

Summary

The present disclosure generally relates to binding agents that are at least bispecific for the binding to CD3 and CLDN6, i.e., they are capable of binding to at least CD3 and CLDN6. Specifically, the present disclosure relates to RNA encoding these binding agents which may be used in the treatment or prevention of cancer in a subject. In particular, RNA encoding a binding agent disclosed herein may be administered to provide (following expression of the RNA by appropriate target cells) binding agent for targeting CD3 and CLDN6.

Thus, a pharmaceutical composition described herein may comprise as the active principle single-stranded RNA that may be translated into the respective encoded polypeptide upon entering cells of a recipient. In addition to sequences encoding the binding agent, the RNA may contain one or more structural elements optimized for maximal efficacy of the RNA with respect to stability and translational efficiency (5'-cap, 5'-UTR, 3'-UTR, poly(A)-tail). In some examples, the RNA contains all of these elements.

The RNA described herein may be complexed with proteins and/or lipids, preferably lipids, to generate RNA particles for administration. Different RNAs may be complexed together or complexed separately with proteins and/or lipids to generate RNA-particles for administration.

In one aspect, the present disclosure provides a composition or medical preparation comprising:

- (i) a first RNA encoding a first polypeptide chain comprising a variable region of a heavy chain (VH) derived from an immunoglobulin with specificity for CD3 (VH(CD3)), a variable region of a heavy chain (VH) derived from an immunoglobulin with specificity for CLDN6 (VH(CLDN6)) and a variable region of a light chain (VL) derived from an immunoglobulin with specificity for CLDN6 (VL(CLDN6)); and
- (ii) a second RNA encoding a second polypeptide chain comprising a variable region of a light chain (VL) derived from an immunoglobulin with specificity for CD3 (VL(CD3)), a variable

region of a heavy chain (VH) derived from an immunoglobulin with specificity for CLDN6 (VH(CLDN6)) and a variable region of a light chain (VL) derived from an immunoglobulin with specificity for CLDN6 (VL(CLDN6)).

In some examples, the first polypeptide chain interacts with the second polypeptide chain to form a binding domain with specificity for CD3 and two binding domains with specificity for CLDN6.

In some examples:

the VH(CD3) of the first polypeptide chain and the VL(CD3) of the second polypeptide chain interact to form a binding domain with specificity for CD3,

the VH(CLDN6) and the VL(CLDN6) of the first polypeptide chain interact to form a binding domain with specificity for CLDN6, and

the VH(CLDN6) and the VL(CLDN6) of the second polypeptide chain interact to form a binding domain with specificity for CLDN6.

In one example, the present disclosure provides a composition or medical preparation comprising:

(i) a first RNA encoding a first polypeptide chain comprising a variable region VH(CD3), a variable region VH(CLDN6) and a variable region VL(CLDN6); and

(ii) a second RNA encoding a second polypeptide chain comprising a variable region VL(CD3), a variable region VH(CLDN6) and a variable region VL(CLDN6),

wherein the VH(CD3) of the first polypeptide chain and the VL(CD3) of the second polypeptide chain interact to form a binding domain with specificity for CD3,

wherein the VH(CLDN6) and the VL(CLDN6) of the first polypeptide chain interact to form a binding domain with specificity for CLDN6, and

wherein the VH(CLDN6) and the VL(CLDN6) of the second polypeptide chain interact to form a binding domain with specificity for CLDN6.

In some examples, the first and the second polypeptide chains comprise a constant region 1 of a heavy chain (CH1) derived from an immunoglobulin or a functional variant thereof and a constant region of a light chain (CL) derived from an immunoglobulin or a functional variant thereof.

In some examples, the immunoglobulin is IgG1.

In some examples, the IgG1 is human IgG1.

In some examples, the VH, the VL, and the CH1 on the first polypeptide chain are arranged, from N-terminus to C-terminus, in the order

VH(CD3)-CH1-VH(CLDN6)-VL(CLDN6), or

VH(CD3)-CH1-VL(CLDN6)-VH(CLDN6).

In some examples, the CH1 is connected to the VH(CLDN6) or VL(CLDN6) by a peptide linker.

In one example, the peptide linker comprises the amino acid sequence SGPGGGRS(G₄S)₂ or a functional variant thereof.

In some examples, the VH, the VL, and the CL on the second polypeptide chain are arranged, from N-terminus to C-terminus, in the order

VL(CD3)-CL-VH(CLDN6)-VL(CLDN6), or

VL(CD3)-CL-VL(CLDN6)-VH(CLDN6).

In some examples, the CL is connected to the VH(CLDN6) or VL(CLDN6) by a peptide linker. In some examples, the peptide linker comprises the amino acid sequence DVPGGG or a functional variant thereof.

In some examples, the VH(CLDN6) and the VL(CLDN6) are connected to one another by a peptide linker. In some examples, the peptide linker comprises the amino acid sequence (G₄S)_x or a functional variant thereof, wherein x is 2, 3, 4, 5 or 6. In one example, the peptide linker comprises the amino acid sequence (G₄S)₄ or a functional variant thereof.

In some examples, the CH1 on the first polypeptide chain interacts with the CL on the second polypeptide chain.

