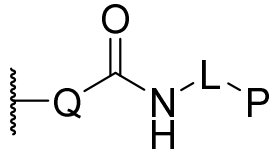
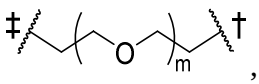
SUMMARY

[0008a] In one aspect, the present disclosure provides conjugate comprising an antibody (Ab) that specifically binds human CD22 and an immunomodulating oligonucleotide (P), wherein the anti-CD22 Ab comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides (Q) having at least one glutamine residue, wherein one Q-tag peptide is linked to the C-terminus of each of the two antibody heavy chains, and wherein the peptide sequence of each Q-tag is independently selected from the group consisting of SEQ ID NOs: 39-55; wherein one of the two Q-tag peptides is linked to the immunomodulating oligonucleotide via an amide bond with the glutamine residue of the Q-tag peptide and a linker (L) as shown in Formula (A):



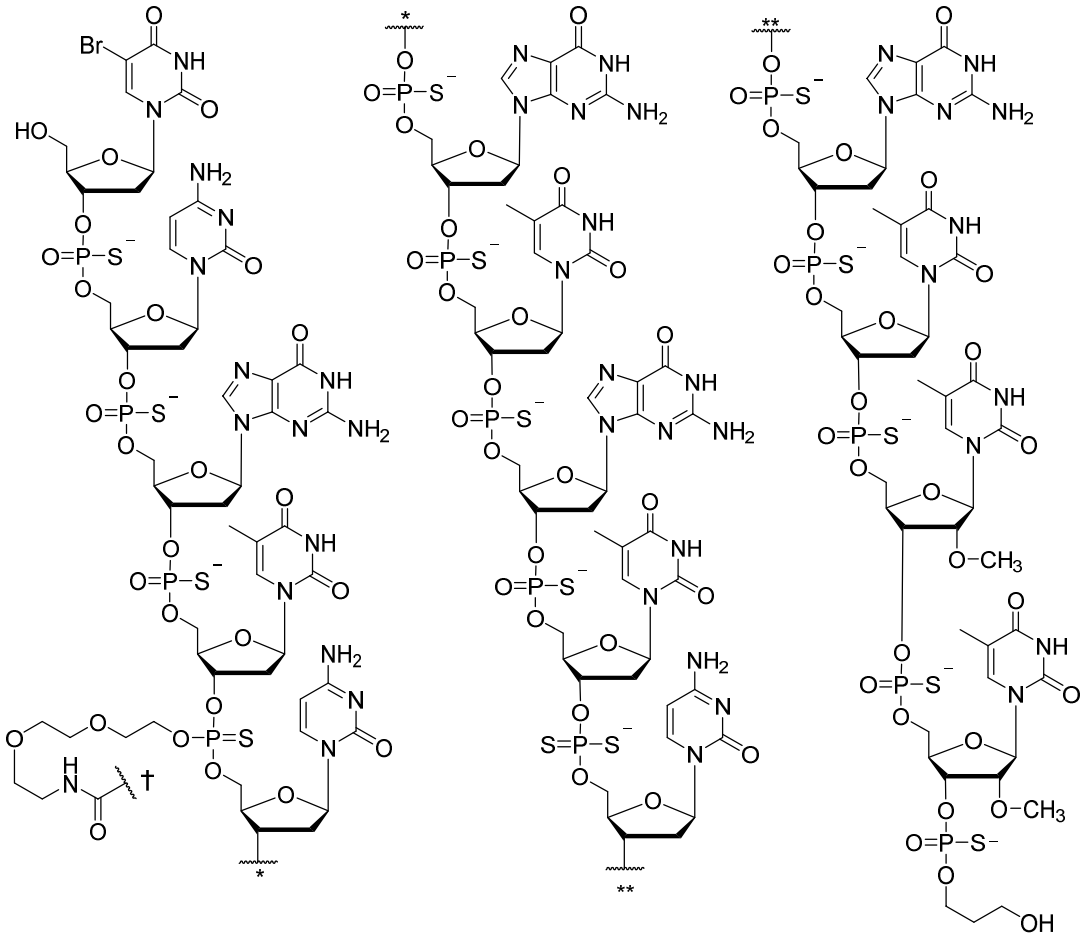
(A);

wherein ~~~ indicates the point of attachment of Q to the antibody (Ab);
wherein each heavy chain of the Ab comprises a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:65, and each light chain of the Ab comprises a light chain variable (VL) domain comprising an amino acid sequence selected from the group consisting of SEQ ID Nos:68, 73, and 87;
wherein the linker L is

