

WE CLAIM:

1. An antibody, antibody-based binding protein or antibody fragment that specifically binds to the extracellular domain of human receptor tyrosine kinase-like orphan receptor 1 (ROR1) comprising heavy chain CDR1, CDR2 and CDR3 sequences and light chain CDR1, CDR2 and CDR3 sequences respectively set forth as SEQ ID Nos:27-29 and SEQ ID Nos:66-68.
2. A pharmaceutical composition comprising (1) a therapeutically effective amount of the antibody, antibody-based binding protein or antibody fragment of claim 1 and (2) a pharmaceutically acceptable carrier.
3. A pharmaceutical composition of claim 2 for use in the treatment of a disease or condition associated with elevated expression of ROR1 in a subject.
4. A polynucleotide encoding an antibody, antibody-based binding protein or antibody fragment that specifically binds to the extracellular domain of human receptor tyrosine kinase-like orphan receptor 1 (ROR1), comprising heavy chain CDR1, CDR2 and CDR3 sequences and light chain CDR1, CDR2 and CDR3 sequences respectively set forth as SEQ ID NOs:27-29 and SEQ ID NOs:66-68.
5. An antibody drug conjugate (ADC), comprising (i) an antibody, antibody-based binding protein or antibody fragment that specifically binds to the extracellular domain of human receptor tyrosine kinase-like orphan receptor 1 (ROR1), comprising heavy chain CDR1, CDR2 and CDR3 sequences and light chain CDR1, CDR2 and CDR3 sequences respectively set forth as SEQ ID NOs:27-29 and SEQ ID NOs:66-68, and (ii) at least one cytotoxic agent.
6. The antibody drug conjugate of claim 5, wherein the cytotoxic agent is a small molecular weight toxin, a peptide toxin, or a protein toxin.
7. The antibody drug conjugate of claim 5, wherein the antibody or antibody fragment is conjugated to the cytotoxic agent via sortase enzyme mediated antibody conjugation (SMAC).

8. The antibody drug conjugate of claim 5, wherein the cytotoxic agent is anthracycline (PNU) toxin derivative Gly(n)-EDA-PNU, where n is any number from 1 to 21.
9. An antibody drug conjugate of claim 5 for use in killing or inhibiting the growth of a tumor cell expressing ROR1 in a subject.
10. A humanized antibody, antibody-based binding protein or antibody fragment that specifically binds to the extracellular domain of human receptor tyrosine kinase-like orphan receptor 1 (ROR1), comprising a heavy chain variable region sequence and a light chain variable region sequence respectively set forth as (1) SEQ ID NO:130 and SEQ ID NO:136; (2) SEQ ID NO:131 and SEQ ID NO:137; (3) SEQ ID NO:132 and SEQ ID NO:138; (4) SEQ ID NO:133 and SEQ ID NO:139; (5) SEQ ID NO:134 and SEQ ID NO:140; or (6) SEQ ID NO:135 and SEQ ID NO:141.
11. A pharmaceutical composition comprising (1) a therapeutically effective amount of the humanized antibody, antibody-based binding protein or antibody fragment of claim 10 and (2) a pharmaceutically acceptable carrier.
12. A pharmaceutical composition of claim 11 for use in the treatment of a disease or condition associated with elevated expression of ROR1 in a subject.
13. A polynucleotide encoding a humanized antibody, antibody-based binding protein or antibody fragment that specifically binds to the extracellular domain of human receptor tyrosine kinase-like orphan receptor 1 (ROR1), comprising a heavy chain variable region sequence and a light chain variable region sequence respectively set forth as (1) SEQ ID NO:130 and SEQ ID NO:136; (2) SEQ ID NO:131 and SEQ ID NO:137; (3) SEQ ID NO:132 and SEQ ID NO:138; (4) SEQ ID NO:133 and SEQ ID NO:139; (5) SEQ ID NO:134 and SEQ ID NO:140; or (6) SEQ ID NO:135 and SEQ ID NO:141.
14. A humanized antibody drug conjugate (hADC), comprising
 - (i) a humanized antibody, antibody-based binding protein or antibody fragment that specifically binds to the extracellular domain of human receptor tyrosine kinase-like orphan receptor 1 (ROR1), comprising a heavy chain variable region sequence and a light chain

variable region sequence respectively set forth as (1) SEQ ID NO:130 and SEQ ID NO:136; (2) SEQ ID NO:131 and SEQ ID NO:137; (3) SEQ ID NO:132 and SEQ ID NO:138; (4) SEQ ID NO:133 and SEQ ID NO:139; (5) SEQ ID NO:134 and SEQ ID NO:140; or (6) SEQ ID NO:135 and SEQ ID NO:141, and (ii) at least one cytotoxic agent.

15. The humanized antibody drug conjugate of claim 14, wherein the cytotoxic agent is a small molecular weight toxin, a peptide toxin, or a protein toxin.

16. The humanized antibody drug conjugate of claim 14, wherein the humanized antibody or antibody fragment is conjugated to the cytotoxic agent via sortase enzyme mediated antibody conjugation (SMAC).

17. The humanized antibody drug conjugate of claim 14, wherein the cytotoxic agent is anthracycline (PNU) toxin derivative Gly(n)-EDA-PNU, where n is any number from 1 to 21.

18. A humanized antibody, antibody-based binding protein or antibody fragment that specifically binds to the extracellular domain of human receptor tyrosine kinase-like orphan receptor 1 (ROR1), comprising a heavy chain variable region sequence and a light chain variable region sequence respectively set forth as SEQ ID NO:133 and SEQ ID NO:139.

19. A pharmaceutical composition comprising (1) a therapeutically effective amount of the antibody, antibody-based binding protein or antibody fragment of claim 18 and (2) a pharmaceutically acceptable carrier.

20. A pharmaceutical composition of claim 19 for use in the treatment of a disease or condition associated with elevated expression of ROR1 in a subject.

21. A polynucleotide encoding an antibody, antibody-based binding protein or antibody fragment that specifically binds to the extracellular domain of human receptor tyrosine kinase-like orphan receptor 1 (ROR1), comprising a heavy chain variable region sequence and a light chain variable region sequence respectively set forth as SEQ ID NO:133 and SEQ ID NO:139.

22. A humanized antibody drug conjugate (hADC), comprising

clean copy of amended claims 300921

(i) a humanized antibody, antibody-based binding protein or antibody fragment that specifically binds to the extracellular domain of human receptor tyrosine kinase-like orphan receptor 1 (ROR1), comprising a heavy chain variable region sequence and a light chain variable region sequence respectively set forth as SEQ ID NO:133 and SEQ ID NO:139, and (ii) at least one cytotoxic agent.

23. The antibody drug conjugate of claim 22, wherein the cytotoxic agent is a small molecular weight toxin, a peptide toxin, or a protein toxin.

24. The antibody drug conjugate of claim 22, wherein the humanized antibody or antibody fragment is conjugated to the cytotoxic agent via sortase enzyme mediated antibody conjugation (SMAC).

25. The antibody drug conjugate of claim 22, wherein the cytotoxic agent is anthracycline (PNU) toxin derivative Gly(n)-EDA-PNU, where n is any number from 1 to 21.