In some examples, the VH(CD3) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 27 to 145 of SEQ ID NO: 4.

In some examples, the VH(CD3) comprises a CDR1 comprising the amino acid sequence GYTFTRYT or a functional variant thereof, a CDR2 comprising the amino acid sequence INPSRGYT or a functional variant thereof, and a CDR3 comprising the amino acid sequence ARYYDDHYSLDY or a functional variant thereof.

In some examples, the VH(CD3) comprises a CDR1 comprising the amino acid sequence GYTFTRYT or a functional variant thereof, a CDR2 comprising the amino acid sequence INPSRGYT or a functional variant thereof, and a CDR3 comprising the amino acid sequence ARYYDDHYCLDY or a functional variant thereof.

In some examples, the VH(CD3) comprises the amino acid sequence of amino acids 27 to 145 of SEQ ID NO: 4 or a functional variant thereof.

In some examples, the VL(CD3) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 27 to 132 of SEQ ID NO: 6.

In some examples, the VL(CD3) comprises a CDR1 comprising the amino acid sequence SSVSY or a functional variant thereof, a CDR2 comprising the amino acid sequence DTS or a functional variant thereof, and a CDR3 comprising the amino acid sequence QQWSSNPLT or a functional variant thereof.

In some examples, the VL(CD3) comprises the amino acid sequence of amino acids 27 to 132 of SEQ ID NO: 6 or a functional variant thereof.

In some examples, the VH(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 267 to 383 of SEQ ID NO: 4.

In some examples, the VH(CLDN6) comprises a CDR1 comprising the amino acid sequence GYSFTGYT or a functional variant thereof, a CDR2 comprising the amino acid sequence INPYNGGT or a functional variant thereof, and a CDR3 comprising the amino acid sequence ARDYGFVLDY or a functional variant thereof.

In some examples, the VH(CLDN6) comprises the amino acid sequence of amino acids 267 to 383 of SEQ ID NO: 4 or a functional variant thereof.

In some examples, the VL(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4.

In some examples, the VL(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4 and a serine residue in position +15 relative to CDR1 (corresponds to position 449 of SEQ ID NO: 4).

In some examples, the VL(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4 and a serine residue in position -3 relative to CDR2 (corresponds to position 449 of SEQ ID NO: 4).

In some examples, the VL(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4, a sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4, and a serine residue in the position corresponding to position 449 of SEQ ID NO: 4.

In some examples, the VL(CLDN6) comprises a CDR1 comprising the amino acid sequence SSVSY or a functional variant thereof, a CDR2 comprising the amino acid sequence STS or a functional variant thereof, and a CDR3 comprising the amino acid sequence QQRSNYPPWT or a functional variant thereof.

In some examples, the VL(CLDN6) comprises the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4 or a functional variant thereof.

In some examples, the VH(CD3) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 27 to 145 of SEQ ID NO: 4, the VL(CD3) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 27 to 132 of SEQ ID NO: 6, the VH(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 267 to 383 of SEQ ID NO: 4, and the VL(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence

of amino acids 404 to 510 of SEQ ID NO: 4, and preferably a serine residue in position +15 relative to CDR1 (corresponds to position 449 of SEQ ID NO: 4) and/or a serine residue in position -3 relative to CDR2 (corresponds to position 449 of SEQ ID NO: 4).

In some examples:

the VH(CD3) comprises the amino acid sequence of amino acids 27 to 145 of SEQ ID NO: 4 or a functional variant thereof,

the VL(CD3) comprises the amino acid sequence of amino acids 27 to 132 of SEQ ID NO: 6 or a functional variant thereof,

the VH(CLDN6) comprises the amino acid sequence of amino acids 267 to 383 of SEQ ID NO: 4 or a functional variant thereof, and/or

the VL(CLDN6) comprises the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4 or a functional variant thereof.

In some examples, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4 or a functional variant thereof.

In some examples, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 6 or a functional variant thereof.

In some examples, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4 or a functional variant thereof and the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 6 or a functional variant thereof.

In some examples, at least one of the first polypeptide and the second polypeptide is encoded by a coding sequence which is codon-optimized and/or the G/C content of which is increased compared to wild type coding sequence, wherein the codon-optimization and/or

the increase in the G/C content preferably does not change the sequence of the encoded amino acid sequence.

In some examples, each of the first polypeptide and the second polypeptide is encoded by a coding sequence which is codon-optimized and/or the G/C content of which is increased compared to wild type coding sequence, wherein the codon-optimization and/or the increase in the G/C content preferably does not change the sequence of the encoded amino acid sequence.

In some examples, the RNA comprises a modified nucleoside in place of uridine. In such a case there is preferably a modified nucleoside in place of each or essentially each uridine in the RNA.

In some examples, the modified nucleoside is selected from pseudouridine (ψ), N1-methyl-pseudouridine ($m_1\psi$), and 5-methyl-uridine (m_5U).

In some examples, at least one RNA comprises the 5' cap $m_2^{7,3'-O}Gppp(m_1^{2'-O})ApG$.

In some examples, each RNA comprises the 5' cap $m_2^{7,3'-O}Gppp(m_1^{2'-O})ApG$.

In some examples, at least one RNA comprises a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 8, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 8.

