

[0006a] In one aspect, the present disclosure refers to an anti-ROR1 antibody or antigen-binding fragment thereof, comprising: a heavy chain variable (V_H) region, and a light chain variable (V_L) region, wherein the V_H region comprises a heavy chain complementarity determining region 1 (CDR-H1), a heavy chain complementarity determining region 2 (CDR-H2) and a heavy chain complementarity determining region 3 (CDR-H3) comprising the sequence set forth in SEQ ID NOS:67, 71 and 73, respectively, and the V_L region comprises a light chain complementarity determining region 1 (CDR-L1), a light chain complementarity determining region 2 (CDR-L2) and a light chain complementarity determining region 3 (CDR-L3) comprising the sequence set forth in SEQ ID NOS:75, 77 and 79, respectively; the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 comprising the sequence set forth in SEQ ID NOS:82, 86 and 88, respectively, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 comprising the sequence set forth in SEQ ID NOS:90, 92 and 94, respectively; the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 comprising the sequence set forth in SEQ ID NOS:52, 56 and 58, respectively, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 comprising the sequence set forth in SEQ ID NOS:60, 62 and 64, respectively; or the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 comprising the sequence set forth in SEQ ID NOS:52, 97 and 99, respectively, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 comprising the sequence set forth in SEQ ID NOS:60, 62 and 64, respectively.

[0007] In some of any such examples: (i) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:67, 71 and 73, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:75, 77 and 79, respectively; (ii) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:65, 69 and 73, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:75, 77 and 79, respectively; (iii) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:66, 70 and 73, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:75, 77 and 79, respectively; or (iv) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:68, 72 and 74, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:76, 78 and 79, respectively.

[0008] In some of any such examples: (i) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:82, 86 and 88, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:90, 92 and 94, respectively; (ii) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:80, 84 and 88, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:90, 92 and 94, respectively; (iii) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:81, 85 and 88, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:90, 92 and 94, respectively; or (iv) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:83, 87 and 89, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:91, 93 and 94, respectively.

[0009] In some of any examples, the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 comprising the sequence set forth in SEQ ID NOS:67, 71 and 73, respectively, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 comprising the sequence set forth in SEQ ID NOS:75, 77 and 79, respectively. In some of any examples, the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 comprising the sequence set forth in SEQ ID NOS:82, 86 and 88, respectively, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 comprising the sequence set forth in SEQ ID NOS:90, 92 and 94, respectively. In some of any such examples, the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 comprising the sequence set forth in SEQ ID NOS:52, 56 and 58, respectively, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 comprising the sequence set forth in SEQ ID NOS:60, 62 and 64, respectively. In some of any such examples, the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 comprising the sequence set forth in SEQ ID NOS:52,

97 and 99, respectively, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 comprising the sequence set forth in SEQ ID NOS:60, 62 and 64, respectively.

[0010] Also provided herein is an anti-ROR1 antibody or antigen-binding fragment thereof, containing: a heavy chain variable (V_H) region and a light chain variable (V_L) region, wherein: the V_H region contains a heavy chain complementarity determining region 1 (CDR-H1), a heavy chain complementarity determining region 2 (CDR-H2) and a heavy chain complementarity determining region 3 (CDR-H3) contained within SEQ ID NO: 112, 121, 103 or 130, and the V_L region contains a light chain complementarity determining region 1 (CDR-L1), a light chain complementarity determining region 2 (CDR-L2) and a light chain complementarity determining region 3 (CDR-L3) contained within SEQ ID NO: 115, 124 or 106.

[0011] Also provided herein is an anti-ROR1 antibody or antigen-binding fragment thereof, containing: a heavy chain variable (V_H) region and a light chain variable (V_L) region, wherein: the V_H region contains a heavy chain complementarity determining region 1 (CDR-H1), a heavy chain complementarity determining region 2 (CDR-H2) and a heavy chain complementarity determining region 3 (CDR-H3) contained within SEQ ID NO:112, and the V_L region contains a light chain complementarity determining region 1 (CDR-L1), a light chain complementarity determining region 2 (CDR-L2) and a light chain complementarity determining region 3 (CDR-L3) contained within SEQ ID NO:115; the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:121, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 124; the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:103, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 106; or the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:130, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 106.

[0011a] In one aspect, the present disclosure refers to an anti-receptor tyrosine kinase-like orphan receptor 1 (ROR1) antibody or antigen-binding fragment thereof, comprising: a heavy chain variable (V_H) region and a light chain variable (V_L) region, wherein: the V_H region comprises a heavy chain complementarity determining region 1 (CDR-H1), a heavy chain complementarity determining region 2 (CDR-H2) and a heavy chain complementarity determining region 3 (CDR-H3) contained within SEQ ID NO:112, and the V_L region comprises a light chain complementarity determining region 1 (CDR-L1), a light chain complementarity determining region 2 (CDR-L2) and a light chain complementarity determining region 3 (CDR-L3) contained within SEQ ID NO:115; the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:121, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 124; the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:103, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 106; or the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:130, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 106.

[0012] In some of any such examples, the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:112, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 115. In some of any such examples, the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:121, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 124. In some of any examples, the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:103, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 106. In some of any examples, the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:130, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 106.

[0013] In some of any such examples, the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 112, 121, 103 or 130, and the V_L region is or contains an amino

[0015] Also provided herein is an anti-ROR1 antibody or antigen-binding fragment thereof, containing: a heavy chain variable (V_H) region and a light chain variable (V_L) region, wherein: the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 112, 121, 103 or 130, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 115, 124 or 106.

[0016] Also provided herein is an anti-ROR1 antibody or antigen-binding fragment thereof, containing: a heavy chain variable (V_H) region and a light chain variable (V_L) region, wherein: the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:112, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 115; the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:121, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:124; the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:103, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:106; or the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:130, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:106.

[0017] In some of any such examples, the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:112, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 115. In some of any such examples, the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:121, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:124.

[0017a] In one aspect, the present disclosure refers to an anti-ROR1 antibody or antigen-binding fragment thereof, comprising: a heavy chain variable (V_H) region and a light chain variable (V_L) region, wherein: the V_H region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:112, and the V_L region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 115; the V_H region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:121, and the V_L region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:124; the V_H region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:103, and the V_L region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:106; the V_H region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:130, and the V_L region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:106; the V_H region and the V_L region are or comprise the sequence set forth in SEQ ID NOS: 112 and 115, respectively; the V_H region and the V_L region are or comprise the sequence set forth in SEQ ID NOS: 121 and 124, respectively; the V_H region and the V_L region are or comprise the sequence set forth in SEQ ID NOS: 103 and 106, respectively; or the V_H region and the V_L region are or comprise the sequence set forth in SEQ ID NOS: 130 and 106, respectively.

[0018] In some of any such examples: the V_H region is or contains the sequence set forth in SEQ ID NO: 112, 121, 103 or 130, and the V_L region is or contains the sequence set forth in SEQ ID NO: 115,

124 or 106. In some of any such examples: the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 112 and 115, respectively; the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 121 and 124, respectively; the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 103 and 106, respectively; or the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 130 and 106, respectively.

[0019] Also provided herein is an anti-ROR1 antibody or antigen-binding fragment thereof, containing: a heavy chain variable (V_H) region and a light chain variable (V_L) region, wherein: the V_H region is or contains the sequence set forth in SEQ ID NO: 112, 121, 103 or 130, and the V_L region is or contains the sequence set forth in SEQ ID NO: 115, 124 or 106.

[0020] Also provided herein is an anti-ROR1 antibody or antigen-binding fragment thereof, containing: a heavy chain variable (V_H) region and a light chain variable (V_L) region, wherein: the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 112 and 115, respectively; the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 121 and 124, respectively; the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 103 and 106, respectively; or the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 130 and 106, respectively.

[0021] In some of any such examples, the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 112 and 115, respectively. In some of any such examples, the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 121 and 124, respectively. In some of any examples, the V_H region and the V_L region are or comprise the sequence set forth in SEQ ID NOS: 103 and 106, respectively. In some of any examples, the V_H region and the V_L region are or comprise the sequence set forth in SEQ ID NOS: 130 and 106, respectively.

[0022] In some of any such examples, the V_H region is or contains the amino acid sequence encoded by SEQ ID NO: 110, 119, 101 or 128 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 110, 119, 101 or 128, and the V_L region is or contains the amino acid sequence encoded by SEQ ID NO: 113, 122 or 104, or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 113, 122 or 104. In some of any such examples, the V_H region is or contains the amino acid sequence encoded by SEQ ID NO: 111, 120, 102 or 129, and the V_L region is or contains the amino acid sequence encoded by SEQ ID NO: 114, 123, 105 or 131. In some of any such examples, the V_H region is or contains the amino acid sequence encoded by SEQ ID NO: 110 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 110, and the V_L region is or contains the amino acid sequence encoded by SEQ ID NO: 113, or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%,

93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 113. In some of any such examples, the V_H region is or contains the amino acid sequence encoded by SEQ ID NO: 111, and the V_L region is or contains the amino acid sequence encoded by SEQ ID NO: 114. In some of any such examples, the V_H region is or contains the amino acid sequence encoded by SEQ ID NO: 119 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 119, and the V_L region is or contains the amino acid sequence encoded by SEQ ID NO: 122, or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 122. In some of any such examples, the V_H region is or contains the amino acid sequence encoded by SEQ ID NO: 120, and the V_L region is or contains the amino acid sequence encoded by SEQ ID NO: 123.

[0023] In some of any examples, the antibody is a full length antibody. In some of any examples, the antibody is an antigen-binding fragment. In some of any such examples, said anti-ROR1 antibody or antigen-binding fragment thereof is isolated. In some of any such examples, said anti-ROR1 antibody or antigen-binding fragment thereof is recombinant. In some of any such examples, at least a portion of the V_H region and the V_L region is human or is from a human protein. In some of any such examples, the antigen-binding fragment thereof is or contains a single chain fragment. In some of any such examples, the antigen-binding fragment thereof is or contains a single chain Fv (scFv).

[0024] In some of any such examples, the V_H region is amino-terminal to the V_L region. In some of any such examples, the V_H region is carboxy-terminal to the V_L region. In some of any such examples, the V_H region and the V_L region are joined by a flexible linker. In some of any such examples, the flexible linker contains the sequence set forth in SEQ ID NO:41.

[0025] In some of any such examples, the scFv is or contains the sequence set forth in SEQ ID NO: 118, 127, 109 or 134, or an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to SEQ ID NO: 118, 127, 109 or 134. In some of any such examples, the scFv is or contains the sequence set forth in SEQ ID NO: 118. In some of any such examples, the scFv is or contains the sequence set forth in SEQ ID NO: 127. In some of any examples, the scFv is or comprises the sequence set forth in SEQ ID NO: 109. In some of any examples, the scFv is or comprises the sequence set forth in SEQ ID NO: 134.

