

WHAT IS CLAIMED IS:

1. An antibody or antigen-binding fragment thereof that binds to CD40 (TNF Receptor Superfamily Member 5) comprising:

a heavy chain variable region (VH) comprising complementarity determining regions (CDRs) 1, 2, and 3, wherein the VH CDR1 region comprises an amino acid sequence that is ~~at least 80%~~ identical to a selected VH CDR1 amino acid sequence, the VH CDR2 region comprises an amino acid sequence that is ~~at least 80%~~ identical to a selected VH CDR2 amino acid sequence, and the VH CDR3 region comprises an amino acid sequence that is ~~at least 80%~~ identical to a selected VH CDR3 amino acid sequence; and

a light chain variable region (VL) comprising CDRs 1, 2, and 3, wherein the VL CDR1 region comprises an amino acid sequence that is ~~at least 80%~~ identical to a selected VL CDR1 amino acid sequence, the VL CDR2 region comprises an amino acid sequence that is ~~at least 80%~~ identical to a selected VL CDR2 amino acid sequence, and the VL CDR3 region comprises an amino acid sequence that is ~~at least 80%~~ identical to a selected VL CDR3 amino acid sequence,

wherein the selected VH CDRs 1, 2, and 3 amino acid sequences and the selected VL CDRs, 1, 2, and 3 amino acid sequences are one of the following:

(1) the selected VH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1, 2, 3, respectively, and the selected VL CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 4, 5, 6, respectively, as defined by Kabat numbering; or, the selected VH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 19, 20, 3, respectively, and the selected VL CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 4, 21, 6, respectively, as defined by Chothia numbering;

(2) the selected VH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 7, 8, 9, respectively, and the selected VL CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 10, 11, 12, respectively, as defined by Kabat numbering; or, the selected VH CDRs 1, 2, 3 amino acid sequences are set

forth in SEQ ID NOs: 22, 23, 9, respectively, and the selected VL CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 10, 11, 12, respectively, as defined by Chothia numbering; or

(3) the selected VH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 13, 14, 15, respectively, and the selected VL CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 16, 17, 18, respectively, as defined by Kabat numbering; or, the selected VH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 24, 25, 15, respectively, and the selected VL CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 16, 17, 18, respectively, as defined by Chothia numbering.

2. The antibody or antigen-binding fragment thereof of claim 1, wherein the VH comprises CDRs 1, 2, 3 with the amino acid sequences set forth in SEQ ID NOs: 1, 2, and 3 respectively, and the VL comprises CDRs 1, 2, 3 with the amino acid sequences set forth in SEQ ID NOs: 4, 5, and 6, respectively, as defined by Kabat numbering; or, the selected VH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 19, 20, 3, respectively, and the selected VL CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 4, 21, 6, respectively, as defined by Chothia numbering.
3. The antibody or antigen-binding fragment thereof of claim 1, wherein the VH comprises CDRs 1, 2, 3 with the amino acid sequences set forth in SEQ ID NOs: 7, 8, and 9, respectively, and the VL comprises CDRs 1, 2, 3 with the amino acid sequences set forth in SEQ ID NOs: 10, 11, and 12, respectively, as defined by Kabat numbering; or, the selected VH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 22, 23, 9, respectively, and the selected VL CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 10, 11, 12, respectively, as defined by Chothia numbering.
4. The antibody or antigen-binding fragment thereof of claim 1, wherein the VH comprises CDRs 1, 2, 3 with the amino acid sequences set forth in SEQ ID NOs: 13, 14, and 15, respectively, and the VL comprises CDRs 1, 2, 3 with the amino acid sequences set forth in SEQ ID NOs: 16, 17, and 18, respectively, as defined

by Kabat numbering; or, the selected VH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 24, 25, 15, respectively, and the selected VL CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 16, 17, 18, respectively, as defined by Chothia numbering.