In some examples, each RNA comprises a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 8, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 8.

In some examples, at least one RNA comprises a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 9, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 9.

In some examples, each RNA comprises a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 9, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 9.

In some examples, at least one RNA comprises a poly-A sequence.

In some examples, each RNA comprises a poly-A sequence.

In some examples, the poly-A sequence comprises at least 100 nucleotides.

In some examples, the poly-A sequence comprises or consists of the nucleotide sequence of SEQ ID NO: 10.

In some examples:

- (i) the first RNA and the second RNA are in a (w/w) ratio of about 1.75:1 to about 1.25:1, or about 1.5:1 to about 1.25:1, or preferably about 1.5:1; and/or
- (ii) the first RNA and the second RNA comprise a modified nucleoside in place of each uridine; and/or
- (iii) the first RNA and the second RNA comprise a modified nucleoside in place of each uridine, wherein the modified nucleoside is independently selected from pseudouridine (ψ), N1-methyl-pseudouridine (m1 ψ), and 5-methyl-uridine (m5U); and/or
- (iv) the first RNA and the second RNA comprise the 5' cap m₂^{7,3'-O}Gppp(m₁^{2'-O})ApG; and/or

- (v) the first RNA and the second RNA comprise a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 8, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 8; and/or
- (vi) the first RNA and the second RNA comprise a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 9, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 9; and/or
- (vii) the first RNA and the second RNA comprise a poly-A tail comprising the nucleotide sequence of SEQ ID NO: 10.

In some examples:

- (i) the first RNA and the second RNA are in a (w/w) ratio of about 1.75:1 to about 1.25:1, or about 1.5:1 to about 1.25:1, or preferably about 1.5:1;
- (ii) the first RNA and the second RNA comprise a modified nucleoside in place of each uridine, wherein the modified nucleoside is N1-methyl-pseudouridine (m1 ψ);
- (iii) the first RNA and the second RNA comprise the 5' cap m₂^{7,3'-O}Gppp(m₁^{2'-O})ApG;
- (iv) the first RNA and the second RNA comprise a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 8;
- (v) the first RNA and the second RNA comprise a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 9; and
- (vi) the first RNA and the second RNA comprise a poly-A tail comprising the nucleotide sequence of SEQ ID NO: 10.

In some examples:

- (i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 4; and/or

(ii) the first RNA comprises the nucleotide sequence of SEQ ID NO: 5, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 5.

In some examples:

- (i) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 6, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 6; and/or
- (ii) the second RNA comprises the nucleotide sequence of SEQ ID NO: 7, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 7.

In one aspect, the present disclosure provides a composition or medical preparation comprising:

- (i) a first RNA encoding a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 4, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 4; and
- (ii) a second RNA encoding a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 6, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 6.

In some examples of all examples, the first RNA comprises the nucleotide sequence of SEQ ID NO: 5, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 5.

In some examples of all examples, the second RNA comprises the nucleotide sequence of SEQ ID NO: 7, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 7.

In one example, the present disclosure provides a composition or medical preparation comprising: a first RNA comprising the nucleotide sequence of SEQ ID NO: 35 or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 35 and/or a second RNA comprising the nucleotide sequence of SEQ ID NO: 36 or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 36.

In one example, the present disclosure provides a composition or medical preparation comprising: a first RNA comprising the nucleotide sequence of SEQ ID NO: 5 and a second RNA comprising the nucleotide sequence of SEQ ID NO: 7, wherein the first RNA and the second RNA are present at a (w/w) ratio of first RNA to second RNA of about 1.5:1.

In some examples of all examples, the RNA is mRNA.

In some examples of all examples, the RNA is formulated as a liquid, formulated as a solid, or a combination thereof.

In some examples of all examples, the RNA is formulated or is to be formulated for injection.

In some examples of all examples, the RNA is formulated or is to be formulated for intravenous administration.

In some examples of all examples, the RNA is formulated or is to be formulated as particles.

In some examples, the particles are lipid nanoparticles (LNP).

In some examples, the LNP particles comprise ((3-hydroxypropyl)azanediyl)bis(nonane-9,1-diyl)bis(2-butyloctanoate), 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 1,2-Distearoyl-sn-glycero-3-phosphocholine, and cholesterol.

In some examples of all examples, the composition or medical preparation is a pharmaceutical composition.

In some examples, the pharmaceutical composition further comprises one or more pharmaceutically acceptable carriers, diluents and/or excipients.

In some examples of all examples, the composition or medical preparation is a kit.

In some examples, the RNA and optionally the particle forming components are in separate vials.

In some examples, the composition or medical preparation further comprises instructions for use of the composition or medical preparation for treating or preventing cancer.

In one example, the present disclosure provides a composition or medical preparation described herein for pharmaceutical use.

In another aspect, the present disclosure provides a composition or medical preparation of the disclosure for use in therapy.

In another aspect, the present disclosure provides a use of the composition or medical preparation of the disclosure, in the preparation of a medicament for treating or preventing cancer.

In some examples, the pharmaceutical use comprises a therapeutic or prophylactic treatment of a disease or disorder.

In some examples, the therapeutic or prophylactic treatment of a disease or disorder comprises treating or preventing cancer.