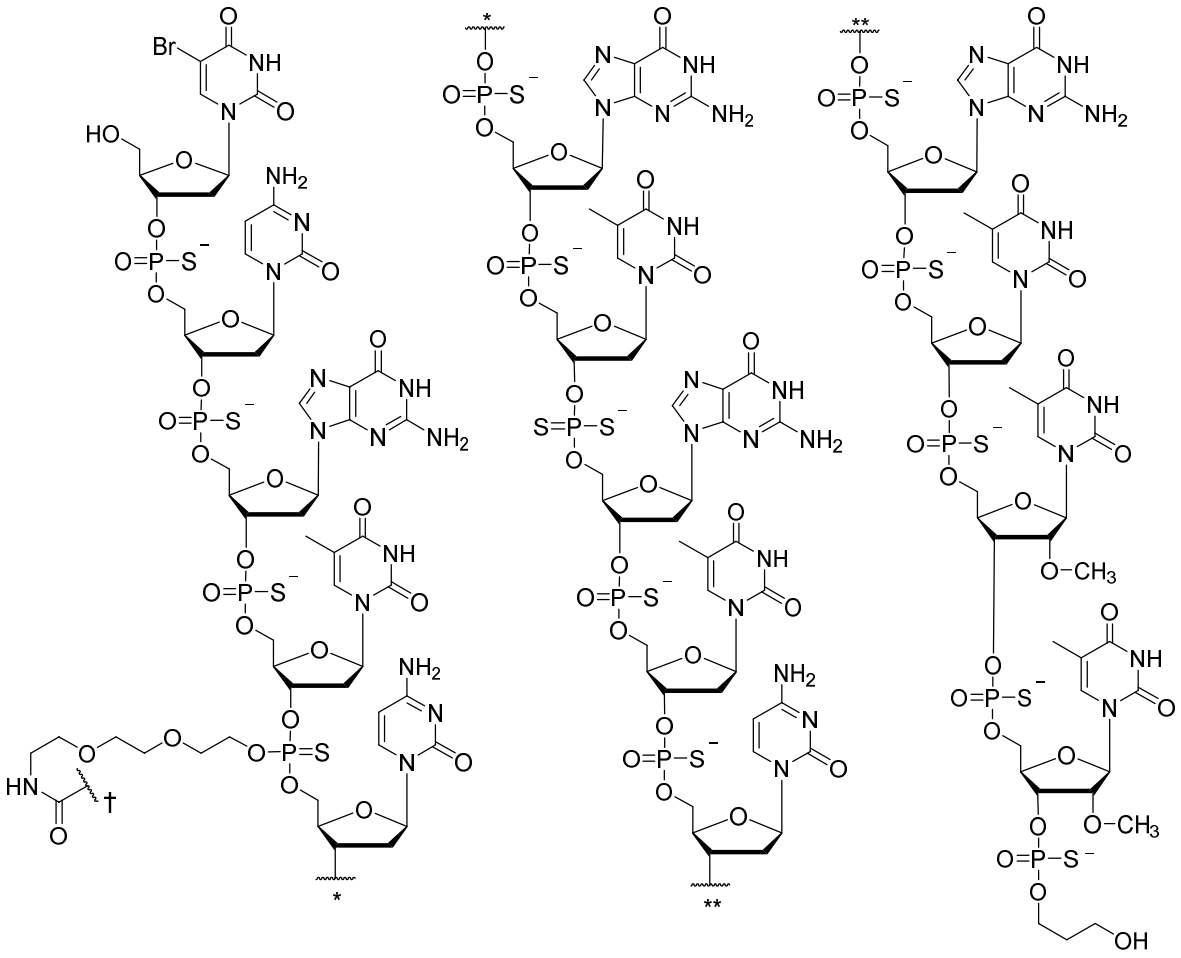


,

wherein m is 24, and wherein ~~~ † indicates the point of attachment to the oligonucleotide P, and ~~~ ‡ indicates the point of attachment to the glutamine residue of the Q-tag; and
wherein the oligonucleotide P comprises the structure



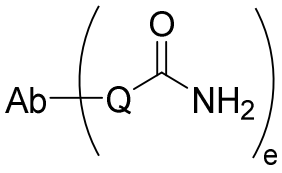
or



or a pharmaceutically acceptable salt thereof,

wherein ~~~ * and ~~~ ** indicate the points of attachment within the oligonucleotide, and wherein ~~~ † indicates the point of attachment to the linker L.

