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(54) Title: MULTIFUNCTIONAL MOLECULES THAT BIND TO CALRETICULIN AND USES THEREOF

(57) **Abrégé/Abstract:**

Multifunctional molecules that include i) an antigen binding domain that binds to a calreticulin protein; and one, two or all of: (ii) an immune cell engager (e.g., chosen from an NK cell engager, a T cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager); (iii) a cytokine molecule; and/or (iv) a stromal modifying moiety are disclosed. Additionally disclosed are nucleic acids encoding the same, methods of producing the aforesaid molecules, and methods of treating a cancer using the aforesaid molecules.

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(54) Title: MULTIFUNCTIONAL MOLECULES THAT BIND TO CALRETICULIN AND USES THEREOF

(57) Abstract: Multifunctional molecules that include i) an antigen binding domain that binds to a calreticulin protein; and one, two or all of: (ii) an immune cell engager (e.g., chosen from an NK cell engager, a T cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager); (iii) a cytokine molecule; and/or (iv) a stromal modifying moiety are disclosed. Additionally disclosed are nucleic acids encoding the same, methods of producing the aforesaid molecules, and methods of treating a cancer using the aforesaid molecules.

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LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

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JUMBO APPLICATIONS/PATENTS

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MULTIFUNCTIONAL MOLECULES THAT BIND TO CALRETICULIN AND USES THEREOF

RELATED APPLICATIONS

5 This application claims priority to U.S. Provisional Application 62/808,779 filed on February 21, 2019, U.S. Provisional Application 62/818,427 filed on March 14, 2019, and U.S. Provisional Application 62/956,866 filed on January 3, 2020, the entire contents of each of which are hereby incorporated by reference.

SEQUENCE LISTING

10 The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on February 19, 2020, is named E2070-7021WO_SL.txt and is 1,760,247 bytes in size.

BACKGROUND

15 Myeloproliferative neoplasms (MPNs) are a group of conditions that cause blood cells to grow abnormally in the bone marrow. Common myeloproliferative neoplasms include primary or idiopathic myelofibrosis (MF), essential thrombocytosis (ET), polycythemia vera (PV), and
20 chronic myelogenous leukemia (CML). Primary myelofibrosis is a chronic blood cancer in which excessive scar tissue forms in the bone marrow and impairs its ability to produce normal blood cells. Given the ongoing need for improved treatment of myeloproliferative neoplasms such as myelofibrosis, new compositions and treatments targeting myeloproliferative neoplasms are highly desirable.

SUMMARY OF THE INVENTION

25 The disclosure relates, inter alia, to novel multispecific or multifunctional molecules that include (i) an antigen binding domain that binds to a calreticulin protein (e.g., a wild-type or mutant calreticulin protein); and one, two or all of: (ii) an immune cell engager (e.g., chosen -
30 from an NK cell engager, a T cell engager, a B cell engager, a dendritic cell engager, or a

macrophage cell engager); (iii) a cytokine molecule; and/or (iv) a stromal modifying moiety. The terms “multispecific” or “multifunctional” are used interchangeably herein.

Without wishing to be bound by theory, the multispecific or multifunctional molecules disclosed herein are expected to target (e.g., localize, bridge and/or activate) an immune cell (e.g., an immune effector cell chosen from an NK cell, a T cell, a B cell, a dendritic cell or a macrophage), at a target cell, e.g., a cancer cell, expressing a calreticulin protein (e.g., a wild-type or mutant calreticulin protein), and/or alter the tumor stroma, e.g., alter the tumor microenvironment near the cancer site. Increasing the proximity and/or activity of the immune cell using the multispecific molecules described herein is expected to enhance an immune response against the target cell (e.g., the cancer cell), thereby providing a more effective therapy (e.g., a more effective cancer therapy). Without being bound by theory, a targeted, localized immune response against the target cell (e.g., the cancer cell) is believed to reduce the effects of systemic toxicity of the multispecific molecules described herein.

Accordingly, provided herein are, *inter alia*, multispecific molecules (e.g., multispecific or multifunctional antibody molecules) that include the aforesaid moieties, nucleic acids encoding the same, methods of producing the aforesaid molecules, and methods of treating a cancer using the aforesaid molecules.

Accordingly, in one aspect, the disclosure features a multifunctional molecule that includes:

(i) a first antigen binding domain that binds to a calreticulin protein (e.g., a wild-type or mutant calreticulin protein),

and

(ii) a second antigen binding domain that binds to TCR β V, e.g., an anti-TCR β V antigen binding domain disclosed in any one of Table 1A, Table 2A, Table 3A, Table 10A, Table 11A, Table 12A, or Table 13A, or a second antigen binding domain that binds to NKp30, e.g., an anti-NKp30 antigen binding domain disclosed in Tables 7-10 or 18.

In some embodiments, the second antigen binding domain binds to TCR β V.

In some embodiments, the second antigen binding domain activates a T cell or the second antigen binding domain does not activate a T cell.

In some embodiments, the second antigen binding domain binds to TCR β V12 or TCR β V6 (e.g., comprising the amino acid sequence of SEQ ID NO: 1044).

In some embodiments, the second antigen binding domain comprises one or more amino acid sequences as listed in Table 1A, Table 2A, Table 3A, Table 10A, Table 11A, Table 12A, or Table 13A.

In some embodiments, the second antigen binding domain comprises:

(a) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises a heavy chain complementarity determining region 1 (VHCDR1) having an amino acid sequence of a VHCDR1 in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 having an amino acid sequence of a VHCDR2 in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 having an amino acid sequence of a VHCDR3 in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions),

(ii) the VL comprises a light chain complementarity determining region 1 (VLCDR1) having an amino acid sequence of a VLCDR1 in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 having an amino acid sequence of a VLCDR2 in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 having an amino acid sequence of a VLCDR3 in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions);

(b) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 3 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 4 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g.,

substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 5 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or

(ii) the VL comprises a light chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 7 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 8 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions);

(c) a heavy chain variable region (VH) and/or a light chain variable region (VL), wherein:

(i) the VH comprises a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 45 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 46 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 47 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or

(ii) the VL comprises a light chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 51 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 52 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 53 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions); and/or

(d) a heavy chain variable region (VH) and/or a light chain variable region (VL), wherein:

(i) the VH comprises a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 48 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 49 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 50 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or

(ii) the VL comprises a light chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 54 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 55 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 56 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

In some embodiments, the second antigen binding domain comprises:

(a) a heavy chain variable region (VH) and/or a light chain variable region (VL),

wherein:

(i) the VH comprises the amino acid sequence of a VH in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and/or

(ii) the VL comprises the amino acid sequence of a VL in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto)

(iii) the VH comprises the amino acid sequence of SEQ ID NO: 9 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and/or

(iv) the VL comprises the amino acid sequence of SEQ ID NO: 10 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto);

(b) a heavy chain variable region (VH) and/or a light chain variable region (VL), wherein:

(i) the VH comprises the amino acid sequence of SEQ ID NO: 9 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and/or

(ii) the VL comprises the amino acid sequence of SEQ ID NO: 11 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto); and/or

(c) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises the amino acid sequence of SEQ ID NO: 1312 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and/or

(ii) the VL comprises the amino acid sequence of SEQ ID NO: 1314 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto).

In some embodiments, the second antigen binding domain comprises:

(a) a heavy chain variable region (VH) and/or a light chain variable region (VL),

wherein:

(i) the VH comprises a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 17 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 19 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or

(ii) the VL comprises a light chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 20 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 21 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 22 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions);

(b) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises a heavy chain complementarity determining region 1
(VHCDR1) amino acid sequence of SEQ ID NO: 57 (or a sequence with no more than 1,
2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid
sequence of SEQ ID NO: 58 (or a sequence with no more than 1, 2, 3, or 4 mutations,
e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of
SEQ ID NO: 59 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g.,
substitutions, additions, or deletions), and/or

(ii) the VL comprises a light chain complementarity determining region 1
(VHCDR1) amino acid sequence of SEQ ID NO: 63 (or a sequence with no more than 1,
2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid
sequence of SEQ ID NO: 64 (or a sequence with no more than 1, 2, 3, or 4 mutations,
e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of
SEQ ID NO: 65 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g.,
substitutions, additions, or deletions); and/or

(c) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises a heavy chain complementarity determining region 1
(VHCDR1) amino acid sequence of SEQ ID NO: 60 (or a sequence with no more than 1,
2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid
sequence of SEQ ID NO: 61 (or a sequence with no more than 1, 2, 3, or 4 mutations,
e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of
SEQ ID NO: 62 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g.,
substitutions, additions, or deletions), and/or

(ii) the VL comprises a light chain complementarity determining region 1
(VHCDR1) amino acid sequence of SEQ ID NO: 66 (or a sequence with no more than 1,
2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid
sequence of SEQ ID NO: 67 (or a sequence with no more than 1, 2, 3, or 4 mutations,

e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 68 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

In some embodiments, the second antigen binding domain comprises:

5 (a) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises the amino acid sequence of SEQ ID NO: 15 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and/or

10 (ii) the VL comprises the amino acid sequence of SEQ ID NO: 16 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto); and/or

(b) a heavy chain variable region (VH) and/or a light chain variable region (VL),
15 wherein:

(i) the VH comprises:

the amino acid sequence of SEQ ID NO: 23 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto),

20 the amino acid sequence of SEQ ID NO: 24 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), or

the amino acid sequence of SEQ ID NO: 25 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto); and/or
25

(ii) the VL comprises:

the amino acid sequence of SEQ ID NO: 26 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto),

the amino acid sequence of SEQ ID NO: 27 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto),

the amino acid sequence of SEQ ID NO: 28 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto),

the amino acid sequence of SEQ ID NO: 29 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), or

the amino acid sequence of SEQ ID NO: 30 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto).

In some embodiments, the multifunctional molecule comprises:

a first polypeptide comprising, e.g., from N-terminus to C-terminus, a first VL and a first CL,

a second polypeptide comprising, e.g., from N-terminus to C-terminus, a first VH, a first CH1, a first dimerization domain (e.g., a first Fc), and a first moiety that binds to TCR (e.g., TCRV β) (e.g., a first scFv that binds to TCR (e.g., TCRV β)),

a third polypeptide comprising, e.g., from N-terminus to C-terminus, a second VH, a second CH1, a second dimerization domain (e.g., a second Fc), and optionally a second moiety that binds to TCR (e.g., TCRV β) (e.g., a second scFv that binds to TCR (e.g., TCRV β)),

a fourth polypeptide comprising, e.g., from N-terminus to C-terminus, a second VL and a second CL,

wherein:

the first VL and the first VH form a first antigen binding domain that binds to a first calreticulin protein, and the second VL and the second VH form a third antigen binding domain that binds to a second calreticulin protein,

optionally wherein the first and second calreticulin proteins comprise the amino acid sequence of SEQ ID NO: 6285 or 6286,

optionally wherein the first and second calreticulin mutant proteins are each independently chosen from: a molecule comprising the amino acid sequence of SEQ ID NO: 6313, or a molecule comprising the amino acid sequence of SEQ ID NO: 6314,

optionally wherein the multifunctional molecule comprises the configuration of FIG. 3A or 3B.

In some embodiments, the second antigen binding domain binds to NKp30.

In some embodiments, the second antigen binding domain is chosen from an antibody molecule, e.g., an antigen binding domain, or ligand that binds to (e.g., activates) NKp30, e.g., the second antigen binding domain is an antibody molecule or ligand that binds to (e.g., activates) NKp30.

In some embodiments, the second antigen binding domain comprises:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) having an amino acid sequence of a VHCDR1 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 having an amino acid sequence of a VHCDR2 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 having an amino acid sequence of a VHCDR3 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or

(ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) having an amino acid sequence of a VLCDR1 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 having an amino acid sequence of a VLCDR2 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 having an amino acid sequence of a VLCDR3 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

In some embodiments, the second antigen binding domain comprises:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 7313 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2

amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 7315 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions; and/or

- 5 (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 7326 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 7327 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of
10 SEQ ID NO: 7329 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

In some embodiments, the second antigen binding domain comprises:

- (i) a VH comprising the amino acid sequence of any of SEQ ID NOs: 7298 or 7300-7304 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence
15 identity to any of SEQ ID NOs: 7298 or 7300-7304); and/or
- (ii) a VL comprising the amino acid sequence of any of SEQ ID NOs: 7299 or 7305-7309 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to any of SEQ ID NOs: 7299 or 7305-7309).

In some embodiments, the second antigen binding domain comprises:

- 20 (i) a VH comprising the amino acid sequence of SEQ ID NO: 7302 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7302), and a VL comprising the amino acid sequence of SEQ ID NO: 7305 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7305); or
- (ii) a VH comprising the amino acid sequence of SEQ ID NO: 7302 (or an amino acid
25 sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7302), and a VL comprising the amino acid sequence of SEQ ID NO: 7309 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7309).

In some embodiments, the second antigen binding domain comprises:

- (i) an amino acid sequence of SEQ ID NO: 7310 (or an amino acid sequence having at
30 least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7310); or

(ii) an amino acid sequence of SEQ ID NO: 7311 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7311).

In some embodiments, the second antigen binding domain comprises:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000, a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002, and

(ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063, a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7293.

In some embodiments, the second antigen binding domain comprises:

(1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) having an amino acid sequence of a VHFWR1 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 having an amino acid sequence of a VHFWR2 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 having an amino acid sequence of a VHFWR3 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VHFWR4 having an amino acid sequence of a VHFWR4 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), and/or

(2) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) having an amino acid sequence of a VLFWR1 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 having an amino acid sequence of a VLFWR2 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 having an amino acid sequence of a VLFWR3 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a

VLFWR4 having an amino acid sequence of a VLFWR4 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

In some embodiments, the second antigen binding domain comprises:

5 (1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, or a VHFWR4 amino acid sequence of SEQ ID NO: 6006, and

10 (3) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 7292, or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

In some embodiments, the second antigen binding domain comprises:

15 (i) a VH comprising the amino acid sequence of a VH of Table 7, Table 9, Table 10, or Table 18 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and/or

(ii) a VL comprising the amino acid sequence of a VL of Table 8, Table 9, Table 10, or Table 18 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity thereto).

20 In some embodiments, the second antigen binding domain comprises a heavy chain comprising the amino acid sequence of a heavy chain of Table 10 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto).

25 In some embodiments, the second antigen binding domain comprises a light chain comprising the amino acid sequence of a light chain of Table 10 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto).

30 In some embodiments, the second antigen binding domain comprises a heavy chain comprising the amino acid sequence of a heavy chain of Table 10 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and a light chain comprising the amino acid sequence of a light chain of Table 10 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto).

In some embodiments, the multispecific molecule comprises:

a first polypeptide comprising, e.g., from N-terminus to C-terminus, a first VL and a first CL,

a second polypeptide comprising, e.g., from N-terminus to C-terminus, a first VH, a first CH1, a first dimerization domain (e.g., a first Fc), and a first moiety that binds to NKp30 (e.g., a first antibody molecule or ligand that binds to NKp30),

a third polypeptide comprising, e.g., from N-terminus to C-terminus, a second VH, a second CH1, a second dimerization domain (e.g., a second Fc), and optionally a second moiety that binds to NKp30 (e.g., a second antibody molecule or ligand that binds to NKp30),

a fourth polypeptide comprising, e.g., from N-terminus to C-terminus, a second VL and a second CL,

wherein:

the first VL and the first VH form a first antigen binding domain that binds to a first calreticulin protein, and the second VL and the second VH form a second antigen binding domain that binds to a second calreticulin protein,

optionally wherein the first and second calreticulin proteins comprise the amino acid sequence of SEQ ID NO: 6285 or 6286,

optionally wherein the first and second calreticulin mutant proteins are each independently chosen from: a molecule comprising the amino acid sequence of SEQ ID NO: 6313, or a molecule comprising the amino acid sequence of SEQ ID NO: 6314,

optionally wherein the multifunctional molecule comprises the configuration of FIG. 3A or 3B.

In some embodiments, the calreticulin protein comprises an amino acid sequence chosen from SEQ ID NOs: 6285-6312, optionally wherein the calreticulin protein comprises an amino acid sequence chosen from SEQ ID NOs: 6313-6346.

In some embodiments, the calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6285.

In some embodiments, the calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286.

In some embodiments, the first antigen binding domain binds to an epitope located within the C-terminus of the calreticulin protein, optionally wherein the first antigen binding domain binds to an epitope located within the amino acid sequence of SEQ ID NO: 6285 or 6286.

In some embodiments, the multispecific molecule further comprises:

a third antigen binding domain that binds to a second calreticulin protein, e.g., wherein the second calreticulin mutant protein comprises the amino acid sequence of SEQ ID NO: 6285 or 6286, optionally wherein:

- 5 (i) the third antigen binding domain is different from the first antigen binding domain, or
- (ii) the third antigen binding domain is the same as the first antigen binding domain.

In some embodiments, the second calreticulin molecule is the same as the calreticulin molecule bound by the first antigen binding domain.

10 In some embodiments, the second calreticulin molecule is different from the calreticulin molecule bound by the first antigen binding domain.

In some embodiments, the second calreticulin protein comprises an amino acid sequence chosen from SEQ ID NOs: 6285-6312, optionally wherein the second calreticulin protein comprises an amino acid sequence chosen from SEQ ID NOs: 6313-6346.

15 In some embodiments, the calreticulin protein bound by the first antigen binding domain comprises the amino acid sequence of SEQ ID NO: 6285, and the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286.

20 In some embodiments, the third antigen binding domain binds to an epitope located within the C-terminus of the second calreticulin protein, optionally wherein the third antigen binding domain binds to an epitope located within the amino acid sequence of SEQ ID NO: 6285 or 6286.

In some embodiments, the first antigen binding domain comprises:

- 25 (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) having an amino acid sequence of a VHCDR1 in Table 4, Table 7A, or Table 17 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 having an amino acid sequence of a VHCDR2 in Table 4, Table 7A, or Table 17 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 having an amino acid sequence of a VHCDR3 in Table 4, Table 7A, or Table 17 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions);
- 30 (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VHCDR1) having an amino acid sequence of a VLCDR1 in Table 5,

Table 7A, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 having an amino acid sequence of a VLCDR2 in Table 5, Table 7A, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 having an amino acid sequence of a VLCDR3 in Table 5, Table 7A, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions);

(iii) a VH comprising the amino acid sequence of a VH in Table 7A or Table 16 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto);

(iv) a VL comprising the amino acid sequence of a VL in Table 7A or Table 16 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity thereto);

(v) a VH comprising a heavy chain framework region 1 (VHFWR1) having an amino acid sequence of a VHFWR1 in Table 4 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), a VHFWR2 having an amino acid sequence of a VHFWR2 in Table 4 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), a VHFWR3 having an amino acid sequence of a VHFWR3 in Table 4 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 having an amino acid sequence of a VHFWR4 in Table 4 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), and/or

(vi) a VL comprising a light chain framework region 1 (VLFWR1) having an amino acid sequence of a VLFWR1 in Table 5 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 having an amino acid sequence of a VLFWR2 in Table 5 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), a VLFWR3 having an amino acid sequence of a VLFWR3 in Table 5 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), and/or a VLFWR4 having an amino acid sequence of a VLFWR4 in Table 5 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions).

In some embodiments, the multifunctional molecule further comprises a tumor-targeting moiety.

In some embodiments, the tumor-targeting moiety binds to a tumor antigen.

In some embodiments, the tumor antigen is selected from G6B, CD34, CD41, P-selectin, Clec2, cKIT, FLT3, MPL, ITGB3, ITGB2, GP5, GP6, GP9, GP1BA, DSC2, FCGR2A, TNFRSF10A, TNFRSF10B, or TM4SF1.

5 In some embodiments, the tumor-targeting moiety comprises an antibody molecule, e.g., that binds to a tumor antigen selected from G6B, CD34, CD41, P-selectin, Clec2, cKIT, FLT3, MPL, ITGB3, ITGB2, GP5, GP6, GP9, GP1BA, DSC2, FCGR2A, TNFRSF10A, TNFRSF10B, or TM4SF1.

10 In some embodiments, the tumor-targeting moiety comprises a VH and/or VL sequence, e.g., as listed in Table A or Table 20.

In some embodiments, the multifunctional molecule preferentially binds to a myeloproliferative neoplasm cell over a non-tumor cell, optionally wherein the binding between the multifunctional molecule and the myeloproliferative neoplasm cell is more than 10, 20, 30, 40, 50-fold greater than the binding between the multifunctional molecule and a non-tumor cell.

15 In some embodiments, the myeloproliferative neoplasm cell is chosen from a myelofibrosis cell, an essential thrombocythemia cell, a polycythemia vera cell, or a chronic myeloid cancer cell, optionally wherein:

the myeloproliferative neoplasm cell does not comprise a JAK2 V617F mutation, or the myeloproliferative neoplasm cell does not comprise a MPL mutation.

20 In some embodiments, the multispecific molecule further comprises a linker, e.g., a linker between the first antigen binding domain and the second antigen binding domain.

In some embodiments, the linker is chosen from: a cleavable linker, a non-cleavable linker, a peptide linker, a flexible linker, a rigid linker, a helical linker, or a non-helical linker.

In some embodiments, the linker is a peptide linker.

25 In some embodiments, the peptide linker comprises Gly and Ser.

In some embodiments, the peptide linker comprises an amino acid sequence chosen from SEQ ID NOs: 6214-6217 or 6220-6221 and 77-78.

In another aspect, the disclosure provides a nucleic acid molecule encoding the multifunctional molecule as described herein.

30 In another aspect, the disclosure provides a vector, e.g., an expression vector, comprising the nucleic acid molecule as described herein.

In another aspect, the disclosure provides a host cell comprising the nucleic acid molecule or a vector as described herein.

In another aspect, the disclosure provides a method of making, e.g., producing, the multifunctional molecule as described herein, comprising culturing the host cell described
5 herein, under suitable conditions, e.g., conditions suitable for gene expression and/or homo- or heterodimerization.

In another aspect, the disclosure provides a pharmaceutical composition comprising the multifunctional molecule as described herein and a pharmaceutically acceptable carrier, excipient, or stabilizer.

10 In another aspect, the disclosure provides a method of treating a cancer, comprising administering to a subject in need thereof the multifunctional molecule as disclosed herein, wherein the multifunctional molecule is administered in an amount effective to treat the cancer.

In another aspect, the disclosure provides a use of the multifunctional molecule as described herein in treating a cancer. In another aspect, the disclosure provides a multifunctional
15 molecule disclosed herein for use in treating a cancer.

In some embodiments, the subject has cancer cells that express the first and/or second calreticulin protein.

In some embodiments, wherein the subject has the JAK2 V617F mutation.

In some embodiments, the subject does not have the JAK2 V617F mutation.

20 In some embodiments, the subject has a MPL mutation.

In some embodiments, the subject does not have a MPL mutation.

In some embodiments, the cancer is a hematological cancer, optionally wherein the cancer is a myeloproliferative neoplasm, e.g., primary or idiopathic myelofibrosis (MF), essential thrombocytosis (ET), polycythemia vera (PV), or chronic myelogenous leukemia (CML),
25 optionally wherein the cancer is myelofibrosis.

In some embodiments, the cancer is a solid tumor cancer.

In some embodiments, the method or use further comprises administering a second therapeutic treatment.

In some embodiments, the second therapeutic treatment comprises a therapeutic agent
30 (e.g., a chemotherapeutic agent, a biologic agent, hormonal therapy), radiation, or surgery.

In some embodiments, the therapeutic agent is selected from: a chemotherapeutic agent, or a biologic agent.

In another aspect, the disclosure features a multifunctional molecule (e.g., polypeptide or nucleic acid encoding the same) that includes:

(i) a first antigen binding domain that binds to a calreticulin protein (e.g., a wild-type or mutant calreticulin protein),

and

(ii) one, two, or all of:

(a) an immune cell engager chosen from a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager;

(b) a cytokine molecule;

(c) a stromal modifying moiety; or

(d) a tumor-targeting moiety that binds to a tumor antigen, e.g., chosen from:

G6B, CD34, CD41, P-selectin, Clec2, cKIT, FLT3, MPL, ITGB3, ITGB2, GP5, GP6, GP9, GP1BA, DSC2, FCGR2A, TNFRSF10A, TNFRSF10B, or TM4SF1.

In an aspect, the disclosure features a multifunctional molecule (e.g., polypeptide or nucleic acid encoding the same) that includes:

(i) a first antigen binding domain that binds to a calreticulin protein (e.g., a wild-type or mutant calreticulin protein), and

(ii) a second antigen binding domain comprising an immune cell engager (e.g., a T cell engager, e.g., an antigen binding domain that binds to TCR β V, e.g., as described herein).

In an aspect, the disclosure features a multifunctional molecule (e.g., polypeptide or nucleic acid encoding the same) that includes:

(i) a first antigen binding domain that binds to a calreticulin protein (e.g., a wild-type or mutant calreticulin protein), and

(ii) a second antigen binding domain comprising a tumor-targeting moiety, e.g., that binds to a tumor antigen chosen from: G6B, CD34, CD41, P-selectin, Clec2, cKIT, FLT3, MPL, ITGB3, ITGB2, GP5, GP6, GP9, GP1BA, DSC2, FCGR2A, TNFRSF10A, TNFRSF10B, or TM4SF1.

In an aspect, the disclosure features a multifunctional molecule (e.g., polypeptide or nucleic acid encoding the same) that includes:

(i) a first antigen binding domain that binds to a calreticulin protein (e.g., a wild-type or mutant calreticulin protein),

5 (ii) a second antigen binding domain comprising an immune cell engager (e.g., a T cell engager, e.g., an antigen binding domain that binds to TCR β V, e.g., as described herein, e.g., an anti-TCR β V antibody molecule described herein), and

(iii) a third antigen binding domain comprising a tumor-targeting moiety, e.g., that binds to a tumor antigen chosen from: G6B, CD34, CD41, P-selectin, Clec2, cKIT, FLT3, MPL, 10 ITGB3, ITGB2, GP5, GP6, GP9, GP1BA, DSC2, FCGR2A, TNFRSF10A, TNFRSF10B, or TM4SF1.

In some embodiments, the multifunctional molecule further comprises a cytokine molecule or a modulator of a cytokine molecule, e.g., a TGF- β inhibitor, e.g., as described herein.

15 In some embodiments, the multifunctional molecule further comprises an NK cell engager, e.g., an antigen binding domain that binds to Nkp30, e.g., as described herein.

In some embodiments, the calreticulin protein (e.g., the wild-type or mutant calreticulin protein) comprises the amino acid sequence of SEQ ID NO: 6285 or 6286. In some embodiments, the wild type calreticulin protein comprises the amino acid sequence of SEQ ID 20 NO: 6285. In some embodiments, the calreticulin mutant protein comprises the amino acid sequence of SEQ ID NO: 6286.

In some embodiments, the first antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6224, a VHFWR2 amino acid sequence of SEQ ID NO: 6226, a VHFWR3 amino acid sequence of SEQ ID NO: 6228, or a VHFWR4 amino acid sequence of SEQ ID NO: 6230. 25 In some embodiments, the first antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6232, a VHFWR2 amino acid sequence of SEQ ID NO: 6234, a VHFWR3 amino acid sequence of SEQ ID NO: 6236, or a VHFWR4 amino acid sequence of SEQ ID NO: 6230. In 30 some embodiments, the first antigen binding domain comprises a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID

NO: 6238, a VLFWR2 amino acid sequence of SEQ ID NO: 6240, a VLFWR3 amino acid sequence of SEQ ID NO: 6242, or a VLFWR4 amino acid sequence of SEQ ID NO: 6244.

In some embodiments, the calreticulin protein (e.g., a wild-type or mutant calreticulin protein) comprises an amino acid sequence chosen from SEQ ID NOs: 6285-6312. In some
5 embodiments, the calreticulin protein (e.g., a wild-type or mutant calreticulin protein) comprises an amino acid sequence chosen from SEQ ID NOs: 6313-6346. In some embodiments, the calreticulin protein (e.g., a wild-type or mutant calreticulin protein) is a calreticulin protein (e.g., a wild-type or mutant calreticulin protein) disclosed in Table 2 or 3. In some embodiments, the calreticulin protein (e.g., a wild-type or mutant calreticulin protein) comprises the amino acid
10 sequence of SEQ ID NO: 6287. In some embodiments, the calreticulin protein (e.g., a wild-type or mutant calreticulin protein) comprises the amino acid sequence of SEQ ID NO: 6313. In some embodiments, the calreticulin protein (e.g., a wild-type or mutant calreticulin protein) comprises the amino acid sequence of SEQ ID NO: 6288. In some embodiments, the calreticulin protein (e.g., a wild-type or mutant calreticulin protein) comprises the amino acid sequence of
15 SEQ ID NO: 6314.

In some embodiments, the multifunctional molecule further comprising a second antigen binding domain that preferentially binds to a second calreticulin protein (e.g., a wild-type or mutant calreticulin protein). In some embodiments, the second calreticulin protein (e.g., a wild-type or mutant calreticulin protein) comprises the amino acid sequence of SEQ ID NO: 6286. In
20 some embodiments, the second antigen binding domain is different from the first antigen binding domain. In some embodiments, the second antigen binding domain is the same as the first antigen binding domain. In some embodiments, the second calreticulin protein (e.g., a wild-type or mutant calreticulin protein) comprises an amino acid sequence chosen from SEQ ID NOs: 6287-6312. In some embodiments, the second calreticulin protein (e.g., a wild-type or mutant calreticulin protein) comprises an amino acid sequence chosen from SEQ ID NOs: 6313-6346.
25 In some embodiments, the second calreticulin protein (e.g., a wild-type or mutant calreticulin protein) is a calreticulin protein (e.g., a wild-type or mutant calreticulin protein) disclosed in Table 2 or 3. In some embodiments, the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6287. In some embodiments, the second calreticulin protein comprises
30 the amino acid sequence of SEQ ID NO: 6313. In some embodiments, the second calreticulin

protein comprises the amino acid sequence of SEQ ID NO: 6288. In some embodiments, the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6314.

In some embodiments, the first calreticulin protein (e.g., a wild-type or mutant calreticulin protein) is a Type 1 calreticulin protein (e.g., a wild-type or mutant calreticulin protein), and the second calreticulin protein (e.g., a wild-type or mutant calreticulin protein) is a Type 2 calreticulin protein (e.g., a wild-type or mutant calreticulin protein). In some embodiments, the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6287, and the second calreticulin protein the amino acid sequence of SEQ ID NO: 6288. In some embodiments, the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6313, and the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6314.

In some embodiments, the wild type calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6285.

In some embodiments, the first antigen binding domain has about the same affinity (e.g., equal affinity) for the first calreticulin protein (e.g., a mutant calreticulin protein) and for a wild-type calreticulin protein.

In some embodiments, the second antigen binding domain has about the same affinity (e.g., equal affinity) for the second calreticulin protein (e.g., a mutant calreticulin protein) and for a wild-type calreticulin protein.

In some embodiments, the first antigen binding domain has a higher affinity for a first calreticulin mutant protein than for the wild type calreticulin protein. In some embodiments, the K_D for the binding between the first antigen binding domain and the first calreticulin mutant protein is no more than 40%, 30%, 20%, 10%, 1%, 0.1%, or 0.01% of the K_D for the binding between the first antigen binding domain and the wild type calreticulin protein. In some embodiments, the first antigen binding domain binds to an epitope located within the C-terminus of the first calreticulin mutant protein. In some embodiments, the first antigen binding domain binds to an epitope located within the amino acid sequence of SEQ ID NO: 6286. In some embodiments, the first antigen binding domain does not bind to the wild type calreticulin protein. In some embodiments, the wild type calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6285.

In some embodiments, the second antigen binding domain has a higher affinity for a second calreticulin mutant protein than for the wild type calreticulin protein. In some embodiments, the K_D for the binding between the second antigen binding domain and the second calreticulin mutant protein is no more than 40%, 30%, 20%, 10%, 1%, 0.1%, or 0.01% of the K_D for the binding between the second antigen binding domain and the wild type calreticulin protein. In some embodiments, the second antigen binding domain binds to an epitope located within the C-terminus of the second calreticulin mutant protein. In some embodiments, the second antigen binding domain binds to an epitope located within the amino acid sequence of SEQ ID NO: 6286. In some embodiments, the second antigen binding domain does not bind to the wild type calreticulin protein. In some embodiments, the wild type calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6285.

In some embodiments, the multifunctional molecule preferentially binds to a myeloproliferative neoplasm cell over a non-tumor cell. In some embodiments, the binding between the multifunctional molecule and the myeloproliferative neoplasm cell is more than 10, 20, 30, 40, 50-fold greater than the binding between the multifunctional molecule and a non-tumor cell. In some embodiments, the myeloproliferative neoplasm cell is chosen from a myelofibrosis cell, an essential thrombocythemia cell, a polycythemia vera cell, or a chronic myeloid cancer cell. In some embodiments, the myeloproliferative neoplasm cell does not comprise a JAK2 V617F mutation. In some embodiments, the myeloproliferative neoplasm cell does not comprise a MPL mutation.

In some embodiments, the first and/or second antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6253 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6254 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6255 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the first and/or second antigen binding domain comprises a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6259 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ

ID NO: 6260 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6261 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

In some embodiments, the first and/or second antigen binding domain comprises:

5 (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6253 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6254 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of
10 SEQ ID NO: 6255 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and

(ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6259 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2
15 amino acid sequence of SEQ ID NO: 6260 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6261 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

In some embodiments, the first and/or second antigen binding domain comprises a VH
20 comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6253, a VHCDR2 amino acid sequence of SEQ ID NO: 6254, and a VHCDR3 amino acid sequence of SEQ ID NO: 6255. In some embodiments, the first and/or second antigen binding domain comprises a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6259, a VLCDR2 amino acid sequence of SEQ ID NO: 6260, and a VLCDR3 amino acid sequence of SEQ ID NO: 6261.

25 In some embodiments, the first and/or second antigen binding domain comprises:

(i) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6253, a VHCDR2 amino acid sequence of SEQ ID NO: 6254, and a VHCDR3 amino acid sequence of SEQ ID NO: 6255, and

(ii) a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6259, a VLCDR2
30 amino acid sequence of SEQ ID NO: 6260, and a VLCDR3 amino acid sequence of SEQ ID NO: 6261.

In some embodiments, the first and/or second antigen binding domain comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6224, a VHFWR2 amino acid sequence of SEQ ID NO: 6226, a VHFWR3 amino acid sequence of SEQ ID NO: 6228, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6230. In some
 5 embodiments, the first and/or second antigen binding domain comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6238, a VLFWR2 amino acid sequence of SEQ ID NO: 6240, a VLFWR3 amino acid sequence of SEQ ID NO: 6242, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6244.

In some embodiments, the first and/or second antigen binding domain comprises:

10 (i) a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6224, a VHFWR2 amino acid sequence of SEQ ID NO: 6226, a VHFWR3 amino acid sequence of SEQ ID NO: 6228, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6230, and

(ii) a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence
 15 of SEQ ID NO: 6238, a VLFWR2 amino acid sequence of SEQ ID NO: 6240, a VLFWR3 amino acid sequence of SEQ ID NO: 6242, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6244.

In some embodiments, the first and/or second antigen binding domain comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6263 (or a sequence with no more
 20 than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions), a VHFWR2 amino acid sequence of SEQ ID NO: 6264 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions), a VHFWR3 amino acid sequence of SEQ ID NO: 6265 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO:
 25 228. In some embodiments, the first and/or second antigen binding domain comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6277 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6278 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6279 (or a sequence with
 30 no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6280.

In some embodiments, the first and/or second antigen binding domain comprises:

(i) a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6263 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions), a VHFWR2 amino acid sequence of SEQ ID NO: 6264 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions), a VHFWR3 amino acid sequence of SEQ ID NO: 6265 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 228, and

(ii) a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6277 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6278 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6279 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6280.

In some embodiments, the first and/or second antigen binding domain comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6263, a VHFWR2 amino acid sequence of SEQ ID NO: 6264, a VHFWR3 amino acid sequence of SEQ ID NO: 6265, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 228. In some embodiments, the first and/or second antigen binding domain comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6277, a VLFWR2 amino acid sequence of SEQ ID NO: 6278, a VLFWR3 amino acid sequence of SEQ ID NO: 6279, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6280.

In some embodiments, the first and/or second antigen binding domain comprises:

(i) a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6263, a VHFWR2 amino acid sequence of SEQ ID NO: 6264, a VHFWR3 amino acid sequence of SEQ ID NO: 6265, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 228, and

(ii) a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6277, a VLFWR2 amino acid sequence of SEQ ID NO: 6278, a VLFWR3 amino acid sequence of SEQ ID NO: 6279, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6280.

In some embodiments, the first and/or second antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6247 (or an amino acid sequence having at

least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6247). In some embodiments, the first and/or second antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6249 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6249).

5 In some embodiments, the first and/or second antigen binding domain comprises:

(i) a VH comprising the amino acid sequence of SEQ ID NO: 6247 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6247), and

(ii) a VL comprising the amino acid sequence of SEQ ID NO: 6249 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6249).

10 In some embodiments, the first and/or second antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6247. In some embodiments, the first and/or second antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6249. In some embodiments, the first and/or second antigen binding domain comprises (i) a VH comprising the amino acid sequence of SEQ ID NO: 6247, and (ii) a VL comprising the amino acid sequence of SEQ ID NO: 6249.

15 In some embodiments, the first and/or second antigen binding domain comprises a VH comprising an amino acid sequence of at least 70% or 75% sequence identity to SEQ ID NO: 6250. In some embodiments, the first and/or second antigen binding domain comprises a VL comprising an amino acid sequence of at least 85% or 90% sequence identity to SEQ ID NO: 20 6252. In some embodiments, the first and/or second antigen binding domain comprises (i) a VH comprising an amino acid sequence of at least 70% or 75% sequence identity to SEQ ID NO: 6250, and (ii) a VL comprising an amino acid sequence of at least 85% or 90% sequence identity to SEQ ID NO: 6252.

25 In some embodiments, the first and/or second antigen binding domain comprises a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6256 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6257 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6258 or 116 (or 30 a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

In some embodiments, the first and/or second antigen binding domain comprises a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6259 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6260 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6261 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

In some embodiments, the first and/or second antigen binding domain comprises:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6256 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6257 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6258 or 116 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and

(ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6259 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6260 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6261 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

In some embodiments, the first and/or second antigen binding domain comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6232, a VHFWR2 amino acid sequence of SEQ ID NO: 6234, a VHFWR3 amino acid sequence of SEQ ID NO: 6236, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6230. In some embodiments, the first and/or second antigen binding domain comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6238, a VLFWR2 amino acid sequence of SEQ ID NO: 6240, a VLFWR3 amino acid sequence of SEQ ID NO: 6242, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6244.

In some embodiments, the first and/or second antigen binding domain comprises:

(i) a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6232, a VHFWR2 amino acid sequence of SEQ ID NO: 6234, a VHFWR3 amino acid sequence of SEQ ID NO: 6236, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6230, and

5 (ii) a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6238, a VLFWR2 amino acid sequence of SEQ ID NO: 6240, a VLFWR3 amino acid sequence of SEQ ID NO: 6242, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6244.

In some embodiments, the first and/or second antigen binding domain comprises a VH
10 comprising a heavy chain framework 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6266 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), a VHFWR2 amino acid sequence of SEQ ID NO: 6267 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHFWR3 amino acid sequence of SEQ ID NO: 6268 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8,
15 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6269. In some embodiments, the first and/or second antigen binding domain comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6277 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6278 (or a sequence with no more than 1
20 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6279 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6280.

In some embodiments, the first and/or second antigen binding domain comprises:

(i) a VH comprising a heavy chain framework 1 (VHFWR1) amino acid sequence of
25 SEQ ID NO: 6266 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), a VHFWR2 amino acid sequence of SEQ ID NO: 6267 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHFWR3 amino acid sequence of SEQ ID NO: 6268 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a
30 VHFWR4 amino acid sequence of SEQ ID NO: 6269, and

(ii) a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6277 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6278 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6279 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6280.

In some embodiments, the first and/or second antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6248 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6248). In some embodiments, the first and/or second antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6249 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6249).

In some embodiments, the first and/or second antigen binding domain comprises

(i) a VH comprising the amino acid sequence of SEQ ID NO: 6248 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6248), and

(ii) a VL comprising the amino acid sequence of SEQ ID NO: 6249 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6249).

In some embodiments, the first and/or second antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6248. In some embodiments, the first and/or second antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6249. In some embodiments, the first and/or second antigen binding domain comprises (i) a VH comprising the amino acid sequence of SEQ ID NO: 6248, and (ii) a VL comprising the amino acid sequence of SEQ ID NO: 6249.

In some embodiments, the first and/or second antigen binding domain comprises a VH comprising an amino acid sequence of at least 70% or 74% sequence identity to SEQ ID NO: 6251. In some embodiments, the first and/or second antigen binding domain comprises a VL comprising an amino acid sequence of at least 85% or 90% sequence identity to SEQ ID NO: 6252. In some embodiments, the first and/or second antigen binding domain comprises (i) a VH comprising an amino acid sequence of at least 70% or 74% sequence identity to SEQ ID NO:

6251, and/or (ii) a VL comprising an amino acid sequence of at least 85% or 90% sequence identity to SEQ ID NO: 6252.

In some embodiments, the multifunctional molecule comprises an immune cell engager chosen from a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager. In some embodiments, the immune cell engager binds to and activates an immune cell, e.g., an effector cell. In some embodiments, the immune cell engager binds to, but does not activate, an immune cell, e.g., an effector cell.

In some embodiments, the immune cell engager is a T cell engager, e.g., a T cell engager that mediates binding to and activation of a T cell, or a T cell engager that mediates binding to but not activation of a T cell. In some embodiments, the T cell engager binds to CD3, TCR α , TCR β , TCR γ , TCR ζ , ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, or CD226. In some embodiments, the T cell engager is an anti-CD3 antibody molecule. In some embodiments, the T cell engager is an anti-TCR β antibody molecule, e.g., an anti-TCR β V antibody molecule described herein.

In some embodiments, the immune cell engager is an NK cell engager, e.g., an NK cell engager that mediates binding to and activation of an NK cell, or an NK cell engager that mediates binding to but not activation of an NK cell. In some embodiments, the NK cell engager is chosen from an antibody molecule, e.g., an antigen binding domain, or ligand that binds to (e.g., activates): NKp30, NKp40, NKp44, NKp46, NKG2D, DNAM1, DAP10, CD16 (e.g., CD16a, CD16b, or both), CRTAM, CD27, PSGL1, CD96, CD100 (SEMA4D), NKp80, CD244 (also known as SLAMF4 or 2B4), SLAMF6, SLAMF7, KIR2DS2, KIR2DS4, KIR3DS1, KIR2DS3, KIR2DS5, KIR2DS1, CD94, NKG2C, NKG2E, or CD160. In some embodiments, the NK cell engager is an antibody molecule or ligand that binds to (e.g., activates) NKp30. In some embodiments, the NK cell engager is an antibody molecule, e.g., an antigen binding domain. In some embodiments, the NK cell engager is an antibody molecule, e.g., an antigen binding domain, that binds to NKp30 or NKp46. In some embodiments, the NK cell engager is a ligand, optionally, the ligand further comprises an immunoglobulin constant region, e.g., an Fc region. In some embodiments, the NK cell engager is a ligand of NKp44 or NKp46, e.g., a viral HA. In some embodiments, the NK cell engager is a ligand of DAP10, e.g., a coreceptor for NKG2D. In some embodiments, the NK cell engager is a ligand of CD16, e.g., a CD16a/b ligand, e.g., a CD16a/b ligand further comprising an antibody Fc region. In some embodiments,

the immune cell engager mediates binding to, or activation of, or both of, one or more of a B cell, a macrophage, and/or a dendritic cell.

In some embodiments, the immune cell engager comprises a B cell, macrophage, and/or dendritic cell engager chosen from one or more of CD40 ligand (CD40L) or a CD70 ligand; an antibody molecule that binds to CD40 or CD70; an antibody molecule to OX40; an OX40 ligand (OX40L); an agonist of a Toll-like receptor (e.g., a TLR4, e.g., a constitutively active TLR4 (caTLR4) or a TLR9 agonist); a 41BB; a CD2 agonist; a CD47; or a STING agonist, or a combination thereof. In some embodiments, the immune cell engager is a B cell engager, e.g., a CD40L, an OX40L, or a CD70 ligand, or an antibody molecule that binds to OX40, CD40 or CD70. In some embodiments, the immune cell engager is a macrophage cell engager, e.g., a CD2 agonist; a CD40L; an OX40L; an antibody molecule that binds to OX40, CD40 or CD70; an agonist of a Toll-like receptor (TLR) (e.g., a TLR4, e.g., a constitutively active TLR4 (caTLR4) or a TLR9 agonist); CD47; or a STING agonist. In some embodiments, the immune cell engager is a dendritic cell engager, e.g., a CD2 agonist, an OX40 antibody, an OX40L, 41BB agonist, a Toll-like receptor agonist or a fragment thereof (e.g., a TLR4, e.g., a constitutively active TLR4 (caTLR4)), CD47 agonist, or a STING agonist. In some embodiments, the STING agonist comprises a cyclic dinucleotide, e.g., a cyclic di-GMP (cdGMP), a cyclic di-AMP (cdAMP), or a combination thereof, optionally with 2',5' or 3',5' phosphate linkages, e.g., wherein the STING agonist is covalently coupled to the multifunctional molecule.

In some embodiments, the multifunctional molecule comprises a cytokine molecule or a modulator thereof. In some embodiments, the cytokine molecule is chosen from TGF- β , interleukin-2 (IL-2), interleukin-7 (IL-7), interleukin-12 (IL-12), interleukin-15 (IL-15), interleukin-18 (IL-18), interleukin-21 (IL-21), or interferon gamma, or a fragment or variant thereof, or a combination of any of the aforesaid cytokines. In some embodiments, the cytokine molecule is a monomer or a dimer. In some embodiments, the cytokine molecule further comprises a receptor dimerizing domain, e.g., an IL15Ralpha dimerizing domain. In some embodiments, the cytokine molecule (e.g., IL-15) and the receptor dimerizing domain (e.g., an IL15Ralpha dimerizing domain) are not covalently linked, e.g., are non-covalently associated.

In some embodiments, the modulator of the cytokine molecule comprises a TGF- β inhibitor.

In some embodiments, the multifunctional molecule comprises a stromal modifying moiety. In some embodiments, the stromal modifying moiety causes one or more of: decreases the level or production of a stromal or extracellular matrix (ECM) component; decreases tumor fibrosis; increases interstitial tumor transport; improves tumor perfusion; expands the tumor microvasculature; decreases interstitial fluid pressure (IFP) in a tumor; or decreases or enhances penetration or diffusion of an agent, e.g., a cancer therapeutic or a cellular therapy, into a tumor or tumor vasculature. In some embodiments, the stromal or ECM component decreased is chosen from a glycosaminoglycan or an extracellular protein, or a combination thereof. In some embodiments, the glycosaminoglycan is chosen from hyaluronan (also known as hyaluronic acid or HA), chondroitin sulfate, chondroitin, dermatan sulfate, heparan sulfate, heparin, entactin, tenascin, aggrecan or keratin sulfate. In some embodiments, the extracellular protein is chosen from collagen, laminin, elastin, fibrinogen, fibronectin, or vitronectin. In some embodiments, the stromal modifying moiety comprises an enzyme molecule that degrades a tumor stroma or extracellular matrix (ECM). In some embodiments, the enzyme molecule is chosen from a hyaluronidase molecule, a collagenase molecule, a chondroitinase molecule, a matrix metalloproteinase molecule (e.g., macrophage metalloelastase), or a variant (e.g., a fragment) of any of the aforesaid. In some embodiments, the stromal modifying moiety decreases the level or production of hyaluronic acid. In some embodiments, the stromal modifying moiety comprises a hyaluronan degrading enzyme, an agent that inhibits hyaluronan synthesis, or an antibody molecule against hyaluronic acid. In some embodiments, the hyaluronan degrading enzyme is a hyaluronidase molecule or a variant (e.g., fragment thereof) thereof. In some embodiments, the hyaluronan degrading enzyme is active in neutral or acidic pH, e.g., pH of about 4-5. In some embodiments, the hyaluronidase molecule is a mammalian hyaluronidase molecule, e.g., a recombinant human hyaluronidase molecule, or a variant thereof (e.g., a truncated form thereof). In some embodiments, the hyaluronidase molecule is chosen from HYAL1, HYAL2, or PH-20/SPAM1, or a variant thereof (e.g., a truncated form thereof). In some embodiments, the truncated form lacks a C-terminal glycosylphosphatidylinositol (GPI) attachment site or a portion of the GPI attachment site. In some embodiments, the hyaluronidase molecule is glycosylated, e.g., comprises at least one N-linked glycan. In some embodiments, the hyaluronidase molecule comprises the amino acid sequence of SEQ ID NO:6213, or a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical

thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 6213). In some embodiments, the hyaluronidase molecule comprises the amino acid residues 36-464 of SEQ ID NO: 6213. In some embodiments, the

5 hyaluronidase molecule comprises the amino acid residues 36-481, 36-482, or 36-483 of PH20, wherein PH20 has the amino acid sequence of SEQ ID NO: 6213. In some embodiments, the hyaluronidase molecule comprises an amino acid sequence having at least 95% to 100 % sequence identity to the polypeptide or truncated form of the amino acid sequence of SEQ ID NO: 6213. In some embodiments, the hyaluronidase molecule comprises an amino acid

10 sequence having 30, 20, 10, 5 or fewer amino acid substitutions to the amino acid sequence of SEQ ID NO: 6213. In some embodiments, the hyaluronidase molecule comprises an amino acid sequence at least 95% (e.g., at least 95%, 96%, 97%, 98%, 99%, 100%) identical to the amino acid sequence of SEQ ID NO: 6213. In some embodiments, the hyaluronidase molecule is encoded by a nucleotide sequence at least 95% (e.g., at least 96%, 97%, 98%, 99%, 100%)

15 identical to the nucleotide sequence of SEQ ID NO: 6213. In some embodiments, the hyaluronidase molecule is PH20, e.g., rHuPH20. In some embodiments, the hyaluronidase molecule is HYAL1 and comprises the amino acid sequence of SEQ ID NO: 6218, or a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen

20 alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 6218). In some embodiments, the hyaluronan degrading enzyme, e.g., the hyaluronidase molecule, further comprises a polymer, e.g., is conjugated to a polymer, e.g., PEG. In some embodiments, the hyaluronan-degrading enzyme is a PEGylated PH20 enzyme (PEGPH20). In some embodiments, the hyaluronan degrading enzyme, e.g., the

25 hyaluronidase molecule, further comprises an immunoglobulin chain constant region (e.g., Fc region) chosen from, e.g., the heavy chain constant regions of IgG1, IgG2, IgG3, or IgG4, more particularly, the heavy chain constant region of human IgG1, IgG2, IgG3, or IgG4. In some embodiments, the immunoglobulin constant region (e.g., the Fc region) is linked, e.g., covalently linked to, the hyaluronan degrading enzyme, e.g., the hyaluronidase molecule. In some

30 embodiments, the immunoglobulin chain constant region (e.g., Fc region) is altered, e.g., mutated, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the

number of cysteine residues, effector cell function, or complement function. In some embodiments, the hyaluronan degrading enzyme, e.g., the hyaluronidase molecule, forms a dimer. In some embodiments, the stromal modifying moiety comprises an inhibitor of the synthesis of hyaluronan, e.g., an HA synthase. In some embodiments, the inhibitor comprises a sense or an antisense nucleic acid molecule against an HA synthase or is a small molecule drug. In some embodiments, the inhibitor is 4- methylumbelliferone (MU) or a derivative thereof (e.g., 6,7-dihydroxy-4-methyl coumarin or 5,7-dihydroxy-4-methyl coumarin), or leflunomide or a derivative thereof. In some embodiments, the stromal modifying moiety comprises a collagenase molecule, e.g., a mammalian collagenase molecule, or a variant (e.g., fragment) thereof. In some embodiments, the collagenase molecule is collagenase molecule IV, e.g., comprising the amino acid sequence of SEQ ID NO: 6219, or a fragment thereof, or an amino acid sequence substantially identical thereto (e.g., 95% to 99.9% identical thereto, or having at least one amino acid alteration, but not more than five, ten or fifteen alterations (e.g., substitutions, deletions, or insertions, e.g., conservative substitutions) to the amino acid sequence of SEQ ID NO: 6219.

In some embodiments, the multifunctional molecule comprises an immune cell engager (e.g., a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager) and a cytokine molecule. In some embodiments, the multifunctional molecule comprises an immune cell engager (e.g., a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager) and a stromal modifying moiety. In some embodiments, the multifunctional molecule comprises a cytokine molecule and a stromal modifying moiety. In some embodiments, the multifunctional molecule comprises an immune cell engager (e.g., a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager), a cytokine molecule, and a stromal modifying moiety.

In some embodiments, the multifunctional molecule comprises at least two non-contiguous polypeptide chains.

In some embodiments, the multifunctional molecule comprises the following configuration:

A, B-[dimerization module]-C, -D

e.g., the configuration shown in FIGs. 1A, 1B, and 1C, wherein:

(1) the dimerization module comprises an immunoglobulin constant domain, *e.g.*, a heavy chain constant domain (*e.g.*, a homodimeric or heterodimeric heavy chain constant region, *e.g.*, an Fc region), or a constant domain of an immunoglobulin variable region (*e.g.*, a Fab region); and

5 (2) A, B, C, and D are independently absent; (i) an antigen binding domain that binds to a calreticulin protein (*e.g.*, a wild type calreticulin protein or a mutant calreticulin protein), wherein the calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286; (ii) an immune cell engager chosen from a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager; (iii) a cytokine molecule; or (iv) a stromal
10 modifying moiety, provided that:

at least one, two, or three of A, B, C, and D comprises an antigen binding domain that binds to a calreticulin protein (*e.g.*, a wild type calreticulin protein or a calreticulin mutant protein), wherein the calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and

15 any of the remaining A, B, C, and D is absent or comprises one of an immune cell engager, a cytokine molecule, or a stromal modifying moiety.

In some embodiments,

(i) A comprises an antigen binding domain that binds to a calreticulin protein (*e.g.*, a wild type calreticulin protein or a calreticulin mutant protein), wherein the calreticulin protein
20 comprises the amino acid sequence of SEQ ID NO: 6286, and B, C, or D comprises an immune cell engager, *e.g.*, a T cell engager, *e.g.*, an anti-CD3 antibody molecule;

(ii) A comprises an antigen binding domain that binds to a calreticulin protein (*e.g.*, a wild type calreticulin protein or a calreticulin mutant protein), wherein the calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and B, C, or D comprises a cytokine
25 molecule;

(iii) A comprises an antigen binding domain that binds to a calreticulin protein (*e.g.*, a wild type calreticulin protein or a calreticulin mutant protein), wherein the calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and B, C, or D comprises a stromal modifying moiety;

30 (iv) A comprises a first antigen binding domain that binds to a first calreticulin protein (*e.g.*, a wild type calreticulin protein or a calreticulin mutant protein), wherein the first

calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, B comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and C or D comprises an immune cell
 5 engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule;

(v) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, B comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type
 10 calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and C or D comprises a cytokine molecule;

(vi) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first
 15 calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, B comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and C or D comprises a stromal modifying moiety;

(vii) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, C comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type
 20 calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and B or D comprises an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule;

(viii) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, C comprises a
 25 second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein

comprises the amino acid sequence of SEQ ID NO: 6286, and B or D comprises a cytokine molecule;

(ix) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, C comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and B or D comprises a stromal modifying moiety;

(x) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and B, C, or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule and (b) a cytokine molecule;

(xi) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and B, C, or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule and (b) a stromal modifying moiety;

(xii) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and B, C, or D comprises (a) a cytokine molecule and (b) a stromal modifying moiety;

(xiii) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, B comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and C or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule and (b) a cytokine molecule;

(xiv) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, B comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and C or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule and (b) a stromal modifying moiety;

(xv) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, B comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and C or D comprises (a) a cytokine molecule and (b) a stromal modifying moiety;

(xvi) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, C comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and B or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule and (b) a cytokine molecule;

(xvii) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, C comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and B or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule and (b) a stromal modifying moiety;

(xviii) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, C comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and B or D comprises (a) a cytokine molecule and (b) a stromal modifying moiety;

(xix) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and B, C, or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule, (b) a cytokine molecule, and (c) a stromal modifying moiety;

(xx) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, B comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and C or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule, (b) a cytokine molecule, and (c) a stromal modifying moiety; or

(xxi) A comprises a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the first calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, C comprises a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), wherein the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286, and B or D comprises (a) an immune cell engager, e.g., a T cell engager, e.g., an anti-CD3 antibody molecule, (b) a cytokine molecule, and (c) a stromal modifying moiety.

In some embodiments, the dimerization module comprises one or more immunoglobulin chain constant regions (e.g., Fc regions) comprising one or more of: a paired cavity-protuberance (“knob-in-a hole”), an electrostatic interaction, or a strand-exchange. In some embodiments, the

one or more immunoglobulin chain constant regions (e.g., Fc regions) comprise an amino acid substitution at a position chosen from one or more of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397, 398, 399, 405, 407, or 409, e.g., of the Fc region of human IgG1. In some embodiments, the one or more immunoglobulin chain constant regions (e.g., Fc regions) comprise an amino acid substitution chosen from: T366S, L368A, or Y407V (e.g., corresponding to a cavity or hole), or T366W (e.g., corresponding to a protuberance or knob), or a combination thereof.

In some embodiments, the multifunctional molecule further comprises a linker, e.g., a linker between one or more of: the antigen binding domain and the immune cell engager, the antigen binding domain and the cytokine molecule, the antigen binding domain and the stromal modifying moiety, the immune cell engager and the cytokine molecule, the immune cell engager and the stromal modifying moiety, the cytokine molecule and the stromal modifying moiety, the antigen binding domain and the dimerization module, the immune cell engager and the dimerization module, the cytokine molecule and the dimerization module, or the stromal modifying moiety and the dimerization module. In some embodiments, the linker is chosen from: a cleavable linker, a non-cleavable linker, a peptide linker, a flexible linker, a rigid linker, a helical linker, or a non-helical linker. In some embodiments, the linker is a peptide linker. In some embodiments, the peptide linker comprises Gly and Ser. In some embodiments, the peptide linker comprises an amino acid sequence chosen from SEQ ID NOs: 6214-6217 or 6220-6221 and 77-78.

In one aspect, the invention provides a multifunctional molecule, comprising:

(i) an antigen binding domain that binds to a calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), e.g., wherein the calreticulin mutant protein comprises the amino acid sequence of SEQ ID NO: 6286, and

(ii) a moiety that binds to CD3, e.g., an antibody molecule that binds to CD3.

In some embodiments, the multifunctional molecule comprises:

a first polypeptide comprising, e.g., from N-terminus to C-terminus, a first VL and a first CL,

a second polypeptide comprising, e.g., from N-terminus to C-terminus, a first VH, a first CH1, a first dimerization domain (e.g., a first Fc), and a first moiety that binds to CD3 (e.g., a first scFv that binds to CD3),

5 a third polypeptide comprising, e.g., from N-terminus to C-terminus, a second VH, a second CH1, a second dimerization domain (e.g., a second Fc), and optionally a second moiety that binds to CD3 (e.g., a second scFv that binds to CD3),

a fourth polypeptide comprising, e.g., from N-terminus to C-terminus, a second VL and a second CL, wherein:

10 the first VL and the first VH form a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild-type calreticulin protein or a calreticulin mutant protein), and the second VL and the second VH form a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild-type calreticulin protein or a calreticulin mutant protein), wherein the first and second calreticulin proteins comprise the amino acid sequence of SEQ ID NO: 6286, optionally wherein the first and second calreticulin proteins are each independently
15 chosen from: a molecule comprising the amino acid sequence of SEQ ID NO: 6313, or a molecule comprising the amino acid sequence of SEQ ID NO: 6314.

In some embodiments, the multifunctional molecule comprises the configuration of FIG. 2A or 2B.

20 In one aspect, the invention provides a multifunctional molecule, comprising:

(i) an antigen binding domain that binds to a calreticulin protein (e.g., a wild type calreticulin protein or a calreticulin mutant protein), e.g., wherein the calreticulin mutant protein comprises the amino acid sequence of SEQ ID NO: 6286, and

25 (ii) a moiety that binds to TCR (e.g., TCR β), e.g., an antibody molecule that binds to TCR (e.g., TCR β).

In some embodiments, the multifunctional molecule comprises:

a first polypeptide comprising, e.g., from N-terminus to C-terminus, a first VL and a first CL,

30 a second polypeptide comprising, e.g., from N-terminus to C-terminus, a first VH, a first CH1, a first dimerization domain (e.g., a first Fc), and a first moiety that binds to TCR (e.g., TCR β) (e.g., a first scFv that binds to TCR (e.g., TCR β)),

a third polypeptide comprising, e.g., from N-terminus to C-terminus, a second VH, a second CH1, a second dimerization domain (e.g., a second Fc), and optionally a second moiety that binds to TCR (e.g., TCR β) (e.g., a second scFv that binds to TCR (e.g., TCR β)),

a fourth polypeptide comprising, e.g., from N-terminus to C-terminus, a second VL and a
5 second CL, wherein:

the first VL and the first VH form a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild-type calreticulin protein or a calreticulin mutant protein), and the second VL and the second VH form a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild-type calreticulin protein or a calreticulin mutant protein),

10 wherein the first and second calreticulin proteins comprise the amino acid sequence of SEQ ID NO: 6286, optionally wherein the first and second calreticulin proteins are each independently chosen from: a molecule comprising the amino acid sequence of SEQ ID NO: 6313, or a molecule comprising the amino acid sequence of SEQ ID NO: 6314.

In some embodiments, the multifunctional molecule comprises the configuration of FIG.
15 3A or 3B.

In one aspect, the invention provides a multifunctional molecule, comprising:

(i) an antigen binding domain that binds to a calreticulin protein (e.g., a wild-type calreticulin protein or a calreticulin mutant protein), e.g., wherein the calreticulin protein
20 comprises the amino acid sequence of SEQ ID NO: 6286, and

(ii) a moiety that binds to NKp30, e.g., an antibody molecule or ligand that binds to (e.g., activates) NKp30.

In some embodiments, the multifunctional molecule comprises:

a first polypeptide comprising, e.g., from N-terminus to C-terminus, a first VL and a first
25 CL,

a second polypeptide comprising, e.g., from N-terminus to C-terminus, a first VH, a first CH1, a first dimerization domain (e.g., a first Fc), and a first moiety that binds to NKp30 (e.g., a first antibody molecule or ligand that binds to NKp30),

a third polypeptide comprising, e.g., from N-terminus to C-terminus, a second VH, a
30 second CH1, a second dimerization domain (e.g., a second Fc), and optionally a second moiety that binds to NKp30 (e.g., a second antibody molecule or ligand that binds to NKp30),

a fourth polypeptide comprising, e.g., from N-terminus to C-terminus, a second VL and a second CL, wherein:

the first VL and the first VH form a first antigen binding domain that binds to a first calreticulin protein (e.g., a wild-type calreticulin protein or a calreticulin mutant protein), and the second VL and the second VH form a second antigen binding domain that binds to a second calreticulin protein (e.g., a wild-type calreticulin protein or a calreticulin mutant protein), wherein the first and second calreticulin proteins comprise the amino acid sequence of SEQ ID NO: 6286, optionally wherein the first and second calreticulin proteins are each independently chosen from: a molecule comprising the amino acid sequence of SEQ ID NO: 6313, or a molecule comprising the amino acid sequence of SEQ ID NO: 6314.

In some embodiments, the multifunctional molecule comprises the configuration of FIG. 4A or 4B.

In another aspect, the disclosure provides an isolated nucleic acid molecule encoding any multispecific or multifunctional molecule described herein. In another aspect, the disclosure provides an isolated nucleic acid molecule, which comprises the nucleotide sequence encoding any of the multispecific or multifunctional molecules described herein, or a nucleotide sequence substantially homologous thereto (e.g., at least 80%, 90%, 95%, or 99.9% identical thereto). In another aspect, the disclosure provides a host cell comprising a nucleic acid molecule or a vector described herein.

In another aspect, the disclosure provides a method of making, e.g., producing, a multispecific or multifunctional molecule polypeptide described herein, comprising culturing a host cell described herein, under suitable conditions, e.g., conditions suitable for gene expression and/or homo- or heterodimerization.

In another aspect, the disclosure provides a pharmaceutical composition comprising a multispecific or multifunctional molecule polypeptide described herein and a pharmaceutically acceptable carrier, excipient, or stabilizer.

In another aspect, the disclosure provides a method of treating a cancer, comprising administering to a subject in need thereof a multispecific or multifunctional molecule polypeptide described herein, wherein the multispecific antibody is administered in an amount effective to treat the cancer. In some embodiments, the subject has cancer cells that express the

first and/or second calreticulin mutant. In some embodiments, the subject has tumor cells that express the first, second, or third tumor antigen, e.g., the subject has tumor cells that express a tumor antigen chosen from G6B, CD34, CD41, P-selectin, Clec2, cKIT, FLT3, MPL, ITGB3, ITGB2, GP5, GP6, GP9, GP1BA, DSC2, FCGR2A, TNFRSF10A, TNFRSF10B, or TM4SF1.

5 In some embodiments, the subject has the JAK2 V617F mutation. In some embodiments, the subject does not have the JAK2 V617F mutation. In some embodiments, the subject has a MPL mutation. In some embodiments, the subject does not have a MPL mutation. In some
embodiments, the cancer is a hematological cancer, optionally wherein the cancer is a
myeloproliferative neoplasm, e.g., primary or idiopathic myelofibrosis (MF), essential
10 thrombocytosis (ET), polycythemia vera (PV), or chronic myelogenous leukemia (CML). In
some embodiments, the cancer is myelofibrosis. In some embodiments, the cancer is a solid
tumor cancer. In some embodiments, the solid tumor cancer is one or more of pancreatic (e.g.,
pancreatic adenocarcinoma), breast, colorectal, lung (e.g., small or non-small cell lung cancer),
skin, ovarian, or liver cancer.

15 In some embodiments, the cancer cell comprises a myeloproliferative neoplasm cell. In
embodiments, the myeloproliferative neoplasm cell is chosen from a myelofibrosis cell, an
essential thrombocythemia cell, a polycythemia vera cell, or a chronic myeloid cancer cell. In
some embodiments, the myeloproliferative neoplasm cell is a myelofibrosis cell. In some
embodiments, the myeloproliferative neoplasm cell is an essential thrombocythemia cell. In
20 some embodiments, the myeloproliferative neoplasm cell is a polycythemia vera cell. In some
embodiments, the myeloproliferative neoplasm cell is a chronic myeloid cancer cell. In some
embodiments, the myeloproliferative neoplasm cell comprises a JAK2 mutation (e.g., a JAK2
V617F mutation). In some embodiments, the myeloproliferative neoplasm cell comprises a
calreticulin mutation. In some embodiments, the myeloproliferative neoplasm cell comprises a
25 MPL mutation.

In some embodiments, the method further comprises administering a second therapeutic
treatment. In some embodiments, second therapeutic treatment comprises a therapeutic agent
(e.g., a chemotherapeutic agent, a biologic agent, hormonal therapy), radiation, or surgery. In
some embodiments, therapeutic agent is selected from: a chemotherapeutic agent, or a biologic
30 agent.

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

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

BRIEF DESCRIPTION OF THE DRAWINGS

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

FIGs. 1A-1B shows the alignment of the Antibody A source mouse VH and VL framework 1, CDR 1, framework 2, CDR 2, framework 3, CDR3, and framework 4 regions with their respective humanized sequences. Kabat CDRs are shown in bold, Chothia CDRs are shown in italics, and combined CDRs are shown in boxes. The framework positions that were back mutated are double underlined. **FIG. 1A** shows VH sequences for murine Antibody A (SEQ ID NO: 1) and humanized Antibody A-H (SEQ ID NO: 9). **FIG. 1B** shows VL sequences for murine Antibody A (SEQ ID NO: 2) and humanized Antibody A-H (SEQ ID NO: 10 and SEQ ID NO: 11).

FIGs. 2A-2B shows the alignment of the Antibody B source mouse VH and VL framework 1, CDR 1, framework 2, CDR 2, framework 3, CDR3, and framework 4 regions with their respective humanized sequences. Kabat CDRs are shown in bold, Chothia CDRs are shown in italics, and combined CDRs are shown in boxes. The framework positions that were back mutated are double underlined. **FIG. 2A** shows the VH sequence for murine Antibody B (SEQ ID NO: 15) and humanized VH sequences B-H.1A to B-H.1C (SEQ ID NOs: 23-25). **FIG. 2B** shows the VL sequence for murine Antibody B (SEQ ID NO: 16) and humanized VL sequences B-H.1D to B-H.1H (SEQ ID NOs: 26-30).

FIG. 3 depicts the phylogenetic tree of TCRBV gene family and subfamilies with corresponding antibodies mapped. Subfamily identities are as follows: Subfamily A: TCR β V6; Subfamily B: TCR β V10; Subfamily C: TCR β V12; Subfamily D: TCR β V5; Subfamily E: TCR β V7; Subfamily F: TCR β V11; Subfamily G: TCR β V14; Subfamily H: TCR β V16; Subfamily I: TCR β V18; Subfamily J: TCR β V9; Subfamily K: TCR β V13; Subfamily L: TCR β V4; Subfamily M: TCR β V3; Subfamily N: TCR β V2; Subfamily O: TCR β V15; Subfamily P: TCR β V30; Subfamily Q: TCR β V19; Subfamily R: TCR β V27; Subfamily S: TCR β V28; Subfamily T: TCR β V24; Subfamily U: TCR β V20; Subfamily V: TCR β V25; and Subfamily W: TCR β V29 subfamily. Subfamily members are described in detail herein in the Section titled “TCR beta V (TCR β V)”.
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FIGs. 4A-4C show human CD3+ T cells activated by anti-TCR V β 13.1 antibody (A-H.1) for 6-days. Human CD3+ T cells were isolated using magnetic-bead separation (negative selection) and activated with immobilized (plate-coated) anti-TCR V β 13.1 (A-H.1) or anti-CD3 ϵ (OKT3) antibodies at 100 nM for 6 days. **FIG. 4A** shows two scatter plots (left: activated with OKT3; and right: activated with A-H.1) of expanded T cells assessed for TCR V β 13.1 surface expression using anti-TCR V β 13.1 (A-H.1) followed by a secondary fluorochrome- conjugated antibody for flow cytometry analysis. **FIG. 4B** shows percentage (%) of TCR V β 13.1 positive T cells activated by anti-TCR V β 13.1 (A-H.1) or anti-CD3 ϵ (OKT3) plotted against total T cells (CD3+). **FIG. 4C** shows relative cell count acquired by counting the number of events in each T cell subset gate (CD3 or TCR V β 13.1) for 20 seconds at a constant rate of 60 μ l/min. Data shown as mean value from 3 donors.
 15
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FIGs. 5A-5B show cytolytic activity of human CD3+ T cells activated by anti-TCR V β 13.1 antibody (A-H.1) against transformed cell line RPMI 8226. **FIG. 5A** depicts target cell lysis of human CD3+ T cells activated with A-H.1 or OKT3. Human CD3+ T cells were isolated using magnetic-bead separation (negative selection) and activated with immobilized (plate-coated) A-H.1 or OKT3 at the indicated concentrations for 4 days prior to co-culture with RPMI 8226 cells at a (E:T) ratio of 5:1 for 2 days. Samples were next analyzed for cell lysis of RPMI 8226 cells by FACS staining for CFSE/CD138-labeled, and membrane-impermeable DNA dyes (DRAQ7) using flow cytometry analysis. **FIG. 5B** shows target cell lysis of human CD3+ T cells activated with A-H.1 or OKT3 incubated with RPMI-8226 at a (E:T) ratio of 5:1 for 6 days followed by cell lysis analysis of RPMI 8226 cells as described above. Percentage (%) target cell
 25
 30

lysis was determined by normalizing to basal target cell lysis (i.e. without antibody treatment) using the following formula, $[(x - \text{basal}) / (100\% - \text{basal})]$, where x is cell lysis of sample]. Data shown is a representative of n=1 donor.

FIGs. 6A-6B show IFN γ production by human PBMCs activated with the indicated antibodies. Human PBMCs were isolated from whole blood from the indicated number of donors, followed by solid-phase (plate-coated) stimulation with the indicated antibodies at 100Nm. Supernatant was collected on Days 1, 2, 3, 5, or 6. **FIG. 6A** is a graph comparing the production of IFN γ in human PBMCs activated with the antibodies indicated activated with anti-TCR V β 13.1 antibodies (A-H.1 or A-H.2) or anti-CD3e antibodies (OKT3 or SP34-2) on Day 1, 2, 3, 5, or 6 post-activation. **FIG. 6B** shows IFN γ production in human PBMCs activated with the antibodies indicated activated with the indicated anti-TCR V β 13.1 antibodies or anti-CD3e antibody (OKT3) on Day 1, 2, 3, 5, or 6 post-activation.

FIGs. 7A-7B show IL-2 production by human PBMCs activated with the indicated antibodies. A similar experimental setup as described for FIGs 6A-6B was used.

FIGs. 8A- 8B show IL-6 production by human PBMCs activated with the indicated antibodies. A similar experimental setup as described for FIGs 6A-6B was used.

FIGs. 9A- 9B show TNF-alpha production by human PBMCs activated with the indicated antibodies. A similar experimental setup as described for FIGs 6A-6B was used.

FIGs. 10A- 10B show IL-1beta production by human PBMCs activated with the indicated antibodies. A similar experimental setup as described for FIGs 6A-6B was used.

FIGs. 11A-11B are graphs showing delayed kinetics of IFN γ secretion in human PMBCs activated by anti-TCR V β 13.1 antibody A-H.1 when compared to PBMCs activated by anti-CD3e antibody OKT3. **FIG. 11A** shows IFN γ secretion data from 4 donors. **FIG. 11B** shows IFN γ secretion data from 4 additional donors. Data shown is representative of n=8 donors.

FIG. 12 depicts increased CD8+ TSCM and Temra T cell subsets in human PBMCs activated by anti-TCR V β 13.1 antibodies (A-H.1 or A-H.2) compared to PBMCs activated by anti-CD3e antibodies (OKT3 or SP34-2).

FIGs. 13A-13F show characterization of an anti-TCRVb antibody. **FIG. 13A** is a graph depicting proliferation of T cells activated with anti-CD3 (OKT3) antibody or anti-TCRVb antibody. **FIG. 13B** shows selective expansion of CD45RA+ effector memory CD8+ and CD4+ T cells (TEMRA) cells with anti- TCRVb antibodies. Tn= naïve T cell; Tscm= stem cell memory

T cell; Tcm= central memory T cell; Tem=effector memory T cell; Temra=effector memory CD45RA+ T cell. **FIG. 13C** is a graph showing IFN-g secretion by PBMCs stimulated with an anti-TCRVb antibody, or anti-CD3 antibodies. **FIG. 13D** shows target cell lysis by T cells stimulated with an anti-TCRVb antibody, or anti-CD3 antibodies. Cells were stimulated for 4 days followed by 2 days incubation with multiple myeloma target cells for assessment of cell killing. **FIG. 13E** is a graph showing perforin secretion by T cells stimulated with an anti-TCRVb antibody, or an anti-CD3 antibody. Perforin was analyzed by FACS staining in TCRVB-positive and TCRVB-negative T cells in PBMCs after 5 days of stimulation with 100ng/ml plate-bound antibody. **FIG. 13F** is a graph showing Granzyme B by T cells stimulated with an anti-TCRVb antibody, or an anti-CD3 antibody. Granzyme B was analyzed by FACS staining in TCRVB-positive and TCRVB-negative T cells in PBMCs after 5 days of stimulation with 100ng/ml plate-bound antibody.

FIGs. 14A-14B show production of IL-2 and IL-15 and expansion of human NK cells by stimulation of PBMCs with anti-TCRVb antibody for 6 days at a dose of 100nM. **FIG. 14A** shows secretion of IL-2 or IL-15 in T cells stimulated with an anti-TCRVb antibody, or anti-CD3 antibodies. **FIG. 14B** depicts flow cytometry dot plots showing NKp46 staining vs CD56 antibody staining in cells stimulated with an anti-TCRVb antibody or an anti-CD3 antibody or a control sample.

FIGs. 15A-15C show secretion of cytokines in PBMCs stimulated with an anti-TCRVb antibody, or anti-CD3 antibodies.

FIGs 16A-16B show killing of MM cells by dual targeting BCMA-TCRVb antibody molecules. **FIG.16A** shows in vitro killing by one of the following dual-targeting antibody molecules: BCMA-TCRVb, BCMA-CD3, or Control-TCRVb; or an isotype control. **FIG. 16B** shows in vivo killing of MM cells by a dual-targeting BCM-TCRVb antibody.

FIG. 17 shows lysis of MM target cells with a dual targeting antibody which recognized FcRH5 on one arm and TCRVb on the other arm.

FIGs. 18A-18C are schematic representations of exemplary formats and configurations of functional moieties attached to a dimerization module, *e.g.*, an immunoglobulin constant domain. **FIG. 18A** depicts moieties A, B, C and D, covalently linked to a heterodimeric Fc domain. **FIG. 18B** depicts moieties A, B, C and D, covalently linked to a homodimeric Fc domain. **FIG. 18C** depicts moieties A, B, C and D, covalently linked to heterodimeric heavy

and light constant domains (*e.g.*, a Fab CH₁ and a Fab CL). In some embodiments, the functional moiety is an antigen binding domain that binds to a calreticulin protein (*e.g.*, a wild-type calreticulin protein and/or a calreticulin mutant protein). In some embodiments, the functional moiety is an antigen binding domain that binds to a wild-type calreticulin protein and a calreticulin mutant protein with approximately the same affinity. In some embodiments, the functional moiety is an antigen binding domain that preferentially binds to a calreticulin mutant protein over a wild type calreticulin protein, *e.g.*, wherein the first calreticulin mutant protein comprises the amino acid sequence of SEQ ID NO: 6286 and the wild type calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6285. In some embodiments, the functional moiety is an immune cell engager chosen from a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager. In some embodiments, the functional moiety is a cytokine molecule. In some embodiments, the functional moiety is a stromal modifying moiety.

FIGs. 19A and 19B are schematic representations of exemplary formats and configurations of a multifunctional molecule comprising a first antigen binding domain (*e.g.*, a first Fab) that binds to a calreticulin protein (*e.g.*, a wild-type calreticulin protein and/or a calreticulin mutant protein), a second antigen binding domain (*e.g.*, a second Fab) that binds to a calreticulin protein (*e.g.*, a wild-type calreticulin protein and/or a calreticulin mutant protein), and one or more moieties that bind to CD3 (*e.g.*, an scFv that binds to CD3). In one embodiment, the first antigen binding domain (*e.g.*, the first Fab) binds to a calreticulin protein (*e.g.*, a wild-type calreticulin protein and/or a calreticulin mutant protein) disclosed herein, *e.g.*, a calreticulin mutant protein disclosed in Table 2 or 3, *e.g.*, Type 1 or Type 2 calreticulin mutant protein disclosed in Table 2 or 3, *e.g.*, a calreticulin mutant protein comprising the amino acid sequence of SEQ ID NO: 6113 or 6314. In one embodiment, the second antigen binding domain (*e.g.*, the second Fab) binds to a calreticulin protein (*e.g.*, a wild-type calreticulin protein and/or a calreticulin mutant protein) disclosed herein, *e.g.*, a calreticulin mutant protein disclosed in Table 2 or 3, *e.g.*, Type 1 or Type 2 calreticulin mutant protein disclosed in Table 2 or 3, *e.g.*, a calreticulin mutant protein comprising the amino acid sequence of SEQ ID NO: 6313 or 6314.

FIGs. 20A and 20B are schematic representations of exemplary formats and configurations of a multifunctional molecule comprising a first antigen binding domain (*e.g.*, a first Fab) that binds to a calreticulin protein (*e.g.*, a wild-type calreticulin protein and/or a

calreticulin mutant protein), a second antigen binding domain (e.g., a second Fab) that binds to a calreticulin protein (e.g., a wild-type calreticulin protein and/or a calreticulin mutant protein), and one or more moieties that bind to TCR (e.g., TCR β) (e.g., an scFv that binds to TCR (e.g., TCR β)). In one embodiment, the first antigen binding domain (e.g., the first Fab) binds to a calreticulin protein (e.g., a wild-type calreticulin protein and/or a calreticulin mutant protein) disclosed herein, e.g., a calreticulin mutant protein disclosed in Table 2 or 3, e.g., Type 1 or Type 2 calreticulin mutant protein disclosed in Table 2 or 3, e.g., a calreticulin mutant protein comprising the amino acid sequence of SEQ ID NO: 6313 or 6314. In one embodiment, the second antigen binding domain (e.g., the second Fab) binds to a calreticulin protein (e.g., a wild-type calreticulin protein and/or a calreticulin mutant protein) disclosed herein, e.g., a calreticulin mutant protein disclosed in Table 2 or 3, e.g., Type 1 or Type 2 calreticulin mutant protein disclosed in Table 2 or 3, e.g., a calreticulin mutant protein comprising the amino acid sequence of SEQ ID NO: 6313 or 6314.

FIGs. 21A and 21B are schematic representations of exemplary formats and configurations of a multifunctional molecule comprising a first antigen binding domain (e.g., a first Fab) that binds to a calreticulin protein (e.g., a wild-type calreticulin protein and/or a calreticulin mutant protein), a second antigen binding domain (e.g., a second Fab) that binds to a calreticulin protein (e.g., a wild-type calreticulin protein and/or a calreticulin mutant protein), and one or more moieties that bind to NKp30 (e.g., an antibody molecule or ligand that binds to NKp30). In one embodiment, the first antigen binding domain (e.g., the first Fab) binds to a calreticulin protein (e.g., a wild-type calreticulin protein and/or a calreticulin mutant protein) disclosed herein, e.g., a calreticulin mutant protein disclosed in Table 2 or 3, e.g., Type 1 or Type 2 calreticulin mutant protein disclosed in Table 2 or 3, e.g., a calreticulin mutant protein comprising the amino acid sequence of SEQ ID NO: 6313 or 6314. In one embodiment, the second antigen binding domain (e.g., the second Fab) binds to a calreticulin protein (e.g., a wild-type calreticulin protein and/or a calreticulin mutant protein) disclosed herein, e.g., a calreticulin mutant protein disclosed in Table 2 or 3, e.g., Type 1 or Type 2 calreticulin mutant protein disclosed in Table 2 or 3, e.g., a calreticulin mutant protein comprising the amino acid sequence of SEQ ID NO: 6313 or 6314.

FIG. 22 is a graph showing binding of NKp30 antibodies to NK92 cells. Data was calculated as the percent-AF747 positive population.

FIG. 23 is a graph showing activation of NK92 cells by NKp30 antibodies. Data were generated using hamster anti-NKp30 mAbs.

FIGs. 24A-24D are schematics showing exemplary multispecific molecules comprising a TGF β inhibitor. In some embodiments, the TGF β inhibitor comprises a TGF-beta receptor ECD homodimer. In some embodiments, the TGF β inhibitor comprises a TGFBR2 ECD heterodimer. In FIGs. 24A and 24B, the two TGFBR ECD domains are linked to the C-terminus of two Fc regions. In some embodiments, the CH1-Fc-TGFBR ECD region shown in FIG. 24A or 24B comprises the amino acid sequence of SEQ ID NO: 6405 or 3193. In some embodiments, the Fc-TGFBR ECD region shown in FIG. 24A or 24B comprises the amino acid sequence of SEQ ID NO: 6407 or 6408. In FIGs. 24C and 24D, the two TGFBR ECD domains are linked to CH1 and CL, respectively. In some embodiments, the TGFBR ECD-CH1-Fc region shown in FIG. 24C or 24D comprises the amino acid sequence of SEQ ID NO: 6409 or 6410. In some embodiments, the TGFBR ECD-CL region shown in FIG. 24C or 24D comprises the amino acid sequence of SEQ ID NO: 6411 or 6412. In some embodiments, the multispecific molecule comprises a binding moiety A and a binding moiety B. In some embodiments, the binding moiety A or binding moiety B is a calreticulin-targeting antigen binding domain disclosed herein.

