CLAIMS

1. An isolated anti-IL-36R antibody or an antigen-binding fragment thereof, wherein the antibody or the antigen-binding fragment thereof comprises heavy chain CDR1, heavy chain CDR2, heavy chain CDR3, light chain CDR1, light chain CDR2, and light chain CDR3, wherein

(1) heavy chain CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 1 or 85, heavy chain CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 2, heavy chain CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 3, light chain CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 4, light chain CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 5, and light chain CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 6;

(2) heavy chain CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 21 or 86, heavy chain CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 22, heavy chain CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 23, light chain CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 24 or 87, light chain CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 25, and light chain CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 26;

(3) heavy chain CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 45 or 88, heavy chain CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 46, heavy chain CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 47, light chain CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 48, light chain CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 49, and light chain CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 50;

(4) heavy chain CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 53 or 89, heavy chain CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 54, heavy chain CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 55, light chain CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 56, light chain CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 57, and light chain CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 58; or

(5) heavy chain CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 61 or 90, heavy chain CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 62, heavy chain CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 63, light chain CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 64, light chain CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 65, and light chain CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 66;

wherein

the amino acid sequence of SEQ ID NO: 2 is $YIX_1YSGYTYYNPSLKS$, the amino acid sequence of SEQ ID NO: 6 is $QQX_2TTSPYT$, wherein

i) X_1 = S or Y, X_2 = F, or

ii) X_1 = S or Y, X_2 = Y;

and the amino acid sequence of SEQ ID NO: 21 is $GYX_3FTSYWMN$, the amino acid sequence of SEQ ID NO: 22 is $X_4IX_5PYDSETRX_6X_7QKFX_8G$, wherein

i) X_3 = F or Y, X_4 = M or Y, X_5 = H or Y, X_6 = L, X_7 = N or A, and X_8 = K, or

ii) X_3 = F or Y, X_4 = M or Y, X_5 = H or Y, X_6 = Y, X_7 = N or A, and X_8 = Q.

2. The antibody or the antigen-binding fragment thereof according to claim 1, wherein heavy chain CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 1 or 85, heavy chain CDR2 comprises an amino acid

sequence set forth in SEQ ID NO: 2, heavy chain CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 3, light chain CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 4, light chain CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 5, and light chain CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 6; and

wherein the amino acid sequence of SEQ ID NO: 2 is $YIX_1YSGYTYYNPSLKS$, the amino acid sequence of SEQ ID NO: 6 is $QQX_2TTSPYT$, wherein X_1 = S and X_2 = F.

3. An isolated anti-IL-36R antibody or an antigen-binding fragment thereof, wherein the antibody or the antigen-binding fragment thereof comprises:

(1) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 7, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 15;

(2) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 9, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 17;

(3) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 11, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 17;

(4) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 13, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 17;

(5) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 9, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 19;

(6) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 11, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 19;

(7) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 13, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 19;

(8) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 27, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 39;

(9) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 29, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 41;

(10) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 31, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 41;

(11) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 33, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 41;
(12) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 35, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 41;
(13) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 37, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 41;
(14) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 29, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 43;
(15) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 31, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 43;
(16) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 33, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 43;
(17) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 35, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 43;
(18) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 37, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 43;
(19) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 51, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 52;
(20) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 59, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 60; or
(21) heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 67, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 68.

4. The antibody or the antigen-binding fragment thereof according to claim 3, wherein the antibody or the antigen-binding fragment thereof comprises: heavy chain CDR1, heavy chain CDR2 and heavy chain CDR3 in a heavy chain variable region set forth in SEQ ID NO: 9, and light chain CDR1, light chain CDR2 and light chain CDR3 in a light chain variable region set forth in SEQ ID NO: 17.

5. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 4, wherein the antibody or the antigen-binding fragment thereof comprises:

(1) a heavy chain variable region comprising an amino acid sequence set forth in SEQ ID NO: 7, 9, 11, 13, 27, 29, 31, 33, 35, 37, 51, 59 or 67;

(2) a light chain variable region comprising an amino acid sequence set forth in SEQ ID NO: 15, 17, 19, 39, 41, 43, 52, 60 or 68; or

(3) a heavy chain variable region set forth in (1) and a light chain variable region set forth in (2).

6. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 5, wherein the antibody or the antigen-binding fragment thereof comprises a heavy chain variable region and a light chain variable region, wherein

(1) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 7, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 15;

(2) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 9, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 17;

(3) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 11, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 17;

(4) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 13, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 17;

(5) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 9, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 19;

(6) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 11, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 19;

(7) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 13, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 19;

(8) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 27, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 39;

(9) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 29, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 41;

(10) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 31, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 41;

(11) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 33, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 41;

(12) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 35, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 41;

(13) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 37, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 41;

(14) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 29, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 43;

(15) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 31, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 43;

(16) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 33, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 43;

(17) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 35, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 43;
(18) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 37, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 43;
(19) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 51, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 52;
(20) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 59, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 60; or
(21) the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 67, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 68.

7. The antibody or the antigen-binding fragment thereof according to claim 6, wherein the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 9, and the light chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 17.

8. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 4, wherein the antibody or the antigen-binding fragment thereof is chimeric or humanized.

9. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 8, the antibody or the antigen-binding fragment thereof is of the IgG1, IgG2 or IgG4 isotype.

10. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 9, wherein the antibody or the antigen-binding fragment thereof further comprises a heavy chain constant region and a light chain constant region, wherein the heavy chain constant region comprises an amino acid sequence set forth in SEQ ID NO: 69 or 71, and the light chain constant region comprises an amino acid sequence set forth in SEQ ID NO: 73.

11. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 10, wherein the antibody or the antigen-binding fragment thereof is selected from a monoclonal antibody, a fusion protein, a recombinant polypeptide, a multispecific antibody, an Fab fragment, an $F(ab')_2$ fragment, an Fd fragment, an Fv fragment, a dAb fragment, an isolated CDR region, a single-chain Fv molecule, or combinations thereof.

12. An isolated nucleic acid molecule encoding the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 11.

13. An immunoconjugate or a multispecific molecule comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 11.

14. A pharmaceutical composition comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 11, and one or more pharmaceutically acceptable excipients, diluents or carriers.

15. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1 to 11, the immunoconjugate or the multispecific molecule according to claim 13, or the pharmaceutical composition according to claim 14, in the manufacturing of a medicament for the treatment or prevention of IL-36/IL-36R-mediated related diseases and conditions.

16. The use according to claim 15, wherein the antibody or the antigen-binding fragment thereof is to be co-administered with one or more other antibodies or drugs capable of preventing, alleviating, ameliorating or treating IL-36/IL-36R-mediated related diseases and conditions.

17. The use according to claims 15 or 16, wherein the IL-36/IL-36R-mediated related diseases and conditions include autoimmune diseases, inflammatory diseases, respiratory diseases, metabolic disorders, or cancer.

18. The use according to claims 15 or 16, wherein the IL-36/IL-36R-mediated related diseases and conditions include multiple sclerosis, scleroderma, asthma, chronic obstructive pulmonary disease, hidradenitis suppurativa, arthritis, ankylosing spondylitis, psoriasis, palmoplantar pustulosis, systemic lupus erythematosus, atopic dermatitis, acne vulgaris, skin rash, allergic rhinitis, nephritis, inflammatory bowel disease, and/or food allergy.

19. The use according to claim 18, wherein the arthritis includes rheumatoid arthritis, and psoriatic arthritis.

20. The use according to claim 18, wherein the psoriasis includes psoriasis vulgaris, pustular psoriasis, local pustular psoriasis, and generalized pustular psoriasis.