X_{34} is G or E or F or H or M or Q or S,

X_{35} is W or A or I or P or Q or T or V,

X_{36} is Y or G or N or Q,

X_{37} is G or S or T, and

X_{38} is Y or I.

[0008a] In one aspect, the present disclosure refers to a conditionally active anti-Ror2 antibody or antibody fragment that specifically binds to Ror2 protein with a ratio of binding affinity to the Ror protein at a value of a pH of pH 5.8 to pH 6.8 in a tumor microenvironment in comparison with a different value of pH 7.0 to pH 7.6 that occurs in a non-tumor microenvironment of at least 1.5:1, said antibody or antibody fragment comprising a heavy chain variable region and a light chain variable region, said heavy chain variable region comprising three complementarity determining regions having H1, H2, and H3 sequences, wherein:

(a) the H1 sequence is $GYTX_1TEX_2X_3X_4H$ (SEQ ID NO:1);
(b) the H2 sequence is $X_5X_6X_7X_8NNGGTGYNQKFKG$ (SEQ ID NO:2); and
(c) the H3 sequence is $X_9X_{10}X_{11}SX_{12}YX_{13}YX_{14}X_{15}SYFX_{16}X_{17}X_{18}$ (SEQ ID NO:3);
wherein
X_1 is F or E,
X_2 is Y or D,
X_3 is T or C,
X_4 is M or D or E or Y,
X_5 is G or S,
X_6 is I or E,
X_7 is N or C or L or V,
X_8 is T or D or E,
X_9 is A or I or M or S or T,
X_{10} is R or Q or H,
X_{11} is G ~~or E~~,
X_{12} is L,
X_{13} is S,
X_{14} is G,
X_{15} is N or E,
X_{16} is D or L,
X_{17} is Y or T, and
X_{18} is W or L, and

said light chain variable region comprising three light chain complementarity determining regions having L1, L2, and L3 sequences, wherein:

(a) the L1 sequence is SATSSX$_{19}$X$_{20}$X$_{21}$MX$_{22}$ (SEQ ID NO:7);

(b) the L2 sequence is X$_{23}$TSNLAS (SEQ ID NO:8); and

(c) the L3 sequence is QX$_{24}$X$_{25}$SX$_{26}$YPFX$_{27}$X$_{28}$ (SEQ ID NO:9);

wherein

X$_{19}$ is V or E,

X$_{20}$ is S or D,

X$_{21}$ is Y or C or D,

X$_{22}$ is H or G or L,

X$_{23}$ is G or C or H or P,

X$_{24}$ is Q or E,

X$_{25}$ is R or H,

X$_{26}$ is S~~ or G or I or Q~~,

X$_{27}$ is T or D,

X$_{28}$ is F or D or E, and

WHAT IS CLAIMED IS:

1. A conditionally active anti-Ror2 antibody or antibody fragment that specifically binds to Ror2 protein with a ratio of binding affinity to the Ror protein at a value of a pH of pH 5.8 to pH 6.8 in a tumor microenvironment in comparison with a different value of pH 7.0 to pH 7.6 that occurs in a non-tumor microenvironment of at least 1.5:1, said antibody or antibody fragment comprising a heavy chain variable region and a light chain variable region, said heavy chain variable region comprising three complementarity determining regions having H1, H2, and H3 sequences, wherein:

(a) the H1 sequence is $GYTX_1TEX_2X_3X_4H$ (SEQ ID NO:1);

(b) the H2 sequence is $X_5X_6X_7X_8NNGGTGYNQKFKG$ (SEQ ID NO:2); and

(c) the H3 sequence is $X_9X_{10}X_{11}SX_{12}YX_{13}YX_{14}X_{15}SYFX_{16}X_{17}X_{18}$ (SEQ ID NO:3);

wherein

X_1 is F or E,

X_2 is Y or D,

X_3 is T or C,

X_4 is M or D or E or Y,

X_5 is G or S,

X_6 is I or E,

X_7 is N or C or L or V,

X_8 is T or D or E,

X_9 is A or I or M or S or T,

X_{10} is R or Q or H,

X_{11} is G ~~or E~~,

X_{12} is L,

X_{13} is S,

X_{14} is G,

X_{15} is N or E,

X_{16} is D or L,

X_{17} is Y or T, and

X_{18} is W or L, and

said light chain variable region comprising three light chain complementarity determining regions having L1, L2, and L3 sequences, wherein:

(a) the L1 sequence is $SATSSX_{19}X_{20}X_{21}MX_{22}$ (SEQ ID NO:7);

(b) the L2 sequence is $X_{23}TSNLAS$ (SEQ ID NO:8); and

(c) the L3 sequence is $QX_{24}X_{25}SX_{26}YPFX_{27}X_{28}$ (SEQ ID NO:9);

wherein

X_{19} is V or E,

X_{20} is S or D,

X_{21} is Y or C or D,

X_{22} is H or G or L,

X_{23} is G or C or H or P,

X_{24} is Q or E,

X_{25} is R or H,

X_{26} is S~~ or G or I or Q~~,

X_{27} is T or D,

X_{28} is F or D or E, and

wherein the antibody or antibody fragment has only one single point mutation in one of the heavy and light chain complementarity determining regions H1, H2, H3, L1, L2, and L3, said one single point mutation being determined in comparison with the parent antibody in which X_1 to X_{28} are F, Y, T, M, G, I, N, T, A, R, G, L, S, G, N, D, Y, W, V, S, Y, H, G, Q, R, S, T, and F, respectively.