[0008b] In one aspect, the present disclosure provides a method for preparing the conjugate of formula (A) of the disclosure comprising contacting a compound of formula (B)



(B),

wherein Ab and Q are as defined for formula (A) above, and e is an integer from 1 to 20,

with one or more immunomodulating oligonucleotides P in the presence of a transglutaminase; and wherein the peptide sequence of each Q-tag independently comprises RPQGF (SEQ ID NO:47), RPQGFPP (SEQ ID NO:48), or RPQGFGPP (SEQ ID NO:49).

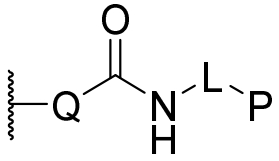
[0008c] In one aspect, the present disclosure provides an antibody or antigen binding fragment thereof that binds to CD22, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain the amino acid sequence of SEQ ID No:65; and
wherein the VL domain comprises the VL domain sequence of SEQ ID No: 87.

[0008d] In one aspect, the present disclosure provides a pharmaceutical composition comprising the conjugate according to the disclosure, or the antibody according to the disclosure, and pharmaceutically acceptable carrier.

[0008e] In one aspect, the present disclosure provides the use of the conjugate according to the disclosure, antibody according to the disclosure, or pharmaceutical composition according to the disclosure for the manufacture of a medicament for treating cancer.

[0008f] In one aspect, the present disclosure provides the conjugate according to the disclosure, antibody according to the disclosure, or pharmaceutical composition according to the disclosure for use in therapy.

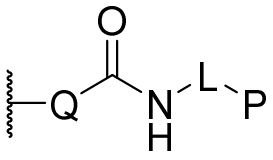
[0009] In one example, provided herein is a conjugate comprising an antibody or antigen-binding fragment thereof and one or more immunomodulating oligonucleotides (P), wherein each immunomodulating oligonucleotide is linked via an amide bond to a glutamine residue (Q) of the antibody or fragment and a linker (L) as shown in Formula (A):



(A),

wherein ~~~ indicates the point of attachment of each Q to the antibody or antigen-binding fragment thereof (Ab). In some examples, the glutamine residue is part of a Q-tag peptide linked to the antibody, *e.g.*, to the C-terminus of the antibody Fc region. In some examples, the glutamine residue is part of the antibody (*e.g.*, part of the Fc region, such as residue Q295). In some examples, the antibody further comprises an N297A mutation. Exemplary Q-tag peptide sequences are provided, *e.g.*, in ***Table 3***. Exemplary immunomodulating oligonucleotides are described herein and provided, *e.g.*, in ***Tables 2 & 9-12***. In some examples, 1-4 immunomodulating oligonucleotides are conjugated to the antibody. Exemplary linkers (L) are described herein. In some examples, the linker comprises a polyethylene glycol moiety.

[0009a] In one example, the present disclosure refers to a conjugate comprising a monoclonal antibody or antigen-binding fragment thereof and one or more immunomodulating oligonucleotides (P), wherein the monoclonal antibody or antigen-binding fragment is linked to one or more Q-tag peptides (Q) comprising at least one glutamine residue, and wherein each immunomodulating oligonucleotide is linked to a Q-tag peptide via an amide bond with the glutamine residue of the Q-tag peptide and a linker (L) as shown in Formula (A):