DETAILED DESCRIPTION OF THE INVENTION

Disclosed herein are multifunctional molecules (also referred to herein as “multispecific molecules”) that include a plurality of (e.g., two or more) functionalities (or binding specificities), comprising (i) an antigen binding domain that binds to a calreticulin protein (e.g., a wild-type calreticulin protein and/or a calreticulin mutant protein), e.g., wherein the calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6285 or 6286, and (ii) one, two, or all of: (a) an immune cell engager chosen from a T cell engager, an NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager; (b) a cytokine molecule; (c) a stromal modifying moiety, and (d) a tumor-targeting moiety (e.g., which binds to a tumor antigen chosen from: G6B, CD34, CD41, P-selectin, Clec2, cKIT, FLT3, MPL, ITGB3, ITGB2, GP5, GP6, GP9, GP1BA, DSC2, FCGR2A, TNFRSF10A, TNFRSF10B, or TM4SF1). In some embodiments, the antigen binding domain binds to a calreticulin protein (e.g., a wild-type calreticulin protein or a mutant calreticulin protein, e.g., as described herein). In some

embodiments, the antigen binding domain binds to a calreticulin mutant protein disclosed in Table 2 or Table 3. In some embodiments, the antigen binding domain binds to Type 1 calreticulin mutant protein disclosed in Table 2 or Table 3. In some embodiments, the antigen binding domain binds to Type 2 calreticulin mutant protein disclosed in Table 2 or Table 3. In some embodiments, the antigen binding domain binds to both Type 1 and Type 2 calreticulin mutant proteins disclosed in Table 2 or Table 3. In some embodiments, the T cell engager comprises an additional antigen binding domain that binds to the variable chain of the beta subunit of TCR (TCR β V), e.g., a TCR β V6 or TCR β V12.

In an embodiment, the multispecific or multifunctional molecule is a bispecific (or bifunctional) molecule, a trispecific (or trifunctional) molecule, or a tetraspecific (or tetrafunctional) molecule. In an embodiment, the multispecific or multifunctional molecule is a bispecific molecule.

Without being bound by theory, the multispecific or multifunctional molecules disclosed herein are expected to localize (e.g., bridge) and/or activate an immune cell (e.g., an immune effector cell chosen from a T cell, an NK cell, a B cell, a dendritic cell or a macrophage), in the presence of a cell expressing the calreticulin protein, e.g., on the surface. Increasing the proximity and/or activity of the immune cell, in the presence of the cell expressing the calreticulin protein, using the multispecific or multifunctional molecules described herein is expected to enhance an immune response against the target cell, thereby providing a more effective therapy.

Novel multifunctional, e.g., multispecific, molecules that include (i) a stromal modifying moiety and (ii) an antigen binding domain that binds to a calreticulin protein (e.g., a wild-type calreticulin protein and/or a calreticulin mutant protein), e.g., wherein the calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6285 or 6286 are disclosed. Without being bound by theory, the multifunctional molecules disclosed herein are believed to inter alia target (e.g., localize to) a cancer site, and alter the tumor stroma, e.g., alter the tumor microenvironment near the cancer site. The multifunctional molecules can further include one or both of: an immune cell engager (e.g., chosen from one, two, three, or all of a T cell engager, NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager); and/or a cytokine molecule. Accordingly, provided herein are, inter alia, multifunctional, e.g., multispecific molecules, that include the aforesaid moieties, nucleic acids encoding the same,

methods of producing the aforesaid molecules, and methods of treating a cancer using the aforesaid molecules.

Accordingly, provided herein are, *inter alia*, multispecific or multifunctional molecules (e.g., multispecific or multifunctional antibody molecules) that include the aforesaid moieties, nucleic acids encoding the same, methods of producing the aforesaid molecules, and methods of treating a disease or disorder, e.g., cancer, using the aforesaid molecules.

Definitions

In some embodiments, the multifunctional molecule includes an immune cell engager.

“An immune cell engager” refers to one or more binding specificities that bind and/or activate an immune cell, e.g., a cell involved in an immune response. In embodiments, the immune cell is chosen from a T cell, an NK cell, a B cell, a dendritic cell, and/or the macrophage cell. The immune cell engager can be an antibody molecule, a receptor molecule (e.g., a full length receptor, receptor fragment, or fusion thereof (e.g., a receptor-Fc fusion)), or a ligand molecule (e.g., a full length ligand, ligand fragment, or fusion thereof (e.g., a ligand-Fc fusion)) that binds to the immune cell antigen (e.g., the T cell, the NK cell antigen, the B cell antigen, the dendritic cell antigen, and/or the macrophage cell antigen). In embodiments, the immune cell engager specifically binds to the target immune cell, e.g., binds preferentially to the target immune cell. For example, when the immune cell engager is an antibody molecule, it binds to an immune cell antigen (e.g., a T cell antigen, an NK cell antigen, a B cell antigen, a dendritic cell antigen, and/or a macrophage cell antigen) with a dissociation constant of less than about 10 nM.

As used herein, the terms “T cell receptor beta variable chain,” “TCRV β ,” “TCRVb,” and “TCR β V” are used interchangeably to refer to an extracellular region of the T cell receptor beta chain which comprises the antigen recognition domain of the T cell receptor. The term TCRV β or TCR β V includes isoforms, mammalian, e.g., human TCR β V, species homologs of human and analogs comprising at least one common epitope with TCR β V. Human TCR β V comprises a gene family comprising subfamilies including, but not limited to: a TCR β V6 subfamily, a TCR β V10 subfamily, a TCR β V12 subfamily, a TCR β V5 subfamily, a TCR β V7 subfamily, a TCR β V11 subfamily, a TCR β V14 subfamily, a TCR β V16 subfamily, a TCR β V18 subfamily, a TCR β V9 subfamily, a TCR β V13 subfamily, a TCR β V4 subfamily, a TCR β V3 subfamily, a TCR β V2 subfamily, a TCR β V15 subfamily, a TCR β V30 subfamily, a TCR β V19 subfamily, a TCR β

V27 subfamily, a TCR β V28 subfamily, a TCR β V24 subfamily, a TCR β V20 subfamily, TCR β V25 subfamily, or a TCR β V29 subfamily. In some embodiments, the TCR β V6 subfamily comprises: TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01. In some
 5 embodiments, TCR β V comprises TCR β V6-5*01. TCR β V6-5*01 is also known as TRBV65; TCRBV6S5; TCRBV13S1, or TCR β V13.1. The amino acid sequence of TCR β V6-5*01, *e.g.*, human TCR β V6-5*01, is known in that art, *e.g.*, as provided by IMGT ID L36092. In some embodiments, TCR β V6-5*01 is encoded by the nucleic acid sequence of SEQ ID NO: 1043, or a sequence having 85%, 90%, 95%, 99% or more identity thereof. In some embodiments, TCR β
 10 V6-5*01 comprises the amino acid sequence of SEQ ID NO: 1044, or a sequence having 85%, 90%, 95%, 99% or more identity thereof.

In some embodiments, the multifunctional molecule includes a cytokine molecule. As used herein, a “cytokine molecule” refers to full length, a fragment or a variant of a cytokine; a cytokine further comprising a receptor domain, *e.g.*, a cytokine receptor dimerizing domain; or
 15 an agonist of a cytokine receptor, *e.g.*, an antibody molecule (*e.g.*, an agonistic antibody) to a cytokine receptor, that elicits at least one activity of a naturally-occurring cytokine. In some embodiments the cytokine molecule is chosen from interleukin-2 (IL-2), interleukin-7 (IL-7), interleukin-12 (IL-12), interleukin-15 (IL-15), interleukin-18 (IL-18), interleukin-21 (IL-21), or interferon gamma, or a fragment or variant thereof, or a combination of any of the aforesaid
 20 cytokines. The cytokine molecule can be a monomer or a dimer. In embodiments, the cytokine molecule can further include a cytokine receptor dimerizing domain. In other embodiments, the cytokine molecule is an agonist of a cytokine receptor, *e.g.*, an antibody molecule (*e.g.*, an agonistic antibody) to a cytokine receptor chosen from an IL-15Ra or IL-21R.

As used herein, the term “molecule” as used in, *e.g.*, antibody molecule, cytokine
 25 molecule, receptor molecule, includes full-length, naturally-occurring molecules, as well as variants, *e.g.*, functional variants (*e.g.*, truncations, fragments, mutated (*e.g.*, substantially similar sequences) or derivatized form thereof), so long as at least one function and/or activity of the unmodified (*e.g.*, naturally-occurring) molecule remains.

In some embodiments, the multifunctional molecule includes a stromal modifying
 30 moiety. A “stromal modifying moiety,” as used herein refers to an agent, *e.g.*, a protein (*e.g.*, an enzyme), that is capable of altering, *e.g.*, degrading a component of, the stroma. In

embodiments, the component of the stroma is chosen from, e.g., an ECM component, e.g., a glycosaminoglycan, e.g., hyaluronan (also known as hyaluronic acid or HA), chondroitin sulfate, chondroitin, dermatan sulfate, heparin sulfate, heparin, entactin, tenascin, aggrecan and keratin sulfate; or an extracellular protein, e.g., collagen, laminin, elastin, fibrinogen, fibronectin, and vitronectin.

Certain terms are defined below.

As used herein, the articles “a” and “an” refer to one or more than one, *e.g.*, to at least one, of the grammatical object of the article. The use of the words “a” or “an” when used in conjunction with the term “comprising” herein may mean “one,” but it is also consistent with the meaning of “one or more,” “at least one,” and “one or more than one.”

As used herein, “about” and “approximately” generally mean an acceptable degree of error for the quantity measured given the nature or precision of the measurements. Exemplary degrees of error are within 20 percent (%), typically, within 10%, and more typically, within 5% of a given range of values.

“Antibody molecule” as used herein refers to a protein, *e.g.*, an immunoglobulin chain or fragment thereof, comprising at least one immunoglobulin variable domain sequence. An antibody molecule encompasses antibodies (*e.g.*, full-length antibodies) and antibody fragments. In an embodiment, an antibody molecule comprises an antigen binding or functional fragment of a full-length antibody, or a full-length immunoglobulin chain. For example, a full-length antibody is an immunoglobulin (Ig) molecule (*e.g.*, an IgG antibody) that is naturally occurring or formed by normal immunoglobulin gene fragment recombinatorial processes). In embodiments, an antibody molecule refers to an immunologically active, antigen-binding portion of an immunoglobulin molecule, such as an antibody fragment. An antibody fragment, *e.g.*, functional fragment, is a portion of an antibody, *e.g.*, Fab, Fab', F(ab')₂, F(ab)₂, variable fragment (Fv), domain antibody (dAb), or single chain variable fragment (scFv). A functional antibody fragment binds to the same antigen as that recognized by the intact (*e.g.*, full-length) antibody. The terms “antibody fragment” or “functional fragment” also include isolated fragments consisting of the variable regions, such as the “Fv” fragments consisting of the variable regions of the heavy and light chains or recombinant single chain polypeptide molecules in which light and heavy variable regions are connected by a peptide linker (“scFv proteins”). In some

embodiments, an antibody fragment does not include portions of antibodies without antigen binding activity, such as Fc fragments or single amino acid residues. Exemplary antibody molecules include full length antibodies and antibody fragments, e.g., dAb (domain antibody), single chain, Fab, Fab', and F(ab')₂ fragments, and single chain variable fragments (scFvs).

5 As used herein, an “immunoglobulin variable domain sequence” refers to an amino acid sequence which can form the structure of an immunoglobulin variable domain. For example, the sequence may include all or part of the amino acid sequence of a naturally-occurring variable domain. For example, the sequence may or may not include one, two, or more N- or C-terminal amino acids, or may include other alterations that are compatible with formation of the protein
10 structure.

In embodiments, an antibody molecule is monospecific, e.g., it comprises binding specificity for a single epitope. In some embodiments, an antibody molecule is multispecific, e.g., it comprises a plurality of immunoglobulin variable domain sequences, where a first immunoglobulin variable domain sequence has binding specificity for a first epitope and a
15 second immunoglobulin variable domain sequence has binding specificity for a second epitope. In some embodiments, an antibody molecule is a bispecific antibody molecule. “Bispecific antibody molecule” as used herein refers to an antibody molecule that has specificity for more than one (e.g., two, three, four, or more) epitope and/or antigen.

“Antigen” (Ag) as used herein refers to a molecule that can provoke an immune response,
20 e.g., involving activation of certain immune cells and/or antibody generation. Any macromolecule, including almost all proteins or peptides, can be an antigen. Antigens can also be derived from genomic recombinant or DNA. For example, any DNA comprising a nucleotide sequence or a partial nucleotide sequence that encodes a protein capable of eliciting an immune response encodes an “antigen.” In embodiments, an antigen does not need to be encoded solely
25 by a full-length nucleotide sequence of a gene, nor does an antigen need to be encoded by a gene at all. In embodiments, an antigen can be synthesized or can be derived from a biological sample, e.g., a tissue sample, a tumor sample, a cell, or a fluid with other biological components. As used, herein a “tumor antigen” or interchangeably, a “cancer antigen” includes any molecule present on, or associated with, a cancer, e.g., a cancer cell or a tumor microenvironment that can
30 provoke an immune response. As used, herein an “immune cell antigen” includes any molecule present on, or associated with, an immune cell that can provoke an immune response.

The “antigen-binding site,” or “binding portion” of an antibody molecule refers to the part of an antibody molecule, e.g., an immunoglobulin (Ig) molecule, that participates in antigen binding. In embodiments, the antigen binding site is formed by amino acid residues of the variable (V) regions of the heavy (H) and light (L) chains. Three highly divergent stretches within the variable regions of the heavy and light chains, referred to as hypervariable regions, are disposed between more conserved flanking stretches called “framework regions,” (FRs). FRs are amino acid sequences that are naturally found between, and adjacent to, hypervariable regions in immunoglobulins. In embodiments, in an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface, which is complementary to the three-dimensional surface of a bound antigen. The three hypervariable regions of each of the heavy and light chains are referred to as “complementarity-determining regions,” or “CDRs.” The framework region and CDRs have been defined and described, e.g., in 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, and Chothia, C. et al. (1987) J. Mol. Biol. 196:901-917. Each variable chain (e.g., variable heavy chain and variable light chain) is typically made up of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the amino acid order: FR1, CDR1, FR2, CDR2, FR3, CDR3, and FR4.

“Cancer” as used herein can encompass all types of oncogenic processes and/or cancerous growths. In embodiments, cancer includes primary tumors as well as metastatic tissues or malignantly transformed cells, tissues, or organs. In embodiments, cancer encompasses all histopathologies and stages, e.g., stages of invasiveness/severity, of a cancer. In embodiments, cancer includes relapsed and/or resistant cancer. The terms “cancer” and “tumor” can be used interchangeably. For example, both terms encompass solid and liquid tumors. As used herein, the term “cancer” or “tumor” includes premalignant, as well as malignant cancers and tumors.

As used herein, an “immune cell” refers to any of various cells that function in the immune system, e.g., to protect against agents of infection and foreign matter. In embodiments, this term includes leukocytes, e.g., neutrophils, eosinophils, basophils, lymphocytes, and monocytes. Innate leukocytes include phagocytes (e.g., macrophages, neutrophils, and dendritic cells), mast cells, eosinophils, basophils, and natural killer cells. Innate leukocytes identify and

eliminate pathogens, either by attacking larger pathogens through contact or by engulfing and then killing microorganisms, and are mediators in the activation of an adaptive immune response. The cells of the adaptive immune system are special types of leukocytes, called lymphocytes. B cells and T cells are important types of lymphocytes and are derived from hematopoietic stem cells in the bone marrow. B cells are involved in the humoral immune response, whereas T cells are involved in cell-mediated immune response. The term “immune cell” includes immune effector cells.

“Immune effector cell,” as that term is used herein, refers to a cell that is involved in an immune response, e.g., in the promotion of an immune effector response. Examples of immune effector cells include, but are not limited to, T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NK T) cells, and mast cells.

The term “effector function” or “effector response” refers to a specialized function of a cell. Effector function of a T cell, for example, may be cytolytic activity or helper activity including the secretion of cytokines.

The compositions and methods of the present invention encompass polypeptides and nucleic acids having the sequences specified, or sequences substantially identical or similar thereto, e.g., sequences at least 80%, 85%, 90%, 95% identical or higher to the sequence specified. In the context of an amino acid sequence, the term "substantially identical" is used herein to refer to a first amino acid that contains a sufficient or minimum number of amino acid residues that are i) identical to, or ii) conservative substitutions of aligned amino acid residues in a second amino acid sequence such that the first and second amino acid sequences can have a common structural domain and/or common functional activity. For example, amino acid sequences that contain a common structural domain having at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, e.g., a sequence provided herein.

In the context of nucleotide sequence, the term "substantially identical" is used herein to refer to a first nucleic acid sequence that contains a sufficient or minimum number of nucleotides that are identical to aligned nucleotides in a second nucleic acid sequence such that the first and second nucleotide sequences encode a polypeptide having common functional activity, or encode a common structural polypeptide domain or a common functional polypeptide activity. For

example, nucleotide sequences having at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to a reference sequence, *e.g.*, a sequence provided herein.

The term “variant” refers to a polypeptide that has a substantially identical amino acid sequence to a reference amino acid sequence, or is encoded by a substantially identical

5 nucleotide sequence. In some embodiments, the variant is a functional variant.

The term “functional variant” refers to a polypeptide that has a substantially identical amino acid sequence to a reference amino acid sequence, or is encoded by a substantially identical nucleotide sequence, and is capable of having one or more activities of the reference amino acid sequence.

10 Calculations of homology or sequence identity between sequences (the terms are used interchangeably herein) are performed as follows.

To determine the percent identity of two amino acid sequences, or of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). In a preferred embodiment, the length of a reference sequence aligned for comparison purposes is at least 30%, preferably at least 40%, more preferably at least 50%, 60%, and even more preferably at least 70%, 80%, 90%, 100% of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared.

20 When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid “identity” is equivalent to amino acid or nucleic acid “homology”).

The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch ((1970) *J. Mol. Biol.* 48:444-453) algorithm which has been incorporated into the GAP program in the GCG software package (available at <http://www.gcg.com>), using either a

Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (available at <http://www.gcg.com>), using a NWSgapdna.CMP matrix and a gap weight
5 of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A particularly preferred set of parameters (and the one that should be used unless otherwise specified) are a Blossum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

The percent identity between two amino acid or nucleotide sequences can be determined using the algorithm of E. Meyers and W. Miller ((1989) *CABIOS*, 4:11-17) which has been
10 incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

The nucleic acid and protein sequences described herein can be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and
15 XBLAST programs (version 2.0) of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to a nucleic acid molecule of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to protein molecules of the invention. To obtain
20 gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, (1997) *Nucleic Acids Res.* 25:3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (*e.g.*, XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>.

It is understood that the molecules of the present invention may have additional
25 conservative or non-essential amino acid substitutions, which do not have a substantial effect on their functions.

The term "amino acid" is intended to embrace all molecules, whether natural or synthetic, which include both an amino functionality and an acid functionality and capable of being included in a polymer of naturally-occurring amino acids. Exemplary amino acids include
30 naturally-occurring amino acids; analogs, derivatives and congeners thereof; amino acid analogs

having variant side chains; and all stereoisomers of any of any of the foregoing. As used herein the term "amino acid" includes both the D- or L- optical isomers and peptidomimetics.

A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine).

The terms "polypeptide", "peptide" and "protein" (if single chain) are used interchangeably herein to refer to polymers of amino acids of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation, such as conjugation with a labeling component. The polypeptide can be isolated from natural sources, can be a produced by recombinant techniques from a eukaryotic or prokaryotic host, or can be a product of synthetic procedures.

The terms "nucleic acid," "nucleic acid sequence," "nucleotide sequence," or "polynucleotide sequence," and "polynucleotide" are used interchangeably. They refer to a polymeric form of nucleotides of any length, either deoxyribonucleotides or ribonucleotides, or analogs thereof. The polynucleotide may be either single-stranded or double-stranded, and if single-stranded may be the coding strand or non-coding (antisense) strand. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and nucleotide analogs. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. The nucleic acid may be a recombinant polynucleotide, or a polynucleotide of genomic, cDNA, semisynthetic, or synthetic origin which either does not occur in nature or is linked to another polynucleotide in a non-natural arrangement.

The term "isolated," as used herein, refers to material that is removed from its original or native environment (*e.g.*, the natural environment if it is naturally occurring). For example, a

naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or polypeptide, separated by human intervention from some or all of the co-existing materials in the natural system, is isolated. Such polynucleotides could be part of a vector and/or such polynucleotides or polypeptides could be part of a composition, and still be isolated in that such vector or composition is not part of the environment in which it is found in nature.

As used herein, the term “transforming growth factor beta-1 (TGF-beta 1)” refers to a protein that in humans is encoded by the gene *TGFB1*, or its orthologs. Swiss-Prot accession number P01137 provides exemplary human TGF-beta 1 amino acid sequences. An exemplary immature human TGF-beta 1 amino acid sequence is provided in SEQ ID NO: 6378. An exemplary mature human TGF-beta 1 amino acid sequence is provided in SEQ ID NO: 6395.

As used herein, the term “transforming growth factor beta-2 (TGF-beta 2)” refers to a protein that in humans is encoded by the gene *TGFB2*, or its orthologs. Swiss-Prot accession number P61812 provides exemplary human TGF-beta 2 amino acid sequences. An exemplary immature human TGF-beta 2 amino acid sequence is provided in SEQ ID NO: 6379. An exemplary mature human TGF-beta 2 amino acid sequence is provided in SEQ ID NO: 6396.

As used herein, the term “transforming growth factor beta-3 (TGF-beta 3)” refers to a protein that in humans is encoded by the gene *TGFB3*, or its orthologs. Swiss-Prot accession number P10600 provides exemplary human TGF-beta 3 amino acid sequences. An exemplary immature human TGF-beta 3 amino acid sequence is provided in SEQ ID NO: 6380. An exemplary mature human TGF-beta 3 amino acid sequence is provided in SEQ ID NO: 6397.

As used herein, a “TGF-beta receptor polypeptide” refers to a TGF-beta receptor (e.g., TGFBR1, TGFBR2, or TGFBR3) or its fragment, or variant thereof.

As used herein, the term “transforming growth factor beta receptor type 1 (TGFB β R1)” (also known as ALK-5 or SKR4) refers to a protein that in humans is encoded by the gene *TGFB β R1*, or its orthologs. Swiss-Prot accession number P36897 provides exemplary human TGFB β R1 amino acid sequences. Exemplary immature human TGFB β R1 amino acid sequences are provided in SEQ ID NOs: 6381, 6382, and 6383. Exemplary mature human TGFB β R1 amino acid sequences are provided in SEQ ID NOs: 6398, 6399, and 6400. As used herein, a “TGFB β R1 polypeptide” refers to a TGFB β R1 or its fragment, or variant thereof.

As used herein, the term “transforming growth factor beta receptor type 2 (TGFB β R2)” refers to a protein that in humans is encoded by the gene *TGFB β R2*, or its orthologs. Swiss-Prot accession number P37173 provides exemplary human TGFB β R2 amino acid sequences. Exemplary immature human TGFB β R2 amino acid sequences are provided in SEQ ID NOs: 6384 and 6385. Exemplary mature human TGFB β R2 amino acid sequences are provided in SEQ ID NOs: 6401 and 6402. As used herein, a “TGFB β R2 polypeptide” refers to a TGFB β R2 or its fragment, or variant thereof.

As used herein, the term “transforming growth factor beta receptor type 3 (TGFB β R3)” refers to a protein that in humans is encoded by the gene *TGFB β R3*, or its orthologs. Swiss-Prot accession number Q03167 provides exemplary human TGFB β R3 amino acid sequences. Exemplary immature human TGFB β R3 amino acid sequences are provided in SEQ ID NOs: 6392 and 6393. Exemplary mature human TGFB β R3 amino acid sequences are provided in SEQ ID NOs: 6403 and 6404. As used herein, a “TGFB β R3 polypeptide” refers to a TGFB β R3 or its fragment, or variant thereof.

Various aspects of the invention are described in further detail below. Additional definitions are set out throughout the specification.

Antibody Molecules

In some embodiments, a multifunctional molecule, multispecific molecule, and/or an antigen binding domain as described herein comprises an antibody molecule. In one embodiment, the antibody molecule binds to a cancer antigen, e.g., a tumor antigen or a stromal antigen. In some embodiments, the cancer antigen is, e.g., a mammalian, e.g., a human, cancer antigen. In other embodiments, the antibody molecule binds to an immune cell antigen, e.g., a mammalian, e.g., a human, immune cell antigen. For example, the antibody molecule binds

specifically to an epitope, *e.g.*, linear or conformational epitope, on the cancer antigen or the immune cell antigen.

In an embodiment, an antibody molecule is a monospecific antibody molecule and binds a single epitope. *E.g.*, a monospecific antibody molecule having a plurality of immunoglobulin
5 variable domain sequences, each of which binds the same epitope.

In an embodiment an antibody molecule is a multispecific or multifunctional antibody molecule, *e.g.*, it comprises a plurality of immunoglobulin variable domains sequences, wherein a first immunoglobulin variable domain sequence of the plurality has binding specificity for a first epitope and a second immunoglobulin variable domain sequence of the plurality has binding
10 specificity for a second epitope. In an embodiment the first and second epitopes are on the same antigen, *e.g.*, the same protein (or subunit of a multimeric protein). In an embodiment the first and second epitopes overlap. In an embodiment the first and second epitopes do not overlap. In an embodiment the first and second epitopes are on different antigens, *e.g.*, the different proteins (or different subunits of a multimeric protein). In an embodiment a multispecific antibody
15 molecule comprises a third, fourth or fifth immunoglobulin variable domain. In an embodiment, a multispecific antibody molecule is a bispecific antibody molecule, a trispecific antibody molecule, or a tetraspecific antibody molecule.

In an embodiment a multispecific antibody molecule is a bispecific antibody molecule. A bispecific antibody has specificity for no more than two antigens. A bispecific antibody
20 molecule is characterized by a first immunoglobulin variable domain sequence which has binding specificity for a first epitope and a second immunoglobulin variable domain sequence that has binding specificity for a second epitope. In an embodiment the first and second epitopes are on the same antigen, *e.g.*, the same protein (or subunit of a multimeric protein). In an embodiment the first and second epitopes overlap. In an embodiment the first and second
25 epitopes do not overlap. In an embodiment the first and second epitopes are on different antigens, *e.g.*, the different proteins (or different subunits of a multimeric protein). In an embodiment a bispecific antibody molecule comprises a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a first epitope and a heavy chain variable domain sequence and a light chain variable domain sequence which have
30 binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a half antibody having binding specificity for a first epitope and a half antibody

having binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a half antibody, or fragment thereof, having binding specificity for a first epitope and a half antibody, or fragment thereof, having binding specificity for a second epitope. In an embodiment a bispecific antibody molecule comprises a scFv or a Fab, or fragment thereof, have binding specificity for a first epitope and a scFv or a Fab, or fragment thereof, have binding specificity for a second epitope.

In an embodiment, an antibody molecule comprises a diabody, and a single-chain molecule, as well as an antigen-binding fragment of an antibody (*e.g.*, Fab, F(ab')₂, and Fv). For example, an antibody molecule can include a heavy (H) chain variable domain sequence (abbreviated herein as VH), and a light (L) chain variable domain sequence (abbreviated herein as VL). In an embodiment an antibody molecule comprises or consists of a heavy chain and a light chain (referred to herein as a half antibody). In another example, an antibody molecule includes two heavy (H) chain variable domain sequences and two light (L) chain variable domain sequence, thereby forming two antigen binding sites, such as Fab, Fab', F(ab')₂, Fc, Fd, Fd', Fv, single chain antibodies (scFv for example), single variable domain antibodies, diabodies (Dab) (bivalent and bispecific), and chimeric (*e.g.*, humanized) antibodies, which may be produced by the modification of whole antibodies or those synthesized de novo using recombinant DNA technologies. These functional antibody fragments retain the ability to selectively bind with their respective antigen or receptor. Antibodies and antibody fragments 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. The a preparation of antibody molecules can be monoclonal or polyclonal. An antibody molecule can also be a human, humanized, CDR-grafted, or *in vitro* generated antibody. The antibody can have a heavy chain constant region chosen from, *e.g.*, IgG1, IgG2, IgG3, or IgG4. The antibody can also have a light chain chosen from, *e.g.*, kappa or lambda. The term "immunoglobulin" (Ig) is used interchangeably with the term "antibody" herein.

Examples of antigen-binding fragments of an antibody molecule include: (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; (ii) a F(ab')₂ fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a diabody (dAb)

fragment, which consists of a VH domain; (vi) a camelid or camelized variable domain; (vii) a single chain Fv (scFv), *see e.g.*, Bird *et al.* (1988) *Science* 242:423-426; and Huston *et al.* (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883); (viii) a single domain antibody. These antibody fragments are obtained using conventional techniques known to those with skill in the art, and
5 the fragments are screened for utility in the same manner as are intact antibodies.

Antibody molecules include intact molecules as well as functional fragments thereof. Constant regions of the antibody molecules can be altered, *e.g.*, mutated, to modify the properties of the antibody (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function).

10 Antibody molecules can also be single domain antibodies. Single domain antibodies can include antibodies whose complementary determining regions are part of a single domain polypeptide. Examples include, but are not limited to, heavy chain antibodies, antibodies naturally devoid of light chains, single domain antibodies derived from conventional 4-chain antibodies, engineered antibodies and single domain scaffolds other than those derived from
15 antibodies. Single domain antibodies may be any of the art, or any future single domain antibodies. Single domain antibodies may be derived from any species including, but not limited to mouse, human, camel, llama, fish, shark, goat, rabbit, and bovine. According to another aspect of the invention, a single domain antibody is a naturally occurring single domain antibody known as heavy chain antibody devoid of light chains. Such single domain antibodies are
20 disclosed in WO 9404678, for example. For clarity reasons, this variable domain derived from a heavy chain antibody naturally devoid of light chain is known herein as a VHH or nanobody to distinguish it from the conventional VH of four chain immunoglobulins. Such a VHH molecule can be derived from antibodies raised in *Camelidae* species, for example in camel, llama, dromedary, alpaca and guanaco. Other species besides *Camelidae* may produce heavy chain
25 antibodies naturally devoid of light chain; such VHHs are within the scope of the invention.

The VH and VL regions can be subdivided into regions of hypervariability, termed "complementarity determining regions" (CDR), interspersed with regions that are more conserved, termed "framework regions" (FR or FW).

The extent of the framework region and CDRs has been precisely defined by a number of
30 methods (*see*, 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. *See, generally, e.g., Protein Sequence and Structure Analysis of Antibody Variable Domains.* In: Antibody Engineering Lab Manual (Ed.: Duebel, S. and Kontermann, R., Springer-Verlag, Heidelberg).

5 The terms “complementarity determining region,” and “CDR,” as used herein refer to the sequences of amino acids within antibody variable regions which confer antigen specificity and binding affinity. In general, there are three CDRs in each heavy chain variable region (HCDR1, HCDR2, HCDR3) and three CDRs in each light chain variable region (LCDR1, LCDR2, LCDR3).

10 The precise amino acid sequence boundaries of a given CDR can be determined using any of a number of known schemes, including those described by Kabat *et al.* (1991), “Sequences of Proteins of Immunological Interest,” 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD (“Kabat” numbering scheme), Al-Lazikani *et al.*, (1997) *JMB* 273,927-948 (“Chothia” numbering scheme). As used herein, the CDRs defined according the
15 “Chothia” number scheme are also sometimes referred to as “hypervariable loops.”

For example, under Kabat, the CDR amino acid residues in the heavy chain variable domain (VH) are numbered 31-35 (HCDR1), 50-65 (HCDR2), and 95-102 (HCDR3); and the CDR amino acid residues in the light chain variable domain (VL) are numbered 24-34 (LCDR1), 50-56 (LCDR2), and 89-97 (LCDR3). Under Chothia, the CDR amino acids in the VH are
20 numbered 26-32 (HCDR1), 52-56 (HCDR2), and 95-102 (HCDR3); and the amino acid residues in VL are numbered 26-32 (LCDR1), 50-52 (LCDR2), and 91-96 (LCDR3).

Each VH and VL typically includes three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4.

25 The antibody molecule can be a polyclonal or a monoclonal antibody.

The terms “monoclonal antibody” or “monoclonal antibody composition” as used herein refer to a preparation of antibody molecules of single molecular composition. A monoclonal antibody composition displays a single binding specificity and affinity for a particular epitope. A monoclonal antibody can be made by hybridoma technology or by methods that do not use
30 hybridoma technology (*e.g.*, recombinant methods).

The antibody can be recombinantly produced, *e.g.*, produced by phage display or by combinatorial methods.

Phage display and 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 Antibod 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, the contents of all of which are incorporated by reference herein).

In one embodiment, the antibody is a fully human antibody (*e.g.*, an antibody made in a mouse which has been genetically engineered to produce an antibody from a human immunoglobulin sequence), or a non-human antibody, *e.g.*, a rodent (mouse or rat), goat, primate (*e.g.*, monkey), camel antibody. Preferably, the non-human antibody is a rodent (mouse or rat antibody). Methods of producing rodent antibodies are known in the art.

Human monoclonal antibodies can be generated using transgenic mice carrying the human immunoglobulin genes rather than the mouse system. Splenocytes from these transgenic mice immunized with the antigen of interest are used to produce hybridomas that secrete human mAbs with specific affinities for epitopes from a human protein (see, *e.g.*, Wood *et al.* International Application WO 91/00906, Kucherlapati *et al.* PCT publication WO 91/10741; Lonberg *et al.* International Application WO 92/03918; Kay *et al.* International Application 92/03917; Lonberg, N. *et al.* 1994 *Nature* 368:856-859; Green, L.L. *et al.* 1994 *Nature Genet.* 7:13-21; Morrison, S.L. *et al.* 1994 *Proc. Natl. Acad. Sci. USA* 81:6851-6855; Bruggeman *et al.* 1993 *Year Immunol* 7:33-40; Tuaillon *et al.* 1993 *PNAS* 90:3720-3724; Bruggeman *et al.* 1991 *Eur J Immunol* 21:1323-1326).

An antibody molecule can be one in which the variable region, or a portion thereof, *e.g.*, the CDRs, are generated in a non-human organism, *e.g.*, a rat or mouse. Chimeric, CDR-grafted, and humanized antibodies are within the invention. Antibody molecules generated in a non-human organism, *e.g.*, a rat or mouse, and then modified, *e.g.*, in the variable framework or
 5 constant region, to decrease antigenicity in a human are within the invention.

An "effectively human" protein is a protein that does substantially not evoke a neutralizing antibody response, *e.g.*, the human anti-murine antibody (HAMA) response. HAMA can be problematic in a number of circumstances, *e.g.*, if the antibody molecule is administered repeatedly, *e.g.*, in treatment of a chronic or recurrent disease condition. A HAMA
 10 response can make repeated antibody administration potentially ineffective because of an increased antibody clearance from the serum (*see, e.g.*, Saleh *et al.*, *Cancer Immunol. Immunother.*, 32:180-190 (1990)) and also because of potential allergic reactions (*see, e.g.*, LoBuglio *et al.*, *Hybridoma*, 5:5117-5123 (1986)).

Chimeric antibodies can be produced by recombinant DNA techniques known in the art
 15 (see Robinson *et al.*, International Patent Publication PCT/US86/02269; Akira, *et al.*, European Patent Application 184,187; Taniguchi, M., European Patent Application 171,496; Morrison *et al.*, European Patent Application 173,494; Neuberger *et al.*, International Application WO 86/01533; Cabilly *et al.* U.S. Patent No. 4,816,567; Cabilly *et al.*, European Patent Application 125,023; Better *et al.* (1988 *Science* 240:1041-1043); Liu *et al.* (1987) *PNAS* 84:3439-3443; Liu
 20 *et al.*, 1987, *J. Immunol.* 139:3521-3526; Sun *et al.* (1987) *PNAS* 84:214-218; Nishimura *et al.*, 1987, *Canc. Res.* 47:999-1005; Wood *et al.* (1985) *Nature* 314:446-449; and Shaw *et al.*, 1988, *J. Natl Cancer Inst.* 80:1553-1559).

A humanized or CDR-grafted antibody will have at least one or two but generally all three recipient CDRs (of heavy and or light immunoglobulin chains) replaced with a donor CDR.
 25 The antibody may be replaced with at least a portion of a non-human CDR or only some of the CDRs may be replaced with non-human CDRs. It is only necessary to replace the number of CDRs required for binding to the antigen. Preferably, the donor will be a rodent antibody, *e.g.*, a rat or mouse antibody, and the recipient will be a human framework or a human consensus framework. Typically, the immunoglobulin providing the CDRs is called the "donor" and the
 30 immunoglobulin providing the framework is called the "acceptor." In one embodiment, the donor immunoglobulin is a non-human (*e.g.*, rodent). The acceptor framework is a naturally-

occurring (*e.g.*, a human) framework or a consensus framework, or a sequence about 85% or higher, preferably 90%, 95%, 99% or higher identical thereto.

As used herein, the term "consensus sequence" refers to the sequence formed from the most frequently occurring amino acids (or nucleotides) in a family of related sequences (See *e.g.*, Winnaker, *From Genes to Clones* (Verlagsgesellschaft, Weinheim, Germany 1987). In a family of proteins, each position in the consensus sequence is occupied by the amino acid occurring most frequently at that position in the family. If two amino acids occur equally frequently, either can be included in the consensus sequence. A "consensus framework" refers to the framework region in the consensus immunoglobulin sequence.

An antibody molecule can be humanized by methods known in the art (*see e.g.*, Morrison, S. L., 1985, *Science* 229:1202-1207, by Oi *et al.*, 1986, *BioTechniques* 4:214, and by Queen *et al.* US 5,585,089, US 5,693,761 and US 5,693,762, the contents of all of which are hereby incorporated by reference).

Humanized or CDR-grafted antibody molecules can be produced by CDR-grafting or CDR substitution, wherein one, two, or all CDRs of an immunoglobulin chain can be replaced. See *e.g.*, U.S. Patent 5,225,539; Jones *et al.* 1986 *Nature* 321:552-525; Verhoeyan *et al.* 1988 *Science* 239:1534; Beidler *et al.* 1988 *J. Immunol.* 141:4053-4060; Winter US 5,225,539, the contents of all of which are hereby expressly incorporated by reference. Winter describes a CDR-grafting method which may be used to prepare the humanized antibodies of the present invention (UK Patent Application GB 2188638A, filed on March 26, 1987; Winter US 5,225,539), the contents of which is expressly incorporated by reference.

Also within the scope of the invention are humanized antibody molecules in which specific amino acids have been substituted, deleted or added. Criteria for selecting amino acids from the donor are described in US 5,585,089, *e.g.*, columns 12-16 of US 5,585,089, *e.g.*, columns 12-16 of US 5,585,089, the contents of which are hereby incorporated by reference. Other techniques for humanizing antibodies are described in Padlan *et al.* EP 519596 A1, published on December 23, 1992.

The antibody molecule can be a single chain antibody. A single-chain antibody (scFV) may be engineered (see, for example, Colcher, D. *et al.* (1999) *Ann N Y Acad Sci* 880:263-80; and Reiter, Y. (1996) *Clin Cancer Res* 2:245-52). The single chain antibody can be dimerized or

multimerized to generate multivalent antibodies having specificities for different epitopes of the same target protein.

In yet other embodiments, the antibody molecule has a heavy chain constant region chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE; particularly, chosen from, *e.g.*, the (*e.g.*, human) heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4. In another embodiment, the antibody molecule has a light chain constant region chosen from, *e.g.*, the (*e.g.*, human) light chain constant regions of kappa or lambda. The constant region can be altered, *e.g.*, mutated, to modify the properties of the antibody (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, and/or complement function). In one embodiment the antibody has: effector function; and can fix complement. In other embodiments the antibody does not; recruit effector cells; or fix complement. In another embodiment, the antibody has reduced or no ability to bind an Fc receptor. For example, it is a isotype or subtype, fragment or other mutant, which does not support binding to an Fc receptor, *e.g.*, it has a mutagenized or deleted Fc receptor binding region.

Methods for altering an antibody constant region are known in the art. Antibodies with altered function, *e.g.* altered affinity for an effector ligand, such as FcR on a cell, or the C1 component of complement can be produced by replacing at least one amino acid residue in the constant portion of the antibody with a different residue (*see e.g.*, EP 388,151 A1, U.S. Pat. No. 5,624,821 and U.S. Pat. No. 5,648,260, the contents of all of which are hereby incorporated by reference). Similar type of alterations could be described which if applied to the murine, or other species immunoglobulin would reduce or eliminate these functions.

An antibody molecule can be derivatized or linked to another functional molecule (*e.g.*, another peptide or protein). As used herein, a "derivatized" antibody molecule is one that has been modified. Methods of derivatization include but are not limited to the addition of a fluorescent moiety, a radionucleotide, a toxin, an enzyme or an affinity ligand such as biotin. Accordingly, the antibody molecules of the invention are intended to include derivatized and otherwise modified forms of the antibodies described herein, including immunoadhesion molecules. For example, an antibody molecule can be functionally linked (by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other molecular entities, such as another antibody (*e.g.*, a bispecific antibody or a diabody), a detectable agent, a cytotoxic

agent, a pharmaceutical agent, and/or a protein or peptide that can mediate association of the antibody or antibody portion with another molecule (such as a streptavidin core region or a polyhistidine tag).

One type of derivatized antibody molecule is produced by crosslinking two or more antibodies (of the same type or of different types, *e.g.*, to create bispecific antibodies). Suitable crosslinkers include those that are heterobifunctional, having two distinctly reactive groups separated by an appropriate spacer (*e.g.*, m-maleimidobenzoyl-N-hydroxysuccinimide ester) or homobifunctional (*e.g.*, disuccinimidyl suberate). Such linkers are available from Pierce Chemical Company, Rockford, Ill.

Multispecific or multifunctional antibody molecules

Exemplary structures of multispecific and multifunctional molecules defined herein are described throughout. Exemplary structures are further described in: Weidle U et al. (2013) The Intriguing Options of Multispecific Antibody Formats for Treatment of Cancer. *Cancer Genomics & Proteomics* 10: 1-18 (2013); and Spiess C et al. (2015) Alternative molecular formats and therapeutic applications for bispecific antibodies. *Molecular Immunology* 67: 95-106; the full contents of each of which is incorporated by reference herein).

In embodiments, multispecific antibody molecules can comprise more than one antigen-binding site, where different sites are specific for different antigens. In embodiments, multispecific antibody molecules can bind more than one (*e.g.*, two or more) epitopes on the same antigen. In embodiments, multispecific antibody molecules comprise an antigen-binding site specific for a target cell (*e.g.*, cancer cell) and a different antigen-binding site specific for an immune effector cell. In embodiments, the multispecific antibody molecule is a bispecific, trispecific, or tetraspecific antibody molecule. In one embodiment, the multispecific antibody molecule is a bispecific antibody molecule. Bispecific antibody molecules can be classified into five different structural groups: (i) bispecific immunoglobulin G (BsIgG); (ii) IgG appended with an additional antigen-binding moiety; (iii) bispecific antibody fragments; (iv) bispecific fusion proteins; and (v) bispecific antibody conjugates.

BsIgG is a format that is monovalent for each antigen. Exemplary BsIgG formats include but are not limited to crossMab, DAF (two-in-one), DAF (four-in-one), DutaMab, DT-IgG, knobs-in-holes common LC, knobs-in-holes assembly, charge pair, Fab-arm exchange,

SEEDbody, triomab, LUZ-Y, Fcab, $\kappa\lambda$ -body, orthogonal Fab. *See* Spiess et al. Mol. Immunol. 67(2015):95-106. Exemplary BsIgGs include catumaxomab (Fresenius Biotech, Trion Pharma, Neopharm), which contains an anti-CD3 arm and an anti-EpCAM arm; and ertumaxomab (Neovii Biotech, Fresenius Biotech), which targets CD3 and HER2. In some embodiments, BsIgG comprises heavy chains that are engineered for heterodimerization. For example, heavy chains can be engineered for heterodimerization using a “knobs-into-holes” strategy, a SEED platform, a common heavy chain (e.g., in $\kappa\lambda$ -bodies), and use of heterodimeric Fc regions. *See* Spiess et al. Mol. Immunol. 67(2015):95-106. Strategies that have been used to avoid heavy chain pairing of homodimers in BsIgG include knobs-in-holes, duobody, azymetric, charge pair, HA-TF, SEEDbody, and differential protein A affinity. *See Id.* BsIgG can be produced by separate expression of the component antibodies in different host cells and subsequent purification/assembly into a BsIgG. BsIgG can also be produced by expression of the component antibodies in a single host cell. BsIgG can be purified using affinity chromatography, e.g., using protein A and sequential pH elution.

IgG appended with an additional antigen-binding moiety is another format of bispecific antibody molecules. For example, monospecific IgG can be engineered to have bispecificity by appending an additional antigen-binding unit onto the monospecific IgG, e.g., at the N- or C-terminus of either the heavy or light chain. Exemplary additional antigen-binding units include single domain antibodies (e.g., variable heavy chain or variable light chain), engineered protein scaffolds, and paired antibody variable domains (e.g., single chain variable fragments or variable fragments). *See Id.* Examples of appended IgG formats include dual variable domain IgG (DVD-Ig), IgG(H)-scFv, scFv-(H)IgG, IgG(L)-scFv, scFv-(L)IgG, IgG(L,H)-Fv, IgG(H)-V, V(H)-IgG, IgG(L)-V, V(L)-IgG, KIH IgG-scFab, 2scFv-IgG, IgG-2scFv, scFv4-Ig, zyboby, and DVI-IgG (four-in-one). *See* Spiess et al. Mol. Immunol. 67(2015):95-106. An example of an IgG-scFv is MM-141 (Merrimack Pharmaceuticals), which binds IGF-1R and HER3. Examples of DVD-Ig include ABT-981 (AbbVie), which binds IL-1 α and IL-1 β ; and ABT-122 (AbbVie), which binds TNF and IL-17A.

Bispecific antibody fragments (BsAb) are a format of bispecific antibody molecules that lack some or all of the antibody constant domains. For example, some BsAb lack an Fc region. In embodiments, bispecific antibody fragments include heavy and light chain regions that are connected by a peptide linker that permits efficient expression of the BsAb in a single host cell.

Exemplary bispecific antibody fragments include but are not limited to nanobody, nanobody-HAS, BiTE, Diabody, DART, TandAb, scDiabody, scDiabody-CH3, Diabody-CH3, triple body, miniantibody, minibody, TriBi minibody, scFv-CH3 KIH, Fab-scFv, scFv-CH-CL-scFv, F(ab')₂, F(ab')₂-scFv₂, scFv-KIH, Fab-scFv-Fc, tetravalent HCAb, scDiabody-Fc, Diabody-Fc, tandem
5 scFv-Fc, and intrabody. *See Id.* For example, the BiTE format comprises tandem scFvs, where the component scFvs bind to CD3 on T cells and a surface antigen on cancer cells

Bispecific fusion proteins include antibody fragments linked to other proteins, e.g., to add additional specificity and/or functionality. An example of a bispecific fusion protein is an immTAC, which comprises an anti-CD3 scFv linked to an affinity-matured T-cell receptor that
10 recognizes HLA-presented peptides. In embodiments, the dock-and-lock (DNL) method can be used to generate bispecific antibody molecules with higher valency. Also, fusions to albumin binding proteins or human serum albumin can be extend the serum half-life of antibody fragments. *See Id.*

In embodiments, chemical conjugation, e.g., chemical conjugation of antibodies and/or
15 antibody fragments, can be used to create BsAb molecules. *See Id.* An exemplary bispecific antibody conjugate includes the CovX-body format, in which a low molecular weight drug is conjugated site-specifically to a single reactive lysine in each Fab arm or an antibody or fragment thereof. In embodiments, the conjugation improves the serum half-life of the low molecular weight drug. An exemplary CovX-body is CVX-241 (NCT01004822), which
20 comprises an antibody conjugated to two short peptides inhibiting either VEGF or Ang2. *See Id.*

The antibody molecules can be produced by recombinant expression, e.g., of at least one or more component, in a host system. Exemplary host systems include eukaryotic cells (e.g., mammalian cells, e.g., CHO cells, or insect cells, e.g., SF9 or S2 cells) and prokaryotic cells (e.g., *E. coli*). Bispecific antibody molecules can be produced by separate expression of the
25 components in different host cells and subsequent purification/assembly. Alternatively, the antibody molecules can be produced by expression of the components in a single host cell. Purification of bispecific antibody molecules can be performed by various methods such as affinity chromatography, e.g., using protein A and sequential pH elution. In other embodiments, affinity tags can be used for purification, e.g., histidine-containing tag, myc tag, or streptavidin
30 tag.

CDR-grafted scaffolds

In embodiments, the antibody molecule is a CDR-grafted scaffold domain. In embodiments, the scaffold domain is based on a fibronectin domain, e.g., fibronectin type III domain. The overall fold of the fibronectin type III (Fn3) domain is closely related to that of the smallest functional antibody fragment, the variable domain of the antibody heavy chain. There are three loops at the end of Fn3; the positions of BC, DE and FG loops approximately correspond to those of CDR1, 2 and 3 of the VH domain of an antibody. Fn3 does not have disulfide bonds; and therefore Fn3 is stable under reducing conditions, unlike antibodies and their fragments (see, e.g., WO 98/56915; WO 01/64942; WO 00/34784). An Fn3 domain can be modified (e.g., using CDRs or hypervariable loops described herein) or varied, e.g., to select domains that bind to an antigen/marker/cell described herein.

In embodiments, a scaffold domain, e.g., a folded domain, is based on an antibody, e.g., a “minibody” scaffold created by deleting three beta strands from a heavy chain variable domain of a monoclonal antibody (see, e.g., Tramontano et al., 1994, J Mol. Recognit. 7:9; and Martin et al., 1994, EMBO J. 13:5303-5309). The “minibody” can be used to present two hypervariable loops. In embodiments, the scaffold domain is a V-like domain (see, e.g., Coia et al. WO 99/45110) or a domain derived from tendamistatin, which is a 74 residue, six-strand beta sheet sandwich held together by two disulfide bonds (see, e.g., McConnell and Hoess, 1995, J Mol. Biol. 250:460). For example, the loops of tendamistatin can be modified (e.g., using CDRs or hypervariable loops) or varied, e.g., to select domains that bind to a marker/antigen/cell described herein. Another exemplary scaffold domain is a beta-sandwich structure derived from the extracellular domain of CTLA-4 (see, e.g., WO 00/60070).

Other exemplary scaffold domains include but are not limited to T-cell receptors; MHC proteins; extracellular domains (e.g., fibronectin Type III repeats, EGF repeats); protease inhibitors (e.g., Kunitz domains, ecotin, BPTI, and so forth); TPR repeats; trifoil structures; zinc finger domains; DNA-binding proteins; particularly monomeric DNA binding proteins; RNA binding proteins; enzymes, e.g., proteases (particularly inactivated proteases), RNase; chaperones, e.g., thioredoxin, and heat shock proteins; and intracellular signaling domains (such as SH2 and SH3 domains). See, e.g., US 20040009530 and US 7,501,121, incorporated herein by reference.

In embodiments, a scaffold domain is evaluated and chosen, e.g., by one or more of the following criteria: (1) amino acid sequence, (2) sequences of several homologous domains, (3) 3-dimensional structure, and/or (4) stability data over a range of pH, temperature, salinity, organic solvent, oxidant concentration. In embodiments, the scaffold domain is a small, stable protein domain, e.g., a protein of less than 100, 70, 50, 40 or 30 amino acids. The domain may include one or more disulfide bonds or may chelate a metal, e.g., zinc.

Antibody-Based Fusions

A variety of formats can be generated which contain additional binding entities attached to the N or C terminus of antibodies. These fusions with single chain or disulfide stabilized Fvs or Fabs result in the generation of tetravalent molecules with bivalent binding specificity for each antigen. Combinations of scFvs and scFabs with IgGs enable the production of molecules which can recognize three or more different antigens.

Antibody-Fab Fusion

Antibody-Fab fusions are bispecific antibodies comprising a traditional antibody to a first target and a Fab to a second target fused to the C terminus of the antibody heavy chain. Commonly the antibody and the Fab will have a common light chain. Antibody fusions can be produced by (1) engineering the DNA sequence of the target fusion, and (2) transfecting the target DNA into a suitable host cell to express the fusion protein. It seems like the antibody-scFv fusion may be linked by a (Gly)-Ser linker between the C-terminus of the CH3 domain and the N-terminus of the scFv, as described by Coloma, J. *et al.* (1997) *Nature Biotech* 15:159.

Antibody-scFv Fusion

Antibody-scFv Fusions are bispecific antibodies comprising a traditional antibody and a scFv of unique specificity fused to the C terminus of the antibody heavy chain. The scFv can be fused to the C terminus through the Heavy Chain of the scFv either directly or through a linker peptide. Antibody fusions can be produced by (1) engineering the DNA sequence of the target fusion, and (2) transfecting the target DNA into a suitable host cell to express the fusion protein. It seems like the antibody-scFv fusion may be linked by a (Gly)-Ser linker between the C-

terminus of the CH3 domain and the N-terminus of the scFv, as described by Coloma, J. *et al.* (1997) *Nature Biotech* 15:159.

Variable Domain Immunoglobulin DVD

5 A related format is the dual variable domain immunoglobulin (DVD), which are composed of VH and VL domains of a second specificity placed upon the N termini of the V domains by shorter linker sequences.

Other exemplary multispecific antibody formats include, e.g., those described in the following US20160114057A1, US20130243775A1, US20140051833, US20130022601, 10 US20150017187A1, US20120201746A1, US20150133638A1, US20130266568A1, US20160145340A1, WO2015127158A1, US20150203591A1, US20140322221A1, US20130303396A1, US20110293613, US20130017200A1, US20160102135A1, WO2015197598A2, WO2015197582A1, US9359437, US20150018529, WO2016115274A1, 15 WO2016087416A1, US20080069820A1, US9145588B, US7919257, and US20150232560A1. Exemplary multispecific molecules utilizing a full antibody-Fab/scFab format include those described in the following, US9382323B2, US20140072581A1, US20140308285A1, US20130165638A1, US20130267686A1, US20140377269A1, US7741446B2, and WO1995009917A1. Exemplary multispecific molecules utilizing a domain exchange format 20 include those described in the following, US20150315296A1, WO2016087650A1, US20160075785A1, WO2016016299A1, US20160130347A1, US20150166670, US8703132B2, US20100316645, US8227577B2, US20130078249.

Fc-containing entities (mini-antibodies)

25 Fc-containing entities, also known as mini-antibodies, can be generated by fusing scFv to the C-termini of constant heavy region domain 3 (CH3-scFv) and/or to the hinge region (scFv-hinge-Fc) of an antibody with a different specificity. Trivalent entities can also be made which have disulfide stabilized variable domains (without peptide linker) fused to the C-terminus of CH3 domains of IgGs.

30

Fc-containing multispecific molecules

In some embodiments, the multispecific molecules disclosed herein includes an immunoglobulin constant region (e.g., an Fc region). Exemplary Fc regions can be chosen from the heavy chain constant regions of IgG1, IgG2, IgG3 or IgG4; more particularly, the heavy chain constant region of human IgG1, IgG2, IgG3, or IgG4.

In some embodiments, the immunoglobulin chain constant region (e.g., the Fc region) is altered, e.g., mutated, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function.

In other embodiments, an interface of a first and second immunoglobulin chain constant regions (e.g., a first and a second Fc region) is altered, e.g., mutated, to increase or decrease dimerization, e.g., relative to a non-engineered interface, e.g., a naturally-occurring interface. For example, dimerization of the immunoglobulin chain constant region (e.g., the Fc region) can be enhanced by providing an Fc interface of a first and a second Fc region with one or more of: a paired protuberance-cavity (“knob-in-a hole”), an electrostatic interaction, or a strand-exchange, such that a greater ratio of heteromultimer to homomultimer forms, e.g., relative to a non-engineered interface.

In some embodiments, the multispecific molecules include a paired amino acid substitution at a position chosen from one or more of 347, 349, 350, 351, 366, 368, 370, 392, 394, 395, 397, 398, 399, 405, 407, or 409, e.g., of the Fc region of human IgG1. For example, the immunoglobulin chain constant region (e.g., Fc region) can include a paired amino acid substitution chosen from: T366S, L368A, or Y407V (e.g., corresponding to a cavity or hole), and T366W (e.g., corresponding to a protuberance or knob).

In other embodiments, the multifunctional molecule includes a half-life extender, e.g., a human serum albumin or an antibody molecule to human serum albumin.

Heterodimerized Antibody Molecules & Methods of Making

Various methods of producing multispecific antibodies have been disclosed to address the problem of incorrect heavy chain pairing. Exemplary methods are described below. Exemplary multispecific antibody formats and methods of making said multispecific antibodies are also disclosed in e.g., Speiss et al. *Molecular Immunology* 67 (2015) 95–106; and Klein et al

mAbs 4:6, 653–663; November/December 2012; the entire contents of each of which are incorporated by reference herein.

Heterodimerized bispecific antibodies are based on the natural IgG structure, wherein the two binding arms recognize different antigens. IgG derived formats that enable defined
 5 monovalent (and simultaneous) antigen binding are generated by forced heavy chain heterodimerization, combined with technologies that minimize light chain mispairing (e.g., common light chain). Forced heavy chain heterodimerization can be obtained using, e.g., knob-in-hole OR strand exchange engineered domains (SEED).

10 Knob-in-Hole

Knob-in-Hole as described in US 5,731,116, US 7,476,724 and Ridgway, J. *et al.* (1996) *Prot. Engineering* 9(7): 617-621, broadly involves: (1) mutating the CH3 domain of one or both antibodies to promote heterodimerization; and (2) combining the mutated antibodies under conditions that promote heterodimerization. “Knobs” or “protuberances” are typically created by
 15 replacing a small amino acid in a parental antibody with a larger amino acid (e.g., T366Y or T366W); “Holes” or “cavities” are created by replacing a larger residue in a parental antibody with a smaller amino acid (e.g., Y407T, T366S, L368A and/or Y407V).

For bispecific antibodies including an Fc domain, introduction of specific mutations into the constant region of the heavy chains to promote the correct heterodimerization of the Fc
 20 portion can be utilized. Several such techniques are reviewed in Klein et al. (mAbs (2012) 4:6, 1-11), the contents of which are incorporated herein by reference in their entirety. These techniques include the “knobs-into-holes” (KiH) approach which involves the introduction of a bulky residue into one of the CH3 domains of one of the antibody heavy chains. This bulky residue fits into a complementary “hole” in the other CH3 domain of the paired heavy chain so as to promote
 25 correct pairing of heavy chains (see e.g., US7642228).

Exemplary KiH mutations include S354C, T366W in the “knob” heavy chain and Y349C, T366S, L368A, Y407V in the “hole” heavy chain. Other exemplary KiH mutations are provided in Table 1, with additional optional stabilizing Fc cysteine mutations.

30 **Table 1.** Exemplary Fc KiH mutations and optional Cysteine mutations

Position	Knob Mutation	Hole Mutation

T366	T366W	T366S
L368	-	L368A
Y407	-	Y407V
Additional Cysteine Mutations to form a stabilizing disulfide bridge		
Position	Knob CH3	Hole CH3
S354	S354C	-
Y349	-	Y349C

Other Fc mutations are provided by Igawa and Tsunoda who identified 3 negatively charged residues in the CH3 domain of one chain that pair with three positively charged residues in the CH3 domain of the other chain. These specific charged residue pairs are: E356-K439, E357-K370, D399-K409 and vice versa. By introducing at least two of the following three mutations in chain A: E356K, E357K and D399K, as well as K370E, K409D, K439E in chain B, alone or in combination with newly identified disulfide bridges, they were able to favor very efficient heterodimerization while suppressing homodimerization at the same time (Martens T et al. A novel one-armed antic- Met antibody inhibits glioblastoma growth in vivo. Clin Cancer Res 2006; 12:6144-52; PMID:17062691). Xencor defined 41 variant pairs based on combining structural calculations and sequence information that were subsequently screened for maximal heterodimerization, defining the combination of S364H, F405A (HA) on chain A and Y349T, T394F on chain B (TF) (Moore GL et al. A novel bispecific antibody format enables simultaneous bivalent and monovalent co-engagement of distinct target antigens. MAbs 2011; 3:546-57; PMID: 22123055).

Other exemplary Fc mutations to promote heterodimerization of multispecific antibodies include those described in the following references, the contents of each of which is incorporated by reference herein, WO2016071377A1, US20140079689A1, US20160194389A1, US20160257763, WO2016071376A2, WO2015107026A1, WO2015107025A1, WO2015107015A1, US20150353636A1, US20140199294A1, US7750128B2, US20160229915A1, US20150344570A1, US8003774A1, US20150337049A1, US20150175707A1, US20140242075A1, US20130195849A1, US20120149876A1,

US20140200331A1, US9309311B2, US8586713, US20140037621A1, US20130178605A1, US20140363426A1, US20140051835A1 and US20110054151A1.

Stabilizing cysteine mutations have also been used in combination with KiH and other Fc heterodimerization promoting variants, see e.g., US7183076. Other exemplary cysteine
5 modifications include, e.g., those disclosed in US20140348839A1, US7855275B2, and US9000130B2.

Strand Exchange Engineered Domains (SEED)

Heterodimeric Fc platform that support the design of bispecific and asymmetric fusion
10 proteins by devising strand-exchange engineered domain (SEED) C(H)3 heterodimers are known. These derivatives of human IgG and IgA C(H)3 domains create complementary human SEED C(H)3 heterodimers that are composed of alternating segments of human IgA and IgG C(H)3 sequences. The resulting pair of SEED C(H)3 domains preferentially associates to form heterodimers when expressed in mammalian cells. SEEDbody (Sb) fusion proteins consist of
15 [IgG1 hinge]-C(H)2-[SEED C(H)3], that may be genetically linked to one or more fusion partners (see e.g., Davis JH et al. SEEDbodies: fusion proteins based on strand exchange engineered domain (SEED) CH3 heterodimers in an Fc analogue platform for asymmetric binders or immunofusions and bispecific antibodies. Protein Eng Des Sel 2010; 23:195-202; PMID:20299542 and US8871912. The contents of each of which are incorporated by reference
20 herein).

Duobody

“Duobody” technology to produce bispecific antibodies with correct heavy chain pairing are known. The DuoBody technology involves three basic steps to generate stable bispecific
25 human IgG1 antibodies in a post-production exchange reaction. In a first step, two IgG1s, each containing single matched mutations in the third constant (CH3) domain, are produced separately using standard mammalian recombinant cell lines. Subsequently, these IgG1 antibodies are purified according to standard processes for recovery and purification. After production and purification (post-production), the two antibodies are recombined under tailored laboratory
30 conditions resulting in a bispecific antibody product with a very high yield (typically >95%) (see

e.g., Labrijn et al, PNAS 2013;110(13):5145-5150 and Labrijn et al. Nature Protocols 2014;9(10):2450-63, the contents of each of which are incorporated by reference herein).

Electrostatic Interactions

5 Methods of making multispecific antibodies using CH3 amino acid changes with charged amino acids such that homodimer formation is electrostatically unfavorable are disclosed. EP1870459 and WO 2009089004 describe other strategies for favoring heterodimer formation upon co-expression of different antibody domains in a host cell. In these methods, one or more residues that make up the heavy chain constant domain 3 (CH3), CH3-CH3 interfaces in both
10 CH3 domains are replaced with a charged amino acid such that homodimer formation is electrostatically unfavorable and heterodimerization is electrostatically favorable. Additional methods of making multispecific molecules using electrostatic interactions are described in the following references, the contents of each of which is incorporated by reference herein, include US20100015133, US8592562B2, US9200060B2, US20140154254A1, and US9358286A1.

Common Light Chain

15 Light chain mispairing needs to be avoided to generate homogenous preparations of bispecific IgGs. One way to achieve this is through the use of the common light chain principle, i.e. combining two binders that share one light chain but still have separate specificities. An
20 exemplary method of enhancing the formation of a desired bispecific antibody from a mixture of monomers is by providing a common variable light chain to interact with each of the heteromeric variable heavy chain regions of the bispecific antibody. Compositions and methods of producing bispecific antibodies with a common light chain as disclosed in, e.g., US7183076B2, US20110177073A1, EP2847231A1, WO2016079081A1, and EP3055329A1, the contents of
25 each of which is incorporated by reference herein.

CrossMab

30 Another option to reduce light chain mispairing is the CrossMab technology which avoids non-specific L chain mispairing by exchanging CH1 and CL domains in the Fab of one half of the bispecific antibody. Such crossover variants retain binding specificity and affinity, but make the two arms so different that L chain mispairing is prevented. The CrossMab technology

(as reviewed in Klein et al. *Supra*) involves domain swapping between heavy and light chains so as to promote the formation of the correct pairings. Briefly, to construct a bispecific IgG-like CrossMab antibody that could bind to two antigens by using two distinct light chain-heavy chain pairs, a two-step modification process is applied. First, a dimerization interface is engineered into the C-terminus of each heavy chain using a heterodimerization approach, e.g., Knob-into-hole (KiH) technology, to ensure that only a heterodimer of two distinct heavy chains from one antibody (e.g., Antibody A) and a second antibody (e.g., Antibody B) is efficiently formed. Next, the constant heavy 1 (CH1) and constant light (CL) domains of one antibody are exchanged (Antibody A), keeping the variable heavy (VH) and variable light (VL) domains consistent. The exchange of the CH1 and CL domains ensured that the modified antibody (Antibody A) light chain would only efficiently dimerize with the modified antibody (antibody A) heavy chain, while the unmodified antibody (Antibody B) light chain would only efficiently dimerize with the unmodified antibody (Antibody B) heavy chain; and thus only the desired bispecific CrossMab would be efficiently formed (see e.g., Cain, C. SciBX 4(28); doi:10.1038/scibx.2011.783, the contents of which are incorporated by reference herein).

Common Heavy Chain

An exemplary method of enhancing the formation of a desired bispecific antibody from a mixture of monomers is by providing a common variable heavy chain to interact with each of the heteromeric variable light chain regions of the bispecific antibody. Compositions and methods of producing bispecific antibodies with a common heavy chain are disclosed in, e.g., US20120184716, US20130317200, and US20160264685A1, the contents of each of which is incorporated by reference herein.

Amino Acid Modifications

Alternative compositions and methods of producing multispecific antibodies with correct light chain pairing include various amino acid modifications. For example, Zymeworks describes heterodimers with one or more amino acid modifications in the CH1 and/or CL domains, one or more amino acid modifications in the VH and/or VL domains, or a combination thereof, which are part of the interface between the light chain and heavy chain and create preferential pairing between each heavy chain and a desired light chain such that when the two heavy chains and two

light chains of the heterodimer pair are co-expressed in a cell, the heavy chain of the first heterodimer preferentially pairs with one of the light chains rather than the other (see e.g., WO2015181805). Other exemplary methods are described in WO2016026943 (Argen-X), US20150211001, US20140072581A1, US20160039947A1, and US20150368352.

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Lambda/Kappa Formats

Multispecific molecules (e.g., multispecific antibody molecules) that include the lambda light chain polypeptide and a kappa light chain polypeptides, can be used to allow for heterodimerization. Methods for generating bispecific antibody molecules comprising the
10 lambda light chain polypeptide and a kappa light chain polypeptides are disclosed in PCT Publication No. WO2018057955 (corresponding to PCT/US17/53053, filed on September 22, 2017), incorporated herein by reference in its entirety.

In embodiments, the multispecific molecules includes a multispecific antibody molecule, e.g., an antibody molecule comprising two binding specificities, e.g., a bispecific antibody
15 molecule. The multispecific antibody molecule includes:

- a lambda light chain polypeptide 1 (LLCP1) specific for a first epitope;
- a heavy chain polypeptide 1 (HCP1) specific for the first epitope;
- a kappa light chain polypeptide 2 (KLCP2) specific for a second epitope; and
- a heavy chain polypeptide 2 (HCP2) specific for the second epitope.

20

“Lambda light chain polypeptide 1 (LLCP1)”, as that term is used herein, refers to a polypeptide comprising sufficient light chain (LC) sequence, such that when combined with a cognate heavy chain variable region, can mediate specific binding to its epitope and complex with an HCP1. In an embodiment it comprises all or a fragment of a CH1 region. In an
25 embodiment, an LLCP1 comprises LC-CDR1, LC-CDR2, LC-CDR3, FR1, FR2, FR3, FR4, and CH1, or sufficient sequence therefrom to mediate specific binding of its epitope and complex with an HCP1. LLCP1, together with its HCP1, provide specificity for a first epitope (while KLCP2, together with its HCP2, provide specificity for a second epitope). As described elsewhere herein, LLCP1 has a higher affinity for HCP1 than for HCP2.

30 “Kappa light chain polypeptide 2 (KLCP2)”, as that term is used herein, refers to a polypeptide comprising sufficient light chain (LC) sequence, such that when combined with a

cognate heavy chain variable region, can mediate specific binding to its epitope and complex with an HCP2. In an embodiment it comprises all or a fragment of a CH1 region. In an embodiment, a KLCP2 comprises LC-CDR1, LC-CDR2, LC-CDR3, FR1, FR2, FR3, FR4, and CH1, or sufficient sequence therefrom to mediate specific binding of its epitope and complex with an HCP2. KLCP2, together with its HCP2, provide specificity for a second epitope (while LLCP1, together with its HCP1, provide specificity for a first epitope).

“Heavy chain polypeptide 1 (HCP1)”, as that term is used herein, refers to a polypeptide comprising sufficient heavy chain (HC) sequence, e.g., HC variable region sequence, such that when combined with a cognate LLCP1, can mediate specific binding to its epitope and complex with an HCP1. In an embodiment it comprises all or a fragment of a CH1 region. In an embodiment, it comprises all or a fragment of a CH2 and/or CH3 region. In an embodiment an HCP1 comprises HC-CDR1, HC-CDR2, HC-CDR3, FR1, FR2, FR3, FR4, CH1, CH2, and CH3, or sufficient sequence therefrom to: (i) mediate specific binding of its epitope and complex with an LLCP1, (ii) to complex preferentially, as described herein to LLCP1 as opposed to KLCP2; and (iii) to complex preferentially, as described herein, to an HCP2, as opposed to another molecule of HCP1. HCP1, together with its LLCP1, provide specificity for a first epitope (while KLCP2, together with its HCP2, provide specificity for a second epitope).

“Heavy chain polypeptide 2 (HCP2)”, as that term is used herein, refers to a polypeptide comprising sufficient heavy chain (HC) sequence, e.g., HC variable region sequence, such that when combined with a cognate LLCP1, can mediate specific binding to its epitope and complex with an HCP1. In an embodiment it comprises all or a fragment of a CH1 region. In an embodiment it comprises all or a fragment of a CH2 and/or CH3 region. In an embodiment an HCP1 comprises HC-CDR1, HC-CDR2, HC-CDR3, FR1, FR2, FR3, FR4, CH1, CH2, and CH3, or sufficient sequence therefrom to: (i) mediate specific binding of its epitope and complex with an KLCP2, (ii) to complex preferentially, as described herein to KLCP2 as opposed to LLCP1; and (iii) to complex preferentially, as described herein, to an HCP1, as opposed to another molecule of HCP2. HCP2, together with its KLCP2, provide specificity for a second epitope (while LLCP1, together with its HCP1, provide specificity for a first epitope).

In some embodiments of the multispecific antibody molecule disclosed herein:

LLCP1 has a higher affinity for HCP1 than for HCP2; and/or

KLCP2 has a higher affinity for HCP2 than for HCP1.

In embodiments, the affinity of LLC1 for HCP1 is sufficiently greater than its affinity for HCP2, such that under preselected conditions, e.g., in aqueous buffer, e.g., at pH 7, in saline, e.g., at pH 7, or under physiological conditions, at least 75, 80, 90, 95, 98, 99, 99.5, or 99.9 % of the multispecific antibody molecule molecules have a LLC1complexed, or interfaced with, a HCP1.

In some embodiments of the multispecific antibody molecule disclosed herein: the HCP1 has a greater affinity for HCP2, than for a second molecule of HCP1; and/or the HCP2 has a greater affinity for HCP1, than for a second molecule of HCP2.

In embodiments, the affinity of HCP1 for HCP2 is sufficiently greater than its affinity for a second molecule of HCP1, such that under preselected conditions, e.g., in aqueous buffer, e.g., at pH 7, in saline, e.g., at pH 7, or under physiological conditions, at least 75%, 80, 90, 95, 98, 99 99.5 or 99.9 % of the multispecific antibody molecule molecules have a HCP1complexed, or interfaced with, a HCP2.

In another aspect, disclosed herein is a method for making, or producing, a multispecific antibody molecule. The method includes:

(i) providing a first heavy chain polypeptide (e.g., a heavy chain polypeptide comprising one, two, three or all of a first heavy chain variable region (first VH), a first CH1, a first heavy chain constant region (e.g., a first CH2, a first CH3, or both));

(ii) providing a second heavy chain polypeptide (e.g., a heavy chain polypeptide comprising one, two, three or all of a second heavy chain variable region (second VH), a second CH1, a second heavy chain constant region (e.g., a second CH2, a second CH3, or both));

(iii) providing a lambda chain polypeptide (e.g., a lambda light variable region (VL λ), a lambda light constant chain (VL λ), or both) that preferentially associates with the first heavy chain polypeptide (e.g., the first VH); and

(iv) providing a kappa chain polypeptide (e.g., a kappa light variable region (VL κ), a kappa light constant chain (VL κ), or both) that preferentially associates with the second heavy chain polypeptide (e.g., the second VH),

under conditions where (i)-(iv) associate.

In embodiments, the first and second heavy chain polypeptides form an Fc interface that enhances heterodimerization.

In embodiments, (i)-(iv) (e.g., nucleic acid encoding (i)-(iv)) are introduced in a single cell, e.g., a single mammalian cell, e.g., a CHO cell. In embodiments, (i)-(iv) are expressed in the cell.

In embodiments, (i)-(iv) (e.g., nucleic acid encoding (i)-(iv)) are introduced in different
5 cells, e.g., different mammalian cells, e.g., two or more CHO cell. In embodiments, (i)-(iv) are expressed in the cells.

In one embodiment, the method further comprises purifying a cell-expressed antibody molecule, e.g., using a lambda- and/or- kappa-specific purification, e.g., affinity chromatography.

10 In embodiments, the method further comprises evaluating the cell-expressed multispecific antibody molecule. For example, the purified cell-expressed multispecific antibody molecule can be analyzed by techniques known in the art, include mass spectrometry. In one embodiment, the purified cell-expressed antibody molecule is cleaved, e.g., digested with papain to yield the Fab moieties and evaluated using mass spectrometry.

15 In embodiments, the method produces correctly paired kappa/lambda multispecific, e.g., bispecific, antibody molecules in a high yield, e.g., at least 75%, 80, 90, 95, 98, 99 99.5 or 99.9 %.

In other embodiments, the multispecific, e.g., a bispecific, antibody molecule that includes:

20 (i) a first heavy chain polypeptide (HCP1) (e.g., a heavy chain polypeptide comprising one, two, three or all of a first heavy chain variable region (first VH), a first CH1, a first heavy chain constant region (e.g., a first CH2, a first CH3, or both)), e.g., wherein the HCP1 binds to a first epitope;

(ii) a second heavy chain polypeptide (HCP2) (e.g., a heavy chain polypeptide
25 comprising one, two, three or all of a second heavy chain variable region (second VH), a second CH1, a second heavy chain constant region (e.g., a second CH2, a second CH3, or both)), e.g., wherein the HCP2 binds to a second epitope;

(iii) a lambda light chain polypeptide (LLCP1) (e.g., a lambda light variable region (VL1), a lambda light constant chain (VL1), or both) that preferentially associates with the first
30 heavy chain polypeptide (e.g., the first VH), e.g., wherein the LLCP1 binds to a first epitope; and

(iv) a kappa light chain polypeptide (KLCP2) (e.g., a lambda light variable region (VLk), a lambda light constant chain (VLk), or both) that preferentially associates with the second heavy chain polypeptide (e.g., the second VH), e.g., wherein the KLCP2 binds to a second epitope.

In embodiments, the first and second heavy chain polypeptides form an Fc interface that enhances heterodimerization. In embodiments, the multispecific antibody molecule has a first binding specificity that includes a hybrid VL1-CL1 heterodimerized to a first heavy chain variable region connected to the Fc constant, CH2-CH3 domain (having a knob modification) and a second binding specificity that includes a hybrid VLk-CLk heterodimerized to a second heavy chain variable region connected to the Fc constant, CH2-CH3 domain (having a hole modification).

Calreticulin-Targeting Antigen Binding Domains

The present disclosure provides, *inter alia*, multispecific (e.g., bi-, tri-, tetra- specific) or multifunctional molecules, that include, e.g., are engineered to contain, one or more antigen binding domains that bind to calreticulin, e.g., a wild-type calreticulin protein or a calreticulin mutant protein. In some embodiments, the multifunctional molecule binds to a wild-type calreticulin protein and a calreticulin mutant protein with similar affinity. In some embodiments, the multifunctional molecule preferentially binds to a calreticulin mutant protein over a wild type calreticulin protein.

An exemplary wild type human calreticulin is shown as SEQ ID NO: 6285.

EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDEEKDKGLQTSQD
ARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPNSLDQTD MHGDSEYNI
MFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCKDDEFTHLYTLIVRPDNTYEVKIDNSQ
VESGSLEDDWDFLPPKKIKDPDASKPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKK
PEDWDEEMDGEWEPPVIQNPEYKGEWKPRQIDNPDYKGTWIHPEIDNPEYSPDPSIYAY
DNFGVLGLDLWQVKSGTIFDNFLITNDEAYAEFEGNETWGVTKAAEKQMKDKQDEEQ
RLKEEEEDKKRKEEEEAEDKEDDEDKDEDEEDEEDKEEDEEEDVPGQAKDEL (SEQ ID
NO: 6285)

Calreticulin mutant proteins have been identified and found to be associated with myeloid cancers, e.g., see Nangalia et al., N Engl J Med. 2013 Dec 19;369(25):2391-2405, Klampfl et al., N Engl J Med. 2013 Dec 19;369(25):2379-90, and US20170269092, herein incorporated by

reference in their entirety. Mutant calreticulin has a frameshift in exon 9 of the coding sequence of wild type calreticulin, resulting in the replacement of the C-terminal negatively charged amino acids of wild type calreticulin by a predominantly positively charged polypeptide. Table 2 discloses full-length amino acid sequences of 36 calreticulin mutant proteins. Table 3 discloses the C-terminal amino acid sequences of the 36 calreticulin mutant proteins. All 36 calreticulin mutant proteins comprise the amino acid sequence of RRKMSPARPRTSCREACLQGWTEA (SEQ ID NO: 6286).

The predominant mutations of calreticulin are Type 1 and Type 2 mutations (see Tables 2 and 3). Type 1 mutation is a 52-bp deletion (c.1092_1143del) whereas Type 2 mutation is a 5-bp insertion (c.1154_1155insTTGTC).