[0026] In some of any such examples, the scFv is or contains the amino acid sequence encoded by SEQ ID NO: 116, 125, 107 or 132 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 116, 125, 107 or 132. In some of any such examples, the scFv is or contains the amino acid sequence encoded by SEQ ID NO: 117, 126, 108 or 133. In some of any such examples, the scFv is or contains the amino acid sequence encoded by SEQ ID NO: 116 or a nucleic

acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 116. In some of any such examples, the scFv is or contains the amino acid sequence encoded by SEQ ID NO: 117. In some of any such examples, the scFv is or contains the amino acid sequence encoded by SEQ ID NO: 125 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 125. In some of any such examples, the scFv is or contains the amino acid sequence encoded by SEQ ID NO: 126.

[0027] In some of any such examples, the anti-ROR1 antibody or fragment further contains at least a portion of an immunoglobulin constant region or a variant thereof. In some of any such examples, the portion of an immunoglobulin constant region contains at least a portion of a hinge region or a variant thereof. In some of any such examples, the at least a portion of an immunoglobulin constant region or a variant thereof contains at least a portion of a C_{H2} region or a variant thereof. In some of any such examples, the at least a portion of an immunoglobulin constant region or a variant thereof contains at least a portion of a C_{H3} region or a variant thereof. In some of any such examples, the at least a portion of an immunoglobulin constant region or a variant thereof contains at least a portion of a C_{H2} region and/or a C_{H3} region or a variant thereof. In some of any such examples, the at least a portion of an immunoglobulin constant region or a variant thereof is human or from a human protein or a variant thereof.

[0028] In some of any such examples, said anti-ROR1 antibody or antigen-binding fragment thereof specifically binds to a Receptor tyrosine kinase-like orphan receptor 1 (ROR1) protein. In some of any such examples, said anti-ROR1 antibody or antigen-binding fragment thereof specifically binds to a human ROR1 protein. In some of any such examples, the human ROR1 protein contains an amino acid sequence set forth in SEQ ID NO: 144, 145 or 146.

[0029] In some of any examples, the anti-ROR1 antibody or antigen-binding fragment thereof specifically binds to an epitope consisting of the sequence set forth in SEQ ID NO:199 or an epitope present within the sequence set forth in SEQ ID NO:199. In some of any examples, the antibody or antigen-binding fragment thereof further binds to one or more epitopes consisting of a sequence selected from among any one of SEQ ID NOS: 200-214 or an epitope present within a sequence selected from among any one of SEQ ID NOS: 200-214. In some of any examples, the one or more epitopes comprises a conformational epitope.

[0030] In some of any such examples, said anti-ROR1 antibody or antigen-binding fragment thereof does not bind to, is not cross-reactive to, or binds at a lower level or degree or affinity to a Receptor tyrosine kinase-like orphan receptor 2 (ROR2) protein. In some of any such examples, said anti-ROR1 antibody or antigen-binding fragment thereof does not bind to, is not cross-reactive to, or binds at a lower level or degree or affinity to a human ROR2 protein. In some of any such examples, the extent, level or degree or affinity of binding of said anti-ROR1 antibody or antigen-binding fragment

thereof to a human ROR2 is at least at or about 75%, 80%, 90%, 95% or 99% less than the extent, level or degree or affinity of binding to a human ROR1 protein.

[0031] In some of any examples, the antibody or antigen-binding fragment thereof binds to human ROR1 protein with an equilibrium dissociation constant (K_D) of from about 1×10^{-11} M to about 1×10^{-7} M. In some of any examples, the antibody or antigen-binding fragment thereof binds to human ROR1 protein with an equilibrium dissociation constant (K_D) of from about 1×10^{-8} M to about 1×10^{-7} M. In some of any examples, the antibody or antigen-binding fragment thereof binds to human ROR1 protein with an equilibrium dissociation constant (K_D) of from about 5×10^{-11} M to about 1×10^{-10} M.

[0032] In some of any examples, the antibody or antigen-binding fragment thereof binds to human ROR1 protein with a dissociation rate constant (k_d or k_{off}) of from about 1×10^{-5} 1/s to about 1×10^{-2} 1/s. In some of any examples, the antibody or antigen-binding fragment thereof binds to human ROR1 protein with a dissociation rate constant (k_d or k_{off}) of from about 1×10^{-3} 1/s to about 1×10^{-2} 1/s. In some of any examples, the antibody or antigen-binding fragment thereof binds to human ROR1 protein with a dissociation rate constant (k_d or k_{off}) of from about 1×10^{-5} 1/s to about 1×10^{-4} 1/s.

[0033] Also provided herein is a single chain cell-surface protein, containing the anti-ROR1 antibody or antigen-binding fragment thereof of any of the examples provided herein.

[0033a] In one aspect, the present disclosure refers to a single chain cell-surface protein, comprising the anti-ROR1 antibody or antigen-binding fragment thereof disclosed herein.

[0034] Also provided herein is a conjugate, containing the anti-ROR1 antibody or antigen-binding fragment thereof of any of the examples provided herein and a heterologous molecule or moiety. In some of any such examples, the heterologous molecule or moiety is a therapeutic moiety.

[0034a] In one aspect, the present disclosure refers to a conjugate, comprising the anti-ROR1 antibody or antigen-binding fragment thereof disclosed herein and a heterologous molecule or moiety.

[0035] Also provided herein is an anti-ROR1 chimeric antigen receptor (CAR) containing an extracellular antigen-binding domain containing the anti-ROR1 antibody or antigen-binding fragment thereof of any of the examples provided herein and an intracellular signaling region.

[0035a] In one aspect, the present disclosure refers to an anti-ROR1 chimeric antigen receptor (CAR) comprising an extracellular antigen-binding domain comprising the anti-ROR1 antibody or antigen-binding fragment thereof disclosed herein, a transmembrane region and an intracellular signaling region.

[0036] Also provided herein is an anti-ROR1 chimeric antigen receptor (CAR) containing an extracellular antigen-binding domain containing the anti-ROR1 antibody or antigen-binding fragment thereof of any of the examples provided herein, a transmembrane region and an intracellular signaling region.

[0037] Also provided herein is an anti-ROR1 chimeric antigen receptor (CAR) containing: an extracellular antigen-binding domain containing a heavy chain variable (V_H) region, and a light chain variable (V_L) region, and an intracellular signaling region, wherein: (i) the V_H region contains a heavy chain complementarity determining region 1 (CDR-H1) containing the sequence set forth in SEQ ID NO: 67, 82 or 52, a heavy chain complementarity determining region 2 (CDR-H2) containing the sequence set forth in SEQ ID NO: 71, 86, 56 or 97, and a heavy chain complementarity determining region 3 (CDR-H3) containing the sequence set forth in SEQ ID NO: 73, 88, 58 or 99, and the V_L region contains a light chain complementarity determining region 1 (CDR-L1) containing the sequence set forth in SEQ ID NO: 75, 90 or 60, a light chain complementarity determining region 2 (CDR-L2) containing the sequence set

containing the sequence set forth in SEQ ID NOS:75, 77 and 79, respectively; the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:80, 84 and 88, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:90, 92 and 94, respectively; the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:50, 54 and 58, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:60, 62 and 64, respectively; or the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:50, 95 and 99, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:60, 62 and 64, respectively; (iii) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:66, 70 and 73, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:75, 77 and 79, respectively; the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:81, 85 and 88, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:90, 92 and 94, respectively; the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:51, 55 and 58, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:60, 62 and 64, respectively; or the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:51, 96 and 99, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:60, 62 and 64, respectively; (iv) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:68, 72 and 74, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:76, 78 and 79, respectively; or the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:83, 87 and 89, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:91, 93 and 94, respectively; the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:53, 57 and 59, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:60, 63 and 64, respectively; or the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:53, 98 and 100, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:61, 63 and 64, respectively.

[0039] In some of any such examples: (i) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:67, 71 and 73, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:75, 77 and 79, respectively; (ii) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3

containing the sequence set forth in SEQ ID NOS:65, 69 and 73, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:75, 77 and 79, respectively; (iii) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:66, 70 and 73, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:75, 77 and 79, respectively; or (iv) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:68, 72 and 74, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:76, 78 and 79, respectively.

[0040] In some of any such examples: (i) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:82, 86 and 88, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:90, 92 and 94, respectively; (ii) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:80, 84 and 88, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:90, 92 and 94, respectively; (iii) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:81, 85 and 88, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:90, 92 and 94, respectively; or (iv) the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 containing the sequence set forth in SEQ ID NOS:83, 87 and 89, respectively, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 containing the sequence set forth in SEQ ID NOS:91, 93 and 94, respectively.

[0041] Also provided herein is an anti-ROR1 chimeric antigen receptor (CAR) containing: an extracellular antigen-binding domain containing a heavy chain variable (V_H) region and a light chain variable (V_L) region, and an intracellular signaling region, wherein: the V_H region contains a heavy chain complementarity determining region 1 (CDR-H1), a heavy chain complementarity determining region 2 (CDR-H2) and a heavy chain complementarity determining region 3 (CDR-H3) contained within SEQ ID NO: 112, 121, 103 or 130, and the V_L region contains a light chain complementarity determining region 1 (CDR-L1), a light chain complementarity determining region 2 (CDR-L2) and a light chain complementarity determining region 3 (CDR-L3) contained within SEQ ID NO: 115, 124 or 106.

[0042] Also provided herein is an anti-ROR1 chimeric antigen receptor (CAR) containing: an extracellular antigen-binding domain containing a heavy chain variable (V_H) region and a light chain variable (V_L) region, and an intracellular signaling region, wherein: the V_H region contains a heavy chain complementarity determining region 1 (CDR-H1), a heavy chain complementarity determining region 2 (CDR-H2) and a heavy chain complementarity determining region 3 (CDR-H3) contained within SEQ ID NO:112, and the V_L region contains a light chain complementarity determining region 1 (CDR-L1), a light chain complementarity determining region 2 (CDR-L2) and a light chain complementarity determining region 3 (CDR-L3) contained within SEQ ID NO:115; the V_H region contains a CDR-H1, a

CDR-H2 and a CDR-H3 contained within SEQ ID NO:121, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 124; the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:103, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 106; or the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:130, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 106.

[0043] In some of any such examples, the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:112, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 115. In some of any such examples, the V_H region contains a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:121, and the V_L region contains a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 124.

[0044] In some of any such examples: the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 112, 121, 103 or 130, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 115, 124 or 106. In some of any such examples: the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:112, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 115; the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:121, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:124; the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:103, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:106; or the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:130, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:106.