2. The antibody or antibody fragment of claim 1, wherein the heavy chain variable region has an amino acid sequence selected from sequences of SEQ ID NOS: 18 and 20-22.

3. The antibody or antibody fragment of ~~any one of claims 1-2~~claim 1, wherein the light chain variable region has an amino acid sequence selected from SEQ ID NOS: 13, 15, and 16.

4. The antibody or antibody fragment of claim 1, wherein the heavy chain variable region has an amino acid sequence of SEQ ID NO: 18 and the light chain variable region has an amino acid sequence of SEQ ID NO: 15.

5. The antibody or antibody fragment of claim 1, wherein the heavy chain variable region has an amino acid sequence selected from sequences of SEQ ID NOS: 20-22 and the light chain variable region has an amino acid sequence selected from sequences of SEQ ID NOS: 13 and 16.

~~4~~6. The antibody or antibody fragment of claim 1, wherein X_1 to X_{28} are F, Y, T, M, G, I, N, T, A, H, G, L, S, G, N, D, Y, W, V, S, Y, H, G, Q, R, S, T and F, respectively.

~~5~~7. The antibody or antibody fragment of claim 1, wherein the heavy chain variable region has an amino acid sequence selected from SEQ ID NOS: 20-22 and the light chain variable region has an amino acid sequence selected from SEQ ID NOS: 15 and 16.

~~6~~8. The antibody or antibody fragment of claim ~~7~~5, wherein the heavy chain variable region has the amino acid sequence of SEQ ID NO: 20 and the light chain variable region has the amino acid sequence of SEQ ID NO: 15.

~~7~~9. The antibody or antibody fragment of claim ~~5~~7, wherein the heavy chain variable region has the amino acid sequence of SEQ ID NO: 21 and the light chain variable region has the amino acid sequence of SEQ ID NO: 16.

~~8~~10. The antibody or antibody fragment of claim ~~5~~7, wherein the heavy chain variable region has the amino acid sequence of SEQ ID NO: 22 and the light chain variable region has the amino acid sequence of SEQ ID NO: 16.

~~9~~11. The antibody or antibody fragment of any one of claims 1-~~8~~10, wherein the antibody or antibody fragment has a ratio of binding affinity to the Ror2 protein in the tumor microenvironment to a binding affinity to the Ror2 protein in the non-tumor microenvironment of at least 2:1, at least 3:1, at least 4:1, at least 5:1, at least 6:1, at least 7:1, at least 8:1, at least 9:1, at least 10:1, at least 20:1, at least 30:1, at least 50:1, at least 70:1, or at least 100:1.

~~10~~12. The antibody or antibody fragment of any of one of claims 1-~~9~~11, wherein the antibody or antibody fragment is a chimeric antibody, a multispecific antibody, or a humanized antibody.

~~11~~13. An immunoconjugate comprising the antibody or antibody fragment of any one of claims 1-~~10~~12.

~~12~~14. The immunoconjugate of claim ~~11~~13, wherein the immunoconjugate comprises at least one agent selected from a chemotherapeutic agent, a radioactive atom, a cytostatic agent and a cytotoxic agent.

~~13~~15. The immunoconjugate of claim ~~12~~14, comprising at least two said agents.

~~14~~16. The immunoconjugate of any one of claims ~~12 13~~14-15, wherein the antibody or antibody fragment and the at least one or two agents are covalently bonded to a linker molecule.

~~15~~17. The immunoconjugate of any one of claims ~~12 14~~14-16, wherein the at least one or two agents are selected from maytansinoids, auristatins, dolastatins, calicheamicin, pyrrolobenzodiazepines, and anthracyclines.

~~16~~18. A pharmaceutical composition comprising:

the antibody or antibody fragment of any one of claims 1-~~10~~12, or the immunoconjugate of any one of claims ~~11 15~~13-17; and

a pharmaceutically acceptable carrier.

~~17~~19. The pharmaceutical composition of claim ~~16~~18, further comprising a tonicity agent.

~~18~~20. A kit for diagnosis or treatment, said kit comprising the antibody or antibody fragment of any one of claims 1-~~10~~12, or the immunoconjugate of any one of claims ~~12 15~~13-17, or the pharmaceutical composition of any one of claims ~~16 17~~18-19 and instructions for using the antibody or antibody fragment, the immunoconjugate and/or the pharmaceutical composition for diagnosis or treatment.