Table 2. Full-length amino acid sequences of calreticulin mutants

SEQ ID NO	Type	Full length sequences of insertion/deletion frameshift mutations of calreticulin
SEQ ID NO: 6313	Type 1	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMHGDSEYNIMFGPDICPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRTTRMMRTKMRMRMRRTTRRKMRKMSPARPRTSCREACLQGWTEA
SEQ ID NO: 6314	Type 2	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMHGDSEYNIMFGPDICPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEDKKRKEEEAEDNCRMMRTKMRMRMRRTTRRKMRKMSPARPRTSCREACLQGWTEA
SEQ ID NO: 6315	Type 3	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMHGDSEYNIMFGPDICPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRQRTTRMMRTKMRMRMRRTTRRKMRKMSPARPRTSCREACLQGWTEA
SEQ ID NO:	Type 4	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN

6316		SLDQTDMMHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEYKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLRRRQRTRRMMRTKMRMRMRRTRRKMRRKMSPARPRTSCR EACLQGWTEA
SEQ ID NO: 6317	Type 5	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMMHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEYKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEGQRTRRMMRTKMRMRMRRTRRKMRRKMSPARPRTSCREACLQ GWTEA
SEQ ID NO: 6318	Type 6	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMMHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEYKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEERRQRTRRMMRTKMRMRMRRTRRKMRRKMSPARPRTSCREACL QGWTEA
SEQ ID NO: 6319	Type 7	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMMHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEYKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLRRMMRTKMRMRMRRTRRKMRRKMSPARPRTSCREACLQ WTEA
SEQ ID NO: 6320	Type 8	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMMHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEYKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKRRQRTRRMMRTKMRMRMRRTRRKMRRKMSPARPRTSC REACLQGWTEA
SEQ ID NO: 6321	Type 9	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMMHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEYKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK

		QDEEQRLKEEEEDKKRKEEERQRTTRMMRTKMRMRRMRRTTRRKMR KMSPARPRTSCREACLQGWTEA
SEQ ID NO: 6322	Type 10	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWHPIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEDKKRKEEEDAEEDMCRMMRTKMRMRRMRRTTRRK RRKMSPARPRTSCREACLQGWTEA
SEQ ID NO: 6323	Type 11	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWHPIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRRRRRQRTTRMMRTKMRMRRMRRTTRRKMRMRRKMSPARPRTSC REACLQGWTEA
SEQ ID NO: 6324	Type 12	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWHPIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRRRRRQRTTRMMRTKMRMRRMRRTTRRKMRMRRKMSPARPRTSC REACLQGWTEA
SEQ ID NO: 6325	Type 13	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWHPIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRRRRRQRTTRMMRTKMRMRRMRRTTRRKMRMRRKMSPARPRTSC REACLQGWTEA
SEQ ID NO: 6316	Type 14	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWHPIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLRRRQRTTRMMRTKMRMRRMRRTTRRKMRMRRKMSPARPRTSC REACLQGWTEA
SEQ ID NO: 6326	Type 15	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK

		DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDNFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWHPIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLRRRERTRRMMRTKMRMRMRRTRRKMRRKMSPARPRTSCR EACLQGWTEA
SEQ ID NO: 6327	Type 16	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDNFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWHPIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLQRRQRTRRMMRTKMRMRMRRTRRKMRRKMSPARPRTSC REACLQGWTEA
SEQ ID NO: 6328	Type 17	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDNFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWHPIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKRRQWTRRMMRTKMRMRMRRTRRKMRRKMSPARPRTSC REACLQGWTEA
SEQ ID NO: 6329	Type 18	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDNFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWHPIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKRRMRTKMRMRMRRTRRKMRRKMSPARPRTSCREACLQ GWTEA
SEQ ID NO: 6330	Type 19	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDNFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWHPIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEERQRTRRMMRTKMRMRMRRTRRKMRRKMSPARPRTSC REACLQGWTEA
SEQ ID NO: 6331	Type 20	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDNFLPPKKIKDPDAS KPEDWDERAKIDDPDTSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWHPIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEGRRQRTRRMMRTKMRMRMRRTRRKMRRKMSPARP

		RTSCREACLQGWTEA
SEQ ID NO: 6332	Type 21	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEAFKRRRMMRTKMRMRMRRTRRKMRRKMSPARPR TSCREACLQGWTEA
SEQ ID NO: 6333	Type 22	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEDNAKRRRRQRTRRMMRTKMRMRMRRTRRKMRRK MSPARPRTSCREACLQGWTEA
SEQ ID NO: 6334	Type 23	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEDCVRRRQRTRRMMRTKMRMRMRRTRRKMRRKM SPARPRTSCREACLQGWTEA
SEQ ID NO: 6335	Type 24	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEDRRQRTRRMMRTKMRMRMRRTRRKMRRKMSPAR RTSCREACLQGWTEA
SEQ ID NO: 6336	Type 25	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEDKRQRTRRMMRTKMRMRMRRTRRKMRRKMSPAR PRTSCREACLQGWTEA
SEQ ID NO: 6337	Type 26	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDHMGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS

		KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNP DYKGTW IHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAE EFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEDKNAKRRRRQRTRMMRTKMRMRRMRRTTRRKMR KMSPARPRTSCREACLOGWTEA
SEQ ID NO: 6338	Type 27	EPAVYFKEQFLDGDGWT SRWIESKHKSDFGK FVLSSGKFYGD EEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTD MHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYE VKIDNSQVESGSLEDDWD FLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNP DYKGTW IHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAE EFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEDKCF AKRRRRQRTRMMRTKMRMRRMRRTTRRKMR RKMSPARPRTSCREACLOGWTEA
SEQ ID NO: 6339	Type 28	EPAVYFKEQFLDGDGWT SRWIESKHKSDFGK FVLSSGKFYGD EEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTD MHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYE VKIDNSQVESGSLEDDWD FLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNP DYKGTW IHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAE EFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEDKKRKRMMRTKMRMRRMRRTTRKMR RKMSPARP RTSCREACLOGWTEA
SEQ ID NO: 6340	Type 29	EPAVYFKEQFLDGDGWT SRWIESKHKSDFGK FVLSSGKFYGD EEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTD MHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYE VKIDNSQVESGSLEDDWD FLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNP DYKGTW IHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAE EFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEDKKRKEPPLCLRRMMRTKMRMRRMRRTTRKMR RK MSPARPRTSCREACLOGWTEA
SEQ ID NO: 6341	Type 30	EPAVYFKEQFLDGDGWT SRWIESKHKSDFGK FVLSSGKFYGD EEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTD MHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYE VKIDNSQVESGSLEDDWD FLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNP DYKGTW IHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAE EFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEDKKRKEDHPCRRMMRTKMRMRRMRRTTRKMR RK SPARPRTSCREACLOGWTEA
SEQ ID NO: 6342	Type 31	EPAVYFKEQFLDGDGWT SRWIESKHKSDFGK FVLSSGKFYGD EEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTD MHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYE VKIDNSQVESGSLEDDWD FLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNP DYKGTW IHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAE EFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEDKKRKEEEEAEGNCRRMMRTKMRMRRMRRTTRKMR RRKMSPARPRTSCREACLOGWTEA

SEQ ID NO: 6343	Type 32	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEDKKRKEEEEAEDCRRMMRTKMRMRMRRTTRRKMRR KMSPARPRTSCREACLQGWTEA
SEQ ID NO: 6344	Type 33	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEDKKRKEEEEAEDCRRMMRTKMRMRMRRTTRRKM RRKMSPARPRTSCREACLQGWTEA
SEQ ID NO: 6345	Type 34	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEDKKRKEEEEAEDTCRRMMRTKMRMRMRRTTRRKM RKMSPARPRTSCREACLQGWTEA
SEQ ID NO: 6346	Type 35	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEDKKRKEEEEAEDICRRMMRTKMRMRMRRTTRRKM RKMSPARPRTSCREACLQGWTEA
SEQ ID NO: 6344	Type 36	EPAVYFKEQFLDGDGWTSRWIESKHKSDFGKFVLSSGKFYGDDEEKDKGL QTSQDARFYALSASFEPFSNKGQTLVVQFTVKHEQNIDCGGGYVKLFPN SLDQTDMHGDSEYNIMFGPDICGPGTKKVHVIFNYKGKNVLINKDIRCK DDEFTHLYTLIVRPDNTYEVKIDNSQVESGSLEDDWDFLPPKKIKDPDAS KPEDWDERAKIDDPTDSKPEDWDKPEHIPDPDAKKPEDWDEEMDGEWE PPVIQNPEYKGEWKPRQIDNPDYKGTWIIHPEIDNPEYSPDPSIAYDNFG VLGLDLWQVKSGTIFDNFLITNDEAYAEFGNETWGVTKAAEKQMKDK QDEEQRLKEEEEDKKRKEEEEAEDCRRMMRTKMRMRMRRTTRRKM RRKMSPARPRTSCREACLQGWTEA

Table 3. The C-terminal amino acid sequences of calreticulin mutants

SEQ ID NO	Type	C-terminal sequences of insertion/deletion frameshift mutations of calreticulin
SEQ ID NO: 6287	Type 1	TRRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6288	Type 2	NCRRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6289	Type 3	QRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6290	Type 4	RRRQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6291	Type 5	GQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6292	Type 6	RRQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6293	Type 7	RRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6292	Type 8	RRQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6294	Type 9	RQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6295	Type 10	MCRRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6296	Type 11	DQRQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 152	Type 12	RRRRQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6297	Type 13	QRRRQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6290	Type 14	RRRQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6298	Type 15	RRRERTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6299	Type 16	QRRQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6300	Type 17	RRQWTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6301	Type 18	RMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6294	Type 19	RQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6302	Type 20	GRRQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6303	Type 21	AFKRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6304	Type 22	NAKRRRRQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA
SEQ ID NO: 6305	Type 23	CVRRRRQRTRMMRTKMRMRMRRTTRRKMRKMSPARPTSCREACLQGWTEA

SEQ ID NO: 6292	Type 24	RRQRTRRMMRTKMRMRRMRRTRRKMRRKMSPARPRTSCR EACLGWTEA
SEQ ID NO: 6294	Type 25	RQRTRRMMRTKMRMRRMRRTRRKMRRKMSPARPRTSCRE ACLGWTEA
SEQ ID NO: 6304	Type 26	NAKRRRRQRTRRMMRTKMRMRRMRRTRRKMRRKMSPARP RTSCREACLGWTEA
SEQ ID NO: 6306	Type 27	CFAKRRRRQRTRRMMRTKMRMRRMRRTRRKMRRKMSPAR PRTSCREACLGWTEA
SEQ ID NO: 6293	Type 28	RRMMRTKMRMRRMRRTRRKMRRKMSPARPRTSCREACLG WTEA
SEQ ID NO: 6307	Type 29	PPLCLRRMMRTKMRMRRMRRTRRKMRRKMSPARPRTSCRE ACLGWTEA
SEQ ID NO: 6308	Type 30	DHPCRRMMRTKMRMRRMRRTRRKMRRKMSPARPRTSCRE ACLGWTEA
SEQ ID NO: 6309	Type 31	GNCRRMMRTKMRMRRMRRTRRKMRRKMSPARPRTSCREA CLGWTEA
SEQ ID NO: 6310	Type 32	CRRMMRTKMRMRRMRRTRRKMRRKMSPARPRTSCREACL QGWTEA
SEQ ID NO: 6310	Type 33	CRRMMRTKMRMRRMRRTRRKMRRKMSPARPRTSCREACL QGWTEA
SEQ ID NO: 6311	Type 34	TCRRMMRTKMRMRRMRRTRRKMRRKMSPARPRTSCREAC LQGWTEA
SEQ ID NO: 6312	Type 35	ICRRMMRTKMRMRRMRRTRRKMRRKMSPARPRTSCREACL QGWTEA
SEQ ID NO: 6310	Type 36	CRRMMRTKMRMRRMRRTRRKMRRKMSPARPRTSCREACL QGWTEA

In some embodiments, the calreticulin-targeting antigen binding domain comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in Tables 4-7.

- 5 In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising one, two, three CDRs from murine 16B11.1 antibody, e.g., as described in Table 4. For example, in some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6358 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g.,
- 10 substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6360 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 227 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising a heavy chain
- 15 complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6358

(or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6360 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 227 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6358 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6360 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 227 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6358 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6360 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 227 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

Alternatively, or in combination with the calreticulin-targeting antigen binding domain comprising the VH comprising one, two, three CDRs from murine 16B11.1 antibody, the calreticulin-targeting antigen binding domain comprises a VL comprising one, two or three CDRs derived from murine 16B11.1 antibody, e.g., as described in Table 4. For example, in some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 251 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 246 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 248 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 251, a VLCDR2 amino acid sequence of SEQ ID NO: 253, and a VLCDR3 amino acid sequence

of SEQ ID NO: 255. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 258, a VLCDR2 amino acid sequence of SEQ ID NO: 260, and a VLCDR3 amino acid sequence of SEQ ID NO: 262. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL
 5 comprising a VLCDR1 amino acid sequence of SEQ ID NO: 265, a VLCDR2 amino acid sequence of SEQ ID NO: 267, and a VLCDR3 amino acid sequence of SEQ ID NO: 269. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 272, a VLCDR2 amino acid sequence of SEQ ID NO: 274, and a VLCDR3 amino acid sequence of SEQ ID NO: 276. In
 10 some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 279, a VLCDR2 amino acid sequence of SEQ ID NO: 281, and a VLCDR3 amino acid sequence of SEQ ID NO: 283.

In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH
 15 comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6253 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6254 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6255 (or a sequence with no more than
 20 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6253, a VHCDR2 amino acid sequence of SEQ ID NO: 6254, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6255.

In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL
 25 comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6259 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6260 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6261 (or a sequence with no more than 1, 2, 3, or
 30 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a VLCDR1 amino acid sequence

of SEQ ID NO: 6259, a VLCDR2 amino acid sequence of SEQ ID NO: 6260, and a VLCDR3 amino acid sequence of SEQ ID NO: 6261.

In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising one, two, three, or four framework regions from humanized 16B11.1 antibody, e.g., as
 5 described in Table 4. For example, in some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6357, a VHFWR2 amino acid sequence of SEQ ID NO: 6359, a VHFWR3 amino acid sequence of SEQ ID NO: 6361, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6273. In some embodiments, the calreticulin-targeting antigen binding
 10 domain comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6362, a VHFWR2 amino acid sequence of SEQ ID NO: 6363, a VHFWR3 amino acid sequence of SEQ ID NO: 226, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 228. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence
 15 of SEQ ID NO: 229, a VHFWR2 amino acid sequence of SEQ ID NO: 6369, a VHFWR3 amino acid sequence of SEQ ID NO: 6371, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 228. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6373, a VHFWR2 amino acid sequence of SEQ ID NO: 6369, a VHFWR3 amino acid sequence
 20 of SEQ ID NO: 6371, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 228.

In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6374, a VLFWR2 amino acid sequence of SEQ ID NO: 6375, a VLFWR3 amino acid sequence of SEQ ID NO: 247, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 249. In some
 25 embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 250, a VLFWR2 amino acid sequence of SEQ ID NO: 252, a VLFWR3 amino acid sequence of SEQ ID NO: 254, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 256. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a
 30 light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 257, a VLFWR2 amino acid sequence of SEQ ID NO: 259, a VLFWR3 amino acid sequence of SEQ

ID NO: 261, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 263. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 264, a VLFWR2 amino acid sequence of SEQ ID NO: 266, a VLFWR3 amino acid sequence of SEQ ID NO: 268, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 270. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 271, a VLFWR2 amino acid sequence of SEQ ID NO: 273, a VLFWR3 amino acid sequence of SEQ ID NO: 275, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 277. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 278, a VLFWR2 amino acid sequence of SEQ ID NO: 280, a VLFWR3 amino acid sequence of SEQ ID NO: 282, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 284.

In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6224, a VHFWR2 amino acid sequence of SEQ ID NO: 6226, a VHFWR3 amino acid sequence of SEQ ID NO: 6228, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6230. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6238, a VLFWR2 amino acid sequence of SEQ ID NO: 6240, a VLFWR3 amino acid sequence of SEQ ID NO: 6242, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6244. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6263 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions), a VHFWR2 amino acid sequence of SEQ ID NO: 6264 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions), a VHFWR3 amino acid sequence of SEQ ID NO: 6265 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 228. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6277 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ

ID NO: 6278 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6279 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6280. In some embodiments, the calreticulin-targeting antigen binding domain
 5 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6263, a VHFWR2 amino acid sequence of SEQ ID NO: 6264, a VHFWR3 amino acid sequence of SEQ ID NO: 6265, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 228. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6277, a VLFWR2 amino acid sequence of SEQ ID NO: 6278, a
 10 VLFWR3 amino acid sequence of SEQ ID NO: 6279, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6280.

In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6347 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6347). In
 15 some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6348 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6348). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6349 (or an amino acid sequence having at
 20 least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6349). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6350 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6350). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH
 25 comprising the amino acid sequence of SEQ ID NO: 6351 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6351). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6352 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6352). In some embodiments,
 30 the calreticulin-targeting antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6353 (or an amino acid sequence having at least about 93%, 95%, or

99% sequence identity to SEQ ID NO: 6353). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6354 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6354). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6355 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6355). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6356 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6356).

In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6247 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6247). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6249 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6249). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6247. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 6249. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6247, and a VL comprising the amino acid sequence of SEQ ID NO: 6249.

Table 4. Exemplary heavy chain CDRs and FWRs of calreticulin-targeting antigen binding domains

Ab ID	VHFWR1	VHCDR1	VHFWR2	VHCDR2	VHFWR3	VHCDR3	VHFWR4
AbH-1H	QVQLVQS GAEVKKP GASVKVS CKASG (SEQ ID NO: 6263)	YSFTGYI H (SEQ ID NO: 6253)	WVRQAP GQELGW MG (SEQ ID NO: 6264)	YISCYNG ASSYNQK FKG (SEQ ID NO: 6254)	RVTMTVD TSISTAYT ELSSLRSE DTATYYC A (SEQ ID NO: 6265)	SSMDY (SEQ ID NO: 6255)	WGQGT LVTVSS (SEQ ID NO: 228)
AbH-2H	QVTLKES GPVLVKP TETLTLC TVSG	YSITSDYA WN (SEQ ID NO: 6256)	WIRQPPG KALEWLA (SEQ ID NO: 6267)	YISYSGST SYNPSLK S (SEQ ID NO: 6257)	RLSITKDT SKSQVVL TMTNMD PVDATY	DPPYY YGS (SEQ ID NO:	WGQGT TVTSS (SEQ ID NO: 6269)

	(SEQ ID NO: 6266)				YCAR (SEQ ID NO: 6268)	6258)	
AbM-1H	EVQLEQS GPVLVKT GASVKIS CKASG (SEQ ID NO: 6270)	YSFTGYI H (SEQ ID NO: 6253)	WVKQSH GKSLEWI G (SEQ ID NO: 6271)	YISCYNG ASSYNQK FKG (SEQ ID NO: 6254)	KATFTVD TSSSTAY MQFNSLT SGDSAVY YCA (SEQ ID NO: 6272)	SSMDY (SEQ ID NO: 6255)	WGQGT S VTVSS (SEQ ID NO: 6273)
AbM-2H	DVQLQES GPGLVKN SQSLSLTC TVTG (SEQ ID NO: 6274)	YSITSDYA WN (SEQ ID NO: 6256)	WIRQFPG NKLEWM G (SEQ ID NO: 6275)	YISYSGST SYNPSLK S (SEQ ID NO: 6257)	RISITRDT SKNQFFL QLNSVTP EDTATYY CAR (SEQ ID NO: 6276)	DPPYY YGSNG T (SEQ ID NO: 6262)	WGQGT S VTVSS (SEQ ID NO: 6273)
Murine anti-calreticulin antibody 16B11.1 heavy chain variable region	EVKLVE SGGGLV KPGGSL KLSCAA SGFA (SEQ ID NO: 6357)	FSRYDM S (SEQ ID NO: 6358)	WVRQTP EKRLEW VA (SEQ ID NO: 6359)	TISSGGS YTYYPD SVKG (SEQ ID NO: 6360)	RFTISR D NARNTL YLQMSS LRSEDTA LYYCAR (SEQ ID NO: 6361)	HSAYY VNYEN AMDY (SEQ ID NO: 227)	WGQGT S VTVSS (SEQ ID NO: 6273)
Humanized anti-calreticulin heavy chain variable region variant 1	QVQLVE SGGGLV KPGGSL RLSCAA SGFA (SEQ ID NO: 6362)	FSRYDM S (SEQ ID NO: 6358)	WIRQAP GKGLEW VA (SEQ ID NO: 6363)	TISSGGS YTYYPD SVKG (SEQ ID NO: 6360)	RFTISR D NAKNSL YLQMNS LRAEDT AVYYCA R (SEQ ID NO: 226)	HSAYY VNYEN AMDY (SEQ ID NO: 227)	WGQGT S LTVSS (SEQ ID NO: 228)
Humanized anti-calreticulin heavy chain variable region variant 2	QVQLVE SGGGVV QPGRSL RLSCAA SGFA (SEQ ID NO: 229)	FSRYDM S (SEQ ID NO: 6358)	WVRQAP GKGLEW VA (SEQ ID NO: 6369)	TISSGGS YTYYPD SVKG (SEQ ID NO: 6360)	RFTISR D NSKNTL YLQMNS LRAEDT AVYYCA R (SEQ ID NO: 6371)	HSAYY VNYEN AMDY (SEQ ID NO: 227)	WGQGT S LTVSS (SEQ ID NO: 228)
Humanized anti-calreticulin heavy chain variable region variant 3	EVQLVE SGGGLV QPGGSL RLSCAA SGFA (SEQ ID NO: 6373)	FSRYDM S (SEQ ID NO: 6358)	WVRQAP GKGLEW VA (SEQ ID NO: 6369)	TISSGGS YTYYPD SVKG (SEQ ID NO: 6360)	RFTISR D NSKNTL YLQMNS LRAEDT AVYYCA R (SEQ ID NO: 6371)	HSAYY VNYEN AMDY (SEQ ID NO: 227)	WGQGT S LTVSS (SEQ ID NO: 228)

Table 5. Exemplary light chain CDRs and FWRs of calreticulin-targeting antigen binding domains

Ab ID	FWR1	CDR1	FWR2	CDR2	FWR3	CDR3	FWR4
AbH-1L /	DVVMTQS	KSSQSLL	WLQQRPG	LVSKLDS	GVPDRFS	WQGT	FGGGTK

AbH-2L	PLSLPVTL GQPASISC (SEQ ID NO: 6277)	DSDGKTY LN (SEQ ID NO: 6259)	QSPRRLIY (SEQ ID NO: 6278)	(SEQ ID NO: 6260)	GSGSGTD FTLKISRV EAEDVGV YHC (SEQ ID NO: 6279)	HFPLYT (SEQ ID NO: 6261)	VEIK (SEQ ID NO: 6280)
AbM-1L / AbM-2L	DVVMQTQ TPLTLSVT IGQPASIS C (SEQ ID NO: 6281)	KSSQSLL DSDGKTY LN (SEQ ID NO: 6259)	WLLQRP QSPKRLIY (SEQ ID NO: 6282)	LVSCLDS (SEQ ID NO: 6260)	GVPDRFT GSGSGTD FTLKISRV EAEDLGV YHC (SEQ ID NO: 6283)	WQGT HFPLYT (SEQ ID NO: 6261)	FGGGTKL EIK (SEQ ID NO: 6284)
Murine anti- calreticulin antibody 16B11.1 light chain variable region	NIVLTQS PASLAVS LGQRATIS C (SEQ ID NO: 6374)	RASESV DSFGISF MH (SEQ ID NO: 251)	WYQQR GQPPKL LIY (SEQ ID NO: 6375)	LASNLES (SEQ ID NO: 246)	GVPARF SGSGSRT DFTLTID PVEADD AATYYC (SEQ ID NO: 247)	QQNN EDPL T (SEQ ID NO: 248)	FGAGTK LELK (SEQ ID NO: 249)
Humanized anti- calreticulin light chain variable region variant 1	DIVLTQT PLSLSVT PGQPASI SC (SEQ ID NO: 250)	RASESV DSFGISF MH (SEQ ID NO: 251)	WYLQKP GQSPQL LIY (SEQ ID NO: 252)	LASNLES (SEQ ID NO: 253)	GVPDRF SGSGSRT DFTLKIS RVEAED VGYYC (SEQ ID NO: 254)	QQNN EDPL T (SEQ ID NO: 255)	FGQGTK LEIK (SEQ ID NO: 256)
Humanized anti- calreticulin light chain variable region variant 2	DIVLTQS PLSLPVT LGQPASI SC (SEQ ID NO: 257)	RASESV DSFGISF MH (SEQ ID NO: 258)	WYQQR GQSPRL LIY (SEQ ID NO: 259)	LASNLES (SEQ ID NO: 260)	GVPDRF SGSGSRT DFTLKIS RVEAED VGYYC (SEQ ID NO: 261)	QQNN EDPL T (SEQ ID NO: 262)	FGQGTK LEIK (SEQ ID NO: 263)
Humanized anti- calreticulin light chain variable region variant 3	DIVLTQT PLSLPVT PGEPASI SC (SEQ ID NO: 264)	RASESV DSFGISF MH (SEQ ID NO: 265)	WYLQKP GQSPQL LIY (SEQ ID NO: 266)	LASNLES (SEQ ID NO: 267)	GVPDRF SGSGSRT DFTLKIS RVEAED VGYYC (SEQ ID NO: 268)	QQNN EDPL T (SEQ ID NO: 269)	FGQGTK LEIK (SEQ ID NO: 270)
Humanized anti- calreticulin light chain variable region variant 4	EIVLTQS PATLSLS PGERATL SC (SEQ ID NO: 271)	RASESV DSFGISF MH (SEQ ID NO: 272)	WYQKP GQAPRL LIY (SEQ ID NO: 273)	LASNLES (SEQ ID NO: 274)	GIPARF SGSGSRT DFTLTIS SLEPEDF AVYYC (SEQ ID NO: 275)	QQNN EDPL T (SEQ ID NO: 276)	FGQGTK LEIK (SEQ ID NO: 277)
Humanized anti- calreticulin light chain	DIQLTQS PSSLSAS VGDRVITI TC (SEQ	RASESV DSFGISF MH (SEQ ID NO:	WYQKP GKAPKL LIY (SEQ ID NO:	LASNLES (SEQ ID NO: 281)	GVPSRFS SGSGSRT DFTFTIS SLQPEDI	QQNN EDPL T (SEQ ID NO:	FGQGTK LEIK (SEQ ID NO: 284)

variable region variant 5	ID NO: 278)	279)	280)		ATYYC (SEQ ID NO: 282)	283)	

Table 6. Exemplary FWRs of calreticulin-targeting antigen binding

SEQ ID NO	Description	Sequence
SEQ ID NO: 6224	Ab-1 VHFWR1	X ₁ VQLX ₂ QSGX ₃ EX ₄ X ₅ KX ₆ GASVKX ₇ SCKASG, wherein: X ₁ is not E, X ₂ is not E, X ₃ is not P, X ₄ is not L, X ₅ is not V, X ₆ is not T, or X ₇ is not I
SEQ ID NO: 6226	Ab-1 VHFWR2	WVX ₁ QX ₂ X ₃ GX ₄ X ₅ LX ₆ WX ₇ G, wherein: X ₁ is not K, X ₂ is not S, X ₃ is not H, X ₄ is not K, X ₅ is not S, X ₆ is not E, or X ₇ is not I
SEQ ID NO: 6228	Ab-1 VHFWR3	X ₁ X ₂ TX ₃ TVDTX ₄ STAYX ₅ X ₆ X ₇ X ₈ SLX ₉ SX ₁₀ DX ₁₁ AX ₁₂ YYCA, wherein: X ₁ is not K, X ₂ is not A, X ₃ is not F, X ₄ is not S, X ₅ is not M, X ₆ is not Q, X ₇ is not F, X ₈ is not N, X ₉ is not T, X ₁₀ is not G, X ₁₁ is not S, or X ₁₂ is not V
SEQ ID NO: 6230	Ab-1 VHFWR4	WGQGTX ₁ VTVSS, wherein: X ₁ is not S
SEQ ID NO: 6232	Ab-2 VHFWR1	X ₁ VX ₂ LX ₃ ESGPX ₄ LVKX ₅ X ₆ X ₇ X ₈ LX ₉ LTCTVX ₁₀ G, wherein: X ₁ is not D, X ₂ is not Q, X ₃ is not Q, X ₄ is not G, X ₅ is not N, X ₆ is not S, X ₇ is not Q, X ₈ is not S, X ₉ is not S, or X ₁₀ is not T

SEQ ID NO: 6234	Ab-2 VHFWR2	WIRQX ₁ PGX ₂ X ₃ LEWX ₄ X ₅ , wherein: X ₁ is not F, X ₂ is not N, X ₃ is not K, X ₄ is not M, or X ₅ is not G
SEQ ID NO: 6236	Ab-2 VHFWR3	RX ₁ SITX ₂ DTSKX ₃ QX ₄ X ₅ LX ₆ X ₇ X ₈ X ₉ X ₁₀ X ₁₁ PX ₁₂ DTATYYCAR, wherein: X ₁ is not I, X ₂ is not R, X ₃ is not N, X ₄ is not F, X ₅ is not F, X ₆ is not Q, X ₇ is not L, X ₈ is not N, X ₉ is not S, X ₁₀ is not V, X ₁₁ is not T, or X ₁₂ is not E
SEQ ID NO: 6230	Ab-2 VHFWR4	WGQGTGX ₁ VTVSS, wherein: X ₁ is not S
SEQ ID NO: 6238	Ab-1/2 VLFWR1	DVVMQTQX ₁ PLX ₂ LX ₃ VTX ₄ GQPASISC, wherein: X ₁ is not T, X ₂ is not T, X ₃ is not S, or X ₄ is not I
SEQ ID NO: 6240	Ab-1/2 VLFWR2	WLX ₁ QRPQGSPX ₂ RLIY, wherein: X ₁ is not L, or X ₂ is not K
SEQ ID NO: 6242	Ab-1/2 VLFWR3	GVPDRFX ₁ GSGSGTDFTLKISRVEAEDX ₂ GVYHC, wherein: X ₁ is not T, or X ₂ is not L
SEQ ID NO: 6244	Ab-1/2 VLFWR4	FGGGTKX ₁ EIK, wherein: X ₁ is not L

Table 7A. Exemplary variable regions of calreticulin-targeting antigen binding (underlining indicates CDR sequences)

SEQ ID NO	Description	Sequence
SEQ ID NO: 6247	AbH-1 heavy chain variable region	QVQLVQSGAEVKKPGASVKVSCKASGYSFTGYYIHWVRQA PGQELGWMGYISCYNGASSYNQKFKGRVTMTVDTSISTAYT ELSSLRSEDATYYCA SSMDYWGQGTLVTVSS
SEQ ID NO: 6248	AbH-2 heavy chain variable region	QVTLKESGPVLVKPTETLTCTVSGYSITSDYAWNWRQPP GKALEWLAYISYSGSTSYNPSLKSRLSITKDTSKSQVVLMT NMDPVDATYYCARDPPYYYGSWGQGTTVTVSS
SEQ ID NO: 6249	AbH-1 / AbH-2 light chain variable region	DVVMTQSPLSLPVTLGQPASISCKSSQSLLDSGKTYLNWLQ QRPQGSPRRLIYLVSKLDSGVPDRFSGSGSGTDFTLKISRVEA EDVGVIHCWQGTHFPYTFGGGTVKVEIK

SEQ ID NO: 6250	AbM-1 heavy chain variable region	EVQLEQSGPELVKTGASVKISCKASGYSTGYIHWVKQSHG KSLEWIGYISCYNGASSYNQKFKGKATFTVDTSSSTAYMQFN SLTSGDSAVYYCA SSMDYWGQGTSTVTVSS
SEQ ID NO: 6251	AbM-2 heavy chain variable region	DVQLQESGPGLVKNSQSLTCTVTGYSITSDYAWNWRQFP GNKLEWMGYISYSGSTSYNPSLKSRSITRDTSKNQFFLQLNS VTPEDTATYYCA RDPPYYYGSNGTWGQGTSTVTVSS
SEQ ID NO: 6252	AbM-1 / AbM- 2 light chain variable region	DVVMQTPTLTLSTIGQPASISCKSSQSLDSDGKTYLNWLL QRPQGSPKRLIYLVSKLDSGVPDRFTGSGSGTDFTLKISRVEA EDLGVYHCWQGTTHFPYTFGGGTKLEIK
SEQ ID NO: 6347	Murine anti- calreticulin antibody 16B11.1 heavy chain variable region	EVKLVESGGGLVKPGGSLKLSAASGFAFSRYDMSWVRQTP EKRLEWVATISSGGSYTYYPDSVKGRFTISRDNARNTLYLQM SSLRSEDALYYCARHSAYYVNYENAMDYWGQGTSTVTVSS
SEQ ID NO: 6348	Murine anti- calreticulin antibody 16B11.1 light chain variable region	NIVLTQSPASLAVSLGQRATISCRASESVDSFGISFMHWYQQR PGQPPKLLIYLASNLESGVPARFSGSGSRTDFTLTIDPVEADD AATYYCQNNEDPLTFGAGTKLELK
SEQ ID NO: 6349	Humanized anti-calreticulin heavy chain variable region variant 1	QVQLVESGGGLVKPGGSLRLSAAASGFAFSRYDMSWVRQAP GKGLEWVATISSGGSYTYYPDSVKGRFTISRDNANKNSLYLQ MNSLRAEDTAVYYCARHSAYYVNYENAMDYWGQGTSLTVV SS
SEQ ID NO: 6350	Humanized anti-calreticulin heavy chain variable region variant 2	QVQLVESGGGVVQPGSLRLSAAASGFAFSRYDMSWVRQAP GKGLEWVATISSGGSYTYYPDSVKGRFTISRDNANKNTLYLQM NSLRAEDTAVYYCARHSAYYVNYENAMDYWGQGTSLTVS S
SEQ ID NO: 6351	Humanized anti-calreticulin heavy chain variable region variant 3	EVQLVESGGGLVQPGGSLRLSAAASGFAFSRYDMSWVRQAP GKGLEWVATISSGGSYTYYPDSVKGRFTISRDNANKNTLYLQM NSLRAEDTAVYYCARHSAYYVNYENAMDYWGQGTSLTVS S
SEQ ID NO: 6352	Humanized anti-calreticulin light chain variable region variant 1	DIVLTQTPLSLSVTPGQPASISCRASESVDSFGISFMHWYLQK PGQSPQLLIYLAASNLESGVPDRFSGSGSRTDFTLKISRVEAED VGVYYCQNNEDPLTFGQGTKEIK
SEQ ID NO: 6353	Humanized anti-calreticulin light chain variable region variant 2	DIVLTQSPLSLPVTLGQPASISCRASESVDSFGISFMHWYQQR PGQSPRLLIYLAASNLESGVPDRFSGSGSRTDFTLKISRVEAED VGVYYCQNNEDPLTFGQGTKEIK
SEQ ID NO: 6354	Humanized anti-calreticulin light chain variable region	DIVLTQTPLSLPVTGEPASISCRASESVDSFGISFMHWYLQKP GQSPQLLIYLAASNLESGVPDRFSGSGSRTDFTLKISRVEAEDV GVYYCQNNEDPLTFGQGTKEIK

	variant 3	
SEQ ID NO: 6355	Humanized anti-calreticulin light chain variable region variant 4	EIVLTQSPATLSLSPGERATLSCRASESVDSEFGISFMHWYQQK PGQAPRLLIYLASNLESGIPARFSGSGSRTDFTLTISSELPEDFA VYYCQONNEDPLTFGQGTKLEIK
SEQ ID NO: 6356	Humanized anti-calreticulin light chain variable region variant 5	DIQLTQSPSSLSASVGDRVTITCRASESVDSFGISFMHWYQQK PGKAPKLLIYLASNLESGVPSRFSGSGSRTDFTFTISLQPEDIA TYYCQONNEDPLTFGQGTKLEIK

Additional calreticulin-targeting antigen binding domains

In some embodiments, the calreticulin-targeting antigen binding domain comprises any CDR amino acid sequence or variable region amino acid sequence disclosed in Tables 16-19. In

5 some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6253 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 243 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions),

10 and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6255 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6253, a VHCDR2 amino acid sequence of SEQ ID NO: 243, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6255. In some embodiments, the

15 calreticulin-targeting antigen binding domain comprises a VL comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6259 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6260 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid

20 sequence of SEQ ID NO: 6261 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6259, a VLCDR2 amino acid sequence of SEQ ID NO: 6260, and a VLCDR3 amino acid sequence of SEQ ID NO: 6261. In some embodiments, the calreticulin-targeting antigen binding

domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 244 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 245 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 244 and/or a VL comprising the amino acid sequence of SEQ ID NO: 245. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6372, 234, 235, 236, or 237, or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VL comprising the amino acid sequence of SEQ ID NO: 238, 239, 240, 241, or 242, or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6372 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 238 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6372 and a VL comprising the amino acid sequence of SEQ ID NO: 238. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 234 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 238 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 234 and a VL comprising the amino acid sequence of SEQ ID NO: 238. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 235 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 238 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99%

sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 235 and a VL comprising the amino acid sequence of SEQ ID NO: 238. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 236 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 238 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 236 and a VL comprising the amino acid sequence of SEQ ID NO: 238. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 237 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 238 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 237 and a VL comprising the amino acid sequence of SEQ ID NO: 238. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6372 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 239 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6372 and a VL comprising the amino acid sequence of SEQ ID NO: 239. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 234 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 239 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 234 and a VL comprising the amino acid sequence of SEQ ID NO: 239. In some embodiments, the

calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 235 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 239 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 235 and a VL comprising the amino acid sequence of SEQ ID NO: 239. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 236 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 239 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 236 and a VL comprising the amino acid sequence of SEQ ID NO: 239. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 237 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 239 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 237 and a VL comprising the amino acid sequence of SEQ ID NO: 239. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6372 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 240 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6372 and a VL comprising the amino acid sequence of SEQ ID NO: 240. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 234 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ

ID NO: 240 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 234 and a VL comprising the amino acid sequence of SEQ ID NO: 240. In some embodiments, the

5 calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 235 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 240 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding

10 domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 235 and a VL comprising the amino acid sequence of SEQ ID NO: 240. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 236 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ

15 ID NO: 240 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 236 and a VL comprising the amino acid sequence of SEQ ID NO: 240. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid

20 sequence of SEQ ID NO: 237 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 240 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 237 and a VL

25 comprising the amino acid sequence of SEQ ID NO: 240. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6372 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 241 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or

30 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6372 and a VL

comprising the amino acid sequence of SEQ ID NO: 241. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 234 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ

5 ID NO: 241 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 234 and a VL comprising the amino acid sequence of SEQ ID NO: 241. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid

10 sequence of SEQ ID NO: 235 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 241 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 235 and a VL

15 comprising the amino acid sequence of SEQ ID NO: 241. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 236 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 241 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99%

20 sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 236 and a VL comprising the amino acid sequence of SEQ ID NO: 241. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 237 (or an amino acid sequence having at least about 80%, 85%, 90%,

25 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 241 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 237 and a VL comprising the amino acid sequence of SEQ ID NO: 241. In some embodiments, the

30 calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6372 (or an amino acid sequence having at least about 80%, 85%,

90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 242 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 6372 and a VL comprising the amino acid sequence of SEQ ID NO: 242. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 234 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 242 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 234 and a VL comprising the amino acid sequence of SEQ ID NO: 242. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 235 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 242 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 235 and a VL comprising the amino acid sequence of SEQ ID NO: 242. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 236 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 242 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 236 and a VL comprising the amino acid sequence of SEQ ID NO: 242. In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 237 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto) and a VL comprising the amino acid sequence of SEQ ID NO: 242 (or an amino acid sequence having at least about 80%, 85%, 90%, 95%, or 99% sequence identity thereto). In some embodiments, the calreticulin-targeting antigen binding

domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 237 and a VL comprising the amino acid sequence of SEQ ID NO: 242.

In some embodiments, the calreticulin-targeting antigen binding domain comprises a VH comprising the amino acid sequence of SEQ ID NO: 236 and a VL comprising the amino acid sequence of SEQ ID NO: 238.

5

Table 16. Exemplary variable regions of additional calreticulin-targeting antigen binding domains

SEQ ID NO	Description	Sequence
SEQ ID NO: 6372	BJ092 (VH)	QVQLVQSGAEVKKPGASVKVSCKASGYSFTGYYIHWVRQA PGQGLEWIGYISAYNGASSYNQKFKGRATFTVDTSTSTAYM ELRSLRSDDMAVYYCASSMDYWGQGLTVTVSS
SEQ ID NO: 234	BJ093 (VH)	QVQLVQSGAEVKKPGASVKVSCKASGYSFTGYYIHWVRQA PGQGLEWIGYISAYNGASSYNQKFKGRATFTVDTSTSTAYM ELRSLRSDDTAVYYCASSMDYWGQGLTVTVSS
SEQ ID NO: 235	BJ094 (VH)	QVQLVQSGAEVKKPGASVKVSCKASGYSFTGYYIHWVRQA PGKGLEWIGYISAYNGASSYNQKFKGRATFTVDTSTSTAYM ELSSLRSEDTAVYYCASSMDYWGQGLTVTVSS
SEQ ID NO: 236	BJ095 (VH)	QVQLVQSGAEVKKPGASVKVSCKASGYSFTGYYIHWVRQA PGQGLEWIGYISAYNGASSYNQKFKGRATFTVDTSTSTAYME LSRLRSDDTAVYYCASSMDYWGQGLTVTVSS
SEQ ID NO: 237	BJ096 (VH)	QVQLVQSGAEVKKPGASVKVSCKASGYSFTGYYIHWVRQA PGQGLEWIGYISAYNGASSYNQKFKGRATFTVDTSTSTAYM ELSSLRSEDTAVYYCASSMDYWGQGLTVTVSS
SEQ ID NO: 244	VH consensus	QVQLVQSGAEVKKPGASVKVSCKASGYSFTGYYIHWVRQA PGX ₁ GLEWIGYISAYNGASSYNQKFKGRATFTVDTSX ₂ STAY MELX ₃ X ₄ LRSDDX ₅ AVYYCASSMDYWGQGLTVTVSS, wherein: X ₁ is Q or K, X ₂ is I or T, X ₃ is S or R, X ₄ is R or S, or X ₅ is T or M
SEQ ID NO: 238	BJ097 (VL)	DVVMTQSPVLTGQPASISCKSSQSLDSDGKTYLNWLQ QRPQGSPKRLIYLVSKLDSGVPDRFSGSGSGTDFTLKISRVEA EDVGVYHCWQGTHFPYTFGQGTKLEIK
SEQ ID NO: 239	BJ098 (VL)	DVVMTQTPLSVTPGQPASISCKSSQSLDSDGKTYLNWLL QKPGQSPKLLIYLVSKLDSGVPDRFSGSGSGTDFTLKISRVEA EDVGVYHCWQGTHFPYTFGQGTKLEIK
SEQ ID NO: 240	BJ099 (VL)	DVVMTQTPLSVTPGQPASISCKSSQSLDSDGKTYLNWLL QKPGQPPKLLIYLVSKLDSGVPDRFSGSGSGTDFTLKISRVEA EDVGVYHCWQGTHFPYTFGQGTKLEIK
SEQ ID NO: 241	BJ100 (VL)	DVVMTQTPLSSPVTGQPASISCKSSQSLDSDGKTYLNWLQ QRPQGPPKLLIYLVSKLDSGVPDRFSGSGAGTDFTLKISRVEA EDVGVYHCWQGTHFPYTFGQGTKLEIK
SEQ ID NO: 242	BJ101 (VL)	DVVMTQSPVLTGPEPASISCKSSQSLDSDGKTYLNWLL QKPGQSPKLLIYLVSKLDSGVPDRFSGSGSGTDFTLKISRVEA

		EDVGVYHCWQGTHFPYTFGQGTKLEIK
SEQ ID NO: 245	VL consensus	DVVMTQX ₁ PLSX ₂ X ₃ VTX ₄ GX ₅ PASISCKSSQSLLSDGKTYLN WLX ₆ QX ₇ PGQX ₈ PKX ₉ LIYLVSKLDSGVPDRFSGSGX ₁₀ GTDFTL KISRVEAEDVGVYHCWQGTHFPYTFGQGTKLEIK, wherein: X ₁ is S or T, X ₂ is L or S, X ₃ is P or S, X ₄ is L or P, X ₅ is Q or E, X ₆ is Q or L, X ₇ is R or K, X ₈ is S or P, X ₉ is R or L, or X ₁₀ is S or A

Table 17. Exemplary heavy chain CDRs of calreticulin-targeting antigen binding domains

VH (SEQ ID NO)	VHCDR1 (SEQ ID NO)	VHCDR2 (SEQ ID NO)	VHCDR3 (SEQ ID NO)
BJ092 (SEQ ID NO: 6372)	YSFTGYYIH (SEQ ID NO: 6253)	YISAYNGASSYNQKFK G (SEQ ID NO: 243)	SSMDY (SEQ ID NO: 6255)
BJ093 (SEQ ID NO: 234)	YSFTGYYIH (SEQ ID NO: 6253)	YISAYNGASSYNQKFK G (SEQ ID NO: 243)	SSMDY (SEQ ID NO: 6255)
BJ094 (SEQ ID NO: 235)	YSFTGYYIH (SEQ ID NO: 6253)	YISAYNGASSYNQKFK G (SEQ ID NO: 243)	SSMDY (SEQ ID NO: 6255)
BJ095 (SEQ ID NO: 236)	YSFTGYYIH (SEQ ID NO: 6253)	YISAYNGASSYNQKFK G (SEQ ID NO: 243)	SSMDY (SEQ ID NO: 6255)
BJ096 (SEQ ID NO: 237)	YSFTGYYIH (SEQ ID NO: 6253)	YISAYNGASSYNQKFK G (SEQ ID NO: 243)	SSMDY (SEQ ID NO: 6255)

Table 18. Exemplary light chain CDRs of calreticulin-targeting antigen binding domains

VL (SEQ ID NO)	VLCDR1 (SEQ ID NO)	VLCDR2 (SEQ ID NO)	VLCDR3 (SEQ ID NO)
BJ097 (SEQ ID NO: 238)	KSSQSLLSDGKTYLN (SEQ ID NO: 6259)	LVSCLDS (SEQ ID NO: 6260)	WQGTHFPYT (SEQ ID NO: 6261)
BJ098 (SEQ ID NO: 239)	KSSQSLLSDGKTYLN (SEQ ID NO: 6259)	LVSCLDS (SEQ ID NO: 6260)	WQGTHFPYT (SEQ ID NO: 6261)
BJ099 (SEQ ID NO: 240)	KSSQSLLSDGKTYLN (SEQ ID NO: 6259)	LVSCLDS (SEQ ID NO: 6260)	WQGTHFPYT (SEQ ID NO: 6261)
BJ100 (SEQ ID NO: 241)	KSSQSLLSDGKTYLN (SEQ ID NO: 6259)	LVSCLDS (SEQ ID NO: 6260)	WQGTHFPYT (SEQ ID NO: 6261)
BJ101 (SEQ ID NO: 242)	KSSQSLLSDGKTYLN (SEQ ID NO: 6259)	LVSCLDS (SEQ ID NO: 6260)	WQGTHFPYT (SEQ ID NO: 6261)

5

Table 19. Exemplary calreticulin-targeting antigen binding domains

Antibody code	VH code	VH germline	VL code	VL germline
BJM0040	BJ092 (SEQ ID NO: 6372)	IGHV1-18*03	BJ097 (SEQ ID NO: 238)	IGKV2-30*01
BJM0041	BJ093 (SEQ ID NO: 234)	IGHV1-18*01	BJ097 (SEQ ID NO: 238)	IGKV2-30*01

BJM0042	BJ094 (SEQ ID NO: 235)	IGHV1-2*02	BJ097 (SEQ ID NO: 238)	IGKV2-30*01
BJM0043	BJ095 (SEQ ID NO: 236)	IGHV1-2*02	BJ097 (SEQ ID NO: 238)	IGKV2-30*01
BJM0044	BJ096 (SEQ ID NO: 237)	IGHV1-2*02	BJ097 (SEQ ID NO: 238)	IGKV2-30*01
BJM0045	BJ092 (SEQ ID NO: 6372)	IGHV1-18*03	BJ098 (SEQ ID NO: 239)	IGKV2-29*02
BJM0046	BJ093 (SEQ ID NO: 234)	IGHV1-18*01	BJ098 (SEQ ID NO: 239)	IGKV2-29*02
BJM0047	BJ094 (SEQ ID NO: 235)	IGHV1-2*02	BJ098 (SEQ ID NO: 239)	IGKV2-29*02
BJM0048	BJ095 (SEQ ID NO: 236)	IGHV1-2*02	BJ098 (SEQ ID NO: 239)	IGKV2-29*02
BJM0049	BJ096 (SEQ ID NO: 237)	IGHV1-2*02	BJ098 (SEQ ID NO: 239)	IGKV2-29*02
BJM0050	BJ092 (SEQ ID NO: 6372)	IGHV1-18*03	BJ099 (SEQ ID NO: 240)	IGKV2D-29*01
BJM0051	BJ093 (SEQ ID NO: 234)	IGHV1-18*01	BJ099 (SEQ ID NO: 240)	IGKV2D-29*01
BJM0052	BJ094 (SEQ ID NO: 235)	IGHV1-2*02	BJ099 (SEQ ID NO: 240)	IGKV2D-29*01
BJM0053	BJ095 (SEQ ID NO: 236)	IGHV1-2*02	BJ099 (SEQ ID NO: 240)	IGKV2D-29*01
BJM0054	BJ096 (SEQ ID NO: 237)	IGHV1-2*02	BJ099 (SEQ ID NO: 240)	IGKV2D-29*01
BJM0055	BJ092 (SEQ ID NO: 6372)	IGHV1-18*03	BJ100 (SEQ ID NO: 241)	IGKV2-24*01
BJM0056	BJ093 (SEQ ID NO: 234)	IGHV1-18*01	BJ100 (SEQ ID NO: 241)	IGKV2-24*01
BJM0057	BJ094 (SEQ ID NO: 235)	IGHV1-2*02	BJ100 (SEQ ID NO: 241)	IGKV2-24*01
BJM0058	BJ095 (SEQ ID NO: 236)	IGHV1-2*02	BJ100 (SEQ ID NO: 241)	IGKV2-24*01
BJM0059	BJ096 (SEQ ID NO: 237)	IGHV1-2*02	BJ100 (SEQ ID NO: 241)	IGKV2-24*01
BJM0060	BJ092 (SEQ ID NO: 6372)	IGHV1-18*03	BJ101 (SEQ ID NO: 242)	IGKV2-28*01
BJM0061	BJ093 (SEQ ID NO: 234)	IGHV1-18*01	BJ101 (SEQ ID NO: 242)	IGKV2-28*01
BJM0062	BJ094 (SEQ ID NO: 235)	IGHV1-2*02	BJ101 (SEQ ID NO: 242)	IGKV2-28*01
BJM0063	BJ095 (SEQ ID NO: 236)	IGHV1-2*02	BJ101 (SEQ ID NO: 242)	IGKV2-28*01
BJM0064	BJ096 (SEQ ID NO: 237)	IGHV1-2*02	BJ101 (SEQ ID NO: 242)	IGKV2-28*01

Immune Cell Engagers

The immune cell engagers of the multispecific or multifunctional molecules disclosed herein can mediate binding to, and/or activation of, an immune cell, e.g., an immune effector cell. In some embodiments, the immune cell is chosen from a T cell, an NK cell, a B cell, a dendritic cell, or a macrophage cell engager, or a combination thereof. In some embodiments, the immune cell engager is chosen from one, two, three, or all of a T cell engager, NK cell engager, a B cell engager, a dendritic cell engager, or a macrophage cell engager, or a combination thereof. The immune cell engager can be an agonist of the immune system. In some embodiments, the immune cell engager can be an antibody molecule, a ligand molecule (e.g., a ligand that further comprises an immunoglobulin constant region, e.g., an Fc region), a small molecule, or a nucleotide molecule.

T Cell Engagers

The present disclosure provides, *inter alia*, multispecific (e.g., bi-, tri-, quad- specific) or multifunctional molecules, that are engineered to contain one or more T cell engager that mediate binding to and/or activation of a T cell. Accordingly, in some embodiments, the T cell engager is selected from an antigen binding domain or ligand that binds to (e.g., and in some embodiments activates) one or more of the variable chain of the beta subunit of a TCR (e.g., TCR β V), CD3, TCR α , TCR β , TCR γ , TCR ζ , ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, or CD226. In other embodiments, the T cell engager is selected from an antigen binding domain or ligand that binds to and does not activate one or more of TCR β V, CD3, TCR α , TCR β , TCR γ , TCR ζ , ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, or CD226. In some embodiments, the T cell engager binds to TCR β V.

Human T cell receptor (TCR) complex

T cell receptors (TCR) can be found on the surface of T cells. TCRs recognize antigens, e.g., peptides, presented on, e.g., bound to, major histocompatibility complex (MHC) molecules on the surface of cells, e.g., antigen-presenting cells. TCRs are heterodimeric molecules and can comprise an alpha chain, a beta chain, a gamma chain or a delta chain. TCRs comprising an alpha chain and a beta chain are also referred to as TCR $\alpha\beta$. The TCR beta chain consists of the

following regions (also known as segments): variable (V), diversity (D), joining (J) and constant (C) (see Mayer G. and Nyland J. (2010) Chapter 10: Major Histocompatibility Complex and T-cell Receptors-Role in Immune Responses. In: Microbiology and Immunology on-line, University of South Carolina School of Medicine). The TCR alpha chain consists of V, J and C regions. The rearrangement of the T-cell receptor (TCR) through somatic recombination of V (variable), D (diversity), J (joining), and C (constant) regions is a defining event in the development and maturation of a T cell. TCR gene rearrangement takes place in the thymus.

TCRs can comprise a receptor complex, known as the TCR complex, which comprises a TCR heterodimer comprising of an alpha chain and a beta chain, and dimeric signaling molecules, *e.g.*, CD3 co-receptors, *e.g.*, CD3 δ/ϵ , and/or CD3 γ/ϵ .

TCR beta V (TCR β V)

Diversity in the immune system enables protection against a huge array of pathogens. Since the germline genome is limited in size, diversity is achieved not only by the process of V(D)J recombination but also by junctional (junctions between V-D and D-J segments) deletion of nucleotides and addition of pseudo-random, non-templated nucleotides. The TCR beta gene undergoes gene arrangement to generate diversity.

The TCR V beta repertoire varies between individuals and populations because of, *e.g.*, frequently occurring inactivating polymorphisms in functional gene segments and a large insertion/deletion-related polymorphism encompassing 2 V beta gene segments. This disclosure provides, *inter alia*, antibody molecules and fragments thereof, that bind, *e.g.*, specifically bind, to a human TCR beta V chain (TCR β V), *e.g.*, a TCR β V gene family (also referred to as a group), *e.g.*, a TCR β V subfamily (also referred to as a subgroup), *e.g.*, as described herein. TCR beta V families and subfamilies are known in the art, *e.g.*, as described in Yassai et al., (2009) *Immunogenetics* 61(7)pp:493-502; Wei S. and Concannon P. (1994) *Human Immunology* 41(3) pp: 201-206. The antibodies described herein can be recombinant antibodies, *e.g.*, recombinant non-murine antibodies, *e.g.*, recombinant human or humanized antibodies.

In an aspect, the disclosure provides an anti-TCR β V antibody molecule that binds to human TCR β V, *e.g.*, a TCR β V family, *e.g.*, gene family or a variant thereof. In some embodiments a TCRBV gene family comprises one or more subfamilies, *e.g.*, as described herein, *e.g.*, in FIG. 3, Table 8A or Table 8B. In some embodiments, the TCR β V gene family

comprises: a TCR β V6 subfamily, a TCR β V10 subfamily, a TCR β V12 subfamily, a TCR β V5 subfamily, a TCR β V7 subfamily, a TCR β V11 subfamily, a TCR β V14 subfamily, a TCR β V16 subfamily, a TCR β V18 subfamily, a TCR β V9 subfamily, a TCR β V13 subfamily, a TCR β V4 subfamily, a TCR β V3 subfamily, a TCR β V2 subfamily, a TCR β V15 subfamily, a TCR β V30 subfamily, a TCR β V19 subfamily, a TCR β V27 subfamily, a TCR β V28 subfamily, a TCR β V24 subfamily, a TCR β V20 subfamily, TCR β V25 subfamily, a TCR β V29 subfamily, a TCR β V1 subfamily, a TCR β V17 subfamily, a TCR β V21 subfamily, a TCR β V23 subfamily, or a TCR β V26 subfamily.

In some embodiments, TCR β V6 subfamily is also known as TCR β V13.1. In some embodiments, the TCR β V6 subfamily comprises: TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-4*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-4*02, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-9*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-8*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-5*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-6*02, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-6*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-2*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-3*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-1*01, or a variant thereof.

In some embodiments, TCR β V6 comprises TCR β V6-5*01, or a variant thereof. In some embodiments, TCR β V6, *e.g.*, TCR β V6-5*01, is recognized, *e.g.*, bound, by SEQ ID NO: 1 and/or SEQ ID NO: 2. In some embodiments, TCR β V6, *e.g.*, TCR β V6-5*01, is recognized, *e.g.*, bound, by SEQ ID NO: 9 and/or SEQ ID NO: 10. In some embodiments, TCR β V6 is recognized, *e.g.*, bound, by SEQ ID NO: 9 and/or SEQ ID NO: 11.

In some embodiments, TCR β V10 subfamily is also known as TCR β V12. In some embodiments, the TCR β V10 subfamily comprises: TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01, or a variant thereof.

In some embodiments, TCR β V12 subfamily is also known as TCR β V8.1. In some embodiments, the TCR β V12 subfamily comprises: TCR β V12-4*01, TCR β V12-3*01, or TCR β

V12-5*01, or a variant thereof. In some embodiments, TCR β V12 is recognized, *e.g.*, bound, by SEQ ID NO: 15 and/or SEQ ID NO: 16. In some embodiments, TCR β V12 is recognized, *e.g.*, bound, by any one of SEQ ID NOs 23-25, and/or any one of SEQ ID NO: 26-30:

In some embodiments, the TCR β V5 subfamily is chosen from: TCR β V5-5*01, TCR β V5-6*01, TCR β V5-4*01, TCR β V5-8*01, TCR β V5-1*01, or a variant thereof.

In some embodiments, the TCR β V7 subfamily comprises TCR β V7-7*01, TCR β V7-6*01, TCR β V7-8*02, TCR β V7-4*01, TCR β V7-2*02, TCR β V7-2*03, TCR β V7-2*01, TCR β V7-3*01, TCR β V7-9*03, or TCR β V7-9*01, or a variant thereof.

In some embodiments, the TCR β V11 subfamily comprises: TCR β V11-1*01, TCR β V11-2*01 or TCR β V11-3*01, or a variant thereof.

In some embodiments, the TCR β V14 subfamily comprises TCR β V14*01, or a variant thereof.

In some embodiments, the TCR β V16 subfamily comprises TCR β V16*01, or a variant thereof.

In some embodiments, the TCR β V18 subfamily comprises TCR β V18*01, or a variant thereof.

In some embodiments, the TCR β V9 subfamily comprises TCR β V9*01 or TCR β V9*02, or a variant thereof.

In some embodiments, the TCR β V13 subfamily comprises TCR β V13*01, or a variant thereof.

In some embodiments, the TCR β V4 subfamily comprises TCR β V4-2*01, TCR β V4-3*01, or TCR β V4-1*01, or a variant thereof.

In some embodiments, the TCR β V3 subfamily comprises TCR β V3-1*01, or a variant thereof.

In some embodiments, the TCR β V2 subfamily comprises TCR β V2*01, or a variant thereof.

In some embodiments, the TCR β V15 subfamily comprises TCR β V15*01, or a variant thereof.

In some embodiments, the TCR β V30 subfamily comprises TCR β V30*01, or TCR β V30*02, or a variant thereof.

In some embodiments, the TCR β V19 subfamily comprises TCR β V19*01, or TCR β V19*02, or a variant thereof.

In some embodiments, the TCR β V27 subfamily comprises TCR β V27*01, or a variant thereof.

5 In some embodiments, the TCR β V28 subfamily comprises TCR β V28*01, or a variant thereof.

In some embodiments, the TCR β V24 subfamily comprises TCR β V24-1*01, or a variant thereof.

10 In some embodiments, the TCR β V20 subfamily comprises TCR β V20-1*01, or TCR β V20-1*02, or a variant thereof.

In some embodiments, the TCR β V25 subfamily comprises TCR β V25-1*01, or a variant thereof.

In some embodiments, the TCR β V29 subfamily comprises TCR β V29-1*01, or a variant thereof.

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Table 8A: List of TCR β V subfamilies and subfamily members

Reference in Fig. 3	Subfamily	Subfamily members
A	TCR β V6 <i>Also referred to as: TCR VB 13.1</i>	TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01.
B	TCR β V10 <i>Also referred to as: TCRβ V12</i>	TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01
C	TCR β V12 <i>Also referred to as: TCRβ V8.1</i>	TCR β V12-4*01, TCR β V12-3*01, or TCR β V12-5*01
D	TCR β V5	TCR β V5-5*01, TCR β V5-6*01, TCR β V5-4*01, TCR β V5-8*01, TCR β V5-1*01
E	TCR β V7	TCR β V7-7*01, TCR β V7-6*01, TCR β V7-8*02, TCR β V7-4*01, TCR β V7-2*02, TCR β V7-2*03, TCR β V7-2*01, TCR β V7-3*01, TCR β V7-9*03, or TCR β V7-9*01
F	TCR β V11	TCR β V11-1*01, TCR β V11-2*01 or TCR β V11-3*01

G	TCR β V14	TCR β V14*01
H	TCR β V16	TCR β V16*01
I	TCR β V18	TCR β V18*01
J	TCR β V9	TCR β V9*01 or TCR β V9*02
K	TCR β V13	TCR β V13*01
L	TCR β V4	TCR β V4-2*01, TCR β V4-3*01, or TCR β V4-1*01
M	TCR β V3	TCR β V3-1*01
N	TCR β V2	TCR β V2*01
O	TCR β V15	TCR β V15*01
P	TCR β V30	TCR β V30*01, or TCR β V30*02
Q	TCR β V19	TCR β V19*01, or TCR β V19*02
R	TCR β V27	TCR β V27*01.
S	TCR β V28	TCR β V28*01.
T	TCR β V24	TCR β V24-1*01
U	TCR β V20	TCR β V20-1*01, or TCR β V20-1*02
V	TCR β V25	TCR β V25-1*01
W	TCR β V29	TCR β V29-1*01

Table 8B: Additional TCR β V subfamilies

Subfamily
TCR β V1
TCR β V17
TCR β V21
TCR β V23
TCR β V26

Anti-TCR β V antibodies

5 Disclosed herein, is the discovery of a novel class of antibodies, i.e. anti-TCR β V antibody molecules disclosed herein, which despite having low sequence similarity (e.g., low sequence identity among the different antibody molecules that recognize different TCR β V subfamilies), recognize a structurally conserved region, e.g., domain, on the TCR β V protein and have a similar function (e.g., a similar cytokine profile). Thus, the anti-TCR β V antibody

10 molecules disclosed herein share a structure-function relationship.

In some embodiments, the anti-TCR β V antibody molecules disclosed herein do not recognize, e.g., bind to, an interface of a TCR β V:TCR α complex.

In some embodiments, the anti-TCR β V antibody molecules disclosed herein do not recognize, e.g., bind to, a constant region of a TCR β V protein. An exemplary antibody that binds

to a constant region of a TCRBV region is JOVI.1 as described in Viney *et al.*, (*Hybridoma*. 1992 Dec;11(6):701-13).

In some embodiments, the anti-TCR β V antibody molecules disclosed herein do not recognize, e.g., bind to, one or more (e.g., all) of a complementarity determining region (e.g., CDR1, CDR2 and/or CDR3) of a TCR β V protein.

In some embodiments, the anti-TCR β V antibody molecules disclosed herein binds (e.g., specifically binds) to a TCR β V region. In some embodiments, binding of anti-TCR β V antibody molecules disclosed herein results in a cytokine profile that differs from a cytokine profile of a T cell engager that binds to a receptor or molecule other than a TCR β V region (“a non-TCR β V-binding T cell engager”). In some embodiments, the non-TCR β V-binding T cell engager comprises an antibody that binds to a CD3 molecule (e.g., CD3 epsilon (CD3e) molecule); or a TCR alpha (TCR α) molecule. In some embodiments, the non-TCR β V-binding T cell engager is an OKT3 antibody or an SP34-2 antibody.

In an aspect, the disclosure provides an anti-TCR β V antibody molecule that binds to human TCR β V, e.g., a TCR β V gene family, e.g., one or more of a TCR β V subfamily, e.g., as described herein, e.g., in **FIG. 3**, Table 8A, or Table 8B. In some embodiments, the anti-TCR β V antibody molecule binds to one or more TCR β V subfamilies chosen from: a TCR β V6 subfamily, a TCR β V10 subfamily, a TCR β V12 subfamily, a TCR β V5 subfamily, a TCR β V7 subfamily, a TCR β V11 subfamily, a TCR β V14 subfamily, a TCR β V16 subfamily, a TCR β V18 subfamily, a TCR β V9 subfamily, a TCR β V13 subfamily, a TCR β V4 subfamily, a TCR β V3 subfamily, a TCR β V2 subfamily, a TCR β V15 subfamily, a TCR β V30 subfamily, a TCR β V19 subfamily, a TCR β V27 subfamily, a TCR β V28 subfamily, a TCR β V24 subfamily, a TCR β V20 subfamily, TCR β V25 subfamily, a TCR β V29 subfamily, a TCR β V1 subfamily, a TCR β V17 subfamily, a TCR β V21 subfamily, a TCR β V23 subfamily, or a TCR β V26 subfamily, or a variant thereof.

In some embodiments, the anti-TCR β V antibody molecule binds to a TCR β V6 subfamily comprising: TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01, or a variant thereof. In some embodiments the TCR β V6 subfamily comprises TCR β V6-5*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-4*01, or a variant

thereof. In some embodiments, TCR β V6 comprises TCR β V6-4*02, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-9*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-8*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-5*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-6*02, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-6*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-2*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-3*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-1*01, or a variant thereof.

In some embodiments, the anti-TCR β V antibody molecule binds to a TCR β V10 subfamily comprising: TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01, or a variant thereof.

In some embodiments, the anti-TCR β V antibody molecule binds to a TCR β V12 subfamily comprising: TCR β V12-4*01, TCR β V12-3*01 or TCR β V12-5*01, or a variant thereof.

In some embodiments, the anti-TCR β V antibody molecule binds to a TCR β V5 subfamily comprising: TCR β V5-5*01, TCR β V5-6*01, TCR β V5-4*01, TCR β V5-8*01, TCR β V5-1*01, or a variant thereof.

In some embodiments, the anti-TCR β V antibody molecule does not bind to TCR β V12, or binds to TCR β V12 with an affinity and/or binding specificity that is less than (*e.g.*, less than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the 16G8 murine antibody or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule binds to TCR β V12 with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the 16G8 murine antibody or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule binds to a TCR β V region other than TCR β V12 (*e.g.*, TCR β V region as described herein, *e.g.*, TCR β V6 subfamily (*e.g.*, TCR β V6-5*01) with an affinity and/or binding specificity that is greater than (*e.g.*, greater than

about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of the 16G8 murine antibody or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule does not bind to TCR β V5-5*01 or TCR β V5-1*01, or binds to TCR β V5-5*01 or TCR β V5-1*01 with an affinity and/or binding specificity that is less than (*e.g.*, less than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of murine Antibody C or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule binds to TCR β V5-5*01 or TCR β V5-1*01 with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of murine Antibody C or a humanized version thereof as described in US Patent 5,861,155.

In some embodiments, the anti-TCR β V antibody molecule binds to a TCR β V region other than TCR β V5-5*01 or TCR β V5-1*01 (*e.g.*, TCR β V region as described herein, *e.g.*, TCR β V6 subfamily (*e.g.*, TCR β V6-5*01) with an affinity and/or binding specificity that is greater than (*e.g.*, greater than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or about 2-, 5-, or 10- fold) the affinity and/or binding specificity of murine Antibody C or a humanized version thereof as described in US Patent 5,861,155.

20 **Anti-TCR β V6 antibodies**

Accordingly, in one aspect, the disclosure provides an anti-TCR β V antibody molecule that binds to human TCR β V6, *e.g.*, a TCR β V6 subfamily comprising: TCR β V6-4*01, TCR β V6-4*02, TCR β V6-9*01, TCR β V6-8*01, TCR β V6-5*01, TCR β V6-6*02, TCR β V6-6*01, TCR β V6-2*01, TCR β V6-3*01 or TCR β V6-1*01. In some embodiments the TCR β V6 subfamily comprises TCR β V6-5*01 or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-4*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-4*02, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-9*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-8*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-5*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-6*02, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-6*01, or a variant thereof. In some embodiments,

TCR β V6 comprises TCR β V6-2*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-3*01, or a variant thereof. In some embodiments, TCR β V6 comprises TCR β V6-1*01, or a variant thereof.

In some embodiments, TCR β V6-5*01 is encoded by the nucleic acid sequence of SEQ ID NO: 43, or a sequence having 85%, 90%, 95%, 99% or more identity thereof.

SEQ ID NO: 43

ATGAGCATCGGCCTCCTGTGCTGTGCAGCCTTGTCTCTCCTGTGGGCAGGTCCAGTG
AATGCTGGTGTCACTCAGACCCCAAAATTCCAGGTCCTGAAGACAGGACAGAGCAT
GACACTGCAGTGTGCCCAGGATATGAACCATGAATACATGTCCTGGTATCGACAAG
ACCCAGGCATGGGGCTGAGGCTGATTCATTACTCAGTTGGTGTGCTGGTATCACTGACC
AAGGAGAAGTCCCCAATGGCTACAATGTCTCCAGATCAACCACAGAGGATTTCCCG
CTCAGGCTGCTGTCTGGCTGCTCCCTCCCAGACATCTGTGTACTTCTGTGCCAGCAGTT
ACTC

In some embodiments, TCR β V6-5*01 comprises the amino acid sequence of SEQ ID NO: 44, or an amino acid sequence having 85%, 90%, 95%, 99% or more identity thereof.

SEQ ID NO: 44

MSIGLLCCAALSLLWAGPVNAGVTQTPKFQVLKTGQSM TLQCAQDMNHEYMSWYRQ
DPGMGLRLIHYSVGAGITDQGEVPNGYNVSRSTTEDFPLRLLSAAPSQTSVYFCASSY

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, is a non-murine antibody molecule, *e.g.*, a human or humanized antibody molecule. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule is a human antibody molecule. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule is a humanized antibody molecule.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, is isolated or recombinant.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises at least one antigen-binding region, *e.g.*, a variable region or an antigen-binding fragment thereof, from an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises at least one, two, three or four variable regions from an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises at least one or two heavy chain variable regions from an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody molecule described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule comprises a heavy chain variable region (VH) having a consensus sequence of SEQ ID NO: 231 or 3290.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises at least one or two light chain variable regions from an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule comprises a light chain variable region (VL) having a consensus sequence of SEQ ID NO: 230 or 3289.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a heavy chain constant region for an IgG4,

e.g., a human IgG4. In still another embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes a heavy chain constant region for an IgG1, *e.g.*, a human IgG1. In one embodiment, the heavy chain constant region comprises an amino sequence set forth in **Table 3A**, or a sequence substantially identical (*e.g.*, at least 80%,
5 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes a kappa light chain constant region, *e.g.*, a human kappa light chain constant region. In one embodiment, the light chain constant region comprises an amino sequence set forth in **Table 3A**, or a sequence substantially identical (*e.g.*, at
10 least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, or three complementarity determining regions (CDRs) from a heavy chain variable region (VH) of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-
15 H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, or three CDRs (or
20 collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, or three complementarity determining regions (CDRs) from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**, or a
25 sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or
30 higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**. In one
 5 embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, three, four, five or six CDRs
 10 (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in **Table 1A**. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 1A**, or encoded by a nucleotide sequence shown in
 15 **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, molecule includes all six CDRs from an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table**
 20 **1A**, or closely related CDRs, *e.g.*, CDRs which are identical or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions). In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, may include any CDR described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes at least one, two, or three CDRs according to Kabat *et al.* (*e.g.*, at least one, two, or three CDRs according to the Kabat definition as set out in **Table 1A**) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody
 25 chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at
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least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Kabat et al. shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes at least one, two, or three CDRs according to Kabat *et al.* (*e.g.*, at least one, two, or three CDRs according to the Kabat definition as set out in **Table 1A**) from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Kabat et al. shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, three, four, five, or six CDRs according to Kabat *et al.* (*e.g.*, at least one, two, three, four, five, or six CDRs according to the Kabat definition as set out in **Table 1A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs according to Kabat et al. shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes all six CDRs according to Kabat *et al.* (*e.g.*, all six CDRs according to the Kabat definition as set out in **Table 1A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid

sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six CDRs according to Kabat et al. shown in **Table 1A**. In one embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, may
 5 include any CDR described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, or three hypervariable loops that have the same canonical structures as the corresponding hypervariable loop of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*,
 10 A-H.1, A-H.2 or A-H.68, *e.g.*, the same canonical structures as at least loop 1 and/or loop 2 of the heavy and/or light chain variable domains of an antibody described herein. See, *e.g.*, Chothia et al., (1992) J. Mol. Biol. 227:799-817; Tomlinson et al., (1992) J. Mol. Biol. 227:776-798 for descriptions of hypervariable loop canonical structures. These structures can be determined by inspection of the tables described in these references.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes at least one, two, or three CDRs according to Chothia et al. (*e.g.*, at least one, two, or three CDRs according to the Chothia definition as set out in **Table 1A**) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or as
 20 described in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Chothia et al. shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes at least one, two, or three CDRs according to Chothia *et al.* (*e.g.*, at least one, two, or three CDRs according to the Chothia definition as set out in **Table 1A**) from a light chain variable region of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody
 30 described in **Table 1A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at

least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Chothia et al. shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes at least one, two, three, four, five, or six CDRs according to Chothia *et al.* (*e.g.*, at least one, two, three, four, five, or six CDRs according to the Chothia definition as set out in **Table 1A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by the nucleotide sequence in **Table 1A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs according to Chothia et al. shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes all six CDRs according to Chothia *et al.* (*e.g.*, all six CDRs according to the Chothia definition as set out in **Table 1A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or an antibody described in **Table 1A**, or encoded by a nucleotide sequence in **Table 1A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six CDRs according to Chothia et al. shown in **Table 1A**. In one embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, may include any CDR described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, molecule includes a combination of CDRs or hypervariable loops defined according to Kabat et al., Chothia et al., or as described in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, can contain any combination of CDRs or hypervariable loops according to the Kabat and Chothia definitions.

In some embodiments, a combined CDR as set out in **Table 1A** is a CDR that comprises
 5 a Kabat CDR and a Chothia CDR.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, molecule includes a combination of CDRs or hypervariable loops identified as combined CDRs in **Table 1A**. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule,
 10 can contain any combination of CDRs or hypervariable loops according the “combined” CDRs are described in **Table 1A**.

In an embodiment, *e.g.*, an embodiment comprising a variable region, a CDR (*e.g.*, a combined CDR, Chothia CDR or Kabat CDR), or other sequence referred to herein, *e.g.*, in **Table 1A**, the antibody molecule is a monospecific antibody molecule, a bispecific antibody
 15 molecule, a bivalent antibody molecule, a biparatopic antibody molecule, or an antibody molecule that comprises an antigen binding fragment of an antibody, *e.g.*, a half antibody or antigen binding fragment of a half antibody. In certain embodiments the antibody molecule comprises a multispecific molecule, *e.g.*, a bispecific molecule, *e.g.*, as described herein.

In an embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes:
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(i) one, two or all of a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 2, SEQ ID NO: 10 or SEQ ID NO: 11, and/or

25 (ii) one, two or all of a heavy chain complementarity determining region 1 (HC CDR1), heavy chain complementarity determining region 2 (HC CDR2), and a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 1 or SEQ ID NO: 9.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises a LC CDR1, LC CDR2, and LC CDR3 of
 30 SEQ ID NO: 2, and a HC CDR1, HC CDR2, and HC CDR3 of SEQ ID NO: 1.

In some embodiments the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises a LC CDR1, LC CDR2, and LC CDR3 of SEQ ID NO: 10, and a HC CDR1, HC CDR2, and HC CDR3 of SEQ ID NO: 9.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises a LC CDR1, LC CDR2, and LC CDR3 of SEQ ID NO: 11, and a HC CDR1, HC CDR2, and HC CDR3 of SEQ ID NO: 9.

In an embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 6, a LC CDR2 amino acid sequence of SEQ ID NO: 7, or a LC CDR3 amino acid sequence of SEQ ID NO: 8; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 3, a HC CDR2 amino acid sequence of SEQ ID NO: 4, or a HC CDR3 amino acid sequence of SEQ ID NO: 5.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 6, a LC CDR2 amino acid sequence of SEQ ID NO: 7, or a LC CDR3 amino acid sequence of SEQ ID NO: 8; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 3, a HC CDR2 amino acid sequence of SEQ ID NO: 4, or a HC CDR3 amino acid sequence of SEQ ID NO: 5.

In an embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 51, a LC CDR2 amino acid sequence of SEQ ID NO: 52, or a LC CDR3 amino acid sequence of SEQ ID NO: 53; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 45, a HC CDR2 amino acid sequence of SEQ ID NO: 46, or a HC CDR3 amino acid sequence of SEQ ID NO: 47.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 51, a LC CDR2 amino acid sequence of SEQ ID NO: 52, or a LC CDR3 amino acid sequence of SEQ ID NO: 53; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 45, a HC CDR2 amino acid sequence of SEQ ID NO: 46, or a HC CDR3 amino acid sequence of SEQ ID NO: 47.

In an embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 54, a LC CDR2 amino acid sequence of SEQ ID NO: 55, or a LC CDR3 amino acid sequence of SEQ ID NO: 56; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 48, a HC CDR2 amino acid sequence of SEQ ID NO: 49, or a HC CDR3 amino acid sequence of SEQ ID NO: 50.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 54, a LC CDR2 amino acid sequence of SEQ ID NO: 55, or a LC CDR3 amino acid sequence of SEQ ID NO: 56; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 48, a HC CDR2 amino acid sequence of SEQ ID NO: 49, or a HC CDR3 amino acid sequence of SEQ ID NO: 50.

In one embodiment, the light or the heavy chain variable framework (*e.g.*, the region encompassing at least FR1, FR2, FR3, and optionally FR4) of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule can be chosen from: (a) a light or heavy chain variable framework including at least 80%, 85%, 87%, 90%, 92%, 93%, 95%, 97%, 98%, or 100% of the amino acid residues from a human light or heavy chain variable framework, *e.g.*, a light or heavy chain variable framework residue from a human mature antibody, a human germline sequence, or a human consensus sequence; (b) a light or heavy chain variable framework including from 20% to 80%, 40% to 60%, 60% to 90%, or 70% to 95% of the amino acid residues from a human light or heavy chain variable framework, *e.g.*, a light or heavy chain variable framework residue from a human mature antibody, a human germline sequence, or a human consensus sequence; (c) a non-human framework (*e.g.*, a rodent framework); or (d) a non-human framework that has been modified, *e.g.*, to remove antigenic or cytotoxic determinants, *e.g.*, deimmunized, or partially humanized. In one embodiment, the light

or heavy chain variable framework region (particularly FR1, FR2 and/or FR3) includes a light or heavy chain variable framework sequence at least 70, 75, 80, 85, 87, 88, 90, 92, 94, 95, 96, 97, 98, 99% identical or identical to the frameworks of a VL or VH segment of a human germline gene.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a heavy chain variable domain having at least one, two, three, four, five, six, seven, ten, fifteen, twenty or more changes, *e.g.*, amino acid substitutions or deletions, from an amino acid sequence of any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, *e.g.*, the amino acid sequence of the FR region in the entire variable
10 region, *e.g.*, shown in **FIG. 1A**, or in SEQ ID NO: 9.

Alternatively, or in combination with the heavy chain substitutions described herein, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain having at least one, two, three, four, five, six, seven, ten, fifteen, twenty or more amino acid changes, *e.g.*, amino acid substitutions or
15 deletions, from an amino acid sequence of any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, *e.g.*, the amino acid sequence of the FR region in the entire variable region, *e.g.*, shown in **FIG. 1B**, or in SEQ ID NO: 10 or SEQ ID NO: 11.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes one, two, three, or four heavy chain
20 framework regions shown in **FIG. 1A**, or a sequence substantially identical thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes one, two, three, or four light chain framework regions shown in **FIG. 1B**, or a sequence substantially identical thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*,
25 anti-TCR β V6-5*01) antibody molecule, comprises the light chain framework region 1 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the light chain framework region 2 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the light chain framework region 3 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the light chain framework region 4 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at position 10 according to Kabat numbering. In some
10 embodiments, the FR1 comprises a Phenylalanine at position 10, *e.g.*, a Serine to Phenylalanine substitution. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain comprising a
15 framework region, *e.g.*, framework region 2 (FR2), comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at a position disclosed herein according to Kabat numbering. In some embodiments, FR2 comprises a Histidine at position 36, *e.g.*, a substitution at position 36 according to Kabat numbering, *e.g.*, a Tyrosine to Histidine substitution. In some embodiments,
20 FR2 comprises an Alanine at position 46, *e.g.*, a substitution at position 46 according to Kabat numbering, *e.g.*, an Arginine to Alanine substitution. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain comprising a
25 framework region, *e.g.*, framework region 3 (FR3), comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at a position disclosed herein according to Kabat numbering. In some embodiments, FR3 comprises a Phenylalanine at position 87, *e.g.*, a substitution at position 87 according to Kabat numbering, *e.g.*, a Tyrosine to Phenylalanine substitution. In some
30 embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain comprising: (a) a framework region 1 (FR1) comprising a Phenylalanine at position 10, *e.g.*, a substitution at position 10 according to Kabat numbering, *e.g.*, a Serine to Phenylalanine substitution; (b) a framework region 2 (FR2) comprising a Histidine at position 36, *e.g.*, a substitution at position 36 according to Kabat numbering, *e.g.*, a Tyrosine to Histidine substitution, and a Alanine at position 46, *e.g.*, a substitution at position 46 according to Kabat numbering, *e.g.*, a Arginine to Alanine substitution; and (c) a framework region 3 (FR3) comprising a Phenylalanine at position 87, *e.g.*, a substitution at position 87 according to Kabat numbering, *e.g.*, a Tyrosine to Phenylalanine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 10. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain comprising: (a) a framework region 2 (FR2) comprising a Histidine at position 36, *e.g.*, a substitution at position 36 according to Kabat numbering, *e.g.*, a Tyrosine to Histidine substitution, and a Alanine at position 46, *e.g.*, a substitution at position 46 according to Kabat numbering, *e.g.*, a Arginine to Alanine substitution; and (b) a framework region 3 (FR3) comprising a Phenylalanine at position 87, *e.g.*, a substitution at position 87 according to Kabat numbering, *e.g.*, a Tyrosine to Phenylalanine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 11. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises a light chain variable domain comprising: (a) a framework region 1 (FR1) comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more (*e.g.*, all) positions disclosed herein according to Kabat numbering, ; (b) a framework region 2 (FR2) comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more (*e.g.*, all) position disclosed herein according to Kabat numbering and (c) a framework region 3 (FR3) comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more (*e.g.*, all) position disclosed herein according to Kabat numbering.

In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*,
5 anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework region 1 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*,
anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework region 2 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1A**

10 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*,
anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework region 3 of A-H.1 or A-H.2, *e.g.*, as shown in **FIG. 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*,
anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework region 4 of A-
15 H.1 or A-H.2, *e.g.*, as shown in **FIG. 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*,
anti-TCR β V6-5*01) antibody molecule, comprises a heavy chain variable domain comprising a
framework region, *e.g.*, framework region 3 (FR3), comprising a change, *e.g.*, a substitution
(*e.g.*, a conservative substitution) at a position disclosed herein according to Kabat numbering. In
20 some embodiments, FR3 comprises a Threonine at position 73, *e.g.*, a substitution at position 73
according to Kabat numbering, *e.g.*, a Glutamic Acid to Threonine substitution. In some
embodiments, FR3 comprises a Glycine at position 94, *e.g.*, a substitution at position 94
according to Kabat numbering, *e.g.*, an Arginine to Glycine substitution. In some embodiments,
the substitution is relative to a human germline heavy chain framework region sequence.

25 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*,
anti-TCR β V6-5*01) antibody molecule, comprises a heavy chain variable domain comprising a
framework region 3 (FR3) comprising a Threonine at position 73, *e.g.*, a substitution at position
73 according to Kabat numbering, *e.g.*, a Glutamic Acid to Threonine substitution, and a Glycine
at position 94, *e.g.*, a substitution at position 94 according to Kabat numbering, *e.g.*, a Arginine
30 to Glycine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 10.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework regions 1-4 of A-H.1 or A-H.2, *e.g.*, SEQ ID NO: 9, or as shown in **FIGs. 1A** and **1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the light chain framework regions 1-4 of A-H.1, *e.g.*, SEQ ID NO: 10, or as shown in **FIGs. 1A** and **1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the light chain framework regions 1-4 of A-H.2, *e.g.*, SEQ ID NO: 11, or as shown in **FIGs. 1A** and **1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework regions 1-4 of A-H.1, *e.g.*, SEQ ID NO: 9; and the light chain framework regions 1-4 of A-H.1, *e.g.*, SEQ ID NO: 10, or as shown in **FIGs. 1A** and **1B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises the heavy chain framework regions 1-4 of A-H.2, *e.g.*, SEQ ID NO: 9; and the light chain framework regions 1-4 of A-H.2, *e.g.*, SEQ ID NO: 11, or as shown in **FIGs. 1A** and **1B**.

In some embodiments, the heavy or light chain variable domain, or both, of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, includes an amino acid sequence, which is substantially identical to an amino acid disclosed herein, *e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical to a variable region of an antibody described herein, *e.g.*, an antibody chosen from any one of A-H.1 to A-H.68, *e.g.*, A-H.1, A-H.2 or A-H.68, or as described in **Table 1A**, or encoded by the nucleotide sequence in **Table 1A**; or which differs at least 1 or 5 residues, but less than 40, 30, 20, or 10 residues, from a variable region of an antibody described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises at least one, two, three, or four antigen-binding regions, *e.g.*, variable regions, having an amino acid sequence as set forth in **Table 1A**, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the sequences shown in **Table 1A**). In another embodiment, the anti-TCR β V antibody

molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule includes a VH and/or VL domain encoded by a nucleic acid having a nucleotide sequence as set forth in **Table 1A**, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 3, 6, 15, 30, or 45 nucleotides from the sequences shown in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 9, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 9, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 9; and/or

a VL domain comprising the amino acid sequence of SEQ ID NO: 10, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 10, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 10.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 9, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 9, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 9; and/or

a VL domain comprising the amino acid sequence of SEQ ID NO: 11, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 11, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 11.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule is a full antibody or fragment thereof (*e.g.*, a Fab, F(ab')₂, Fv, or a single chain Fv fragment (scFv)). In embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule is a monoclonal antibody or an antibody with single specificity. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, can also be a

humanized, chimeric, camelid, shark, or an *in vitro*-generated antibody molecule. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, is a humanized antibody molecule. The heavy and light chains of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, can be full-length (*e.g.*, an antibody can include at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains) or can include an antigen-binding fragment (*e.g.*, a Fab, F(ab')₂, Fv, a single chain Fv fragment, a single domain antibody, a diabody (dAb), a bivalent antibody, or bispecific antibody or fragment thereof, a single domain variant thereof, or a camelid antibody).

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, is in the form of a multispecific molecule, *e.g.*, a bispecific molecule, *e.g.*, as described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, has a heavy chain constant region (Fc) chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE. In some embodiments, the Fc region is chosen from the heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4. In some embodiments, the Fc region is chosen from the heavy chain constant region of IgG1 or IgG2 (*e.g.*, human IgG1, or IgG2). In some embodiments, the heavy chain constant region is human IgG1. In some embodiments, the Fc region comprises a Fc region variant, *e.g.*, as described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule, has a light chain constant region chosen from, *e.g.*, the light chain constant regions of kappa or lambda, preferably kappa (*e.g.*, human kappa). In one embodiment, the constant region is altered, *e.g.*, mutated, to modify the properties of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function). For example, the constant region is mutated at positions 296 (M to Y), 298 (S to T), 300 (T to E), 477 (H to K) and 478 (N to F) to alter Fc receptor binding (*e.g.*, the mutated positions correspond to positions 132 (M to Y), 134 (S to T), 136 (T to E), 313 (H to K) and 314 (N to F) of SEQ ID NOs: 212 or

214; or positions 135 (M to Y), 137 (S to T), 139 (T to E), 316 (H to K) and 317 (N to F) of SEQ ID NOs: 215, 216, 217, or 218), *e.g.*, relative to human IgG1.