[0045] In some of any such examples, the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:112, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or

99% identity to SEQ ID NO: 115. In some of any such examples, the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:121, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:124.

[0046] Also provided herein is an anti-ROR1 chimeric antigen receptor (CAR) containing: an extracellular antigen-binding domain containing a heavy chain variable (V_H) region and a light chain variable (V_L) region, and an intracellular signaling region, wherein: the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 112, 121, 103 or 130, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 115, 124 or 106.

[0047] Also provided herein is an anti-ROR1 chimeric antigen receptor (CAR) containing: an extracellular antigen-binding domain containing a heavy chain variable (V_H) region and a light chain variable (V_L) region, and an intracellular signaling region, wherein: the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:112, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 115; the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:121, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:124; the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:103, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:106; or the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:130, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:106.

[0048] In some of any such examples, the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:112, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 115. In some of any such examples, the V_H region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%,

95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:121, and the V_L region is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:124.

[0049] In some of any such examples: the V_H region is or contains the sequence set forth in SEQ ID NO: 112, 121, 103 or 130, and the V_L region is or contains the sequence set forth in SEQ ID NO: 115, 124 or 106.

[0050] In some of any such examples: the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 112 and 115, respectively; the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 121 and 124, respectively; the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 103 and 106, respectively; or the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 130 and 106, respectively.

[0051] Also provided herein is an anti-ROR1 chimeric antigen receptor (CAR) containing: an extracellular antigen-binding domain containing a heavy chain variable (V_H) region and a light chain variable (V_L) region, and an intracellular signaling region, wherein: the V_H region is or contains the sequence set forth in SEQ ID NO: 112, 121, 103 or 130, and the V_L region is or contains the sequence set forth in SEQ ID NO: 115, 124 or 106.

[0052] Also provided herein is an anti-ROR1 chimeric antigen receptor (CAR) containing: an extracellular antigen-binding domain containing a heavy chain variable (V_H) region and a light chain variable (V_L) region, and an intracellular signaling region, wherein: the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 112 and 115, respectively; the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 121 and 124, respectively; the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 103 and 106, respectively; or the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 130 and 106, respectively.

[0053] In some of any such examples, the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS: 112 and 115, respectively. In some of any such examples, the V_H region and the V_L region are or contain the sequence set forth in SEQ ID NOS:121 and 124, respectively.

[0054] In some of any such examples, the V_H region is or contains the amino acid sequence encoded by SEQ ID NO: 110, 119, 101 or 128 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 110, 119, 101 or 128, and the V_L region is or contains the amino acid sequence encoded by SEQ ID NO: 113, 122 or 104, or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 113, 122 or 104. In some of any such examples, the V_H region is or contains the amino acid sequence encoded by SEQ ID NO: 111, 120, 102 or 129, and the V_L region

is or contains the amino acid sequence encoded by SEQ ID NO: 114, 123, 105 or 131. In some of any such examples, the V_H region is or contains the amino acid sequence encoded by SEQ ID NO: 110 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 110, and the V_L region is or contains the amino acid sequence encoded by SEQ ID NO: 113, or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 113. In some of any such examples, the V_H region is or contains the amino acid sequence encoded by SEQ ID NO: 111, and the V_L region is or contains the amino acid sequence encoded by SEQ ID NO: 114. In some of any such examples, the V_H region is or contains the amino acid sequence encoded by SEQ ID NO: 119 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 119, and the V_L region is or contains the amino acid sequence encoded by SEQ ID NO: 122, or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 122. In some of any such examples, the V_H region is or contains the amino acid sequence encoded by SEQ ID NO: 120, and the V_L region is or contains the amino acid sequence encoded by SEQ ID NO: 123.

[0055] In some of any such examples, said anti-ROR1 antibody or antigen-binding fragment thereof is isolated. In some of any such examples, said anti-ROR1 antibody or antigen-binding fragment thereof is recombinant. In some of any such examples, at least a portion of the V_H region and the V_L region is human or is from a human protein.

[0056] In some of any such examples, the antigen-binding fragment thereof is or contains a single chain fragment. In some of any such examples, the antigen-binding fragment thereof is or contains a single chain Fv (scFv).

[0057] In some of any such examples, the V_H region is amino-terminal to the V_L region. In some of any such examples, the V_H region is carboxy-terminal to the V_L region. In some of any such examples, the V_H region and the V_L region are joined by a flexible linker. In some of any such examples, the flexible linker contains the sequence set forth in SEQ ID NO:41.

[0058] In some of any such examples, the scFv is or contains the sequence set forth in SEQ ID NO: 118, 127, 109 or 134, or an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to SEQ ID NO: 118, 127, 109 or 134. In some of any such examples, the scFv is or contains the sequence set forth in SEQ ID NO: 118. In some of any such examples, the scFv is or contains the sequence set forth in SEQ ID NO: 127. In some of any such examples, the scFv is or contains the amino acid sequence encoded by SEQ ID NO: 116, 125, 107 or 132 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%

identity to SEQ ID NO: 116, 125, 107 or 132. In some of any such examples, the scFv is or contains the amino acid sequence encoded by SEQ ID NO: 117, 126, 108 or 133. In some of any such examples, the scFv is or contains the amino acid sequence encoded by SEQ ID NO: 116 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 116. In some of any such examples, the scFv is or contains the amino acid sequence encoded by SEQ ID NO: 117. In some of any such examples, the scFv is or contains the amino acid sequence encoded by SEQ ID NO: 125 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 125. In some of any such examples, the scFv is or contains the amino acid sequence encoded by SEQ ID NO: 126.

[0059] In some of any such examples, the anti-ROR1 chimeric antigen receptor further contains a spacer between the extracellular antigen-binding domain and the transmembrane domain. In some of any such examples, the spacer contains at least a portion of an immunoglobulin or a variant thereof. In some of any such examples, the spacer contains at least a portion of a hinge region of an immunoglobulin or a variant thereof. In some of any such examples, the spacer is less than at or about 15 amino acids in length. In some of any such examples, the spacer is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 1, 26, 27, 29, 31, 32, 33 or 135.

[0060] In some of any such examples, the at least a portion of a hinge region contains all or a portion of an IgG4 hinge region. In some of any such examples, the at least a portion of a hinge region contains all or a portion of a human IgG4 hinge region, or a variant thereof. In some of any such examples, the at least a portion of a hinge region contains all or a portion of an IgG2 hinge region. In some of any such examples, the at least a portion of a hinge region contains all or a portion of a human IgG2 hinge region, or a variant thereof.

[0061] In some of any such examples, the spacer is or contains the sequence set forth in SEQ ID NO: 1. In some of any such examples, the spacer is or contains the amino acid sequence encoded by SEQ ID NO: 2 or 30 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 2 or 30. In some of any such examples, the spacer is or contains the amino acid sequence encoded by SEQ ID NO: 30.

[0062] In some of any such examples, the spacer is or contains the sequence set forth in SEQ ID NO: 135. In some of any such examples, the spacer is or contains the amino acid sequence encoded by SEQ ID NO: 192 or 136 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 192 or 136. In some of any such examples, the spacer is or contains the amino acid sequence encoded by SEQ ID NO: 136.

[0063] In some of any such examples, the spacer contains at least a portion of a C_{H3} region of an immunoglobulin or a variant thereof. In some of any such examples, the at least a portion of a C_{H3} region contains all or a portion of an IgG4 C_{H3}. In some of any such examples, the at least a portion of a C_{H3} region contains all or a portion of an IgG2 C_{H3}. In some of any such examples, the at least a portion of a C_{H3} region contains all or a portion of an IgG4 C_{H3} and/or an IgG2 C_{H3}. In some of any such examples, the IgG4 C_{H3} is a human IgG4 C_{H3} and the IgG2 C_{H3} is a human IgG2 C_{H3}. In some of any such examples, the spacer contains at least a portion of a hinge region and at least a portion of a C_{H3} region of an immunoglobulin or a variant thereof. In some of any such examples, the spacer is at or about 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124 or 125 amino acids in length, or has a length between any of the foregoing. In some of any such examples, the spacer is at or about 120 amino acids in length.

[0064] In some of any such examples, the spacer is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 138. In some of any such examples, the spacer is or contains the sequence set forth in SEQ ID NO:138. In some of any such examples, the spacer is or contains the amino acid sequence encoded by SEQ ID NO: 193 or 139 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 193 or 139. In some of any such examples, the spacer is or contains the amino acid sequence encoded by SEQ ID NO: 139.

[0065] In some of any such examples, the spacer is at or about 120 amino acids in length. In some of any such examples, the spacer is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 3. In some of any such examples, the spacer is or contains the sequence set forth in SEQ ID NO:3. In some of any such examples, the spacer is or contains the amino acid sequence encoded by SEQ ID NO: 4 or 137 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 4 or 137. In some of any such examples, the spacer is or contains the amino acid sequence encoded by SEQ ID NO: 137.

[0066] In some of any such examples, the spacer contains at least a portion of a C_{H2} of an immunoglobulin or a variant thereof. In some of any such examples, the at least a portion of a C_{H2} region contains all or a portion of an IgG4 C_{H2}. In some of any such examples, the at least a portion of a C_{H2} region contains all or a portion of an IgG2 C_{H2}. In some of any such examples, the at least a portion of a C_{H2} region contains all or a portion of an IgG4 C_{H2} and/or an IgG2 C_{H2}. In some of any such examples, the IgG4 C_{H2} is a human IgG4 C_{H2} and the IgG2 C_{H2} is a human IgG2 C_{H2}. In some of any such examples, the spacer contains at least a portion of a hinge region, at least a portion of a C_{H2} and at least a portion of a C_{H3} region of an immunoglobulin or a variant thereof. In some of any such

examples, the spacer is at or about 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229 or 230 amino acids in length, or has a length between any of the foregoing. In some of any such examples, one or more of the hinge region, the C_{H2} region and the C_{H3} region contains all or a portion of a C_{H2} region and all or a portion of a C_{H3} region from human IgG4. In some of any such examples, one or more of the hinge region, the C_{H2} region and the C_{H3} region is chimeric and contains a hinge, a C_{H2} region and a C_{H3} region from human IgG4 and human IgG2.

[0067] In some of any such examples, the spacer contains a IgG4/2 chimeric hinge region or a modified IgG4 hinge region containing at least one amino acid replacement compared to a human IgG4 hinge; an IgG2/4 chimeric C_{H2} region; and an IgG4 C_{H3} region.