In some examples, the therapeutic or prophylactic treatment of a disease or disorder further comprises administering a further therapy.

In some examples, the further therapy comprises one or more selected from the group consisting of: (i) surgery to excise, resect, or debulk a tumor, (ii) radiotherapy, and (iii) chemotherapy.

In some examples, the further therapy comprises administering a further therapeutic agent.

In some examples, the further therapeutic agent comprises an anti-cancer therapeutic agent.

In some examples, the composition or medical preparation described herein is for administration to a human.

In one example, the present disclosure provides a method of treating cancer in a subject comprising administering to the subject:

(i) a first RNA encoding a first polypeptide chain comprising a variable region of a heavy chain (VH) derived from an immunoglobulin with specificity for CD3 (VH(CD3)), a variable region of a heavy chain (VH) derived from an immunoglobulin with specificity for CLDN6 (VH(CLDN6)) and a variable region of a light chain (VL) derived from an immunoglobulin with specificity for CLDN6 (VL(CLDN6)); and

(ii) a second RNA encoding a second polypeptide chain comprising a variable region of a light chain (VL) derived from an immunoglobulin with specificity for CD3 (VL(CD3)), a variable region of a heavy chain (VH) derived from an immunoglobulin with specificity for CLDN6 (VH(CLDN6)) and a variable region of a light chain (VL) derived from an immunoglobulin with specificity for CLDN6 (VL(CLDN6)).

In some examples, the first polypeptide chain interacts with the second polypeptide chain to form a binding domain with specificity for CD3 and two binding domains with specificity for CLDN6.

In some examples:

the VH(CD3) of the first polypeptide chain and the VL(CD3) of the second polypeptide chain interact to form a binding domain with specificity for CD3,

the VH(CLDN6) and the VL(CLDN6) of the first polypeptide chain interact to form a binding domain with specificity for CLDN6, and

the VH(CLDN6) and the VL(CLDN6) of the second polypeptide chain interact to form a binding domain with specificity for CLDN6.

In one example, the present disclosure provides a method of treating cancer in a subject comprising administering to the subject:

(i) a first RNA encoding a first polypeptide chain comprising a variable region VH(CD3), a variable region VH(CLDN6) and a variable region VL(CLDN6); and

(ii) a second RNA encoding a second polypeptide chain comprising a variable region VL(CD3), a variable region VH(CLDN6) and a variable region VL(CLDN6),

wherein the VH(CD3) of the first polypeptide chain and the VL(CD3) of the second polypeptide chain interact to form a binding domain with specificity for CD3,

wherein the VH(CLDN6) and the VL(CLDN6) of the first polypeptide chain interact to form a binding domain with specificity for CLDN6, and
wherein the VH(CLDN6) and the VL(CLDN6) of the second polypeptide chain interact to form a binding domain with specificity for CLDN6.

In some examples, the first and the second polypeptide chains comprise a constant region 1 of a heavy chain (CH1) derived from an immunoglobulin or a functional variant thereof and a constant region of a light chain (CL) derived from an immunoglobulin or a functional variant thereof.

In some examples, the immunoglobulin is IgG1.

In some examples, the IgG1 is human IgG1.

In some examples, the VH, the VL, and the CH1 on the first polypeptide chain are arranged, from N-terminus to C-terminus, in the order
VH(CD3)-CH1-VH(CLDN6)-VL(CLDN6), or
VH(CD3)-CH1-VL(CLDN6)-VH(CLDN6).

In some examples, the CH1 is connected to the VH(CLDN6) or VL(CLDN6) by a peptide linker.
In some examples, the peptide linker comprises the amino acid sequence SGPGGGRS(G₄S)₂ or a functional variant thereof.

In some examples, the VH, the VL, and the CL on the second polypeptide chain are arranged, from N-terminus to C-terminus, in the order
VL(CD3)-CL-VH(CLDN6)-VL(CLDN6), or
VL(CD3)-CL-VL(CLDN6)-VH(CLDN6).

In some examples, the CL is connected to the VH(CLDN6) or VL(CLDN6) by a peptide linker. In some examples, the peptide linker comprises the amino acid sequence DVPGGG or a functional variant thereof.

In some examples, the VH(CLDN6) and the VL(CLDN6) are connected to one another by a peptide linker. In some examples, the peptide linker comprises the amino acid sequence (G₄S)_x or a functional variant thereof, wherein x is 2, 3, 4, 5 or 6. In some examples, the peptide linker comprises the amino acid sequence (G₄S)₄ or a functional variant thereof.

In some examples, the CH1 on the first polypeptide chain interacts with the CL on the second polypeptide chain.

In some examples, the VH(CD3) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 27 to 145 of SEQ ID NO: 4.

In some examples, the VH(CD3) comprises a CDR1 comprising the amino acid sequence GYTFTRYT or a functional variant thereof, a CDR2 comprising the amino acid sequence INPSRGYT or a functional variant thereof, and a CDR3 comprising the amino acid sequence ARYYDDHYSLDY or a functional variant thereof.

In some examples, the VH(CD3) comprises a CDR1 comprising the amino acid sequence GYTFTRYT or a functional variant thereof, a CDR2 comprising the amino acid sequence INPSRGYT or a functional variant thereof, and a CDR3 comprising the amino acid sequence ARYYDDHYCLDY or a functional variant thereof.