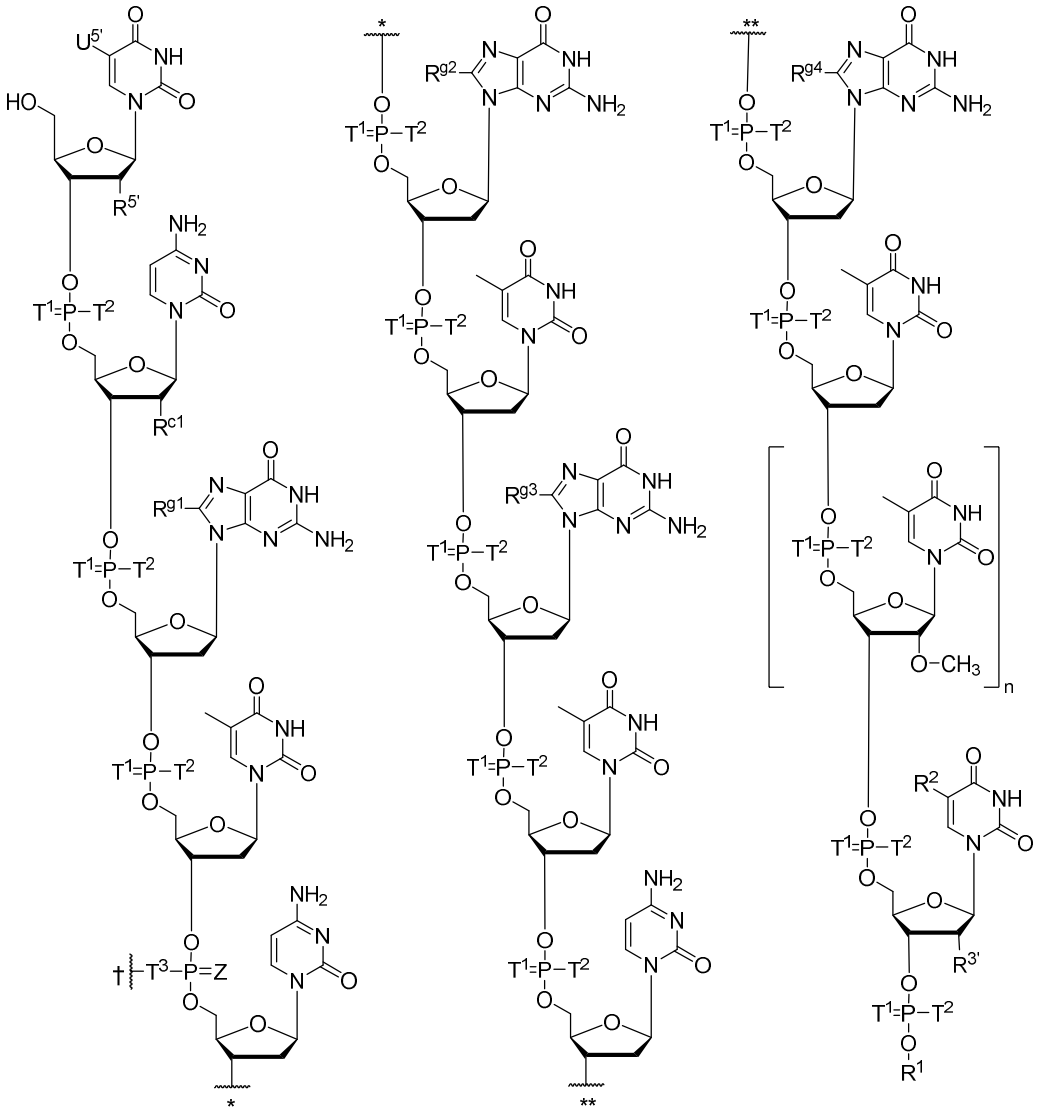


(A);

wherein ~~~ indicates the point of attachment of each Q to the antibody or antigen-binding fragment thereof (Ab); and wherein:

(a) each of the one or more Q-tag peptides (Q) comprises the amino acid sequence RPQGF (SEQ ID NO:47); and/or

(b) each P is independently an immunomodulating oligonucleotide having the structure

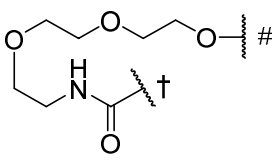


wherein

〰 * and 〰 ** indicate the points of attachment within the oligonucleotide, and wherein 〰 † indicates the point of attachment to the linker L;

each T^1 is independently O or S;

each T^2 is S^-;



T^3 is a group , wherein 〰 † indicates the point of attachment to L and wherein 〰 # indicates the point of attachment to the rest of the oligonucleotide;

Z is O or S;

$U^{5'}$ is –H or halogen;

$R^{5'}$ is -H or methoxy;

R^{c1} is -H or methoxy;

R^{g1}, R^{g2}, R^{g3}, and R^{g4} are H;

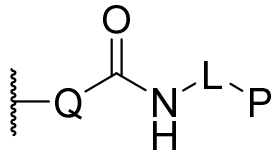
$R^{3'}$ is methoxy;

R^{1} is $-(CH_2)_3-OH$;

R^{2} is -H or methyl; and

n is an integer from 0 to 2.

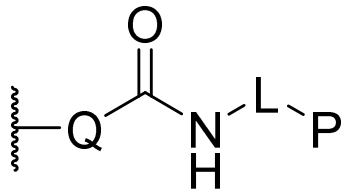
[0010] In one example, provided herein is a conjugate comprising an antibody or antigen-binding fragment thereof and one or more immunomodulating oligonucleotides (P), wherein the antibody or antigen-binding fragment is linked to one or more Q-tag peptides (Q) that comprise the amino acid sequence RPQGF (SEQ ID NO:47), wherein each immunomodulating oligonucleotide is linked to a Q-tag peptide via an amide bond with the glutamine residue of the Q-tag peptide and a linker (L) as shown in Formula (A):



(A),

wherein 〰 indicates the point of attachment of each Q to the antibody or antigen-binding fragment thereof (Ab).