[0068] In some of any such examples, the spacer is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:194. In some of any such examples, the spacer is or contains the sequence set forth in SEQ ID NO: 194. In some of any such examples, the spacer is or contains the amino acid sequence encoded by SEQ ID NO: 195 or 196 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 195 or 196. In some of any such examples, the spacer is or contains the amino acid sequence encoded by SEQ ID NO: 196.

[0069] In some of any such examples, the spacer is or contains an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:37. In some of any such examples, the spacer is or contains the sequence set forth in SEQ ID NO: 37. In some of any such examples, the spacer is or contains the amino acid sequence encoded by SEQ ID NO: 38 or 140 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 38 or 140. In some of any such examples, the spacer is or contains the amino acid sequence encoded by SEQ ID NO: 140.

[0070] In some of any such examples, the intracellular signaling region contains an intracellular signaling domain. In some of any such examples, the intracellular signaling domain is capable of inducing a primary activation signal in a T cell, is a T cell receptor (TCR) component or contains an immunoreceptor tyrosine-based activation motif (ITAM). In some of any such examples, the intracellular signaling domain is or contains a cytoplasmic signaling domain of a CD3-zeta (CD3ζ) chain or a functional variant or signaling portion thereof. In some of any such examples, the intracellular signaling domain is human or is from a human protein. In some of any such examples, the intracellular signaling domain is or contains the sequence set forth in SEQ ID NO:13, 14 or 15, or an amino acid sequence having at least at or about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to SEQ ID NO:13, 14 or 15. In some of any such examples, the intracellular signaling domain is or contains the sequence set forth in SEQ ID NO:13.

[0071] In some of any such examples, the intracellular signaling region further contains a costimulatory signaling region. In some of any such examples, the costimulatory signaling region contains an intracellular signaling domain of a T cell costimulatory molecule or a signaling portion thereof. In some of any such examples, the costimulatory signaling region contains an intracellular signaling domain of CD28, 4-1BB, or ICOS, or a signaling portion thereof. In some of any such examples, the costimulatory signaling region is human or is from a human protein. In some of any such examples, the costimulatory signaling region contains an intracellular signaling domain of CD28. In some of any such examples, the costimulatory signaling region is or contains the sequence set forth in SEQ ID NO:10 or an amino acid sequence having at least at or about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to SEQ ID NO:10. In some of any such examples, the costimulatory signaling region contains an intracellular signaling domain of 4-1BB. In some of any such examples, the costimulatory signaling region is or contains the sequence set forth in SEQ ID NO:12 or an amino acid sequence having at least at or about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to SEQ ID NO: 12.

[0072] In some of any such examples, the anti-ROR1 chimeric antigen receptor further contains a transmembrane region. In some of any such examples, the costimulatory signaling region is between the transmembrane region and the intracellular signaling domain. In some of any such examples, the transmembrane region is or contains a transmembrane domain from CD4, CD28, or CD8. In some of any such examples, the transmembrane region is or contains a transmembrane domain from CD28. In some of any such examples, the transmembrane region is human or is from a human protein.

[0073] In some of any such examples, the transmembrane domain is or contains SEQ ID NO: 8 or an amino acid sequence having at least at or about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to SEQ ID NO: 8. In some of any such examples, the transmembrane domain is or contains the sequence set forth in SEQ ID NO: 8. In some of any such examples, the transmembrane domain is or contains the amino acid sequence encoded by SEQ ID NO: 197 or 198 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 197 or 198. In some of any such examples, the transmembrane domain is or contains the amino acid sequence encoded by SEQ ID NO: 198.

[0074] In some of any such examples, the transmembrane domain is or contains SEQ ID NO: 149 or an amino acid sequence having at least at or about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to SEQ ID NO: 149. In some of any such examples, the transmembrane domain is or contains the sequence set forth in SEQ ID NO: 149. In some of any such examples, the transmembrane domain is or contains the amino acid sequence encoded by SEQ ID NO: 147 or 148 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%,

86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 147 or 148. In some of any such examples, the transmembrane domain is or contains the amino acid sequence encoded by SEQ ID NO: 148.

[0075] In some of any such examples, the encoded chimeric antigen receptor contains from its N to C terminus in order: the extracellular antigen-binding domain, the spacer, the transmembrane region and the intracellular signaling region. In some of any such examples, the encoded chimeric antigen receptor contains, from its N to C terminus in order: an extracellular antigen-binding domain containing an scFv, a spacer containing a modified IgG4 hinge; a transmembrane domain; and an intracellular signaling region containing a cytoplasmic signaling domain of a CD3-zeta (CD3 ζ) chain and an intracellular signaling domain of a costimulatory signaling region. In some of any such examples, the encoded chimeric antigen receptor contains, from its N to C terminus in order: an extracellular antigen-binding domain containing an scFv, a spacer containing a modified IgG4 hinge containing the sequence set forth in SEQ ID NO:135; a transmembrane domain from a human CD28; and an intracellular signaling region containing a cytoplasmic signaling domain of a CD3-zeta (CD3 ζ) chain and an intracellular signaling domain of a costimulatory signaling region containing an intracellular signaling domain of 4-1BB. In some of any such examples, the encoded chimeric antigen receptor contains, from its N to C terminus in order: an extracellular antigen-binding domain containing an scFv, a spacer containing a modified IgG4 hinge-C_H3; a transmembrane domain; and an intracellular signaling region containing a cytoplasmic signaling domain of a CD3-zeta (CD3 ζ) chain and an intracellular signaling domain of a costimulatory signaling region. In some of any such examples, the encoded chimeric antigen receptor contains, from its N to C terminus in order: an extracellular antigen-binding domain containing an scFv, a spacer containing a modified IgG4 hinge-C_H3 containing the sequence set forth in SEQ ID NO: 138; a transmembrane domain from a human CD28; and an intracellular signaling region containing a cytoplasmic signaling domain of a CD3-zeta (CD3 ζ) chain and an intracellular signaling domain of a costimulatory signaling region containing an intracellular signaling domain of 4-1BB. In some of any such examples, the extracellular antigen-binding domain is an scFv.

[0076] In some of any such examples, the anti-ROR1 chimeric antigen receptor is or contains the sequence set forth in SEQ ID NO: 184, 185, 186, 187, 188 or 189 or a sequence that exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO: 184, 185, 186, 187, 188 or 189.

[0077] In some of any such examples, the anti-ROR1 chimeric antigen receptor is or contains the sequence set forth in SEQ ID NO: 184 or a sequence that exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO: 184. In some of any such examples, the anti-ROR1 chimeric antigen receptor is or contains the sequence set forth in SEQ ID NO: 184. In some of any such examples, the anti-ROR1 chimeric antigen receptor is or contains the sequence set forth in SEQ ID NO: 185 or a sequence that

exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO:185. In some of any such examples, the anti-ROR1 chimeric antigen receptor is or contains the sequence set forth in SEQ ID NO: 185. In some of any examples, the anti-ROR1 chimeric antigen receptor is or comprises the sequence set forth in SEQ ID NO: 186 or a sequence that exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO: 186. In some of any examples, the anti-ROR1 chimeric antigen receptor is or comprises the sequence set forth in SEQ ID NO: 186. In some of any examples, the anti-ROR1 chimeric antigen receptor is or comprises the sequence set forth in SEQ ID NO: 187 or a sequence that exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO:187. In some of any examples, the anti-ROR1 chimeric antigen receptor is or comprises the sequence set forth in SEQ ID NO: 187. In some of any examples, the anti-ROR1 chimeric antigen receptor is or comprises the sequence set forth in SEQ ID NO: 188 or a sequence that exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO: 188. In some of any examples, the anti-ROR1 chimeric antigen receptor is or comprises the sequence set forth in SEQ ID NO: 188. In some of any examples, the anti-ROR1 chimeric antigen receptor is or comprises the sequence set forth in SEQ ID NO: 189 or a sequence that exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO:189. In some of any examples, the anti-ROR1 chimeric antigen receptor is or comprises the sequence set forth in SEQ ID NO: 189.

[0078] In some of any such examples, the anti-ROR1 chimeric antigen receptor is encoded by the sequence set forth in SEQ ID NO: 156, 157, 158, 159, 160 or 161 or a sequence that exhibits at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO: 156, 157, 158, 159, 160 or 161. In some of any such examples, the anti-ROR1 chimeric antigen receptor is encoded by the sequence set forth in SEQ ID NO: 156 or a sequence that exhibits at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO: 156. In some of any such examples, the anti-ROR1 chimeric antigen receptor is encoded by the sequence set forth in SEQ ID NO: 156. In some of any such examples, the anti-ROR1 chimeric antigen receptor is encoded by the sequence set forth in SEQ ID NO: 157 or a sequence that exhibits at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO: 157. In some of any such examples, the anti-ROR1 chimeric antigen receptor is encoded by the sequence set forth in SEQ ID NO: 157.

[0079] In some of any such examples, said anti-ROR1 chimeric antigen receptor specifically binds to a receptor tyrosine kinase-like orphan receptor 1 (ROR1) protein. In some of any such examples, said anti-ROR1 chimeric antigen receptor specifically binds to a human ROR1 protein. In some of any such examples, the human ROR1 protein contains an amino acid sequence set forth in SEQ ID NO: 144, 145 or 146. In some of any such examples, said anti-ROR1 chimeric antigen receptor does not bind to, is not cross-reactive to, or binds at a lower level or degree or affinity to a receptor tyrosine kinase-like orphan receptor 2 (ROR2) protein. In some of any such examples, said anti-ROR1 chimeric antigen receptor does not bind to, is not cross-reactive to, or binds at a lower level or degree or affinity to a human ROR2.

[0080] In some of any such examples, the extent, level or degree or affinity of binding of said anti-ROR1 chimeric antigen receptor to a human ROR2 is at least at or about 75%, 80%, 90%, 95% or 99% less than the extent, level or degree or affinity of binding to a human ROR1. In some of any such examples, binding is compared under the same or substantially the same conditions or assay. In some of any such examples, said anti-ROR1 chimeric antigen receptor exhibits the same, substantially the same or lower level or degree of signaling or activity in the presence of a ROR2 protein, compared to the level or degree of signaling or activity in the presence of a ROR1 protein. In some of any such examples, said anti-ROR1 chimeric antigen receptor exhibits the same, substantially the same or lower level or degree of signaling or activity in the presence of a human ROR2 protein, compared to the level or degree of signaling or activity in the presence of a human ROR1 protein. In some of any such examples, activity is compared under the same or substantially the same conditions or assay. In some of any such examples, said anti-ROR1 chimeric antigen receptor exhibits a level or degree of signaling or activity in the presence of a human ROR2 that is at least at or about 75%, 80%, 90%, 95% or 99% less than the level or degree of signaling or activity in the presence of a human ROR1. In some of any such examples, activity is compared under the same or substantially the same conditions or assay.