Antibody A-H.1 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 3278 and a light chain comprising the amino acid sequence of SEQ ID NO: 72. Antibody A-H.2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 3278 and a light chain comprising the amino acid sequence of SEQ ID NO: 3279. Antibody A-H.68 comprises the amino acid sequence of SEQ ID NO: 1337, or a sequence having at least 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity thereto.

Additional exemplary humanized anti-TCRB V6 antibodies are provided in **Table 1A**. In some embodiments, the anti-TCR β V6 is antibody A, *e.g.*, humanized antibody A (antibody A-H), as provided in **Table 1A**. In some embodiments, the anti-TCR β V antibody comprises one or more (*e.g.*, all three) of a LC CDR1, LC CDR2, and LC CDR3 provided in **Table 1A**; and/or one or more (*e.g.*, all three) of a HC CDR1, HC CDR2, and HC CDR3 provided in **Table 1A**, or a sequence with at least 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity thereto. In some embodiments, antibody A comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Table 1A**, or a sequence with at least 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity thereto.

Table 1A: Amino acid and nucleotide sequences for murine, chimeric and humanized antibody molecules which bind to TCRVB 6, *e.g.*, TCRVB 6-5. The antibody molecules include murine mAb Antibody A, and humanized mAb Antibody A-H Clones A-H.1 to A-H.68. The amino acid the heavy and light chain CDRs, and the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the heavy and light chains are shown.

Antibody A (murine)		
SEQ ID NO: 3	HC CDR1 (Combined)	GYSFTTYIH
SEQ ID NO: 4	HC CDR2 (Combined)	WFFPGSGNIKYNEKFKG
SEQ ID NO: 5	HC CDR3 (Combined)	SYYSYDVLDY
SEQ ID NO: 45	HC CDR1 (Kabat)	TYYIH
SEQ ID NO: 46	HC CDR2 (Kabat)	WFFPGSGNIKYNEKFKG
SEQ ID NO: 47	HC CDR3 (Kabat)	SYYSYDVLDY
SEQ ID NO: 48	HC CDR1 (Chothia)	GYSFTTY
SEQ ID NO: 49	HC CDR2 (Chothia)	FPGSGN
SEQ ID NO: 50	HC CDR3 (Chothia)	SYYSYDVLDY
SEQ ID NO: 1	VH	QVQLQQSGPELVKPGTSVKISCKASGYSFTTYI HWVKQRPQGGLWIGWFFPGSGNIKYNEKFKG

		KATLTADTSSSTAYMQLSSLTSEESAVYFCAGS YYSYDVLDDYWGHTTLTVSS
SEQ ID NO: 6	LC CDR1 (Combined)	KASQNVGINVV
SEQ ID NO: 7	LC CDR2 (Combined)	SSSHRYS
SEQ ID NO: 8	LC CDR3 (Combined)	QQFKSYPLT
SEQ ID NO: 51	LC CDR1 (Kabat)	KASQNVGINVV
SEQ ID NO: 52	LC CDR2 (Kabat)	SSSHRYS
SEQ ID NO: 53	LC CDR3 (Kabat)	QQFKSYPLT
SEQ ID NO: 54	LC CDR1 (Chothia)	KASQNVGINVV
SEQ ID NO: 55	LC CDR2 (chothia)	SSSHRYS
SEQ ID NO: 56	LC CDR3 (chothia)	QQFKSYPLT
SEQ ID NO: 2	VL	DILMTQSQKFMSTSLGDRVSVSCKASQNVGINV VWHQQKPGQSPKALIISSSHRYSGVPDRFTGSG SGTDFTLTINNVSQEDLAIEYFCQQFKSYPLTFGA GTKLELK
Antibody A humanized (A-H antibody)		
A-H.1 antibody		
SEQ ID NO: 3	HC CDR1 (Combined)	GYSFTTYIYH
SEQ ID NO: 4	HC CDR2 (Combined)	WFFPGSGNIKYNEKFKG
SEQ ID NO: 5	HC CDR3 (Combined)	SYYSYDVLDDY
SEQ ID NO: 9	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDDYWGQGTITVTVSS
SEQ ID NO: 12	DNA VH	CAGGTGCAGCTGGTTCAGTCTGGCGCCGAAGT GAAGAAACCTGGCTCCTCCGTGAAGGTGTCCT GCAAGGCTTCCGGCTACTCCTCACCACCTAC TACATCCACTGGGTCCGACAGGCCCTGGACA AGGATTGGAATGGATGGGCTGGTTCCTCCCCG GCTCCGGCAACATCAAGTACAACGAGAAGTT CAAGGGCCGCGTGACCATCACCGCCGACACC TCTACCTCTACCGCCTACATGGAAGTGTCCAG CCTGAGATCTGAGGACACCGCCGTGTACTACT GCGCCGGCTCCTACTACTCTTACGACGTGCTG GATTACTGGGGCCAGGGCACCACAGTGACAG TGTCCTCT
SEQ ID NO: 69	VH-IgM constant delta CDC	METDTLLLWVLLWVPGSTGQVQLVQSGAEVK KPGSSVKVSCKASGYSFTTYIHWVRQAPGQGL EWMGWFFPGSGNIKYNEKFKGRVTITADTSTST AYMELSSLRSEDNAVYYCAGSYYSYDVLDDYWG QGTTVTVSSGSASAPTLFPLVSCENSPSDTSSVA VGCLAQDFLPDSITFSWKYKNNSDISSTRGFPSV LRGGKYAATSQVLLPSKDVMQGTDEHVVCKV QHPNGNKEKNVPLPVIAELPPKVSFVPPRDGFF GNPRKSKLICATGFSPRQIQVSWLREGKQVGS GVTTDQVQAEAKESGPTYTKVTSTLTIKESDWL GQSMFTCRVDHRLTFQQNASSMCPDQDTAI RVFAIPPSFASIFLTKSTKLTLVTDLTYSVTIS WTRQNGEAVKTHTNISESHPNATFSAVGEASIC EDDWNNGERFTCTVTHTDLASSLKQTISRPKG

		ALHRPDVYLLPPAREQLNLRESATITCLVTGFSP ADV FVQWMQRGQPLSPEKYVTSAPMPEPQAPG RYFAHSILTVSEEWNTGETYTCVVAHEALPNR VTERTVDKSTGKPTLYNVSLVMSDTAGTCY
SEQ ID NO: 70	VH-IgGA1	METDTLLLWVLLLWVPGSTGQVQLVQSGAEVK KPGSSVKV SCKASGYSFTTYYIHWVRQAPGQGL EWMGWFFPGSGNIKYNEKFKGRVTITADTSTST AYMELSSLRSEDTAVYYCAGSYYSYDVLDYWG QGTTVTVSSASPTSPKVFPLSLCSTQPDGNVIA CLVQGGFFPQEPLSVTWSESGQGV TARNFPSSQD ASGDLYTTSSQLTLPATQCLAGKSVTCHVKHYT NPSQDVTVP CPVPSTPPTPSPSTPPTPSPSCCHPR LSLHRPALEDLLLGSEANLTCTLTGLRDASGVTF TWT PSSGKSAVQGP PERDLCGCYSVSSVLP GCA EPWNH GKTF TCTAAYPESKTPLTATLSKSGNTF RPEVHLLPPPSEELALNELVTLTCLARGFSPKDV LVRWLQGSQELPREKYLTWASRQEPSQGTTTFA VTSILRVA AEDWKKGDTFSCMV GHEALPLAFT QKTIDRLAGKPTHVNVSVVMAEVDGTCY
SEQ ID NO: 71	VH-IgGA2	METDTLLLWVLLLWVPGSTGQVQLVQSGAEVK KPGSSVKV SCKASGYSFTTYYIHWVRQAPGQGL EWMGWFFPGSGNIKYNEKFKGRVTITADTSTST AYMELSSLRSEDTAVYYCAGSYYSYDVLDYWG QGTTVTVSSASPTSPKVFPLSLDSTPQDGNVV ACL VQGGFFPQEPLSVTWSESGQNV TARNFPSSQ DASGDLYTTSSQLTLPATQCPDGKSVTCHVKHY TNSSQDVTVP CRVPPPPPCCHPRLSLHRPAEDL LLGSEANLTCTLTGLRDASGATFTWTPSSGKSA VQGP PERDLCGCYSVSSVLP GCAQPWNHGETFT CTAAHPELKTPLTANITKSGNTFRPEVHLLPPPS EELALNELVTLTCLARGFSPKDV LVRWLQGSQE LPREKYLTWASRQEPSQGTTTYAVTSILRVA AE DWKKGETFSCMV GHEALPLAFTQKTIDRMAGK PTHINVSVM AEADGTCY
SEQ ID NO: 3278	Heavy chain	METDTLLLWVLLLWVPGSTGQVQLVQSGAEVK KPGSSVKV SCKASGYSFTTYYIHWVRQAPGQGL EWMGWFFPGSGNIKYNEKFKGRVTITADTSTST AYMELSSLRSEDTAVYYCAGSYYSYDVLDYWG QGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQ SSGLYSLSSVTV PSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLF PPKPKDTLMISRTPEVTCVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAK GQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTTPVLDSDGSFLL YSKLTVDKSRWQQGNV FSCSV MHEALHNHYT QKSLSLSPGK
SEQ ID NO: 6	LC CDR1 (Combined)	KASQNVGINVV

SEQ ID NO: 7	LC CDR2 (Combined)	SSSHRYS
SEQ ID NO: 8	LC CDR3 (Combined)	QQFKSYPLT
SEQ ID NO: 10	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVGINVV WHQQKPGKAPKALIISSSHRYSGVPSRFSGSGS GTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 13	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTTCCT GTCCGCCTCTGTGGGCGACAGAGTGACCATCA CATGCAAGGCCTCTCAGAACGTGGGCATCAA CGTCGTGTGGCACCAGCAGAAGCCTGGCAAG GCTCCTAAGGCTCTGATCTACTCCTCCAGCCA CCGGTACTCTGGCGTGCCCTCTAGATTTTCCG GCTCTGGCTCTGGCACCGAGTTTACCCTGACA ATCTCCAGCCTGCAGCCTGAGGACTTCGCCAC CTACTTTTGCCAGCAGTTCAAGAGCTACCCTC TGACCTTTGGCCAGGGCACCAAGCTGGAAAT CAAG
SEQ ID NO: 72	VL and kappa constant region/light chain	METDTLLLWVLLLWVPGSTGDIQMTQSPSFLSA SVGDRVITITCKASQNVGINVVWHQQKPGKAPK ALIISSSHRYSGVPSRFSGSGSGTEFTLTISLQPE DFATYFCQQFKSYPLTFGQGTKLEIKRTVAAPS VFIFPPSDEQLKSGTASVCLNNFYPREAKVQ WKVDNALQSGNSQESVTEQDSKSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRG EC
A-H.2 antibody		
SEQ ID NO: 3	HC CDR1 (Combined)	GYSFTTYIH
SEQ ID NO: 4	HC CDR2 (Combined)	WFFPGSGNIKYNEKFKG
SEQ ID NO: 5	HC CDR3 (Combined)	SYYSYDVLDY
SEQ ID NO: 9	VH	QVQLVQSGAEVKKPGSSVKVSKASGYSFTTY YIHWVRQAPGQGLEWMGWFFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDYWGQGTITVTVSS
SEQ ID NO: 12	DNA VH	CAGGTGCAGCTGGTTCAGTCTGGCGCCGAAGT GAAGAAACCTGGCTCCTCCGTGAAGGTGTCCT GCAAGGCTTCCGGCTACTCCTTACCACCTAC TACATCCACTGGGTCCGACAGGCCCTGGACA AGGATTGGAATGGATGGGCTGGTCTTCCCCG GCTCCGGCAACATCAAGTACAACGAGAAGTT CAAGGGCCGCGTGACCATCACCGCCGACACC TCTACCTCTACCGCCTACATGGAAGTGTCCAG CCTGAGATCTGAGGACACCGCCGTGTACTACT GCGCCGGCTCCTACTACTCTTACGACGTGCTG GATTACTGGGGCCAGGGCACACAGTGACAG TGTCTCT
SEQ ID NO: 3278	Heavy chain	METDTLLLWVLLLWVPGSTGQVQLVQSGAEVK KPGSSVKVSKASGYSFTTYIHWVRQAPGQGL EWMGWFFPGSGNIKYNEKFKGRVTITADTSTST AYMELSSLRSEDNAVYYCAGSYYSYDVLDYWG QGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAAL

		GCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMHREALHNYHTQKSLSLSPGK
SEQ ID NO: 6	LC CDR1 (Combined)	KASQNVGINVV
SEQ ID NO: 7	LC CDR2 (Combined)	SSSHRYS
SEQ ID NO: 8	LC CDR3 (Combined)	QQFKSYPLT
SEQ ID NO: 11	VL	DIQMTQSPSSLSASVGDRVITITCKASQNVGINVVWHQQKPGKVPKALIIYSSSHRYSVPSRFSGSGSGTDFTLTISLQPEDVATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 14	DNA VL	GACATCCAGATGACCCAGTCTCCATCCTCTCTGTCCGCCTCTGTGGGCGACAGAGTGACCATCATGCAAGGCCTCTCAGAACGTGGGCATCAACGTCGTGTGGCACCAGCAGAAACCTGGCAAGGTGCCCAAGGCTCTGATCTACTCCTCCAGCCAAGATACTCCGGCGTGGCCTCTAGATTCTCCGGCTCTGGCTCTGGCACCGACTTTACCCTGACAATCTCCAGCCTGCAGCCTGAGGACGTGGCCACCTACTTTTGCCAGCAGTTCAAGAGCTACCCTCTGACCTTTGGCCAGGGCACCAAGCTGGAAATCAAG
SEQ ID NO: 3279	Light chain	METDTLLLWVLLWVPGSTGDIQMTQSPSSLSASVGDRVITITCKASQNVGINVVWHQQKPGKVPKALIIYSSSHRYSVPSRFSGSGSGTDFTLTISLQPEDVATYFCQQFKSYPLTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSPVTKSFNRGEC
A-H.3 antibody		
SEQ ID NO: 80	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDfkLT YIHWVRQAPGQGLEWMGRVSPGSGNTKYNEKFKGRVTITADTSTSTAYMELSSLRSED TAVYYCAGSYYSYDVL DYWGQGTTVTVSSGGGGSGGGSGGGGGSGGGGSDIQMTQSPSFLSASVGDRVITITCKASQNVEDRVAWYQQKPGKAPKALIIYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 81	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVEDRVAWYQQKPGKAPKALIIYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 82	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDfkLT

		YIHWVRQAPGQGLEWMGRVSPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGT TVTVSS
A-H.4		
SEQ ID NO: 83	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTD FDKIY IHWVRQAPGQGLEWMGRISAGSGNVKYNEKFK GRVTITADTSTSTAYMELSSLRSEDTAVYYCAG SYYSYDVLDYWGQGT TVTVSSGGGGSGGGGSG GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITCK ASQNVEDRVAWYQQKPGKAPKALIYSSSHRYK GVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQF KSYPLTFGQGTKLEIK
SEQ ID NO: 84	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVEDRV AWYQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 85	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTD FDKIY IHWVRQAPGQGLEWMGRISAGSGNVKYNEKFK GRVTITADTSTSTAYMELSSLRSEDTAVYYCAG SYYSYDVLDYWGQGT TVTVSS
A-H.5		
SEQ ID NO: 86	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRDF YIHWVRQAPGQGLEWMGRVYPGSGSYRYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGT TVTVSSGGGGSGGGG SGGGGSGGGGSDIQMTQSPSFLSASVGDRVTI TCKASQNVDDRVAWYQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 87	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDDRVA AWYQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 88	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRDF YIHWVRQAPGQGLEWMGRVYPGSGSYRYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGT TVTVSS
A-H.6		
SEQ ID NO: 89	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDFKLT YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDTAVYYCA GSYYSYDVLDYWGQGT TVTVSSGGGGSGGGGSG GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVNDRVAWYQQKPGKAPKALIYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 90	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVNDRVA AWYQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK

SEQ ID NO: 91	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDFKLT YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVL DYWGQGT TVTVSS
A-H.7		
SEQ ID NO: 92	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTD F KLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVL DYWGQGT TVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVENKVAWHQQKPGKAPKALIYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGT KLEIK
SEQ ID NO: 93	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVENKV AWHQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 94	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTD F KLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVL DYWGQGT TVTVSS
A-H.8		
SEQ ID NO: 95	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTD FDKIY IHWVRQAPGQGLEWMGRIFAGSGNTKYNEKFK GRVTITADTSTSTAYMELSSLRSEDNAVYYCAG SYYSYDVL DYWGQGT TVTVSSGGGGSGGGGSG GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITCK ASQNVDDRVAWYQQKPGKAPKALIYSSSHRYK GVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQF KSYPLTFGQGT KLEIK
SEQ ID NO: 96	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDDRVA WYQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 97	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTD FDKIY IHWVRQAPGQGLEWMGRIFAGSGNTKYNEKFK GRVTITADTSTSTAYMELSSLRSEDNAVYYCAG SYYSYDVL DYWGQGT TVTVSS
A-H.9		
SEQ ID NO: 98	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDFDKF YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVL DYWGQGT TVTVSSGGGGSGGGG SGGGGGSGGGGSDIQMTQSPSFLSASVGDRVTI TCKASQNVGNRVAWYQQKPGKAPKALIYSSSH RYSGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGT KLEIK

SEQ ID NO: 99	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVGNRV AWYQQKPGKAPKALIISSSHRYSGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 100	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDFDKF YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVL DYWGQGTTTVTVSS
A-H.10		
SEQ ID NO: 101	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDFDKF YIHWVRQAPGQGLEWMGRIFAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVL DYWGQGTTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITITC KASQNVGDRV AWYQQKPGKAPKALIISSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIKs
SEQ ID NO: 102	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVGDRV AWYQQKPGKAPKALIISSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 103	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDFDKF YIHWVRQAPGQGLEWMGRIFAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVL DYWGQGTTTVTVSS
A-H.11		
SEQ ID NO: 104	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDfKLT YIHWVRQAPGQGLEWMGRVSPGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVL DYWGQGTTTVTVSSGGGGSGGGG SGGGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVGDRV AWYQQKPGKAPKALIISSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 105	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVGDRV AWYQQKPGKAPKALIISSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 106	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDfKLT YIHWVRQAPGQGLEWMGRVSPGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVL DYWGQGTTTVTVSS
A-H.12		
SEQ ID NO: 107	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDfDKIY IHWVRQAPGQGLEWMGRVSAGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVL DYWGQGTTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITITC KASQNVGNRV AWYQQKPGKAPKALIISSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ

		FKSYPLTFGQGTKLEIK
SEQ ID NO: 108	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVGNRV AWYQQKPGKAPKALIISSSHRYKGVPSRFGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 109	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFDKIY IHWVRQAPGQGLEWMGRVSAGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLVDYWGQGTITVTVSS
A-H.13		
SEQ ID NO: 110	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDFKLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLVDYWGQGTITVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITITC KASQNVGNRV AWYQQKPGKAPKALIISSSHRY KGVPSRFGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 111	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVGNRV AWYQQKPGKAPKALIISSSHRYKGVPSRFGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 112	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFKLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLVDYWGQGTITVTVSS
A-H.14		
SEQ ID NO: 113	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDFDKIY IHWVRQAPGQGLEWMGRISAGSGNTKYNEKFK GRVTITADTSTSTAYMELSSLRSEDNAVYYCAG SYYSYDVLVDYWGQGTITVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITITC ASQNVDDRVAWYQQKPGKAPKALIISSSHRYK GVPSRFGSGSGTEFTLTISLQPEDFATYFCQQF KSYPLTFGQGTKLEIK
SEQ ID NO: 114	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVDDRVA AWYQQKPGKAPKALIISSSHRYKGVPSRFGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 115	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFDKIY IHWVRQAPGQGLEWMGRISAGSGNTKYNEKFK GRVTITADTSTSTAYMELSSLRSEDNAVYYCAG SYYSYDVLVDYWGQGTITVTVSS
A-H.15		
SEQ ID NO: 116	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDFRLT YIHWVRQAPGQGLEWMGRVSPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVLVDYWGQGTITVTVSSGGGGSGGG GSGGGSGGGGSDIQMTQSPSFLSASVGDRVIT

		TCKASQNVDNKNVAWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 117	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVDNKNV AWHQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 118	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFTLT YIHWVRQAPGQGLEWMGRVSPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVLDYWGQGTITVTVSS
A-H.16		
SEQ ID NO: 119	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGGTFTLT YIHWVRQAPGQGLEWMGRVYPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVLDYWGQGTITVTVSSGGGGSGGG GGGGGGGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVDNRVAWYQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 120	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVDNRV AWYQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 121	VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFTLT YIHWVRQAPGQGLEWMGRVYPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVLDYWGQGTITVTVSS
A-H.17		
SEQ ID NO: 122	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDFTLT YIHWVRQAPGQGLEWMGRIFPGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDYWGQGTITVTVSSGGGGSGGGGS GGGGSGGGGGSDIQMTQSPSFLSASVGDRVITITC KASQNVDNRVAWYQQKPGKAPKALIYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 123	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVDNRV AWYQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 124	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFTLT YIHWVRQAPGQGLEWMGRIFPGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDYWGQGTITVTVSS
A-H.18		
SEQ ID NO: 125	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDFTLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDYWGQGTITVTVSSGGGGSGGGGS

		GGGSGGGGSDIQMTQSPSFLSASVGDRVITIC KASQNVEDRVAWYQQKPGKAPKALYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 126	VL	DIQMTQSPSFLSASVGDRVITICKASQNVEDRV AWYQQKPGKAPKALYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 127	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFKLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDATVYYCA GSYYSYDVLVDYWGQGTITVTVSS
A-H.19		
SEQ ID NO: 128	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGGTFRLT YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDATVYYCA GSYYSYDVLVDYWGQGTITVTVSSGGGGSGGGGS GGGSGGGGSDIQMTQSPSFLSASVGDRVITIC KASQNVGDRVAWYQQKPGKAPKALYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 129	VL	DIQMTQSPSFLSASVGDRVITICKASQNVGDRV AWYQQKPGKAPKALYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 130	VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFRLT YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDATVYYCA GSYYSYDVLVDYWGQGTITVTVSS
A-H.20		
SEQ ID NO: 131	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGGTFDKT YIHWVRQAPGQGLEWMGRISAGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDATVYYCA GSYYSYDVLVDYWGQGTITVTVSSGGGGSGGGGS GGGSGGGGSDIQMTQSPSFLSASVGDRVITIC KASQNVDDRVAWYQQKPGKAPKALYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 132	VL	DIQMTQSPSFLSASVGDRVITICKASQNVDDRVAWYQQKPGKAPKALYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 133	VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFDKT YIHWVRQAPGQGLEWMGRISAGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDATVYYCA GSYYSYDVLVDYWGQGTITVTVSS
A-H.21		
SEQ ID NO: 134	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDFDKF YIHWVRQAPGQGLEWMGRISAGSGNTKYNEKF

		KGRVTITADTSTSTAYMELSSLRSED TAVYYCA GSYYSYDVLDYWGQGT TTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVDDRVAWYQQKPGKAPKALYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 135	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDDRVAWYQQKPGKAPKALYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 136	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHD FDKF YIHWVRQAPGQGLEWMGRISAGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSED TAVYYCA GSYYSYDVLDYWGQGT TTVTVSS
A-H.22		
SEQ ID NO: 137	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTD FKL T YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSED TAVYYCA GSYYSYDVLDYWGQGT TTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNV DNKVAWHQQKPGKAPKALYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 138	VL	DIQMTQSPSFLSASVGDRVTITCKASQNV DNKV AWHQQKPGKAPKALYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 139	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTD FKL T YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSED TAVYYCA GSYYSYDVLDYWGQGT TTVTVSS
A-H.23		
SEQ ID NO: 140	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHD FRL T YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSED TAVYYCA GSYYSYDVLDYWGQGT TTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVADRV AWYQQKPGKAPKALYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 141	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVADRV AWYQQKPGKAPKALYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 142	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHD FRL T YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSED TAVYYCA GSYYSYDVLDYWGQGT TTVTVSS
A-H.24		
SEQ ID NO: 143	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHD FHLW

		YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSED TAVYYC AGSYYSYDVLDYWGQGT TTVTVSSGGGGSGGG GSGGGSGGGGSDIQMTQSPSFLSASVGDRVTI TCKASQNV DNKVAWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 144	VL	DIQMTQSPSFLSASVGDRVTITCKASQNV DNKVAWHQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 145	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDFHLW YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSED TAVYYC AGSYYSYDVLDYWGQGT TTVTVSS
A-H.25		
SEQ ID NO: 146	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDFHLW YIHWVRQAPGQGLEWMGRVFAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSED TAVYYC AGSYYSYDVLDYWGQGT TTVTVSSGGGGSGGG GSGGGSGGGGSDIQMTQSPSFLSASVGDRVTI TCKASQNV EDKVAWYQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 147	VL	DIQMTQSPSFLSASVGDRVTITCKASQNV EDKVAWYQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 148	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDFHLW YIHWVRQAPGQGLEWMGRVFAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSED TAVYYC AGSYYSYDVLDYWGQGT TTVTVSS
A-H.26		
SEQ ID NO: 149	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTD FKLTYIHWVRQAPGQGLEWMGRIFPGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSED TAVYYCA GSYYSYDVLDYWGQGT TTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVDDRVAWYQQKPGKAPKALIYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 150	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDDRVAWYQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGT KLEIK
SEQ ID NO: 151	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTD FKLTYIHWVRQAPGQGLEWMGRIFPGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSED TAVYYCA GSYYSYDVLDYWGQGT TTVTVSS
A-H.27		

SEQ ID NO: 153	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDfKLT YIHWVRQAPGQGLEWMGRVSAsgsnvkyNEK FKGRVTITADTSTSTAYMELSSLRSEDtAVYYC AGSYYSYDVLdYWGQgTTVTvSSGGGGSGGGG SGGGSGGGGSDIQMTQSPSFLSASVGDRVTI TCKASQNVGNrVAWYQQKPGKAPKALiYSSSH RYKGVPSRFSGSGSGTEFTLTISSLQPEDfATyFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 154	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGNrV AWYQQKPGKAPKALiYSSSHRYKGVPSRFSGSG SGTEFTLTISSLQPEDfATyFCQQFKSYPLTFGQg TKLEIK
SEQ ID NO: 155	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDfKLT YIHWVRQAPGQGLEWMGRVSAsgsnvkyNEK FKGRVTITADTSTSTAYMELSSLRSEDtAVYYC AGSYYSYDVLdYWGQgTTVTvSS
A-H.28		
SEQ ID NO: 156	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDfKLT YIHWVRQAPGQGLEWMGRISPGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDtAVYYCA GSYYSYDVLdYWGQgTTVTvSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVGDRVAWYQQKPGKAPKALiYSSSHRY KGVPSRFSGSGSGTEFTLTISSLQPEDfATyFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 157	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGDRV AWYQQKPGKAPKALiYSSSHRYKGVPSRFSGSG SGTEFTLTISSLQPEDfATyFCQQFKSYPLTFGQg TKLEIK
SEQ ID NO: 158	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDfKLT YIHWVRQAPGQGLEWMGRISPGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDtAVYYCA GSYYSYDVLdYWGQgTTVTvSS
A-H.29		
SEQ ID NO: 159	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDFHLW YIHWVRQAPGQGLEWMGRISPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDtAVYYCA GSYYSYDVLdYWGQgTTVTvSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVGDRVAWHQQKPGKAPKALiYSSSHRY KGVPSRFSGSGSGTEFTLTISSLQPEDfATyFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 160	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGDRV AWHQQKPGKAPKALiYSSSHRYKGVPSRFSGSG SGTEFTLTISSLQPEDfATyFCQQFKSYPLTFGQg TKLEIK
SEQ ID NO: 161	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDFHLW YIHWVRQAPGQGLEWMGRISPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDtAVYYCA GSYYSYDVLdYWGQgTTVTvSS

A-H.31		
SEQ ID NO: 162	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGHDFKLT YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSDVLDYWGQGTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITIC KASQNVDDRVAWYQQKPGKAPKALYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 163	VL	DIQMTQSPSFLSASVGDRVITICKASQNVDDRVAWYQQKPGKAPKALYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 164	VH	QVQLVQSGAEVKKPGSSVKVSCASGHDFKLT YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSDVLDYWGQGTTVTVSS
A-H.31		
SEQ ID NO: 165	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTDHFLW YIHWVRQAPGQGLEWMGRVFAGSGSYRYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVLDYWGQGTTVTVSSGGGGSGGG GSGGGSGGGGSDIQMTQSPSFLSASVGDRVITIC KASQNVDDRVAWYQQKPGKAPKALYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 166	VL	DIQMTQSPSFLSASVGDRVITICKASQNVDDRVAWYQQKPGKAPKALYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 167	VH	QVQLVQSGAEVKKPGSSVKVSCASGTDHFLW YIHWVRQAPGQGLEWMGRVFAGSGSYRYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVLDYWGQGTTVTVSS
A-H.32		
SEQ ID NO: 168	VH+VL	QVQLVQSGAEVKKPGSSVKVSCASGTDFDKIY IHWVRQAPGQGLEWMGRISAGSGNTKYNEKFK GRVTITADTSTSTAYMELSSLRSEDNAVYYCAG SYYSYDVLDYWGQGTTVTVSSGGGGSGGGGSG GGSGGGGSDIQMTQSPSFLSASVGDRVITICK ASQNVADRVAWYQQKPGKAPKALYSSSHRYK GVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQF KSYPLTFGQGTKLEIK
SEQ ID NO: 169	VL	DIQMTQSPSFLSASVGDRVITICKASQNVADRVAWYQQKPGKAPKALYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK

SEQ ID NO: 170	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFDKIY IHWVRQAPGQGLEWMGRISAGSGNTKYNEKF GRVTITADTSTSTAYMELSSLRSEDNAVYYCAG SYYSYDVL DYWGQGT TVTVSS
A-H.33		
SEQ ID NO: 171	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDFKLT YIHWVRQAPGQGLEWMGRISAGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVL DYWGQGT TVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVEDRVAWYQQKPGKAPKALYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 172	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVEDRV AWYQQKPGKAPKALYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 173	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFKLT YIHWVRQAPGQGLEWMGRISAGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVL DYWGQGT TVTVSS
A-H.34		
SEQ ID NO: 174	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDFRLT YIHWVRQAPGQGLEWMGRISPGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVL DYWGQGT TVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVGNRVAWYQQKPGKAPKALYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 175	VL	DIQMTQSPSFLSASVGDRVTITCKASQNVGNRV AWYQQKPGKAPKALYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQG TKLEIK
SEQ ID NO: 176	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFRLT YIHWVRQAPGQGLEWMGRISPGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVL DYWGQGT TVTVSS
A-H.35		
SEQ ID NO: 177	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDFDKT YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVL DYWGQGT TVTVSSGGGGSGGGG SGGGSGGGGSDIQMTQSPSFLSASVGDRVTI TCKASQNVEDRVAWYQQKPGKAPKALYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC

		QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 178	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVEDRV AWYQQKPGKAPKALIISSSHRYKGVPSRFGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 179	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDFDKT YIHWVRQAPGQGLEWMGRVSAAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVLDYWGQGTITVTVSS
A-H.36		
SEQ ID NO: 180	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDFKLT YIHWVRQAPGQGLEWMGRVSPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVLDYWGQGTITVTVSSGGGGSGGG GGGGGGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVEDRVAVHWQKPGKAPKALIISSSH RYKGVPSRFGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 181	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVEDRV AWHWQKPGKAPKALIISSSHRYKGVPSRFGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 182	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDFKLT YIHWVRQAPGQGLEWMGRVSPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVLDYWGQGTITVTVSS
A-H.37		
SEQ ID NO: 183	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDFDKT YIHWVRQAPGQGLEWMGRIYPSGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDYWGQGTITVTVSSGGGGSGGGG GGGGGGGGGSDIQMTQSPSFLSASVGDRVITIT KASQNVADRVAVYQQKPGKAPKALIISSSHRY KGVPSRFGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 184	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVADRV AWYQQKPGKAPKALIISSSHRYKGVPSRFGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 185	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDFDKT YIHWVRQAPGQGLEWMGRIYPSGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDYWGQGTITVTVSS
A-H.38		
SEQ ID NO: 186	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDFDKT YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA

		GSYYSYDVLDYWGQGTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITITC KASQNVDDRVAWYQQKPGKAPKALIYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 187	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVDDRVAWYQQKPGKAPKALIYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 188	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFDKTYIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDTAVYYCAGSYYSYDVLDYWGQGTTVTVSS
A-H.39		
SEQ ID NO: 189	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDFDKIYIHWVRQAPGQGLEWMGRISAGSGNIKYNEKFK GRVTITADTSTSTAYMELSSLRSEDTAVYYCAGSYYSYDVLDYWGQGTTVTVSSGGGGSGGGGSG GGGGSGGGGSDIQMTQSPSFLSASVGDRVITITCKASQNVDDRVAWYQQKPGKAPKALIYSSSHRYK GVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 190	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVDDRVAWYQQKPGKAPKALIYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 191	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFDKIYIHWVRQAPGQGLEWMGRISAGSGNIKYNEKFK GRVTITADTSTSTAYMELSSLRSEDTAVYYCAGSYYSYDVLDYWGQGTTVTVSS
A-H.40		
SEQ ID NO: 192	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDFDKIYIHWVRQAPGQGLEWMGRISAGSGNVKYNEKFK GRVTITADTSTSTAYMELSSLRSEDTAVYYCAGSYYSYDVLDYWGQGTTVTVSSGGGGSGGGGSG GGGGSGGGGSDIQMTQSPSFLSASVGDRVITITCKASQNVGDRVVAWYQQKPGKAPKALIYSSSHRYK GVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 193	VL	DIQMTQSPSFLSASVGDRVITITCKASQNVGDRVVAWYQQKPGKAPKALIYSSSHRYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK
SEQ ID NO: 194	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDFDKIYIHWVRQAPGQGLEWMGRISAGSGNVKYNEKFK GRVTITADTSTSTAYMELSSLRSEDTAVYYCAGSYYSYDVLDYWGQGTTVTVSS

A-H.41		
SEQ ID NO: 195	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGGTFKLT YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGTTVTVSSGGGGSGGG GSGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVDDRVAWYQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 196	VL	DIQMTQSPSFLSASVGDRVITCKASQNVDDR AWYQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 197	VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFKLT YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGTTVTVSS
A-H.42		
SEQ ID NO: 198	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDKLT YIHWVRQAPGQGLEWMGRISPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDTAVYYCA GSYYSYDVLDYWGQGTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITC KASQNVNDRVAWHQQKPGKAPKALIYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 199	VL	DIQMTQSPSFLSASVGDRVITCKASQNVNDR VAWHQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 200	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDKLT YIHWVRQAPGQGLEWMGRISPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDTAVYYCA GSYYSYDVLDYWGQGTTVTVSS
A-H.43		
SEQ ID NO: 201	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGHDFDKF YIHWVRQAPGQGLEWMGRVSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGTTVTVSSGGGGSGGG GSGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVNDRVAWYQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 202	VL	DIQMTQSPSFLSASVGDRVITCKASQNVNDR AWYQQKPGKAPKALIYSSSHRYKGVPSRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK

SEQ ID NO: 203	VH	QVQLVQSGAEVKKPGSSVKVSCKASGHDGDFKF YIHWVRQAPGQGLEWMGRVSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGTTVTVSS
A-H.44		
SEQ ID NO: 204	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGTDGDFKF YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGTTVTVSSGGGGSGGG GSGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVGDRVVWYQQKPGKAPKALIISSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 205	VH	QVQLVQSGAEVKKPGSSVKVSCKASGTDGDFKF YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGTTVTVSS
A-H.45		
SEQ ID NO: 206	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AVSYYSYDVLDYWGQGTTVTVSSGGGGSGGG GSGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVGINVWVHQQKPGKAPKALIISSSH RYSQVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 207	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AVSYYSYDVLDYWGQGTTVTVSS
A-H.46		
SEQ ID NO: 208	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGTTVTVSSGGGGSGGG GSGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVGINVWVHQQKPGKAPKALIISSSH RYSQVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 209	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGTTVTVSS
A-H.47		
SEQ ID NO: 210	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFFPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGTTVTVSSGGGGSGGG

		GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVITI TCKASQNVGINVVWHQQKPGKAPKALIYSSSH RYSGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 211	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFFPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVLDYWGQGTITVTVSS
A-H.48		
SEQ ID NO: 212	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFFPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTITVTVSSGSGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVITI TCKASQNVGINVVWHQQKPGKAPKALIYSSSH RYSGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 213	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFFPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTITVTVSS
A-H.49		
SEQ ID NO: 214	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFFPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVLDYWGQGTITVTVSSGSGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVITI TCKASQNVGINVVWHQQKPGKAPKALIYSSSH RYSGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
SEQ ID NO: 215	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFFPGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AGSYYSYDVLDYWGQGTITVTVSS
A-H.50		
SEQ ID NO: 216	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGRIFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDYWGQGTITVTVSSGSGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITITC KASQNVGINVVWHQQKPGKAPKALIYSSSHRY SGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 217	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGRIFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA

		GSYYSYDVLDDYWGQGTTVTVSS
A-H.51		
SEQ ID NO: 218	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSIYSAGVLDYWGQGTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITC KASQNVGINVVWHQKPGKAPKALIYSSSHRY SGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 219	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSIYSAGVLDYWGQGTTVTVSS
A-H.52		
SEQ ID NO: 220	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTLG YIHWVRQAPGQGLEWMGWFFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDDYWGQGTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITC KASQNVGINVVWHQKPGKAPKALIYSSSHRY SGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 221	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTLG YIHWVRQAPGQGLEWMGWFFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDDYWGQGTTVTVSS
A-H.53		
SEQ ID NO: 222	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFRLT YIHWVRQAPGQGLEWMGWFFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDDYWGQGTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITC KASQNVGINVVWHQKPGKAPKALIYSSSHRY SGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 223	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFRLT YIHWVRQAPGQGLEWMGWFFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDDYWGQGTTVTVSS
A-H.54		
SEQ ID NO: 224	VH+VL	QVQLVQSGAEVKKPGSSVKVSCKASGYSFHNW YIHWVRQAPGQGLEWMGWFFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDDYWGQGTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITC KASQNVGINVVWHQKPGKAPKALIYSSSHRY

		SGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
SEQ ID NO: 225	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFHNW YIHWVRQAPGQGLEWMGWFFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDTAVYYCA GSYYSDVLDYWGQGTTVTVSS
A-H.55 antibody		
SEQ ID NO: 3	HC CDR1 (Combined)	GYSFTTYIH
SEQ ID NO: 4	HC CDR2 (Combined)	WFFPGSGNIKYNEKFKG
SEQ ID NO: 5	HC CDR3 (Combined)	SYYSYDVLDY
SEQ ID NO: 45	HC CDR1 (Kabat)	TYYIH
SEQ ID NO: 46	HC CDR2 (Kabat)	WFFPGSGNIKYNEKFKG
SEQ ID NO: 47	HC CDR3 (Kabat)	SYYSYDVLDY
SEQ ID NO: 48	HC CDR1 (Chothia)	GYSFTTY
SEQ ID NO: 49	HC CDR2 (Chothia)	FPGSGN
SEQ ID NO: 50	HC CDR3 (Chothia)	SYYSYDVLDY
SEQ ID NO: 1100	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYSFTTY YIHWVRQAPGQGLEWMGWFFPGSGNIKYNEKF KGRVTITADTSTSTAYMELSSLRSEDTAVYYCA GSYYSDVLDYWGQGTTVTVSS
SEQ ID NO: 6	LC CDR1 (Combined)	KASQNVGINVV
SEQ ID NO: 7	LC CDR2 (Combined)	SSSHRYS
SEQ ID NO: 8	LC CDR3 (Combined)	QQFKSYPLT
SEQ ID NO: 51	LC CDR1 (Kabat)	KASQNVGINVV
SEQ ID NO: 52	LC CDR2 (Kabat)	SSSHRYS
SEQ ID NO: 53	LC CDR3 (Kabat)	QQFKSYPLT
SEQ ID NO: 54	LC CDR1 (Chothia)	KASQNVGINVV
SEQ ID NO: 55	LC CDR2 (chothia)	SSSHRYS
SEQ ID NO: 56	LC CDR3 (chothia)	QQFKSYPLT
SEQ ID NO: 1101	VL	QSVLTQPPSVSEAPRQRTISCKASQNVGINVV WHQQLPGKAPKALIYSSSHRYSVSDRFSGSGS GTSFSLAISGLQSEADYFCQQFKSYPLTFGTG TKVTVL
A-H.56		
SEQ ID NO: 1309	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFDKF YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AGSYYSYDVLDYWGQGTTVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVTI TCKASQNVGNRVAWYQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.57		
SEQ ID NO: 1326	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRLT YIHWVRQAPGQGLEWMGRVSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDTAVYYC AVSYYSYDVLDYWGQGTTVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVTI

		TCKASQNVGDRVVWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.58		
SEQ ID NO: 1327	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRLT YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTTTVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVGNRVVWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.59		
SEQ ID NO: 1328	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRLT YIHWVRQAPGQGLEWMGRIVAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTTTVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVADRVVWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.60		
SEQ ID NO: 1329	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFKLT YIHWVRQAPGQGLEWMGRVSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTTTVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVGDRVAWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.61		
SEQ ID NO: 1330	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFKLT YIHWVRQAPGQGLEWMGRVSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTTTVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVNDRVAWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.62		
SEQ ID NO: 1331	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRLT YIHWVRQAPGQGLEWMGRVSAGSGNVKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTTTVTVSSGGGGSGGG GSGGGGSGGGGSDIQMTQSPSFLSASVGDRVIT TCKASQNVADRVVWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.63		
SEQ ID NO: 1332	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRLT

		YIHWVRQAPGQGLEWMGRVYAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTTVTVSSGGGGSGGG GSGGGSGGGGSDIQMTQSPSFLSASVGDRVTI TCKASQNVEDRVVWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.64		
SEQ ID NO: 1333	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFKLT YIHWVRQAPGQGLEWMGRVSAGSGNTKYNEK FKGRVTITADTSTSTAYMELSSLRSEDNAVYYC AVSYYSYDVLDYWGQGTTVTVSSGGGGSGGG GSGGGSGGGGSDIQMTQSPSFLSASVGDRVTI TCKASQNVADRVVWHQQKPGKAPKALIYSSSH RYKGVPSRFSGSGSGTEFTLTISLQPEDFATYFC QQFKSYPLTFGQGTKLEIK
A-H.65		
SEQ ID NO: 1334	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFKLT YIHWVRQAPGQGLEWMGRISAGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA VSYYSYDVLDYWGQGTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVGDRVVWHQQKPGKAPKALIYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
A-H.66		
SEQ ID NO: 1335	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFKLT YIHWVRQAPGQGLEWMGRISAGSGNTKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA VSYYSYDVLDYWGQGTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVGDRVVWHQQKPGKAPKALIYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
A-H.67		
SEQ ID NO: 1336	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGTDKLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA VSYYSYDVLDYWGQGTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVNDRVAWYQQKPGKAPKALIYSSSHRY KGVPSRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
A-H.68		
SEQ ID NO: 1337	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGHDFRLT YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA VSYYSYDVLDYWGQGTTVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVTITC KASQNVADRVAWYQQKPGKAPKALIYSSSHRY

		KGVPSPRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
A-H.69		
SEQ ID NO: 1344	VH+ VL (ScFv)	QVQLVQSGAEVKKPGSSVKVSCKASGTDKLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDDYWGQGTITVTVSSGGGGSGGGGS GGGGSGGGGSDIQMTQSPSFLSASVGDRVITC KASQNVNDRVAWYQQKPKAPKALYSSSHRY KGVPSPRFSGSGSGTEFTLTISLQPEDFATYFCQQ FKSYPLTFGQGTKLEIK
A-H humanized-matured VH		
SEQ ID NO: 1310	VH-humanized matured 1	QVQLVQSGAEVKKPGSSVKVSCKASGTDKLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA GSYYSYDVLDDYWGQGTITVTVSS
SEQ ID NO: 1311	VH-humanized matured 2	QVQLVQSGAEVKKPGSSVKVSCKASGTDKLT YIHWVRQAPGQGLEWMGRIFPGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA VSYYSYDVLDDYWGQGTITVTVSS
SEQ ID NO: 1312	VH-humanized matured 3	QVQLVQSGAEVKKPGSSVKVSCKASGHDRLT YIHWVRQAPGQGLEWMGRISAGSGNVKYNEKF KGRVTITADTSTSTAYMELSSLRSEDNAVYYCA VSYYSYDVLDDYWGQGTITVTVSS
A-H humanized-matured VL		
SEQ ID NO: 1313	VL-humanized matured 1	DIQMTQSPSFLSASVGDRVITCKASQNVNDRV AWYQQKPKAPKALYSSSHRYKGVPSPRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK
SEQ ID NO: 1314	VL-humanized matured 2	DIQMTQSPSFLSASVGDRVITCKASQNVADRV AWYQQKPKAPKALYSSSHRYKGVPSPRFSGSG SGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQ TKLEIK

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises a VH and/or a VL of an antibody described in **Table 1A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule comprises a VH and a VL of an antibody described in **Table 1A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

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Alignment of affinity matured humanized Antibody A-H VL sequences (SEQ ID NOS 3377-3389, respectively, in order of appearance)

5 a5-VL 60
c1d2d4-VL 60
h3-VL 60
f5-VL 60
e4b6g3c6h2c2d1a6c3a3e6d6g2-VL 60
e3-VL 60
d5-VL 60
10 d3f1g1-VL 60
c4f4f2a2a1-VL 60
b5h4a4-VL 60
b2c5b3e2g4h6-VL 60
b1-VL 60
15 b4e1f3-VL 60
*****:****:*****.****

20

25 a5-VL 107
c1d2d4-VL 107
h3-VL 107
f5-VL 107
e4b6g3c6h2c2d1a6c3a3e6d6g2-VL 107
e3-VL 107
d5-VL 107
30 d3f1g1-VL 107
c4f4f2a2a1-VL 107
b5h4a4-VL 107
b2c5b3e2g4h6-VL 107
b1-VL 107
b4e1f3-VL 107
35 *****

Consensus VL: SEQ ID NO: 230

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DIQMTQSPSFLSASVGDRVTITCKASQNV G/E/A/D N/D R/K VAW Y/H QQKPKAPKALIISSSHRY K/S
GVPSRFGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK

Consensus VL: SEQ ID NO: 3289

DIQMTQSPSFLSASVGDRVTITCKASQNVX₁X₂X₃VAWX₄QQKPKAPKALIISSSHRYX₅

5 GVPSRFGSGSGTEFTLTISLQPEDFATYFCQQFKSYPLTFGQGTKLEIK, wherein X₁ is G, E, A or D; X₂ is N or D; X₃ is R or K; X₄ is Y or H; and X₅ is K or S

Alignment of affinity matured humanized Antibody A-H VH sequences (SEQ ID NOS 3390-3436, respectively, in order of appearance)

A-H. 52-VH QVQLVQSGAEVKKPGSSVKVCKASGYSFTLGYIHWVRQAPQGQLEWMGWFFPFGSGNIKY 60
A-H. 53-VH QVQLVQSGAEVKKPGSSVKVCKASGYSFRLTYIHWVRQAPQGQLEWMGWFFPFGSGNIKY 60
A-H. 54-VH QVQLVQSGAEVKKPGSSVKVCKASGYSFHNWYIHWVRQAPQGQLEWMGWFFPFGSGNIKY 60
A-H. 51-VH QVQLVQSGAEVKKPGSSVKVCKASGYSFTTYIHWVRQAPQGQLEWMGWFFPFGSGNIKY 60
A-H. 50-VH QVQLVQSGAEVKKPGSSVKVCKASGYSFTTYIHWVRQAPQGQLEWMGRIFPFGSGNIKY 60
A-H. 47-VH QVQLVQSGAEVKKPGSSVKVCKASGYSFTTYIHWVRQAPQGQLEWMGWFFPFGSGNTKY 60
A-H. 49-VH QVQLVQSGAEVKKPGSSVKVCKASGYSFTTYIHWVRQAPQGQLEWMGWFFPFGSGNTKY 60
A-H. 48-VH QVQLVQSGAEVKKPGSSVKVCKASGYSFTTYIHWVRQAPQGQLEWMGWFFPFGSGNTKY 60
A-H. 45-VH QVQLVQSGAEVKKPGSSVKVCKASGYSFTTYIHWVRQAPQGQLEWMGWFFPFGSGNTKY 60
A-H. 46-VH QVQLVQSGAEVKKPGSSVKVCKASGYSFTTYIHWVRQAPQGQLEWMGWFFPFGSGNTKY 60
c2-VH QVQLVQSGAEVKKPGSSVKVCKASGHDGFKLTYIHWVRQAPQGQLEWMGRVSPFGSGNTKY 60
f5-VH QVQLVQSGAEVKKPGSSVKVCKASGHDGFKLTYIHWVRQAPQGQLEWMGRVSPFGSGNTKY 60
f3-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRISPGSGNTKY 60
e2-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRISPGSGNTKY 60
e1-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRVSAGSGNVKY 60
c1-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRVSPFGSGNTKY 60
a1-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRVSPFGSGNTKY 60
b3-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRVSPFGSGNVKY 60
h3-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRISPGSGNVKY 60
c3-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRIFPFGSGNTKY 60
a5b5c4-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRIFPFGSGNVKY 60
d6-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRIFPFGSGNTKY 60
h2-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRVSAGSGNVKY 60
c5-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRISAGSGNVKY 60
f2-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRISAGSGNTKY 60
d3-VH QVQLVQSGAEVKKPGSSVKVCKASGHDGFKLTYIHWVRQAPQGQLEWMGRISAGSGNVKY 60
a4e4-VH QVQLVQSGAEVKKPGSSVKVCKASGHDGFKLTYIHWVRQAPQGQLEWMGRISAGSGNVKY 60
d2-VH QVQLVQSGAEVKKPGSSVKVCKASGTDGFKLTYIHWVRQAPQGQLEWMGRISAGSGNVKY 60

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g1-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFDKTYIHVVRQAPGQGLEWMGRISAGSGNVKY 60
c6-VH QVQLVQSGAEVKKPKGSSVKVSKASGGTDFDKTYIHVVRQAPGQGLEWMGRISAGSGNTKY 60
g2-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKTYIHVVRQAPGQGLEWMGRISAGSGNVKY 60
b4-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKIYIHVVRQAPGQGLEWMGRVSAGSGNTKY 60
a6-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKIYIHVVRQAPGQGLEWMGRIFAGSGNTKY 60
a2g4-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKIYIHVVRQAPGQGLEWMGRISAGSGNVKY 60
b6f1-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKIYIHVVRQAPGQGLEWMGRISAGSGNTKY 60
g3-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKIYIHVVRQAPGQGLEWMGRISAGSGNIKY 60
d1-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFDKFYIHVVRQAPGQGLEWMGRISAGSGNTKY 60
h4-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFDKFYIHVVRQAPGQGLEWMGRVSAGSGNTKY 60
b2-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFDKFYIHVVRQAPGQGLEWMGRIFAGSGNVKY 60
h6-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFDKFYIHVVRQAPGQGLEWMGRVSAGSGNVKY 60
b1-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFDKFYIHVVRQAPGQGLEWMGRVSAGSGNVKY 60
f4-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFDKTYIHVVRQAPGQGLEWMGRVSAGSGNVKY 60
a3-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFRDFYIHVVRQAPGQGLEWMGRVYPGSGSYRY 60
e6-VH QVQLVQSGAEVKKPKGSSVKVSKASGTDFHLWYIHVVRQAPGQGLEWMGRVFAGSGSYRY 60
e3-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFHLWYIHVVRQAPGQGLEWMGRISPGSGNVKY 60
d4-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFHLWYIHVVRQAPGQGLEWMGRVSAGSGNVKY 60
d5-VH QVQLVQSGAEVKKPKGSSVKVSKASGHDFHLWYIHVVRQAPGQGLEWMGRVFAGSGNTKY 60
***** * ***** . ***. : *

A-H. 52-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
A-H. 53-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
A-H. 54-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
A-H. 51-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSIYSAGVLDYWGGTTTVTVSS 119
A-H. 50-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
A-H. 47-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
A-H. 49-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
A-H. 48-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYCAVSYSDVLDYWGGTTTVTVSS 119
A-H. 45-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYCAVSYSDVLDYWGGTTTVTVSS 119
A-H. 46-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
c2-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
f5-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
f3-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
e2-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
e1-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
c1-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
a1-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119
b3-VH NEKFKGRVTITADTSTSTAYMELSSLRSEDNAVYACAGSYSDVLDYWGGTTTVTVSS 119

[illegible]

Consensus VH: SEQ ID NO: 231
QVQLVQSGAEVKKPGSSVKVCKASG H/T/G/Y D/T/S F H/R/D/K/T L/D/K/T/N W/F/T/I/Y/G YHWVVRQAPGGQGLEWMG
R/W V/I/F F/S/Y A/P GSG N/S T/V/Y/I K/R YNEKFKGRVTITADTSTAYMELSSLRSEDTAVYYCA G/V S Y/I YS Y/A D/G
VLDYWGQGTTVTVSS

Consensus VH: SEQ ID NO: 3290

QVQLVQSGAEVKKPGSSVKVSCKASGX₁X₂FX₃X₄X₅YIHWVVRQAPGQGLEWMGX₆X₇X₈X₉GSGX₁₀X₁₁X₁₂YNEKFKGRVTIT
ADTSTSTAYMELSSLRSEDTAVYYCAX₁₃SX₁₄YSX₁₅X₁₆VLDYWGGQTTTVTVSS, wherein: X1 is H or T or G or Y; X2 is D or
T or S; X3 is H or R or D or K or T; X4 is L or D or K or T or N; X5 is W or F or T or I or Y or G; X6 is R or W; X7 is V or I or F;
X8 is F or S or Y; X9 is A or P; X10 is N or S; X11 is T or V or Y or I; X12 is K or R; X13 is G or V; X14 is Y or I; X15 is Y or A;
and X16 is D or G

5

In some embodiments, an anti-TCRVb antibody disclosed herein has an antigen binding domain having a VL having a consensus sequence of SEQ ID NO: 230, wherein position 30 is G, E, A or D; position 31 is N or D; position 32 is R or K; position 36 is Y or H; and/or position 56 is K or S.

5 In some embodiments, an anti-TCRVb antibody disclosed herein has an antigen binding domain having a VH having a consensus sequence of SEQ ID NO: 231, wherein: position 27 is H or T or G or Y; position 28 is D or T or S; position 30 is H or R or D or K or T; position 31 is L or D or K or T or N; position 32 is W or F or T or I or Y or G; position 49 is R or W; position 50 is V or I or F; position 51 is F or S or Y; position 52 is A or P; position 56 is N or S; position 10 57 is T or V or Y or I; position 58 is K or R; position 97 is G or V; position 99 is Y or I; position 102 is Y or A; and/or position 103 is D or G.

Anti-TCR β V12 antibodies

Accordingly, in one aspect, the disclosure provides an anti-TCR β V antibody molecule 15 that binds to human TCR β V12, *e.g.*, a TCR β V12 subfamily comprising: TCR β V12-4*01, TCR β V12-3*01 or TCR β V12-5*01. In some embodiments the TCR β V12 subfamily comprises TCR β V12-4*01. In some embodiments the TCR β V12 subfamily comprises TCR β V12-3*01.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, is a non-murine antibody molecule, *e.g.*, a human or humanized antibody molecule. In 20 some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule is a human antibody molecule. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule is a humanized antibody molecule.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, is isolated or recombinant.

25 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, comprises at least one antigen-binding region, *e.g.*, a variable region or an antigen-binding fragment thereof, from an antibody described herein, *e.g.*, an antibody described in **Table 2A**, or encoded by a nucleotide sequence in **Table 2A**, or a sequence substantially

identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, comprises at least one, two, three or four variable regions from an antibody described
5 herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by a nucleotide sequence in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, comprises at least one or two heavy chain variable regions from an antibody described
10 herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by a nucleotide sequence in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, comprises at least one or two light chain variable regions from an antibody described
15 herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by a nucleotide sequence in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, comprises a heavy chain constant region for an IgG4, *e.g.*, a human IgG4. In still
20 another embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes a heavy chain constant region for an IgG1, *e.g.*, a human IgG1. In one embodiment, the heavy chain constant region comprises an amino sequence set forth in **Table 3A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes a kappa light chain constant region, *e.g.*, a human kappa light chain constant region. In one embodiment, the light chain constant region comprises an amino sequence set forth in **Table 3A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%,
25 95%, 97%, 98%, 99% or higher identical) thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes at least one, two, or three complementarity determining regions (CDRs) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**, or a sequence substantially
5 identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes at least one, two, or three CDRs (or collectively all of the CDRs) from a heavy chain variable region comprising an amino acid sequence shown in **Table 2A**, or encoded
10 by a nucleotide sequence shown in **Table 2A**. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes at least one, two, or three complementarity determining regions (CDRs) from a light chain variable region of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**, or a sequence substantially
15 identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes at least one, two, or three CDRs (or collectively all of the CDRs) from a light chain variable region comprising an amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino
20 acid substitutions or deletions, relative to the amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, includes at least one, two, three, four, five or six CDRs (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown

in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**. In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions or deletions, relative to the amino acid sequence shown in **Table 2A**, or encoded by a nucleotide sequence shown in **Table 2A**.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, molecule includes all six CDRs from an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**, or closely related CDRs, *e.g.*, CDRs which are identical or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*,
10 conservative substitutions). In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, may include any CDR described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three CDRs according to Kabat *et al.* (*e.g.*, at least one, two, or three CDRs according to the Kabat definition as set out in **Table 2A**) from a heavy chain
15 variable region of an antibody described herein, *e.g.*, an antibody chosen as described in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to
20 Kabat *et al.* shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three CDRs according to Kabat *et al.* (*e.g.*, at least one, two, or three CDRs according to the Kabat definition as set out in **Table 2A**) from a light chain
25 variable region of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Kabat *et al.* shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, three, four, five, or six CDRs according to Kabat *et al.* (*e.g.*, at least one, two, three, four, five, or six CDRs according to the Kabat definition as set out in **Table 2A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*,
 5 an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs
 10 according to Kabat *et al.* shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes all six CDRs according to Kabat *et al.* (*e.g.*, all six CDRs according to the Kabat definition as set out in **Table 2A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the
 15 nucleotide sequence in **Table 2A**; or encoded by the nucleotide sequence in **Table 2A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six CDRs according to Kabat *et al.*
 20 shown in **Table 2A**. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule may include any CDR described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three hypervariable loops that have the same canonical structures as the corresponding hypervariable loop of an antibody described herein, *e.g.*, an
 25 antibody described in **Table 2A**, *e.g.*, the same canonical structures as at least loop 1 and/or loop 2 of the heavy and/or light chain variable domains of an antibody described herein. See, *e.g.*, Chothia *et al.*, (1992) *J. Mol. Biol.* 227:799-817; Tomlinson *et al.*, (1992) *J. Mol. Biol.* 227:776-798 for descriptions of hypervariable loop canonical structures. These structures can be determined by inspection of the tables described in these references.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three CDRs according to Chothia *et al.* (*e.g.*, at least one, two, or three CDRs according to the Chothia definition as set out in **Table 2A**) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen as described in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Chothia et al. shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three CDRs according to Chothia *et al.* (*e.g.*, at least one, two, or three CDRs according to the Chothia definition as set out in **Table 2A**) from a light chain variable region of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to Chothia et al. shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, three, four, five, or six CDRs according to Chothia *et al.* (*e.g.*, at least one, two, three, four, five, or six CDRs according to the Chothia definition as set out in **Table 2A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs according to Chothia et al. shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes all six CDRs according to Chothia *et al.* (*e.g.*, all six CDRs according to the Chothia definition as set out in **Table 2A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or encoded by the nucleotide sequence in **Table 2A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six CDRs according to Chothia *et al.* shown in **Table 2A**. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule may include any CDR described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three CDRs according to a combined CDR (*e.g.*, at least one, two, or three CDRs according to the combined CDR definition as set out in **Table 2A**) from a heavy chain variable region of an antibody described herein, *e.g.*, an antibody chosen as described in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to combined CDR shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, or three CDRs according to a combined CDR (*e.g.*, at least one, two, or three CDRs according to the combined CDR definition as set out in **Table 2A**) from a light chain variable region of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions,

deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, or three CDRs according to a combined CDR shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes at least one, two, three, four, five, or six CDRs according to a combined CDR. (5 *e.g.*, at least one, two, three, four, five, or six CDRs according to the combined CDR definition as set out in **Table 2A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one (10 amino acid alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to one, two, three, four, five, or six CDRs according to a combined CDR shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes all six CDRs according to a combined CDR (*e.g.*, all six CDRs according to (15 the combined CDR definition as set out in **Table 2A**) from the heavy and light chain variable regions of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or encoded by the nucleotide sequence in **Table 2A**; or a sequence substantially identical (*e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical) to any of the aforesaid sequences; or which have at least one amino acid (20 alteration, but not more than two, three or four alterations (*e.g.*, substitutions, deletions, or insertions, *e.g.*, conservative substitutions) relative to all six CDRs according to a combined CDR shown in **Table 2A**. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule may include any CDR described herein.

(25 In some embodiments, a combined CDR as set out in **Table 1A** is a CDR that comprises a Kabat CDR and a Chothia CDR.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, molecule includes a combination of CDRs or hypervariable loops identified as combined CDRs in **Table 1A**. In some embodiments, the anti-TCR β V antibody molecule,

e.g., anti-TCR β V12 antibody molecule, can contain any combination of CDRs or hypervariable loops according the “combined” CDRs are described in **Table 1A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes a combination of CDRs or hypervariable loops defined according to the Kabat et al. and Chothia et al., or as described in **Table 1A**

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule can contain any combination of CDRs or hypervariable loops according to the Kabat and Chothia definitions.

In an embodiment, *e.g.*, an embodiment comprising a variable region, a CDR (*e.g.*, a combined CDR, Chothia CDR or Kabat CDR), or other sequence referred to herein, *e.g.*, in **Table 2A**, the antibody molecule is a monospecific antibody molecule, a bispecific antibody molecule, a bivalent antibody molecule, a biparatopic antibody molecule, or an antibody molecule that comprises an antigen binding fragment of an antibody, *e.g.*, a half antibody or antigen binding fragment of a half antibody. In certain embodiments the antibody molecule comprises a multispecific molecule, *e.g.*, a bispecific molecule, *e.g.*, as described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes:

(i) one, two or all of a light chain complementarity determining region 1 (LC CDR1), a light chain complementarity determining region 2 (LC CDR2), and a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 16, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29 or SEQ ID NO: 30, and/or

(ii) one, two or all of a heavy chain complementarity determining region 1 (HC CDR1), heavy chain complementarity determining region 2 (HC CDR2), and a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 15, SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 20, a LC CDR2 amino acid sequence of SEQ ID NO: 21, or a LC CDR3 amino acid sequence of SEQ ID NO: 22; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 17, a HC CDR2 amino acid sequence of SEQ ID NO: 18, or a HC CDR3 amino acid sequence of SEQ ID NO: 19.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

5 (i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 20, a LC CDR2 amino acid sequence of SEQ ID NO: 21, and a LC CDR3 amino acid sequence of SEQ ID NO: 2; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 17, a HC CDR2 amino acid sequence of SEQ ID NO: 18, and a HC CDR3 amino
10 acid sequence of SEQ ID NO: 19.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 63, a LC CDR2 amino acid sequence of SEQ ID NO: 64, or a LC CDR3 amino acid sequence of SEQ ID NO: 65; and/or

15 (ii) a HC CDR1 amino acid sequence of SEQ ID NO: 57, a HC CDR2 amino acid sequence of SEQ ID NO: 58, or a HC CDR3 amino acid sequence of SEQ ID NO: 59.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of
20 SEQ ID NO: 63, a LC CDR2 amino acid sequence of SEQ ID NO: 64, or a LC CDR3 amino acid sequence of SEQ ID NO: 65; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 57, a HC CDR2 amino acid sequence of SEQ ID NO: 58, or a HC CDR3 amino acid sequence of SEQ ID NO: 59.

25 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

(i) a LC CDR1 amino acid sequence of SEQ ID NO: 66, a LC CDR2 amino acid sequence of SEQ ID NO: 67, or a LC CDR3 amino acid sequence of SEQ ID NO: 68; and/or

(ii) a HC CDR1 amino acid sequence of SEQ ID NO: 60, a HC CDR2 amino acid sequence of SEQ ID NO: 61, or a HC CDR3 amino acid sequence of SEQ ID NO: 62.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

(i) a light chain variable region (VL) comprising a LC CDR1 amino acid sequence of SEQ ID NO: 63, a LC CDR2 amino acid sequence of SEQ ID NO: 64, or a LC CDR3 amino acid sequence of SEQ ID NO: 65; and/or

(ii) a heavy chain variable region (VH) comprising a HC CDR1 amino acid sequence of SEQ ID NO: 57, a HC CDR2 amino acid sequence of SEQ ID NO: 58, or a HC CDR3 amino acid sequence of SEQ ID NO: 59.

In one embodiment, the light or the heavy chain variable framework (*e.g.*, the region encompassing at least FR1, FR2, FR3, and optionally FR4) of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule can be chosen from: (a) a light or heavy chain variable framework including at least 80%, 85%, 87%, 90%, 92%, 93%, 95%, 97%, 98%, or 100% of the amino acid residues from a human light or heavy chain variable framework, *e.g.*, a light or heavy chain variable framework residue from a human mature antibody, a human germline sequence, or a human consensus sequence; (b) a light or heavy chain variable framework including from 20% to 80%, 40% to 60%, 60% to 90%, or 70% to 95% of the amino acid residues from a human light or heavy chain variable framework, *e.g.*, a light or heavy chain variable framework residue from a human mature antibody, a human germline sequence, or a human consensus sequence; (c) a non-human framework (*e.g.*, a rodent framework); or (d) a non-human framework that has been modified, *e.g.*, to remove antigenic or cytotoxic determinants, *e.g.*, deimmunized, or partially humanized. In one embodiment, the light or heavy chain variable framework region (particularly FR1, FR2 and/or FR3) includes a light or heavy chain variable framework sequence at least 70, 75, 80, 85, 87, 88, 90, 92, 94, 95, 96, 97, 98, 99% identical or identical to the frameworks of a VL or VH segment of a human germline gene.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, comprises a heavy chain variable domain having at least one, two, three, four, five,

six, seven, ten, fifteen, twenty or more changes, *e.g.*, amino acid substitutions or deletions, from an amino acid sequence described in **Table 2A** *e.g.*, the amino acid sequence of the FR region in the entire variable region, *e.g.*, shown in **FIGs. 2A** and **2B**, or in SEQ ID NOs: 23-25.

Alternatively, or in combination with the heavy chain substitutions described herein the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain variable domain having at least one, two, three, four, five, six, seven, ten, fifteen, twenty or more amino acid changes, *e.g.*, amino acid substitutions or deletions, from an amino acid sequence of an antibody described herein *e.g.*, the amino acid sequence of the FR region in the entire variable region, *e.g.*, shown in **FIGs. 2A** and **2B**, or in SEQ ID NOs: 26-30.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes one, two, three, or four heavy chain framework regions shown in **FIG. 2A**, or a sequence substantially identical thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes one, two, three, or four light chain framework regions shown in **FIG. 2B**, or a sequence substantially identical thereto.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the light chain framework region 1 *e.g.*, as shown in **FIG. 2B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the light chain framework region 2 *e.g.*, as shown in **FIG. 2B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the light chain framework region 3, *e.g.*, as shown in **FIG. 2B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the light chain framework region 4, *e.g.*, as shown in **FIG. 2B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more, *e.g.*, all, position disclosed herein according to Kabat numbering. In some embodiments, FR1 comprises an Aspartic Acid at position 1, *e.g.*, a substitution at position 1 according to Kabat numbering, *e.g.*, an Alanine to Aspartic Acid substitution. In some embodiments, FR1 comprises

an Asparagine at position 2, *e.g.*, a substitution at position 2 according to Kabat numbering, *e.g.*, an Isoleucine to Asparagine substitution, Serine to Asparagine substitution or Tyrosine to Asparagine substitution. In some embodiments, FR1 comprises a Leucine at position 4, *e.g.*, a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising a substitution at position 1 according to Kabat numbering, *e.g.*, an Alanine to Aspartic Acid substitution, a substitution at position 2 according to Kabat numbering, *e.g.*, an Isoleucine to Asparagine substitution, Serine to Asparagine substitution or Tyrosine to Asparagine substitution, and a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising a substitution at position 1 according to Kabat numbering, *e.g.*, an Alanine to Aspartic Acid substitution, and a substitution at position 2 according to Kabat numbering, *e.g.*, an Isoleucine to Asparagine substitution, Serine to Asparagine substitution or Tyrosine to Asparagine substitution. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising a substitution at position 1 according to Kabat numbering, *e.g.*, an Alanine to Aspartic Acid substitution, and a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 1 (FR1), comprising a substitution at position 2 according to Kabat numbering, *e.g.*, an Isoleucine to Asparagine substitution, Serine to Asparagine substitution or Tyrosine to Asparagine substitution, and a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more, *e.g.*, all, position disclosed herein according to Kabat numbering. In some embodiments, FR3
 5 comprises a Glycine at position 66, *e.g.*, a substitution at position 66 according to Kabat numbering, *e.g.*, a Lysine to Glycine substitution, or a Serine to Glycine substitution. In some embodiments, FR3 comprises an Asparagine at position 69, *e.g.*, a substitution at position 69 according to Kabat numbering, *e.g.*, a Tyrosine to Asparagine substitution. In some
 10 embodiments, FR3 comprises a Tyrosine at position 71, *e.g.*, a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, or an Alanine to Tyrosine substitution.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising a substitution at position 66 according to Kabat numbering, *e.g.*, a Lysine to
 15 Glycine substitution, or a Serine to Glycine substitution, and a substitution at position 69 according to Kabat numbering, *e.g.*, a Tyrosine to Asparagine substitution. . In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising a substitution at position 66 according to Kabat numbering, *e.g.*, Lysine to Glycine
 20 substitution, or a Serine to Glycine substitution, and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, or an Alanine to Tyrosine substitution. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising a substitution at position 69 according to Kabat numbering, *e.g.*, a
 25 Tyrosine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, or an Alanine to Tyrosine substitution. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising a framework region, *e.g.*, framework region 3 (FR3), comprising a substitution at position 66 according to Kabat numbering, *e.g.*, a Lysine to

Glycine substitution, or a Serine to Glycine substitution, a substitution at position 69 according to Kabat numbering, *e.g.*, a Tyrosine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, or an Alanine to Tyrosine substitution. In some embodiments, the substitution is relative to a human germline
5 light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising: a framework region 1 (FR1) comprising a substitution at position 2 according to Kabat numbering, *e.g.*, a Isoleucine to Asparagine
10 substitution; and a framework region 3 (FR3), comprising a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 26. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising: (a) a framework region 1 (FR1) comprising a substitution at position 1 according to Kabat numbering, *e.g.*, a Alanine to Aspartic Acid substitution, and a substitution at position 2 according to Kabat numbering, *e.g.*, a Isoleucine to Asparagine substitution; and (b) a framework region 3 (FR3), comprising a substitution at
20 position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 27. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising: (a) a framework region 1 (FR1) comprising a substitution at position 2 according to Kabat numbering, *e.g.*, a Serine to Asparagine substitution; and a substitution at position 4 according to Kabat numbering, *e.g.*, a Methionine to Leucine substitution; and (b) a framework region 3 (FR3), comprising a substitution at position
25

69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution and a substitution at position 71 according to Kabat numbering, *e.g.*, a Phenylalanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 28. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising: (a) a framework region 1 (FR1) comprising a substitution at position 2 according to Kabat numbering, *e.g.*, a Serine to Asparagine substitution; and (b) a framework region 3 (FR3) comprising a substitution at position 66 according to Kabat numbering, *e.g.*, a Lysine to Glycine substitution; a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution; and a substitution at position 71 according to Kabat numbering, *e.g.*, a Alanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 29. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

15 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain comprising: (a) a framework region 1 (FR1) comprising a substitution at position 2 according to Kabat numbering, *e.g.*, a Tyrosine to Asparagine substitution; and (b) a framework region 3 (FR3) comprising a substitution at position 66 according to Kabat numbering, *e.g.*, a Serine to Glycine substitution; a substitution at position 69 according to Kabat numbering, *e.g.*, a Threonine to Asparagine substitution; and a substitution at position 71 according to Kabat numbering, *e.g.*, a Alanine to Tyrosine substitution, *e.g.*, as shown in the amino acid sequence of SEQ ID NO: 29. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

25 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises a light chain variable domain comprising: (a) a framework region 1 (FR1) comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more (*e.g.*, all) positions disclosed herein according to Kabat numbering, and (b) a framework region 3 (FR3) comprising a change, *e.g.*, a substitution (*e.g.*, a conservative substitution) at one or more

(*e.g.*, all) position disclosed herein according to Kabat numbering. In some embodiments, the substitution is relative to a human germline light chain framework region sequence.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the heavy chain framework region 1, *e.g.*, as shown in **FIG. 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the heavy chain framework region 2, *e.g.*, as shown in **FIG. 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the heavy chain framework region 3, *e.g.*, as shown in **FIG. 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the heavy chain framework region 4, *e.g.*, as shown in **FIG. 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the heavy chain framework regions 1-4, *e.g.*, SEQ ID NOS: 20-23, or as shown in **FIG. 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the light chain framework regions 1-4, *e.g.*, SEQ ID NOS: 26-30, or as shown in **FIG. 2B**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises the heavy chain framework regions 1-4, *e.g.*, SEQ ID NOS: 23-25; and the light chain framework regions 1-4, *e.g.*, SEQ ID NOS: 26-30, or as shown in **FIGs. 2A and 2B**.

In some embodiments, the heavy or light chain variable domain, or both, of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes an amino acid sequence, which is substantially identical to an amino acid disclosed herein, *e.g.*, at least 80%, 85%, 90%, 92%, 95%, 97%, 98%, 99% or higher identical to a variable region of an antibody described herein, *e.g.*, an antibody as described in **Table 2A**, or encoded by the nucleotide sequence in **Table 2A**; or which differs at least 1 or 5 residues, but less than 40, 30, 20, or 10 residues, from a variable region of an antibody described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises at least one, two, three, or four antigen-binding regions, *e.g.*, variable regions, having an amino acid sequence as set forth in **Table 2A**, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the sequences shown in **Table 2A**. In another embodiment, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule includes a VH and/or VL domain encoded by a nucleic acid having a nucleotide sequence as set forth in **Table 2A**, or a sequence substantially identical thereto (*e.g.*, a sequence at least about 85%, 90%, 95%, 99% or more identical thereto, or which differs by no more than 3, 6, 15, 30, or 45 nucleotides from the sequences shown in **Table 2A**.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising an amino acid sequence chosen from the amino acid sequence of SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23, SEQ ID NO: 24, or SEQ ID NO: 25; and/or

a VL domain comprising an amino acid sequence chosen from the amino acid sequence of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, or SEQ ID NO: 30.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ

ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 26, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 26, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 27, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 27, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 27.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 28, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 28, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 28.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

5 a VL domain comprising the amino acid sequence of SEQ ID NO: 29, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 29, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 29.

10 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 23, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 23, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 23; and

15 a VL domain comprising the amino acid sequence of SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 30.

20 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

25 a VL domain comprising the amino acid sequence of SEQ ID NO: 26, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 26, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 27, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 27, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 27.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 28, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 28, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 28.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 29, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ

ID NO: 29, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 29.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

5 a VH domain comprising the amino acid sequence of SEQ ID NO: 24, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 24, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 24; and

10 a VL domain comprising the amino acid sequence of SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 30.

15 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

20 a VL domain comprising the amino acid sequence of SEQ ID NO: 26, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 26, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 26.

25 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 27, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 27, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 27.

5 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 28, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 28, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 28.

15 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 29, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 29, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 29.

25 In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule comprises:

a VH domain comprising the amino acid sequence of SEQ ID NO: 25, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ

ID NO: 25, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 25; and

a VL domain comprising the amino acid sequence of SEQ ID NO: 30, an amino acid sequence at least about 85%, 90%, 95%, 99% or more identical to the amino acid sequence SEQ ID NO: 30, or an amino acid sequence which differs by no more than 1, 2, 5, 10, or 15 amino acid residues from the amino acid sequence of SEQ ID NO: 30.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule is a full antibody or fragment thereof (*e.g.*, a Fab, F(ab')₂, Fv, or a single chain Fv fragment (scFv)). In embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V6 (*e.g.*, anti-TCR β V6-5*01) antibody molecule is a monoclonal antibody or an antibody with single specificity. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule, can also be a humanized, chimeric, camelid, shark, or an *in vitro*-generated antibody molecule. In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule is a humanized antibody molecule. The heavy and light chains of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule can be full-length (*e.g.*, an antibody can include at least one, and preferably two, complete heavy chains, and at least one, and preferably two, complete light chains) or can include an antigen-binding fragment (*e.g.*, a Fab, F(ab')₂, Fv, a single chain Fv fragment, a single domain antibody, a diabody (dAb), a bivalent antibody, or bispecific antibody or fragment thereof, a single domain variant thereof, or a camelid antibody).

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule is in the form of a multispecific molecule, *e.g.*, a bispecific molecule, *e.g.*, as described herein.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule has a heavy chain constant region (Fc) chosen from, *e.g.*, the heavy chain constant regions of IgG1, IgG2, IgG3, IgG4, IgM, IgA1, IgA2, IgD, and IgE. In some embodiments, the Fc region is chosen from the heavy chain constant regions of IgG1, IgG2, IgG3, and IgG4. In some embodiments, the Fc region is chosen from the heavy chain constant region of IgG1 or

IgG2 (*e.g.*, human IgG1, or IgG2). In some embodiments, the heavy chain constant region is human IgG1.

In some embodiments, the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule has a light chain constant region chosen from, *e.g.*, the light chain constant regions of kappa or lambda, preferably kappa (*e.g.*, human kappa). In one embodiment, the constant region is altered, *e.g.*, mutated, to modify the properties of the anti-TCR β V antibody molecule, *e.g.*, anti-TCR β V12 antibody molecule (*e.g.*, to increase or decrease one or more of: Fc receptor binding, antibody glycosylation, the number of cysteine residues, effector cell function, or complement function). For example, the constant region is mutated at positions 296 (M to Y), 298 (S to T), 300 (T to E), 477 (H to K) and 478 (N to F) to alter Fc receptor binding (*e.g.*, the mutated positions correspond to positions 132 (M to Y), 134 (S to T), 136 (T to E), 313 (H to K) and 314 (N to F) of SEQ ID NOs: 212 or 214; or positions 135 (M to Y), 137 (S to T), 139 (T to E), 316 (H to K) and 317 (N to F) of SEQ ID NOs: 215, 216, 217, or 218).

Antibody B-H.1 comprises a first chain comprising the amino acid sequence of SEQ ID NO: 3280 and a second chain comprising the amino acid sequence of SEQ ID NO: 3281.

Additional exemplary anti-TCR β V12 antibodies of the disclosure are provided in **Table 2A**. In some embodiments, the anti-TCR β V12 is antibody B, *e.g.*, humanized antibody B (antibody B-H), as provided in **Table 2A**. In some embodiments, the anti-TCR β V antibody comprises one or more (*e.g.*, all three) of a LC CDR1, LC CDR2, and LC CDR3 provided in **Table 2A**; and/or one or more (*e.g.*, all three) of a HC CDR1, HC CDR2, and HC CDR3 provided in **Table 2A**, or a sequence with at least 95% identity thereto. In some embodiments, antibody B comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Table 2A**, or a sequence with at least 95% identity thereto.

Table 2A: Amino acid and nucleotide sequences for murine and humanized antibody molecules which bind to TCRVB 12, e.g., TCRVB 12-3 or TCRVB 12-4. The antibody molecules include murine mAb Antibody B and humanized mAb Antibody B-H.1to B-H.6. The amino acid the heavy and light chain CDRs, and the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the heavy and light chains are shown.

