NO: 120, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 120; and/or

(c) a VH comprising an amino acid sequence of SEQ ID NO: 146, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 146; and

a VL comprising an amino acid sequence of SEQ ID NO: 188, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 188.

11. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-10, wherein the second antigen-binding domain that selectively binds an immune effector cell antigen comprises:

(a) a VH comprising an amino acid sequence of SEQ ID NO: 37, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 37; and

a VL comprising an amino acid sequence of SEQ ID NO: 65, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 65;

(b) a VH comprising an amino acid sequence of SEQ ID NO: 173, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 173; and

a VL comprising an amino acid sequence of SEQ ID NO: 201, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 201; and/or

(c) a VH comprising an amino acid sequence of SEQ ID NO: 105, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 105; and

a VL comprising an amino acid sequence of SEQ ID NO: 133, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 133.

12. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-11, wherein the third antigen-binding domain that selectively binds to B7-H7 or an immune effector cell antigen comprises:

(a) a VH comprising an amino acid sequence of SEQ ID NO: 23, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 23; and

a VL comprising an amino acid sequence of SEQ ID NO: 52, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 52;

(b) a VH comprising an amino acid sequence of SEQ ID NO: 91, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 91; and

a VL comprising an amino acid sequence of SEQ ID NO: 120, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 120; and/or

(c) a VH comprising an amino acid sequence of SEQ ID NO: 159, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 159; and

a VL comprising an amino acid sequence of SEQ ID NO: 188, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 188.

13. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-12, wherein the multispecific antibody or antigen-binding fragment thereof comprises:

- (a) a heavy chain comprising an amino acid sequence of SEQ ID NO: 12, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 12; and a light chain comprising an amino acid sequence of SEQ ID NO: 54, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 54; and/or a second heavy chain comprising an amino acid sequence of SEQ ID NO: 39, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 39; and a second light chain comprising an amino acid sequence of SEQ ID NO: 67, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 67;
 - (b) a heavy chain comprising an amino acid sequence of SEQ ID NO: 80, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 80; and a light chain comprising an amino acid sequence of SEQ ID NO: 122, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 122; and/or a second heavy chain comprising an amino acid sequence of SEQ ID NO: 107, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 107; and a second light chain comprising an amino acid sequence of SEQ ID NO: 135, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 135;
- or

(c) a heavy chain comprising an amino acid sequence of SEQ ID NO: 148, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 148; and a light chain comprising an amino acid sequence of SEQ ID NO: 190, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 190; and/or a second heavy chain comprising an amino acid sequence of SEQ ID NO: 175, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 175; and a second light chain comprising an amino acid sequence of SEQ ID NO: 203, or an amino acid sequence at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or higher identical to SEQ ID NO: 203.

14. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-13, wherein the multispecific antibody or antigen-binding fragment thereof comprises:

- (a) a first heavy chain comprising an amino acid sequence of SEQ ID NO: 12; a light chain comprising an amino acid sequence of SEQ ID NO: 54; and
- (b) a second heavy chain comprising an amino acid sequence of SEQ ID NO: 39; a light chain comprising an amino acid sequence of SEQ ID NO: 67.

15. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-14, wherein the multispecific antibody or antigen-binding fragment thereof comprises a linker comprising an amino acid sequence of SEQ ID NO: 27.

16. The multispecific antibody or antigen-binding fragment of any one of claims 1-15, wherein the multispecific antibody or antigen-binding fragment thereof, comprises or is:

- (i) a chimeric, human, or humanized bispecific antibody or antigen-binding fragment thereof;
- (ii) a monoclonal bispecific antibody or antigen-binding fragment thereof; and/or
- (iii) a knob-into-hole bispecific antibody, a 1:1 bispecific antibody, or a 2:1 bispecific antibody.

17. The multispecific antibody or antigen-binding fragment thereof, of any one of claims 1-16, wherein the multispecific antibody or antigen-binding fragment thereof, comprises:

- (i) a heavy chain constant region chosen from IgG1, IgG2, IgG3, or IgG4, and/or

(ii) a light chain constant region chosen from light chain constant regions of kappa or lambda.

18. The multispecific antibody or antigen-binding fragment thereof of any one of claims 1-17, wherein the multispecific antibody or antigen-binding fragment thereof, comprises an Fc region with reduced effector function relative to a reference agent.

19. The multispecific antibody or antigen-binding fragment thereof, of any one of claims 1-18, wherein an Fc region comprises one or more amino acid substitutions of L234A, L235A, and/or P329A numbering according to EU index.

20. A pharmaceutical composition comprising a multispecific antibody or antigen-binding fragment thereof of any one of claims 1-19, and a pharmaceutically acceptable carrier.

21. A method of treating a subject having a disease, disorder, or condition and/or modulating an immune response in a subject comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 20.

22. The method of claim 21, wherein the subject has or is at risk of developing a cancer.

23. The method of claim 21 or 22, wherein the subject has a solid tumor or a hematological cancer.

24. The method of claim 23, wherein the solid tumor is or comprises one or more of: a renal cancer, a bone cancer, a skin cancer, a breast cancer, a cervical cancer, a colorectal cancer, an endometrial cancer, a lung cancer, an ovarian cancer, a liver cancer, cholangiocarcinoma, a thyroid cancer, a prostate cancer, a bladder cancer, a brain cancer, a retinoblastoma cancer, an esophageal cancer, a gastric cancer, a stomach cancer, a testicular cancer, a head and neck cancer, a metastatic cancer, a neuroblastoma cancer, a pancreatic cancer, or a small intestine cancer.

25. The method of claim 23 or 24, wherein the hematological cancer comprises or is a leukemia or lymphoma.
26. The method of claim 25, wherein the leukemia comprises or is acute lymphocytic leukemia, acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, chronic leukemia, or acute leukemia.
27. The method of claim 25, wherein the lymphoma comprises or is Hodgkin lymphoma (HL), non-Hodgkin's lymphoma, lymphocytic lymphoma, or diffuse large B cell lymphoma (DLBCL).
28. The method of any one of claims 21-27, wherein the pharmaceutical composition is administered in combination with at least one additional agent.
29. The method of any one of claims 21-28, wherein the pharmaceutical composition is administered to the subject in accordance with a dosage regimen of at least about 1 $\mu\text{g/kg}$, 3 $\mu\text{g/kg}$, 10 $\mu\text{g/kg}$, 100 $\mu\text{g/kg}$, 300 $\mu\text{g/kg}$, 1000 $\mu\text{g/kg}$ or more.
30. The method of any one of claims 21-29, wherein the pharmaceutical composition is administered to the subject at least once or at least twice during the course of treatment of the subject.
31. A nucleic acid encoding a multispecific antibody or antigen-binding fragment thereof of any one of claims 1-19.
32. An expression vector comprising the nucleic acid of claim 31.
33. A host cell comprising or expressing a multispecific antibody or antigen-binding fragment thereof of any one of claims 1-19, the nucleic acid of claim 31, or the expression vector of claim 32.
34. A method of making a multispecific antibody or antigen-binding fragment thereof, comprising:

(i) culturing a host cell comprising the nucleic acid of claim 31 or the expression vector of claim 32 under conditions suitable for expression of the multispecific antibody or antigen-binding fragment thereof, and

(ii) recovering the multispecific antibody or antigen-binding fragment thereof.

35. A kit comprising a multispecific antibody or antigen-binding fragment thereof of any one of claims 1-19 or pharmaceutical composition of claim 20, and instructions for use.