[0081] In some of any such examples, said anti-ROR1 chimeric antigen receptor exhibits the same, substantially the same or lower level or degree of signaling or activity in the presence of a ROR2 protein compared to a reference ROR1-specific chimeric antigen receptor. In some of any such examples, said anti-ROR1 chimeric antigen receptor exhibits the same, substantially the same or lower level or degree of signaling or activity in the presence of a human ROR2, compared to a reference ROR1-specific chimeric antigen receptor. In some of any examples, activity is compared under the same or substantially the same conditions or assay.

[0082] In some of any such examples, said anti-ROR1 chimeric antigen receptor exhibits the same, substantially the same or lower level or degree of signaling or activity in the presence of a ROR2 protein, compared to a reference ROR1-specific chimeric antigen receptor. In some of any such examples, said anti-ROR1 chimeric antigen receptor exhibits the same, substantially the same or

lower level or degree of signaling or activity in the presence of a human ROR2 protein, compared to a reference ROR1-specific chimeric antigen receptor. In some of any such examples, activity is compared under the same or substantially the same conditions or assay. In some of any such examples, said anti-ROR1 chimeric antigen receptor exhibits the same, substantially the same or higher antigen-specific signaling or antigen dependent activity or signaling compared to a reference ROR1-specific chimeric antigen receptor. In some of any such examples, activity is compared under the same or substantially the same conditions or assay. In some of any such examples, said anti-ROR1 chimeric antigen receptor exhibits the same, substantially the same or lower tonic signaling or antigen independent activity or signaling compared to a reference ROR1-specific chimeric antigen receptor. In some of any such examples, activity is compared under the same or substantially the same conditions or assay. In some of any such examples, said anti-ROR1 chimeric antigen receptor exhibits a level or degree of tonic signaling or antigen independent activity or signaling that is at least at or about 75%, 80%, 90%, 95% or 99% less than the level or degree of tonic signaling or antigen independent activity of a reference ROR1-specific chimeric antigen receptor. In some of any such examples, activity is compared under the same or substantially the same conditions or assay.

[0083] In some of any such examples, the reference ROR1-specific chimeric antigen receptor contains the anti-ROR1 antibody R12 or the anti-ROR1 antibody 2A2 or an antigen-binding fragment thereof. In some of any such examples, the reference ROR1-specific chimeric antigen receptor contains an scFv from R12 or 2A2. In some of any such examples, the reference ROR1-specific chimeric antigen receptor contains the anti-ROR1 antibody R12 or an scFv from R12 or 2A2.

[0084] Also provided herein is a polynucleotide containing a nucleic acid encoding all or a portion of the anti-ROR1 antibody or antigen-binding domain thereof of any of the examples provided herein, the single chain cell surface protein of any of the examples provided herein, the conjugate of any of the examples provided herein, or the anti-ROR1 chimeric antigen receptor of any of the examples provided herein.

[0084a] In one aspect, the present disclosure refers to a polynucleotide comprising a nucleic acid encoding the anti-ROR1 antibody or antigen-binding domain thereof disclosed herein or the anti-ROR1 chimeric antigen receptor disclosed herein.

[0085] In some of any such examples, said polynucleotide contains a nucleic acid encoding the V_H containing the sequence set forth in SEQ ID NO: 110, 119, 101 or 128 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 110, 119, 101 or 128, and a nucleic acid encoding the V_L containing the sequence set forth in SEQ ID NO: 113, 122 or 104, or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 113, 122 or 104. In some of any such examples, said polynucleotide contains a nucleic acid encoding the V_H containing the sequence set forth in SEQ ID NO: 110 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 110, and a nucleic acid encoding the V_L containing the sequence set forth in SEQ ID NO:

113, or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 113. In some of any such examples, said polynucleotide contains a nucleic acid encoding the V_H containing the sequence set forth in SEQ ID NO: 119 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 119, and a nucleic acid encoding the V_L containing the sequence set forth in SEQ ID NO: 122, or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 122.

[0086] In some of any such examples, said polynucleotide contains a nucleic acid encoding the scFv containing the sequence set forth in SEQ ID NO: 116, 125, 107 or 132 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 116, 125, 107 or 132. In some of any such examples, said polynucleotide contains a nucleic acid encoding the scFv containing the sequence set forth in SEQ ID NO: 116 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 116. In some of any such examples, said polynucleotide contains a nucleic acid encoding the scFv containing the sequence set forth in SEQ ID NO: 125 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 125.

[0087] In some of any such examples, said polynucleotide contains a nucleic acid encoding the spacer containing the sequence set forth in SEQ ID NO: 192 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 192. In some of any such examples, said polynucleotide contains a nucleic acid encoding the spacer containing the sequence set forth in SEQ ID NO: 193 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 193. In some of any such examples, said polynucleotide contains a nucleic acid encoding the spacer containing the sequence set forth in SEQ ID NO: 195 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 195.

[0088] In some of any such examples, the nucleic acid encoding the anti-ROR1 antibody or antigen-binding domain thereof, the single chain cell surface protein, the conjugate or the anti-ROR1 chimeric antigen receptor contains at least one modified splice donor or splice acceptor site or both, said modified splice donor and/or acceptor site containing one or more nucleotide modifications corresponding to a reference splice donor site and/or reference splice acceptor site. In some of any such

examples, the one or more nucleotide modifications contain a nucleic acid substitution. In some of any such examples, the reference splice donor and/or reference splice acceptor sites are canonical, non-canonical, or cryptic splice sites. In some of any examples, the polynucleotide is optimized by splice site elimination.

[0089] In some of any such examples: the reference splice donor or reference splice acceptor site(s) or both has a splice site prediction score of at least at or about 0.4, 0.5, 0.6, 0.70, 0.75, 0.80, 0.85, 0.90, 0.95, 0.99 or 1.0; or the reference splice donor or reference splice acceptor site(s) or both is/are predicted to be involved in a splice event with a probability of at least at or about 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 99% or 100%.

[0090] In some of any such examples: the reference splice donor or reference splice acceptor site(s) or both has a splice site prediction score of at least at or about 0.70, 0.75, 0.80, 0.85, 0.90, 0.95, 0.99 or 1.0; and/or the reference splice donor or reference splice acceptor site(s) or both is/are predicted to be involved in a splice event with a probability of at least at or about 70%, 75%, 80%, 85%, 90%, 95%, 99% or 100%.

[0091] In some of any such examples, at least one of the one or more nucleotide modifications are within 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 residues of the splice site junction of the reference splice acceptor and/or reference splice donor site. In some of any such examples, the one or more nucleotide modifications is silent or results in a degenerate codon or does not change the amino acid sequence of the encoded protein, or one or more or all of the foregoing.

[0092] In some of any such examples, upon expression of the polynucleotide in a cell, the transcribed RNA from the polynucleotide, exhibits at least at or about 70%, at or about 75%, at or about 80%, at or about 85%, at or about 90%, or at or about 95% RNA homogeneity. In some of any such examples, upon expression in a cell, the transcribed RNA from the polynucleotide exhibits reduced heterogeneity compared to the heterogeneity of the mRNA transcribed from a reference polynucleotide, said reference polynucleotide encoding the same amino acid sequence as the polynucleotide, wherein the reference polynucleotide differs by the presence of one or more splice donor site or one or more splice acceptor site or both, in the nucleic acid encoding the spacer or contains one or more nucleotide modifications compared to the polynucleotide. In some of any such examples, the RNA heterogeneity is reduced by greater than at or about 10%, 15%, 20%, 25%, 30%, 40% or 50% or more. In some of any such examples, the transcribed RNA from the reference polynucleotide exhibits greater than at or about 10%, 15%, 20%, 25%, 30%, 40% or 50% or more RNA heterogeneity. In some of any such examples, the transcribed RNA messenger RNA (mRNA). In some of any such examples, the RNA homogeneity or heterogeneity or both is determined by agarose gel electrophoresis, chip-based capillary electrophoresis, analytical ultracentrifugation, field flow fractionation, or liquid chromatography.

[0093] In some of any such examples, the polynucleotide is codon-optimized for expression in a human cell.

[0094] In some of any such examples, said polynucleotide contains a nucleic acid encoding the V_H containing the sequence set forth in SEQ ID NO: 111, 120, 102 or 129, and a nucleic acid encoding the V_L containing the sequence set forth in SEQ ID NO: 114, 123, 105 or 131. In some of any such examples, said polynucleotide contains a nucleic acid encoding the V_H containing the sequence set forth in SEQ ID NO: 111, and a nucleic acid encoding the V_L containing the sequence set forth in SEQ ID NO: 114. In some of any such examples, said polynucleotide contains a nucleic acid encoding the V_H containing the sequence set forth in SEQ ID NO: 120, and a nucleic acid encoding the V_L containing the sequence set forth in SEQ ID NO: 123.

[0095] In some of any such examples, said polynucleotide contains a nucleic acid encoding the scFv containing the sequence set forth in SEQ ID NO: 117, 126, 108 or 133. In some of any such examples, said polynucleotide contains a nucleic acid encoding the scFv containing the sequence set forth in SEQ ID NO: 117. In some of any such examples, said polynucleotide contains a nucleic acid encoding the scFv containing the sequence set forth in SEQ ID NO: 126.

[0096] In some of any such examples, said polynucleotide contains a nucleic acid encoding the spacer containing the sequence set forth in SEQ ID NO:136. In some of any such examples, said polynucleotide contains a nucleic acid encoding the spacer containing the sequence set forth in SEQ ID NO:139. In some of any such examples, said polynucleotide contains a nucleic acid encoding the spacer containing the sequence set forth in SEQ ID NO:196.

[0097] In some of any such examples, said polynucleotide contains the sequence set forth in SEQ ID NO: 156, 157, 158, 159, 160 or 161 or a sequence that exhibits at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO: 156, 157, 158, 159, 160 or 161. In some of any such examples, said polynucleotide contains the sequence set forth in SEQ ID NO: 156 or a sequence that exhibits at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO: 156. In some of any such examples, said polynucleotide contains the sequence set forth in SEQ ID NO: 156. In some of any such examples, said polynucleotide contains the sequence set forth in SEQ ID NO: 157 or a sequence that exhibits at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO: 157. In some of any such examples, said polynucleotide contains the sequence set forth in SEQ ID NO: 157.

[0098] In some of any such examples, the polynucleotide further contains a CD33 signal sequence, a GM-CSF signal sequence, a CD8 signal sequence or an Ig kappa signal sequence. In some of any such examples, the polynucleotide further contains a CD33 signal sequence. In some of any

such examples, the CD33 signal sequence is set forth in SEQ ID NO:190 or a nucleic acid sequence having at least at or about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:190.

