

WHAT IS CLAIMED IS:

1. An antibody or antigen-binding fragment thereof that binds to OX40 (TNF Receptor Superfamily Member 4) 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 identical to a selected VH CDR1 amino acid sequence, the VH CDR2 region comprises an amino acid sequence that is identical to a selected VH CDR2 amino acid sequence, and the VH CDR3 region comprises an amino acid sequence that is 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 identical to a selected VL CDR1 amino acid sequence, the VL CDR2 region comprises an amino acid sequence that is identical to a selected VL CDR2 amino acid sequence, and the VL CDR3 region comprises an amino acid sequence that is 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;

(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;

(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; and

(4) the selected VH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 19, 20, 21, respectively, and the selected VL CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 22, 23, 24, respectively.

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.

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: 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.

4. The antibody or antigen-binding fragment thereof of any one of claims 1-4, wherein the antibody or antigen-binding fragment is a humanized antibody or antigen-binding fragment thereof, or a single-chain variable fragment (scFV).

5. 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: 56, 57, 58, or 80, binds to OX40;
- (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: 53, 54, 55, or 79, binds to OX40;

- (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: 62, 63, 64, 65, or 82, binds to OX40; or
- (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: 59, 60, 61, or 81, binds to OX40;
- (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, and 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 NOs: 69, 70, 71, 72, or 84 binds to OX40;
- (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 NOs: 66, 67, 68, or 83, binds to OX40;
- (7) 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: 19, 20, and 21, respectively, and wherein the VH, when paired with a light chain variable region (VL) comprising the amino acid sequence set forth in SEQ ID NOs: 76, 77, 78, or 86, binds to OX40;
- (8) 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: 22, 23, and 24, respectively, and wherein the VL, when paired

with a VH comprising the amino acid sequence set forth in SEQ ID NO: 73, 74, 75, or 85, binds to OX40.

6. A vector comprising one or more of the nucleic acids of claim 5.
7. A cell comprising the vector of claim 6.
8. The cell of claim 7, wherein the cell is a CHO cell.
9. A method of producing an antibody or an antigen-binding fragment thereof, the method comprising
 - (a) culturing the cell of claim 7 or 8 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.
10. An antibody or antigen-binding fragment thereof that binds to OX40 comprising a heavy chain variable region (VH) comprising an amino acid sequence that is identical to a selected VH sequence, and a light chain variable region (VL) comprising an amino acid sequence that is 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: 53, 54, 55, or 79, and the selected VL sequence is SEQ ID NO: 56, 57, 58, or 80;
 - (2) the selected VH sequence is SEQ ID NO: 59, 60, 61, or 81, and the selected VL sequence is SEQ ID NO: 62, 63, 64, 65, or 82;
 - (3) the selected VH sequence is SEQ ID NO: 66, 67, 68, or 83, and the selected VL sequence is SEQ ID NO: 69, 70, 71, 72, or 84;
 - (4) the selected VH sequence is SEQ ID NO: 73, 74, 75, or 85, and the selected VL sequence is SEQ ID NO: 76, 77, 78, or 86.

11. The antibody or antigen-binding fragment thereof of claim 10, wherein the VH comprises the sequence of SEQ ID NO: 53 and the VL comprises the sequence of SEQ ID NO: 56.

12. The antibody or antigen-binding fragment thereof of claim 10, wherein the VH comprises the sequence of SEQ ID NO: 55 and the VL comprises the sequence of SEQ ID NO: 58.

13. The antibody or antigen-binding fragment thereof of claim 10, wherein the VH comprises the sequence of SEQ ID NO: 55 and the VL comprises the sequence of SEQ ID NO: 56.

14. The antibody or antigen-binding fragment thereof of claim 10, wherein the VH comprises the sequence of SEQ ID NO: 73 and the VL comprises the sequence of SEQ ID NO: 77.

~~15. An antibody or antigen-binding fragment thereof that binds to OX40, 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: 53, 54, 55, or 79, and the VL CDRs 1, 2, 3 are identical to complementary determining regions in SEQ ID NO: 56, 57, 58, or 80;~~

~~(2) the VH CDRs 1, 2, 3 are identical to complementarity determining regions in SEQ ID NO: 59, 60, 61, or 81, and the VL CDRs 1, 2, 3 amino acid sequences are identical to complementary determining regions in SEQ ID NO: 62, 63, 64, 65, or 82;~~

~~(3) the VH CDRs 1, 2, 3 are identical to complementarity determining regions in SEQ ID NO: 66, 67, 68, or 83, and the VL CDRs 1, 2, 3 are identical to complementary determining regions in SEQ ID NO: 69, 70, 71, 72, or 84; or—~~

~~(4) the VH CDRs 1, 2, 3 are identical to complementarity determining regions in SEQ ID NO: 73, 74, 75, or 85, and the VL CDRs 1, 2, 3 are identical to complementarity determining regions in SEQ ID NO: 76, 77, 78, or 86.~~

~~16~~15. An antibody-drug conjugate comprising the antibody or antigen-binding fragment thereof of any one of claims 1-4 and ~~10-15~~14 covalently bound to a therapeutic agent.

~~17~~16. The antibody drug conjugate of claim ~~16~~15, wherein the therapeutic agent is a cytotoxic or cytostatic agent.

~~18~~17. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-4 and ~~10-15~~14, and a pharmaceutically acceptable carrier.

~~19~~18. A pharmaceutical composition comprising the antibody drug conjugate of claim ~~16-15~~15 or ~~17~~16, and a pharmaceutically acceptable carrier.

~~20~~19. Use of the antibody or antigen-binding fragment thereof of any one of claims 1-4 and ~~10-15~~14 in the manufacture of a medicament for preventing or treating a cancer, wherein the cancer is selected from unresectable melanoma, metastatic melanoma, sarcoma, small cell lung cancer, non-small cell lung cancer (NSCLC), squamous cell carcinoma of the head and neck (SCCHN), renal cell carcinoma (RCC), melanoma, bladder, triple-negative breast cancer (TNBC), and colorectal carcinoma.