5. An antibody or antigen-binding fragment thereof that binds to ~~OX40~~CD40, comprising a heavy chain variable region comprising VH CDRs 1, 2, 3, and a light chain variable region comprising VL CDRs 1, 2, 3, wherein

- (1) the VH CDRs 1, 2, 3 are identical to complementarity determining regions in SEQ ID NO: 30, 31, 32, or 52, and the VL CDRs 1, 2, 3 are identical to complementary determining regions in SEQ ID NO: 33, 34, 35, 36, or 53;

- (2) the VH CDRs 1, 2, 3 are identical to complementarity determining regions in SEQ ID NO: 37, 38, 39, 40, or 54, and the VL CDRs 1, 2, 3 amino acid sequences are identical to complementary determining regions in SEQ ID NO: 41, 42, 43, or 55;

- (3) the VH CDRs 1, 2, 3 are identical to complementarity determining regions in SEQ ID NO: 44, 45, 46, 47, or 56, and the VL CDRs 1, 2, 3 are identical to complementary determining regions in SEQ ID NO: 48, 49, 50, 51, or 57.

6. An antibody or antigen-binding fragment thereof that binds to CD40 comprising a heavy chain variable region (VH) comprising an amino acid sequence that is ~~at least 90%~~-identical to a selected VH sequence, and a light chain variable region (VL) comprising an amino acid sequence that is ~~at least 90%~~-identical to a selected VL sequence, wherein the selected VH sequence and the selected VL sequence are one of the following:

- (1) the selected VH sequence is SEQ ID NO: 30, 31, 32, or 52, and the selected VL sequence is SEQ ID NO: 33, 34, 35, 36, or 53;

- (2) the selected VH sequence is SEQ ID NO: 37, 38, 39, 40, or 54, and the selected VL sequence is SEQ ID NO: 41, 42, 43, or 55;

- (3) the selected VH sequence is SEQ ID NO: 44, 45, 46, 47, or 56, and the selected VL sequence is SEQ ID NO: 48, 49, 50, 51, or 57.

7. The antibody or antigen-binding fragment thereof of claim 6, wherein the VH comprises the sequence of SEQ ID NO: 40 and the VL comprises the sequence of SEQ ID NO: 42.
8. The antibody or antigen-binding fragment thereof of claim 6, wherein the VH comprises the sequence of SEQ ID NO: 39 and the VL comprises the sequence of SEQ ID NO: 43.
9. The antibody or antigen-binding fragment thereof of any one of claims 1-8, wherein the antibody or antigen-binding fragment is a humanized antibody or antigen-binding fragment thereof, and/or wherein the antibody or antigen-binding fragment is a single-chain variable fragment (scFV).
10. A nucleic acid comprising a polynucleotide encoding a polypeptide comprising:
 - (1) an immunoglobulin heavy chain or a fragment thereof comprising a heavy chain variable region (VH) comprising complementarity determining regions (CDRs) 1, 2, and 3 comprising the amino acid sequences set forth in SEQ ID NOs: 1, 2, and 3, respectively, and wherein the VH, when paired with a light chain variable region (VL) comprising the amino acid sequence set forth in SEQ ID NO: 33, 34, 35, 36, or 53 binds to CD40;
 - (2) an immunoglobulin light chain or a fragment thereof comprising a VL comprising CDRs 1, 2, and 3 comprising the amino acid sequences set forth in SEQ ID NOs: 4, 5, and 6, respectively, and wherein the VL, when paired with a VH comprising the amino acid sequence set forth in SEQ ID NO: 30, 31, 32, or 52 binds to CD40;
 - (3) an immunoglobulin heavy chain or a fragment thereof comprising a heavy chain variable region (VH) comprising CDRs 1, 2, and 3 comprising the amino acid sequences set forth in SEQ ID NOs: 7, 8, and 9, respectively, and wherein the VH, when paired with a light chain variable region (VL) comprising the amino acid sequence set forth in SEQ ID NO: 41, 42, 43, or 55 binds to CD40;
 - (4) an immunoglobulin light chain or a fragment thereof comprising a VL comprising CDRs 1, 2, and 3 comprising the amino acid sequences set forth in SEQ ID NOs: 10, 11, and 12, respectively, and wherein the VL, when paired with

a VH comprising the amino acid sequence set forth in SEQ ID NO: 37, 38, 39, 40, or 54 binds to CD40;

