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 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;

(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;

(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 1-3, wherein the antibody or antigen-binding fragment specifically binds to human OX40.

5. 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.

6. The antibody or antigen-binding fragment thereof of any one of claims 1-5, wherein the antibody or antigen-binding fragment is a single-chain variable fragment (scFV).

7. 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.

8. The nucleic acid of claim 7, 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.

9. The nucleic acid of claim 7, 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.

10. The nucleic acid of claim 7, 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.

11. The nucleic acid of claim 7, 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.

12. The nucleic acid of any one of claims 7-11, wherein the VH when paired with a VL specifically binds to human OX40, or the VL when paired with a VH specifically binds to human OX40.

13. The nucleic acid of any one of claims 7-12, wherein the immunoglobulin heavy chain or the fragment thereof is a humanized immunoglobulin heavy chain or a fragment thereof, and the immunoglobulin light chain or the fragment thereof is a humanized immunoglobulin light chain or a fragment thereof.

14. The nucleic acid of any one of claims 7-13, wherein the nucleic acid encodes a single-chain variable fragment (scFv).

15. The nucleic acid of any one of claims 7-14, wherein the nucleic acid is cDNA.

16. A vector comprising one or more of the nucleic acids of any one of claims 7-15.

17. A vector comprising two of the nucleic acids of any one of claims 7-15, wherein the vector encodes the VL region and the VH region that together bind to OX40.

18. A pair of vectors, wherein each vector comprises one of the nucleic acids of any one of claims 7-15, wherein together the pair of vectors encodes the VL region and the VH region that together bind to OX40.

19. A cell comprising the vector of claim 16 or 17, or the pair of vectors of claim 18.

20. The cell of claim 19, wherein the cell is a CHO cell.

21. A cell comprising one or more of the nucleic acids of any one of claims 7-15.

22. A cell comprising two of the nucleic acids of any one of claims 7-15.

23. The cell of claim 22, wherein the two nucleic acids together encode the VL region and the VH region that together bind to OX40.

24. A method of producing an antibody or an antigen-binding fragment thereof, the method comprising

(a) culturing the cell of any one of claims 19-23 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.

25. 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 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: 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.

26. The antibody or antigen-binding fragment thereof of claim 25, wherein the VH comprises the sequence of SEQ ID NO: 53 and the VL comprises the sequence of SEQ ID NO: 56.

27. The antibody or antigen-binding fragment thereof of claim 25, wherein the VH comprises the sequence of SEQ ID NO: 55 and the VL comprises the sequence of SEQ ID NO: 58.

28. The antibody or antigen-binding fragment thereof of claim 25, wherein the VH comprises the sequence of SEQ ID NO: 55 and the VL comprises the sequence of SEQ ID NO: 56.

29. The antibody or antigen-binding fragment thereof of claim 25, wherein the VH comprises the sequence of SEQ ID NO: 73 and the VL comprises the sequence of SEQ ID NO: 77.

30. The antibody or antigen-binding fragment thereof of any one of claims 25-29, wherein the antibody or antigen-binding fragment specifically binds to human OX40.

31. The antibody or antigen-binding fragment thereof of any one of claims 25-30, wherein the antibody or antigen-binding fragment is a humanized antibody or antigen-binding fragment thereof.

32. The antibody or antigen-binding fragment thereof of any one of claims 25-31, wherein the antibody or antigen-binding fragment is a single-chain variable fragment (scFV).

33. An antibody-drug conjugate comprising the antibody or antigen-binding fragment thereof of any one of claims 1-6 and 25-32 covalently bound to a therapeutic agent.

34. The antibody drug conjugate of claim 33, wherein the therapeutic agent is a cytotoxic or cytostatic agent.

35. A method of treating a subject having cancer, the method comprising administering a therapeutically effective amount of a composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-6 and 25-32, or the antibody-drug conjugate of claims 33 or 34, to the subject.

36. The method of claim 35, wherein the subject has a solid tumor.

37. The method of claim 35, wherein the cancer is unresectable melanoma or metastatic melanoma.

38. The method of claim 35, wherein the cancer is 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), or colorectal carcinoma.

39. A method of decreasing the rate of tumor growth, the method comprising contacting a tumor cell with an effective amount of a composition comprising an antibody or antigen-binding fragment thereof of any one of claims 1-6 and 25-32, or the antibody-drug conjugate of claims 33 or 34.

40. A method of killing a tumor cell, the method comprising contacting a tumor cell with an effective amount of a composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-6 and 25-32, or the antibody-drug conjugate of claims 33 or 34.

41. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-6 and 25-32, and a pharmaceutically acceptable carrier.

42. A pharmaceutical composition comprising the antibody drug conjugate of claim 33 or 34, and a pharmaceutically acceptable carrier.