[0010a] In one example, the present disclosure refers to a conjugate comprising an antibody or antigen-binding fragment thereof (Ab) and one or more immunomodulating oligonucleotides (P), wherein the antibody or antigen-binding fragment is linked to one or more Q-tag peptides (Q) comprising a Q-tag peptide sequence RPQGF (SEQ ID NO:47), and wherein each immunomodulating oligonucleotide is linked to a Q-tag peptide via an amide bond with the glutamine residue of the Q-tag peptide and a linker (L) as shown in Formula (A)

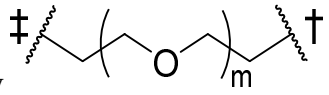


(A),

wherein:

〰 indicates the point of attachment of each Q to the antibody or antigen-binding fragment thereof (Ab)

each Q independently comprises a Q-tag peptide sequence RPQGF (SEQ ID NO:47);

each L is independently a bond or a linker moiety 

,

wherein m is an integer ranging from about 0 to about 50, and wherein 〰 † indicates the point of attachment to P, and 〰 ‡ indicates the point of attachment to the rest of the conjugate connected to Q via an amide bond with the glutamine residue; and

each P is independently an immunomodulating oligonucleotide having the structure

R^{c1} is -H or methoxy;

R^{g1}, R^{g2}, R^{g3}, and R^{g4} are H;

$R^{3'}$ is methoxy;

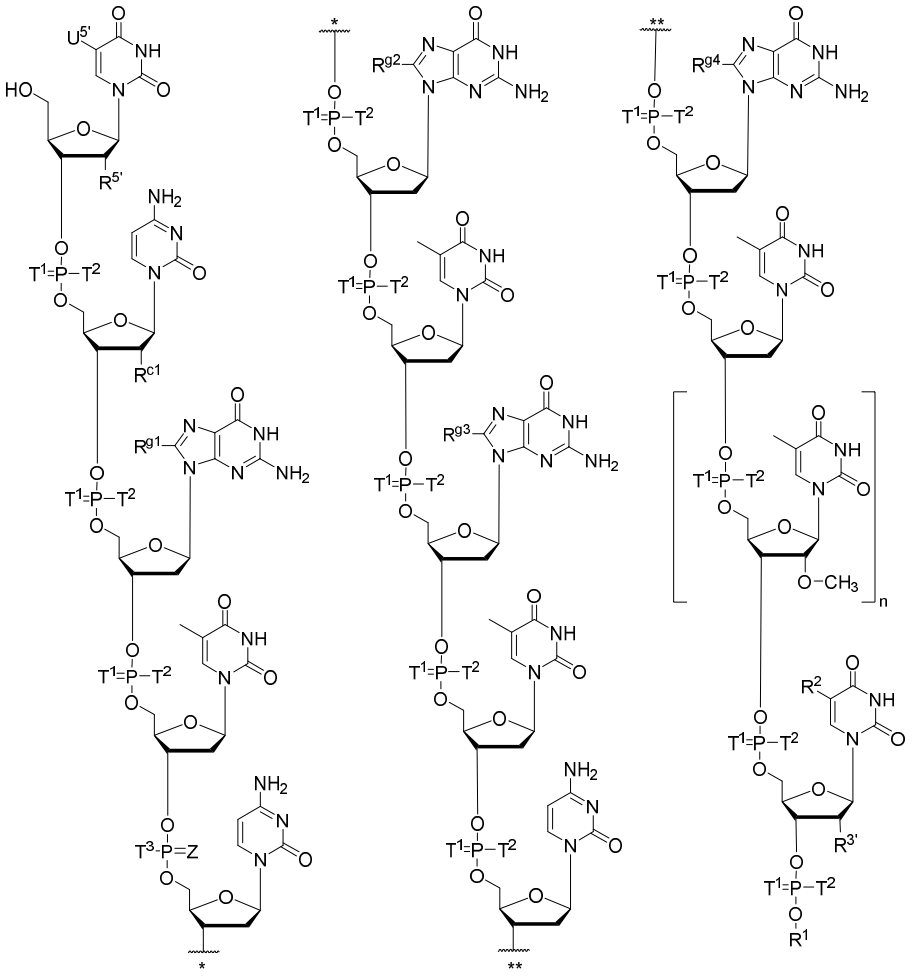
R^1 is $-(CH_2)_3$-OH;

R^2 is -H or methyl; and

n is an integer from 0 to 2,

or a pharmaceutically acceptable salt thereof.