[0099] Also provided herein is a vector, containing the polynucleotide of any of the examples provided herein. In some examples, the vector is a viral vector. In some examples, the viral vector is a retroviral vector or a lentiviral vector.

[0099a] In one aspect, the present disclosure refers to a vector, comprising the polynucleotide disclosed herein.

[0100] Also provided herein is a cell containing the anti-ROR1 chimeric antigen receptor of any of the examples provided herein. Also provided herein is a cell containing the polynucleotide of any of the examples provided herein, or the vector of any of the examples provided herein. Also provided herein is a cell containing the anti-ROR1 antibody or antigen-binding fragment thereof of the examples provided herein, the conjugate of any of the examples provided herein, the single chain cell surface protein of any of the examples provided herein, the anti-ROR1 chimeric antigen receptor of any of the examples provided herein, the polynucleotide of any of the examples provided herein, or the vector of any of the examples provided herein.

[0100a] In one aspect, the present disclosure refers to a cell comprising the anti-ROR1 antibody or antigen-binding fragment thereof disclosed herein, the chimeric antigen receptor disclosed herein, the polynucleotide disclosed herein, or the vector disclosed herein.

[0101] In some examples, the cell is a lymphocyte. In some examples, the cell is an NK cell or a T cell. In some of any such examples, the cell is a T cell and the T cell is a CD4⁺ or a CD8⁺ T cell. In some of any such examples, the cell is a primary cell obtained from a subject.

[0101a] In one aspect, the present disclosure refers to a T cell comprising the chimeric antigen receptor disclosed herein or the polynucleotide disclosed herein.

[0102] In some of any such examples, among a plurality of the cells, less than at or about 10%, at or about 9%, at or about 8%, at or about 7%, at or about 5%, at or about 4%, at or about 3%, at or about 2% or at or about 1% of the cells in the plurality contain an anti-ROR1 chimeric antigen receptor that exhibits tonic signaling or antigen independent activity or signaling.

[0103] Also provided herein is a composition containing the anti-ROR1 antibody or antigen-binding fragment thereof of any of the examples provided herein, the conjugate of any of the examples provided herein, the single chain cell surface protein of any of the examples provided herein or the anti-ROR1 chimeric antigen receptor of any of the examples provided herein.

[0104] Also provided herein is a composition containing the cell of any of the examples provided herein. In some of any such examples, the composition further contains a pharmaceutically acceptable excipient. In some of any such examples, the composition contains CD4⁺ and CD8⁺ T cells and the ratio of CD4⁺ to CD8⁺ T cells is from at or about 1:3 to 3:1. In some of any such examples, the composition contains CD4⁺ and CD8⁺ T cells and the ratio of CD4⁺ to CD8⁺ T cells is at or about 1:2 to 2:1. In some of any such examples, the composition contains CD4⁺ and CD8⁺ T cells and the ratio of CD4⁺ to CD8⁺ T cells is at or about 1:1.

[0104a] In one aspect, the present disclosure refers to a composition comprising the cell disclosed herein.

[0104b] In one aspect, the present disclosure refers to a composition comprising the anti-ROR1 antibody or antigen-binding fragment thereof disclosed herein, the single chain cell surface protein disclosed herein, the conjugate disclosed herein, the chimeric antigen receptor disclosed herein, the polynucleotide disclosed herein, or the vector disclosed herein.

[0105] In some of any such examples, among a plurality of the cells in the composition, less than at or about 10%, at or about 9%, at or about 8%, at or about 7%, at or about 5%, at or about 4%, at or about 3%, at or about 2% or at or about 1% of the cells in the plurality contain an anti-ROR1 chimeric antigen receptor that exhibits tonic signaling or antigen independent activity or signaling.

[0106] Also provided herein is a method of treatment, containing administering the composition of any of the examples provided herein to a subject having a disease or disorder associated with ROR1.

[0107] Also provided herein is a method of treatment, containing administering the anti-ROR1 antibody or antigen-binding fragment thereof of any of the examples provided herein, the conjugate of any of the examples provided herein, the single chain cell surface protein of any of the examples provided herein, the anti-ROR1 chimeric antigen receptor of any of the examples provided herein, the polynucleotide of any of the examples provided herein, the vector of any of the examples provided herein, or the cell of any of the examples provided herein to a subject having a disease or disorder associated with ROR1. Also provided herein is a composition of any of the examples provided herein for use in treating a disease or disorder associated with ROR1. Also provided herein is a use of a composition of any of the examples provided herein for the manufacture of a medicament for treating a disease or disorder associated with ROR1. Also provided herein is a use of a composition of any of the examples provided herein for the treatment of a disease or disorder associated with ROR1. Also provided herein is a method of treatment, containing administering the cells of any of the examples provided herein to a subject having a disease or disorder associated with ROR1.

[0108] Also provided herein is a method of treatment, containing administering the anti-ROR1 antibody or antigen-binding fragment thereof of any of the examples provided herein, the conjugate of any of the examples provided herein, the single chain cell surface protein of any of the examples provided herein, the anti-ROR1 chimeric antigen receptor of any of the examples provided herein, the polynucleotide of any of the examples provided herein, the vector of any of the examples provided herein, or the cell of any of the examples provided herein to a subject having a disease or disorder associated with ROR1. Also provided herein is a cell of any of the examples provided herein for use in treating a disease or disorder associated with ROR1. Also provided herein is a use of a cell of any of the examples provided herein for the manufacture of a medicament for treating a disease or disorder associated with ROR1. Also provided herein is a use of a cell of any of the examples provided herein for the treatment of a disease or disorder associated with ROR1.

[0108a] In one aspect, the present disclosure refers to the anti-ROR1 antibody or antigen-binding fragment thereof disclosed herein, the single chain cell surface protein disclosed herein, the conjugate disclosed herein, the anti-ROR1 chimeric antigen receptor disclosed herein, the polynucleotide disclosed herein, the vector disclosed herein, the cell disclosed herein or the composition disclosed herein for use in treating a disease or disorder associated with ROR1.

[0108b] In one aspect, the present disclosure refers to use of the anti-ROR1 antibody or antigen-binding fragment thereof disclosed herein, the single chain cell surface protein disclosed herein, the conjugate disclosed herein, the anti-ROR1 chimeric antigen receptor disclosed herein, the polynucleotide disclosed herein, the vector disclosed herein, the cell disclosed herein or the composition disclosed herein for the manufacture of a medicament for treating a disease or disorder associated with ROR1.

[0109] In some of any of the provided examples, the disease or disorder associated with ROR1 is a cancer. In some of any of the provided examples, the cancer is a ROR1-expressing cancer. In some of any of the provided examples, the cancer is associated with a ROR1-expressing solid tumor or a ROR1-expressing hematologic malignancy.

[0110] In some of any of the provided examples, the cancer is associated with a ROR1-expressing solid tumor. In some of any of the provided examples, the cancer associated with a solid tumor is selected from the group consisting of neuroblastoma, renal cell carcinoma, colon cancer, colorectal cancer, breast cancer, epithelial squamous cell cancer, melanoma, myeloma, stomach cancer, brain cancer, lung cancer, pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer,

prostate cancer, testicular cancer, thyroid cancer, uterine cancer, adrenal cancer and head and neck cancer. In some of any of the provided examples, the lung cancer is a non-small cell lung cancer (NSCLC), lung adenocarcinoma, adenocarcinoma, squamous cell carcinoma, small cell carcinoma, and atypical carcinoid. In some of any of the provided examples, the lung cancer is a non-small cell lung cancer (NSCLC). In some of any of the provided examples, the breast cancer is a triple negative breast cancer (TNBC).

[0111] In some of any of the provided examples, the cancer is associated with a ROR1-expressing hematologic malignancy. In some of any of the provided examples, the hematologic malignancy is selected from the group consisting of B cell leukemia, lymphoma, B cell chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), Burkitt's Lymphoma or mantle cell lymphoma (MCL).

[0112] In some examples of the methods provided herein, the disease or disorder associated with ROR1 is a cancer. In some examples of the methods provided herein, the cancer is a ROR1-expressing cancer. In some examples of the methods provided herein, the cancer is associated with a ROR1-expressing solid tumor or a ROR1-expressing hematologic malignancy.

[0113] In some examples of the methods provided herein, the cancer is associated with a ROR1-expressing solid tumor. In some examples of the methods provided herein, the cancer associated with a solid tumor is selected from the group consisting of neuroblastoma, renal cell carcinoma, colon cancer, colorectal cancer, breast cancer, epithelial squamous cell cancer, melanoma, myeloma, stomach cancer, brain cancer, lung cancer, pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer, prostate cancer, testicular cancer, thyroid cancer, uterine cancer, adrenal cancer and head and neck cancer. In some examples of the methods provided herein, the lung cancer is a non-small cell lung cancer (NSCLC), lung adenocarcinoma, adenocarcinoma, squamous cell carcinoma, small cell carcinoma, and atypical carcinoid. In some examples of the methods provided herein, the lung cancer is a non-small cell lung cancer (NSCLC). In some examples of the methods provided herein, the breast cancer is a triple negative breast cancer (TNBC).

[0114] In some examples of the methods provided herein, the cancer is associated with a ROR1-expressing hematologic malignancy. In some examples of the methods provided herein, the hematologic malignancy is selected from the group consisting of B cell leukemia, lymphoma, B cell chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), Burkitt's Lymphoma or mantle cell lymphoma (MCL).

[0115] In some examples of the cells or compositions for use provided herein, the disease or disorder associated with ROR1 is a cancer. In some examples of the cells or compositions for use provided herein, the cancer is a ROR1-expressing cancer. In some examples of the cells or compositions for use provided herein, the cancer is associated with a ROR1-expressing solid tumor or a ROR1-expressing hematologic malignancy.

[0116] In some examples of the cells or compositions for use provided herein, the cancer is associated with a ROR1-expressing solid tumor. In some examples of the cells or compositions for use provided herein, the cancer associated with a solid tumor is selected from the group consisting of neuroblastoma, renal cell carcinoma, colon cancer, colorectal cancer, breast cancer, epithelial squamous cell cancer, melanoma, myeloma, stomach cancer, brain cancer, lung cancer, pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer, prostate cancer, testicular cancer, thyroid cancer, uterine cancer, adrenal cancer and head and neck cancer. In some examples of the cells or compositions for use provided herein, the lung cancer is a non-small cell lung cancer (NSCLC), lung adenocarcinoma, adenocarcinoma, squamous cell carcinoma, small cell carcinoma, and atypical carcinoid. In some examples of the cells or compositions for use provided herein, the lung cancer is a non-small cell lung cancer (NSCLC). In some examples of the cells or compositions for use provided herein, the breast cancer is a triple negative breast cancer (TNBC).

