

CLAIMS

1. An isolated anti-OX40 antibody or antigen-binding fragment thereof, comprising
(1) one to three selected from HCDR1, HCDR2 and HCDR3 of a heavy chain variable region
5 (VH), wherein the amino acid sequence of the VH is as set forth in SEQ ID NO: 1, 2, 3, 4 or 5;
and/or

(2) one to three selected from LCDR1, LCDR2 and LCDR3 of a light chain variable region
(VL), wherein the amino acid sequence of the VL is as set forth in SEQ ID NO: 6, 7, 8, 9 or 10;

Wherein, the antibody or antigen-binding fragment thereof does not comprise an Fc region
10 variant which is human IgG1 N297A.

2. The antibody or antigen-binding fragment thereof of claim 1, comprising HCDR1,
HCDR2 and HCDR3 of the VH and LCDR1, LCDR2 and LCDR3 of the VL, wherein the VH and
VL are selected from

15 (1) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 1, and a VL
comprising the amino acid sequence as set forth in SEQ ID NO: 6;

(2) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 2, and a VL
comprising the amino acid sequence as set forth in SEQ ID NO: 7 or 9;

(3) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 3, and a VL
20 comprising the amino acid sequence as set forth in SEQ ID NO: 9; or

(4) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 4 and a VL
comprising the amino acid sequence as set forth in SEQ ID NO: 7 or 8.

3. An isolated anti-OX40 antibody or antigen-binding fragment thereof, comprising
25 (1) one to three selected from heavy chain complementary determining region 1 (HCDR1),
HCDR2 and HCDR3, wherein the HCDR1 comprises the amino acid sequence as set forth in SEQ
ID NO: 11, the HCDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 12, and the
HCDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 13; and/or

(2) one to three selected from light chain complementary determining region 1 (LCDR1),
30 LCDR2 and LCDR3, wherein the LCDR1 comprises the amino acid sequence as set forth in SEQ
ID NO: 14, the LCDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 15, and the
LCDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 16;

Wherein, the antibody or antigen-binding fragment thereof does not comprise an Fc region
variant which is human IgG1 N297A.

4. The antibody or antigen-binding fragment thereof of any one of claims 1-3, comprising
(1) heavy chain complementary determining regions (HCDRs), HCDR1, HCDR2 and HCDR3,
wherein the HCDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 11, the
HCDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 12, and the HCDR3
5 comprises the amino acid sequence as set forth in SEQ ID NO: 13; and/or

(2) light chain complementary determining regions (LCDRs), LCDR1, LCDR2 and LCDR3,
wherein the LCDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 14, the LCDR2
comprises the amino acid sequence as set forth in SEQ ID NO: 15, and the LCDR3 comprises the
amino acid sequence as set forth in SEQ ID NO: 16.

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5. The antibody or antigen-binding fragment thereof of any one of claims 1-3, comprising
(1) a heavy chain variable region (VH) comprising an amino acid sequence identical to or
having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the
amino acid sequence as set forth in SEQ ID NO: 1, 2, 3, 4 or 5; and/or
15 (2) a light chain variable region (VL) comprising an amino acid sequence identical to or
having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to the
amino acid sequence as set forth in SEQ ID NO: 6, 7, 8, 9 or 10.

6. The antibody or antigen-binding fragment thereof of any one of claims 1-3, comprising a
20 heavy chain variable region (VH) and/or a light chain variable region (VL), wherein the VH
comprises the amino acid sequence as set forth in any one of SEQ ID NO: 2, 3, 4 or 5, and the VL
comprises the amino acid sequence as set forth in any one of SEQ ID NO: 7, 8, 9 or 10.

7. The antibody or antigen-binding fragment thereof of claim 6, comprising a heavy chain
25 variable region (VH) and a light chain variable region (VL), wherein the VH and VL are selected
from

(1) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 1, and a VL
comprising the amino acid sequence as set forth in SEQ ID NO: 6;

(2) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 2, and a VL
30 comprising the amino acid sequence as set forth in SEQ ID NO: 7 or 9;

(3) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 3, and a VL
comprising the amino acid sequence as set forth in SEQ ID NO: 9; or

(4) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 4 and a VL
comprising the amino acid sequence as set forth in SEQ ID NO: 7 or 8.

8. The antibody or antigen-binding fragment thereof of claim 7, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises the amino acid sequence as set forth in SEQ ID NO: 2, and wherein the VL comprises the amino acid sequence as set forth in SEQ ID NO: 7.