In some examples, the VH(CD3) comprises the amino acid sequence of amino acids 27 to 145 of SEQ ID NO: 4 or a functional variant thereof.

In some examples, the VL(CD3) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 27 to 132 of SEQ ID NO: 6.

In some examples, the VL(CD3) comprises a CDR1 comprising the amino acid sequence SSVSY or a functional variant thereof, a CDR2 comprising the amino acid sequence DTS or a functional variant thereof, and a CDR3 comprising the amino acid sequence QQWSSNPLT or a functional variant thereof.

In some examples, the VL(CD3) comprises the amino acid sequence of amino acids 27 to 132 of SEQ ID NO: 6 or a functional variant thereof.

In some examples, the VH(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 267 to 383 of SEQ ID NO: 4.

In some examples, the VH(CLDN6) comprises a CDR1 comprising the amino acid sequence GYSFTGYT or a functional variant thereof, a CDR2 comprising the amino acid sequence INPYNGGT or a functional variant thereof, and a CDR3 comprising the amino acid sequence ARDYGFVLDY or a functional variant thereof.

In some examples, the VH(CLDN6) comprises the amino acid sequence of amino acids 267 to 383 of SEQ ID NO: 4 or a functional variant thereof.

In some examples, the VL(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4.

In some examples, the VL(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4 and a serine residue in position +15 relative to CDR1 (corresponds to position 449 of SEQ ID NO: 4).

In some examples, the VL(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4 and a serine residue in position -3 relative to CDR2 (corresponds to position 449 of SEQ ID NO: 4).

In some examples, the VL(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4, a sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4, and a serine residue in the position corresponding to position 449 of SEQ ID NO: 4.

In some examples, the VL(CLDN6) comprises a CDR1 comprising the amino acid sequence SSVSY or a functional variant thereof, a CDR2 comprising the amino acid sequence STS or a functional variant thereof, and a CDR3 comprising the amino acid sequence QQRSNYPPWT or a functional variant thereof.

In some examples, the VL(CLDN6) comprises the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4 or a functional variant thereof.

In some examples, the VH(CD3) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 27 to 145 of SEQ ID NO: 4, the VL(CD3) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 27 to 132 of SEQ ID NO: 6, the VH(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 267 to 383 of

SEQ ID NO: 4, and the VL(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4 and preferably a serine residue in position +15 relative to CDR1 (corresponds to position 449 of SEQ ID NO: 4) and/or a serine residue in position -3 relative to CDR2 (corresponds to position 449 of SEQ ID NO: 4).

In some examples:

the VH(CD3) comprises the amino acid sequence of amino acids 27 to 145 of SEQ ID NO: 4 or a functional variant thereof,

the VL(CD3) comprises the amino acid sequence of amino acids 27 to 132 of SEQ ID NO: 6 or a functional variant thereof,

the VH(CLDN6) comprises the amino acid sequence of amino acids 267 to 383 of SEQ ID NO: 4 or a functional variant thereof, and/or

the VL(CLDN6) comprises the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4 or a functional variant thereof.

In some examples, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4 or a functional variant thereof.

In some examples, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 6 or a functional variant thereof.

In some examples, the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4 or a functional variant thereof and the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 6 or a functional variant thereof.

In some examples, at least one of the first polypeptide and the second polypeptide is encoded by a coding sequence which is codon-optimized and/or the G/C content of which is

increased compared to wild type coding sequence, wherein the codon-optimization and/or the increase in the G/C content preferably does not change the sequence of the encoded amino acid sequence.

In some examples, each of the first polypeptide and the second polypeptide is encoded by a coding sequence which is codon-optimized and/or the G/C content of which is increased compared to wild type coding sequence, wherein the codon-optimization and/or the increase in the G/C content preferably does not change the sequence of the encoded amino acid sequence.

In some examples, the RNA comprises a modified nucleoside in place of uridine. In such a case there is preferably a modified nucleoside in place of each or essentially each uridine in the RNA.

In some examples, the modified nucleoside is selected from pseudouridine (ψ), N1-methyl-pseudouridine ($m1\psi$), and 5-methyl-uridine ($m5U$).

In some examples, at least one RNA comprises the 5' cap $m_2^{7,3'-O}Gppp(m_1^{2'-O})ApG$.

In some examples, each RNA comprises the 5' cap $m_2^{7,3'-O}Gppp(m_1^{2'-O})ApG$.

In some examples, at least one RNA comprises a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 8, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 8.

In some examples, each RNA comprises a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 8, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 8.

In some examples, at least one RNA comprises a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 9, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 9.

In some examples, each RNA comprises a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 9, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 9.

In some examples, at least one RNA comprises a poly-A sequence.

In some examples, each RNA comprises a poly-A sequence.

In some examples, the poly-A sequence comprises at least 100 nucleotides.

In some examples, the poly-A sequence comprises or consists of the nucleotide sequence of SEQ ID NO: 10.