[0117] In some examples of the cells or compositions for use provided herein, the cancer is associated with a ROR1-expressing hematologic malignancy. In some examples of the cells or compositions for use provided herein, the hematologic malignancy is selected from the group consisting of B cell leukemia, lymphoma, B cell chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), Burkitt's Lymphoma or mantle cell lymphoma (MCL).

[0118] In some examples of the uses provided herein, the disease or disorder associated with ROR1 is a cancer. In some examples of the uses provided herein, the cancer is a ROR1-expressing cancer. In some examples of the uses provided herein, the cancer is associated with a ROR1-expressing solid tumor or a ROR1-expressing hematologic malignancy.

[0119] In some examples of the uses provided herein, the cancer is associated with a ROR1-expressing solid tumor. In some examples of the uses provided herein, the cancer associated with a solid tumor is selected from the group consisting of neuroblastoma, renal cell carcinoma, colon cancer, colorectal cancer, breast cancer, epithelial squamous cell cancer, melanoma, myeloma, stomach cancer, brain cancer, lung cancer, pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer, prostate cancer, testicular cancer, thyroid cancer, uterine cancer, adrenal cancer and head and neck cancer. In some examples of the uses provided herein, the lung cancer is a non-small cell lung cancer (NSCLC). In some examples of the uses provided herein, the breast cancer is a triple negative breast cancer (TNBC).

[0120] In some examples of the uses provided herein, the cancer is associated with a ROR1-expressing hematologic malignancy. In some examples of the uses provided herein, the hematologic malignancy is selected from the group consisting of B cell leukemia, lymphoma, B cell chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), Burkitt's Lymphoma or mantle cell lymphoma (MCL).

[0121] In some of any such examples, the disease or disorder associated with ROR1 is associated with ROR1 expression. In some of any such examples, the disease or disorder associated with ROR1 is a B cell-related disorder. In some of any such examples, the disease or disorder associated with ROR1 is a cancer. In some of any such examples, the cancer is a ROR1-expressing cancer. In some of any such examples, the ROR1-expressing cancer is selected from the group consisting of B cell leukemia, lymphoma, B cell chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), Burkitt's Lymphoma, mantle cell lymphoma (MCL), non-small cell lung cancer (NSCLC), neuroblastoma, renal cell carcinoma, colon cancer, colorectal cancer, breast cancer, epithelial squamous cell cancer, melanoma, myeloma, stomach cancer, brain cancer, lung cancer, pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer, prostate cancer, testicular cancer, thyroid cancer, uterine cancer, adrenal cancer and head and neck cancer.

[0122] Also provided herein is a kit containing the anti-ROR1 antibody or antigen-binding fragment thereof of any of the examples provided herein, the single chain cell surface protein of any of the examples provided herein, the conjugate of any of the examples provided herein, the anti-ROR1 chimeric antigen receptor of any of the examples provided herein, the cell of any of the examples provided herein, or the composition of any of the examples provided herein, and instructions for use. In some of any such examples, the instructions are for administering the anti-ROR1 antibody or antigen-binding fragment thereof, the single chain cell surface protein, the conjugate, the anti-ROR1 chimeric antigen receptor, the cell or the composition. In some of any such examples, the instructions are in accord with the method, the composition for use or the use of any of the examples provided herein.

[0122a] In one aspect, the present disclosure refers to a kit comprising the anti-ROR1 antibody or antigen-binding fragment thereof disclosed herein, the single chain surface protein disclosed herein, the conjugate disclosed herein, the anti-ROR1 chimeric antigen receptor disclosed herein, the polynucleotide disclosed herein, the vector disclosed herein, the cell disclosed herein, or the composition disclosed herein, and instructions for use.

[0123] Also provided herein is an article of manufacture containing the anti-ROR1 antibody or antigen-binding fragment thereof of any of the examples provided herein, the single chain cell surface protein of any of the examples provided herein, the conjugate of any of the examples provided herein, the anti-ROR1 chimeric antigen receptor of any of the examples provided herein, the cell of any of the examples provided herein, the composition of any of the examples provided herein, or the kit of any of the examples provided herein.

[0123a] In one aspect, the present disclosure refers to an article of manufacture comprising the anti-ROR1 antibody or antigen-binding fragment thereof disclosed herein, the single chain surface protein disclosed herein, the conjugate disclosed herein, the anti-ROR1 chimeric antigen receptor disclosed herein, the polynucleotide disclosed herein, the vector disclosed herein, the cell disclosed herein, or the composition disclosed herein.

Brief Description of the Drawings

[0124] **FIG. 1** depicts the relative intracellular IFN- γ , TNF- α or IL-2 expression levels by ICS in GFP+ CD4+ T cells compared to the levels of each cytokine in cells expressing the reference anti-ROR1 (R12) CAR, after 24 hours stimulation with plate-bound recombinant ROR1-Fc, in primary T cells expressing select candidate anti-ROR1 CAR-expressing T cells from a screen as described in Example 1.

[0125] **FIG. 2** shows the relative intracellular IFN- γ , TNF- α or IL-2 expression levels by ICS in primary T cells expressing select candidate anti-ROR1 CAR-expressing T cells from a screen as

Claims

1. An anti-receptor tyrosine kinase-like orphan receptor 1 (ROR1) antibody or antigen-binding fragment thereof, comprising: a heavy chain variable (V_H) region and a light chain variable (V_L) region, wherein:

the V_H region comprises a heavy chain complementarity determining region 1 (CDR-H1), a heavy chain complementarity determining region 2 (CDR-H2) and a heavy chain complementarity determining region 3 (CDR-H3) contained within SEQ ID NO:112, and the V_L region comprises a light chain complementarity determining region 1 (CDR-L1), a light chain complementarity determining region 2 (CDR-L2) and a light chain complementarity determining region 3 (CDR-L3) contained within SEQ ID NO:115;

the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:121, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 124;

the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:103, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 106; or

the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 contained within SEQ ID NO:130, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 contained within SEQ ID: NO 106.

2. An anti-ROR1 antibody or antigen-binding fragment thereof, comprising: a heavy chain variable (V_H) region, and a light chain variable (V_L) region, wherein the V_H region comprises a heavy chain complementarity determining region 1 (CDR-H1), a heavy chain complementarity determining region 2 (CDR-H2) and a heavy chain complementarity determining region 3 (CDR-H3) comprising the sequence set forth in SEQ ID NOS:67, 71 and 73, respectively, and the V_L region comprises a light chain complementarity determining region 1 (CDR-L1), a light chain complementarity determining region 2 (CDR-L2) and a light chain complementarity determining region 3 (CDR-L3) comprising the sequence set forth in SEQ ID NOS:75, 77 and 79, respectively;

the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 comprising the sequence set forth in SEQ ID NOS:82, 86 and 88, respectively, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 comprising the sequence set forth in SEQ ID NOS:90, 92 and 94, respectively;

the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 comprising the sequence set forth in SEQ ID NOS:52, 56 and 58, respectively, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 comprising the sequence set forth in SEQ ID NOS:60, 62 and 64, respectively; or

the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 comprising the sequence set forth in SEQ ID NOS:52, 97 and 99, respectively, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 comprising the sequence set forth in SEQ ID NOS:60, 62 and 64, respectively.

3. The anti-ROR1 antibody or antigen-binding fragment thereof of claim 1 or 2, wherein the V_H region comprises a CDR-H1, a CDR-H2 and a CDR-H3 comprising the sequence set forth in SEQ ID NOS:67, 71 and 73, respectively, and the V_L region comprises a CDR-L1, a CDR-L2 and a CDR-L3 comprising the sequence set forth in SEQ ID NOS:75, 77 and 79, respectively.

4. The anti-ROR1 antibody or antigen-binding fragment thereof of any one of claims 1-3: the V_H region comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:112, and the V_L region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 115;

the V_H region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:121, and the V_L region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:124;

the V_H region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:103, and the V_L region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:106; or

the V_H region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:130, and the V_L region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:106.

5. An anti-ROR1 antibody or antigen-binding fragment thereof, comprising: a heavy chain variable (V_H) region and a light chain variable (V_L) region, wherein:

the V_H region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:112, and the V_L region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 115;

the V_H region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:121,

and the V_L region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:124;

the V_H region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:103, and the V_L region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:106;

the V_H region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:130, and the V_L region is or comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:106;

the V_H region and the V_L region are or comprise the sequence set forth in SEQ ID NOS: 112 and 115, respectively;

the V_H region and the V_L region are or comprise the sequence set forth in SEQ ID NOS: 121 and 124, respectively;

the V_H region and the V_L region are or comprise the sequence set forth in SEQ ID NOS: 103 and 106, respectively; or

the V_H region and the V_L region are or comprise the sequence set forth in SEQ ID NOS: 130 and 106, respectively.

6. The anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-6, wherein the V_H region and the V_L region comprise the sequence set forth in SEQ ID NOS: 112 and 115, respectively.

7. The anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-6, wherein the antibody is a full length antibody or an antigen-binding fragment.

8. The anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-7, wherein the antigen-binding fragment thereof comprises a single chain Fv (scFv).

9. The anti-ROR1 antibody or antigen-binding fragment thereof of claim 8, wherein the scFv comprises the sequence set forth in SEQ ID NO: 118, 127, 109 or 134, or an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to SEQ ID NO: 118, 127, 109 or 134.

10. The anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-9, wherein the scFv comprises the sequence set forth in SEQ ID NO: 118.

11. A single chain cell-surface protein, comprising the anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-10.
12. A conjugate, comprising the anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-11 and a heterologous molecule or moiety.
13. An anti-ROR1 chimeric antigen receptor (CAR) comprising an extracellular antigen-binding domain comprising the anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-12, a transmembrane region and an intracellular signaling region.
14. The anti-ROR1 chimeric antigen receptor of claim 13, further comprising a spacer between the extracellular antigen-binding domain and the transmembrane domain.
15. The anti-ROR1 chimeric antigen receptor of claim 14, wherein the spacer comprises at least a portion of a hinge region of an immunoglobulin or a variant thereof.
16. The anti-ROR1 chimeric antigen receptor of claim 14 or claim 15, wherein the spacer comprises an amino acid sequence having at least at or about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO:1, 26, 27, 29, 31, 32, 33 or 135.
17. The anti-ROR1 chimeric antigen receptor of any of claims 14-16, wherein the at least a portion of a hinge region comprises all or a portion of an IgG4 hinge region, optionally a human IgG4 hinge region, or a variant thereof.
18. The anti-ROR1 chimeric antigen receptor of any of claims 14-17, wherein the spacer comprises the sequence set forth in SEQ ID NO: 135.
19. The anti-ROR1 chimeric antigen receptor of any of claims 13-18, wherein the transmembrane region comprises a transmembrane domain from CD28, optionally a human CD28.
20. The anti-ROR1 chimeric antigen receptor of any of claims 13-19, wherein the transmembrane domain comprises SEQ ID NO: 8 or an amino acid sequence having at least at or about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to SEQ ID NO: 8.
21. The anti-ROR1 chimeric antigen receptor of any of claims 13-20, wherein the transmembrane domain comprises SEQ ID NO:8.