Antibody B (murine)		
SEQ ID NO: 17	HC CDR1 (Combined)	GFTFSNFGMH
SEQ ID NO: 18	HC CDR2 (Combined)	YISSGSSTIYYADTLKG
SEQ ID NO: 19	HC CDR3 (Combined)	RGEGAMDY
SEQ ID NO: 57	HC CDR1 (Kabat)	NFGMH
SEQ ID NO: 58	HC CDR2 (Kabat)	YISSGSSTIYYADTLKG
SEQ ID NO: 59	HC CDR3 (Kabat)	RGEGAMDY
SEQ ID NO: 60	HC CDR1 (Chothia)	GFTFSNF
SEQ ID NO: 61	HC CDR2 (Chothia)	SSGSST
SEQ ID NO: 62	HC CDR3 (Chothia)	RGEGAMDY
SEQ ID NO: 15	VH	DVQLVESGGGLVQPGGSRKLSAASGF TFSNFGMHWVRQAPDKGLEWVAYISS GSSTIYYADTLKGRFTISRDNPKNLFL QMTSLRSEDAMYYCARRGEGAMDY WGQGSVTVSS
SEQ ID NO: 20	LC CDR1 (Combined)	RASSSVNYIY
SEQ ID NO: 21	LC CDR2 (Combined)	YTSNLAP
SEQ ID NO: 22	LC CDR3(Combined)	QQFTSSPFT
SEQ ID NO: 63	LC CDR1 (Kabat)	RASSSVNYIY
SEQ ID NO: 64	LC CDR2 (Kabat)	YTSNLAP
SEQ ID NO: 65	LC CDR3 (Kabat)	QQFTSSPFT
SEQ ID NO: 66	LC CDR1 (Chothia)	RASSSVNYIY
SEQ ID NO: 67	LC CDR2 (Chothia)	YTSNLAP
SEQ ID NO: 68	LC CDR3 (Chothia)	QQFTSSPFT
SEQ ID NO: 16	VL	ENVLTQSPAIMSASLGEKVTMSCRASSS VNYIYWYQQKSDASPKLWIYYTSNLAP GVPTRFSGSGSGNSYSLTISMEGEDAA TYYCQQFTSSPFTFGSGTKLEIK
Antibody B humanized (B-H)		
Antibody B-H.1A HC-1		
SEQ ID NO: 17	HC CDR1 (Combined)	GFTFSNFGMH
SEQ ID NO: 18	HC CDR2 (Combined)	YISSGSSTIYYADTLKG
SEQ ID NO: 19	HC CDR3 (Combined)	RGEGAMDY
SEQ ID NO: 23	VH	EVQLVESGGGLVQPGGSLRLSAAASGF TFSNFGMHWVRQAPGKGLEWVSYISSG SSTIYYADTLKGRFTISRDNAKNSLYLQ MNSLRAEDTAVYYCARRGEGAMDYW

		GQGTTVTVSS
SEQ ID NO: 31	DNA VH	GAGGTGCAGCTGGTTGAATCTGGCGG AGGATTGGTTCAGCCTGGCGGCTCTCT GAGACTGTCTTGTGCCGCTTCTGGCTT CACCTTCTCCAACCTTCGGCATGCACTG GGTCCGACAGGCCCCTGGAAAAGGAC TGGAATGGGTGTCCTACATCTCCTCCG GCTCCTCCACCATCTACTACGCTGACA CCCTGAAGGGCAGATTCACCATCTCT CGGGACAACGCCAAGAACTCCCTGTA CCTGCAGATGAACAGCCTGAGAGCCG AGGACACCGCCGTGTACTACTGTGCT AGAAGAGGCGAGGGCGCCATGGATTA TTGGGGCCAGGGAACCACAGTGACCG TGTCTAGC
Antibody B-H.1B HC-2		
SEQ ID NO: 17	HC CDR1 (Combined)	GFTFSNFGMH
SEQ ID NO: 18	HC CDR2 (Combined)	YISSGSSTIYYADTLKG
SEQ ID NO: 19	HC CDR3 (Combined)	RGEGAMDY
SEQ ID NO: 24	VH	EVQLVESGGGLVQPGGSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVSYISSG SSTIYYADTLKGRFTISRDN SKNTLYLQ MNSLRAEDTAVYYCARRGEGAMDYW GQGTTVTVSS
SEQ ID NO: 32	DNA VH	GAGGTGCAGCTGGTTGAATCTGGCGG AGGATTGGTTCAGCCTGGCGGCTCTCT GAGACTGTCTTGTGCCGCTTCTGGCTT CACCTTCTCCAACCTTCGGCATGCACTG GGTCCGACAGGCCCCTGGAAAAGGAC TGGAATGGGTGTCCTACATCTCCTCCG GCTCCTCCACCATCTACTACGCTGACA CCCTGAAGGGCAGATTCACCATCAGC CGGGACAACCTCCAAGAACACCCTGTA CCTGCAGATGAACTCCCTGAGAGCCG AGGACACCGCCGTGTACTACTGTGCT AGAAGAGGCGAGGGCGCCATGGATTA TTGGGGCCAGGGAACCACAGTGACCG TGTCTAGC
Antibody B-H.1C HC-3		
SEQ ID NO: 17	HC CDR1 (Combined)	GFTFSNFGMH
SEQ ID NO: 18	HC CDR2 (Combined)	YISSGSSTIYYADTLKG
SEQ ID NO: 19	HC CDR3 (Combined)	RGEGAMDY
SEQ ID NO: 25	VH	QVQLVESGGGVVQPGRSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVAYISS GSSTIYYADTLKGRFTISRDN SKNTLYL QMNSLRAEDTAVYYCARRGEGAMDY

		WGQGTTVTVSS
SEQ ID NO: 33	DNA VH	CAGGTGCAGCTGGTGGGAATCTGGTGG CGGAGTTGTGCAGCCTGGCAGATCCC TGAGACTGTCTTGTGCCGCCTCTGGCT TCACCTTCTCCAACCTTCGGCATGCACT GGGTCCGACAGGCCCTGGAAAAGGA TTGGAGTGGGTTCGCCTACATCTCCTCC GGCTCCTCCACCATCTACTACGCTGAC ACCCTGAAGGGCAGATTACCATCAG CCGGGACAACCTCCAAGAACACCCTGT ACCTGCAGATGAACTCCCTGAGAGCC GAGGACACCGCCGTGTACTACTGTGC TAGAAGAGGCGAGGGCGCCATGGATT ATTGGGGCCAGGGAACACAGTGACC GTGTCTAGC
Antibody B-H.1D LC-1		
SEQ ID NO: 20	LC CDR1 (Combined)	RASSSVNYIY
SEQ ID NO: 21	LC CDR2 (Combined)	YTSNLAP
SEQ ID NO: 22	LC CDR3(Combined)	QQFTSSPFT
SEQ ID NO: 26	VL	DNQLTQSPSFLSASVGDRVITICRASSS VNYIYWYQQKPGKAPKLLIYYTSNLAP GVPSRFSGSGSGNEYTLTISSLQPEDFAT YYCQQFTSSPFTFGQGTKLEIK
SEQ ID NO: 34	DNA VL	GATAACCAGCTGACCCAGTCTCCTAG CTTCCTGTCTGCCTCTGTGGGCGACAG AGTGACAATTACCTGCCGGGCCTCCT CCTCCGTGAACTACATCTACTGGTATC AGCAGAAGCCCGGCAAGGCCCTAAG CTGCTGATCTACTACACCTCCAATCTG GCCCCTGGCGTGCCCTCTAGATTTTCC GGATCTGGCTCCGGCAACGAGTATAC CCTGACAATCTCCAGCCTGCAGCCTG AGGACTTCGCCACCTACTACTGCCAG CAGTTCACCTCCTCTCCATTCACCTTT GGCCAGGGCACCAAGCTGGAAATCAA A
Antibody B-H.1E LC-2		
SEQ ID NO: 20	LC CDR1 (Combined)	RASSSVNYIY
SEQ ID NO: 21	LC CDR2 (Combined)	YTSNLAP
SEQ ID NO: 22	LC CDR3(Combined)	QQFTSSPFT
SEQ ID NO: 27	VL	DNQLTQSPSSLASVGDRVITICRASSS VNYIYWYQQKPGKAPKLLIYYTSNLAP GVPSRFSGSGSGNDYTLTISSLQPEDFAT YYCQQFTSSPFTFGQGTKLEIK
SEQ ID NO: 35	DNA VL	ATAACCAGCTGACCCAGTCTCCTTCCA GCCTGTCTGCTTCTGTGGGCGACAGA

		GTGACAATTACCTGCCGGGCCTCCTCC TCCGTGAACTACATCTACTGGTATCAG CAGAAGCCCGGCAAGGCCCTAAGCT GCTGATCTACTACACCTCCAATCTGGC CCCTGGCGTGCCCTCTAGATTTTCCGG ATCTGGCTCCGGCAACGACTATACCC TGACAATCTCCAGCCTGCAGCCTGAG GACTTCGCCACCTACTACTGCCAGCA GTTACCTCCTCTCCATTACCTTTGG CCAGGGCACCAAGCTGGAAATCAAA
Antibody B-H.1F LC-3		
SEQ ID NO: 20	LC CDR1 (Combined)	RASSSVNYIY
SEQ ID NO: 21	LC CDR2 (Combined)	YTSNLAP
SEQ ID NO: 22	LC CDR3(Combined)	QQFTSSPFT
SEQ ID NO: 28	VL	ENVLTQSPATLSVSPGERATLSCRASS VNYIYWYQQKPGQAPRLLIYYTSNLAP GIPARFSGSGSGNEYTLTISSLQSEDFAV YYCQQFTSSPFTFGQGTKLEIK
SEQ ID NO: 36	DNA VL	GAGAATGTGCTGACCCAGTCTCCTGC CACTGTCTGTAGCCCTGGCGAGA GAGCTACCCTGAGCTGCAGAGCCTCT TCCTCCGTGAACTACATCTACTGGTAT CAGCAGAAGCCCGGCCAGGCTCCTAG ACTGCTGATCTACTACACCTCCAATCT GGCCCTGGCATCCCTGCCAGATTTTC CGGATCTGGCTCCGGCAACGAGTATA CCCTGACCATCTCCAGCCTGCAGTCCG AGGACTTTGCTGTGTACTATTGCCAGC AGTTCACAAGCAGCCCTTTCACCTTTG GCCAGGGCACCAAGCTGGAAATCAAA
Antibody B-H.1G LC-4		
SEQ ID NO: 20	LC CDR1 (Combined)	RASSSVNYIY
SEQ ID NO: 21	LC CDR2 (Combined)	YTSNLAP
SEQ ID NO: 22	LC CDR3(Combined)	QQFTSSPFT
SEQ ID NO: 29	VL	QNVLTQPPSASGTPGQRVTISCRASSV NYIYWYQQLPGTAPKLLIYYTSNLAPG VPDRFSGSGSGNSYSLAISGLRSEDEAD YYCQQFTSSPFTFGTGTKVTVL
SEQ ID NO: 37	DNA VL	CAGAATGTGCTGACCCAACCTCCTTCC GCCTCTGGCACACCTGGACAGAGAGT GACAATCTCCTGCCGGGCCTCCTCCTC CGTGAACCTACATCTACTGGTATCAGC AGCTGCCCCGGCACCGCTCCTAAACTG CTGATCTACTACACCTCCAATCTGGCC CCTGGCGTGCCCGATAGATTTTCCGG ATCTGGCTCCGGCAACTCCTACAGCCT

		GGCTATCTCTGGCCTGAGATCTGAGG ACGAGGCCGACTACTACTGCCAGCAG TTCACCTCCTCTCCATTACCTTTGGC ACCGGCACCAAAGTGACAGTTCTT
Antibody B-H.1H LC-5		
SEQ ID NO: 20	LC CDR1 (Combined)	RASSSVNYIY
SEQ ID NO: 21	LC CDR2 (Combined)	YTSNLAP
SEQ ID NO: 22	LC CDR3(Combined)	QQFTSSPFT
SEQ ID NO: 30	VL	SNELTQPPSVSVSPGQTARITCRASSSVN YIYWYQQKSGQAPVLVIYYTSNLAPGIP ERFSGSGSGNMYTLTISGAQVEDEADY YCQQFTSSPFTFGTGTKVTVL
SEQ ID NO: 38	DNA VL	TCTAATGAGCTGACCCAGCCTCCTTCC GTGTCCGTGTCTCCTGGACAGACCGC CAGAATTACCTGCCGGGCCTCCTCCTC CGTGAACCTACATCTACTGGTATCAGC AGAAGTCCGGCCAGGCTCCTGTGCTC GTGATCTACTACACCTCCAATCTGGCC CCTGGCATCCCTGAGAGATTCTCCGG ATCTGGCTCCGGCAACATGTACACCC TGACCATCTCTGGCGCCAGGTGGAA GATGAGGCCGACTACTACTGCCAGCA GTTACCTCCTCTCCATTACCTTTGG CACCGGCACCAAAGTGACAGTTCTT
Antibody B-H.1		
SEQ ID NO: 3280	Chain1: Fc only	METDTLLLWVLLLVWPGSTGDKTHTCP PCPAPELLGGPSVFLFPPKPKDTLMISRT PEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPCREEMTKNQV SLWCLVKGFYPSDIAVEWESNGQPENN YKTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNRTQKSLSLS PGK
SEQ ID NO: 3281	Chain2: humanized B-H scFv	METDTLLLWVLLLVWPGSTGEVQLVES GGGLVQPGGSLRLSCAASGFTFSNFGM HWVRQAPGKGLEWVSYISSGSSTIYYA DTLKGRFTISRDNKNTLYLQMNSLRA EDTAVYYCARRGEGAMDYWGQGTTV TVSSGGGGSGGGGSGGGGSGGGGSDN QLTQSPSFLSASVGDRVITTCRASSSVN YIYWYQQKPGKAPKLLIYYTSNLAPGV PSRFSGSGSGNEYTLTISSLQPEDFATYY CQQFTSSPFTFGQGTKLEIKGGGSDKT HTCPPCPAPELLGGPSVFLFPPKPKDTL

		MISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVS VLTVLHQDWLNGKEYKCKVSNKALPA PIEKTISKAKGQPREPQVCTLPSSREEMT KNQVSLSCAVKGFYPSDIAVEWESNGQ PENNYKTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGKGGGGSGGGGSGGLNDIFEAQKI EWHE
SEQ ID NO: 1343	scFv	EVQLVESGGGLVQPGGSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVSYISSG SSTIYYADTLKGRFTISRDN SKNTLYLQ MNSLRAEDTAVYYCARRGEGAMDYW GQGTTTVTVSSGGGGSGGGGSGGGGSG GGGSDNQLTQSPSFLSASVGDRVITICR ASSSVNYIYWYQQKPGKAPKLLIYYTS NLAPGVPSRFSGSGSGNEYTLTISSLQPE DFATYYCQQFTSSPFTFGQGTKLEIK
Antibody B-H.2		
SEQ ID NO: 1338	scFv	EVQLVESGGGLVQPGGSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVSYISSG SSTIYYADTLKGRFTISRDN SKNTLYLQ MNSLRAEDTAVYYCARRGEGAMDYW GQGTTTVTVSSGGGGSGGGGSGGGGSG GGGSDNQLTQSPSFLSASVGDRVITICR ASSSVNYIYWYQQKPGKAPKLLIYYTS NLAPGVPSRFSGSGSGNDYTLTISSLQPE DFATYYCQQFTSSPFTFGQGTKLEIK
Antibody B-H.3		
SEQ ID NO: 1339	scFv	EVQLVESGGGLVQPGGSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVSYISSG SSTIYYADTLKGRFTISRDN SKNTLYLQ MNSLRAEDTAVYYCARRGEGAMDYW GQGTTTVTVSSGGGGSGGGGSGGGGSG GGGSSNELTQPPSVSVSPGQTARITCRA SSSVNYIYWYQQKSGQAPVLVIYYTSN LAPGIPERFSGSGSGNMYTLTISGAQVE DEADYYCQQFTSSPFTFGTGKVTVL
Antibody B-H.4		
SEQ ID NO: 1340	scFv	QVQLVESGGGVVQPGRSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVAYISS GSSTIYYADTLKGRFTISRDN SKNTLYLQ QMNSLRAEDTAVYYCARRGEGAMDY WGQGTTTVTVSSGGGGSGGGGSGGGGSG GGGGSDNQLTQSPSFLSASVGDRVITIC RASSSVNYIYWYQQKPGKAPKLLIYYT

		SNLAPGVPSRFSGSGSGNEYTLTISSLQP EDFATYYCQQFTSSPFTFGQGTKLEIK
Antibody B-H.5		
SEQ ID NO: 1341	scFv	QVQLVESGGGVVQPGRSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVAYISS GSSTIYYADTLKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCARRGEGAMDY WGQGTTVTVSSGGGGSGGGGSGGGGS GGGGSDNQLTQSPSSLSASVGDRVITC RASSSVNYIYWYQQKPGKAPKLLIYYT SNLAPGVPSRFSGSGSGNDYTLTISSLQP EDFATYYCQQFTSSPFTFGQGTKLEIK
Antibody B-H.6		
SEQ ID NO: 1342	scFv	QVQLVESGGGVVQPGRSLRLSCAASGF TFSNFGMHWVRQAPGKGLEWVAYISS GSSTIYYADTLKGRFTISRDNSKNTLYL QMNSLRAEDTAVYYCARRGEGAMDY WGQGTTVTVSSGGGGSGGGGSGGGGS GGGGSSNELTQPPSVSVSPGQTARITCR ASSSVNYIYWYQQKSGQAPVLVIYYTS NLAPGIPERFSGSGSGNMYTLTISGAQV EDEADYYCQQFTSSPFTFGTGTGKVTVL

Table 3A. Constant region amino acid sequences of human IgG heavy chains and human kappa light chain

Human kappa constant region SEQ ID NO: 39	LC	RTVAAPSVFI FPPSDEQLKS GTASVVCLLN NFYPREAKVQ WKVDNALQSG NSQESVTEQD SKDSTYSLSS TLTLISKADYE KHKVYACEVT HQGLSSPVTK SFNRGEC
IgG4 (S228P) mutant constant region (EU Numbering) SEQ ID NO: 40	HC	ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTQYTCNVDHKPSNT KVDKRVESKYGPCCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEV TCVVVDVSDQEDPEVKFNWYVDGVEVHNAKTKPREEQFNSTYRVV SVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQ KSLSLSLG
IgG1 wild type SEQ ID NO: 41	HC	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTQYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRT EVTCTVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSVELTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK

IgG1 (N297A) mutant constant region (EU Numbering) SEQ ID NO: 42	HC	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYR VVSVELTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMHEALHNHY TQKSLSLSPGK
IgM constant delta CDC (P311A, P313S) SEQ ID NO: 73	HC	GSASAPTLFPLVSCENSPSDTSSVAVGCLAQDFLPDSITFSWKYKNN SDISSTRGFPSVLRGGKYAATSQVLLPSKDVMQGTDEHVVCVKVQH PNGNKEKNVPLPVIAELPPKVSFVPPRDRGFFGNPRKSKLICQATGF SPRQIQVSWLREGKQVSGSVTTDQVQAEAKESGPTTYKVTSTLTIK ESDWLGQSMFTCRVDHRGLTFQQNASSMCVPDQDTAIRVFAIPPSF ASIFLTKSTKLTCVTDLTITYDSVTISWTRQNGEAVKTHTNISESH NATFSAVGEASICEDDWNSEGERFTCTVTHTDLASSLKQTISRPGV ALHRPDVYLLPPAREQLNLRESATITCLVTGFSPADV FVQWMQRG QPLSPEKYVTSAPMPEPQAPGRYFAHSILTVSEEWNTGETYTCVV AHEALPNRVTERTVDKSTGKPTLYNVSLVMSDTAGTCY
IgGA1 SEQ ID NO: 74	HC	ASPTSPKVFPLSLCSTQPDGNVVIACLVQGFFPQEPLSVTWSESGQG VTARNFPPSQDASGDLYTTSSQLTLPATQCLAGKSVTCHVKHYTNP SQDVTVPFVPPSTPPTPSPSTPPTPSPSCCHPRLSLHRPALEDLLGSE ANLTCTLTGLRDASGVFTFTWTPSSGKSAVQGPPERDLCGCYSVSSV LPGCAEPWNHGKTFTCTAAYPESKTPLTATLSKSGNTFRPEVHLLP PPSEELALNELVTLTCLARGFSPKDVLRWLQGSQELPREKYLTW ASRQEPSQGTTFFAVTSILRVA AEDWKKGDTFSCMVGHEALPLAF TQKTIDRLAGKPTHVNVSVVMAEVDGTCY
IgGA2 SEQ ID NO: 75	HC	ASPTSPKVFPLSLDSTPQDGNVVVACL VQGFFPQEPLSVTWSESGQ NVTARNFPPSQDASGDLYTTSSQLTLPATQCPDGKSVTCHVKHYT NSSQDVTVPFVPPPPPCCHPRLSLHRPALEDLLGSEANLTCTLTG LRDASGATFTWTPSSGKSAVQGPPERDLCGCYSVSSVLPGCAQPW NHGETFTCTAAHPELKTPLTANITKSGNTFRPEVHLLPPPSEELALN ELVTLTCLARGFSPKDVLRWLQGSQELPREKYLTWASRQEPSQG TTTYAVTSILRVA AEDWKKGETFSCMVGHEALPLAFTQKTIDRMA GKPTHINVSVMMAEADGTCY
Human Ig_J chain SEQ ID NO: 76	HC	MKNHLLFWGVLAVFIKAVHVKAQEDERIVLVDNKCKCARITSRIIR SSEDPNEDIVERNIRIIVPLNNRENISDPTSPLRTRFVYHLSDLCKKC DPTEVELDNQIVTATQSNICDEDSATETCYTYDRNKCYTAVVPLVY GGETKMOVETALTPDACYPD

Anti-TCR β V5 antibodies

Accordingly, in one aspect, the disclosure provides an anti-TCR β V antibody molecule that binds to human TCR β V5. In some embodiments, the TCR β V5 subfamily comprises TCR β V5-5*01, TCR β V5-6*01, TCR β V5-4*01, TCR β V5-8*01, TCR β V5-1*01, or a variant thereof.

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Exemplary anti-TCR β V5 antibodies of the disclosure are provided in **Table 10A**. In some embodiments, the anti-TCR β V5 is antibody C, e.g., humanized antibody C (antibody C-H), as provided in **Table 10A**. In some embodiments, the anti-TCR β V antibody comprises one or more (e.g., all three) of a LC CDR1, LC CDR2, and LC CDR3 provided in **Table 10A**; and/or one or more (e.g., all three) of a HC CDR1, HC CDR2, and HC CDR3 provided in **Table 10A**, or a sequence with at least 95% identity thereto. In some embodiments, antibody C comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Table 10A**, or a sequence with at least 95% identity thereto.

10 **Table 10A: Amino acid sequences for anti TCR β V5 antibodies**

Amino acid and nucleotide sequences for murine and humanized antibody molecules which bind to TCRVB 5 (e.g., TCRVB 5-5 or TCRVB 5-6). The amino acid the heavy and light chain CDRs, and the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the heavy and light chains are shown.

Murine antibody C		
SEQ ID NO: 1315	HC CDR1 (Kabat)	AYGVN
SEQ ID NO: 1316	HC CDR2 (Kabat)	MIWGDGNTDYN SALKS
SEQ ID NO: 1317	HC CDR3 (Kabat)	DRVTATLYAMDY
SEQ ID NO: 1318	HC CDR1 (Chothia)	GFSLTAY
SEQ ID NO: 1319	HC CDR2 (Chothia)	WGDGN
SEQ ID NO: 1317	HC CDR3 (Chothia)	DRVTATLYAMDY
SEQ ID NO: 1320	HC CDR1 (Combined)	GFSLTAYGVN
SEQ ID NO: 1316	HC CDR2 (Combined)	MIWGDGNTDYN SALKS
SEQ ID NO: 1317	HC CDR3(Combined)	DRVTATLYAMDY
SEQ ID NO: 1321	LC CDR1 (Kabat)	SASQGISNYLN
SEQ ID NO: 1322	LC CDR2 (Kabat)	YTSSLHS
SEQ ID NO: 1323	LC CDR3 (Kabat)	QQYSKLPRT
SEQ ID NO: 1321	LC CDR1 (Chothia)	SASQGISNYLN
SEQ ID NO: 1322	LC CDR2 (Chothia)	YTSSLHS
SEQ ID NO: 1323	LC CDR3 (Chothia)	QQYSKLPRT
SEQ ID NO: 1321	LC CDR1 (Combined)	SASQGISNYLN
SEQ ID NO: 1322	LC CDR2	YTSSLHS

	(Combined)	
SEQ ID NO: 1323	LC CDR3(Combined)	QQYSKLPRT
SEQ ID NO: 232	VH	DIQMTQTTSSLSASLGDRVTISCSASQGISNYLN WYQQKPDGTVKLLIYYTSSLHSGVPSRFSGSGSG TDYSLTISNLEPEDIATYYCQQYSKLPRTFGGGT KVEIK
SEQ ID NO: 233	VL	QVQLKESGPGLVAPSQSLSTCTVSGFSLTAYGV NWVRQPPGKGLEWLGMIWGDGNTDYN SALKS RLSISKDNSKSVFLKMNSLQTD TARY YCARD RVTATLYAMDYWGQGTSTVTVSS
Humanized antibody C		
C-H-1 antibody		
SEQ ID NO: 1315	HC CDR1 (Kabat)	AYGVN
SEQ ID NO: 1316	HC CDR2 (Kabat)	MIWGDGNTDYN SALKS
SEQ ID NO: 1317	HC CDR3 (Kabat)	DRVTATLYAMDY
SEQ ID NO: 1318	HC CDR1 (Chothia)	GFSLTAY
SEQ ID NO: 1319	HC CDR2 (Chothia)	WGDGN
SEQ ID NO: 1317	HC CDR3 (Chothia)	DRVTATLYAMDY
SEQ ID NO: 1320	HC CDR1 (Combined)	GFSLTAYGVN
SEQ ID NO: 1316	HC CDR2 (Combined)	MIWGDGNTDYN SALKS
SEQ ID NO: 1317	HC CDR3(Combined)	DRVTATLYAMDY
SEQ ID NO: 1321	LC CDR1 (Kabat)	SASQGISNYLN
SEQ ID NO: 1322	LC CDR2 (Kabat)	YTSSLHS
SEQ ID NO: 1323	LC CDR3 (Kabat)	QQYSKLPRT
SEQ ID NO: 1321	LC CDR1 (Chothia)	SASQGISNYLN
SEQ ID NO: 1322	LC CDR2 (Chothia)	YTSSLHS
SEQ ID NO: 1323	LC CDR3 (Chothia)	QQYSKLPRT
SEQ ID NO: 1321	LC CDR1 (Combined)	SASQGISNYLN
SEQ ID NO: 1322	LC CDR2 (Combined)	YTSSLHS
SEQ ID NO: 1323	LC CDR3(Combined)	QQYSKLPRT
SEQ ID NO: 1324	VL	DIQMTQSPSSLSASVGDRTITCSASQGISNYLNW YQQTPGKAPKLLIYYTSSLHSGVPSRFSGSGSGTD

			YTFTISSLQPEDATYYCQQYSKLPRTFGGQTKLQIT
SEQ ID NO: 1325	VH		QVQLQESGPGLVPRPSQTLSTCTVSGFSLTAYGV NWVRQPPGRGLEWLGMIWGDGNTDYNALKSR VTMLKDTSKNQFSLRLSSVTAADTAVYYCARDR VTATLYAMDYWGQGSGLTVSS
Humanized antibody C Variable light chain (VL)			
SEQ ID NO: 3000	VL	C-H-VL.1	DIQMTQSPSFLSASVGDRVTITCSASQGISNYLN WYQQKPGKAVKLLIYYTSSLHSGVPSRFSGSGS GTEYTLTISSLQPEDFATYYCQQYSKLPRTFGGG TKVEIK
SEQ ID NO: 3001	VL	C-H-VL.2	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKAVKLLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISSLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3002	VL	C-H-VL.3	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKVVKLLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISSLQPEDVATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3003	VL	C-H-VL.4	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISSLQPEDVATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3004	VL	C-H-VL.5	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKAVKLLIYYTSSLHSGVPSRFSGSGSGTDYTF ISSLQPEDATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3005	VL	C-H-VL.6	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKTVKLLIYYTSSLHSGIPSRFSGSGSGTDYTLT IRSLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3006	VL	C-H-VL.7	AIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKAVKLLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISSLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3007	VL	C-H-VL.8	DIQMTQSPSSVSASVGDRVTITCSASQGISNYLNWYQ QKPGKAVKLLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISSLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3008	VL	C-H-VL.9	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKAVKRLIYYTSSLHSGVPSRFSGSGSGTEYTLT ISNLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3009	VL	C-H-VL.10	AIRMTQSPFSLSASVGDRVTITCSASQGISNYLNWYQ QKPAKAVKLFIIYYTSSLHSGVPSRFSGSGSGTDYTLT ISSLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3010	VL	C-H-VL.11	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKAVKRLIYYTSSLHSGVPSRFSGSGSGTEYTLT ISSLQPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3011	VL	C-H-VL.12	DIQMTQSPSTLSASVGDRVTITCSASQGISNYLNWYQ QKPGKAVKLLIYYTSSLHSGVPSRFSGSGSGTEYTLT ISSLQPDDEFATYYCQQYSKLPRTFGGGTKVEIK

SEQ ID NO: 3012	VL	C-H-VL.13	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKAVKSLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISSLPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3013	VL	C-H-VL.14	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPGKAVKSLIYYTSSLHSGVPSKFSGSGSGTDYTLT ISSLPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3014	VL	C-H-VL.15	DIQMTQSPSSLSASVGDRVTITCSASQGISNYLNWYQ QKPEKAVKSLIYYTSSLHSGVPSRFSGSGSGTDYTLT ISSLPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3015	VL	C-H-VL.16	DIQMTQSPSAMSASVGDRVTITCSASQGISNYLNWYQ QKPGKVVKRLIYYTSSLHSGVPSRFSGSGSGTEYTLT ISSLPEDFATYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3016	VL	C-H-VL.17	DIVMTQSPDSLAVSLGERATINCSASQGISNYLNWYQ QKPGQPVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLT ISSLQAEDVAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3017	VL	C-H-VL.18	EIVMTQSPGTLTLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPDRFSGSGSGTDYTLT ISRLEPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3018	VL	C-H-VL.19	EIVMTQSPPTLTLSPGERVTLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGSGTDYTLT ISSLPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3019	VL	C-H-VL.20	EIVMTQSPPTLTLSPGERVTLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSSIPARFSGSGSGTDYTLT ISSLPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3020	VL	C-H-VL.21	EIVMTQSPATLTLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGSGTDYTLT ISSLEPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3021	VL	C-H-VL.22	EIVMTQSPATLTLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGSGTDYTLT ISRLEPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3022	VL	C-H-VL.23	EIVMTQSPATLTLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPDRFSGSGSGTDYTLT ISRLEPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3023	VL	C-H-VL.24	EIVMTQSPATLTLSPGERATLSCSASQGISNYLNWYQ QKPGGLAVKLLIYYTSSLHSGIPDRFSGSGSGTDYTLT ISRLEPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3024	VL	C-H-VL.25	DIQMTQSPSFLSASVGDRVSIICSASQGISNYLNWYL QKPGKSVKLFIIYYTSSLHSGVSSRFSGRSGSGTDYTLT IISLKPEDFAAAYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3025	VL	C-H-VL.26	EIVMTQSPATLTLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGSGTDYTLT ISSLPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3026	VL	C-H-VL.27	EIVMTQSPATLTLSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGPGTDYTLT ISSLEPEDFAVYYCQQYSKLPRTFGGGTKVEIK
SEQ ID NO: 3027	VL	C-H-VL.28	DIVMTQTPLSLSVTPGQPASISCSASQGISNYLNWYL QKPGQSVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLK

			ISRVEAEDVGVIYCYCQYYSKLPRTFGGGKVEIK
SEQ ID NO: 3028	VL	C-H-VL.29	DIVMTQTPLSLSVTPGQPASISCSASQGISNYLNWYL QKPGQPVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDVGVIYCYCQYYSKLPRTFGGGKVEIK
SEQ ID NO: 3029	VL	C-H-VL.30	DIVMTQSPAFLSVTPGKVTITCSASQGISNYLNWYQ QKPDQAVKLLIYYTSSLHSGVPSRFSGSGSGTDYTF ISSLEAEDAATYYCYCQYYSKLPRTFGGGKVEIK
SEQ ID NO: 3030	VL	C-H-VL.31	DIVMTQSPLSLPVTGPGEASISCSASQGISNYLNWYL QKPGQSVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDVGVIYCYCQYYSKLPRTFGGGKVEIK
SEQ ID NO: 3031	VL	C-H-VL.32	DIVMTQTPLSLPVTGPGEASISCSASQGISNYLNWYL QKPGQSVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDVGVIYCYCQYYSKLPRTFGGGKVEIK
SEQ ID NO: 3032	VL	C-H-VL.33	EIVMTQSPATLSVSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGSGTEYTLT ISILQSEDFAVIYCYCQYYSKLPRTFGGGKVEIK
SEQ ID NO: 3033	VL	C-H-VL.34	EIVMTQSPATLSVSPGERATLSCSASQGISNYLNWYQ QKPGQAVKLLIYYTSSLHSGIPARFSGSGSGTEYTLT ISSLQSEDFAVIYCYCQYYSKLPRTFGGGKVEIK
SEQ ID NO: 3034	VL	C-H-VL.35	DIVMTQSPLSLPVTLGQPASISCSASQGISNYLNWYQ QKPGQSVKRLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDVGVIYCYCQYYSKLPRTFGGGKVEIK
SEQ ID NO: 3035	VL	C-H-VL.36	EITMTQSPAFMASATPGDKVNISCSASQGISNYLNWYQ QKPGQAVKFIYYTSSLHSGIPRFSGSGYGTDTLT INNIESEDAAYYCYCQYYSKLPRTFGGGKVEIK
SEQ ID NO: 3036	VL	C-H-VL.37	DIVMTQTPLSSPVTLGQPASISCSASQGISNYLNWYQ QKPGQPVKLLIYYTSSLHSGVPDRFSGSGAGTDYTLK ISRVEAEDVGVIYCYCQYYSKLPRTFGGGKVEIK
SEQ ID NO: 3037	VL	C-H-VL.38	EIVMTQSPDFQSVTPKEKVTITCSASQGISNYLNWYQ QKPDQSVKLLIYYTSSLHSGVPSRFSGSGSGTDYTLT INSLEAEDAATYYCYCQYYSKLPRTFGGGKVEIK
SEQ ID NO: 3038	VL	C-H-VL.39	EIVMTQTPLSLSITPGEQASISCSASQGISNYLNWYL QKARPVVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDFGVIYCYCQYYSKLPRTFGGGKVEIK
SEQ ID NO: 3039	VL	C-H-VL.40	EIVMTQTPLSLSITPGEQASMSCSASQGISNYLNWYL QKARPVVKLLIYYTSSLHSGVPDRFSGSGSGTDYTLK ISRVEAEDFGVIYCYCQYYSKLPRTFGGGKVEIK
Humanized antibody C Variable HEAVY chain (VH)			
SEQ ID NO: 3040	VH	C-H-VH.1	QVTLKESGPVLVKPTETLTCTVSGFSLTAYGVNVV RQPPGKALEWLGMIWGDGNTDYNALKSRITISKDNS KSQVVLMTNMDPVDATATYTCARDRVATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3041	VH	C-H-VH.2	QVTLKESGPALVKPTETLTCTVSGFSLTAYGVNVV RQPPGKALEWLGMIWGDGNTDYNALKSRLLISKDNS KSQVVLMTNMDPVDATATYTCARDRVATLYAMDYWG QGTLLTVSS

SEQ ID NO: 3042	VH	C-H-VH.3	QVTLKESGPALVKPTQTLTLTCTVSGFSLTAYGVNWV RQPPGKALEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVVLMTNMDPVDATATYYCARDRVATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3043	VH	C-H-VH.4	QVQLQESGPGLVKPSGTLTLTCAVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3044	VH	C-H-VH.5	QVTLKESGPTLVKPTQTLTLTCTVSGFSLTAYGVNWV RQPPGKALEWLGMIWGDGNTDYNALKSRLTITKDNS KSQVVLMTNMDPVDATATYYCARDRVATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3045	VH	C-H-VH.6	QVTLKESGPALVKPTQTLTLTCTVSGFSLTAYGVNWV RQPPGKALEWLGMIWGDGNTDYNALKSRLTITKDNS KSQVVLMTNMDPVDATATYYCARDRVATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3046	VH	C-H-VH.7	QVQLQESGPGLVKPSQTLTLTCTVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3047	VH	C-H-VH.8	QVQLQESGPGLVKPSSETLSLTCTVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3048	VH	C-H-VH.9	QVQLQESGPGLVKPSQTLTLTCAVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3049	VH	C-H-VH.10	QVQLQESGPGLVKPSDTLSLTCTVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3050	VH	C-H-VH.11	QVQLQESGPGLVKPSQTLTLTCTVSGFSLTAYGVNWV RQHPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3051	VH	C-H-VH.12	QVQLQESGPGLVKPSQTLTLTCTVSGFSLTAYGVNWV RQPAGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3052	VH	C-H-VH.13	QVQLQESGPGLVKPSQTLTLTCAVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLTVSS
SEQ ID NO: 3053	VH	C-H-VH.14	QVQLQESGPGLVKPSSETLSLTCTVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSHVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG

			QGTLLVTVSS
SEQ ID NO: 3054	VH	C-H-VH.15	QVQLQESGPGLVKPSSETLSLTCAVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3055	VH	C-H-VH.16	QVQLQESGPGLVKPSQTLSTCAVYGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3056	VH	C-H-VH.17	RVQLQESGPGLVKPSSETLSLTCTVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVPLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3057	VH	C-H-VH.18	QVQLQESGPGLVKPSQTLSTCTVSGFSLTAYGVNWV RQHPGKGLEWLGMIWGDGNTDYNALKSLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3058	VH	C-H-VH.19	QVQLQESGPGLVKPSDTLSLTCAVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTALDTAVYYCARDRVATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3059	VH	C-H-VH.20	QVQLQESGPGLVKPSDTLSLTCAVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAVDTAVYYCARDRVATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3060	VH	C-H-VH.21	QVQLQESGSGLVKPSQTLSTCAVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3061	VH	C-H-VH.22	EVQLVESGGGLVQPGRSLRLSCTVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSIVYLQMNSLKTEDTAVYYCARDRVATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3062	VH	C-H-VH.23	EVQLVESGGGLVQPGPSLRLSCTVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSIVYLQMNSLKTEDTAVYYCARDRVATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3063	VH	C-H-VH.24	QVQLQESGSGLVKPSQTLSTCAVSGFSLTAYGVNWV RQSPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3064	VH	C-H-VH.25	QVQLQESGPGLVKPSSETLSLTCTVSGFSLTAYGVNWV RQPAGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRVATLYAMDYWG QGTLLVTVSS
SEQ ID NO: 3065	VH	C-H-VH.26	EVQLVESGGGLVQPGPSLRLSCTVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS

			KSIVYLQMNSLKTEDTAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3066	VH	C-H- VH.27	QVQLQESGPGLVKPS ETL SLTCAVYGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSQVYLKLSSVTAADTAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3067	VH	C-H- VH.28	QVQLQESGPGLVKPS DTL SLTCAVSGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSQVSLKLSSVTAVD TG VYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3068	VH	C-H- VH.29	EVQLVESGGGLVQP GGS LRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSSVYLQMNSLKTEDTAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3069	VH	C-H- VH.30	EVQLVESGGGLV K P GGS LRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSTVYLQMNSLKTEDTAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3070	VH	C-H- VH.31	QVQLQQSGPGLVKPS QTL SLTCAVSGFSLTAYGVNWV RQSPSRGLEWLGMIWGDGNTDYN SALKSRLTINKDNS KSQVSLQLNSVTPEDTAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3071	VH	C-H- VH.32	QVQLVESGGGLVQP GGS LRLSCSVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSTVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3072	VH	C-H- VH.33	QVQLQQWGAGLLKP SETL SLTCAVYGFSLTAYGVNWV RQPPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSQVSLKLSSVTAADTAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3073	VH	C-H- VH.34	QVQLVESGGGVVQP GRSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS TSTVFLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3074	VH	C-H- VH.35	EVQLVESGGGLVQP GGS LRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSTVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3075	VH	C-H- VH.36	EVQLVESGGGLVQP GGS LRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNA KSSVYLQMNSLRDEDTAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3076	VH	C-H- VH.37	EVQLLESGGGLVQP GGS LRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSTVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVT VSS
SEQ ID NO: 3077	VH	C-H-	QVQLVESGGGLV K P GGS LRLSCAVSGFSLTAYGVNWV

		VH.38	RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNA KSSVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVTVSS
SEQ ID NO: 3078	VH	C-H- VH.39	EVQLVESGGGLVQPGGSLRLSCAVSGFSLTAYGVNWV RQASGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSTVYLQMNSLKTEDTAVYYCARDRV TATLYAMDYWG QGT LVTVSS
SEQ ID NO: 3079	VH	C-H- VH.40	QVQLLES GGGVLVKPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNA KSSVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVTVSS
SEQ ID NO: 3080	VH	C-H- VH.41	QVQLVES GGGVVQPGRSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSTVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVTVSS
SEQ ID NO: 3081	VH	C-H- VH.42	QVQLVES GGGVVQPGRSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSRVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVTVSS
SEQ ID NO: 3082	VH	C-H- VH.43	QVQLVES GGGVVQPGRSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLAIS KDNS KSTVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVTVSS
SEQ ID NO: 3083	VH	C-H- VH.44	QVQLVES GGGVVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSTVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVTVSS
SEQ ID NO: 3084	VH	C-H- VH.45	EVQLVES GGGGLVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNA KSTVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVTVSS
SEQ ID NO: 3085	VH	C-H- VH.46	EVQLVES GGGGLVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNA KSSVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVTVSS
SEQ ID NO: 3086	VH	C-H- VH.47	EVQLVES GGGVVVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNS KSSVYLQMNSLRTE DTALYYCARDRV TATLYAMDYWG QGT LVTVSS
SEQ ID NO: 3087	VH	C-H- VH.48	EVQLVES GGGGLVQPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKHNS KSTVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVTVSS
SEQ ID NO: 3088	VH	C-H- VH.49	EVQLVES GGGVLVKPGGSLRLSCAVSGFSLTAYGVNWV RQAPGKGLEWLGMIWGDGNTDYN SALKSRLTISKDNA KSSVYLQMNSLRAEDTAVYYCARDRV TATLYAMDYWG QGT LVTVSS

SEQ ID NO: 3089	VH	C-H-VH.50	EVQLVESGGGLIQPGGSLRLSCAVSGFSLTAYGVNWW RQPPGKGLEWLGMIWGDGNTDYNALKSRLTISKDNS KSTVYLMNSLRAEDTAVYYCARDRTATLYAMDYWG QGTLLTVSS

Exemplary anti-TCR β V5 antibodies of the disclosure are provided in **Table 11A**. In some embodiments, the anti-TCR β V5 is antibody E, e.g., humanized antibody E (antibody E-H), as provided in **Table 11A**. In some embodiments, the anti-TCR β V antibody comprises one or more (e.g., all three) of a LC CDR1, LC CDR2, and LC CDR3 provided in **Table 11A**; and/or one or more (e.g., all three) of a HC CDR1, HC CDR2, and HC CDR3 provided in **Table 11A**, or a sequence with at least 95% identity thereto. In some embodiments, antibody E comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Table 11A**, or a sequence with at least 95% identity thereto.

In some embodiments, antibody E comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 3284 and/or a light chain comprising the amino acid sequence of SEQ ID NO: 3285, or sequence with at least 95% identity thereto.

Table 11A: Amino acid sequences for anti TCR β V5 antibodies

Amino acid and nucleotide sequences for murine and humanized antibody molecules which bind to TCRVB 5 (e.g., TCRVB 5-5 or TCRVB 5-6). The amino acid the heavy and light chain CDRs, and the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the heavy and light chains are shown.

Murine antibody E		
SEQ ID NO: 1298	HC CDR1 (Kabat)	SSWMN
SEQ ID NO: 1299	HC CDR2 (Kabat)	RIYPGDGDTKYNGKFKG
SEQ ID NO: 1300	HC CDR3 (Kabat)	RGTGGWYFDV
SEQ ID NO: 1302	HC CDR1 (Chothia)	GYAFSSS
SEQ ID NO: 1303	HC CDR2 (Chothia)	YPGDGD
SEQ ID NO: 1301	HC CDR3 (Chothia)	RGTGGWYFDV
SEQ ID NO: 1304	HC CDR1 (Combined)	GYAFSSSWMN
SEQ ID NO: 1299	HC CDR2 (Combined))	RIYPGDGDTKYNGKFKG

SEQ ID NO: 1301	HC CDR3(Combined)	RGTGGWYFDV
SEQ ID NO: 1305	LC CDR1 (Kabat)	RASESVDSSGNSFMH
SEQ ID NO: 1306	LC CDR2 (Kabat)	RASNLES
SEQ ID NO: 1307	LC CDR3 (Kabat)	QQSFDDPFT
SEQ ID NO: 1308	LC CDR1 (Chothia)	SESVDSSGNSF
SEQ ID NO: 1306	LC CDR2 (Chothia)	RASNLES
SEQ ID NO: 1307	LC CDR3 (Chothia)	QQSFDDPFT
SEQ ID NO: 1305	LC CDR1 (Combined)	RASESVDSSGNSFMH
SEQ ID NO: 1306	LC CDR2 (Combined)	RASNLES
SEQ ID NO: 1307	LC CDR3(Combined)	QQSFDDPFT
SEQ ID NO: 3091	VH	QVQLQQSGPELVKPGASVKISCKASGYAFSSSW MNWVKQRPGQGLEWIGRIYPGDGDTKYNGKFK GKATLTADKSSSTAYMHLSSLTSVDSAVYFCAR RGTGGWYFDVWGAGTTVTVSS
SEQ ID NO: 3284	Heavy chain	METDTLLLWVLLLWVPGSTGQVQLQQSGPELV KPGASVKISCKASGYAFSSSWMNWVKQRPGQ LEWIGRIYPGDGDTKYNGKFKGKATLTADKSS TAYMHLSSLTSVDSAVYFCARRGTGGWYFDVW GAGTTVTVSSAKTTAPSVYPLAPVCGDTTGSSVT LGCLVKGYFPEPVTLTWNSGSLSSGVHTFPAVL QSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTK VDKKIEPRGPTIKCPPCKCPAPNLLGGPSVFIFPP KIKDVLMISSLPIVTCVVVDVSEDDPDVQISWV NNVEVHTAQTQTHREDYNSTLRVVSALPIQHQD WMSGKEFKCKVNNKDLPAPIERTISKPKGSVRA PQVYVLPPEEEMTKKQVTLTCMVTDFMPEDIY VEWTNNGKTELNYKNTEPVLDSDGSYFMYSKL RVEKKNWVERNSYSCSVVHEGLHNHHTTKSFSR TPGK
SEQ ID NO: 3092	VL	DIVLTQSPASLAVSLGQRATISCRASESVDSSGNS FMHWYQQKPGQPPQLLIYRASNLESGIPARFSGS GSRTDFTLTINPVEADDVATFYCQQSFDDPFTFG SGTKLEIK
SEQ ID NO: 3285	Light chain	METDTLLLWVLLLWVPGSTGDIVLTQSPASLAV SLGQRATISCRASESVDSSGNSFMHWYQQKPGQ PPQLLIYRASNLESGIPARFSGSGSRTDFTLTINPV EADDVATFYCQQSFDDPFTFGSGTKLEIKRADA APTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINV KWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTL TLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNE C
Humanized antibody E (E-H antibody)		

<i>Variable light chain (VL)</i>			
SEQ ID NO: 3093	VL	E-H.1	DIVLTQSPDSLAVSLGERATINCRASESVDSGNS FMHWYQQKPGQPPQLLIYRASNLESGVPDRFSGSG SRTDFTLTISLQAEDVAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3094	VL	E-H.2	EIVLTQSPATLSLSPGERATLSCRASESVDSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG SRTDFTLTISLLEPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3095	VL	E-H.3	EIVLTQSPATLSLSPGERATLSCRASESVDSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG SRTDFTLTISRLEPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3096	VL	E-H.4	EIVLTQSPATLSLSPGERATLSCRASESVDSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG SRTDFTLTISLQPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3097	VL	E-H.5	DIQLTQSPSSLSASVGDRVITITCRASESVDSGNS FMHWYQQKPGQAPQLLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDVATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3098	VL	E-H.6	EIVLTQSPATLSLSPGERATLSCRASESVDSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG PRTDFTLTISLLEPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3099	VL	E-H.7	EIVLTQSPATLSLSPGERATLSCRASESVDSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPDRFSGSG SRTDFTLTISRLEPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3100	VL	E-H.8	DIQLTQSPSSLSASVGDRVITITCRASESVDSGNS FMHWYQQKPGKVPQLLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDVATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3101	VL	E-H.9	DIQLTQSPSSLSASVGDRVITITCRASESVDSGNS FMHWYQQKPGKTPQLLIYRASNLESGIPSRFSGSG SRTDFTLTIRSLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3102	VL	E-H.10	EIVLTQSPGTLSPGERATLSCRASESVDSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPDRFSGSG SRTDFTLTISRLEPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3103	VL	E-H.11	EIVLTQSPATLSLSPGERATLSCRASESVDSGNS FMHWYQQKPGGLAPQLLIYRASNLESGIPDRFSGSG SRTDFTLTISRLEPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3104	VL	E-H.12	DIQLTQSPSSLSASVGDRVITITCRASESVDSGNS FMHWYQQKPGKAPQLLIYRASNLESGVPSRFSGSG

			SRTDFTLTISLQPEDFATYYCQQSFDPPFTFGQG TKLEIK
SEQ ID NO: 3105	VL	E-H.13	DIQLTQSPSSVSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQLLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSFDPPFTFGQG TKLEIK
SEQ ID NO: 3106	VL	E-H.14	AIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQLLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSFDPPFTFGQG TKLEIK
SEQ ID NO: 3107	VL	E-H.15	DIQLTQSPSFLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQLLIYRASNLESGVPSRFSGSG SRTEFTLTISLQPEDFATYYCQQSFDPPFTFGQG TKLEIK
SEQ ID NO: 3108	VL	E-H.16	DIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQLLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSFDPPFTFGQG TKLEIK
SEQ ID NO: 3109	VL	E-H.17	EIVLTQSPATLSVSPGERATLSCRASESVDSSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG SRTEFTLTISILQSEDFAVYYCQQSFDPPFTFGQG TKLEIK
SEQ ID NO: 3110	VL	E-H.18	EIVLTQSPATLSVSPGERATLSCRASESVDSSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG SRTEFTLTISLQSEDFAVYYCQQSFDPPFTFGQG TKLEIK
SEQ ID NO: 3111	VL	E-H.19	AIRLTQSPFSLASVGDRVTITCRASESVDSSGNS FMHWYQQKPAKAPQLFIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSFDPPFTFGQG TKLEIK
SEQ ID NO: 3112	VL	E-H.20	DIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQSLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSFDPPFTFGQG TKLEIK
SEQ ID NO: 3113	VL	E-H.21	DIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQRLIYRASNLESGVPSRFSGSG SRTEFTLTISNLQPEDFATYYCQQSFDPPFTFGQG TKLEIK
SEQ ID NO: 3114	VL	E-H.22	DIQLTQSPSTLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQLLIYRASNLESGVPSRFSGSG SRTEFTLTISLQPDFFATYYCQQSFDPPFTFGQG TKLEIK
SEQ ID NO: 3115	VL	E-H.23	EIVLTQSPDFQSVTPKEKVTITCRASESVDSSGNS FMHWYQQKPDQSPQLLIYRASNLESGVPSRFSGSG SRTDFTLTINSLEAEDAATYYCQQSFDPPFTFGQG TKLEIK
SEQ ID NO: 3116	VL	E-H.24	DIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS

			FMHWYQQKPGKAPQSLIYRASNLESGVPSKFSGSG SRTDFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3117	VL	E-H.25	DIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKAPQRLIYRASNLESGVPSRFSGSG SRTEFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3118	VL	E-H.26	DIVLTQTPLSLSVTPGQPASISCRASESVDSSGNS FMHWYLQKPGQPPQLLIYRASNLESGVPDRFSGSG SRTDFTLKISRVEAEDVGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3119	VL	E-H.27	DIQLTQSPSSLSASVGDRVTITCRASESVDSSGNS FMHWYQQKPEKAPQSLIYRASNLESGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3120	VL	E-H.28	EIVLTQSPPTLSLSPGERVTLSRASESVDSSGNS FMHWYQQKPGQAPQLLIYRASNLESGIPARFSGSG SRTDFTLTISLQPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3121	VL	E-H.29	DIQLTQSPSAMSASVGDRVTITCRASESVDSSGNS FMHWYQQKPGKVPQRLIYRASNLESGVPSRFSGSG SRTEFTLTISLQPEDFATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3122	VL	E-H.30	DIVLTQSPPLSLPVTGPGEASISCRASESVDSSGNS FMHWYLQKPGQSPQLLIYRASNLESGVPDRFSGSG SRTDFTLKISRVEAEDVGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3123	VL	E-H.31	DIVLTQTPLSLPVTGPGEASISCRASESVDSSGNS FMHWYLQKPGQSPQLLIYRASNLESGVPDRFSGSG SRTDFTLKISRVEAEDVGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3124	VL	E-H.32	DIVLTQTPLSLSVTPGQPASISCRASESVDSSGNS FMHWYLQKPGQSPQLLIYRASNLESGVPDRFSGSG SRTDFTLKISRVEAEDVGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3125	VL	E-H.33	EIVLTQSPPTLSLSPGERVTLSRASESVDSSGNS FMHWYQQKPGQAPQLLIYRASNLESSIPARFSGSG SRTDFTLTISLQPEDFAVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3126	VL	E-H.34	DIVLTQSPPLSLPVTLGQPASISCRASESVDSSGNS FMHWYQQRPGQSPQRLIYRASNLESGVPDRFSGSG SRTDFTLKISRVEAEDVGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3127	VL	E-H.35	DIVLTQTPLSSPVTLGQPASISCRASESVDSSGNS FMHWYQQRPGQPPQLLIYRASNLESGVPDRFSGSG ARTDFTLKISRVEAEDVGVYYCQQSFDDPFTFGQG TKLEIK

SEQ ID NO: 3128	VL	E-H.36	DIVLTQSPAFLSVTPGEKVTITCRASESVDSSGNS FMHWYQQKPDQAPQLLIYRASNLESGVPSRFSGSG SRTDFTFTISSLEAEDAATYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3129	VL	E-H.37	DIQLIQSPSFLSASVGDRVSIICRASESVDSSGNS FMHWYLQKPGKSPQLFIYRASNLESGVSSRFSGRG SRTDFTLTIIISLKPEDFAAYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3130	VL	E-H.38	EIVLTQTPLSLSITPGEQASISCRASESVDSSGNS FMHWYLQKARPVPQLLIYRASNLESGVPDRFSGSG SRTDFTLKISRVEAEDFGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3131	VL	E-H.39	EIVLTQTPLSLSITPGEQASMSCRASESVDSSGNS FMHWYLQKARPVPQLLIYRASNLESGVPDRFSGSG SRTDFTLKISRVEAEDFGVYYCQQSFDDPFTFGQG TKLEIK
SEQ ID NO: 3132	VL	E-H.40	EITLTQSPAFMSATPGDKVNISCRASESVDSSGNS FMHWYQQKPGGEAPQFIIYRASNLESGIPPRFSGSG YRTDFTLTINNIESEDAAYYCQQSFDDPFTFGQG TKLEIK
Variable HEAVY chain (VH)			
SEQ ID NO: 3133	VH	E-H.1	QVQLVQSGAEVKKPGASVKVSCASGYAFSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFGRATL TADKSTSTAYMELSSLRSEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3134	VH	E-H.2	QVQLVQSGAEVKKPGSSVKVSCASGYAFSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFGRATL TADKSTSTAYMELSSLRSEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3135	VH	E-H.3	QVQLVQSGAEVKKPGASVKVSCASGYAFSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFGRATL TADKSTSTAYMELSSLRSEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3136	VH	E-H.4	QVQLVQSGAEVKKPGASVKVSCASGYAFSSWMN WVRQAPGQLEWIGRIYPGDGDTKYNGKFGRATL TADKSISTAYMELSSLRSEDTATYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3137	VH	E-H.5	EVQLVQSGAEVKKPGATVKISCKASGYAFSSWMN WVQQAPGKGLEWIGRIYPGDGDTKYNGKFGRATL TADKSTSTAYMELSSLRSEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3138	VH	E-H.6	QVQLVQSGAEVKKTGSSVKVSCASGYAFSSWMN WVRQAPGQALEWIGRIYPGDGDTKYNGKFGRATL TADKSMSTAYMELSSLRSEDTAMYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3139	VH	E-H.7	QVQLVQSGAEVKKPGASVKVSCASGYAFSSWMN WVRQAPGQRLWIGRIYPGDGDTKYNGKFGRATL

			TADKSASTAYMELSSLRSEDMAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3140	VH	E-H.8	QVQLVQSGAEVKKPGASVKVSCASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRATL TADKSTSTAYMELRSLRSDDMAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3141	VH	E-H.9	QVQLVQSGAEVKKPGASVKVSCASGYAFSSSWMN WVRQAPGQRLWIGRIYPGDGDTKYNGKFKGRATL TADKSASTAYMELSSLRSEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3142	VH	E-H.10	QVQLVQSGAEVKKPGASVKVSCASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRATL TADKSTSTAYMELRSLRSDDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3143	VH	E-H.11	QVQLVQSGAEVKKPGASVKVSCASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRATL TADKSISTAYMELRSLRSDDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3144	VH	E-H.12	QVQLVQSGAEVKKPGASVKVSCASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRATL TADKSISTAYMELRSLRSDDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3145	VH	E-H.13	QVQLVQSGAEVKKPGASVKVSCASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGWATL TADKSISTAYMELRSLRSDDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3146	VH	E-H.14	QVQLVQSGAEVKKPGASVKVSCASGYAFSSSWMN WVRQATGQGLEWIGRIYPGDGDTKYNGKFKGRATL TANKSISTAYMELSSLRSEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3147	VH	E-H.15	QVQLVQSGSELKKPGASVKVSCASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSVSTAYLQISSLKAEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3148	VH	E-H.16	QVQLVQSGPEVKKPGTSVKVSCASGYAFSSSWMN WVRQARGQRLWIGRIYPGDGDTKYNGKFKGRATL TADKSTSTAYMELSSLRSEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3149	VH	E-H.17	EVQLVQSGAEVKKPGESLKISKASGYAFSSSWMN WVRQMPGKGLEWIGRIYPGDGDTKYNGKFKGQATL SADKSISTAYLQWSSLKASDTAMYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3150	VH	E-H.18	QVQLVQSGSELKKPGASVKVSCASGYAFSSSWMN WVRQAPGQGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSVSMAYLQISSLKAEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3151	VH	E-H.19	QVQLVQSGHEVKQPGASVKVSCASGYAFSSSWMN

			WVPQAPGQGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSASTAYLQISSLKAEDMAMYYCARRGTGGWY FDVWGQGTDTVTVSS
SEQ ID NO: 3152	VH	E-H.20	EVQLVQSGAEVKKPAGESLKISCKASGYAFSSSWMN WVRQMPGKGLEWIGRIYPGDGDTKYNGKFKGQATL SADKPISTAYLQWSSLKASDTAMYYCARRGTGGWY FDVWGQGTDTVTVSS
SEQ ID NO: 3153	VH	E-H.21	EVQLVQSGAEVKKPAGESLRISCKASGYAFSSSWMN WVRQMPGKGLEWIGRIYPGDGDTKYNGKFKGQATL SADKSIISTAYLQWSSLKASDTAMYYCARRGTGGWY FDVWGQGTDTVTVSS
SEQ ID NO: 3154	VH	E-H.22	EVQLVQSGAEVKKPAGESLRISCKASGYAFSSSWMN WVRQMPGKGLEWIGRIYPGDGDTKYNGKFKGHATL SADKSIISTAYLQWSSLKASDTAMYYCARRGTGGWY FDVWGQGTDTVTVSS
SEQ ID NO: 3155	VH	E-H.23	QVQLVQSGAEVKKTGSSVKVSKASGYAFSSSWMN WVRQAPRQALEWIGRIYPGDGDTKYNGKFKGRAVL TADKSMSTAYMELSSLRSEDAMYYCARRGTGGWY FDVWGQGTDTVTVSS
SEQ ID NO: 3156	VH	E-H.24	EVQLVESGGGLVQPGRSLRLSCTASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSKSIAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTDTVTVSS
SEQ ID NO: 3157	VH	E-H.25	EVQLVESGGGLVQPGPSLRLSCTASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSKSIAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTDTVTVSS
SEQ ID NO: 3158	VH	E-H.26	QVQLQESGPGGLVKPSQTLSTCTASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTDTVTVSS
SEQ ID NO: 3159	VH	E-H.27	QVQLQESGPGGLVKPSGTLSTCTCAASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTDTVTVSS
SEQ ID NO: 3160	VH	E-H.28	EVQLVESGGGLVQPGRSLRLSCTASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSKSIAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTDTVTVSS
SEQ ID NO: 3161	VH	E-H.29	EVQLVESGGGLVQPGGSLKLSAASGYAFSSSWMN WVRQASGKGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSKSTAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTDTVTVSS
SEQ ID NO: 3162	VH	E-H.30	QVQLQESGPGGLVKPSQTLSTCTCAASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRAVL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTDTVTVSS

SEQ ID NO: 3163	VH	E-H.31	EVQLVESGGGLVKPGGSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSTAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3164	VH	E-H.32	EVQLVESGGALVKPGGSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSTAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3165	VH	E-H.33	QVQLQESGPGLVKPSQTLSTLCAAYGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3166	VH	E-H.34	QVQLQESGSGLVKPSQTLSTLCAASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3167	VH	E-H.35	EVQLVESGGGLVQPGGSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSSAYLQMNSLKTEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3168	VH	E-H.36	QVQLQESGPGLVKPSDTLSLTCTASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3169	VH	E-H.37	QVQLQESGPGLVKPSQTLSTLCTASGYAFSSSWMN WVRQHPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3170	VH	E-H.38	QVQLQESGPGLVKPSQTLSTLCTASGYAFSSSWMN WVRQHPGKGLEWIGRIYPGDGDTKYNGKFGLATL SADKSKSQASLKLSSVTAADTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3171	VH	E-H.39	QVQLVESGGGVVQPGRSRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSTAYLQMSSLRAEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3172	VH	E-H.40	QVQLVESGGGLVKPGGSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKAKSSAYLQMNSLRAEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3173	VH	E-H.41	QVQLVESGGGLVQPGGSLRLSCSASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKSKSTAYLQMNSLRAEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3174	VH	E-H.42	QVQLLES GGGLVKPGGSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFKGRATL SADKAKSSAYLQMNSLRAEDTAVYYCARRGTGGWY

			FDVWGQGTTVTVSS
SEQ ID NO: 3175	VH	E-H.43	EVQLVESGGGLVQPGGSLRLSCSASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFGRATL SADKSKSTAYLQMSSLRAEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3176	VH	E-H.44	QVQLQESGPGGLVKPSDTLSLTCAASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFGRATL SADKSKSQASLKLSSVTAVDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3177	VH	E-H.45	QVQLQESGPGGLVKPSQTLSTCAASGYAFSSSWMN WVRQPPGKGLEWIGRIYPGDGDTKYNGKFGRATL SADKSKSQASLKLSSVTAVDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3178	VH	E-H.46	EVQLVESGGGLVQPGGSLRLSCSASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFGRATL SADKSKSTAYVQMSSLRAEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3179	VH	E-H.47	QVQLVDSGGGVVQPGRSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFGRATL SADKSKSTAYLQMNSLRAEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3180	VH	E-H.48	QVQLVESGGGVVQPGRSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFGRATL SADKSKSTAYLQMNSLRAEGTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3181	VH	E-H.49	QVQLVESGGGVVQPGRSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFGRATL SADKSKSTAYLQMNSLRAEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS
SEQ ID NO: 3182	VH	E-H.50	EVQLVESGGGLVQPGGSLRLSCAASGYAFSSSWMN WVRQAPGKGLEWIGRIYPGDGDTKYNGKFGRATL SADKSKSTAYLQMNSLRAEDTAVYYCARRGTGGWY FDVWGQGTTVTVSS

In some embodiments, the anti-TCR β V5 antibody molecule comprises a VH and/or a VL of an antibody described in **Table 10A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

- 5 In some embodiments, the anti-TCR β V5 antibody molecule comprises a VH and a VL of an antibody described in **Table 10A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

In some embodiments, the anti-TCR β V5 antibody molecule comprises a VH and/or a VL of an antibody described in **Table 11A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

In some embodiments, the anti-TCR β V5 antibody molecule comprises a VH and a VL of an antibody described in **Table 11A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

Anti-TCR β V10 antibodies

Accordingly, in one aspect, the disclosure provides an anti-TCR β V antibody molecule that binds to a human TCR β V10 subfamily member. In some embodiments, TCR β V10 subfamily is also known as TCR β V12. In some embodiments, the TCR β V10 subfamily comprises: TCR β V10-1*01, TCR β V10-1*02, TCR β V10-3*01 or TCR β V10-2*01, or a variant thereof.

Exemplary anti-TCR β V10 antibodies of the disclosure are provided in **Table 12A**. In some embodiments, the anti-TCR β V10 is antibody D, e.g., humanized antibody D (antibody D-H), as provided in **Table 12A**. In some embodiments, antibody D comprises one or more (e.g., three) light chain CDRs and/or one or more (e.g., three) heavy chain CDRs provided in **Table 12A**, or a sequence with at least 95% identity thereto. In some embodiments, antibody D comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Table 12A**, or a sequence with at least 95% identity thereto.

Table 12A: Amino acid sequences for anti TCR β V10 antibodies

Amino acid and nucleotide sequences for murine and humanized antibody molecules which bind to TCRBV 10 (e.g., TCRBV 10-1, TCRBV 10-2 or TCRBV 10-3). The amino acid the heavy and light chain CDRs, and the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the heavy and light chains are shown.

Murine antibody D		
SEQ ID NO: 1288	HC CDR1 (Kabat)	SYGMS

SEQ ID NO: 1289	HC CDR2 (Kabat)	LISSGGSYTTYTDSVKG
SEQ ID NO: 1290	HC CDR3 (Kabat)	HGGNFFDY
SEQ ID NO: 1291	HC CDR1 (Chothia)	GFTFRSY
SEQ ID NO: 1292	HC CDR2 (Chothia)	SSGGSY
SEQ ID NO: 1290	HC CDR3 (Chothia)	HGGNFFDY
SEQ ID NO: 1293	HC CDR1 (Combined)	GFTFRSYGMS
SEQ ID NO: 1289	HC CDR2 (Combined))	LISSGGSYTTYTDSVKG
SEQ ID NO: 1290	HC CDR3(Combined)	HGGNFFDY
SEQ ID NO: 1294	LC CDR1 (Kabat)	SVSSSVSYMH
SEQ ID NO: 1295	LC CDR2 (Kabat)	DTSKLAS
SEQ ID NO: 1296	LC CDR3 (Kabat)	QQWSSNPQYT
SEQ ID NO: 1297	LC CDR1 (Chothia)	SSSVSY
SEQ ID NO: 1295	LC CDR2 (Chothia)	DTSKLAS
SEQ ID NO: 1296	LC CDR3 (Chothia)	QQWSSNPQYT
SEQ ID NO: 1294	LC CDR1 (Combined)	SVSSSVSYMH
SEQ ID NO: 1295	LC CDR2 (Combined)	DTSKLAS
SEQ ID NO: 1296	LC CDR3 (Combined)	QQWSSNPQYT
SEQ ID NO: 3183	VH	EVQLVESGGDLVKPGGSLKLSCAVSGFTFRSYGMS WVRQTPDKRLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNTLYLQMSSLKSEDTAIYYCSRHGGNFFD YWGQGTTTLTVSS
SEQ ID NO: 3184	VL	QIVLTQSPSIMSASPGEKVTMTCSVSSSVSYMHWY QQKSGTSPKRWIYDTSKLASGVPARFSGSGSGTSYS LTISSMEAEDAATYYCQQWSSNPQYTFGGGTKLEI K
Humanized antibody D (D-H antibody)		
Variable light chain (VL)		
SEQ ID NO: 3185	VL	D-VL-H.1
		DIVLTQSPAFLSVTPGEKVTITCSVSSSVSYMHWY

			QQKPDQAPKLLIYDTSKLASGVPSRFSGSGSGTDY TFTISSLEAEDAATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3186	VL	D-VL-H.2	AIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3187	VL	D-VL-H.3	DIQLTQSPSFLSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTEY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3188	VL	D-VL-H.4	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3189	VL	D-VL-H.5	DIQLTQSPSSVSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3190	VL	D- VL-H.6	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGKVPKLLIYDTSKLASGVPSRFSGSGSGTDY TLTISSLQPEDVATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3191	VL	D- VL-H.7	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLASGVPSRFSGSGSGTDY TLTISSLQPEDVATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3192	VL	D- VL-H.8	EIVLTQSPDFQSVTPKEKVTITCSVSSSVSYMHWY QQKPDQSPKLLIYDTSKLASGVPSRFSGSGSGTDY TLTINSLEAEDAATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3193	VL	D- VL-H.9	AIRLTQSPFSLASVGDRVTITCSVSSSVSYMHWY QQKPAKAPKLFYDTSKLASGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3194	VL	D- VL- H.10	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTDY TFTISSLQPEDATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3195	VL	D- VL- H.11	EIVLTQSPATLSLSPGERATLSCSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLASGIPARFSGSGSGTDY TLTISSLEPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3196	VL	D- VL- H.12	DIQLTQSPSTLSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGTEY TLTISSLQPDDFATYYCQQWSSNPQYTFGQGTKLE IK

SEQ ID NO: 3197	VL	D- VL-H.13	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGKTPKLLIYDTSKLAGIPSRFSGSGSGTDY TLTIRSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3198	VL	D- VL-H.14	EIVLTQSPPTLSLSPGERVTLSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGSGTDY TLTISSLQPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3199	VL	D- VL-H.15	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKRLIYDTSKLAGVPSRFSGSGSGTEY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3200	VL	D- VL-H.16	EIVLTQSPATLSLSPGERATLSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGPGTDY TLTISSLEPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3201	VL	D- VL-H.17	EIVLTQSPATLSLSPGERATLSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGSGTDY TLTISRLEPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3202	VL	D- VL-H.18	EIVLTQSPATLSLSPGERATLSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGSGTDY TLTISSLQPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3203	VL	D- VL-H.19	EIVLTQSPATLSVSPGERATLSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGSGTEY TLTISSLQSEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3204	VL	D- VL-H.20	EIVLTQSPATLSVSPGERATLSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLAGIPARFSGSGSGTEY TLTISILQSEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3205	VL	D- VL-H.21	EIVLTQSPPTLSLSPGERVTLSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLASSIPARFSGSGSGTDY TLTISSLQPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3206	VL	D- VL-H.22	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKSLIYDTSKLAGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3207	VL	D- VL-H.23	DIQLTQSPSSLSASVGDRVTITCSVSSSVSYMHWY QQKPGKAPKRLIYDTSKLAGVPSRFSGSGSGTEY TLTISNLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3208	VL	D- VL-H.24	DIQLTQSPSAMSASVGDRVTITCSVSSSVSYMHWY QQKPGKVPKRLIYDTSKLAGVPSRFSGSGSGTEY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK

			IK
SEQ ID NO: 3209	VL	D- VL-H.25	EIVLTQSPATLSLSPGERATLSCSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLASGIPDRFSGSGSGTDY TLTISRLEPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3210	VL	D- VL-H.26	EIVLTQSPATLSLSPGERATLSCSVSSSVSYMHWY QQKPGGLAPKLLIYDTSKLASGIPDRFSGSGSGTDY TLTISRLEPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3211	VL	D- VL-H.27	EIVLTQSPGTLSSLSPGERATLSCSVSSSVSYMHWY QQKPGQAPKLLIYDTSKLASGIPDRFSGSGSGTDY TLTISRLEPEDFAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3212	VL	D- VL-H.28	DIQLTQSPSSLSASVGDRTITCSVSSSVSYMHWY QQKPGKAPKSLIYDTSKLASGVPSKFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3213	VL	D- VL-H.29	DIQLTQSPSSLSASVGDRTITCSVSSSVSYMHWY QQKPEKAPKSLIYDTSKLASGVPSRFSGSGSGTDY TLTISSLQPEDFATYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3214	VL	D- VL-H.30	DIVLTQSPDSLAVSLGERATINCSVSSSVSYMHWY QQKPGQPPKLLIYDTSKLASGVDPDRFSGSGSGTDY TLTISSLQAEDVAVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3215	VL	D- VL-H.31	EIVLTQTPLSLSLITPGEQASMSCSVSSSVSYMHWY LQKARPVPKLLIYDTSKLASGVDPDRFSGSGSGTDY TLKISRVEAEDFGVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3216	VL	D- VL-H.32	EIVLTQTPLSLSLITPGEQASISCSVSSSVSYMHWY LQKARPVPKLLIYDTSKLASGVDPDRFSGSGSGTDY TLKISRVEAEDFGVYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3217	VL	D- VL-H.33	DIVLTQSPSLPVTTPGEPASISCSVSSSVSYMHWY LQKPGQSPKLLIYDTSKLASGVDPDRFSGSGSGTDY TLKISRVEAEDVGYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3218	VL	D- VL-H.34	DIVLTQSPSLPVTLGQPASISCSVSSSVSYMHWY QQRPGQSPKRLIYDTSKLASGVDPDRFSGSGSGTDY TLKISRVEAEDVGYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3219	VL	D- VL-H.35	DIVLTQTPLSLPVTTPGEPASISCSVSSSVSYMHWY LQKPGQSPKLLIYDTSKLASGVDPDRFSGSGSGTDY TLKISRVEAEDVGYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3220	VL	D- VL-H.36	DIVLTQTPLSLSVTPGQPASISCSVSSSVSYMHWY LQKPGQSPKLLIYDTSKLASGVDPDRFSGSGSGTDY

			TLKISRVEAEDVGYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3221	VL	D- VL- H.37	DIVLTQTPLSLSVTPGQPASISCSVSSSVSYMHWY LQKPGQPPKLLIYDTSKLAGVDPDRFSGSGSGTDY TLKISRVEAEDVGYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3222	VL	D- VL- H.38	DIQLIQSPSFLSASVGDRVSIICSVSSSVSYMHWY LQKPGKSPKLFIIYDTSKLAGVSSRFSGRSGTDY TLTIISLKPEDFAAYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3223	VL	D- VL- H.39	DIVLTQTPLSSPVTLGQPASISCSVSSSVSYMHWY QQRPGQPPKLLIYDTSKLAGVDPDRFSGSGAGTDY TLKISRVEAEDVGYYCQQWSSNPQYTFGQGTKLE IK
SEQ ID NO: 3224	VL	D- VL- H.40	EITLTQSPAFMSATPGDKVNISCSVSSSVSYMHWY QQKPGEAPKFIIYDTSKLAGIPPRFSGSGYGTDY TLTINNIESEDAAYYCQQWSSNPQYTFGQGTKLE IK
Variable HEAVY chain (VH)			
SEQ ID NO: 3225	VH	D-VH-H.1	EVQLVESGGGLVKPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTYTDSVKGRFTI SRDNSKNTLYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3226	VH	D- VH-H.2	EVQLVESGGALVKPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTYTDSVKGRFTI SRDNSKNTLYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3227	VH	D- VH-H.3	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTYTDSVKGRFTI SRDNAKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3228	VH	D- VH-H.4	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3229	VH	D- VH-H.5	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTYTDSVKGRFTI SRDNSKNSLYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3230	VH	D- VH-H.6	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDMAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3231	VH	D- VH-H.7	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTYTDSVKGRFTI SRDNAKNTLYLQMNSLRAEDMAVYYCSRHGGNFFD YWGQGTITVTVSS

SEQ ID NO: 3232	VH	D- VH-H.8	EVQLVESGGGLVKPGRSLRLSCTVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNILYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTTTVTVSS
SEQ ID NO: 3233	VH	D- VH-H.9	EVQLVESGGGLVKPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTTTVTVSS
SEQ ID NO: 3234	VH	D- VH-H.10	EVQLVESGGGLVQPGGSLKLSCAVSGFTFRSYGMS WVRQASGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTTTVTVSS
SEQ ID NO: 3235	VH	D- VH-H.11	QVQLVESGGGVVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTTTVTVSS
SEQ ID NO: 3236	VH	D- VH-H.12	QVQLVESGGGVVQPGRLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMSSLRAEDTAVYYCSRHGGNFFD YWGQGTTTVTVSS
SEQ ID NO: 3237	VH	D- VH-H.13	EVQLVESGGGLVQPGGSLRLSCPVSFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNANNSLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTTTVTVSS
SEQ ID NO: 3238	VH	D- VH-H.14	EVQLVESGGGLVQPGRLRLSCTVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNILYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTTTVTVSS
SEQ ID NO: 3239	VH	D- VH-H.15	EVQLVESGGGLVQPGPSRLRLSCTVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNILYLQMNSLKTEDTAVYYCSRHGGNFFD YWGQGTTTVTVSS
SEQ ID NO: 3240	VH	D- VH-H.16	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTTTVTVSS
SEQ ID NO: 3241	VH	D- VH-H.17	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRDEDTAVYYCSRHGGNFFD YWGQGTTTVTVSS
SEQ ID NO: 3242	VH	D- VH-H.18	QVQLVESGGGLVKPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTTTVTVSS
SEQ ID NO: 3243	VH	D- VH-H.19	QVQLVESGGGVVQPGRLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD

			YWGQGTTVTVSS
SEQ ID NO: 3244	VH	D- VH- H.20	EVQLLES GGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTTVTVSS
SEQ ID NO: 3245	VH	D- VH- H.21	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRHNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTTVTVSS
SEQ ID NO: 3246	VH	D- VH- H.22	EVQLVESGGGLIQPGGSLRLSCAVSGFTFRSYGMS WVRQPPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTTVTVSS
SEQ ID NO: 3247	VH	D- VH- H.23	EVQLVESGGGLIQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTTVTVSS
SEQ ID NO: 3248	VH	D- VH- H.24	EVQLVESGGGLVQPGRSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDTALYYCSRHGGNFFD YWGQGTTVTVSS
SEQ ID NO: 3249	VH	D- VH- H.25	QVQLVESGGGVVQPGRSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNRLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTTVTVSS
SEQ ID NO: 3250	VH	D- VH- H.26	QVQLVESGGGVVQPGRSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEGTAVYYCSRHGGNFFD YWGQGTTVTVSS
SEQ ID NO: 3251	VH	D- VH- H.27	QVQLVESGGGVVQPGRSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFAI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTTVTVSS
SEQ ID NO: 3252	VH	D- VH- H.28	QVQLVDSGGGVVQPGRSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGGNFFD YWGQGTTVTVSS
SEQ ID NO: 3253	VH	D- VH- H.29	EVQLVESGGGVVRPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDTALYHCSRHGGNFFD YWGQGTTVTVSS
SEQ ID NO: 3254	VH	D- VH- H.30	EVQLVESGGVVVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNSLYLQMNSLRAEDTALYYCSRHGGNFFD YWGQGTTVTVSS
SEQ ID NO: 3255	VH	D- VH- H.31	EVQLVESGGGVVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI

			SRDNSKNSLYLQMNSLRTEDTALYYCSRHGNNFFD YWGQGTTVTVSS
SEQ ID NO: 3256	VH	D- VH- H.32	EVQLVESGGVVVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNSLYLQMNSLRTEDTALYYCSRHGNNFFD YWGQGTTVTVSS
SEQ ID NO: 3257	VH	D- VH- H.33	EVQLVETGGGLIQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGNNFFD YWGQGTTVTVSS
SEQ ID NO: 3258	VH	D- VH- H.34	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQATGKGLEWVALISSGGSYTTYTDSVKGRFTI SRENAKNSLYLQMNSLRAGDTAVYYCSRHGNNFFD YWGQGTTVTVSS
SEQ ID NO: 3259	VH	D- VH- H.35	EVQLVESRGVLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLHLQMNSLRAEDTAVYYCSRHGNNFFD YWGQGTTVTVSS
SEQ ID NO: 3260	VH	D- VH- H.36	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDMALYYCSRHGNNFFD YWGQGTTVTVSS
SEQ ID NO: 3261	VH	D- VH- H.37	QVQLVESGGGLVQPGGSLRLSCSVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCSRHGNNFFD YWGQGTTVTVSS
SEQ ID NO: 3262	VH	D- VH- H.38	EVQLVESGGGLVQPGGSLRLSCSVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMSSLRAEDTAVYYCSRHGNNFFD YWGQGTTVTVSS
SEQ ID NO: 3263	VH	D- VH- H.39	QVQLVESGGGVVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSNTLFLQMNSLRAEDTAVYYCSRHGNNFFD YWGQGTTVTVSS
SEQ ID NO: 3264	VH	D- VH- H.40	QVQLLES GGGLVKPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNAKNSLYLQMNSLRAEDTAVYYCSRHGNNFFD YWGQGTTVTVSS
SEQ ID NO: 3265	VH	D- VH- H.41	EVQLVESGEGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMGLRAEDMAVYYCSRHGNNFFD YWGQGTTVTVSS
SEQ ID NO: 3266	VH	D- VH- H.42	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMGLRAEDMAVYYCSRHGNNFFD YWGQGTTVTVSS
SEQ ID NO: 3267	VH	D- VH-	EVQLVESGGGLVQPGGSLRLSCSVSGFTFRSYGMS

		H.43	WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYVQMSSLRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3268	VH	D- VH- H.44	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSRNSLYLQKNRRRAEDMAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3269	VH	D- VH- H.45	EVQLVESGGGLVQPGGSLRLSCAVSGFTFRSYGMS WVHQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSRNTLYLQTNLSRAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3270	VH	D- VH- H.46	EVHLVESGGGLVQPGGALRLSCAVSGFTFRSYGMS WVRQATGKGLEWVALISSGGSYTTYTDSVKGRFTI SRENAKNSLYLQMNSLRAGDTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3271	VH	D- VH- H.47	EVQLVESGGGLVQPRGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNNLRAEGTAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3272	VH	D- VH- H.48	EVQLVESGGGLVQPRGSLRLSCAVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI SRDNSKNTLYLQMNNLRAEGTAAYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3273	VH	D- VH- H.49	QVQLVQSGAEVKKPGASVKVSKVSGFTFRSYGMS WVRQAPGKGLEWVALISSGGSYTTYTDSVKGRFTI TRDNSTNTLYMELSSLRSED TAVYYCSRHGGNFFD YWGQGTITVTVSS
SEQ ID NO: 3274	VH	D- VH- H.50	QVQLVQSGSELKKPGASVKVSKVSGFTFRSYGMS WVRQAPGQGLEWVALISSGGSYTTYTDSVKGRFVI SRDNSVNTLYLQISSLKAEDTAVYYCSRHGGNFFD YWGQGTITVTVSS

In some embodiments, the anti-TCR β V10 antibody molecule comprises a VH or a VL of an antibody described in **Table 12A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

- 5 In some embodiments, the anti-TCR β V10 antibody molecule comprises a VH and a VL of an antibody described in **Table 12A**, or a sequence with at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identity thereto.

Additional anti-TCRV β antibodies

Additional exemplary anti-TCRV β antibodies of the disclosure are provided in **Table 13A**. In some embodiments, the anti-TCRV β antibody is a humanized antibody, e.g., as provided in **Table 13A**. In some embodiments, the anti-TCRV β antibody comprises one or more (e.g., all three) of a LC CDR1, LC CDR2, and LC CDR3 provided in **Table 13A**; and/or one or more (e.g., all three) of a HC CDR1, HC CDR2, and HC CDR3 provided in **Table 13A**, or a sequence with at least 95% identity thereto. In some embodiments, the anti-TCRV β antibody comprises a variable heavy chain (VH) and/or a variable light chain (VL) provided in **Table 13A**, or a sequence with at least 95% identity thereto.

Table 13A: Amino acid sequences for additional anti-TCRV β V antibodies

Amino acid and nucleotide sequences for murine and humanized antibody molecules which bind to various TCRVB families are disclosed. The amino acid the heavy and light chain CDRs, and the amino acid and nucleotide sequences of the heavy and light chain variable regions, and the heavy and light chains are shown. Antibodies disclosed in the table include, MPB2D5, CAS1.1.3, IMMU222, REA1062, and JOVI-3. MPB2D5 binds human TCR β V 20-1 (TCRV β V2 per old nomenclature). CAS1.1.3 binds human TCR β V 27 (TCRV β V14 per old nomenclature). IMMU 222 binds human TCR β V 6-5, TCR β V 6-6, or TCR β V 6-9 (TCRV β V13.1 per old nomenclature). REA1062 binds human TCR β V 5-1). JOVI-3 binds human TCR β V 28 (TCRV β V3.1 per old nomenclature).