In some examples:

- (i) the first RNA and the second RNA are in a (w/w) ratio of about 1.75:1 to about 1.25:1, or about 1.5:1 to about 1.25:1, or preferably about 1.5:1; and/or
- (ii) the first RNA and the second RNA comprise a modified nucleoside in place of each uridine; and/or

- (iii) the first RNA and the second RNA comprise a modified nucleoside in place of each uridine, wherein the modified nucleoside is independently selected from pseudouridine (ψ), N1-methyl-pseudouridine (m1 ψ), and 5-methyl-uridine (m5U); and/or
- (iv) the first RNA and the second RNA comprise the 5' cap $m_2^{7,3'-O}Gppp(m_1^{2'-O})ApG$; and/or
- (v) the first RNA and the second RNA comprise a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 8, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 8; and/or
- (vi) the first RNA and the second RNA comprise a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 9, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 9; and/or
- (vii) the first RNA and the second RNA comprise a poly-A tail comprising the nucleotide sequence of SEQ ID NO: 10.

In some examples:

- (i) the first RNA and the second RNA are in a (w/w) ratio of about 1.75:1 to about 1.25:1, or about 1.5:1 to about 1.25:1, or preferably about 1.5:1;
- (ii) the first RNA and the second RNA comprise a modified nucleoside in place of each uridine, wherein the modified nucleoside is N1-methyl-pseudouridine (m1 ψ);
- (iii) the first RNA and the second RNA comprise the 5' cap $m_2^{7,3'-O}Gppp(m_1^{2'-O})ApG$;
- (iv) the first RNA and the second RNA comprise a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 8;
- (v) the first RNA and the second RNA comprise a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 9; and
- (vi) the first RNA and the second RNA comprise a poly-A tail comprising the nucleotide sequence of SEQ ID NO: 10.

In some examples:

- (i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 4; and/or
- (ii) the first RNA comprises the nucleotide sequence of SEQ ID NO: 5, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 5.

In some examples:

- (i) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 6, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 6; and/or
- (ii) the second RNA comprises the nucleotide sequence of SEQ ID NO: 7, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 7.

In one example, the present disclosure provides a method of treating cancer in a subject comprising administering to the subject:

- (i) a first RNA encoding a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 4, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 4; and
- (ii) a second RNA encoding a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 6, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 6.

In some examples of all examples, the first RNA comprises the nucleotide sequence of SEQ ID NO: 5, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 5.

In some examples of all examples, the second RNA comprises the nucleotide sequence of SEQ ID NO: 7, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 7.

In one example, the present disclosure provides a method of treating cancer in a subject comprising administering to the subject: a first RNA comprising the nucleotide sequence of SEQ ID NO: 35 or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 35 and/or a second RNA comprising the nucleotide sequence of SEQ ID NO: 36 or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 36.

In one example, the present disclosure provides a method of treating cancer in a subject comprising administering to the subject: a first RNA comprising the nucleotide sequence of SEQ ID NO: 5 and a second RNA comprising the nucleotide sequence of SEQ ID NO: 7, wherein the first RNA and the second RNA are administered at a (w/w) ratio of first RNA to second RNA of about 1.5:1.

In some examples of all examples, the RNA is mRNA.

In some examples of all examples, the RNA is formulated as a liquid, formulated as a solid, or a combination thereof.

In some examples of all examples, the RNA is administered by injection.

In some examples of all examples, the RNA is administered once weekly.

In some examples of all examples, the RNA is administered by intravenous administration.

In some examples of all examples, the RNA is formulated as particles.

In some examples, the particles are lipid nanoparticles (LNP).

In some examples, the LNP particles comprise ((3-hydroxypropyl)azanediyl)bis(nonane-9,1-diyl) bis(2-butyloctanoate), 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 1,2-Distearoyl-sn-glycero-3-phosphocholine, and cholesterol.

In some examples of all examples, the RNA is formulated in a pharmaceutical composition.

In some examples, the pharmaceutical composition further comprises one or more pharmaceutically acceptable carriers, diluents and/or excipients.

In some examples of all examples, the method described herein further comprises administering a further therapy.

In some examples, the further therapy comprises one or more selected from the group consisting of: (i) surgery to excise, resect, or debulk a tumor, (ii) radiotherapy, and (iii) chemotherapy.

In some examples, the further therapy comprises administering a further therapeutic agent.

In some examples, the further therapeutic agent comprises an anti-cancer therapeutic agent.

In some examples of all examples, the subject is a human.

In some examples of all examples, the cancer is CLDN6-positive cancer.

In one example, the present disclosure provides a composition or medical preparation described herein for use in a method described herein.

In one example, the disclosure relates to an agent or composition described herein for use in a method described herein.

Claims

1. A composition or medical preparation comprising:

(i) a first RNA encoding a first polypeptide chain comprising a variable region of a heavy chain (VH) derived from an immunoglobulin with specificity for CD3 (VH(CD3)), a variable region of a heavy chain (VH) derived from an immunoglobulin with specificity for CLDN6 (VH(CLDN6)) and a variable region of a light chain (VL) derived from an immunoglobulin with specificity for CLDN6 (VL(CLDN6)); and

(ii) a second RNA encoding a second polypeptide chain comprising a variable region of a light chain (VL) derived from an immunoglobulin with specificity for CD3 (VL(CD3)), a variable region of a heavy chain (VH) derived from an immunoglobulin with specificity for CLDN6 (VH(CLDN6)) and a variable region of a light chain (VL) derived from an immunoglobulin with specificity for CLDN6 (VL(CLDN6)).

