

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 method of treating a disease or condition associated with elevated expression of ROR1 in a subject, comprising administering the pharmaceutical composition of claim 2 to a subject having a disease or condition associated with elevated expression of ROR1, thereby treating the disease or condition associated with elevated expression of ROR1 in the 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. A method of killing or inhibiting the growth of a tumor cell expressing ROR1 in a subject, comprising administering the antibody drug conjugate of claim 5 to a subject in need thereof, thereby killing or inhibiting the growth of the tumor cell expressing ROR1 in the 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 method of treating a disease or condition associated with elevated expression of ROR1 in a subject, comprising administering the pharmaceutical composition of claim 11 to a subject having a disease or condition associated with elevated expression of ROR1, thereby treating the disease or condition associated with elevated expression of ROR1 in the 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 method of treating a disease or condition associated with elevated expression of ROR1 in a subject, comprising administering the pharmaceutical composition of claim 18 to a subject having a disease or condition associated with elevated expression of ROR1, thereby treating the disease or condition associated with elevated expression of ROR1 in the 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
(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.