22. The anti-ROR1 chimeric antigen receptor of any of claims 13-21, wherein the intracellular signaling domain is or comprises a cytoplasmic signaling domain of a CD3-zeta (CD3ζ) chain, optionally a human CD3ζ chain.

23. The anti-ROR1 chimeric antigen receptor of any of claims 13-22, wherein the intracellular signaling domain is or comprises the sequence set forth in SEQ ID NO:13, 14 or 15, or an amino acid sequence having at least at or about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to SEQ ID NO:13, 14 or 15.

24. The anti-ROR1 chimeric antigen receptor of any of claims 13-23, wherein the intracellular signaling domain is or comprises the sequence set forth in SEQ ID NO:13.

25. The anti-ROR1 chimeric antigen receptor of any of claims 13-24, wherein the intracellular signaling region further comprises a costimulatory signaling region.

26. The anti-ROR1 chimeric antigen receptor of claim 25, wherein the costimulatory signaling region is between the transmembrane region and the intracellular signaling domain.

27. The anti-ROR1 chimeric antigen receptor of claim 25 or 26, wherein the costimulatory signaling region comprises an intracellular signaling domain of a T cell costimulatory molecule or a signaling portion thereof.

28. The anti-ROR1 chimeric antigen receptor of any of claims 25-27, wherein the costimulatory signaling region comprises an intracellular signaling domain of CD28, 4-1BB, or ICOS.

29. The anti-ROR1 chimeric antigen receptor of any of claims 25-28, wherein the costimulatory signaling region comprises an intracellular signaling domain of CD28, optionally a human CD28.

30. The anti-ROR1 chimeric antigen receptor of any of claims 25-26, wherein the costimulatory signaling region comprises an intracellular signaling domain of 4-1BB, optionally a human 4-1BB.

31. The anti-ROR1 chimeric antigen receptor of any of claims 25-28 or 30, wherein the costimulatory signaling region is or comprises the sequence set forth in SEQ ID NO:12 or an amino acid

sequence having at least at or about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to SEQ ID NO: 12.

32. The anti-ROR1 chimeric antigen receptor of any of claims 25-31, wherein the encoded chimeric antigen receptor comprises from its N to C terminus in order: the extracellular antigen-binding domain, the spacer, the transmembrane region and the intracellular signaling region.

33. The anti-ROR1 chimeric antigen receptor of any of claims 25-32, wherein the antigen-binding domain is an scFv and the encoded chimeric antigen receptor comprises, from its N to C terminus in order: an extracellular antigen-binding domain comprising the scFv, a spacer comprising a modified IgG4 hinge-CH3, optionally comprising the sequence set forth in SEQ ID NO: 138; a transmembrane domain, optionally a transmembrane domain from a human CD28; and an intracellular signaling region comprising a cytoplasmic signaling domain of a CD3-zeta (CD3 ζ) chain and an intracellular signaling domain of a costimulatory signaling region, optionally comprising an intracellular signaling domain of 4-1BB.

34. The anti-ROR1 chimeric antigen receptor of any of claims 13-33, wherein the anti-ROR1 chimeric antigen receptor comprises the sequence set forth in SEQ ID NO: 184, 185, 186, 187, 188 or 189 or a sequence that exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO: 184, 185, 186, 187, 188 or 189.

35. The anti-ROR1 chimeric antigen receptor of any of claims 13-34, wherein the anti-ROR1 chimeric antigen receptor comprises the sequence set forth in SEQ ID NO: 184 or a sequence that exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the sequence set forth in SEQ ID NO: 184.

36. The anti-ROR1 chimeric antigen receptor of any of claims 13-35, wherein the anti-ROR1 chimeric antigen receptor is or comprises the sequence set forth in SEQ ID NO: 184.

37. A polynucleotide comprising a nucleic acid encoding the anti-ROR1 antibody or antigen-binding domain thereof of any of claims 1-12 or the anti-ROR1 chimeric antigen receptor of any of claims 13-36.

38. A vector, comprising the polynucleotide of claim 37.

39. The vector of claim 38, wherein the vector is a viral vector.
40. A cell comprising the anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-12, the chimeric antigen receptor of any of claims 13-36, the polynucleotide of claim 37, or the vector of claim 38 or claim 39.
41. The cell of claim 40, that is a lymphocyte.
42. The cell of any of claims 40 or 41, that is an NK cell or a T cell.
43. A T cell comprising the chimeric antigen receptor of any of claims 13-36 or the polynucleotide of claim 37.
44. The cell of any of claims 39-43, wherein the cell is a T cell and the T cell is a CD4⁺ T cell or a CD8⁺ T cell.
45. The cell of any of claims 40-44, wherein the cell is a primary cell obtained from a subject.
46. A composition comprising the cell of any of claims 40-45.
47. A composition comprising the anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-10, the single chain cell surface protein of claim 11, the conjugate of claim 12, the chimeric antigen receptor of any of claims 13-36, the polynucleotide of claim 37, or the vector of claim 38 or claim 39.
48. The composition of claim 46 or 47, further comprising a pharmaceutically acceptable excipient.
49. The composition of claim 46 or 48, wherein the composition comprises CD4⁺ and CD8⁺ T cells and the ratio of CD4⁺ to CD8⁺ T cells is from at or about 1:3 to 3:1, optionally at or about 1:2 to 2:1, optionally at or about 1:1.
50. The composition of any of claims 46, 48, or 49, wherein, among a plurality of the cells in the composition, less than at or about 10%, at or about 9%, at or about 8%, at or about 7%, at or about 5%, at or about 4%, at or about 3%, at or about 2% or at or about 1% of the cells in the plurality comprise

an anti-ROR1 chimeric antigen receptor that exhibits tonic signaling and/or antigen independent activity or signaling.

51. The anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-10, the single chain cell surface protein of claim 11, the conjugate of claim 12, the anti-ROR1 chimeric antigen receptor of any of claims 13-36, the polynucleotide of claim 37, the vector of claim 38 or 39, the cell of any one of claims 40-45 or the composition of any one or claims 46-50 for use in treating a disease or disorder associated with ROR1.

52. Use of the anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-10, the single chain cell surface protein of claim 11, the conjugate of claim 12, the anti-ROR1 chimeric antigen receptor of any of claims 13-36, the polynucleotide of claim 37, the vector of claim 38 or 39, the cell of any one of claims 40-45 or the composition of any one or claims 46-50 for the manufacture of a medicament for treating a disease or disorder associated with ROR1.

53. The antibody or antigen-binding fragment thereof, single chain cell surface protein, conjugate, chimeric antigen receptor, polynucleotide, vector, cell or composition for use or the use of claims 51 or 52, wherein the disease or disorder associated with ROR1 is a cancer.

54. The antibody or antigen-binding fragment thereof, single chain cell surface protein, conjugate, chimeric antigen receptor, polynucleotide, vector, cell or composition for use or the use of claim 53, wherein the cancer is a ROR1-expressing cancer.

55. The antibody or antigen-binding fragment thereof, single chain cell surface protein, conjugate, chimeric antigen receptor, polynucleotide, vector, cell or composition for use or the use of any of claims 51-54, wherein the cancer is associated with a ROR1-expressing solid tumor or a ROR1-expressing hematologic malignancy.

56. The antibody or antigen-binding fragment thereof, single chain cell surface protein, conjugate, chimeric antigen receptor, polynucleotide, vector, cell or composition for use or the use of any of claims 51-55, wherein the cancer is associated with a ROR1-expressing solid tumor.

57. The antibody or antigen-binding fragment thereof, single chain cell surface protein, conjugate, chimeric antigen receptor, polynucleotide, vector, cell or composition for use or the use of claim 55 or 56, wherein the cancer associated with a solid tumor is selected from the group consisting of neuroblastoma, renal cell carcinoma, colon cancer, colorectal cancer, breast cancer, epithelial squamous

cell cancer, melanoma, myeloma, stomach cancer, brain cancer, lung cancer, pancreatic cancer, cervical cancer, ovarian cancer, liver cancer, bladder cancer, prostate cancer, testicular cancer, thyroid cancer, uterine cancer, adrenal cancer and head and neck cancer.

58. The antibody or antigen-binding fragment thereof, single chain cell surface protein, conjugate, chimeric antigen receptor, polynucleotide, vector, cell or composition for use or the use of claim 57, wherein the cancer associated with a solid tumor is lung cancer and wherein the lung cancer is a NSCLC.

59. The antibody or antigen-binding fragment thereof, single chain cell surface protein, conjugate, chimeric antigen receptor, polynucleotide, vector, cell or composition for use or the use of claim 57, wherein the cancer associated with a solid tumor is breast cancer and wherein the breast cancer is a triple negative breast cancer (TNBC).

60. The antibody or antigen-binding fragment thereof, single chain cell surface protein, conjugate, chimeric antigen receptor, polynucleotide, vector, cell or composition for use or the use of any of claims 51-55, wherein the cancer is associated with a ROR1-expressing hematologic malignancy.

61. The antibody or antigen-binding fragment thereof, single chain cell surface protein, conjugate, chimeric antigen receptor, polynucleotide, vector, cell or composition for use or the use of claim 60, wherein the hematologic malignancy is selected from the group consisting of B cell leukemia, lymphoma, B cell chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), Burkitt's Lymphoma or mantle cell lymphoma (MCL).

62. A kit comprising the anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-10, the single chain cell surface protein of claim 11, the conjugate of claim 12, the anti-ROR1 chimeric antigen receptor of any of claims 13-36, the polynucleotide of claim 37, the vector of claim 38 or 39, the cell of any one of claims 40-45, or the composition of any of one of claims 46-50, and instructions for use.

63. An article of manufacture comprising the anti-ROR1 antibody or antigen-binding fragment thereof of any of claims 1-10, the single chain cell surface protein of claim 11, the conjugate of claim 12, the anti-ROR1 chimeric antigen receptor of any of claims 13-36, the polynucleotide of claim 37, the vector of claim 38 or 39, the cell of any one of claims 40-45, or the composition of any of one of claims 46-50.