2. The composition or medical preparation of claim 1, wherein the first polypeptide chain interacts with the second polypeptide chain to form a binding domain with specificity for CD3 and two binding domains with specificity for CLDN6 , wherein optionally the VH(CD3) of the first polypeptide chain and the VL(CD3) of the second polypeptide chain interact to form a binding domain with specificity for CD3, the VH(CLDN6) and the VL(CLDN6) of the first polypeptide chain interact to form a binding domain with specificity for CLDN6, and the VH(CLDN6) and the VL(CLDN6) of the second polypeptide chain interact to form a binding domain with specificity for CLDN6.

3. The composition or medical preparation of claim 1 or 2, wherein the first and the second polypeptide chains comprise a constant region 1 of a heavy chain (CH1) derived from an immunoglobulin or a functional variant thereof and a constant region of a light chain (CL) derived from an immunoglobulin or a functional variant thereof.

4. The composition or medical preparation of any one of claims 1 to 3, wherein the immunoglobulin is IgG1, optionally human IgG1.

5. The composition or medical preparation of claim 3 or 4, wherein the VH, the VL, and the CH1 on the first polypeptide chain are arranged, from N-terminus to C-terminus, in the order VH(CD3)-CH1-VH(CLDN6)-VL(CLDN6), or VH(CD3)-CH1-VL(CLDN6)-VH(CLDN6).
6. The composition or medical preparation of any one of claims 3 to 5, wherein the CH1 is connected to the VH(CLDN6) or VL(CLDN6) by a peptide linker, wherein optionally the peptide linker comprises the amino acid sequence SGPGGGRS(G₄S)₂ or a functional variant thereof.
7. The composition or medical preparation of any one of claims 3 to 6, wherein the VH, the VL, and the CL on the second polypeptide chain are arranged, from N-terminus to C-terminus, in the order VL(CD3)-CL-VH(CLDN6)-VL(CLDN6), or VL(CD3)-CL-VL(CLDN6)-VH(CLDN6).
8. The composition or medical preparation of any one of claims 3 to 7, wherein the CL is connected to the VH(CLDN6) or VL(CLDN6) by a peptide linker, wherein optionally the peptide linker comprises the amino acid sequence DVPGGG or a functional variant thereof.
9. The composition or medical preparation of any one of claims 1 to 8, wherein the VH(CLDN6) and the VL(CLDN6) are connected to one another by a peptide linker, wherein optionally the peptide linker comprises the amino acid sequence (G₄S)_x or a functional variant thereof, wherein x is 2, 3, 4, 5 or 6, and wherein further optionally the peptide linker comprises the amino acid sequence (G₄S)₄ or a functional variant thereof.
10. The composition or medical preparation of any one of claims 3 to 9, wherein the CH1 on the first polypeptide chain interacts with the CL on the second polypeptide chain.
11. The composition or medical preparation of any one of claims 1 to 10, wherein:
- a) the VH(CD3) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 27 to 145 of SEQ ID NO: 4;

- b) the VL(CD3) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 27 to 132 of SEQ ID NO: 6;
- c) the VH(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 267 to 383 of SEQ ID NO: 4;
- d) the VL(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4 and preferably a serine residue in position +15 relative to CDR1 and/or a serine residue in position -3 relative to CDR2;
- e) the VH(CD3) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 27 to 145 of SEQ ID NO: 4, the VL(CD3) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 27 to 132 of SEQ ID NO: 6, the VH(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 267 to 383 of SEQ ID NO: 4, and the VL(CLDN6) comprises CDR1, CDR2 and CDR3 of the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4 and preferably the VL(CLDN6) comprises a serine residue in position +15 relative to CDR1 and/or a serine residue in position -3 relative to CDR2; and/or
- f) the VH(CD3) comprises the amino acid sequence of amino acids 27 to 145 of SEQ ID NO: 4 or a functional variant thereof,
the VL(CD3) comprises the amino acid sequence of amino acids 27 to 132 of SEQ ID NO: 6 or a functional variant thereof,
the VH(CLDN6) comprises the amino acid sequence of amino acids 267 to 383 of SEQ ID NO: 4 or a functional variant thereof, and/or
the VL(CLDN6) comprises the amino acid sequence of amino acids 404 to 510 of SEQ ID NO: 4 or a functional variant thereof.

12. The composition or medical preparation of any one of claims 1 to 11, wherein:

- a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4 or a functional variant thereof;
- b) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 6 or a functional variant thereof; and/or
- c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4 or a functional variant thereof and the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 6 or a functional variant thereof.

13. The composition or medical preparation of any one of claims 1 to 12, wherein:

- a) at least one of the first polypeptide and the second polypeptide is encoded by a coding sequence which is codon-optimized and/or the G/C content of which is increased compared to wild type coding sequence, wherein the codon-optimization and/or the increase in the G/C content preferably does not change the sequence of the encoded amino acid sequence; and/or
- b) each of the first polypeptide and the second polypeptide is encoded by a coding sequence which is codon-optimized and/or the G/C content of which is increased compared to wild type coding sequence, wherein the codon-optimization and/or the increase in the G/C content preferably does not change the sequence of the encoded amino acid sequence.