Antibody G (murine) binds to human TCRVβ 20-1		
SEQ ID NO: 1102	HC CDR1 (Kabat)	SAYMH
SEQ ID NO: 1103	HC CDR2 (Kabat)	RIDPATGKTKYAPKFQA
SEQ ID NO: 1104	HC CDR3 (Kabat)	SLNWDYGLDY
SEQ ID NO: 1105	HC CDR1 (Chothia)	GFNIKSA
SEQ ID NO: 1106	HC CDR2 (Chothia)	DPATGK
SEQ ID NO: 1104	HC CDR3 (Chothia)	SLNWDYGLDY
SEQ ID NO: 6376	HC CDR1 (Combined)	GFNIKSAAYMH
SEQ ID NO: 1103	HC CDR2 (Combined)	RIDPATGKTKYAPKFQA
SEQ ID NO: 1104	HC CDR3 (Combined)	SLNWDYGLDY
SEQ ID NO: 1107	LC CDR1 (Kabat)	RASKSVSILGTHLIH
SEQ ID NO: 1108	LC CDR2 (Kabat)	AASNLES
SEQ ID NO: 1109	LC CDR3 (Kabat)	QQSIEDPWT

SEQ ID NO: 1110	LC CDR1 (Chothia)	SKSVSILGTHL
SEQ ID NO: 1108	LC CDR2 (Chothia)	AASNLES
SEQ ID NO: 1109	LC CDR3 (Chothia)	QQSIEDPWT
SEQ ID NO: 1107	LC CDR1 (Combined)	RASKSVSILGTHLIH
SEQ ID NO: 1108	LC CDR2 (Combined)	AASNLES
SEQ ID NO: 1109	LC CDR3(Combined)	QQSIEDPWT
SEQ ID NO: 1111	VL	DIVLTQSPASLAVSLGQRATISCRASKSVSILGTHL IHWYQQKPGQPPKLLIYAASNLESGVPARFSGSGS ETVFTLNIHPVEEEDAATYFCQQSIEDPWTFGGGT KLGK
SEQ ID NO: 1112	VH	EVQLQQSVADLVRPGASLKLSTASGFNIKSAYM HWVIQRPDQGPECLGRIDPATGKTKYAPKFQAKA TITADTSSNTAYLQLSSLTSEDTAIYYCTRSLNWD YGLDYWGQGTSTVTVSS
Antibody G-H (humanized) VHs binds to human TCRVβ 20-1		
SEQ ID NO: 1113	VH - 1	QVQLVQSGAEVKKPGASVKVSCKASGFNIKSAY MHWVRQAPGQGLEWMGRIDPATGKTKYAPKFQ ARVTMTADTSTNTAYMELSSLRSEDTAVYYCARS LNWDYGLDYWGQGTSLTVTVSS
SEQ ID NO: 1114	VH - 2	QVQLVQSGAEVKKPGASVKVSCKASGFNIKSAY MHWVRQAPGQEPGCMGRIDPATGKTKYAPKFQA RVTMTADTSINTAYTELSSLRSEDTATYYCARSLN WDYGLDYWGQGTSLTVTVSS
SEQ ID NO: 1115	VH - 3	QVQLVQSGAEVKKPGSSVKVSCKASGFNIKSAYM HWVRQAPGQGLEWMGRIDPATGKTKYAPKFQA RVTITADTSTNTAYMELSSLRSEDTAVYYCARSL NWDYGLDYWGQGTSLTVTVSS
SEQ ID NO: 1116	VH - 4	QVQLVQSGAEVKKPGASVKVSCKASGFNIKSAY MHWVRQAPGQRLEWMGRIDPATGKTKYAPKFQ ARVTITADTSANTAYMELSSLRSEDTAVYYCARS LNWDYGLDYWGQGTSLTVTVSS
Antibody G-H (humanized) VLs binds to human TCRVβ 20-1		
SEQ ID NO: 1117	VL - 1	EIVLTQSPATLSLSPGERATLSCRASKSVSILGTHLI HWYQQKPGQAPRLLIYAASNLESGIPARFSGSGSE TDFTLTISLEPEDFAVYFCQQSIEDPFGGGTKEI K
SEQ ID NO: 1118	VL - 2	EIVLTQSPATLSLSPGERATLSCRASKSVSILGTHLI HWYQQKPGAPRLLIYAASNLESGIPDRFSGSGSE TDFTLTISRLEPEDFAVYFCQQSIEDPFGGGTKEI K
SEQ ID NO: 1119	VL - 3	EIVLTQSPGTLSPGERATLSCRASKSVSILGTHLI HWYQQKPGQAPRLLIYAASNLESGIPDRFSGSGSE TDFTLTISRLEPEDFAVYFCQQSIEDPFGGGTKEI K
Antibody H (murine) binds to human TCRVβ 27		
SEQ ID NO: 1120	HC CDR1 (Kabat)	DTYMY

SEQ ID NO: 1121	HC CDR2 (Kabat)	RIDPANGNTKYDPKFQD
SEQ ID NO: 1122	HC CDR3 (Kabat)	GSYYYAMDY
SEQ ID NO: 1123	HC CDR1 (Chothia)	GFKTEDT
SEQ ID NO: 1124	HC CDR2 (Chothia)	DPANGN
SEQ ID NO: 1122	HC CDR3 (Chothia)	GSYYYAMDY
SEQ ID NO: 1125	HC CDR1 (Combined)	GFKTEDTYMY
SEQ ID NO: 1121	HC CDR2 (Combined)	RIDPANGNTKYDPKFQD
SEQ ID NO: 1122	HC CDR3(Combined)	GSYYYAMDY
SEQ ID NO: 1126	LC CDR1 (Kabat)	RASESVDSYGNSFMH
SEQ ID NO: 1127	LC CDR2 (Kabat)	RASNLES
SEQ ID NO: 1128	LC CDR3 (Kabat)	QQSNEPDT
SEQ ID NO: 6377	LC CDR1 (Chothia)	SESVDSYGNSF
SEQ ID NO: 1127	LC CDR2 (Chothia)	RASNLES
SEQ ID NO: 1128	LC CDR3 (Chothia)	QQSNEPDT
SEQ ID NO: 1126	LC CDR1 (Combined)	RASESVDSYGNSFMH
SEQ ID NO: 1127	LC CDR2 (Combined)	RASNLES
SEQ ID NO: 1128	LC CDR3(Combined)	QQSNEPDT
SEQ ID NO: 1129	VL	DIVLTQSPASLAVSLGQRATISCRASESVDSYGNSF MHWYQQKPGQPPKLLIYRASNLESGIPARFSGSGS RTDFTLTINPVEADDVATYYCQQSNEPDTFTGGG TKLEIK
SEQ ID NO: 1130	VH	EVQLQQSGAELVKPGASVKLSCTASGFKTEDTYM YWVKQRPEQGLEWIGRIDPANGNTKYDPKFQDK ATITADSSNTAYLQLSSLPSEDTAVYYCARGSY YAMDYWGQGTSTVSS
Antibody H-H (humanized) VHs binds to human TCRVβ 27		
SEQ ID NO: 1131	VH - 1	QVQLVQSGAEVKKPGSSVKVSCASGFKTEDTY MYWVRQAPGQGLEWIGRIDPANGNTKYDPKFQD RATITADSSNTAYMELSSLRSEDVAVYYCARGS YYYAMDYWGQGTSLTVSS
SEQ ID NO: 1132	VH - 2	QVQLVQSGAEVKKPGASVKVSCASGFKTEDTY MYWVRQAPGQRLWIGRIDPANGNTKYDPKFQD RATITADSSANTAYMELSSLRSEDVAVYYCARGS YYYAMDYWGQGTSLTVSS
SEQ ID NO: 1133	VH - 3	EVQLVESGGGLVQPGGSLKLSCAASGFKTEDTYM YWVRQASGKGLEWIGRIDPANGNTKYDPKFQDR ATISADSSKNTAYLQMNSLKTEDTAVYYCARGSY YYAMDYWGQGTSLTVSS
SEQ ID NO: 1134	VH - 4	EVQLVQSGAEVKKPGESLRISCKASGFKTEDTYM YWVRQMPGKGLEWIGRIDPANGNTKYDPKFQDQ ATISADSSINTAYLQWSSLKASDTAMYYCARGSY YYAMDYWGQGTSLTVSS
SEQ ID NO: 1135	VH - 5	QVQLVQSGSELKKPGASVKVSCASGFKTEDTY MYWVRQAPGQGLEWIGRIDPANGNTKYDPKFQD RAVISADSSVNTAYLQISSLKAEEDTAVYYCARGS

		YYYAMDYWGQGLTVTVSS
Antibody H-H (humanized) VLs Binds to human TCRVβ 27		
SEQ ID NO: 1136	VL - 1	DIVLTQSPDSLAVSLGERATINCRASESVDSYGNS FMHWYQQKPGQPPKLLIYRASNLSEGVDPDRFSGS GSRTDFTLTISLQAEDVAVYYCQQSNEDPYTFGQ GTKLEIK
SEQ ID NO: 1137	VL - 2	EIVLTQSPATLSLSPGERATLSCRASESVDSYGNSF MHWYQQKPGQAPKLLIYRASNLSEGVDPDRFSGS SRTDFTLTISRLEPEDFAVYYCQQSNEDPYTFGQ TKLEIK
SEQ ID NO: 1138	VL - 3	DIQLTQSPSSLSASVGDRVTITCRASESVDSYGNSF MHWYQQKPGQAPKLLIYRASNLSEGVPSRFSGSG SRTDFTLTISLQPEDVATYYCQQSNEDPYTFGQ TKLEIK
SEQ ID NO: 1139	VL - 4	AIQLTQSPSSLSASVGDRVTITCRASESVDSYGNSF MHWYQQKPGKAPKLLIYRASNLSEGVPSRFSGSG SRTDFTLTISLQPEDFATYYCQQSNEDPYTFGQ TKLEIK
SEQ ID NO: 1140	VL - 5	EIVLTQSPDFQSVTPKEKVTITCRASESVDSYGNSF MHWYQQKPDQSPKLLIYRASNLSEGVPSRFSGSG SRTDFTLTINSLEAEDAATYYCQQSNEDPYTFGQ TKLEIK
Antibody I(murine) binds to human TCRVβ 6-5,6-6,6-9		
SEQ ID NO: 1141	HC CDR1 (Kabat)	SYAMS
SEQ ID NO: 1142	HC CDR2 (Kabat)	HISNGGDYIYYADTVKG
SEQ ID NO: 1143	HC CDR3 (Kabat)	PSYYSDPWFFDV
SEQ ID NO: 1144	HC CDR1 (Chothia)	GFTFRSY
SEQ ID NO: 1145	HC CDR2 (Chothia)	SNGGDY
SEQ ID NO: 1143	HC CDR3 (Chothia)	PSYYSDPWFFDV
SEQ ID NO: 1146	HC CDR1 (Combined)	GFTFRSYAMS
SEQ ID NO: 1142	HC CDR2 (Combined)	HISNGGDYIYYADTVKG
SEQ ID NO: 1143	HC CDR3(Combined)	PSYYSDPWFFDV
SEQ ID NO: 1147	LC CDR1 (Kabat)	SAGSSVSFMH
SEQ ID NO: 1148	LC CDR2 (Kabat)	DTSKLAS
SEQ ID NO: 1149	LC CDR3 (Kabat)	LQGSGFPLT
SEQ ID NO: 1150	LC CDR1 (Chothia)	GSSVSF
SEQ ID NO: 1148	LC CDR2 (Chothia)	DTSKLAS
SEQ ID NO: 1149	LC CDR3 (Chothia)	LQGSGFPLT
SEQ ID NO: 1147	LC CDR1 (Combined)	SAGSSVSFMH
SEQ ID NO: 1148	LC CDR2 (Combined)	DTSKLAS
SEQ ID NO: 1149	LC CDR3(Combined)	LQGSGFPLT
SEQ ID NO: 1151	VL	ENVLTQSPAIMASAPGEKVTMTCSAGSSVSFMHW YQQKSSTSPKLWIYDTSKLASGVPGRFSGSGS FSLTISSMEAEDVAIYYCLQGSGFPLTFGSGTKLEI K

SEQ ID NO: 1152	VH	DVKLVESGEGLVKPGGSLKLSAASGFTFRSYAM SWVRQTPEKRLEWVAHISNGGDYIYYADTVKGR FTISRDNARNTLYLQMSSLKSEDTAMYYCTRPSY YSDPWFFDVWGTGTTVTVSS
Antibody I-H (humanized) VHs Binds to human TCRVβ 6-5,6-6,6-9		
SEQ ID NO: 1153	VH - 1	EVQLVESGGGLVQPGGSLRLSCAASGFTFRSYAM SWVRQAPGKGLEWVAHISNGGDYIYYADTVKGR FTISRDNANKNSLYLQMNSLRAEDTAVYYCTRPSY YSDPWFFDVWGQGTITVTVSS
SEQ ID NO: 1154	VH - 2	QVQLVESGGGVVQPGRSLRLSCAASGFTFRSYAM SWVRQAPGKGLEWVAHISNGGDYIYYADTVKGR FTISRDNKNTLYLQMSSLRAEDTAVYYCTRPSY YSDPWFFDVWGQGTITVTVSS
SEQ ID NO: 1155	VH - 3	EVQLVESGGGLVQPGGSLRLSCAASGFTFRSYAM SWVRQAPGKGLEWVAHISNGGDYIYYADTVKGR FTISRDNKNTLYLQMNSLRAEDTAVYYCTRPSY YSDPWFFDVWGQGTITVTVSS
SEQ ID NO: 1156	VH - 4	QVQLVQSGSELKKPGASVKVSCASGFTFRSYAM SWVRQAPGQGLEWVAHISNGGDYIYYADTVKGR FVISRDNSVNTLYLQISSLKAEDTAVYYCTRPSY SDPWFFDVWGQGTITVTVSS
SEQ ID NO: 1157	VH - 5	QVQLVQSGAEVKKPGASVKVSCASGFTFRSYA MSWVRQAPGQRLEWVAHISNGGDYIYYADTVKG RFTITRDNSANTLYMELSSLRSEDTAVYYCTRPSY YSDPWFFDVWGQGTITVTVSS
Antibody I-H (humanized) VLs Binds to human TCRVβ 6-5,6-6,6-9		
SEQ ID NO: 1158	VL - 1	ENVLTQSPATLSLSPGERATLSCSAGSSVSFMHWY QQKPGQAPKLLIYDTSKLASGIPARFSGSGSGNDF TLTISSLEPEDFAVYYCLQGSGFPLTFGQGGTKLEIK
SEQ ID NO: 1159	VL - 2	ENVLTQSPDFQSVTPKEKVTITCSAGSSVSFMHW YQQKPDQSPKLLIYDTSKLASGVPSRFSGSGSGND FTLTINSLEAEDAATYYCLQGSGFPLTFGQGGTKLEI K
SEQ ID NO: 1160	VL - 3	DNQLTQSPSSLSASVGDRVTITCSAGSSVSFMHW YQQKPGKVPKLLIYDTSKLASGVPSRFSGSGSGND FTLTISLQPEDVATYYCLQGSGFPLTFGQGGTKLEI K
SEQ ID NO: 1161	VL - 4	ANQLTQSPSSLSASVGDRVTITCSAGSSVSFMHW YQQKPGKAPKLLIYDTSKLASGVPSRFSGSGSGND FTLTISLQPEDFATYYCLQGSGFPLTFGQGGTKLEI K
SEQ ID NO: 1162	VL - 5	DNVLTQSPDSLAVSLGERATINCSAGSSVSFMHW YQQKPGQPPKLLIYDTSKLASGVDPDRFSGSGSGND FTLTISLQAEDVAVYYCLQGSGFPLTFGQGGTKLEI

		IK
Antibody IJ (murine), Binds to human TCRVβ 5-1		
SEQ ID NO: 1163	HC CDR1 (Kabat)	DYNIH
SEQ ID NO: 1164	HC CDR2 (Kabat)	YINPYNGRTGYNQKFKA
SEQ ID NO: 1165	HC CDR3 (Kabat)	WDGSSYFDY
SEQ ID NO: 1166	HC CDR1 (Chothia)	GYTFTDYNIH
SEQ ID NO: 1167	HC CDR2 (Chothia)	NPYNGR
SEQ ID NO: 1165	HC CDR3 (Chothia)	WDGSSYFDY
SEQ ID NO: 1166	HC CDR1 (Combined)	GYTFTDYNIH
SEQ ID NO: 1164	HC CDR2 (Combined)	YINPYNGRTGYNQKFKA
SEQ ID NO: 1165	HC CDR3 (Combined)	WDGSSYFDY
SEQ ID NO: 1168	LC CDR1 (Kabat)	SASSSVSYMH
SEQ ID NO: 1169	LC CDR2 (Kabat)	EISKLAS
SEQ ID NO: 1170	LC CDR3 (Kabat)	QQWNYPLLT
SEQ ID NO: 1297	LC CDR1 (Chothia)	SSSVSY
SEQ ID NO: 1169	LC CDR2 (Chothia)	EISKLAS
SEQ ID NO: 1170	LC CDR3 (Chothia)	QQWNYPLLT
SEQ ID NO: 1168	LC CDR1 (Combined)	SASSSVSYMH
SEQ ID NO: 1169	LC CDR2 (Combined)	EISKLAS
SEQ ID NO: 1170	LC CDR3 (Combined)	QQWNYPLLT
SEQ ID NO: 1171	VL	EIVLTQSPAITAASLGQKVTITCSASSSVSYMHWY QQKSGTSPKPWIYEISKLASGVPARFSGSGSGTSY SLTISSMEAEDAAIYYCQQWNYPLLTFGAGTKLE LK
SEQ ID NO: 1172	VH	EVQLQQSGPVLVKPGASVRMSCKASGYTFTDYNI HWVKQSHGRSLEWVGYNPYNGRTGYNQKFKA KATLTVDKSSSTAYMDLRSLTSEDSAVYYCARW DGSSYFDYWGQGTTLTVSS
Antibody J-H(humanized) VHs Binds to human TCRVβ 5-1		
SEQ ID NO: 1173	VH - 1	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTDYNI HWVRQAPGQGLEWVGYNPYNGRTGYNQKFKA RATLTVDKSTSTAYMELSSLRSEDNAVYYCARW DGSSYFDYWGQGTTLTVSS
SEQ ID NO: 1174	VH - 2	QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYNI HWVRQAPGQGLEWVGYNPYNGRTGYNQKFKA RATLTVDKSTSTAYMELRSLRSDDMNAVYYCARW DGSSYFDYWGQGTTLTVSS
SEQ ID NO: 1175	VH - 3	QVQLVQSGAEVKKPGASVKVSCKASGYTFTDYNI HWVRQATGQGLEWVGYNPYNGRTGYNQKFKA RATLTVNKSISTAYMELSSLRSEDNAVYYCARWD GSSYFDYWGQGTTLTVSS
SEQ ID NO: 1176	VH - 4	EVQLVESGGGLVQPGRSLRLSCTASGYTFTDYNIH WVRQAPGKGLEWVGYNPYNGRTGYNQKFKAR ATLSVDKSKSIAYLQMNSLKTEDNAVYYCARWD

		GSSYFDYWGQGTTVTVSS
SEQ ID NO: 1177	VH - 5	QVQLVQSGSELKKPGASVKVSCASGYTFTDYN HWVRQAPGQGLEWVGYINPYNGRTGYNQKFA RAVLSVDKSVSTAYLQISSLKAEDTAVYYCARWD GSSYFDYWGQGTTVTVSS
Antibody J-H (humanized) VLs Binds to human TCRVβ 5-1		
SEQ ID NO: 1178	VL - 1	EIVLTQSPATLSLSPGERATLSCSASSSVSYMH WYQQKPGQAPKLLIYEISKLASGIPARFSGSG SGTDYTLTISSLEPEDFAVYYCQQWNYPLLT FGQGGTKLEIK
SEQ ID NO: 1179	VL - 2	EIVLTQSPATLSLSPGERATLSCSASSSVSYMH WYQQKPGQAPKLLIYEISKLASGIPARFSGSG SGTDYTLTISRLEPEDFAVYYCQQWNYPLLT FGQGGTKLEIK
SEQ ID NO: 1180	VL - 3	EIVLTQSPDFQSVTPKEKVTITCSASSSVSYMH WYQQKPDQSPKLLIYEISKLASGVPSRFSGSG SGTDYTLTINSLEAEDAATYYCQQWNYPLLT FGQGGTKLEIK
SEQ ID NO: 1181	VL - 4	DIQLTQSPSFLSASVGDRVTITCSASSSVSYMH WYQQKPGKAPKLLIYEISKLASGVPSRFSGSG SGTEYTLTISSLQPEDFATYYCQQWNYPLLT FGQGGTKLEIK
SEQ ID NO: 1182	VL - 5	AIQLTQSPSSLSASVGDRVTITCSASSSVSYMH WYQQKPGKAPKLLIYEISKLASGVPSRFSGSG SGTDYTLTISSLQPEDFATYYCQQWNYPLLT FGQGGTKLEIK
SEQ ID NO: 1183	VL - 6	AIRLTQSPFSLASVGDRVTITCSASSSVSYMH WYQQKPAKAPKLFIIYEISKLASGVPSRFSGSG SGTDYTLTISSLQPEDFATYYCQQWNYPLLT FGQGGTKLEIK
SEQ ID NO: 1184	VL - 7	DIVLTQSPDSLAVSLGERATINCSASSSVSYMH WYQQKPGQPPKLLIYEISKLASGVDPDRFSGSG SGTDYTLTISSLQAEDVAVYYCQQWNYPLLT FGQGGTKLEIK
Antibody K (murine), binds to human TCRVβ 28		
SEQ ID NO: 1185	HC CDR1 (Kabat)	GSWMN
SEQ ID NO: 1186	HC CDR2 (Kabat)	RIYPGDGDTDYSGKFKG
SEQ ID NO: 1187	HC CDR3 (Kabat)	SGYFNYVPVFDY
SEQ ID NO: 1188	HC CDR1 (Chothia)	GYTFSGS
SEQ ID NO: 1189	HC CDR2 (Chothia)	YPGDGD
SEQ ID NO: 1187	HC CDR3 (Chothia)	SGYFNYVPVFDY
SEQ ID NO: 1190	HC CDR1 (Combined)	GYTFSGSWMN
SEQ ID NO: 1186	HC CDR2 (Combined)	RIYPGDGDTDYSGKFKG
SEQ ID NO: 1187	HC CDR3 (Combined)	SGYFNYVPVFDY
SEQ ID NO: 1191	LC CDR1 (Kabat)	SANSTVGYIH
SEQ ID NO: 1192	LC CDR2 (Kabat)	TTSNLAS
SEQ ID NO: 1193	LC CDR3 (Kabat)	HQWSFYPT
SEQ ID NO: 1194	LC CDR1 (Chothia)	NSTVGY

SEQ ID NO: 1192	LC CDR2 (Chothia)	TTSNLAS
SEQ ID NO: 1193	LC CDR3 (Chothia)	HQWSFYPT
SEQ ID NO: 1191	LC CDR1 (Combined)	SANSTVGYIH
SEQ ID NO: 1192	LC CDR2 (Combined)	TTSNLAS
SEQ ID NO: 1193	LC CDR3(Combined)	HQWSFYPT
SEQ ID NO: 1195	VL	QIVLTQSPAISASLGEIALTCSANSTVGYIHWY QQKSGTSPKLLIYTTSNLASGVPSRFSGSGSGTFYS LTISSVEAEDAADYFCHQWSFYPTFGGGTKLEIK
SEQ ID NO: 1196	VH	QIQLQSQSGPEVVKPGASVQISCKASGYTFSGSWM NWVKQRPKGKLEWIGRIYPGDGDDTDYSGKFKGR ATLTADKSSSTAYMRLSSLTSEDSAVYFCARSGYF NYVPVFDYWGQGTTLVS
Antibody K-H(humanized) VHs Binds to human TCRVβ 28		
SEQ ID NO: 1197	VH - 1	QIQLVQSGAEVKKPGASVKVSCASGYTFSGSW MNWVRQAPGQGLEWIGRIYPGDGDDTDYSGKFKG RATLTADKSTSTAYMELSSLRSEDNAVYYCARSG YFNYVPVFDYWGQGTTVTVSS
SEQ ID NO: 1198	VH - 2	QIQLVQSGAEVKKPGSSVKVSCASGYTFSGSWM NWVRQAPGQGLEWIGRIYPGDGDDTDYSGKFKGR ATLTADKSTSTAYMELSSLRSEDNAVYYCARSGY FNYVPVFDYWGQGTTVTVSS
SEQ ID NO: 1199	VH - 3	EIQLVQSGAEVKKPGESLKISCKASGYTFSGSWM NWVRQMPGKLEWIGRIYPGDGDDTDYSGKFKGQ ATLSADKSISTAYLQWSSLKASDTAMYYCARSGY FNYVPVFDYWGQGTTVTVSS
SEQ ID NO: 1200	VH - 4	QIQLVQSGSELKKPGASVKVSCASGYTFSGSWM NWVRQAPGQGLEWIGRIYPGDGDDTDYSGKFKGR AVLSADKSVSTAYLQISSLKAEDNAVYYCARSGY FNYVPVFDYWGQGTTVTVSS
SEQ ID NO: 1201	VH - 5	QIQLVQSGSELKKPGASVKVSCASGYTFSGSWM NWVRQAPGQGLEWIGRIYPGDGDDTDYSGKFKGR AVLSADKSVSMAYLQISSLKAEDNAVYYCARSGY FNYVPVFDYWGQGTTVTVSS
SEQ ID NO: 1202	VH - 6	EIQLVESGGGLVQPGRSLRLSCTASGYTFSGSWM NWVRQAPGKLEWIGRIYPGDGDDTDYSGKFKGR ATLSADKSKSIAYLQMNSLKTEDNAVYYCARSGY FNYVPVFDYWGQGTTVTVSS
Antibody K-H (humanized) VLs Binds to human TCRVβ 28		
SEQ ID NO: 1203	VL - 1	EIVLTQSPATLSLSPGERATLSCSANSTVGYIHWY QQKPGQAPKLLIYTTSNLASGIPARFSGSGSGTDY TLTISSLEPEDFAVYFCHQWSFYPTFGQGTKLEIK
SEQ ID NO: 1204	VL - 2	DIQLTQSPSFLSASVGDRTITCSANSTVGYIHWY QQKPGKAPKLLIYTTSNLASGVPSRFSGSGSGTEY TLTISSLQPEDFATYFCHQWSFYPTFGQGTKLEIK

SEQ ID NO: 1205	VL - 3	EIVLTQSPATLSLSPGERATLSCSANSTVGYIHWY QQKPGQAPKLLIYTTSNLASGIPARFSGSGPGTDY TLTISSLEPEDFAVYFCHQWSFYPTFGQGTKLEIK
SEQ ID NO: 1206	VL - 4	DIVLTQSPDSLAVSLGERATINCSANSTVGYIHWY QQKPGQPPKLLIYTTSNLASGVDPDRFSGSGSGTDY TLTISSLQAEDVAVYFCHQWSFYPTFGQGTKLEIK
SEQ ID NO: 1207	VL - 5	EIVLTQSPDFQSVTPKEKVTITCSANSTVGYIHWY QQKPDQSPKLLIYTTSNLASGVPSRFSGSGSGTDY TLTINSLEAEDAATYFCHQWSFYPTFGQGTKLEIK
Antibody L (murine), binds to human TCRVβ 4-1,4-2,4-3		
SEQ ID NO: 1208	HC CDR1 (Kabat)	DYYMY
SEQ ID NO: 1209	HC CDR2 (Kabat)	TISGGGSYTYSPDSVKG
SEQ ID NO: 1210	HC CDR3 (Kabat)	ERDIYYGNFNAMVY
SEQ ID NO: 1211	HC CDR1 (Chothia)	GFTFSDY
SEQ ID NO: 1212	HC CDR2 (Chothia)	SGGGSY
SEQ ID NO: 1210	HC CDR3 (Chothia)	ERDIYYGNFNAMVY
SEQ ID NO: 1213	HC CDR1 (Combined)	GFTFSDYYMY
SEQ ID NO: 1209	HC CDR2 (Combined)	TISGGGSYTYSPDSVKG
SEQ ID NO: 1210	HC CDR3(Combined)	ERDIYYGNFNAMVY
SEQ ID NO: 1214	LC CDR1 (Kabat)	RASKSVSTSGYSYMH
SEQ ID NO: 1215	LC CDR2 (Kabat)	LASNLES
SEQ ID NO: 1216	LC CDR3 (Kabat)	QHSRDLPWT
SEQ ID NO: 1217	LC CDR1 (Chothia)	SKSVSTSGYSY
SEQ ID NO: 1215	LC CDR2 (Chothia)	LASNLES
SEQ ID NO: 1216	LC CDR3 (Chothia)	QHSRDLPWT
SEQ ID NO: 1214	LC CDR1 (Combined)	RASKSVSTSGYSYMH
SEQ ID NO: 1215	LC CDR2 (Combined)	LASNLES
SEQ ID NO: 1216	LC CDR3(Combined)	QHSRDLPWT
SEQ ID NO: 1218	VL	DIVLTQSPVSLTVSLGQRATISCRASKSVSTSGYSY MHWYQQKPGQPPKLLIYLASNLESGVPARFSGSG SGTDFTLNHPVEEEDAATYYCQHSRDLPWTFFG GTKLEIK
SEQ ID NO: 1219	VH	EVQLVESGGGLVQPGGSLKLSCAASGFTFSDYYM YWVRQTPEKRLEWVATISGGGSYTYSPDSVKGRF TISRDNANKNNLYLQMSSLRSEDTAMYFCARERDI YYGNFNAMVYWGRGTSVTVSS
Antibody L-H (humanized) VHs Binds to human TCRVβ 4-1,4-2,4-3		
SEQ ID NO: 1220	VH - 1	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYM YWVRQAPGKGLEWVATISGGGSYTYSPDSVKGR FTISRDNANKNTLYLQMNSLRAEDTAVYYCARERD IYYGNFNAMVYWGRGTLTVSS
SEQ ID NO: 1221	VH - 2	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYM YWVRQAPGKGLEWVATISGGGSYTYSPDSVKGR FTISRDNANKNSLYLQMNSLRAEDTAVYYCARERD

		IYYGNFNAMVYWGRGTLTVSS
SEQ ID NO: 1222	VH - 3	QVQLVESGGGVVQPGRSLRLSCAASGFTFSDYY MYWVRQAPGKGLEWVATISGGGSYTYSPDSVK GRFTISRDNKNTLYLQMNSLRAEDTAVYYCAR ERDIYYGNFNAMVYWGRGTLTVSS
SEQ ID NO: 1223	VH - 4	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYM YWIRQAPGKGLEWVATISGGGSYTYSPDSVKGRF TISRDNKNSLYLQMNSLRAEDTAVYYCARERDI YYGNFNAMVYWGRGTLTVSS
Antibody L-H(humanized) VLs Binds to human TCRVβ 4-1,4-2,4-3		
SEQ ID NO: 1224	VL - 1	EIVLTQSPGTLSPGERATLSCRASKSVSTSGYSY MHWYQQKPGQAPRLIYLASNLESGIPDRFSGSGS GTDFTLTISRLEPEDFAVYYCQHSRDLPWTFGGGT KVEIK
SEQ ID NO: 1225	VL - 2	EIVLTQSPATLSLSPGERATLSCRASKSVSTSGYSY MHWYQQKPGQAPRLIYLASNLESGIPARFSGSGS GTDFTLTISLEPEDFAVYYCQHSRDLPWTFGGGT KVEIK
SEQ ID NO: 1226	VL - 3	DIQLTQSPSTLSASVGDRVTITCRASKSVSTSGYSY MHWYQQKPGKAPKLLIYLASNLESGVPSRFSGSG SGTEFTLTISLQPDDEFATYYCQHSRDLPWTFGGG TKVEIK
SEQ ID NO: 1227	VL - 4	AIQLTQSPSSLSASVGDRVTITCRASKSVSTSGYSY MHWYQQKPGKAPKLLIYLASNLESGVPSRFSGSG SGTDFTLTISLQPEDFATYYCQHSRDLPWTFGGG TKVEIK
Antibody M (murine), binds to human TCRVβ 19		
SEQ ID NO: 1229	HC CDR1 (Kabat)	GYFWN
SEQ ID NO: 1230	HC CDR2 (Kabat)	YISYDGSNNYNPSLKN
SEQ ID NO: 1231	HC CDR3 (Kabat)	PSPGTGYAVDY
SEQ ID NO: 1232	HC CDR1 (Chothia)	GYSITSGY
SEQ ID NO: 1233	HC CDR2 (Chothia)	SYDGSN
SEQ ID NO: 1231	HC CDR3 (Chothia)	PSPGTGYAVDY
SEQ ID NO: 1234	HC CDR1 (Combined)	GYSITSGYFWN
SEQ ID NO: 1230	HC CDR2 (Combined)	YISYDGSNNYNPSLKN
SEQ ID NO: 1231	HC CDR3(Combined)	PSPGTGYAVDY
SEQ ID NO: 1235	LC CDR1 (Kabat)	RSSQSLVHSNGNTYLH
SEQ ID NO: 1236	LC CDR2 (Kabat)	KVSNRFS
SEQ ID NO: 1237	LC CDR3 (Kabat)	SQSTHVPFT
SEQ ID NO: 1238	LC CDR1 (Chothia)	SQSLVHSNGNTY
SEQ ID NO: 1236	LC CDR2 (Chothia)	KVSNRFS
SEQ ID NO: 1237	LC CDR3 (Chothia)	SQSTHVPFT
SEQ ID NO: 1235	LC CDR1 (Combined)	RSSQSLVHSNGNTYLH
SEQ ID NO: 1236	LC CDR2 (Combined)	KVSNRFS

SEQ ID NO: 1237	LC CDR3(Combined)	SQSTHVPFT
SEQ ID NO: 1239	VL	NVVMQTQTPLSLPVSLGDQASISCRSSQSLVHSNGN TYLHWYQLKPGQSPKFLIYKVSNRFSGVPDRFSG GGSGTEFTLKISRVEAEDLGVYFCSQSTHVPFTFG SGTKLEIK
SEQ ID NO: 1240	VH	NVQLQESGPGLVKPSQSLSLTCSVAGYSITSGYFW NWIRQPPGNKLEWMGYISYDGSNNYNPSLKNRISI TRDTSKNQFFLKLNSVTTEDTATYYCASPSPGTGY AVDYWGQGTSTVTVSS
Antibody M-H (humanized) VHs Binds to human TCRVβ 19		
SEQ ID NO: 1241	VH - 1	QVQLQESGPGLVKPSETLSLTCTVSGYSITSGYFW NWIRQPPGKGLEWIGYISYDGSNNYNPSLKNRVTI SRDTSKNQFSLKLSSVTAADTAVYYCASPSPGTG YAVDYWGQGTSLTVTVSS
SEQ ID NO: 1242	VH - 2	QVQLQESGPGLVKPSETLSLTCTVSGYSITSGYFW NWIRQPPGKGLEWIGYISYDGSNNYNPSLKNRVTI SRDTSKNQFSLKLSSVTAADTAVYYCASPSPGTG YAVDYWGQGTSLTVTVSS
SEQ ID NO: 1243	VH - 3	QVQLVESGGGLVQPGGSLRLSCSVSGYSITSGYF WNWVRQAPGKGLEWVGYISYDGSNNYNPSLKN RFTISRDTSKNTFYLMNSLRAEDTAVYYCASPS GTGYAVDYWGQGTSLTVTVSS
Antibody M-H (humanized) VLs Binds to human TCRVβ 19		
SEQ ID NO: 1244	VL - 1	VVMTQSPGTLSPGERATLSCRSSQSLVHSNGNT YLHWYQQKPGQAPRFLIYKVSNRFSGIPDRFSGS SGTDFTLTISRLEPEDFAVYFCSQSTHVPFTFGQGT KLEIK
SEQ ID NO: 1245	VL - 2	EVVMTQSPATLSLSPGERATLSCRSSQSLVHSNGN TYLHWYQQKPGQAPRFLIYKVSNRFSGIPARFSGS GSGTDFTLTISLEPEDFAVYFCSQSTHVPFTFGQG TKLEIK
SEQ ID NO: 1246	VL - 3	EVVMTQSPATLSVSPGERATLSCRSSQSLVHSNGN TYLHWYQQKPGQAPRFLIYKVSNRFSGIPARFSGS GSGTEFTLTISLQSEDFAVYFCSQSTHVPFTFGQG TKLEIK
SEQ ID NO: 1247	VL - 4	DVQMTQSPSSLSASVGDRVTITCRSSQSLVHSNGN TYLHWYQQKPGKAPKFLIYKVSNRFSGVPSPRFS SGSGTDFTFTISLQPEDATYFCSQSTHVPFTFGQ GTKLEIK
Antibody N(murine), binds to human TCRVβ 9		
SEQ ID NO: 1248	HC CDR1 (Kabat)	DYIVH
SEQ ID NO: 1249	HC CDR2 (Kabat)	WINTYTGTPTYADDFEG
SEQ ID NO: 1250	HC CDR3 (Kabat)	SWRRGIRGIGFDY
SEQ ID NO: 1251	HC CDR1 (Chothia)	GYTFTDY

SEQ ID NO: 1252	HC CDR2 (Chothia)	NTYTGT
SEQ ID NO: 1250	HC CDR3 (Chothia)	SWRRGIRGIGFDY
SEQ ID NO: 1253	HC CDR1 (Combined)	GYTFTDYIVH
SEQ ID NO: 1249	HC CDR2 (Combined)	WINTYTGTPTYADDFEG
SEQ ID NO: 1250	HC CDR3(Combined)	SWRRGIRGIGFDY
SEQ ID NO: 1254	LC CDR1 (Kabat)	KASKSINKYLA
SEQ ID NO: 1255	LC CDR2 (Kabat)	DGSTLQS
SEQ ID NO: 1256	LC CDR3 (Kabat)	QQHNEYPPT
SEQ ID NO: 1257	LC CDR1 (Chothia)	SKSINKY
SEQ ID NO: 1255	LC CDR2 (Chothia)	DGSTLQS
SEQ ID NO: 1256	LC CDR3 (Chothia)	QQHNEYPPT
SEQ ID NO: 1254	LC CDR1 (Combined)	KASKSINKYLA
SEQ ID NO: 1255	LC CDR2 (Combined)	DGSTLQS
SEQ ID NO: 1256	LC CDR3(Combined)	QQHNEYPPT
SEQ ID NO: 1258	VL	DVQMTQSPYNLAASPGESVSINCKASKSINKYLA WYQQKPGKPNKLLIYDGSTLQSGIPSRFSGSGSGT DFTLTIRGLEPEDFGLYYCQQHNEYPPTFGAGTKL ELK
SEQ ID NO: 1259	VH	QLQLVQSGPELREPGEVKISCKASGYTFTDYIVH WVKQAPGKGLKWMGWINTYTGTPTYADDFEGR FVFSLEASASTANLQISNLKNEDTATYFCARSWRR GIRGIGFDYWGQGMVTVSS
Antibody N-H (humanized) VH's Binds to human TCRVβ 9		
SEQ ID NO: 1260	VH - 1	QLQLVQSGAEVKKPGASVKVSCKASGYTFTDYIV HWVRQAPGQGLEWMGWINTYTGTPTYADDFEG WVTMTLDASISTAYMELSRLSDDTAVYYCARS WRRGIRGIGFDYWGQGMVTVSS
SEQ ID NO: 1261	VH - 2	QLQLVQSGAEVKKPGASVKVSCKASGYTFTDYIV HWVRQAPGQGLEWMGWINTYTGTPTYADDFEG RVTMTLDASTSTAYMELSSLRSEDVAVYYCARS WRRGIRGIGFDYWGQGMVTVSS
SEQ ID NO: 1262	VH - 3	QLQLVQSGAEVKKPGASVKVSCKASGYTFTDYIV HWVRQAPGQRLWMGWINTYTGTPTYADDFEG RVTITLDASASTAYMELSSLRSEDMVAVYYCARSW RRGIRGIGFDYWGQGMVTVSS
SEQ ID NO: 1263	VH - 4	QLQLVQSGAEVKKPGASVKVSCKASGYTFTDYIV HWVRQATGQGLEWMGWINTYTGTPTYADDFEG RVTMTLNASISTAYMELSSLRSEDVAVYYCARSW RRGIRGIGFDYWGQGMVTVSS
Antibody N-H (humanized) VL's Binds to human TCRVβ 9		
SEQ ID NO: 1264	VL - 1	EVVMTQSPGTLSPGERATLSCASKSINKYLA WYQQKPGQAPRLIYDGSTLQSGIPDRFSGSGSGT DFTLTISRLEPEDFAVYYCQQHNEYPPTFGQGTKL EIK

SEQ ID NO: 1265	VL - 2	EVVMTQSPATLSLSPGERATLSCKASKSINKYLA WYQQKPGQAPRLLIYDGSTLQSGIPARFSGSGSGT DFTLTISSELPEDFAVYYCQQHNEYPPFTFGQGTKL EIK
SEQ ID NO: 1266	VL - 3	DVQMTQSPSSLSASVGDRTITCKASKSINKYLA WYQQKPGKAPKLLIYDGSTLQSGVPSRFSGSGSG TDFTLTISLQPEDFATYYCQQHNEYPPFTFGQGTK LEIK
SEQ ID NO: 1267	VL - 4	AVRMTQSPSSFSASTGDRVTITCKASKSINKYLA WYQQKPGKAPKLLIYDGSTLQSGVPSRFSGSGSGTD FTLTISCLQSEDFATYYCQQHNEYPPFTFGQGTKLEI K
Antibody O (murine) binds to TRVβ 11-2		
SEQ ID NO: 1268	HC CDR1 (Kabat)	NYGVH
SEQ ID NO: 1269	HC CDR2 (Kabat)	VIWSDGSTDYDTAFIS
SEQ ID NO: 1270	HC CDR3 (Kabat)	RAVVADFDY
SEQ ID NO: 1271	HC CDR1 (Chothia)	GFSLTN
SEQ ID NO: 1272	HC CDR2 (Chothia)	VIWSDGSTD
SEQ ID NO: 1270	HC CDR3 (Chothia)	RAVVADFDY
SEQ ID NO: 1273	HC CDR1 (combined)	GFSLTNYGVH
SEQ ID NO: 1269	HC CDR2 (combined)	VIWSDGSTDYDTAFIS
SEQ ID NO: 1270	HC CDR3 (combined)	RAVVADFDY
SEQ ID NO: 1274	VH	QVQLKQSGPGLLQPSQSLITCTVSGFSLTNYGVH WVRQSPGKGLEWLGVIWSDGSTDYDTAFISRLSIS KDNSKSKVFFKLNSLQADDTAIYYCARRAVVADF DYWGQGTTTLTVSS
SEQ ID NO: 1275	LC CDR1 (Kabat)	KASKEVTIFGSISALH
SEQ ID NO: 1276	LC CDR2 (Kabat)	NGAKLES
SEQ ID NO: 1277	LC CDR3 (Kabat)	LQNKEVPFT
SEQ ID NO: 1275	LC CDR1 (Chothia)	KASKEVTIFGSISALH
SEQ ID NO: 1276	LC CDR2 (Chothia)	NGAKLES
SEQ ID NO: 1277	LC CDR3 (Chothia)	LQNKEVPFT
SEQ ID NO: 1275	LC CDR1 (combined)	KASKEVTIFGSISALH
SEQ ID NO: 1276	LC CDR2 (combined)	NGAKLES
SEQ ID NO: 1277	LC CDR3 (combined)	LQNKEVPFT
SEQ ID NO: 1278	VL	DIVLTQSPASLAVSLGQKATISCKASKEVTIFGSIS ALHWYQQKPGQPPKLLIYNGAKLESGVSARFSDS GSQNRSPFGNQLSFTLTIAPEADDAATYYCLQN KEVPFTFGSGTKLEIK
Antibody O-H (humanized) VL binds to TRVβ 11-2		
SEQ ID NO: 1279	VL-1	DIVLTQSPDSLAVSLGERATINCKASKEVTIFGSIS ALHWYQQKPGQPPKLLIYNGAKLESGVSARFGVP DRFSRSGSLDFTLTISLQAEDVAVYYCLQNKE VPFTFGQGTKLEIK
SEQ ID NO: 1280	VL-2	EIVLTQSPDFQSVTPKEKVTITCKASKEVTIFGSIS

		ALHWYQQKPDQSPKLLYNGAKLESGVSARFGVP SRFSRSGSGLDFTLTINSLEAEDAATYYCLQNKE VPFTFGQGTKLEIK
SEQ ID NO: 1281	VL-3	AIQLTQSPSSLSASVGDRVITITCKASKEVTIFGSIS ALHWYQQKPGKAPKLLYNGAKLESGVSARFGV PSRFSRSGSGLDFTLTISLQPEDFATYYCLQNKE VPFTFGQGTKLEIK
SEQ ID NO: 1282	VL-4	DIVLTQTPLSLSVTPGQPASISCKASKEVTIFGSIS ALHWYLQKPGQPPKLLYNGAKLESGVSARFGVP DRFSRSGSGLDFTLKISRVEAEDVGVYYCLQNKE VPFTFGQGTKLEIK
Antibody O-H (humanized) VH, binds to TRVβ 11-2		
SEQ ID NO: 1283	VH-1	QVTLKESGPVLVKPTETLTCTVSGFSLTNYGV HWVRQPPGKALEWLGVIWSDGSTDYDTAFISRL TISKDNSKSQVVLTMNMDPVDATYYCARRAV VADFDYWGQGTTVTVSS
SEQ ID NO: 1284	VH-2	QVQLQESGPGLVKPSGTLSTCAVSGFSLTNYGV HWVRQPPGKGLEWLGVIWSDGSTDYDTAFISRL TISKDNSKSQVSLKLSSVTAADTAVYYCARRAV VADFDYWGQGTTVTVSS
SEQ ID NO: 1285	VH-3	QVQLQQSGPGLVKPSQTLSTCAVSGFSLTNYGV HWVRQSPSRGLEWLGVIWSDGSTDYDTAFISRLT INKDNSKSQVSLQLNSVTPEDTAVYYCARRAV VADFDYWGQGTTVTVSS
SEQ ID NO: 1286	VH-4	EVQLVESGGGLVQPGPSLRLSCTVSGFSLTNYGV HWVRQAPGKGLEWLGVIWSDGSTDYDTAFISRL TISKDNSKSIVYLQMNSLKTEDTAVYYCARRAV VADFDYWGQGTTVTVSS
SEQ ID NO: 1287	VH-5	EVQLVQSGAEVKKPGESLRISCKVSGFSLTNYGV HWVRQMPGKGLEWLGVIWSDGSTDYDTAFISQL TISKDNSISTVYLQWSSLKASDTAMYYCARRAV VADFDYWGQGTTVTVSS

Anti-TCRV β antibody effector function and Fc variants

In some embodiments, an anti-TCRV β antibody disclosed herein comprises an Fc region, e.g., as described herein. In some embodiments, the Fc region is a wildtype Fc region, e.g., a wildtype human Fc region. In some embodiments, the Fc region comprises a variant, e.g., an Fc region comprising an addition, substitution, or deletion of at least one amino acid residue in the Fc region which results in, e.g., reduced or ablated affinity for at least one Fc receptor.

The Fc region of an antibody interacts with a number of receptors or ligands including Fc Receptors (e.g., FcγRI, FcγRIIA, FcγRIIIA), the complement protein C1q, and other molecules such as proteins A and G. These interactions are essential for a variety of effector functions and downstream signaling events including: antibody dependent cell-mediated cytotoxicity (ADCC),
 5 Antibody-dependent cellular phagocytosis (ADCP) and complement dependent cytotoxicity (CDC).

In some embodiments, an anti-TCRVβ antibody comprising a variant Fc region has reduced, e.g., ablated, affinity for an Fc receptor, e.g., an Fc receptor described herein. In some
 10 embodiments, the reduced affinity is compared to an otherwise similar antibody with a wildtype Fc region.

In some embodiments, an anti-TCRVβ antibody comprising a variant Fc region has one or more of the following properties: (1) reduced effector function (e.g., reduced ADCC, ADCP and/or CDC); (2) reduced binding to one or more Fc receptors; and/or (3) reduced binding to C1q complement. In some embodiments, the reduction in any one, or all of properties (1)-(3) is
 15 compared to an otherwise similar antibody with a wildtype Fc region.

In some embodiments, an anti-TCRVβ antibody comprising a variant Fc region has reduced affinity to a human Fc receptor, e.g., FcγR I, FcγR II and/or FcγR III. In some
 20 embodiments, the anti-TCRVβ antibody comprising a variant Fc region comprises a human IgG1 region or a human IgG4 region.

In some embodiments, an anti-TCRVβ antibody comprising a variant Fc region activates and/or expands T cells, e.g., as described herein. In some embodiments, an anti-TCRVβ antibody comprising a variant Fc region has a cytokine profile described herein, e.g., a cytokine profile that differs from a cytokine profile of a T cell engager that binds to a receptor or molecule other than a TCRβV region (“a non-TCRβV-binding T cell engager”). In some embodiments, the non-
 25 TCRβV-binding T cell engager comprises an antibody that binds to a CD3 molecule (e.g., CD3 epsilon (CD3e) molecule); or a TCR alpha (TCRα) molecule.

Exemplary Fc region variants are provided in **Table 21A** and also disclosed in Saunders O, (2019) *Frontiers in Immunology*; vol 10, article1296, the entire contents of which is hereby incorporated by reference.

In some embodiments, an anti-TCRV β antibody disclosed herein comprises any one or all, or any combination of Fc region variants, e.g., mutations, disclosed in **Table 21A**. In some embodiments, an anti-TCRV β antibody disclosed herein comprise an Asn297Ala (N297A) mutation. In some embodiments, an anti-TCRV β antibody disclosed herein comprise a

5 Leu234Ala/Leu235Ala (LALA) mutation.

Table 21A: Exemplary Fc modifications

Modification or mutation	Altered effector function
Leu235Glu	ADCC;
Leu234Ala/Leu235Ala (LALA)	ADCC; ADCP; CDC
Ser228Pro/Leu235Glu	
Leu234Ala/Leu235Ala/Pro329Gly	ADCP
Pro331Ser/Leu234Glu/Leu235Phe	CDC
Asp265Ala	ADCC, ADCP
Gly237Ala	ADCP
Glu318Ala	ADCP
Glu233Pro	
Gly236Arg/Leu328Arg	ADCC
His268Gln/Val309Leu/Ala330Ser/Pro331Ser	ADCC; ADCP; CDC
Val234Ala/Gly237Ala/Pro238Ser/ His268Ala/Val309Leu/Ala330Ser/Pro331Ser	ADCC; ADCP; CDC
Leu234Ala/L235Ala/Gly237Ala/P238Ser/ His268Ala/Ala330Ser/Pro331Ser	ADCC; CDC
Ala330Leu	CDC
Asp270Ala	CDC
Lys322Ala	CDC
Pro329Ala	CDC
Pro331Ala	CDC

Val264Ala	CDC
High mannose glycosylation	CDC
Phe241Ala	CDC
Asn297Ala or Gly or Gln	ADCC; ADCP; CDC
S228P/Phe234Ala/Leu235Ala	ADCC; CDC

Natural Killer Cell Engagers

Natural Killer (NK) cells recognize and destroy tumors and virus-infected cells in an antibody-independent manner. The regulation of NK cells is mediated by activating and inhibiting receptors on the NK cell surface. One family of activating receptors is the natural cytotoxicity receptors (NCRs) which include NKp30, NKp44 and NKp46. The NCRs initiate tumor targeting by recognition of heparan sulfate on cancer cells. NKG2D is a receptor that provides both stimulatory and costimulatory innate immune responses on activated killer (NK) cells, leading to cytotoxic activity. DNAM1 is a receptor involved in intercellular adhesion, lymphocyte signaling, cytotoxicity and lymphokine secretion mediated by cytotoxic T-lymphocyte (CTL) and NK cell. DAP10 (also known as HCST) is a transmembrane adapter protein which associates with KLRK1 to form an activation receptor KLRK1-HCST in lymphoid and myeloid cells; this receptor plays a major role in triggering cytotoxicity against target cells expressing cell surface ligands such as MHC class I chain-related MICA and MICB, and U(optionally L1)6-binding proteins (ULBPs); it KLRK1-HCST receptor plays a role in immune surveillance against tumors and is required for cytolysis of tumors cells; indeed, melanoma cells that do not express KLRK1 ligands escape from immune surveillance mediated by NK cells. CD16 is a receptor for the Fc region of IgG, which binds complexed or aggregated IgG and also monomeric IgG and thereby mediates antibody-dependent cellular cytotoxicity (ADCC) and other antibody-dependent responses, such as phagocytosis.

The present disclosure provides, *inter alia*, multispecific (e.g., bi-, tri-, quad- specific) or multifunctional molecules, that are engineered to contain one or more NK cell engagers that mediate binding to and/or activation of an NK cell. Accordingly, in some embodiments, the NK

cell engager is selected from an antigen binding domain or ligand that binds to (e.g., activates): NKp30, NKp40, NKp44, NKp46, NKG2D, DNAM1, DAP10, CD16 (e.g., CD16a, CD16b, or both), CRTAM, CD27, PSGL1, CD96, CD100 (SEMA4D), NKp80, CD244 (also known as SLAMF4 or 2B4), SLAMF6, SLAMF7, KIR2DS2, KIR2DS4, KIR3DS1, KIR2DS3, KIR2DS5,
 5 KIR2DS1, CD94, NKG2C, NKG2E, or CD160.

In some embodiments, the NK cell engager is an antigen binding domain that binds to NKp30 (e.g., NKp30 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or
 10 variable region amino acid sequence disclosed in Tables 7-10. In some embodiments, the NK cell engager is an antigen binding domain that binds to NKp30 (e.g., NKp30 present, e.g., expressed or displayed, on the surface of an NK cell) and comprises any CDR amino acid sequence, framework region (FWR) amino acid sequence, or variable region amino acid sequence disclosed in U.S. Patent No. 6,979,546, U.S. Patent No. 9,447,185, PCT Application
 15 No. WO2015121383A1, PCT Application No. WO2016110468A1, PCT Application No. WO2004056392A1, or U.S. Application Publication No. US20070231322A1, the sequences of which are hereby incorporated by reference. In some embodiments, binding of the NK cell engager, e.g., antigen binding domain that binds to NKp30, to the NK cell activates the NK cell. An antigen binding domain that binds to NKp30 (e.g., NKp30 present, e.g., expressed or
 20 displayed, on the surface of an NK cell) may be said to target NKp30, the NK cell, or both.

In some embodiments, the antigen binding domain that binds to NKp30 comprises one or more CDRs (e.g., VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and/or VLCDR3) disclosed in Table 7, Table 18, or Table 8, or a sequence having at least 85%, 90%, 95%, or 99%
 25 identity thereto. In some embodiments, the antigen binding domain that binds to NKp30 comprises one or more framework regions (e.g., VHFWR1, VHFWR2, VHFWR3, VHFWR4, VLFWR1, VLFWR2, VLFWR3, and/or VLFWR4) disclosed in Table 7, Table 18, or Table 8, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto. In some embodiments, the antigen binding domain that binds to NKp30 comprises a VH and/or a VL disclosed in Table 9,

or a sequence having at least 85%, 90%, 95%, or 99% identity thereto. In some embodiments, any of the VH domains disclosed in Table 9 may be paired with any of the VL domains disclosed in Table 9 to form the antigen binding domain that binds to NKp30. In some embodiments, the antigen binding domain that binds to NKp30 comprises an amino acid sequence disclosed in
5 Table 10, or a sequence having at least 85%, 90%, 95%, or 99% identity thereto.

In some embodiments, the antigen binding domain that binds to NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1), a VHCDR2, and a VHCDR3, and a VL comprising a light chain complementarity determining region 1 (VLCDR1), a VLCDR2, and a VLCDR3.

10 In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, and 7315, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, and 6002, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some
15 embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6008, and 6009, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7385, and 7315, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the
20 VHCDR1, VHCDR2, and VHCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 7318, and 6009, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7326, 7327, and 7329, respectively (or a sequence having at least
25 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 6063, 6064, and 7293, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 6070, 6071, and 6072, respectively (or a sequence having at least 85%, 90%, 95%,

or 99% identity thereto). In some embodiments, the VLCDR1, VLCDR2, and VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 6070, 6064, and 7321, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and
 5 VLCDR3 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, 7315, 7326, 7327, and 7329, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3
 10 comprise the amino acid sequences of SEQ ID NOs: 7313, 6001, 6002, 6063, 6064, and 7293, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some
 15 embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3
 20 comprise the amino acid sequences of SEQ ID NOs: 7313, 7385, 7315, 6070, 6064, and 7321, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some
 25 embodiments, the VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2, and VLCDR3
 30 comprise the amino acid sequences of SEQ ID NOs: 7313, 7318, 6009, 6070, 6064, and 7321, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the VH comprises an amino acid sequence selected from the
 20 group consisting of SEQ ID NOs: 7298 or 7300-7304 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto) and/or the VL comprises an amino acid sequence selected from the
 25 group consisting of SEQ ID NOs: 7299 or 7305-7309 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid
 30 sequences of SEQ ID NOs: 7302 and 7305, respectively (or a sequence having at least 85%,
 35 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino
 40 acid sequences of SEQ ID NOs: 7302 and 7309, respectively (or a sequence having at least 85%,
 45 90%, 95%, or 99% identity thereto).

In some embodiments, the VH comprises an amino acid sequence selected from the
 group consisting of SEQ ID NOs: 6121 or 6123-6128 (or a sequence having at least 85%, 90%,

95%, or 99% identity thereto) and/or the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 7294 or 6137-6141 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 6122 or 6129-6134 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto) and/or the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 6136 or 6142-6147 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid sequences of SEQ ID NOs: 7295 and 7296, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid sequences of SEQ ID NOs: 7297 and 7296, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the VH and VL comprise the amino acid sequences of SEQ ID NOs: 6122 and 6136, respectively (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the antigen binding domain that binds to NKp30 comprises the amino acid sequence of SEQ ID NO: 7310 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the antigen binding domain that binds to NKp30 comprises the amino acid sequence of SEQ ID NO: 7311 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto). In some embodiments, the antigen binding domain that binds to NKp30 comprises the amino acid sequence of SEQ ID NO: 6187, 6188, 6189 or 6190 (or a sequence having at least 85%, 90%, 95%, or 99% identity thereto).

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the NKp30 antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of

SEQ ID NO: 6000, a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002.

5 In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6064 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7293 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the antigen
10 binding domain that targets NKp30 comprises a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6063, a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and a VLCDR3 amino acid sequence of SEQ ID NO: 7293.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid
15 sequence of SEQ ID NO: 6000 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and a VL comprising a light
20 chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6064 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7293 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the NKp30 antigen binding
25 domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6000, a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002, and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6063,

a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and a VLCDR3 amino acid sequence of SEQ ID NO: 7293.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid
5 sequence of SEQ ID NO: 6007 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6008 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the
10 NKp30 antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6007, a VHCDR2 amino acid sequence of SEQ ID NO: 6008, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence
15 of SEQ ID NO: 6070 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6071 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6072 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the antigen
20 binding domain that targets NKp30 comprises a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6070, a VLCDR2 amino acid sequence of SEQ ID NO: 6071, and a VLCDR3 amino acid sequence of SEQ ID NO: 6072.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid
25 sequence of SEQ ID NO: 6007 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6008 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and a VL comprising a light

chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6070 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 6071 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 6072 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions). In some embodiments, the NKp30 antigen binding domain comprises a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO: 6007, a VHCDR2 amino acid sequence of SEQ ID NO: 6008, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6009, and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO: 6070, a VLCDR2 amino acid sequence of SEQ ID NO: 6071, and a VLCDR3 amino acid sequence of SEQ ID NO: 6072.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 7292, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6006, and a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 7292, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6003 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a

VHFWR2 amino acid sequence of SEQ ID NO: 6004 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6005 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid
 5 sequence of SEQ ID NO: 6006.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6066 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6067 (or a sequence with no more than 1 mutation, e.g., substitution,
 10 addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 7292 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6003 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a
 15 VHFWR2 amino acid sequence of SEQ ID NO: 6004 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6005 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid
 20 sequence of SEQ ID NO: 6006, and a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6066 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6067 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 7292 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or
 25 deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010, a VHFWR2 amino acid sequence of SEQ ID NO: 6011, a VHFWR3 amino acid sequence of SEQ ID NO: 6012, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6073, a VLFWR2 amino acid sequence of SEQ ID NO: 6074, a VLFWR3 amino acid sequence of SEQ ID NO: 6075, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

5 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6010, a VHFWR2 amino acid sequence of SEQ ID NO: 6011, a VHFWR3 amino acid sequence of SEQ ID NO: 6012, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013, and a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 10 6073, a VLFWR2 amino acid sequence of SEQ ID NO: 6074, a VLFWR3 amino acid sequence of SEQ ID NO: 6075, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6010 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a 15 VHFWR2 amino acid sequence of SEQ ID NO: 6011 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6012 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013.

20 In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6073 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6074 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6075 (or a sequence with 25 no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6010 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a

VHFWR2 amino acid sequence of SEQ ID NO: 6011 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6012 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6013, and a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6073 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6074 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6075 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6076.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6014, a VHFWR2 amino acid sequence of SEQ ID NO: 6015, a VHFWR3 amino acid sequence of SEQ ID NO: 6016, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6017.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6014 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6015 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6016 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6017.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6077, a VLFWR2 amino acid sequence of SEQ ID NO: 6078, a VLFWR3 amino acid sequence of SEQ ID NO: 6079, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6080.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6077 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid

sequence of SEQ ID NO: 6078 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6079 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6080.

5 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6018, a VHFWR2 amino acid sequence of SEQ ID NO: 6019, a VHFWR3 amino acid sequence of SEQ ID NO: 6020, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6021.

10 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6018 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6019 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6020 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15 or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6021.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6081, a VLFWR2 amino acid sequence of SEQ ID NO: 6082, a VLFWR3 amino acid sequence of SEQ ID NO: 6083, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6084.

20 In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6081 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6082 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6083 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6084.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO:

6022, a VHFWR2 amino acid sequence of SEQ ID NO: 6023, a VHFWR3 amino acid sequence of SEQ ID NO: 6024, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6025.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6022 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a
5 VHFWR2 amino acid sequence of SEQ ID NO: 6023 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6024 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid
10 sequence of SEQ ID NO: 6025.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6085, a VLFWR2 amino acid sequence of SEQ ID NO: 6086, a VLFWR3 amino acid sequence of SEQ ID NO: 6087, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6088.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6085 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6086 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6087 (or a sequence with
20 no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6088.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6026, a VHFWR2 amino acid sequence of SEQ ID NO: 6027, a VHFWR3 amino acid sequence of SEQ ID NO: 6028, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6029.
25

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6026 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6027 (or a sequence with no more than 1, 2, 3,

4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6028 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6029.

5 In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6089, a VLFWR2 amino acid sequence of SEQ ID NO: 6090, a VLFWR3 amino acid sequence of SEQ ID NO: 6091, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6092.

10 In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6089 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6090 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6091 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid
15 sequence of SEQ ID NO: 6092.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6030, a VHFWR2 amino acid sequence of SEQ ID NO: 6032, a VHFWR3 amino acid sequence of SEQ ID NO: 6033, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6034.

20 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6030 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6032 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino
25 acid sequence of SEQ ID NO: 6033 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6034.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO:

6093, a VLFWR2 amino acid sequence of SEQ ID NO: 6094, a VLFWR3 amino acid sequence of SEQ ID NO: 6095, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6096.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6093 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6094 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6095 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6096.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6035, a VHFWR2 amino acid sequence of SEQ ID NO: 6036, a VHFWR3 amino acid sequence of SEQ ID NO: 6037, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6038.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6035 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6036 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6037 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6038.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6039, a VHFWR2 amino acid sequence of SEQ ID NO: 6040, a VHFWR3 amino acid sequence of SEQ ID NO: 6041, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6042.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6039 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6040 (or a sequence with no more than 1, 2, 3,

4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6041 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6042.

5 In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6097, a VLFWR2 amino acid sequence of SEQ ID NO: 6098, a VLFWR3 amino acid sequence of SEQ ID NO: 6099, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6100.

10 In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6097 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6098 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6099 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid
15 sequence of SEQ ID NO: 6100.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6043, a VHFWR2 amino acid sequence of SEQ ID NO: 6044, a VHFWR3 amino acid sequence of SEQ ID NO: 6045, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6046.

20 In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6043 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6044 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino
25 acid sequence of SEQ ID NO: 6045 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6046.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO:

6101, a VLFWR2 amino acid sequence of SEQ ID NO: 6102, a VLFWR3 amino acid sequence of SEQ ID NO: 6103, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6104.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6101 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6102 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6103 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6104.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6047, a VHFWR2 amino acid sequence of SEQ ID NO: 6048, a VHFWR3 amino acid sequence of SEQ ID NO: 6049, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6050.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6047 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6048 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6049 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6050.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6105, a VLFWR2 amino acid sequence of SEQ ID NO: 6106, a VLFWR3 amino acid sequence of SEQ ID NO: 6107, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6108.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6105 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6106 (or a sequence with no more than 1 mutation, e.g., substitution,

addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6107 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6108.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6051, a VHFWR2 amino acid sequence of SEQ ID NO: 6052, a VHFWR3 amino acid sequence of SEQ ID NO: 6053, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6054.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6051 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6052 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6053 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6054.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6109, a VLFWR2 amino acid sequence of SEQ ID NO: 6110, a VLFWR3 amino acid sequence of SEQ ID NO: 6111, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6112.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6109 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6110 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6111 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6112.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO:

6055, a VHFWR2 amino acid sequence of SEQ ID NO: 6056, a VHFWR3 amino acid sequence of SEQ ID NO: 6057, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6058.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6055 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a
5 VHFWR2 amino acid sequence of SEQ ID NO: 6056 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6057 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid
10 sequence of SEQ ID NO: 6058.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6113, a VLFWR2 amino acid sequence of SEQ ID NO: 6114, a VLFWR3 amino acid sequence of SEQ ID NO: 6115, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6116.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6113 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6114 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6115 (or a sequence with
20 no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6116.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6059, a VHFWR2 amino acid sequence of SEQ ID NO: 6060, a VHFWR3 amino acid sequence of SEQ ID NO: 6061, and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6062.
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In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising a VHFWR1 amino acid sequence of SEQ ID NO: 6059 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 amino acid sequence of SEQ ID NO: 6060 (or a sequence with no more than 1, 2, 3,

4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 amino acid sequence of SEQ ID NO: 6061 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 amino acid sequence of SEQ ID NO: 6062.

5 In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6117, a VLFWR2 amino acid sequence of SEQ ID NO: 6118, a VLFWR3 amino acid sequence of SEQ ID NO: 6119, and/or a VLFWR4 amino acid sequence of SEQ ID NO: 6120.

10 In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising a VLFWR1 amino acid sequence of SEQ ID NO: 6117 (or a sequence with no more than 1, 2, or 3 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 amino acid sequence of SEQ ID NO: 6118 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), a VLFWR3 amino acid sequence of SEQ ID NO: 6119 (or a sequence with no more than 1 mutation, e.g., substitution, addition, or deletion), and/or a VLFWR4 amino acid
15 sequence of SEQ ID NO: 6120.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6148 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6148). In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising
20 the amino acid sequence of SEQ ID NO: 6149 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6149). In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6150 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6150). In some embodiments, antigen
25 binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6148. In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6149. In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6150.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6148, and a VL comprising the amino acid sequence of SEQ ID NO: 6150. In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6149, and a VL comprising the amino acid sequence of SEQ ID NO: 6150.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6151 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6151). In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6152 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 6152). In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6153 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to SEQ ID NO: 6153). In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6151. In some embodiments, antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6152. In some embodiments, the antigen binding domain that targets NKp30 comprises a VL comprising the amino acid sequence of SEQ ID NO: 6153.

In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6151, and a VL comprising the amino acid sequence of SEQ ID NO: 6153. In some embodiments, the antigen binding domain that targets NKp30 comprises a VH comprising the amino acid sequence of SEQ ID NO: 6152, and a VL comprising the amino acid sequence of SEQ ID NO: 6153.

In some embodiments, the antigen binding domain that targets NKp30 comprises an scFv. In some embodiments, the scFv comprises an amino acid sequence selected from SEQ ID NOs: 6187-6190, or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity thereto.

Table 7. Exemplary heavy chain CDRs and FWRs of NKp30-targeting antigen binding domains

Ab ID	VHFWR1	VHCDR1	VHFWR2	VHCDR2	VHFWR3	VHCDR3	VHFWR4
9G1-HC	QIQLQES GPGLVKP SQSLSLTC SVTGFSIN (SEQ ID NO: 6003)	TGGYHW N (SEQ ID NO: 6000)	WIRQFPG KKLEWM G (SEQ ID NO: 6004)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	RISITRDT SKNQFFL QLNSVTT EDTATYY CAR (SEQ ID NO: 6005)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6006)
15H6-HC	QIQLQES GPGLVKP SQSLSLTC SVTGFSIN (SEQ ID NO: 6010)	TGGYHW N (SEQ ID NO: 6007)	WIRQFPG KKLEWM G (SEQ ID NO: 6011)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	RISITRDT SKNQFFL QLNSVTP EDTATYY CTR (SEQ ID NO: 6012)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VAVSS (SEQ ID NO: 6013)
9G1-HC_1	QIQLQES GPGLVKP SETLSLTC TVSGFSIN (SEQ ID NO: 6014)	TGGYHW N (SEQ ID NO: 6000)	WIRQPAG KGLEWIG (SEQ ID NO: 6015)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	RVTMSRD TSKNQFS LKLSSVT AADTAVY YCAR (SEQ ID NO: 6016)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6017)
9G1-HC_2	QIQLQES GPGLVKP SQTLSTC TVSGFSIN (SEQ ID NO: 6018)	TGGYHW N (SEQ ID NO: 6000)	WIRQHPG KGLEWIG (SEQ ID NO: 6019)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	LVTISRDT SKNQFSL KLSSVTA ADTAVYY CAR (SEQ ID NO: 6020)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6021)
9G1-HC_3	EIQLLESG GGLVQPG GSLRLSC AVSGFSIN (SEQ ID NO: 6022)	TGGYHW N (SEQ ID NO: 6000)	WVRQAP GKLEW VG (SEQ ID NO: 6023)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	RFTISRDT SKNTFY LMNSLRA EDTAVYY CAR (SEQ ID NO: 6024)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6025)
9G1-HC_4	QIQLVQS GAEVKKP GSSVKVS CKVSGFSI N (SEQ ID NO: 6026)	TGGYHW N (SEQ ID NO: 6000)	WVRQAP GQGLEW MG (SEQ ID NO: 6027)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	RVTITRDT STNTFY MELSSLRSE DTAVYYC AR (SEQ ID NO: 6028)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6029)
9G1-HC_5	EIQLVESG GGLVQPG GSLRLSC AVSGFSIN	TGGYHW N (SEQ ID NO: 6000)	WVRQAP GKLEW VG (SEQ ID NOL	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	RFTISRDT AKNSFY LMNSLRA EDTAVYY	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6034)

	(SEQ ID NO: 6030)		6032)		CAR (SEQ ID NO: 6033)		
9G1-HC_6	QIQLVQS GAEVKKP GASVKVS CKVSGFSI N (SEQ ID NO: 6035)	TGGYHW N (SEQ ID NO: 6000)	WVRQAP GQGLEW MG (SEQ ID NO: 6036)	YIYSSGST SYNPSLK S (SEQ ID NO: 6001)	RVTMTRD TSTNTFY MELSSLR SEDTAVY YCAR (SEQ ID NO: 6037)	GNWHYF DF (SEQ ID NO: 6002)	WGQGT M VTVSS (SEQ ID NO: 6038)
15H6-HC_1	QIQLQES GPGLVKP SQTLSTC TVSGFSIN (SEQ ID NO: 6039)	TGGYHW N (SEQ ID NO: 6007)	WIRQHPG KGLEWIG (SEQ ID NO: 6040)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	LVTISRDT SKNQFSL KLSSVTA ADTAVYY CAR (SEQ ID NO: 6041)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VTVSS (SEQ ID NO: 6042)
15H6-HC_2	QIQLQES GPGLVKP SETLSLTC TVSGFSIN (SEQ ID NO: 6043)	TGGYHW N (SEQ ID NO: 6007)	WIRQPAG KGLEWIG (SEQ ID NO: 6044)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	RVTMSRD TSKNQFS LKLSSVT AADTAVY YCAR (SEQ ID NO: 6045)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VTVSS (SEQ ID NO: 6046)
15H6-HC_3	EIQLLES GGGLVQPG GSLRLSC AVSGFSIN (SEQ ID NO: 6047)	TGGYHW N (SEQ ID NO: 6007)	WVRQAP GKGLEW VG (SEQ ID NO: 6048)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	RFTISRDT SKNTFY L QMNSLRA EDTAVYY CAR (SEQ ID NO: 6049)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VTVSS (SEQ ID NO: 6050)
15H6-HC_4	QIQLVES GGGLVKP GGSLRLS CAVSGFSI N (SEQ ID NO: 6051)	TGGYHW N (SEQ ID NO: 6007)	WIRQAPG KGLEWV G (SEQ ID NO: 6052)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	RFTISRDT AKNSFY L QMNSLRA EDTAVYY CAR (SEQ ID NO: 6053)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VTVSS (SEQ ID NO: 6054)
15H6-HC_5	QIQLVQS GAEVKKP GASVKVS CKVSGFSI N (SEQ ID NO: 6055)	TGGYHW N (SEQ ID NO: 6007)	WVRQAP GQGLEW MG (SEQ ID NO: 6056)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	RVTMTRD TSTNTFY MELSSLR SEDTAVY YCAR (SEQ ID NO: 6057)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VTVSS (SEQ ID NO: 6058)
15H6-HC_6	EIQLVQS GAEVKKP GATVKIS CKVSGFSI N (SEQ ID NO: 6059)	TGGYHW N (SEQ ID NO: 6007)	WVQAP GKGLEW MG (SEQ ID NO: 6060)	YIYSSGTT RYNPSLK S (SEQ ID NO: 6008)	RVTITRDT STNTFY M ELSSLRSE DTAVYYC AR (SEQ ID NO: 6062)	GNWHYF DY (SEQ ID NO: 6009)	WGQGT L VTVSS (SEQ ID NO: 6062)

					6061)		

Table 18. Exemplary heavy chain CDRs and FWRs of NKp30-targeting antigen binding domains (according to the Kabat numbering scheme)

Ab ID	VHFWR1	VHCDR1	VHFWR2	VHCDR2	VHFWR3	VHCDR3	VHFWR4
9G1-HC	QIQLQESG PGLVKPSQ SLSLTCSV TGFSINTG (SEQ ID NO: 7317)	GYHWN (SEQ ID NO: 7313)	WIRQFPGK KLEWMG (SEQ ID NO: 6004)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RISITRDT SKNQFFLQ LNSVTIED TATYYCAR (SEQ ID NO: 6005)	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMTV VSS (SEQ ID NO: 6006)
15H6-HC	QIQLQESG PGLVKPSQ SLSLTCSV TGFSINTG (SEQ ID NO: 7317)	GYHWN (SEQ ID NO: 7313)	WIRQFPGK KLEWMG (SEQ ID NO: 6011)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	RISITRDT SKNQFFLQ LNSVTPED TATYYCTR (SEQ ID NO: 6012)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTMLV VSS (SEQ ID NO: 6013)
9G1-HC_1	QIQLQESG PGLVKPSE TLSLTCTV SGFSINTG (SEQ ID NO: 7371)	GYHWN (SEQ ID NO: 7313)	WIRQPAGK GLEWIG (SEQ ID NO: 6015)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RVTMSRDT SKNQFSLK LSSVTAAD TAVYYCAR (SEQ ID NO: 6016)	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMTV VSS (SEQ ID NO: 6017)
9G1-HC_2	QIQLQESG PGLVKPSQ TLSLTCTV SGFSINTG (SEQ ID NO: 7372)	GYHWN (SEQ ID NO: 7313)	WIRQHPGK GLEWIG (SEQ ID NO: 6019)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	LVTISRDT SKNQFSLK LSSVTAAD TAVYYCAR (SEQ ID NO: 6020)	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMTV VSS (SEQ ID NO: 6021)
9G1-HC_3	EIQLLESG GGLVQPGG SLRLSCAV SGFSINTG (SEQ ID NO: 7373)	GYHWN (SEQ ID NO: 7313)	WVRQAPGK GLEWVG (SEQ ID NO: 6023)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RFTISRDT SKNTFYLLQ MNSLRAED TAVYYCAR (SEQ ID NO: 6024)	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMTV VSS (SEQ ID NO: 6025)
9G1-HC_4	QIQLVQSG AEVKKPGS SVKVSCKV SGFSINTG (SEQ ID NO: 7374)	GYHWN (SEQ ID NO: 7313)	WVRQAPGQ GLEWMG (SEQ ID NO: 6027)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RVITRDT STNTFYME LSSLRSED TAVYYCAR (SEQ ID NO: 6028)	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMTV VSS (SEQ ID NO: 6029)
9G1-HC_5	EIQLVESG GGLVQPGG	GYHWN (SEQ ID	WVRQAPGK GLEWVG	YIYSSGST SYNPSLKS	RFTISRDT AKNSFYLLQ	GNWHYFDF (SEQ ID	WGQGTMTV VSS (SEQ

	SLRLSCAV SGFSINTG (SEQ ID NO: 7375)	NO: 7313)	(SEQ ID NOL 6032)	(SEQ ID NO: 6001)	MNSLRAED TAVYYCAR (SEQ ID NO: 6033)	NO: 6002)	ID NO: 6034)
9G1-HC_6	QIQLVQSG AEVKKPGA SVKVSCKV SGFSINTG (SEQ ID NO: 7376)	GYHWN (SEQ ID NO: 7313)	WVRQAPGQ GLEWMG (SEQ ID NO: 6036)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RVTMTRDT STNTFYME LSSLRSED TAVYYCAR (SEQ ID NO: 6037)	GNWHYFDF (SEQ ID NO: 6002)	WGQGTMTVT VSS (SEQ ID NO: 6038)
15H6-HC_1	QIQLQESG PGLVKPSQ TLSLTCTV SGFSINTG (SEQ ID NO: 7372)	GYHWN (SEQ ID NO: 7313)	WIRQHPGK GLEWIG (SEQ ID NO: 6040)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	LVTISRDT SKNQFSLK LSSVTAAD TAVYYCAR (SEQ ID NO: 6041)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTTLVT VSS (SEQ ID NO: 6042)
15H6-HC_2	QIQLQESG PGLVKPSE TLSLTCTV SGFSINTG (SEQ ID NO: 7371)	GYHWN (SEQ ID NO: 7313)	WIRQPAGK GLEWIG (SEQ ID NO: 6044)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	RVTMSRDT SKNQFSLK LSSVTAAD TAVYYCAR (SEQ ID NO: 6045)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTTLVT VSS (SEQ ID NO: 6046)
15H6-HC_3	EIQLLESG GGLVQPGG SLRLSCAV SGFSINTG (SEQ ID NO: 7373)	GYHWN (SEQ ID NO: 7313)	WVRQAPGK GLEWVG (SEQ ID NO: 6048)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	RFTISRDT SKNTFYLQ MNSLRAED TAVYYCAR (SEQ ID NO: 6049)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTTLVT VSS (SEQ ID NO: 6050)
15H6-HC_4	QIQLVESG GGLVKPGG SLRLSCAV SGFSINTG (SEQ ID NO: 7377)	GYHWN (SEQ ID NO: 7313)	WIRQAPGK GLEWVG (SEQ ID NO: 6052)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	RFTISRDT AKNSFYLQ MNSLRAED TAVYYCAR (SEQ ID NO: 6053)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTTLVT VSS (SEQ ID NO: 6054)
15H6-HC_5	QIQLVQSG AEVKKPGA SVKVSCKV SGFSINTG (SEQ ID NO: 7376)	GYHWN (SEQ ID NO: 7313)	WVRQAPGQ GLEWMG (SEQ ID NO: 6056)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	RVTMTRDT STNTFYME LSSLRSED TAVYYCAR (SEQ ID NO: 6057)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTTLVT VSS (SEQ ID NO: 6058)
15H6-HC_6	EIQLVQSG AEVKKPGA TVKISCKV SGFSINTG (SEQ ID	GYHWN (SEQ ID NO: 7313)	WVQQAPGK GLEWMG (SEQ ID NO: 6060)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	RVTITRDT STNTFYME LSSLRSED TAVYYCAR (SEQ ID	GNWHYFDY (SEQ ID NO: 6009)	WGQGTTLVT VSS (SEQ ID NO: 6062)

	NO: 7378)				NO: 6061)		
9D9-HC	QIQIQESG PGLVKPSQ SLSLSCSV TGFSINTG (SEQ ID NO: 7312)	GYHWN (SEQ ID NO: 7313)	WIRQFPGK KVEWMG (SEQ ID NO: 7314)	YIYSSGTT KYNPSLKS (SEQ ID NO: 7385)	RISITRDT SKNQFFLQ LNSVTTED TATYYCAR (SEQ ID NO: 6005)	GDWHYFDY (SEQ ID NO: 7315)	WGQGTMTVA VSS (SEQ ID NO: 7316)
3A12-HC	QIQIQESG PGLVKPSQ SLSLTCSV TGFSINTG (SEQ ID NO: 7317)	GYHWN (SEQ ID NO: 7313)	WIRQFPGK KLEWMG (SEQ ID NO: 6004)	YIYSSGST RYNPSLKS (SEQ ID NO: 7318)	RFSITRDT SKNQFFLQ LNSVTTED TATYYCTR (SEQ ID NO: 7319)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTMTVA VSS (SEQ ID NO: 6013)
12D10-HC	QIQIQESG PGLVKPSQ SLSLTCSV TGFSINTG (SEQ ID NO: 7317)	GYHWN (SEQ ID NO: 7313)	WIRQFPGK KLEWMG (SEQ ID NO: 6004)	YIYSSGTT RYNPSLKS (SEQ ID NO: 6008)	RISITRDT SKNQFFLQ LNSVTPED TATYYCTR (SEQ ID NO: 6012)	GNWHYFDY (SEQ ID NO: 6009)	WGQGTMTVA VSS (SEQ ID NO: 6013)
15E1-HC	QIQIQESG PGLVKPSQ SLSLSCSV TGFSITTT (SEQ ID NO: 7322)	GYHWN (SEQ ID NO: 7313)	WIRQFPGK KLEWMG (SEQ ID NO: 6004)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RFSITRDT SKNQFFLQ LNSVTTED TATYYCAR (SEQ ID NO: 7323)	GDWHYFDY (SEQ ID NO: 7315)	WGPMTMT VSS (SEQ ID NO: 7324)
15E1_Hum anized variant_VH 1	QIQIQESG PGLVKPSQ TLSLTCTV SGFSITTT (SEQ ID NO: 7330)	GYHWN (SEQ ID NO: 7313)	WIRQHPGK GLEWIG (SEQ ID NO: 6019)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	LVTISRDT SKNQFSLK LSSVTAAD TAVYYCAR (SEQ ID NO: 6020)	GDWHYFDY (SEQ ID NO: 7315)	WGQGTMT VSS (SEQ ID NO: 6006)
15E1_Hum anized variant_VH 2	QIQLVESG GGLVKPGG SLRLSCAV SGFSITTT (SEQ ID NO: 7331)	GYHWN (SEQ ID NO: 7313)	WIRQAPGK GLEWVG (SEQ ID NO: 6052)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RFTISRDT AKNSFYLO MNSLRAED TAVYYCAR (SEQ ID NO: 6033)	GDWHYFDY (SEQ ID NO: 7315)	WGQGTMT VSS (SEQ ID NO: 6006)
15E1_Hum anized variant_VH 3	EIQLLVSG GGLVQPGG SLRLSCAV SGFSITTT (SEQ ID NO: 7332)	GYHWN (SEQ ID NO: 7313)	WVRQAPGK GLEWVG (SEQ ID NO: 6023)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RFTISRDT SKNTFYLO MNSLRAED TAVYYCAR (SEQ ID NO: 6024)	GDWHYFDY (SEQ ID NO: 7315)	WGQGTMT VSS (SEQ ID NO: 6006)
15E1_Hum	EIQLVESG	GYHWN	WVRQAPGK	YIYSSGST	RFTISRDT	GDWHYFDY	WGQGTMT

anized variant_VH 4	GGLVQPGG SLRLSCAV SGFSITTT (SEQ ID NO: 7333)	(SEQ ID NO: 7313)	GLEWVG (SEQ ID NO: 6023)	SYNPSLKS (SEQ ID NO: 6001)	AKNSFYLQ MNSLRAED TAVYYCAR (SEQ ID NO: 6033)	(SEQ ID NO: 7315)	VSS (SEQ ID NO: 6006)
15E1_Hum anized variant_VH 5	QIQLVQSG AEVKKPGA SVKVSCKV SGFSITTT (SEQ ID NO: 7334)	GYHWN (SEQ ID NO: 7313)	WVRQAPGQ GLEWMG (SEQ ID NO: 6027)	YIYSSGST SYNPSLKS (SEQ ID NO: 6001)	RVTMTRDT STNTFYME LSSLRSED TAVYYCAR (SEQ ID NO: 6037)	GDWHYFDY (SEQ ID NO: 7315)	WGQGTMTV VSS (SEQ ID NO: 6006)

Table 8. Exemplary light chain CDRs and FWRs of NKp30-targeting antigen binding domains

Ab ID	VLFWR1	VLCDR1	VLFWR2	VLCDR2	VLFWR3	VLCDR3	VLFWR4
9G1-LC	SYTLTQPP LLSVALG HKATITC (SEQ ID NO: 6066)	SGERLSD KYVH (SEQ ID NO: 6063)	WYQQKP GRAPVM VIY (SEQ ID NO: 6067)	ENDKRPS (SEQ ID NO: 6064)	GIPDQFSG SNSGNIAT LTISKAQ AGYEADY YC (SEQ ID NO: 7292)	QSWDSTN SAV (SEQ ID NO: 7293)	FGSGTQL TVL (SEQ ID NO: 6069)
15H6-LC	SYTLTQPP SLSVAPG QKATIIC (SEQ ID NO: 6073)	SGENLSD KYVH (SEQ ID NO: 6070)	WYQQKP GRAPVM VIY (SEQ ID NO: 6074)	ENEKRPS (SEQ ID NO: 6071)	GIPDQFSG SNSGNIAT LTISKAQP GSEADYYC (SEQ ID NO: 6075)	HYWESIN SVV (SEQ ID NO: 6072)	FGSGTHL TVL (SEQ ID NO: 6076)
9G1-LC_1	QSVTTQP PSVSGAP GQRTVIS C (SEQ ID NO: 6077)	SGERLSD KYVH (SEQ ID NO: 6063)	WYQQLP GTAPKML IY (SEQ ID NO: 6078)	ENDKRPS (SEQ ID NO: 6064)	GVPDRFS GSNSGNS ASLAITGL QAEDEAD YYC (SEQ ID NO: 6079)	QSWDSTN SAV (SEQ ID NO: 7293)	FGGGTQL TVL (SEQ ID NO: 6080)
9G1-LC_2	QSVTTQP PSASGTP GQRTVIS C (SEQ ID NO: 6081)	SGERLSD KYVH (SEQ ID NO: 6063)	WYQQLP GTAPKML IY (SEQ ID NO: 6082)	ENDKRPS (SEQ ID NO: 6064)	GVPDRFS GSNSGNS ASLAISGL QSEDEAD YYC (SEQ ID NO: 6083)	QSWDSTN SAV (SEQ ID NO: 7293)	FGGGTQL TVL (SEQ ID NO: 6084)
9G1-LC_3	QSVTTQP PSASGTP GQRTVIS C (SEQ ID NO: 6085)	SGERLSD KYVH (SEQ ID NO: 6063)	WYQQLP GTAPKML IY (SEQ ID NO: 6086)	ENDKRPS (SEQ ID NO: 6064)	GVPDRFS GSNSGNS ASLAISGL RSEDEAD YYC (SEQ	QSWDSTN SAV (SEQ ID NO: 7293)	FGGGTQL TVL (SEQ ID NO: 6088)

					ID NO: 6087)		
9G1-LC_4	SSETTQPH SVSVATA QMARITC (SEQ ID NO: 6089)	SGERLSD KYVH (SEQ ID NO: 6063)	WYQQKP GQDPVM VIY (SEQ ID NO: 6090)	ENDKRPS (SEQ ID NO: 6064)	GIPERFSG SNPGNTA TLTISRIE AGDEADY YC (SEQ ID NO: 6091)	QSWDSTN SAV (SEQ ID NO: 7293)	FGGGTQL TVL (SEQ ID NO: 6092)
9G1-LC_5	DIQMTQS PSTLSASV GDRVTIT C (SEQ ID NO: 6093)	SGERLSD KYVH (SEQ ID NO: 6063)	WYQQKP GKAPKML IY (SEQ ID NO: 6094)	ENDKRPS (SEQ ID NO: 6064)	GVPSRFS GSNSGNE ATLTISSL QPDDFAT YYC (SEQ ID NO: 6095)	QSWDSTN SAV (SEQ ID NO: 7293)	FGQGTVK EIK (SEQ ID NO: 6096)
15H6-LC_1	QYVLTQP PSASGTP GQRTVIS C (SEQ ID NO: 6097)	SGENLSD KYVH (SEQ ID NO: 6070)	WYQQLP GTAPKML IY (SEQ ID NO: 6098)	ENEKRPS (SEQ ID NO: 6071)	GVPDRFS GSNSGNS ASLAISGL QSEDEAD YYC (SEQ ID NO: 6099)	HYWESIN SVV (SEQ ID NO: 6072)	FGGTEL TVL (SEQ ID NO: 6100)
15H6-LC_2	QYVLTQP PSASGTP GQRTVIS C (SEQ ID NO: 6101)	SGENLSD KYVH (SEQ ID NO: 6070)	WYQQLP GTAPKML IY (SEQ ID NO: 6102)	ENEKRPS (SEQ ID NO: 6071)	GVPDRFS GSNSGNS ASLAISGL RSEDEAD YYC (SEQ ID NO: 6103)	HYWESIN SVV (SEQ ID NO: 6072)	FGGTEL TVL (SEQ ID NO: 6104)
15H6-LC_3	SYELTQPP SVSVSPG QTASITC (SEQ ID NO: 6105)	SGENLSD KYVH (SEQ ID NO: 6070)	WYQQKP GQSPVMV IY (SEQ ID NO: 6106)	ENEKRPS (SEQ ID NO: 6071)	GIPERFSG SNSGNTA TLTISGTQ AMDEAD YYC (SEQ ID NO: 6107)	HYWESIN SVV (SEQ ID NO: 6072)	FGGTEL TVL (SEQ ID NO: 6108)
15H6-LC_4	DYVLTQS PLSLPVT GEPASISC (SEQ ID NO: 6109)	SGENLSD KYVH (SEQ ID NO: 6070)	WYLQKP GQSPQML IY (SEQ ID NO: 6110)	ENEKRPS (SEQ ID NO: 6071)	GVPDRFS GSNSGND ATLKISRV EAEDVGV YYC (SEQ ID NO: 6111)	HYWESIN SVV (SEQ ID NO: 6072)	FGQGTVK EIK (SEQ ID NO: 6112)
15H6-LC_5	AYQLTQS PSSLSASV GDRVTIT C (SEQ ID NO: 6113)	SGENLSD KYVH (SEQ ID NO: 6070)	WYQQKP GKAPKML IY (SEQ ID NO: 6114)	ENEKRPS (SEQ ID NO: 6071)	GVPSRFS GSNSGND ATLTISSL QPEDFAT YYC (SEQ ID NO: 6115)	HYWESIN SVV (SEQ ID NO: 6072)	FGQGTVK EIK (SEQ ID NO: 6116)

15H6-LC_6	EYVLTQS PATLSVSP GERATLS C (SEQ ID NO: 6117)	SGENLSD KYVH (SEQ ID NO: 6070)	WYQQKP GQAPRML IY (SEQ ID NO: 6118)	ENEKRPS (SEQ ID NO: 6071)	GIPARFSG SNSGNEA TLTISSLQ SEDFAVY YC (SEQ ID NO: 6119)	HYWESIN SVV (SEQ ID NO: 6072)	FGQGTKV EIK (SEQ ID NO: 6120)
9D9-LC	SYTLTQPP LVSVALG QKATIIC (SEQ ID NO: 7320)	SGENLSD KYVH (SEQ ID NO: 6070)	WYQQKP GRAPVM VIY (SEQ ID NO: 6067)	ENDKRPS (SEQ ID NO: 6064)	GIPDQFSG SNSGNIAT LTISKAQ AGYEADY YC (SEQ ID NO: 7292)	HCWDSTN SAV (SEQ ID NO: 7321)	FGSGTHL TVL (SEQ ID NO: 6076)
3A12-LC	SYTLTQPP LVSVALG QKATIIC (SEQ ID NO: 7320)	SGENLSD KYVH (SEQ ID NO: 6070)	WYQQKP GRAPVM VIY (SEQ ID NO: 6067)	ENDKRPS (SEQ ID NO: 6064)	GIPDQFSG SNSGNIAT LTISKAQ AGYEADY YC (SEQ ID NO: 7292)	HCWDSTN SAV (SEQ ID NO: 7321)	FGSGTHL TVL (SEQ ID NO: 6076)
12D10-LC	SYTLTQPP SLSVAPG QKATIIC (SEQ ID NO: 6073)	SGENLSD KYVH (SEQ ID NO: 6070)	WYQQKP GRAPVM VIY (SEQ ID NO: 6074)	ENEKRPS (SEQ ID NO: 6071)	GIPDQFSG SNSGNIAT LTISKAQP GSEADYY C (SEQ ID NO: 6075)	HYWESIN SVV (SEQ ID NO: 6072)	FGSGTHL TVL (SEQ ID NO: 6076)
15E1-LC	SFTLTQPP LVSVAVG QVATITC (SEQ ID NO: 7325)	SGEKLSD KYVH (SEQ ID NO: 7326)	WYQQKP GRAPVM VIY (SEQ ID NO: 6067)	ENDRRPS (SEQ ID NO: 7327)	GIPDQFSG SNSGNIAS LTISKAQ AGDEADY FC (SEQ ID NO: 7328)	QFWDSTN SAV (SEQ ID NO: 7329)	FGGGTQL TVL (SEQ ID NO: 6080)
15E1_Hum anized variant_VL 1	SSETTQPP SVSVSPG QTASITC (SEQ ID NO: 7335)	SGEKLSD KYVH (SEQ ID NO: 7326)	WYQQKP GQSPVMV IY (SEQ ID NO: 6106)	ENDRRPS (SEQ ID NO: 7327)	GIPERFSG SNSGNTA TLTISGTQ AMDEAD YFC (SEQ ID NO: 7336)	QFWDSTN SAV (SEQ ID NO: 7329)	FGGGTQL TVL (SEQ ID NO: 6080)
15E1_Hum anized variant_VL 2	SSETTQPH SVSVATA QMARITC (SEQ ID NO: 6089)	SGEKLSD KYVH (SEQ ID NO: 7326)	WYQQKP GQDPVM VIY (SEQ ID NO: 6090)	ENDRRPS (SEQ ID NO: 7327)	GIPERFSG SNPGNTA TLTISRIE AGDEADY FC (SEQ ID NO: 7337)	QFWDSTN SAV (SEQ ID NO: 7329)	FGGGTQL TVL (SEQ ID NO: 6080)
15E1_Hum anized variant_VL	QSVTTQP PSASGTP GQRVITIS	SGEKLSD KYVH (SEQ ID	WYQQLP GTAPKML IY (SEQ ID	ENDRRPS (SEQ ID NO: 7327)	GVPDRFS GSNSGNS ASLAISGL	QFWDSTN SAV (SEQ ID NO:	FGGGTQL TVL (SEQ ID NO:

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
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NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

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NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

We claim:

1. A multifunctional molecule comprising:

(i) a first antigen binding domain that binds to a calreticulin protein (e.g., a wild-type or
5 mutant calreticulin protein),

and

(ii) a second antigen binding domain that binds to TCR β V, e.g., an anti-TCR β V antigen
binding domain disclosed in any one of Table 1A, Table 2A, Table 3A, Table 10A, Table 11A,
Table 12A, or Table 13A, or

10 a second antigen binding domain that binds to NKp30, e.g., an anti-NKp30 antigen
binding domain disclosed in Tables 7-10 or 18.