(5) an immunoglobulin heavy chain or a fragment thereof comprising a heavy chain variable region (VH) comprising CDRs 1, 2, and 3 comprising the amino acid sequences set forth in SEQ ID NOs: 13, 14, 15, respectively, and wherein the VH, when paired with a light chain variable region (VL) comprising the amino acid sequence set forth in SEQ ID NO: 48, 49, 50, 51, or 57 binds to CD40;

(6) an immunoglobulin light chain or a fragment thereof comprising a VL comprising CDRs 1, 2, and 3 comprising the amino acid sequences set forth in SEQ ID NOs: 16, 17, and 18, respectively, and wherein the VL, when paired with a VH comprising the amino acid sequence set forth in SEQ ID NO: 44, 45, 46, 47, or 56 binds to CD40.

11. The nucleic acid of claim 10, wherein the nucleic acid comprises a polynucleotide encoding a polypeptide comprising an immunoglobulin heavy chain or a fragment thereof comprising a VH comprising CDRs 1, 2, and 3 comprising the amino acid sequences set forth in SEQ ID NOs: 1, 2, and 3, respectively, and ~~or~~ wherein the nucleic acid comprises a polynucleotide encoding a polypeptide comprising an immunoglobulin light chain or a fragment thereof comprising a VL comprising CDRs 1, 2, and 3 comprising the amino acid sequences set forth in SEQ ID NOs: 4, 5, and 6, respectively.
12. The nucleic acid of claim 10, wherein the nucleic acid comprises a polynucleotide encoding a polypeptide comprising an immunoglobulin heavy chain or a fragment thereof comprising a VH comprising CDRs 1, 2, and 3 comprising the amino acid sequences set forth in SEQ ID NOs: 7, 8, and 9, respectively, and ~~or~~ the nucleic acid comprises a polynucleotide encoding a polypeptide comprising an immunoglobulin light chain or a fragment thereof comprising a VL comprising CDRs 1, 2, and 3 comprising the amino acid sequences set forth in SEQ ID NOs: 10, 11, and 12, respectively.
13. The nucleic acid of claim 10, wherein the nucleic acid comprises a polynucleotide encoding a polypeptide comprising an immunoglobulin heavy chain or a fragment

thereof comprising a VH comprising CDRs 1, 2, and 3 comprising the amino acid sequences set forth in SEQ ID NOs: 13, 14, and 15, respectively, and/or wherein the nucleic acid comprises a polynucleotide encoding a polypeptide comprising an immunoglobulin light chain or a fragment thereof comprising a VL comprising CDRs 1, 2, and 3 comprising the amino acid sequences set forth in SEQ ID NOs: 16, 17, and 18, respectively.

14. A vector comprising one or more of the nucleic acids of any one of claims 10-13.
15. A cell comprising one or more of the nucleic acids of any one of claims 10-13.
16. A method of producing an antibody or an antigen-binding fragment thereof, the method comprising
 - (a) culturing the cell of any one of claim 15 under conditions sufficient for the cell to produce the antibody or the antigen-binding fragment; and
 - (b) collecting the antibody or the antigen-binding fragment produced by the cell.
17. An antibody-drug conjugate comprising the antibody or antigen-binding fragment thereof of any one of claims 1-9 covalently bound to a therapeutic agent.
18. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-9, and a pharmaceutically acceptable carrier.
19. A pharmaceutical composition for use in the treatment or prevention of a cancer, the pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-9, wherein the cancer is selected from melanoma, pancreatic carcinoma, mesothelioma, hematological malignancy, Non-Hodgkin's lymphoma, lymphoma, or chronic lymphocytic leukemia.
20. A pharmaceutical composition, comprising the antibody drug conjugate of claim 17, and a pharmaceutically acceptable carrier.