14. The composition or medical preparation of any one of claims 1 to 13, wherein the RNA comprises a modified nucleoside in place of uridine, wherein optionally the modified nucleoside is selected from pseudouridine (ψ), N1-methyl-pseudouridine (m1 ψ), and 5-methyl-uridine (m5U).

15. The composition or medical preparation of any one of claims 1 to 14, wherein:

- a) at least one RNA comprises the 5' cap $m_2^{7,3'-O}Gppp(m_1^{2'-O})ApG$, wherein optionally each RNA comprises the 5' cap $m_2^{7,3'-O}Gppp(m_1^{2'-O})ApG$;
- b) at least one RNA comprises a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 8, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 8, wherein optionally each RNA comprises a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 8, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 8;
- c) at least one RNA comprises a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 9, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 9, wherein optionally each RNA comprises a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 9, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 9; and/or

d) at least one RNA comprises a poly-A sequence, wherein optionally each RNA comprises a poly-A sequence, the poly-A sequence comprises at least 100 nucleotides and/or the poly-A sequence comprises or consists of the nucleotide sequence of SEQ ID NO: 10.

16. The composition or medical preparation of any one of claims 1 to 15, wherein

- (i) the first RNA and the second RNA are in a (w/w) ratio of about 1.75:1 to about 1.25:1, or about 1.5:1 to about 1.25:1, or preferably about 1.5:1; and/or
- (ii) the first RNA and the second RNA comprise a modified nucleoside in place of each uridine; and/or
- (iii) the first RNA and the second RNA comprise a modified nucleoside in place of each uridine, wherein the modified nucleoside is independently selected from pseudouridine (ψ), N1-methyl-pseudouridine (m1 ψ), and 5-methyl-uridine (m5U); and/or
- (iv) the first RNA and the second RNA comprise the 5' cap m₂^{7,3'-O}Gppp(m₁^{2'-O})ApG; and/or
- (v) the first RNA and the second RNA comprise a 5' UTR comprising the nucleotide sequence of SEQ ID NO: 8, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 8; and/or
- (vi) the first RNA and the second RNA comprise a 3' UTR comprising the nucleotide sequence of SEQ ID NO: 9, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 9; and/or
- (vii) the first RNA and the second RNA comprise a poly-A tail comprising the nucleotide sequence of SEQ ID NO: 10.

17. The composition or medical preparation of any one of claims 1 to 16, wherein

- (i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 4, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 4; and/or
- (ii) the first RNA comprises the nucleotide sequence of SEQ ID NO: 5, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 5.

18. The composition or medical preparation of any one of claims 1 to 17, wherein

- (i) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 6, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 6; and/or
- (ii) the second RNA comprises the nucleotide sequence of SEQ ID NO: 7, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 7.

19. A composition or medical preparation comprising:

- (i) a first RNA encoding a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 4, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 4; and
- (ii) a second RNA encoding a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 6, or an amino acid sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the amino acid sequence of SEQ ID NO: 6.

20. The composition or medical preparation of any one of claims 1 to 19, wherein the first RNA comprises the nucleotide sequence of SEQ ID NO: 5, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 5, and/or wherein the second RNA comprises the nucleotide sequence of SEQ ID NO: 7, or a nucleotide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, or 80% identity to the nucleotide sequence of SEQ ID NO: 7.

21. The composition or medical preparation of any one of claims 1 to 20, wherein

- a) the RNA is mRNA;
- b) the RNA is formulated as a liquid, formulated as a solid, or a combination thereof;
- c) the RNA is formulated or is to be formulated for injection; and/or
- d) the RNA is formulated or is to be formulated for intravenous administration.

22. The composition or medical preparation of any one of claims 1 to 21, wherein the RNA is formulated or is to be formulated as particles, wherein optionally the particles are lipid nanoparticles (LNP).

23. The composition or medical preparation of any one of claims 1 to 22, which is a pharmaceutical composition, wherein the pharmaceutical composition preferably comprises a dose of 0.05 µg/kg or more, or 0.05 µg/kg to 5 mg/kg, or 0.05 µg/kg to 500 µg/kg, or 0.5 µg/kg to 500 µg/kg, or 1 µg/kg to 50 µg/kg, or 5 µg/kg to 150 µg/kg, or 15 µg/kg to 150 µg/kg RNA encoding the first and second polypeptide, wherein kg refers to kg body weight of a subject to be treated, wherein optionally the pharmaceutical composition further comprises one or more pharmaceutically acceptable carriers, diluents and/or excipients.

24. The composition or medical preparation of any one of claims 1 to 22, wherein the medical preparation is a kit, wherein optionally the RNA and optionally the particle forming components are in separate vials.

25. The composition or medical preparation of claim 24, further comprising instructions for use of the composition or medical preparation for treating or preventing cancer.

26. The composition or medical preparation of any one of claims 1 to 25, which is for administration to a human.

27. The composition or medical preparation of any one of claims 1 to 26 for use in therapy.

28. Use of the composition or medical preparation of any one of claims 1 to 26, in the preparation of a medicament for treating or preventing cancer.