9. The antibody or antigen-binding fragment thereof of any of the preceding claims, which is a murine antibody, a chimeric antibody or a humanized antibody.

10. The antibody or antigen-binding fragment thereof of any of the preceding claims, which is a full-length antibody, a single-domain antibody (such as a VHH), a Fab, a Fab' antibody, a Fab'-SH, a (Fab')₂ antibody, a single-chain antibody (such as a scFv), a Fv, a dAb (domain antibody) or a bis(multi)-specific antibody.

11. The antibody or antigen-binding fragment thereof of any of the preceding claims, comprising an Fc region, wherein the amino acid sequence of the Fc region is identical to the sequence of the Fc region of human IgG1, IgG2 or IgG4, or is a variant thereof.

12. The antibody or antigen-binding fragment thereof of any one of the preceding claims, which has a binding affinity (K_D) for human OX40 of less than 10 nM.

13. The antibody or antigen-binding fragment thereof of any one of the preceding claims, which blocks the binding of OX40 to its ligand OX40L.

14. The antibody or antigen-binding fragment thereof of any one of claims 1-13, which is an OX40 antibody agonist and has an activity of activating OX40-mediated signal transduction.

15. The antibody or antigen-binding fragment thereof of claim 14, comprising an Fc region that binds to FcγR.

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16. The antibody or antigen-binding fragment thereof of claim 14, comprising an Fc region, wherein the amino acid sequence of the Fc region is identical to the sequence of the Fc region of human IgG1, IgG2 or IgG4.

17. The antibody or antigen-binding fragment thereof of any one of claims 1-13, which is an OX40 antibody antagonist and has an activity of blocking OX40-mediated signal transduction.

18. The antibody or antigen-binding fragment thereof of claim 17, comprising an Fc region
5 variant, wherein the binding of the Fc region variant to FcγR is reduced or eliminated.

19. An isolated nucleic acid, encoding the antibody or antigen-binding fragment thereof of any one of claims 1-18.

10 20. A recombinant vector or an expression vector, comprising one or more nucleic acids of claim 19, wherein the vector is suitable for recombinant production of the antibody or antigen-binding fragment thereof of any one of claims 1-18.

21. A host cell, comprising one or more recombinant vectors or expression vectors of claim
15 20.

22. An immunoconjugate or immune fusion, comprising the antibody or antigen-binding fragment thereof of any one of claims 1-18.

20 23. A pharmaceutical composition, comprising the antibody or antigen-binding fragment thereof of any one of claims 1-18, the nucleic acid of claim 19, the vector of claim 20, the host cell of claim 21, or the immunoconjugate or immune fusion of claim 22, and optionally comprising at least one pharmaceutically acceptable excipient.

25 24. Use of the antibody or antigen-binding fragment thereof of any one of claims 1-18, the nucleic acid of claim 19, the vector of claim 20, the host cell of claim 21, or the immunoconjugate or immune fusion of claim 22 in the preparation of a drug for treating or preventing an OX40-related disease or condition.

30 25. Use of the antibody or antigen-binding fragment thereof of any one of claims 14-16, the nucleic acid of claim 19, the vector of claim 20, the host cell of claim 21, or the immunoconjugate or immune fusion of claim 22 in the preparation of a drug for treating or preventing a cancer, such as melanoma, preferably metastatic melanoma.

26. Use of the antibody or antigen-binding fragment thereof of any one of claims 17-18, the nucleic acid of claim 19, the vector of claim 20, the host cell of claim 21, or the immunoconjugate or immune fusion of claim 22 in the preparation of a drug for treating or preventing inflammation and/or autoimmune disease, such as graft-versus-host disease.

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27. A method for treating or preventing an OX40-related disease or condition, comprising administering to a subject an effective amount of the antibody or antigen-binding fragment thereof of any one of claims 1-18, the nucleic acid of claim 19, the vector of claim 20, the host cell of claim 21, or the immunoconjugate or immune fusion of claim 22.

10 28. The method of claims 27, wherein the OX40-related disease or condition is inflammation and/or autoimmune disease, such as graft-versus-host disease.

29. The method of claims 27, wherein the OX40-related disease or condition is a cancer, such as melanoma, preferably metastatic melanoma.

30. A method for detecting OX40 in a sample, comprising:

15 (a) contacting the sample with the antibody or antigen-binding fragment thereof of any one of claims 1-18 or the immunoconjugate or immune fusion of claim 22; and

(b) detecting the formation of the complex of the antibody or antigen-binding fragment thereof or the immunoconjugate or the immune fusion with the OX40 protein.

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