2. The multifunctional molecule of claim 1, wherein the second antigen binding domain
binds to TCR β V.

15 3. The multifunctional molecule of claim 2, wherein the second antigen binding domain
activates a T cell or the second antigen binding domain does not activate a T cell.

4. The multifunctional molecule of claim 2 or 3, wherein the second antigen binding
20 domain binds to TCR β V12 or TCR β V6 (e.g., comprising the amino acid sequence of SEQ ID
NO: 1044).

5. The multifunctional molecule of any of claims 2-4, wherein the second antigen
binding domain comprises one or more amino acid sequences as listed in Table 1A, Table 2A,
25 Table 3A, Table 10A, Table 11A, Table 12A, or Table 13A.

6. The multifunctional molecule of any of claims 2-5, wherein the second antigen
binding domain comprises:

(a) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises a heavy chain complementarity determining region 1 (VHCDR1) having an amino acid sequence of a VHCDR1 in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 having an amino acid sequence of a VHCDR2 in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 having an amino acid sequence of a VHCDR3 in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions),

(ii) the VL comprises a light chain complementarity determining region 1 (VLCDR1) having an amino acid sequence of a VLCDR1 in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 having an amino acid sequence of a VLCDR2 in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 having an amino acid sequence of a VLCDR3 in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions);

(b) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 3 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 4 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID

NO: 5 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or

(ii) the VL comprises a light chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 7 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 8 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions);

(c) a heavy chain variable region (VH) and/or a light chain variable region (VL), wherein:

(i) the VH comprises a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 45 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 46 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 47 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or

(ii) the VL comprises a light chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 51 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 52 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 53 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions); and/or

(d) a heavy chain variable region (VH) and/or a light chain variable region (VL), wherein:

(i) the VH comprises a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 48 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 49 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 50 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or

(ii) the VL comprises a light chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 54 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 55 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 56 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

7. The multifunctional molecule of any of claims 2-5, wherein the second antigen binding domain comprises:

(a) a heavy chain variable region (VH) and/or a light chain variable region (VL), wherein:

(i) the VH comprises the amino acid sequence of a VH in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and/or

(ii) the VL comprises the amino acid sequence of a VL in Table 1A, Table 2A, Table 10A, Table 11A, Table 12A, or Table 13A (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto)

(iii) the VH comprises the amino acid sequence of SEQ ID NO: 9 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and/or

(iv) the VL comprises the amino acid sequence of SEQ ID NO: 10 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto);

5 (b) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises the amino acid sequence of SEQ ID NO: 9 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and/or

10 (ii) the VL comprises the amino acid sequence of SEQ ID NO: 11 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto); and/or

15 (c) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises the amino acid sequence of SEQ ID NO: 1312 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and/or

20 (ii) the VL comprises the amino acid sequence of SEQ ID NO: 1314 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto).

8. The multifunctional molecule of any of claims 2-5, wherein the second antigen binding domain comprises:

25 (a) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 17 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid

sequence of SEQ ID NO: 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 19 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or

5 (ii) the VL comprises a light chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 20 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 21 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of
10 SEQ ID NO: 22 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions);

(b) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

15 (i) the VH comprises a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 57 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 58 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of
20 SEQ ID NO: 59 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or

(ii) the VL comprises a light chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 63 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid
25 sequence of SEQ ID NO: 64 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 65 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions); and/or

(c) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 60 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 61 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 62 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or

(ii) the VL comprises a light chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 66 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 67 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of SEQ ID NO: 68 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

9. The multifunctional molecule of any of claims 2-5, wherein the second antigen binding domain comprises:

(a) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises the amino acid sequence of SEQ ID NO: 15 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and/or

(ii) the VL comprises the amino acid sequence of SEQ ID NO: 16 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto); and/or

(b) a heavy chain variable region (VH) and/or a light chain variable region (VL),
wherein:

(i) the VH comprises:

the amino acid sequence of SEQ ID NO: 23 (or an amino acid sequence
having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity
thereto),

the amino acid sequence of SEQ ID NO: 24 (or an amino acid sequence
having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity
thereto), or

the amino acid sequence of SEQ ID NO: 25 (or an amino acid sequence
having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity
thereto); and/or

(ii) the VL comprises:

the amino acid sequence of SEQ ID NO: 26 (or an amino acid sequence
having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity
thereto),

the amino acid sequence of SEQ ID NO: 27 (or an amino acid sequence
having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity
thereto),

the amino acid sequence of SEQ ID NO: 28 (or an amino acid sequence
having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity
thereto),

the amino acid sequence of SEQ ID NO: 29 (or an amino acid sequence
having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity
thereto), or

the amino acid sequence of SEQ ID NO: 30 (or an amino acid sequence
having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity
thereto).

10. The multifunctional molecule of any of claims 2-9, comprising:

a first polypeptide comprising, e.g., from N-terminus to C-terminus, a first VL and a first CL,

5 a second polypeptide comprising, e.g., from N-terminus to C-terminus, a first VH, a first CH1, a first dimerization domain (e.g., a first Fc), and a first moiety that binds to TCR (e.g., TCRV β) (e.g., a first scFv that binds to TCR (e.g., TCRV β)),

a third polypeptide comprising, e.g., from N-terminus to C-terminus, a second VH, a second CH1, a second dimerization domain (e.g., a second Fc), and optionally a second moiety that binds to TCR (e.g., TCRV β) (e.g., a second scFv that binds to TCR (e.g., TCRV β)),

10 a fourth polypeptide comprising, e.g., from N-terminus to C-terminus, a second VL and a second CL,

wherein:

the first VL and the first VH form a first antigen binding domain that binds to a first calreticulin protein, and the second VL and the second VH form a third antigen binding domain
15 that binds to a second calreticulin protein,

optionally wherein the first and second calreticulin proteins comprise the amino acid sequence of SEQ ID NO: 6285 or 6286,

optionally wherein the first and second calreticulin mutant proteins are each independently chosen from: a molecule comprising the amino acid sequence of SEQ ID NO:
20 6313, or a molecule comprising the amino acid sequence of SEQ ID NO: 6314,

optionally wherein the multifunctional molecule comprises the configuration of FIG. 3A or 3B.

11. The multifunctional molecule of claim 1, wherein the second antigen binding domain
25 binds to NKp30.

12. The multifunctional molecule of claim 11, wherein the second antigen binding domain is chosen from an antibody molecule, e.g., an antigen binding domain, or ligand that

binds to (e.g., activates) NKp30, e.g., the second antigen binding domain is an antibody molecule or ligand that binds to (e.g., activates) NKp30.

13. The multifunctional molecule of claim 11 or 12, wherein the second antigen binding domain comprises:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) having an amino acid sequence of a VHCDR1 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 having an amino acid sequence of a VHCDR2 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 having an amino acid sequence of a VHCDR3 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or

(ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) having an amino acid sequence of a VLCDR1 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 having an amino acid sequence of a VLCDR2 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 having an amino acid sequence of a VLCDR3 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

14. The multifunctional molecule of claim 13, wherein the second antigen binding domain comprises:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 7313 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 amino acid sequence of SEQ ID NO: 6001 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 amino acid sequence of

SEQ ID NO: 7315 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions; and/or

(ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 7326 (or a sequence with
 5 no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 amino acid sequence of SEQ ID NO: 7327 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7329 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions).

10

15. The multifunctional molecule of claim 13 or 14, wherein the second antigen binding domain comprises:

(i) a VH comprising the amino acid sequence of any of SEQ ID NOs: 7298 or 7300-7304 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence
 15 identity to any of SEQ ID NOs: 7298 or 7300-7304); and/or

(ii) a VL comprising the amino acid sequence of any of SEQ ID NOs: 7299 or 7305-7309 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity to any of SEQ ID NOs: 7299 or 7305-7309).

20 16. The multifunctional molecule of any of claims 13-15, wherein the second antigen binding domain comprises:

(i) a VH comprising the amino acid sequence of SEQ ID NO: 7302 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7302), and a VL comprising the amino acid sequence of SEQ ID NO: 7305 (or an amino acid sequence
 25 having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7305); or

(ii) a VH comprising the amino acid sequence of SEQ ID NO: 7302 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7302), and a VL comprising the amino acid sequence of SEQ ID NO: 7309 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7309).

17. The multifunctional molecule of any of claims 13-16, wherein the second antigen binding domain comprises:

- (i) an amino acid sequence of SEQ ID NO: 7310 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7310); or
- (ii) an amino acid sequence of SEQ ID NO: 7311 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to 7311).

18. The multifunctional molecule of claim 11 or 12, wherein the second antigen binding domain comprises:

- (i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) amino acid sequence of SEQ ID NO: 6000, a VHCDR2 amino acid sequence of SEQ ID NO: 6001, and/or a VHCDR3 amino acid sequence of SEQ ID NO: 6002, and
- (ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VLCDR1) amino acid sequence of SEQ ID NO: 6063, a VLCDR2 amino acid sequence of SEQ ID NO: 6064, and/or a VLCDR3 amino acid sequence of SEQ ID NO: 7293.

19. The multifunctional molecule of any of claims 11, 12, or 18, wherein the second antigen binding domain comprises:

- (1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) having an amino acid sequence of a VHFWR1 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR2 having an amino acid sequence of a VHFWR2 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VHFWR3 having an amino acid sequence of a VHFWR3 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a

VHFWR4 having an amino acid sequence of a VHFWR4 of Table 7, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), and/or

(2) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) having an amino acid sequence of a VLFWR1 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR2 having an amino acid sequence of a VLFWR2 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), a VLFWR3 having an amino acid sequence of a VLFWR3 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom), or a VLFWR4 having an amino acid sequence of a VLFWR4 of Table 8, Table 9, Table 10, or Table 18 (or a sequence with no more than 1, 2, 3, 4, 5, or 6 mutations, e.g., substitutions, additions, or deletions, therefrom).

15

20. The multifunctional molecule of claim 19, wherein the second antigen binding domain comprises:

(1) a heavy chain variable region (VH) comprising a heavy chain framework region 1 (VHFWR1) amino acid sequence of SEQ ID NO: 6003, a VHFWR2 amino acid sequence of SEQ ID NO: 6004, a VHFWR3 amino acid sequence of SEQ ID NO: 6005, or a VHFWR4 amino acid sequence of SEQ ID NO: 6006, and

(3) a light chain variable region (VL) comprising a light chain framework region 1 (VLFWR1) amino acid sequence of SEQ ID NO: 6066, a VLFWR2 amino acid sequence of SEQ ID NO: 6067, a VLFWR3 amino acid sequence of SEQ ID NO: 7292, or a VLFWR4 amino acid sequence of SEQ ID NO: 6069.

25

21. The multifunctional molecule of any one of claims 11, 12, or 18-20, wherein the second antigen binding domain comprises:

(i) a VH comprising the amino acid sequence of a VH of Table 7, Table 9, Table 10, or Table 18 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and/or

5 (ii) a VL comprising the amino acid sequence of a VL of Table 8, Table 9, Table 10, or Table 18 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity thereto).

22. The multifunctional molecule of either of claims 11, 12, or 18-21, wherein the second antigen binding domain comprises a heavy chain comprising the amino acid sequence of a heavy
10 chain of Table 10 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto).

23. The multifunctional molecule of either of claims 11, 12, or 18-22, wherein the second antigen binding domain comprises a light chain comprising the amino acid sequence of a light
15 chain of Table 10 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto).

24. The multifunctional molecule of either of claims 11, 12, or 18-23, wherein the second antigen binding domain comprises a heavy chain comprising the amino acid sequence of a heavy
20 chain of Table 10 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto), and a light chain comprising the amino acid sequence of a light chain of Table 10 (or an amino acid sequence having at least about 75%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto).

25. The multifunctional molecule of any of claims 11-24, comprising:
a first polypeptide comprising, e.g., from N-terminus to C-terminus, a first VL and a first
CL,

a second polypeptide comprising, e.g., from N-terminus to C-terminus, a first VH, a first CH1, a first dimerization domain (e.g., a first Fc), and a first moiety that binds to NKp30 (e.g., a first antibody molecule or ligand that binds to NKp30),

5 a third polypeptide comprising, e.g., from N-terminus to C-terminus, a second VH, a second CH1, a second dimerization domain (e.g., a second Fc), and optionally a second moiety that binds to NKp30 (e.g., a second antibody molecule or ligand that binds to NKp30),

a fourth polypeptide comprising, e.g., from N-terminus to C-terminus, a second VL and a second CL,

wherein:

10 the first VL and the first VH form a first antigen binding domain that binds to a first calreticulin protein, and the second VL and the second VH form a third antigen binding domain that binds to a second calreticulin protein,

optionally wherein the first and second calreticulin proteins comprise the amino acid sequence of SEQ ID NO: 6285 or 6286,

15 optionally wherein the first and second calreticulin mutant proteins are each independently chosen from: a molecule comprising the amino acid sequence of SEQ ID NO: 6313, or a molecule comprising the amino acid sequence of SEQ ID NO: 6314,

optionally wherein the multifunctional molecule comprises the configuration of FIG. 3A or 3B.

20

26. The multifunctional molecule of any of the preceding claims, wherein the calreticulin protein comprises an amino acid sequence chosen from SEQ ID NOs: 6285-6312, optionally wherein the calreticulin protein comprises an amino acid sequence chosen from SEQ ID NOs: 6313-6346.

25

27. The multifunctional molecule of any of the preceding claims, wherein the calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6285.

28. The multifunctional molecule of any of the preceding claims, wherein the calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286.

29. The multifunctional molecule of any of the preceding claims, wherein the first
5 antigen binding domain binds to an epitope located within the C-terminus of the calreticulin protein, optionally wherein the first antigen binding domain binds to an epitope located within the amino acid sequence of SEQ ID NO: 6285 or 6286.

30. The multifunctional molecule of any of the preceding claims, further comprising a
10 third antigen binding domain that binds to a second calreticulin protein, e.g., wherein the second calreticulin mutant protein comprises the amino acid sequence of SEQ ID NO: 6285 or 6286, optionally wherein:

- (i) the third antigen binding domain is different from the first antigen binding domain, or
- (ii) the third antigen binding domain is the same as the first antigen binding domain.

15 31. The multifunctional molecule of claim 30, wherein the second calreticulin molecule is the same as the calreticulin molecule bound by the first antigen binding domain.

32. The multifunctional molecule of claim 30, wherein the second calreticulin molecule
20 is different from the calreticulin molecule bound by the first antigen binding domain.

33. The multifunctional molecule of any of claims 30-32, wherein the second calreticulin protein comprises an amino acid sequence chosen from SEQ ID NOs: 6285-6312, optionally wherein the second calreticulin protein comprises an amino acid sequence chosen from SEQ ID
25 NOs: 6313-6346.

34. The multifunctional molecule of claim 33, wherein the calreticulin protein bound by the first antigen binding domain comprises the amino acid sequence of SEQ ID NO6285, and the second calreticulin protein comprises the amino acid sequence of SEQ ID NO: 6286.

35. The multifunctional molecule of any of claims 30-34, wherein the third antigen binding domain binds to an epitope located within the C-terminus of the second calreticulin protein, optionally wherein the third antigen binding domain binds to an epitope located within the amino acid sequence of SEQ ID NO: 6285 or 6286.

36. The multifunctional molecule of any of the preceding claims, wherein the first antigen binding domain comprises:

(i) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (VHCDR1) having an amino acid sequence of a VHCDR1 in Table 4, Table 7A, or Table 17 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VHCDR2 having an amino acid sequence of a VHCDR2 in Table 4, Table 7A, or Table 17 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VHCDR3 having an amino acid sequence of a VHCDR3 in Table 4, Table 7A, or Table 17 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions);

(ii) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (VHCDR1) having an amino acid sequence of a VLCDR1 in Table 5, Table 7A, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), a VLCDR2 having an amino acid sequence of a VLCDR2 in Table 5, Table 7A, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions), and/or a VLCDR3 having an amino acid sequence of a VLCDR3 in Table 5, Table 7A, or Table 18 (or a sequence with no more than 1, 2, 3, or 4 mutations, e.g., substitutions, additions, or deletions);

(iii) a VH comprising the amino acid sequence of a VH in Table 7A or Table 16 (or an amino acid sequence having at least about 77%, 80%, 85%, 90%, 95%, or 99% sequence identity thereto);

(iv) a VL comprising the amino acid sequence of a VL in Table 7A or Table 16 (or an amino acid sequence having at least about 93%, 95%, or 99% sequence identity thereto);

(v) a VH comprising a heavy chain framework region 1 (VHFWR1) having an amino acid sequence of a VHFWR1 in Table 4 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), a VHFWR2 having an amino acid sequence of a VHFWR2 in Table 4 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), a VHFWR3 having an amino acid sequence of a VHFWR3 in Table 4 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), and/or a VHFWR4 having an amino acid sequence of a VHFWR4 in Table 4 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), and/or

(vi) a VL comprising a light chain framework region 1 (VLFWR1) having an amino acid sequence of a VLFWR1 in Table 5 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), a VLFWR2 having an amino acid sequence of a VLFWR2 in Table 5 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), a VLFWR3 having an amino acid sequence of a VLFWR3 in Table 5 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions), and/or a VLFWR4 having an amino acid sequence of a VLFWR4 in Table 5 or Table 6 (or a sequence with no more than 1, 2, 3, 4, 5, 6, 7, 8, or 9 mutations, e.g., substitutions, additions, or deletions).

37. The multifunctional molecule of any of the preceding claims, wherein the multifunctional molecule further comprises a tumor-targeting moiety.

38. The multifunctional molecule of claim 37, wherein the tumor-targeting moiety binds to a tumor antigen.

39. The multifunctional molecule of claim 38, wherein the tumor antigen is selected from G6B, CD34, CD41, P-selectin, Clec2, cKIT, FLT3, MPL, ITGB3, ITGB2, GP5, GP6, GP9, GP1BA, DSC2, FCGR2A, TNFRSF10A, TNFRSF10B, or TM4SF1.

40. The multifunctional molecule of claim 37, wherein the tumor-targeting moiety comprises an antibody molecule, e.g., that binds to a tumor antigen selected from G6B, CD34, CD41, P-selectin, Clec2, cKIT, FLT3, MPL, ITGB3, ITGB2, GP5, GP6, GP9, GP1BA, DSC2, FCGR2A, TNFRSF10A, TNFRSF10B, or TM4SF1.

5

41. The multifunctional molecule of claim 40, wherein the tumor-targeting moiety comprises a VH and/or VL sequence, e.g., as listed in Table A or Table 20.

42. The multifunctional molecule of any one of the preceding claims, wherein the
10 multifunctional molecule preferentially binds to a myeloproliferative neoplasm cell over a non-tumor cell, optionally wherein the binding between the multifunctional molecule and the myeloproliferative neoplasm cell is more than 10, 20, 30, 40, 50-fold greater than the binding between the multifunctional molecule and a non-tumor cell.

15 43. The multifunctional molecule of claim 42, wherein the myeloproliferative neoplasm cell is chosen from a myelofibrosis cell, an essential thrombocythemia cell, a polycythemia vera cell, or a chronic myeloid cancer cell, optionally wherein:

the myeloproliferative neoplasm cell does not comprise a JAK2 V617F mutation, or
the myeloproliferative neoplasm cell does not comprise a MPL mutation.

20

44. The multifunctional molecule of any one of the preceding claims, further comprising a linker, e.g., a linker between the first antigen binding domain and the second antigen binding domain.

25 45. The multifunctional molecule of claim 44, wherein the linker is chosen from: a cleavable linker, a non-cleavable linker, a peptide linker, a flexible linker, a rigid linker, a helical linker, or a non-helical linker.

46. The multifunctional molecule of claim 44 or 45, wherein the linker is a peptide linker.

47. The multifunctional molecule of 46, wherein the peptide linker comprises Gly and Ser.

5 48. The multifunctional molecule of 46, wherein the peptide linker comprises an amino acid sequence chosen from SEQ ID NOs: 6214-6217 or 6220-6221 and 77-78.

49. A nucleic acid molecule encoding the multifunctional molecule of any of the preceding claims.

10

50. A vector, e.g., an expression vector, comprising the nucleic acid molecule of claim 49.

15

51. A cell comprising the nucleic acid molecule of claim 49 or the vector of claim 50.

52. A method of making, e.g., producing, the multifunctional molecule of any one of claims 1-48, comprising culturing the cell of claim 51, under suitable conditions, e.g., conditions suitable for gene expression and/or homo- or heterodimerization.

20 53. A pharmaceutical composition comprising the multifunctional molecule of any one of claims 1-48 and a pharmaceutically acceptable carrier, excipient, or stabilizer.

54. A method of treating a cancer, comprising administering to a subject in need thereof the multifunctional molecule of any one of claims 1-48, wherein the multifunctional molecule is
25 administered in an amount effective to treat the cancer.

55. Use of the multifunctional molecule of any one of claims 1-48 for the manufacture of a medicament for treating a cancer.

56. The method of claim 54 or the use of claim 55, wherein the subject has cancer cells that express the first and/or second calreticulin protein.

57. The method of claim 54 or 56 or the use of claim 55 or 56, wherein the subject has
5 the JAK2 V617F mutation.

58. The method of claim 54 or 56 or the use of claim 55 or 56, wherein the subject does not have the JAK2 V617F mutation.

10 59. The method of any one of claims 54 or 56-58 or the use of any one of claims 55-58, wherein the subject has a MPL mutation.

60. The method of any one of claims 54 or 56-58 or the use of any one of claims 55-58, wherein the subject does not have a MPL mutation.

15 61. The method of any one of claims 54 or 56-60 or the use of any one of claims 55-60, wherein the cancer is a hematological cancer, optionally wherein the cancer is a myeloproliferative neoplasm, e.g., primary or idiopathic myelofibrosis (MF), essential thrombocytosis (ET), polycythemia vera (PV), or chronic myelogenous leukemia (CML),
20 optionally wherein the cancer is myelofibrosis.

62. The method of any one of claims 54 or 56-60 or the use of any one of claims 55-60, the cancer is a solid tumor cancer.

25 63. The method of any of claims 54 or 56-62 or the use of any one of claims 55-62, further comprising administering a second therapeutic treatment.

64. The method of claim 63 or the use of claim 63, wherein the second therapeutic treatment comprises a therapeutic agent (e.g., a chemotherapeutic agent, a biologic agent, hormonal therapy), radiation, or surgery.

- 5 65. The method of claim 64 or the use of claim 64, wherein the therapeutic agent is selected from: a chemotherapeutic agent, or a biologic agent.

VH	Framework 1										CDR 1																								
SEQ ID NO: 1	1	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	31	32	33	34	35
SEQ ID NO: 9	Q	V	Q	L	Q	Q	S	G	P	E	L	V	K	P	G	T	S	V	K	I	S	C	K	A	S	G	Y	S	F	T	T	Y	Y	I	H
	Q	V	Q	L	V	Q	S	G	A	E	V	K	K	P	G	S	S	V	K	V	S	C	K	A	S	G	Y	S	F	T	T	Y	Y	I	H
	Framework 2										CDR 2																								
SEQ ID NO: 1	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	52a	53	54	55	56	57	58	59	60	61	62	63	64	65				
SEQ ID NO: 9	W	V	K	Q	R	P	G	Q	G	L	E	W	I	G	W	F	F	P	G	S	G	N	I	K	Y	N	E	K	F	K	G				
	W	V	R	Q	A	P	G	Q	G	L	E	W	M	G	W	F	F	P	G	S	G	N	I	K	Y	N	E	K	F	K	G				
	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	82a	82b	82c	83	84	85	86	87	88	89	90	91	92	93	94			
SEQ ID NO: 1	K	A	T	L	T	A	D	T	S	S	S	T	A	Y	M	Q	L	S	S	L	T	S	E	E	S	A	V	Y	F	C	A	G			
SEQ ID NO: 9	R	V	T	I	T	A	D	I	S	T	S	T	A	Y	M	E	L	S	S	L	R	S	E	D	T	A	V	Y	C	A	G				
	CDR 3										Framework 4																								
SEQ ID NO: 1	95	96	97	98	99	100	100a	100b	101	102	103	104	105	106	107	108	109	110	111	112	113														
SEQ ID NO: 9	S	Y	Y	S	Y	D	V	L	D	Y	W	G	H	G	T	T	L	T	V	S	S														
	S	Y	Y	S	Y	D	V	L	D	Y	W	G	Q	G	T	T	V	T	V	S	S														

FIG. 1A

VL	Framework 1																																		CDR 1																																	
	1	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	31	32	33	34																																		
SEQ ID NO: 2	D	I	L	M	T	Q	S	Q	K	F	M	S	T	S	L	G	D	R	V	S	V	S	C	K	A	S	Q	N	V	G	I	N	V	V																																		
SEQ ID NO: 10	D	I	Q	M	T	Q	S	P	S	F	L	S	A	S	V	G	D	R	V	T	I	T	C	K	A	S	Q	N	V	G	I	N	V	V																																		
SEQ ID NO: 11	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	K	A	S	Q	N	V	G	I	N	V	V																																		
	Framework 2																																		CDR 2																																	
	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56																																														
SEQ ID NO: 2	W	H	Q	Q	K	P	G	Q	S	P	K	A	L	I	Y	S	S	S	H	R	Y	S																																														
SEQ ID NO: 10	W	H	Q	Q	K	P	G	K	A	P	K	A	L	I	Y	S	S	S	H	R	Y	S																																														
SEQ ID NO: 11	W	H	Q	Q	K	P	G	K	V	P	K	A	L	I	Y	S	S	S	H	R	Y	S																																														
	Framework 3																																																																			
	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88																																				
SEQ ID NO: 2	G	V	P	D	R	F	T	G	S	G	S	G	T	D	F	T	L	T	I	N	N	V	Q	S	E	D	L	A	E	Y	F	C																																				
SEQ ID NO: 10	G	V	P	S	R	F	S	G	S	G	S	G	T	E	F	T	L	T	I	S	S	L	Q	P	E	D	F	A	T	Y	F	C																																				
SEQ ID NO: 11	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P	E	D	V	A	T	Y	F	C																																				
	CDR 3																																		Framework 4																																	
	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107																																																	
SEQ ID NO: 2	Q	Q	F	K	S	Y	P	L	T	F	G	A	G	T	K	L	E	L	K																																																	
SEQ ID NO: 10	Q	Q	F	K	S	Y	P	L	T	F	G	Q	G	T	K	L	E	I	K																																																	
SEQ ID NO: 11	Q	Q	F	K	S	Y	P	L	T	F	G	Q	G	T	K	L	E	I	K																																																	

FIG. 1B

VH		Framework 1										CDR 1										CDR 2														
SEQ ID NO: 15		1	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	31	32	33	34	35
SEQ ID NO: 25		D	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	R	K	L	S	C	A	A	S	G	F	T	F	S	N	F	G	M	H
SEQ ID NO: 23		Q	V	Q	L	V	E	S	G	G	G	V	V	Q	P	G	R	S	L	R	L	S	C	A	A	S	G	F	T	F	S	N	F	G	M	H
SEQ ID NO: 24		E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	N	F	G	M	H
SEQ ID NO: 24		E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	N	F	G	M	H
		Framework 2										CDR 2																								
SEQ ID NO: 15		36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	52a	53	54	55	56	57	58	59	60	61	62	63	64	65				
SEQ ID NO: 25		W	V	R	Q	A	P	D	K	G	L	E	W	V	A	Y	I	S	S	G	S	S	T	I	Y	Y	A	D	T	L	K	G				
SEQ ID NO: 23		W	V	R	Q	A	P	G	K	G	L	E	W	V	A	Y	I	S	S	G	S	S	T	I	Y	Y	A	D	T	L	K	G				
SEQ ID NO: 24		W	V	R	Q	A	P	G	K	G	L	E	W	V	S	Y	I	S	S	G	S	S	T	I	Y	Y	A	D	T	L	K	G				
SEQ ID NO: 24		W	V	R	Q	A	P	G	K	G	L	E	W	V	S	Y	I	S	S	G	S	S	T	I	Y	Y	A	D	T	L	K	G				
		Framework 3																																		
SEQ ID NO: 15		66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	82a	82b	82c	83	84	85	86	87	88	89	90	91	92	93	94			
SEQ ID NO: 25		R	F	T	I	S	R	D	N	P	K	N	T	L	F	L	Q	M	T	S	L	R	S	E	D	T	A	M	Y	Y	C	A	R			
SEQ ID NO: 23		R	F	T	I	S	R	D	N	S	K	N	T	L	Y	L	Q	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	A	R			
SEQ ID NO: 24		R	F	T	I	S	R	D	N	S	K	N	T	L	Y	L	Q	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	A	R			
SEQ ID NO: 24		R	F	T	I	S	R	D	N	S	K	N	T	L	Y	L	Q	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	A	R			
		CDR 3										Framework 4																								
SEQ ID NO: 15		95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113																
SEQ ID NO: 25		R	G	E	G	A	M	D	Y	W	G	Q	G	T	S	V	T	V	S	S																
SEQ ID NO: 23		R	G	E	G	A	M	D	Y	W	G	Q	G	T	T	V	T	V	S	S																
SEQ ID NO: 24		R	G	E	G	A	M	D	Y	W	G	Q	G	T	T	V	T	V	S	S																

FIG. 2A

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VL		Framework 1																														CDR 1									
		1	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	31	32	33	34						
SEQ ID NO: 16	E	N	V	L	T	Q	S	P	A	I	M	S	A	S	L	G	E	K	V	T	M	S	C	R	A	S	S	S	V	-	N	Y	I	Y							
SEQ ID NO: 26	D	N	Q	L	T	Q	S	P	S	F	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	S	S	V	-	N	Y	I	Y							
SEQ ID NO: 27	D	N	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	S	S	V	-	N	Y	I	Y							
SEQ ID NO: 28	E	N	V	L	T	Q	S	P	A	T	L	S	V	S	P	G	E	R	A	T	L	S	C	R	A	S	S	S	V	-	N	Y	I	Y							
SEQ ID NO: 29	Q	N	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	R	A	S	S	S	V	-	N	Y	I	Y							
SEQ ID NO: 30	S	N	E	L	T	Q	P	P	S	-	V	S	V	S	P	G	Q	T	A	R	I	T	C	R	A	S	S	S	V	-	N	Y	I	Y							

		Framework 2																			CDR 2						
		35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56				
SEQ ID NO: 16	W	Y	Q	Q	K	S	D	A	S	P	K	L	W	I	Y	Y	Y	T	S	N	L	A	P				
SEQ ID NO: 26	W	Y	Q	Q	K	P	G	K	A	P	K	L	L	I	Y	Y	Y	T	S	N	L	A	P				
SEQ ID NO: 27	W	Y	Q	Q	K	P	G	K	A	P	K	L	L	I	Y	Y	Y	T	S	N	L	A	P				
SEQ ID NO: 28	W	Y	Q	Q	K	P	G	Q	A	P	R	L	L	I	Y	Y	Y	T	S	N	L	A	P				
SEQ ID NO: 29	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	Y	Y	Y	T	S	N	L	A	P				
SEQ ID NO: 30	W	Y	Q	Q	K	S	G	Q	A	P	V	L	V	I	Y	Y	Y	T	S	N	L	A	P				

FIG. 2B

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Framework 3	
SEQ ID NO: 16	57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88
SEQ ID NO: 26	G V P T R F S G S G S G N S Y S L T I S S M E G E D A A T Y Y C
SEQ ID NO: 27	G V P S R F S G S G S G N S Y T L T I S S L Q P E D F A T Y Y C
SEQ ID NO: 28	G V P A R F S G S G S G N S Y T L T I S S L Q P E D F A T Y Y C
SEQ ID NO: 29	G V P D R F S G S G S G N S Y T L T I S S L Q R S E D F A D Y Y C
SEQ ID NO: 30	G I P E R F S G S G S G N S Y T L T I S S L Q R S E D F A D Y Y C
CDR 3	
Framework 4	
SEQ ID NO: 16	89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107
SEQ ID NO: 26	Q Q F T S S P F T F G S G T K L E I K
SEQ ID NO: 27	Q Q F T S S P F T F G Q G T K L E I K
SEQ ID NO: 28	Q Q F T S S P F T F G Q G T K L E I K
SEQ ID NO: 29	Q Q F T S S P F T F G Q G T K L E I K
SEQ ID NO: 30	Q Q F T S S P F T F G T G T K V T V L

FIG. 2B
(Continued)

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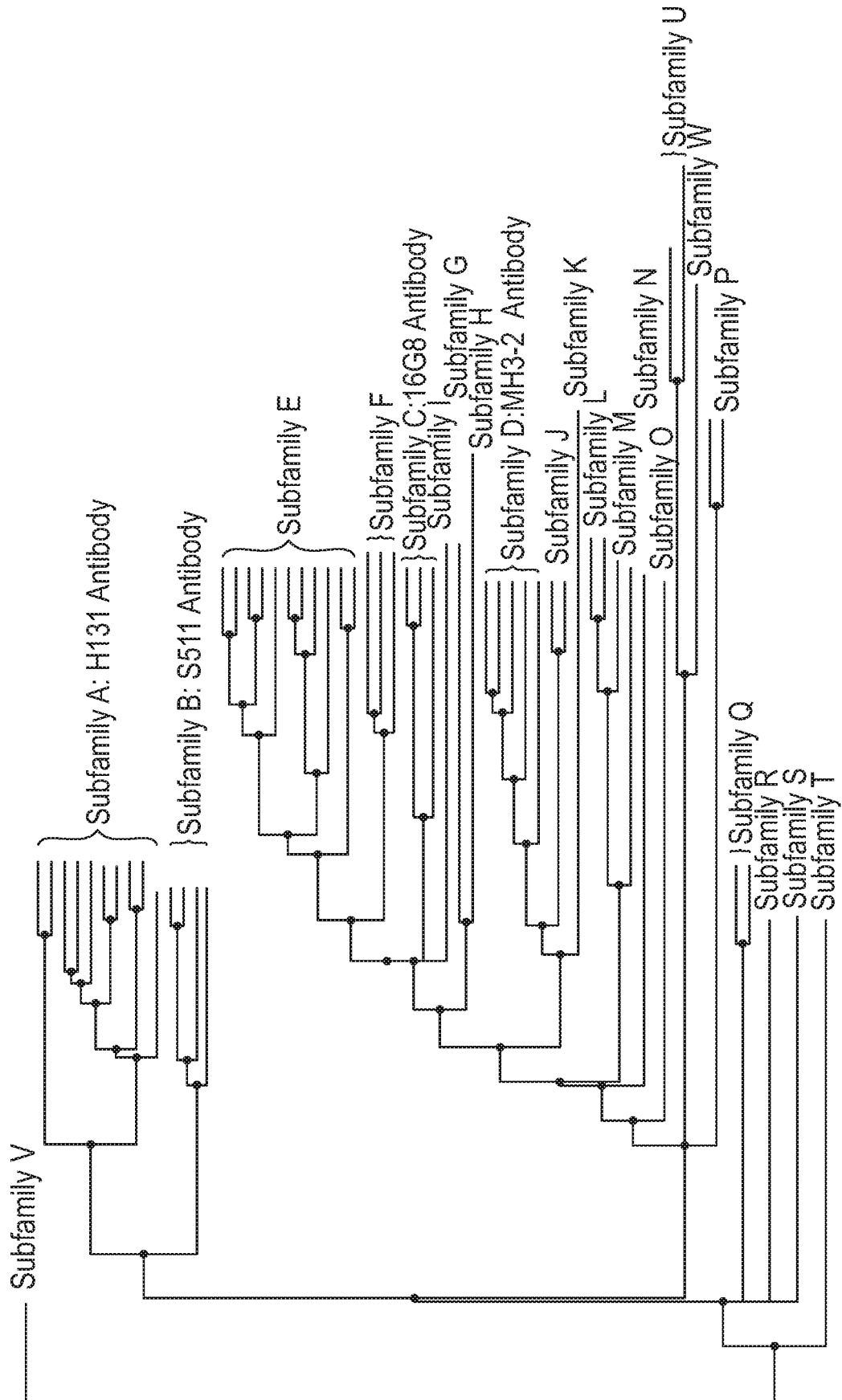


FIG. 3

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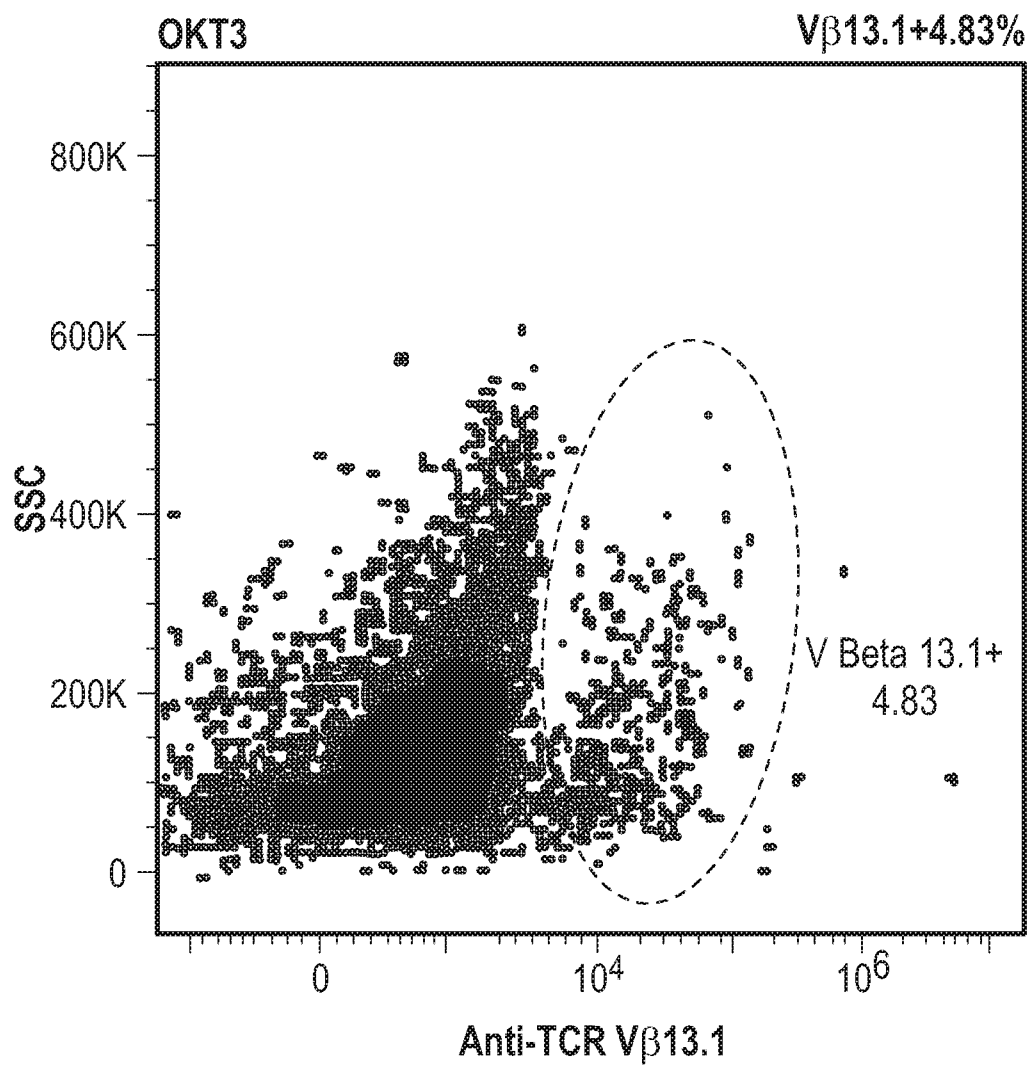


FIG. 4A

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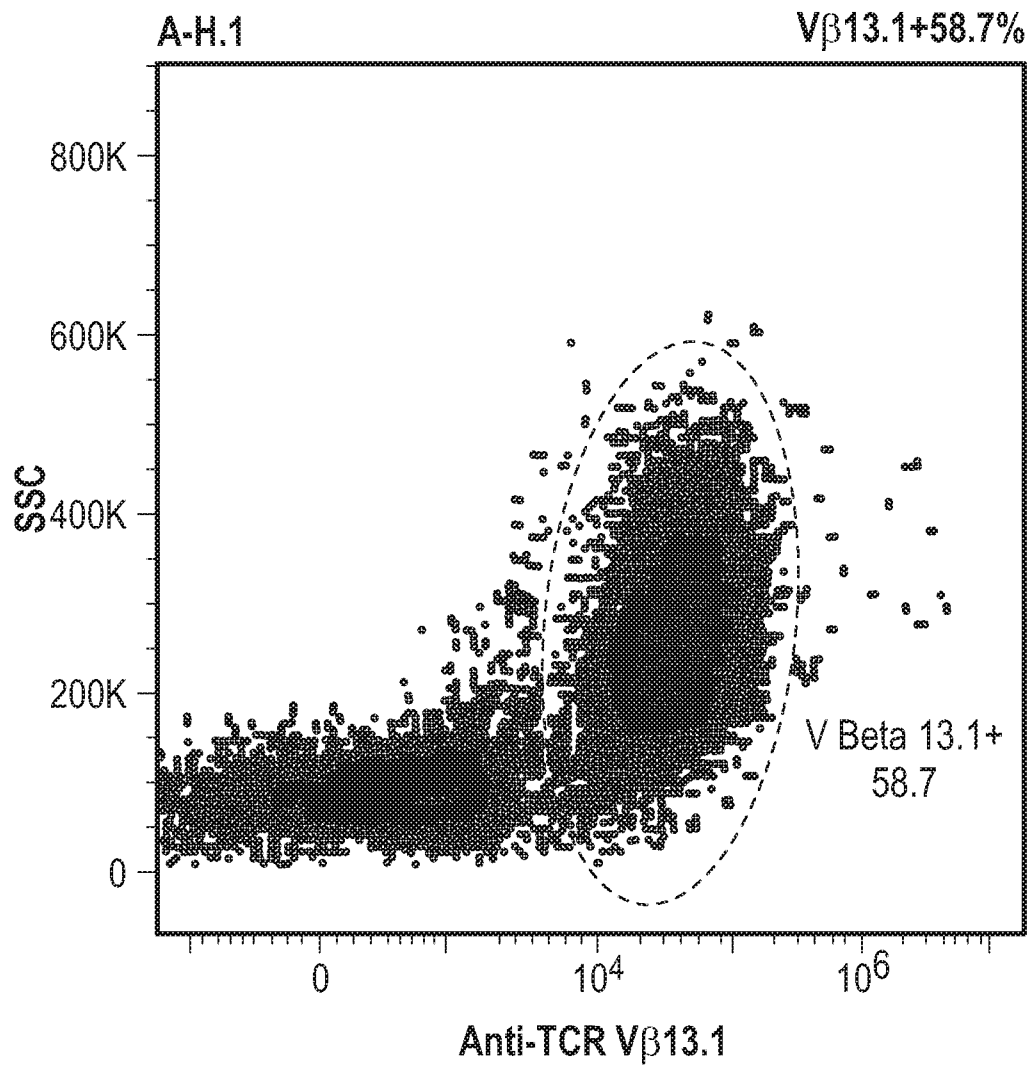


FIG. 4A
(Continued)

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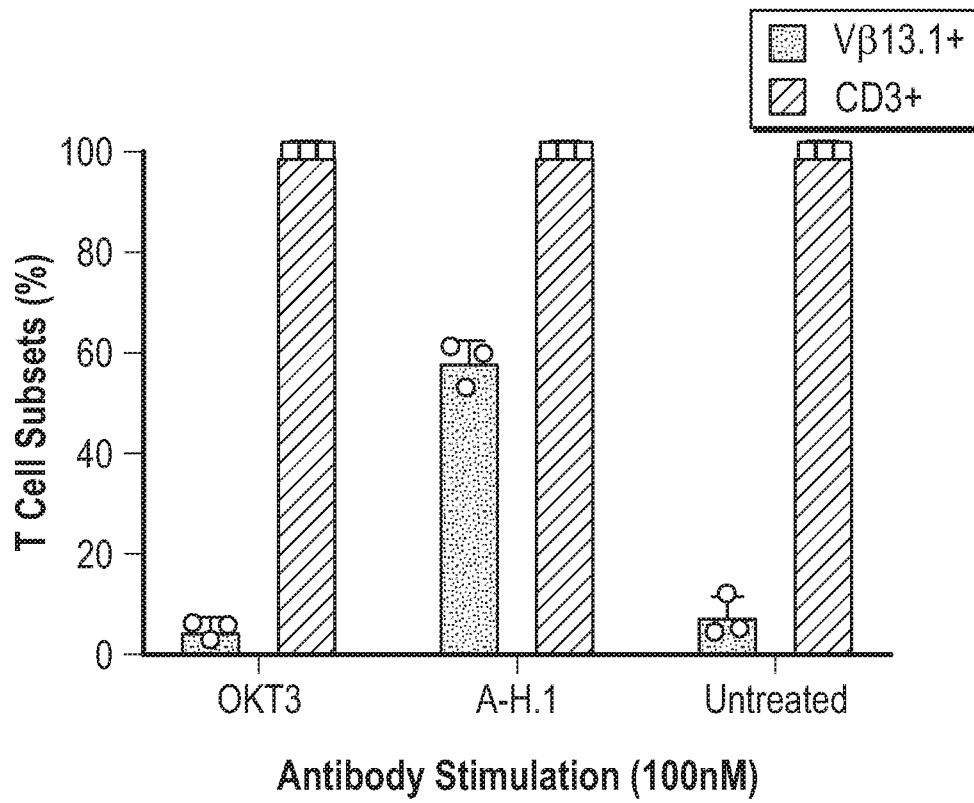


FIG. 4B

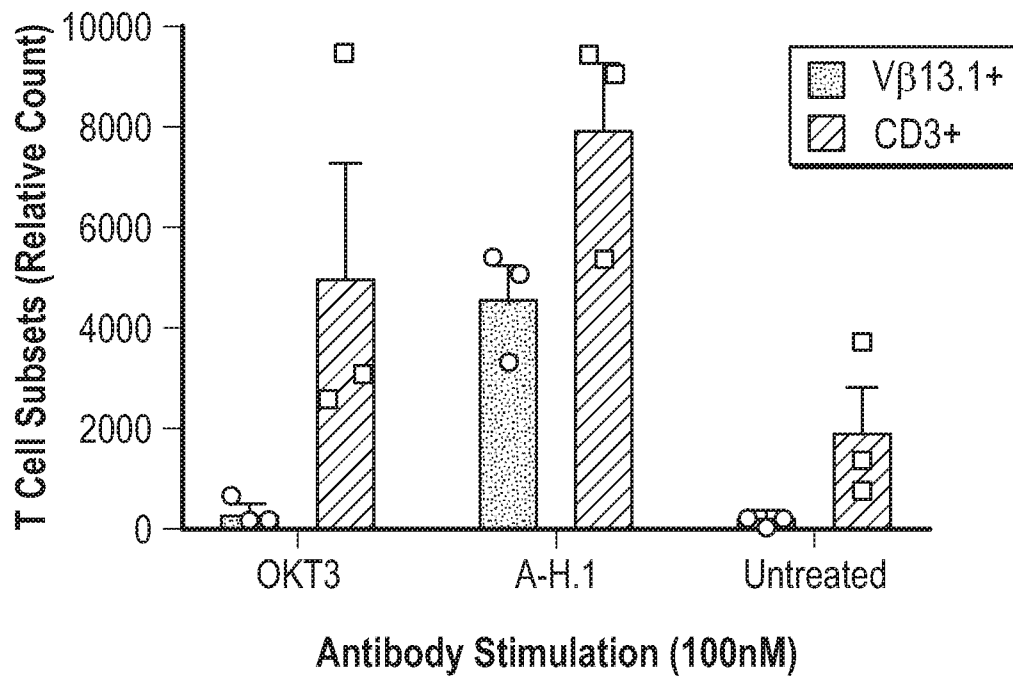


FIG. 4C

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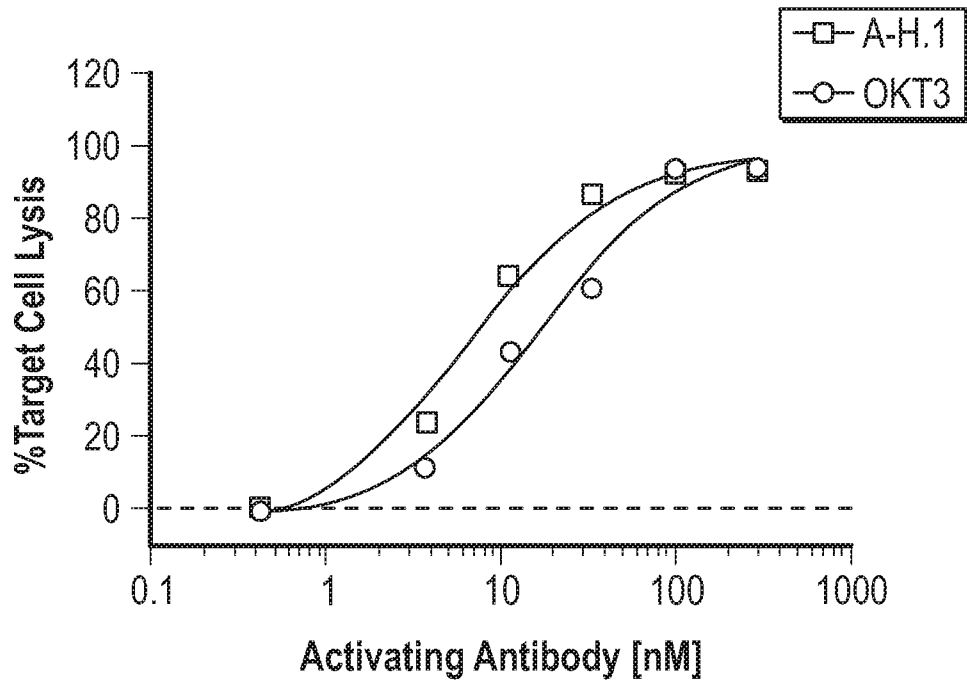


FIG. 5A

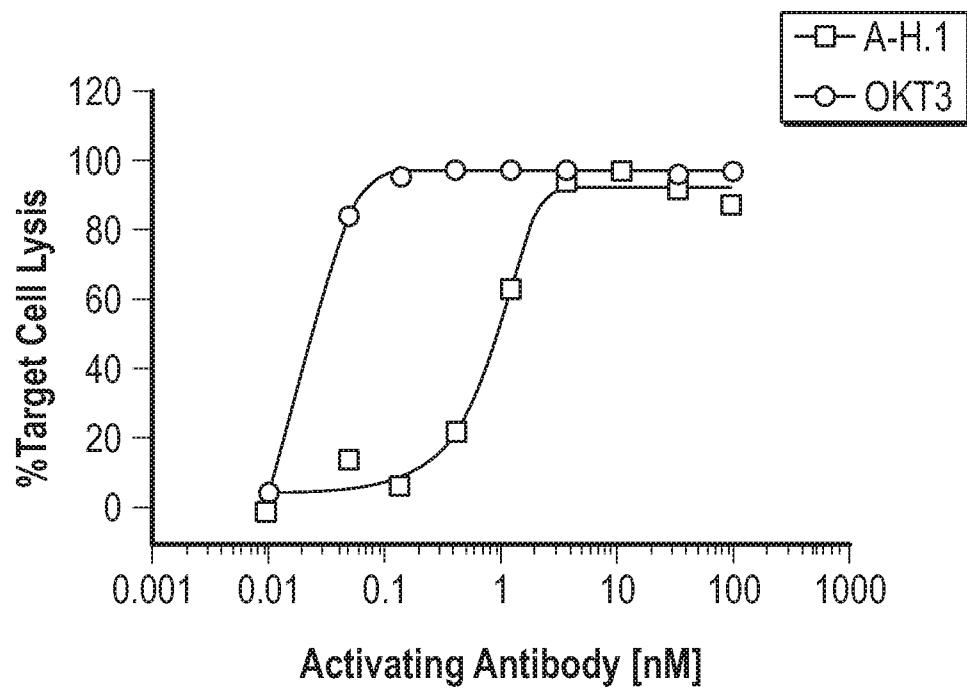


FIG. 5B

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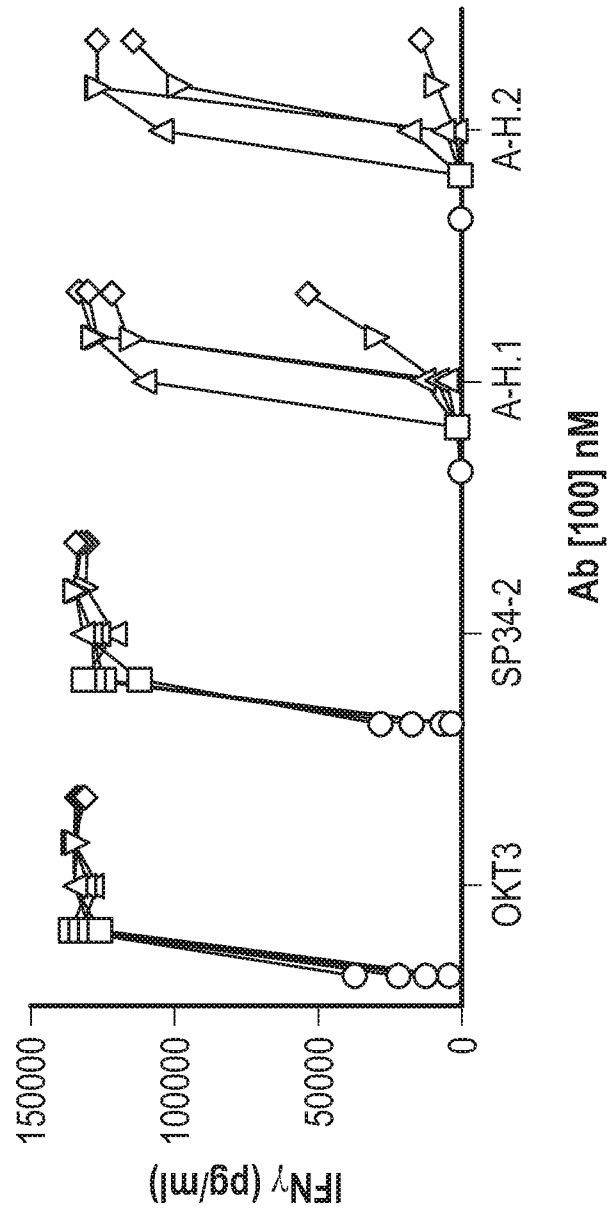
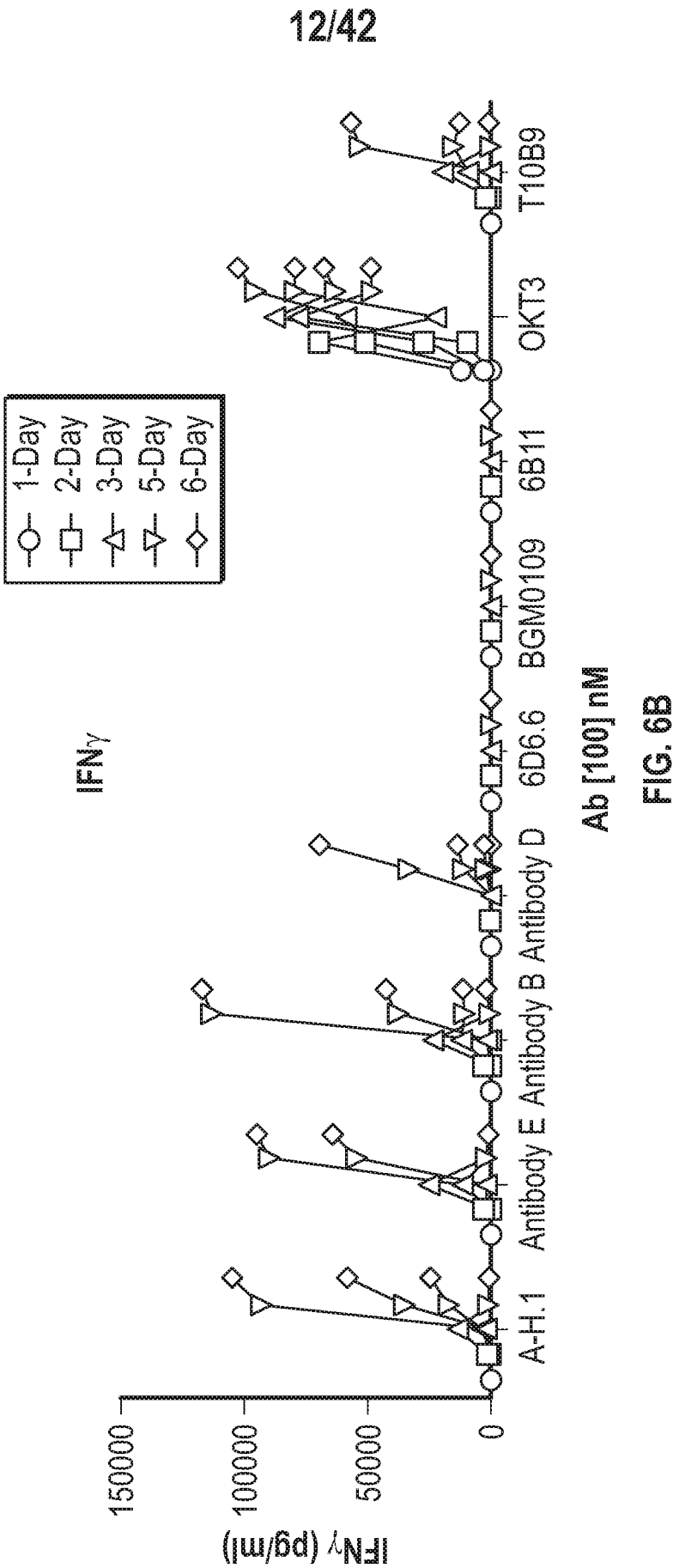


FIG. 6A



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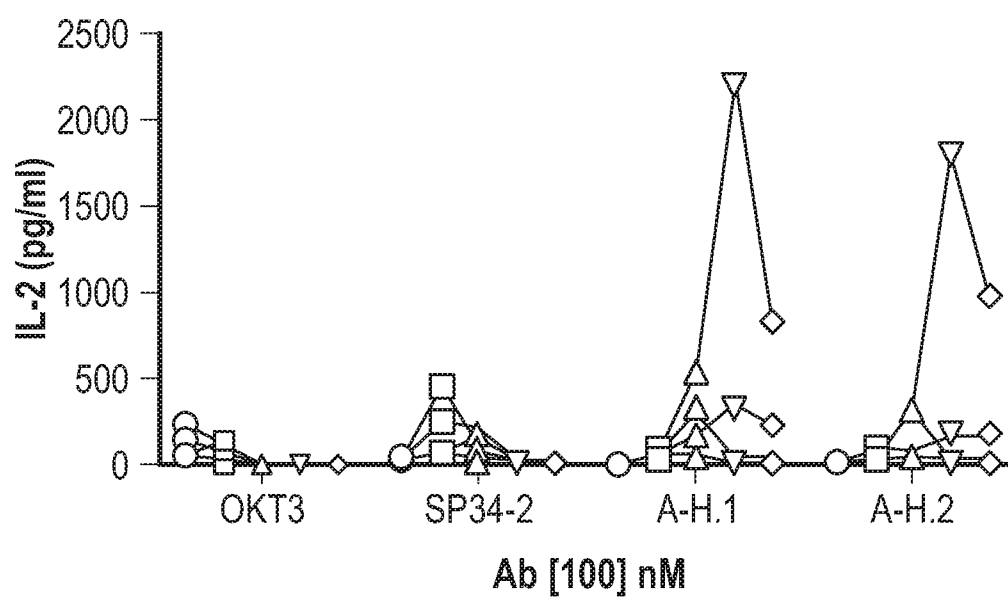


FIG. 7A

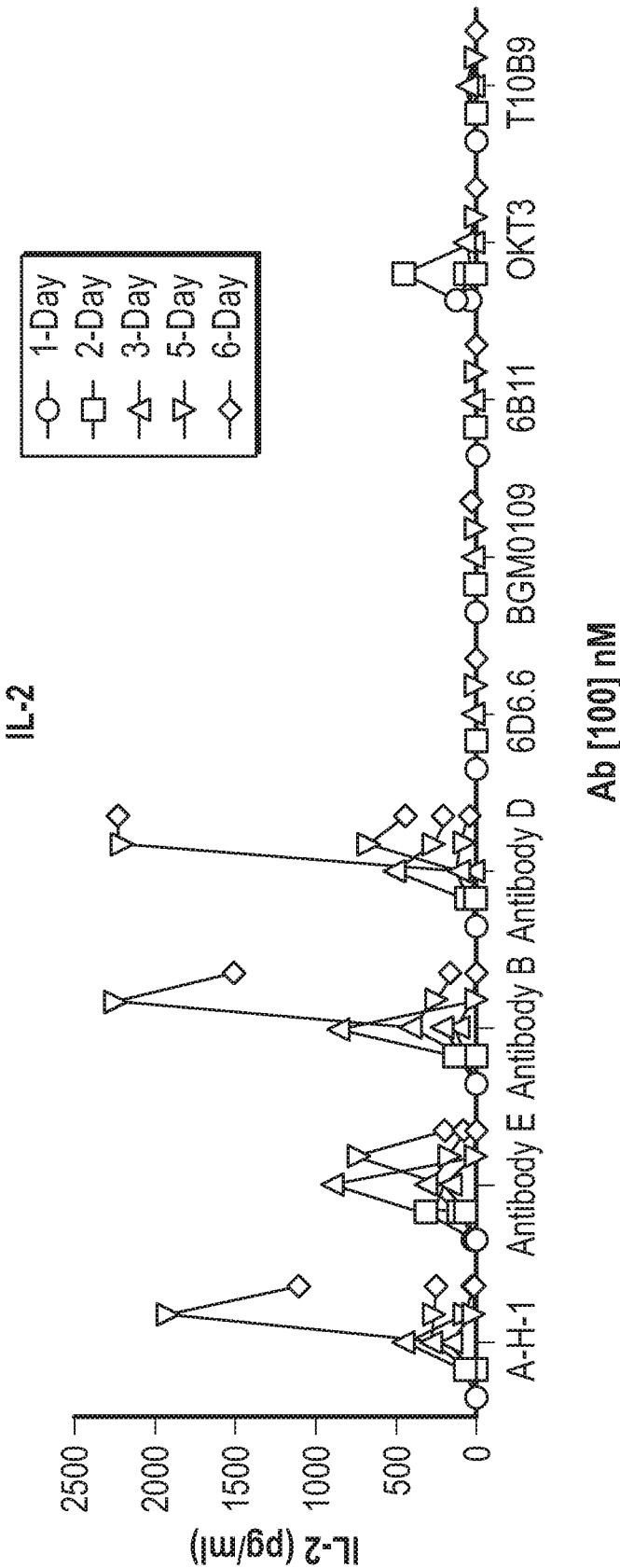


FIG. 7B

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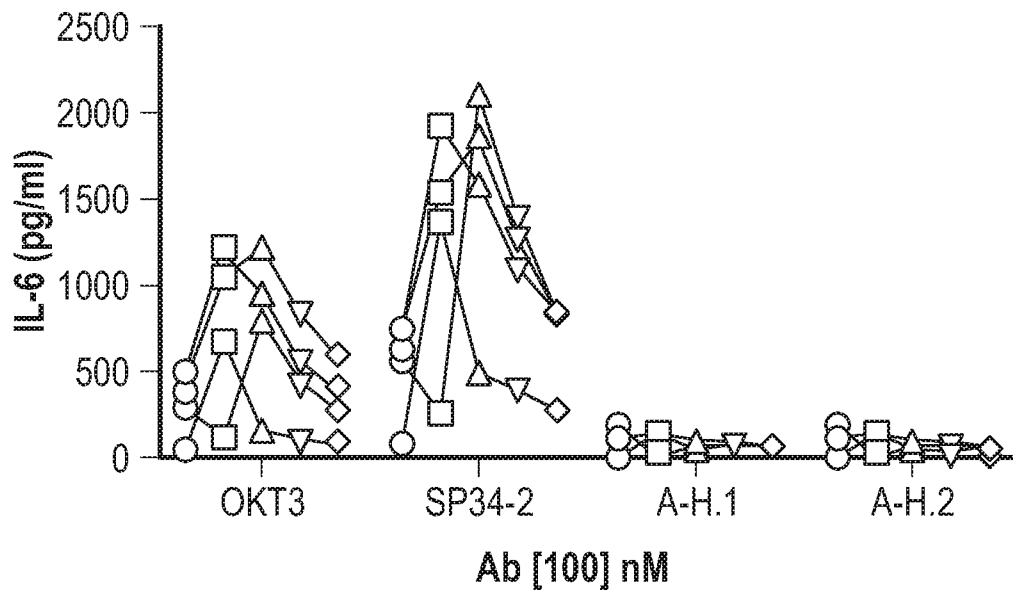


FIG. 8A

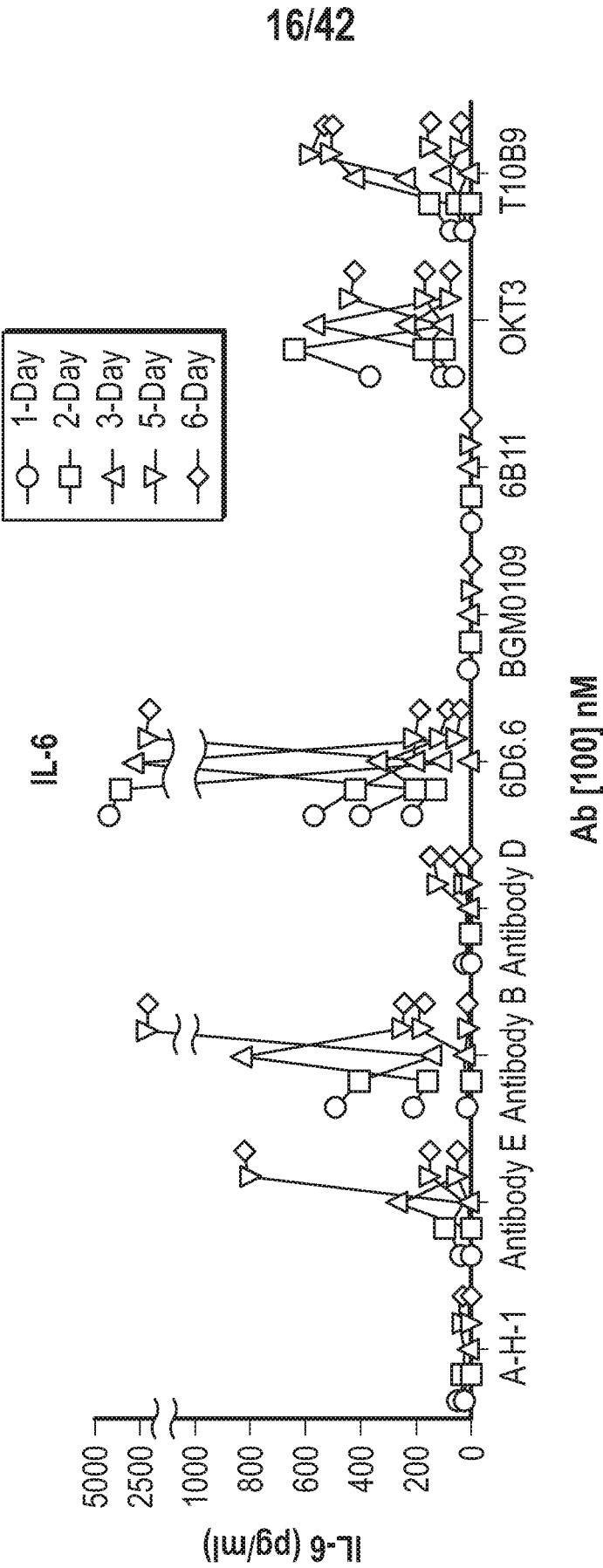
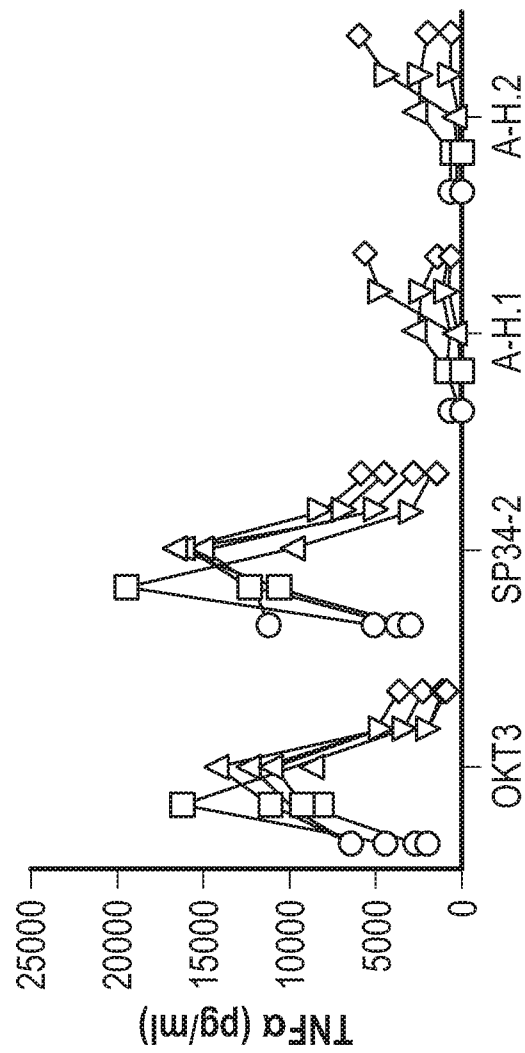


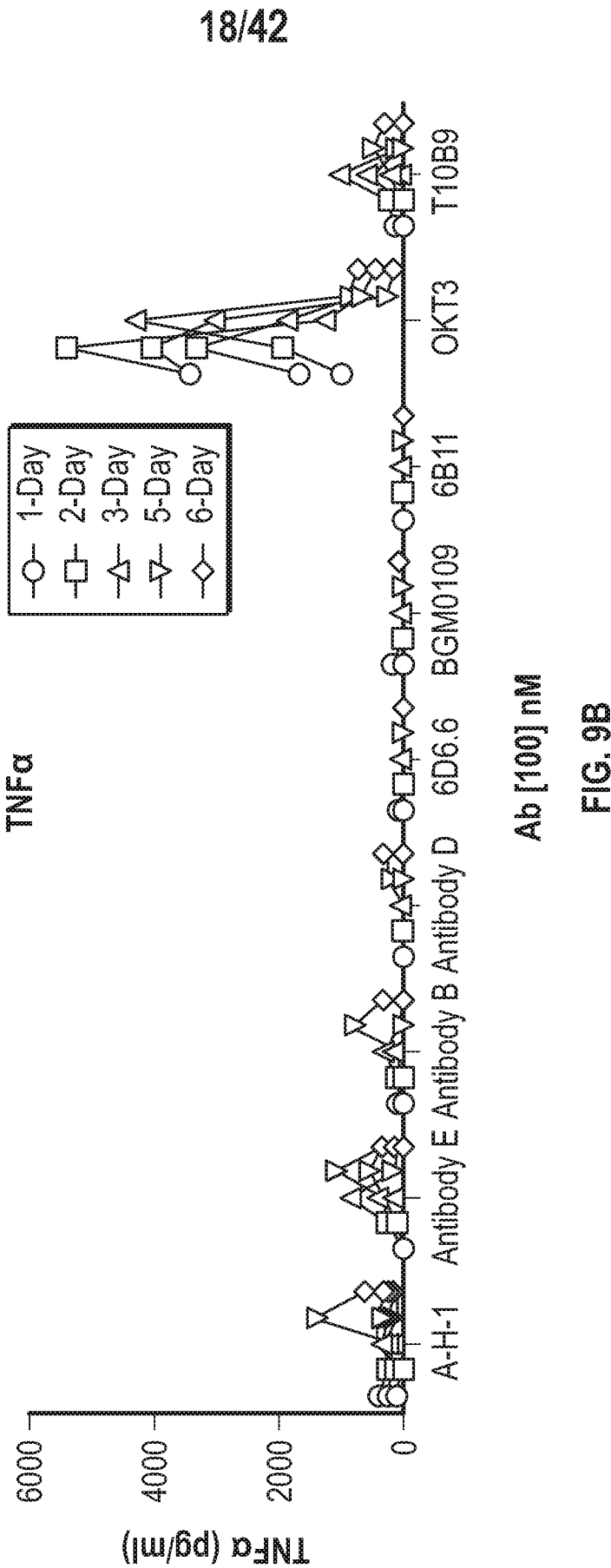
FIG. 8B

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Ab [100] nM

FIG. 9A



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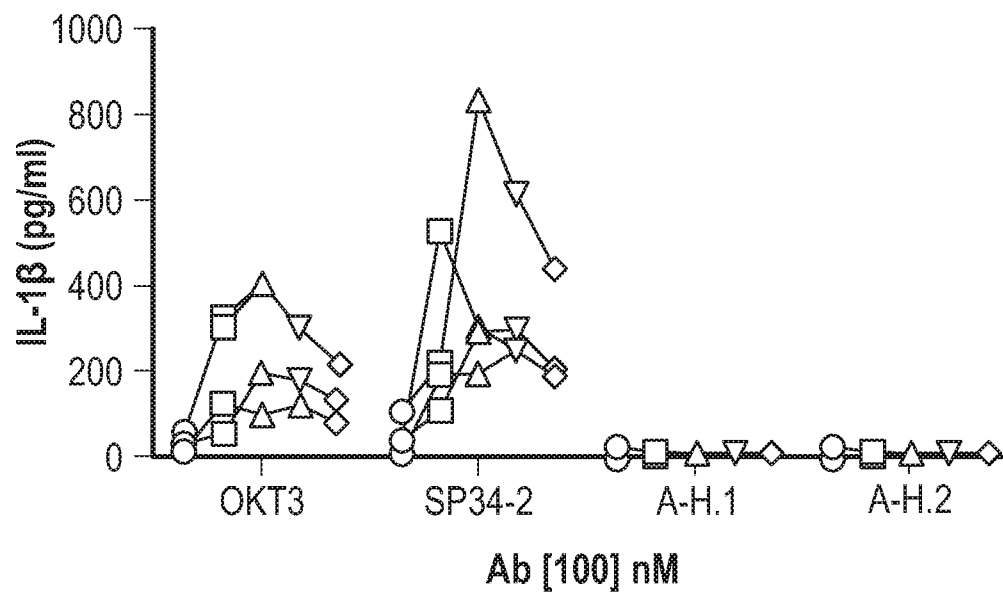


FIG. 10A

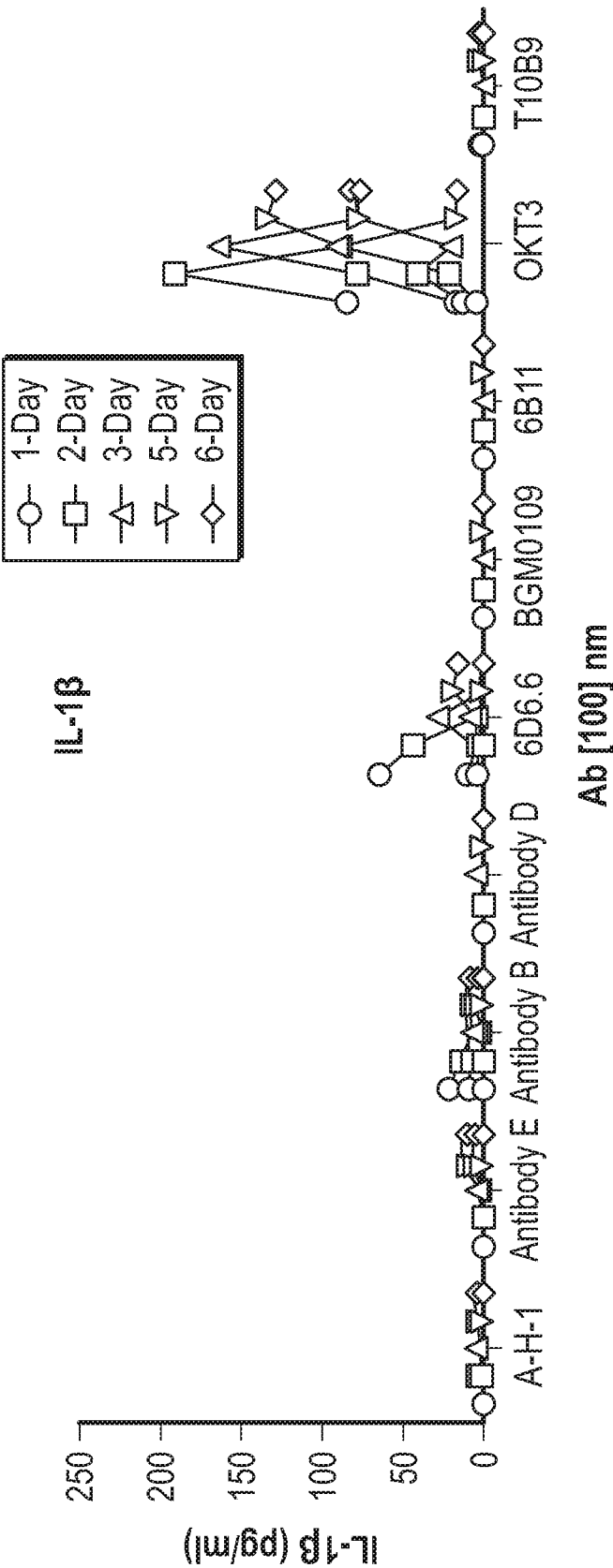


FIG. 10B

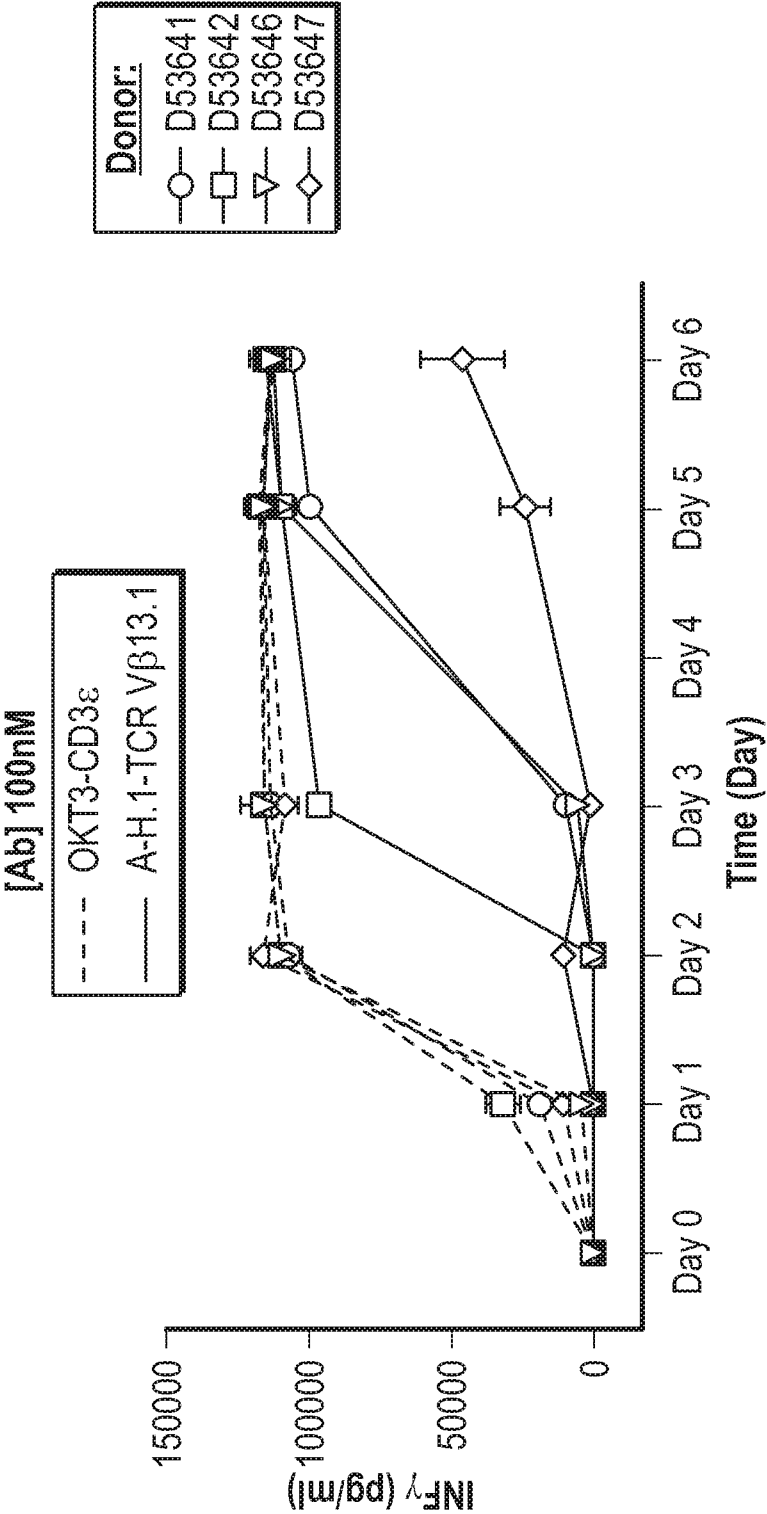


FIG. 11A

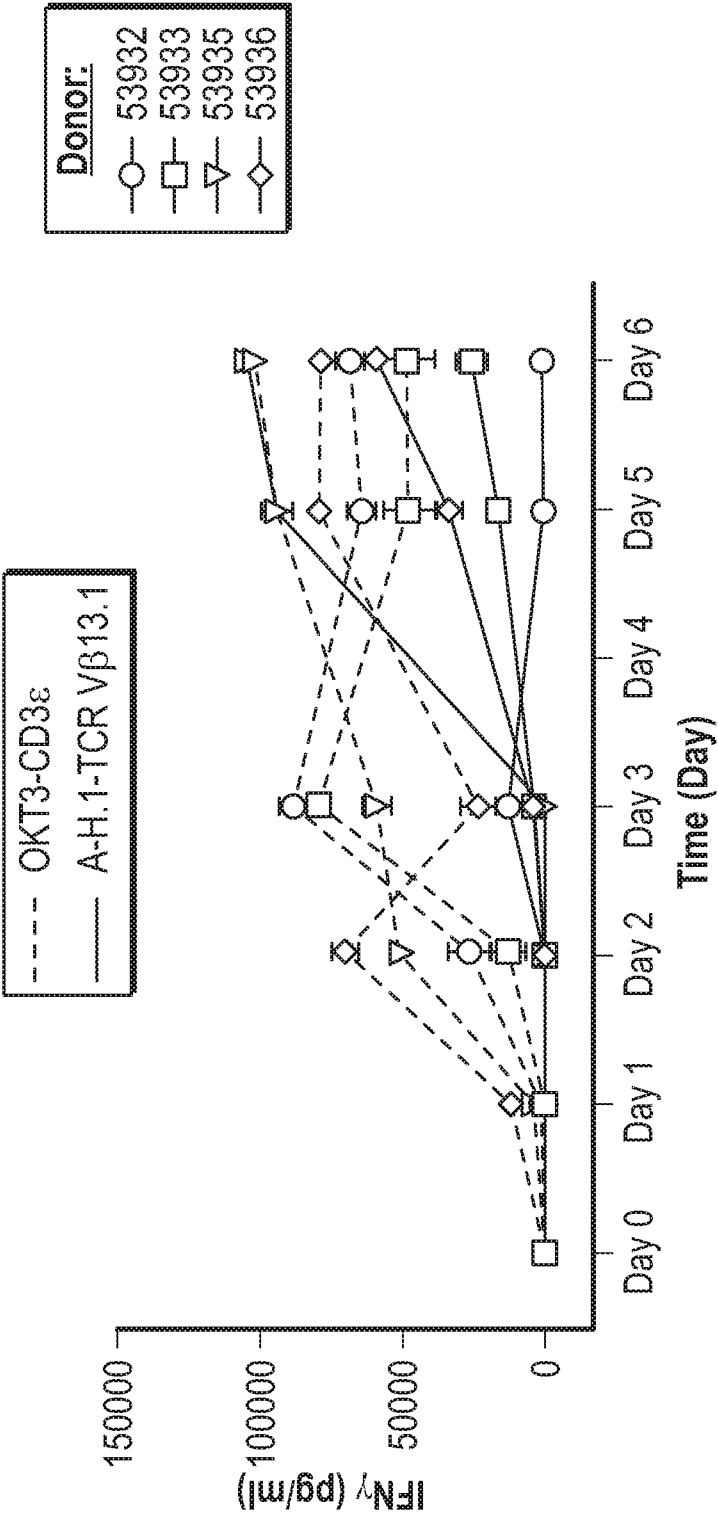
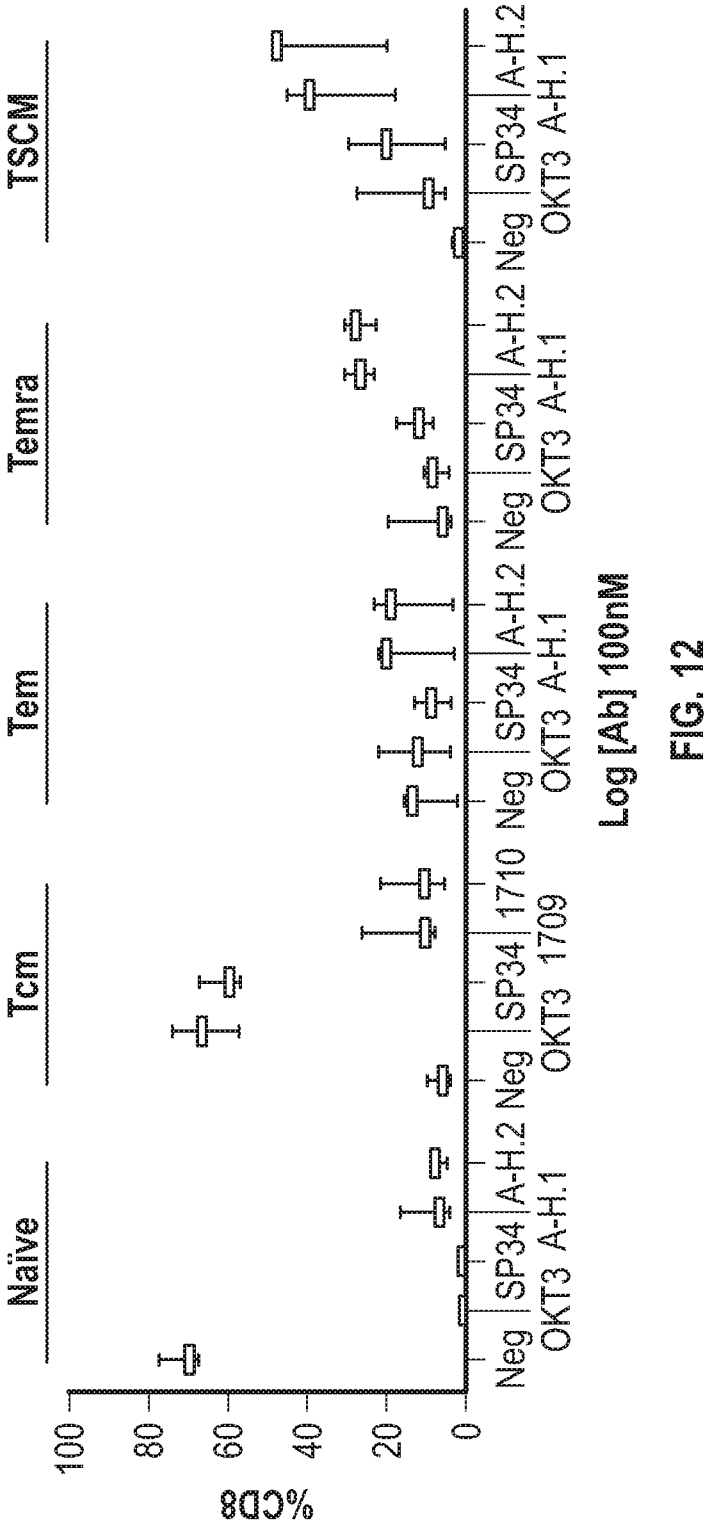


FIG. 11B



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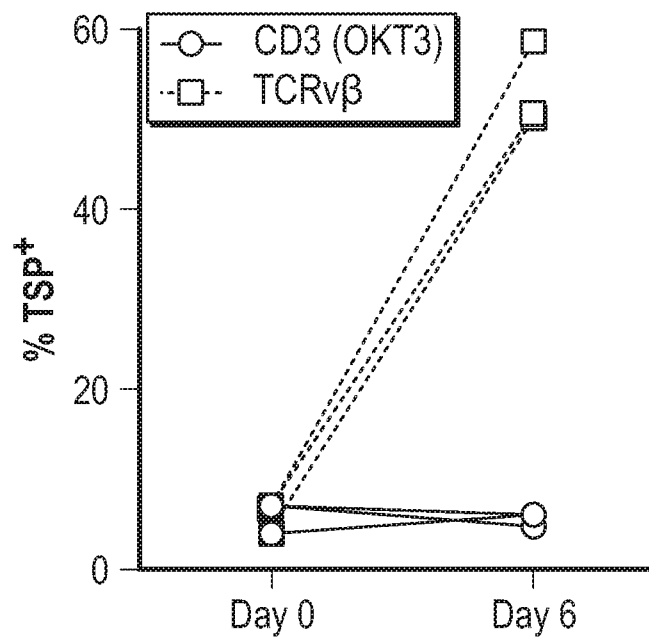


FIG. 13A

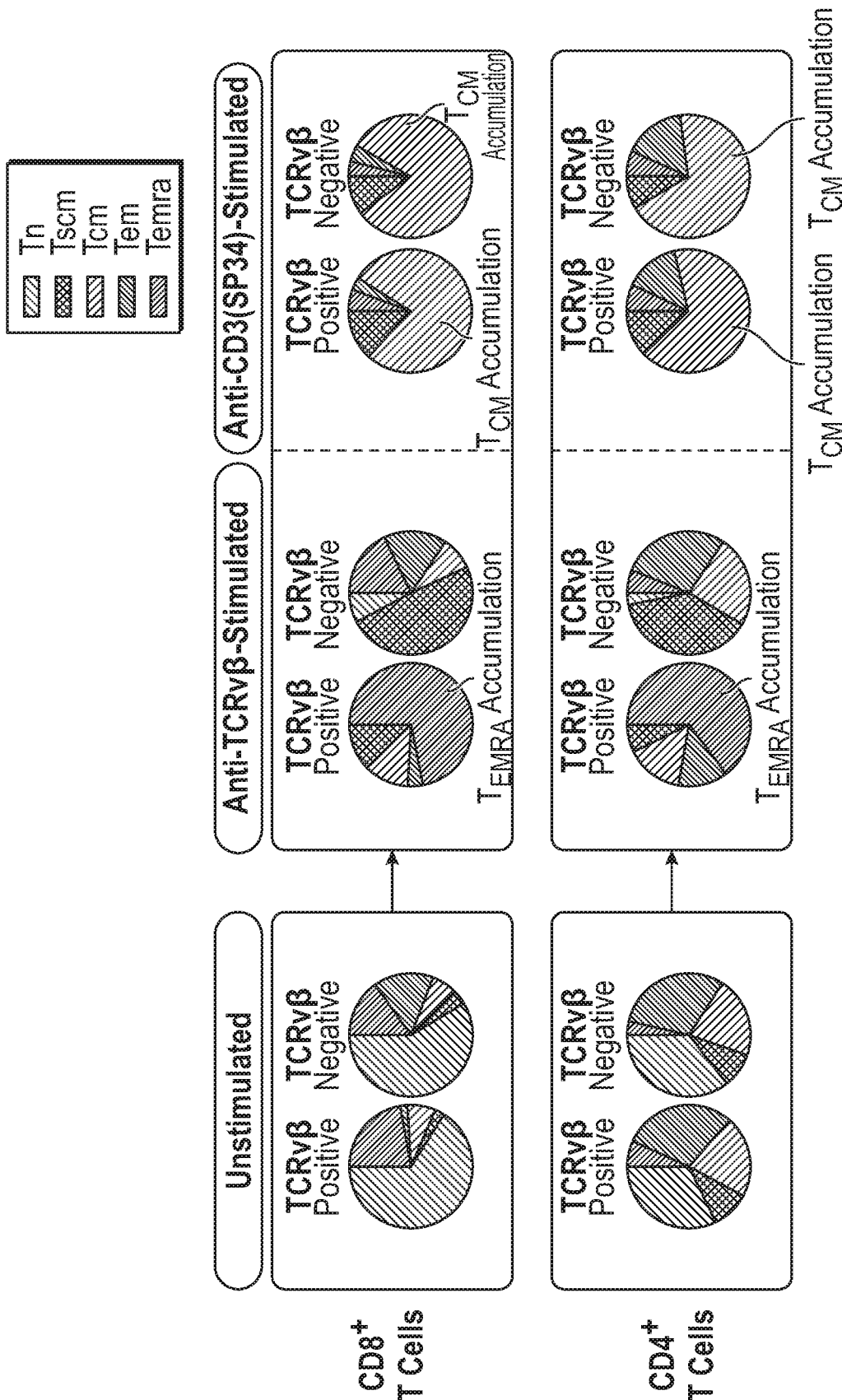


FIG. 13B

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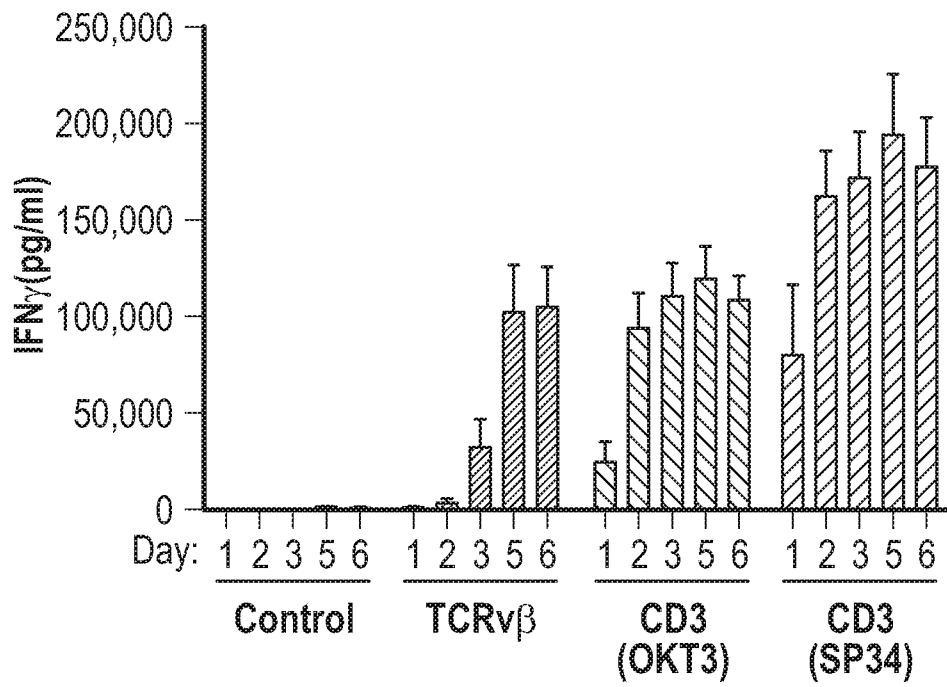


FIG. 13C

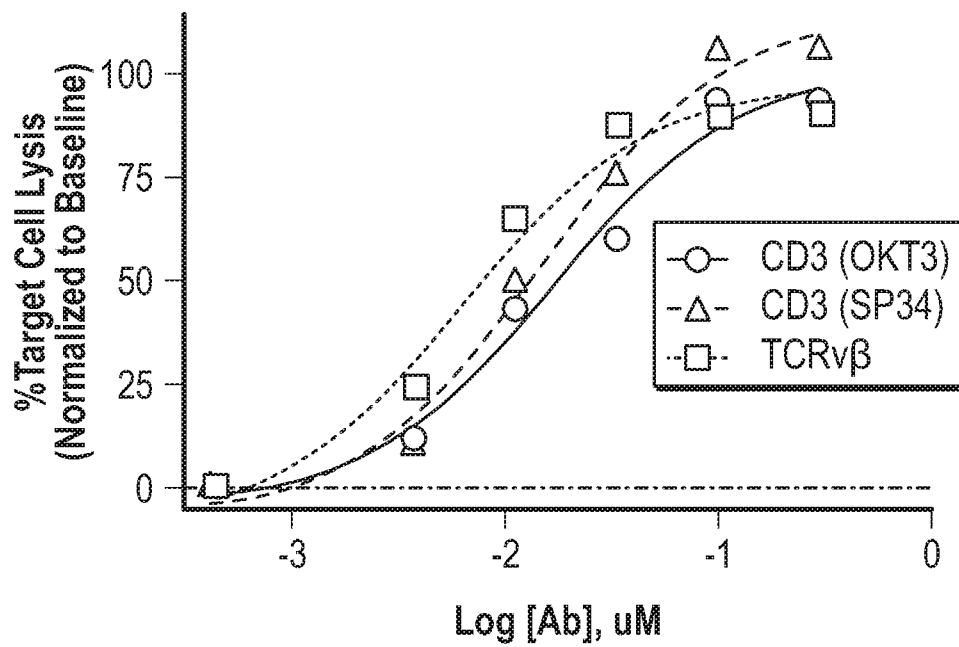


FIG. 13D

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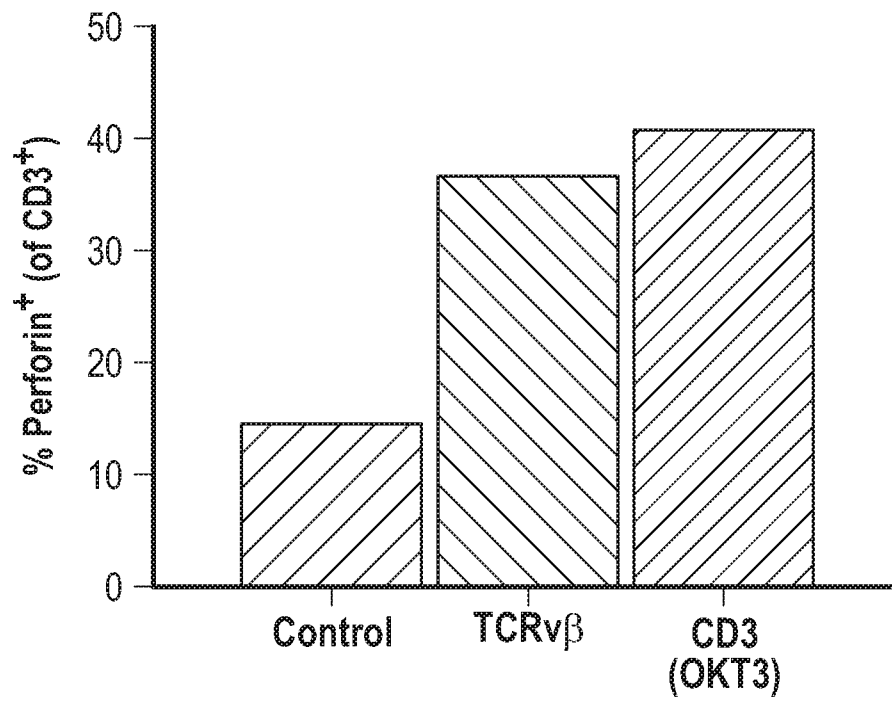


FIG. 13E

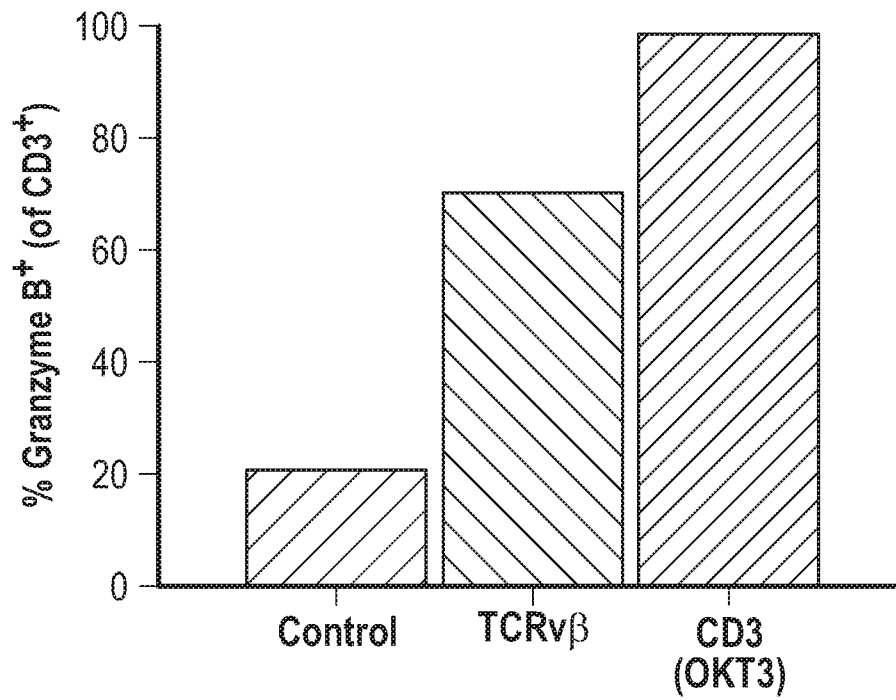


FIG. 13F

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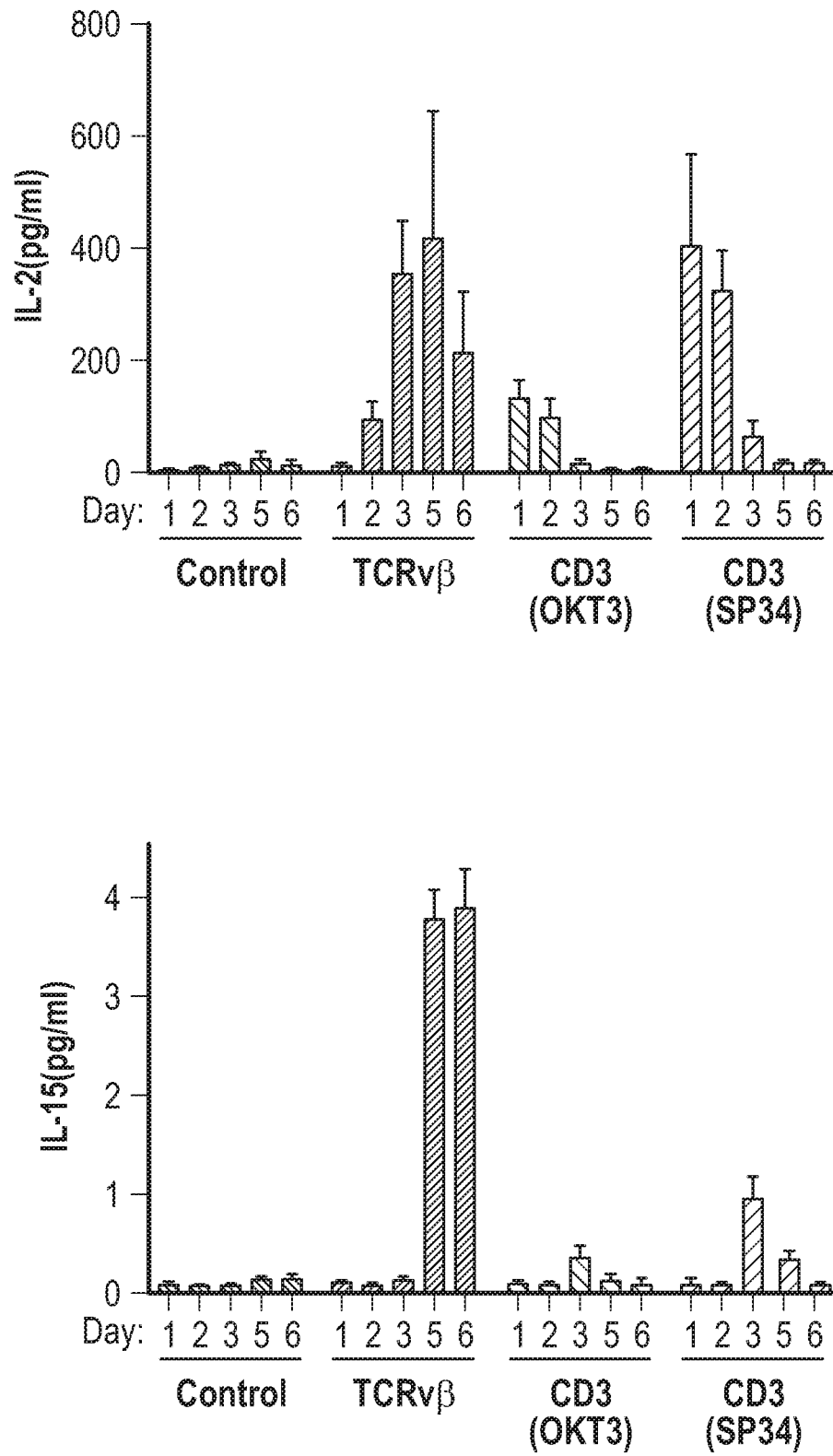


FIG. 14A

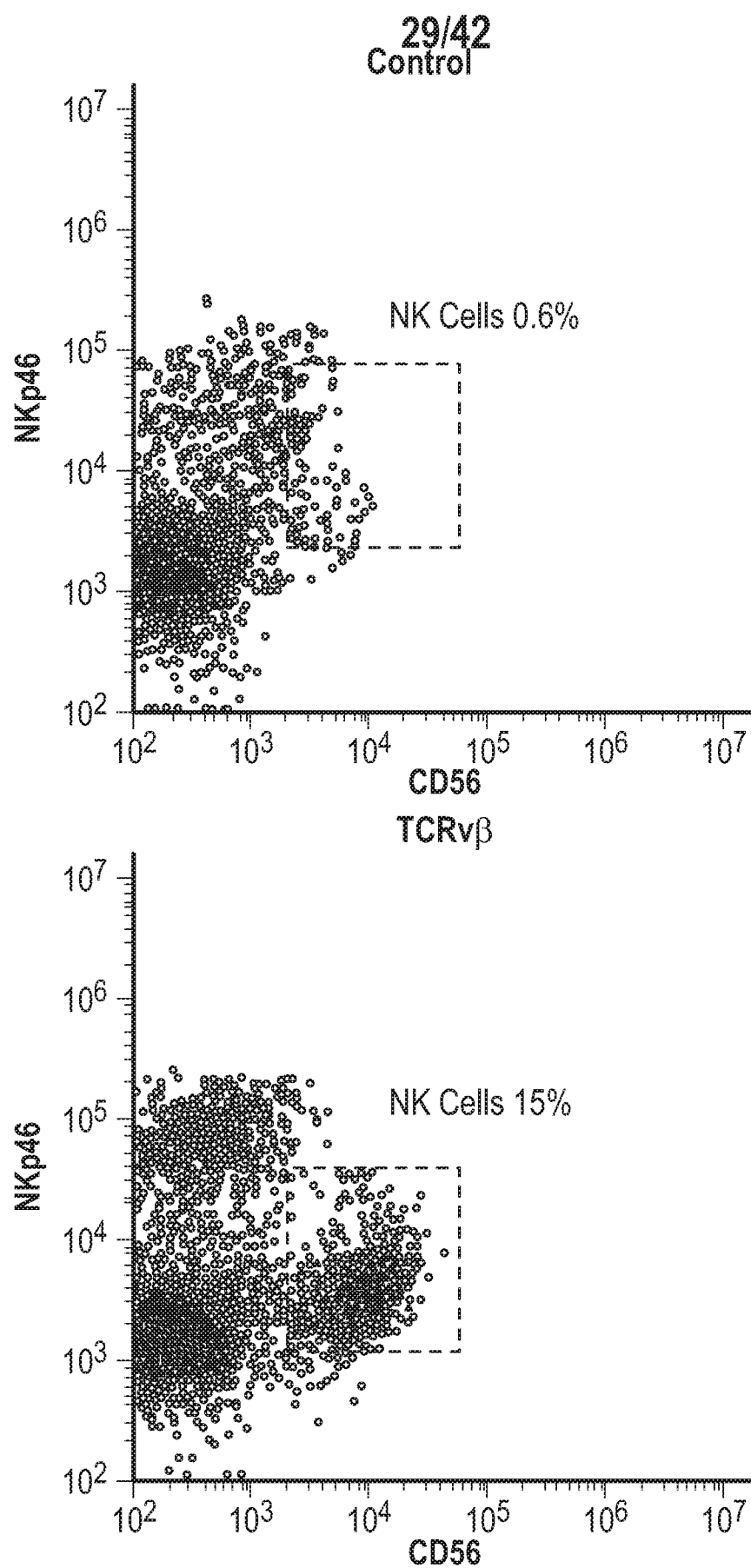


FIG. 14B

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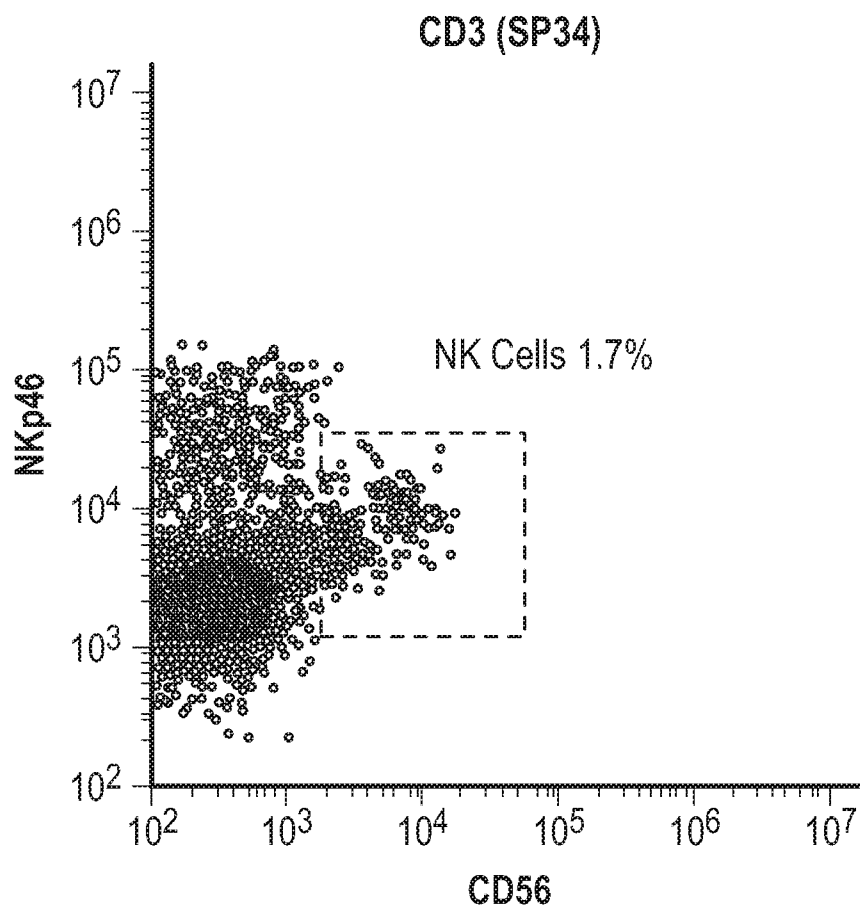


FIG. 14B
(Continued)

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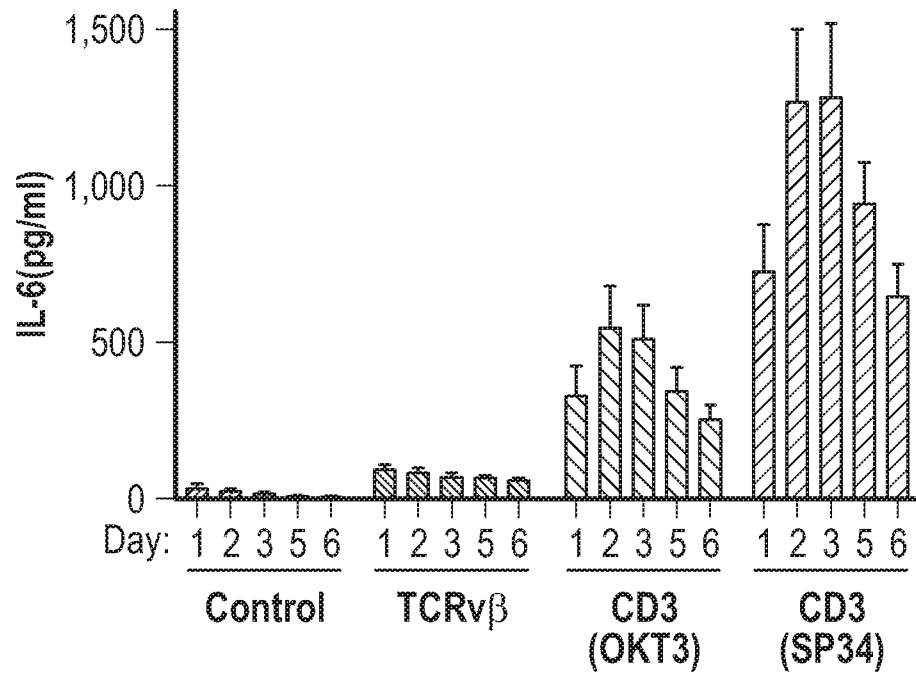


FIG. 15A

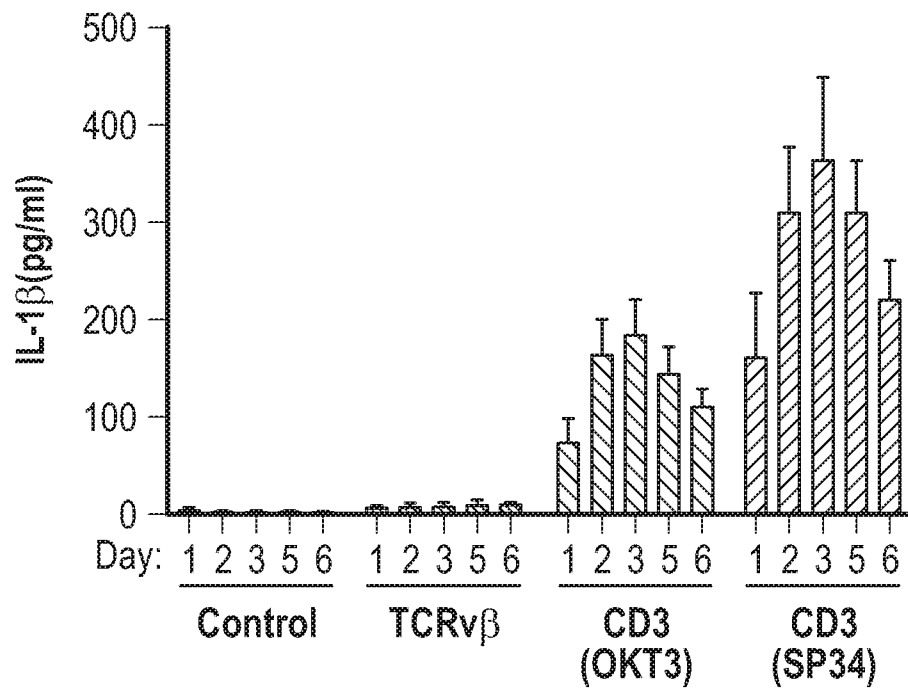


FIG. 15B

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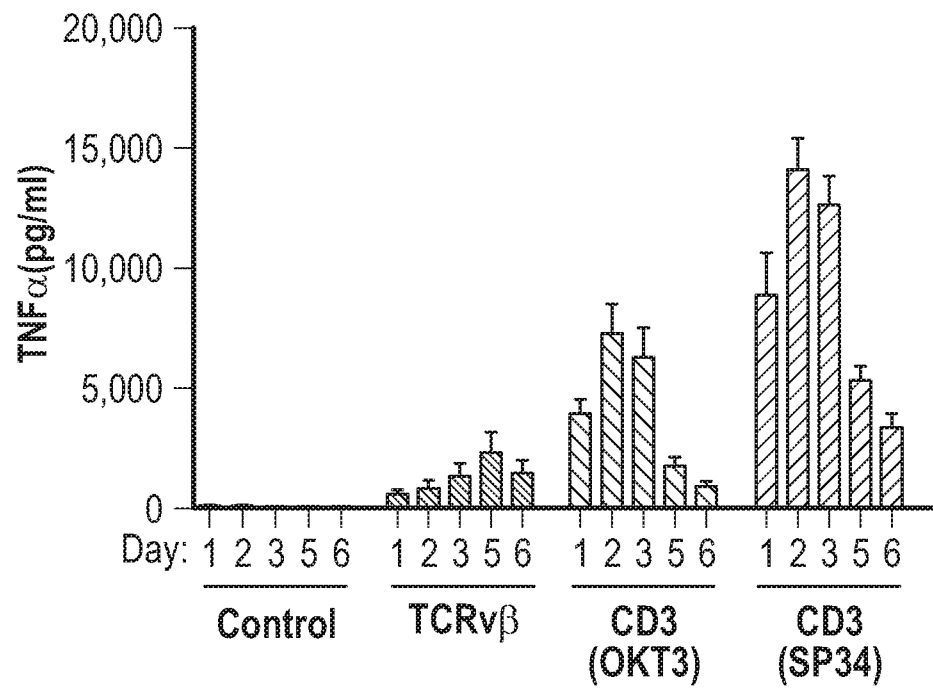


FIG. 15C

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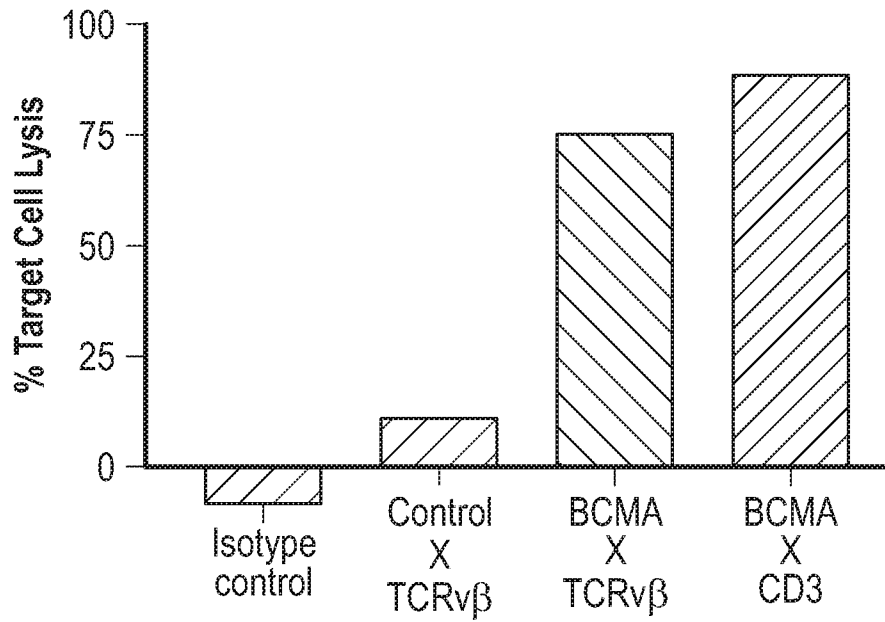


FIG. 16A

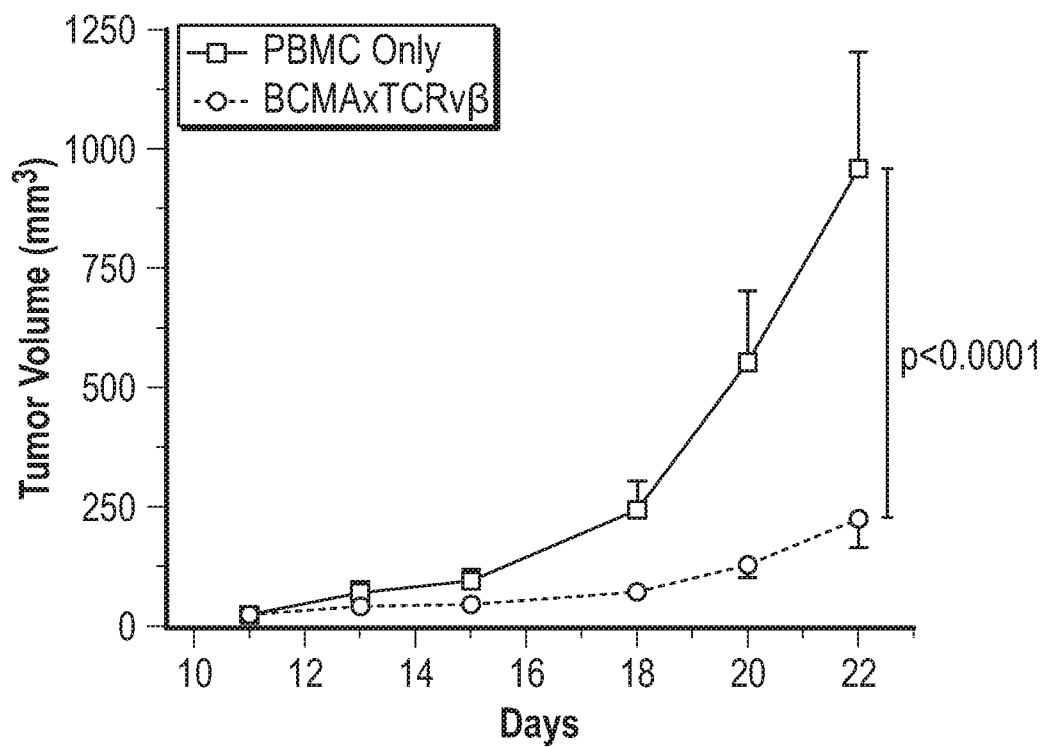


FIG. 16B

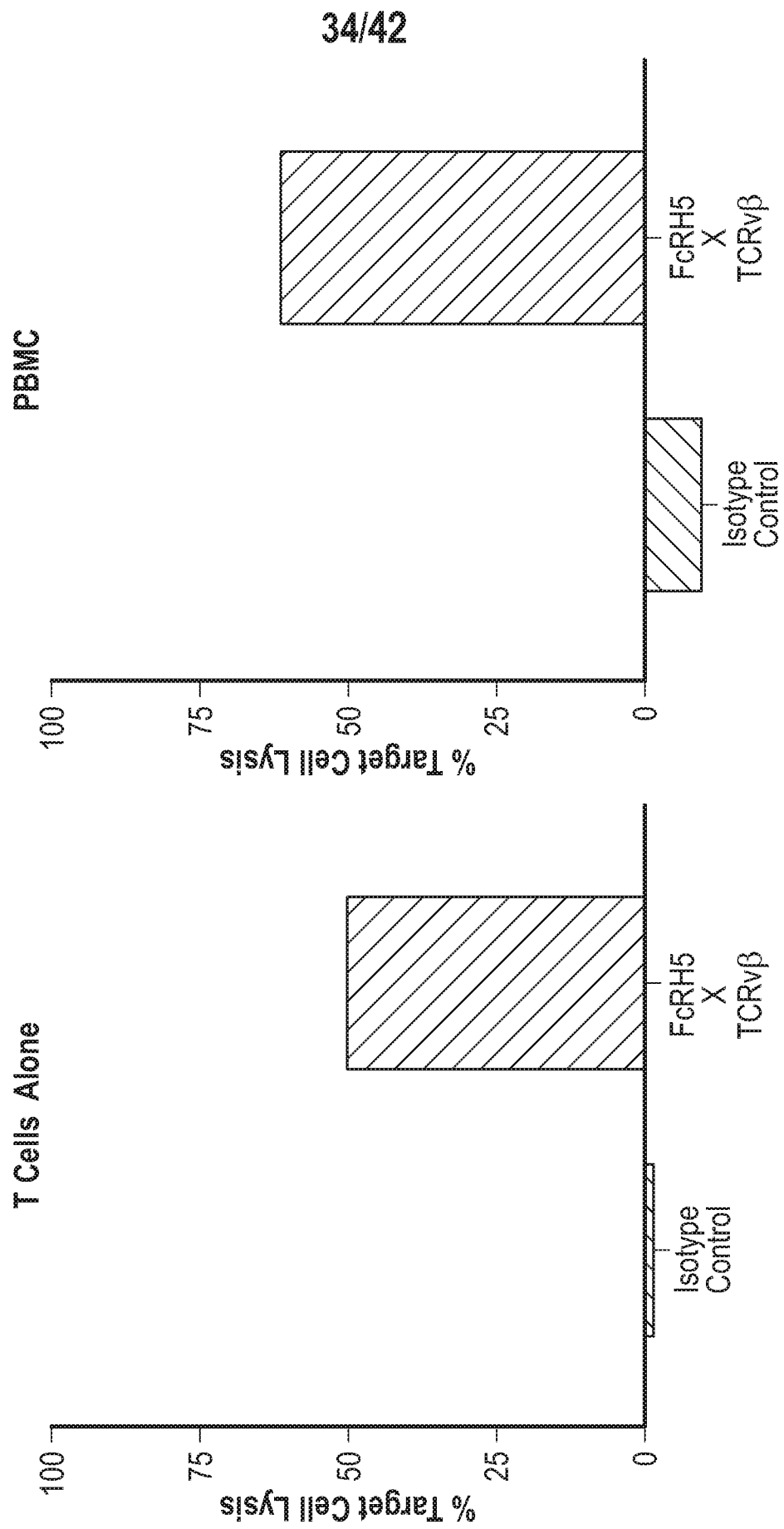


FIG. 17

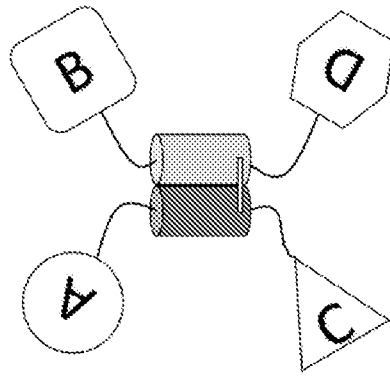


FIG. 18C

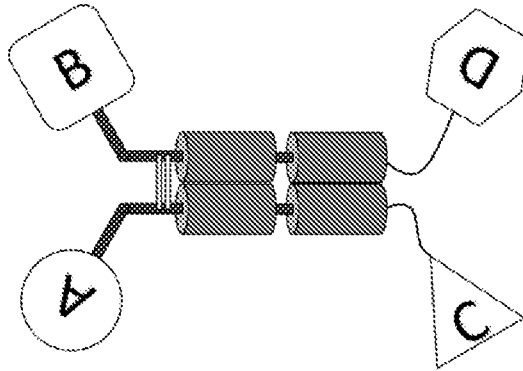


FIG. 18B

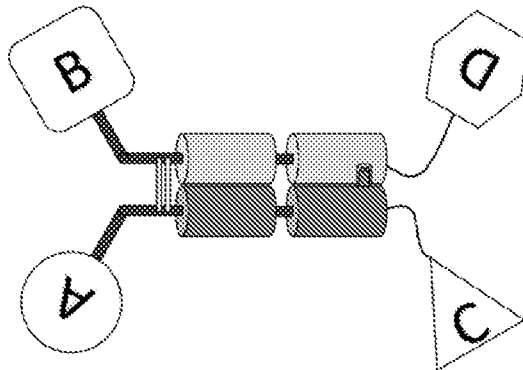


FIG. 18A

FIG. 19A

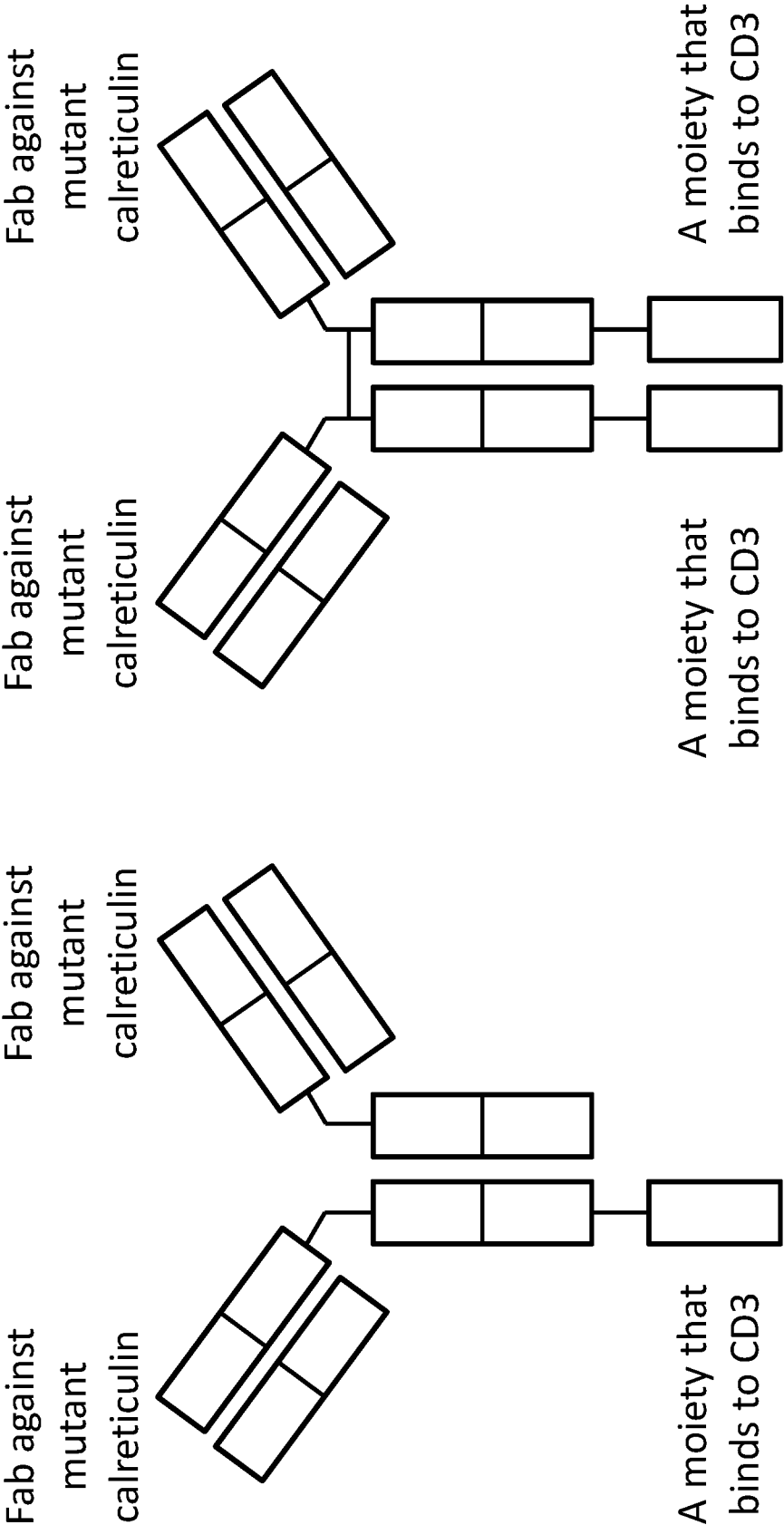


FIG. 19B

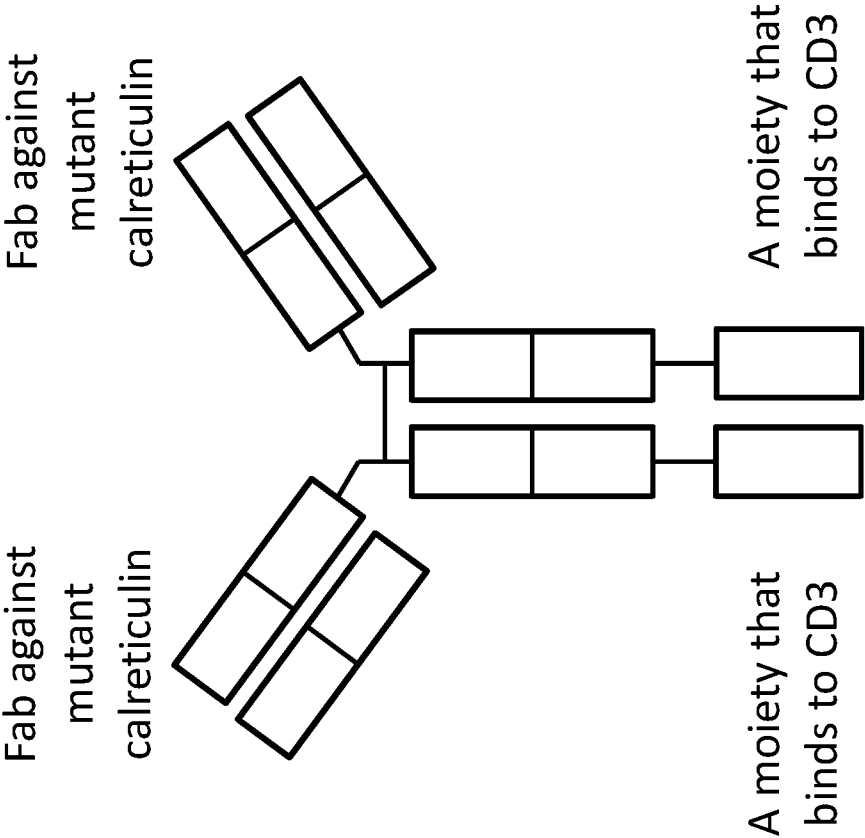


FIG. 20A

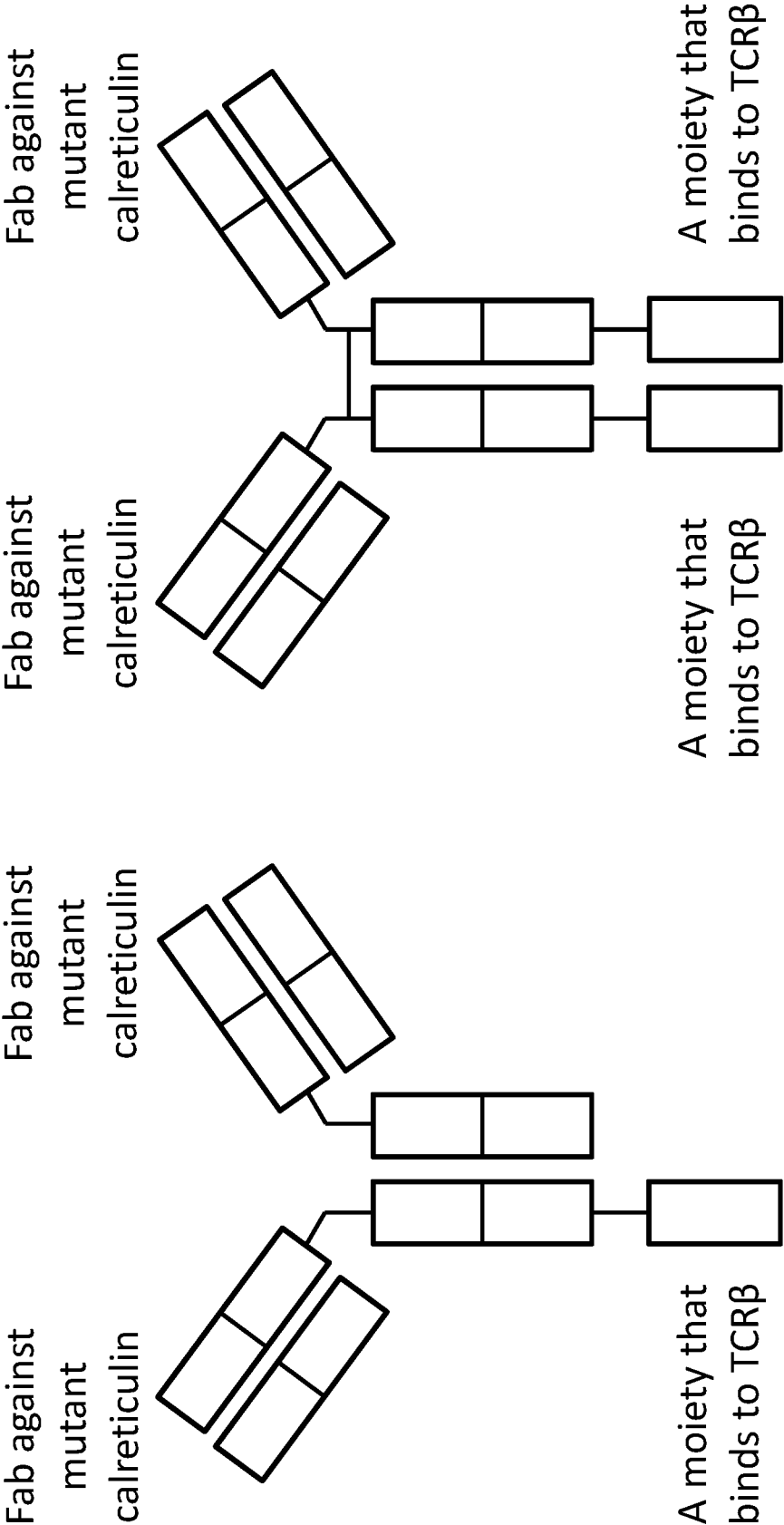


FIG. 20B

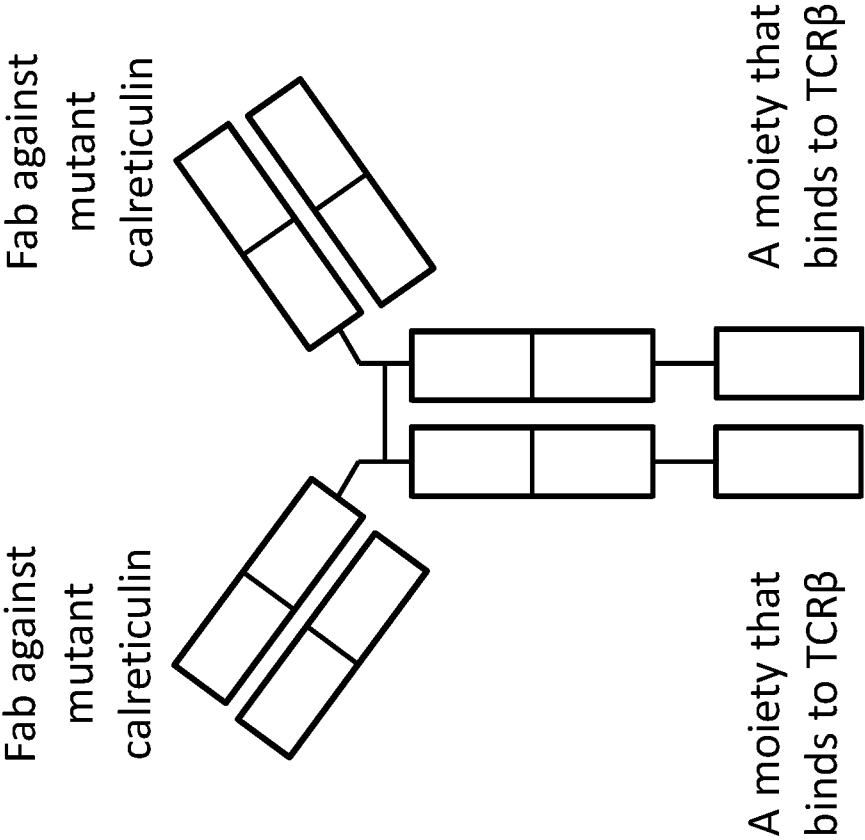


FIG. 21A

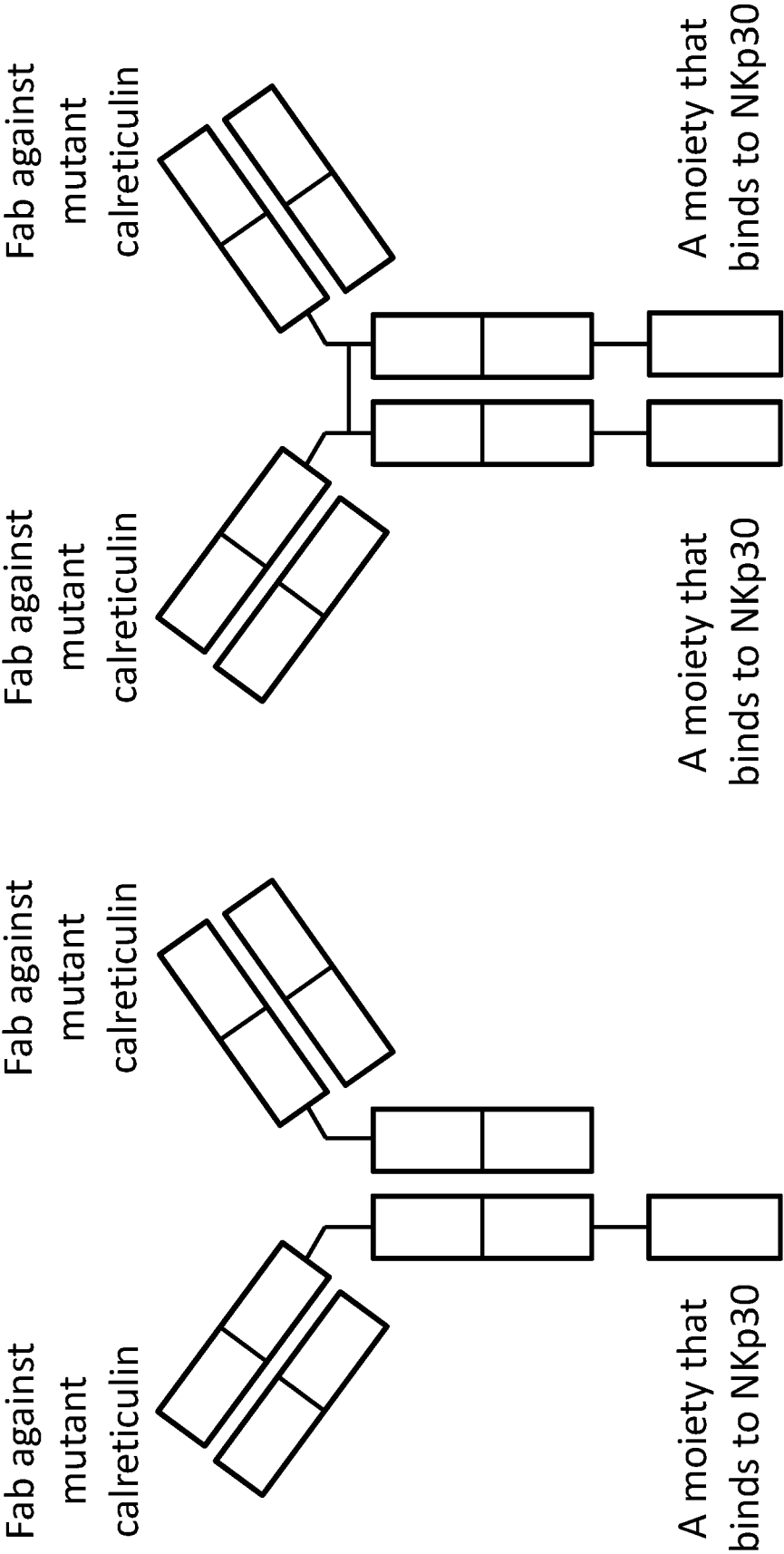
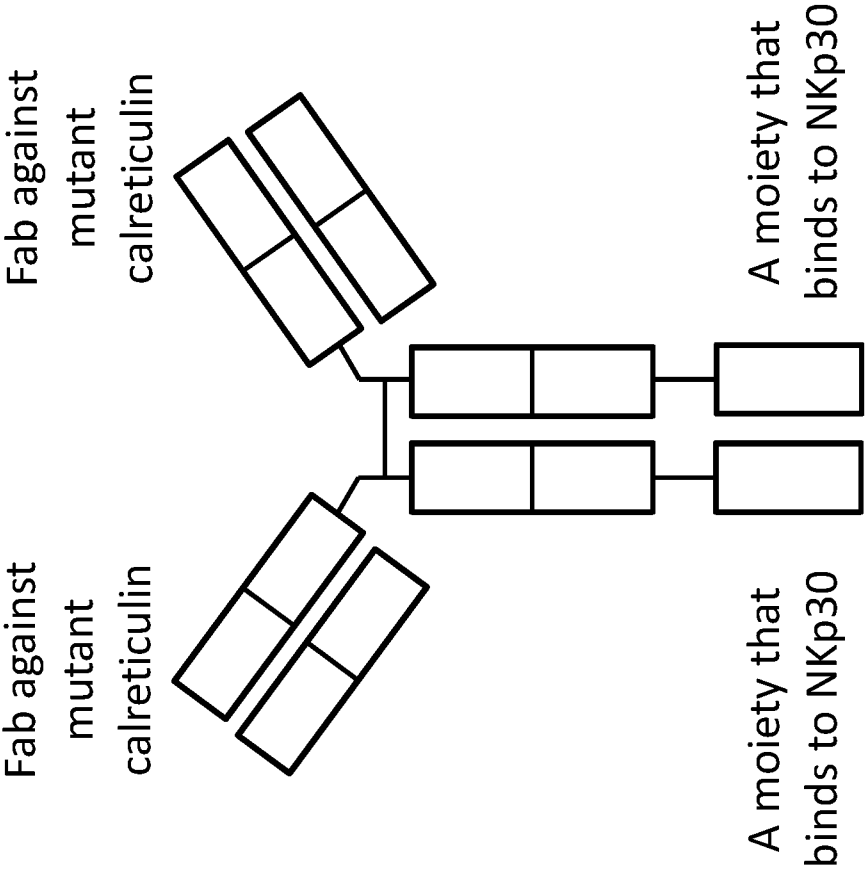


FIG. 21B



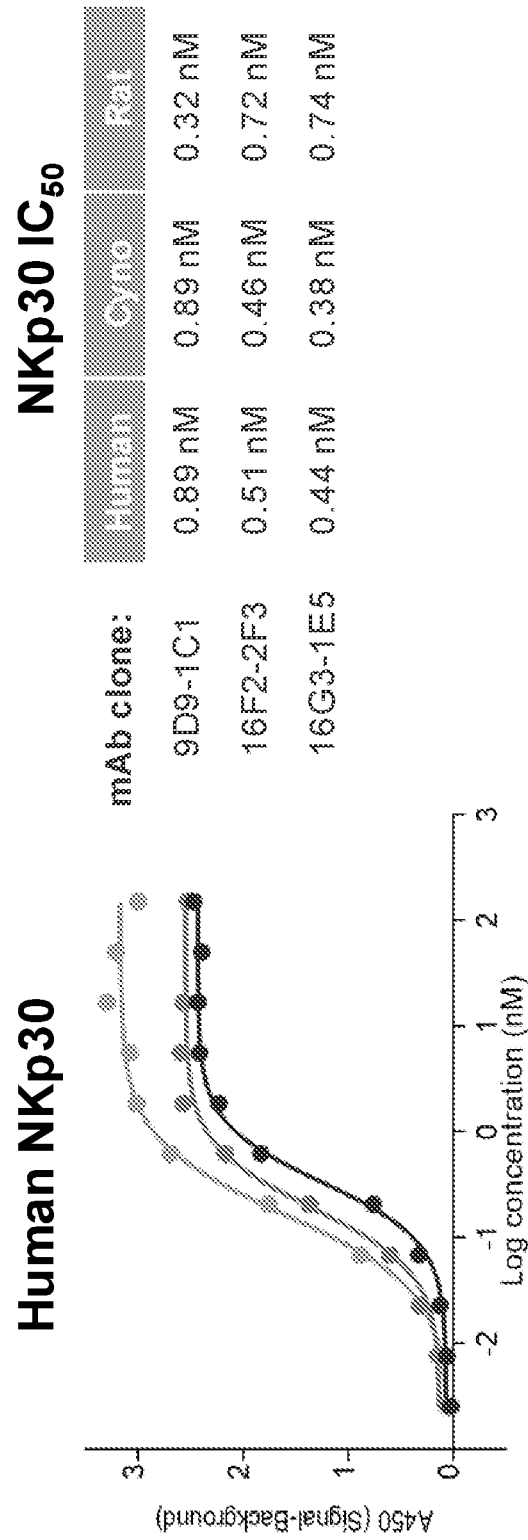


FIG. 22

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Activation of NK92 cells by NK p30 Ab

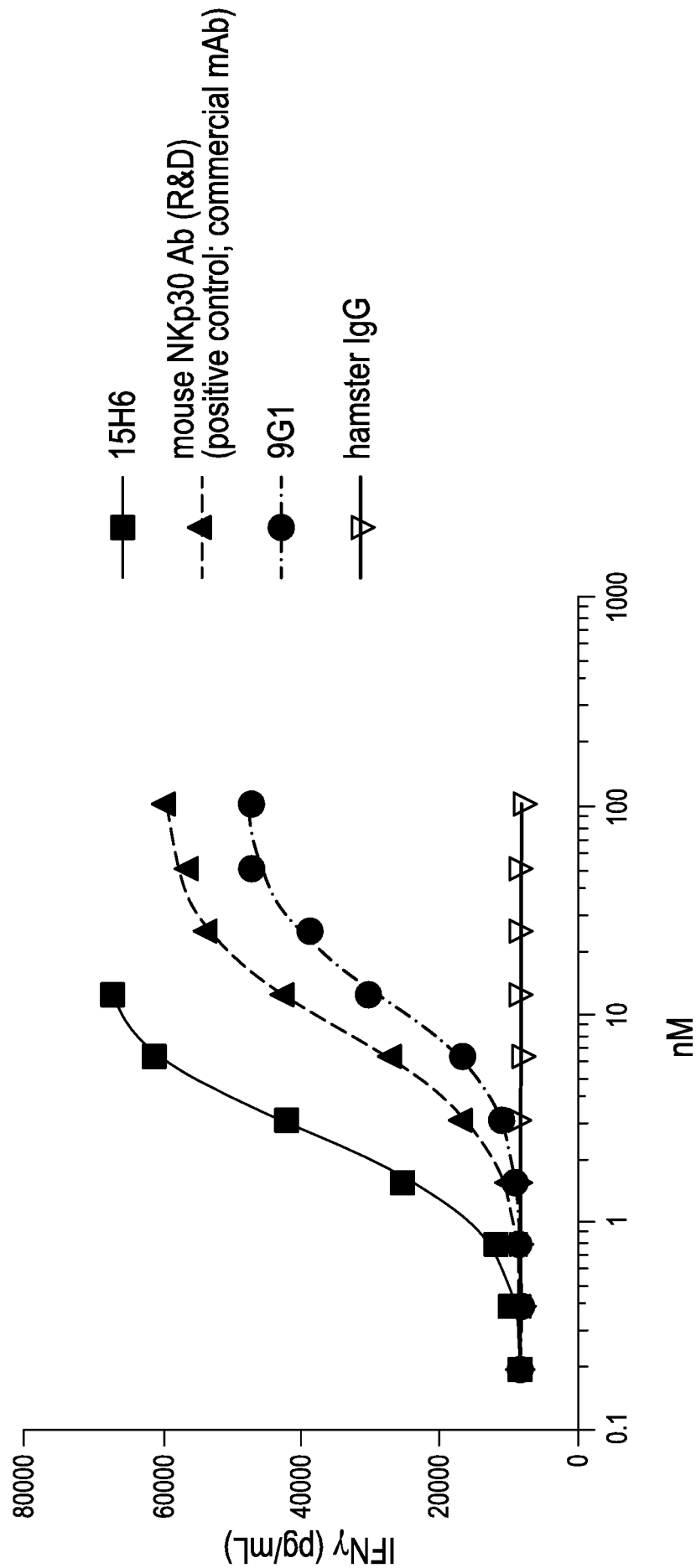


FIG. 23

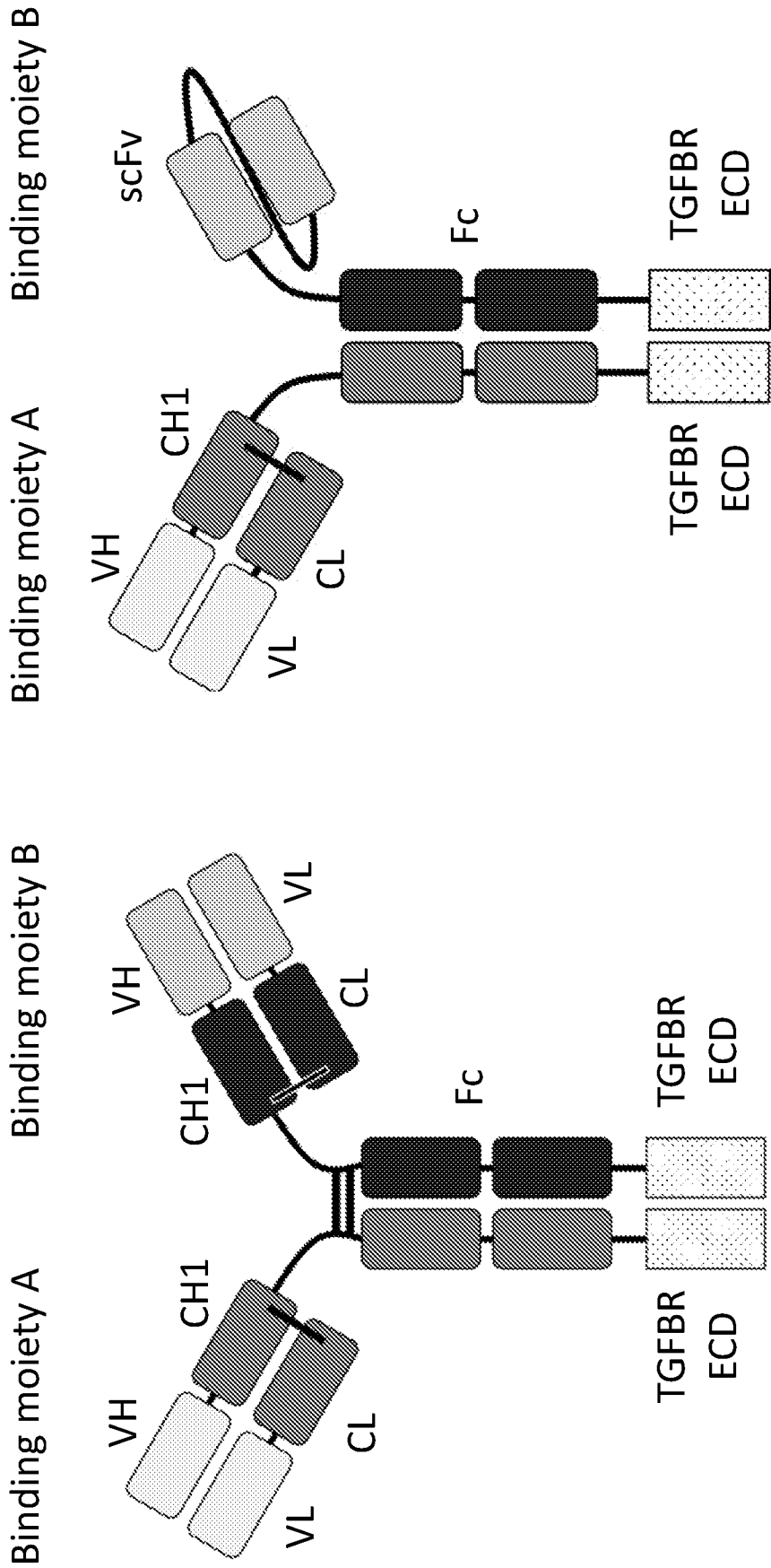


FIG. 24A

FIG. 24B

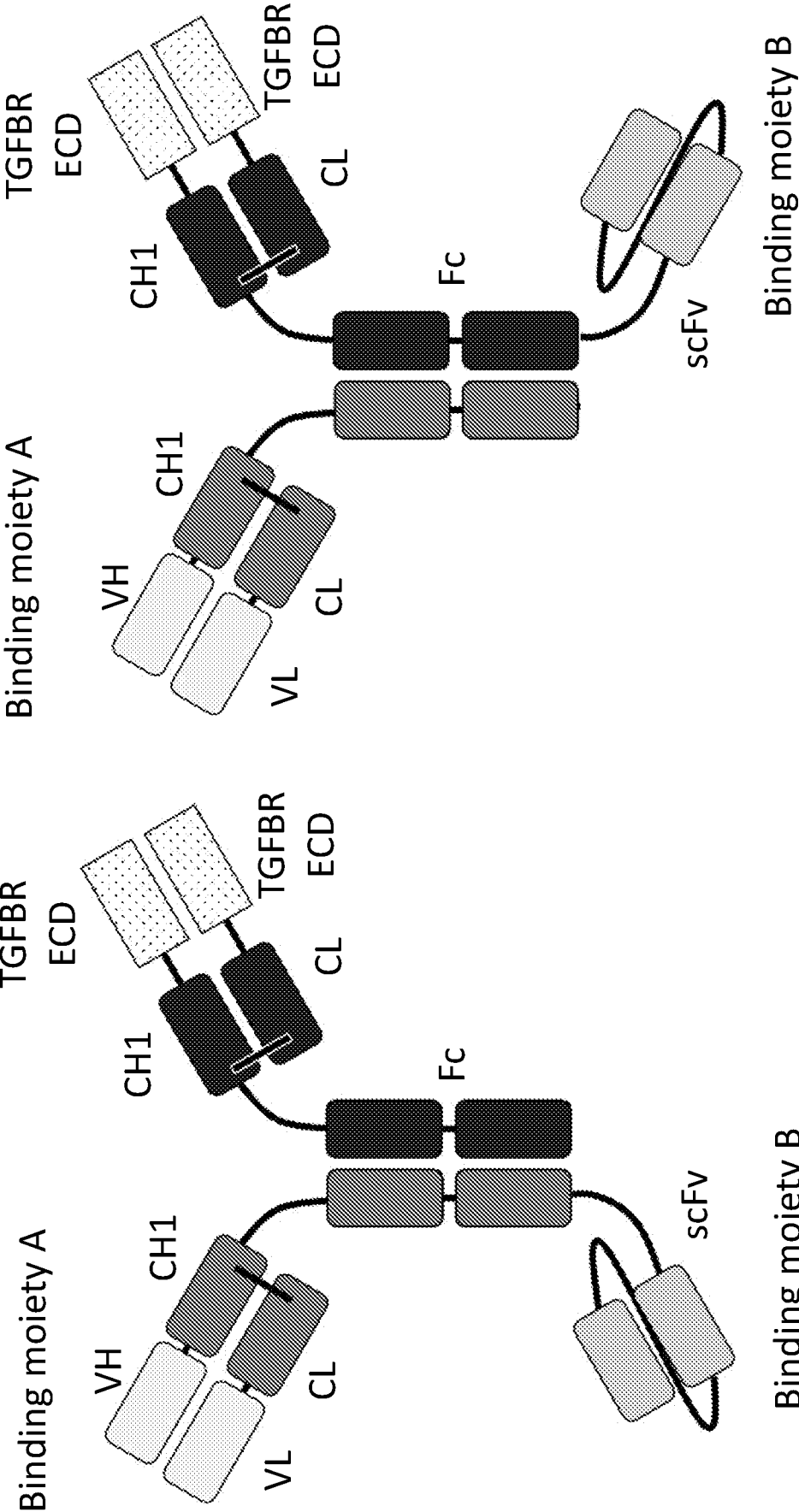


FIG. 24C

FIG. 24D