[0039a] In one example, the present disclosure refers to an immunomodulating oligonucleotide of Formula (C):



(C),

wherein

〰 * and 〰 ** indicate the points of attachment within the oligonucleotide;

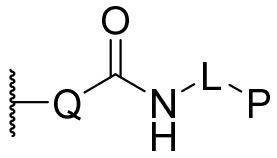
each T^1 is independently O or S;

each T^2 is S^-;

consisting of SEQ ID NOs: 39-55. In some examples, immunomodulatory oligonucleotide has a sequence selected from the group consisting of the oligonucleotides of ***Table 10*** and ***Table 12***. In further examples, the antibody comprises a light chain variable domain (VL) and a heavy chain variable domain (VH), and wherein VH comprises the sequence SEQ ID NO: 56; and VL comprises the sequence SEQ ID NO: 57.

[0050a] In one example, the present disclosure refers to a conjugate comprising a protein, at least one Q tag peptide sequence comprising a glutamine residue, and at least one immunomodulatory oligonucleotide, wherein the Q-tag peptide sequence is naturally occurring or synthetic, and wherein each immunomodulatory oligonucleotide is linked to a Q-tag via an amide bond with the glutamine residue, wherein at least one Q-tag peptide sequence is selected from the group consisting of SEQ ID NOs: 40-55.

[0051] In still yet another example, the present disclosure provides a conjugate comprising an antibody linked to two Q-tag peptides (Q) and an immunomodulating oligonucleotide (P); wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the Q-tag peptides is linked to the C-terminus of one of the antibody heavy chains; and wherein one of the Q-tag peptides is linked to the immunomodulating oligonucleotide via an amide bond with the glutamine residue of the Q-tag peptide and a linker (L) as shown in Formula (A):



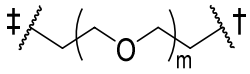
(A),

wherein 〰 indicates the point of attachment of each Q to the antibody.

[0052] In some examples, each Q-tag peptide comprises the amino acid sequence RPQGF (SEQ ID NO:47). In some examples, each L is a linker as described herein. In some examples, each (P) is an immunomodulating oligonucleotide as described herein. In some examples, the antibody is an antibody as described herein. In some examples, the antibody binds to CD22 (*e.g.*, human CD22).

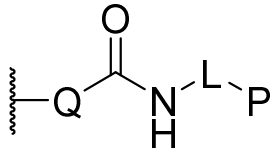
[0053] In yet another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence RPQGF (SEQ ID NO:47); wherein each of the Q-tag peptides is linked to the C-terminus of one of the antibody heavy chains; wherein one of the two Q-tag peptides is linked to the immunomodulating oligonucleotide via an amide bond with the glutamine residue of the Q-tag peptide and a linker (L) as shown in Formula (A):

antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; wherein each of the Q-tag peptides is linked to the C-terminus of one of the antibody heavy chains; wherein one of the two Q-tag peptides is linked to the immunomodulating oligonucleotide via an amide bond with the glutamine residue of the Q-tag peptide and a linker (L), wherein the two antibody heavy chains comprise a VH domain comprising the sequence of SEQ ID NO:65 and a constant region comprising the sequence of SEQ ID NO:92, wherein the two antibody light chains comprise a VL domain comprising the sequence of SEQ ID NO:87 and a constant region comprising the sequence of SEQ ID NO:108, and wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:163. In some examples, the linker comprises the linker moiety



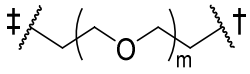
, wherein m is an integer 24, and wherein ~~~ † indicates the point of attachment to P, and ~~~ ‡ indicates the point of attachment to the rest of the conjugate connected to Q via an amide bond with the glutamine residue.

[0054a] In one example, the present disclosure refers to a conjugate comprising an anti-CD22 antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the Ab comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides (Q) having at least one glutamine residue; wherein one Q-tag peptide is linked to the C-terminus of each of the two antibody heavy chains; wherein one of the two Q-tag peptides is linked to the immunomodulating oligonucleotide via an amide bond with the glutamine residue of the Q-tag peptide and a linker (L) as shown in Formula (A):



(A),

wherein ~~~ indicates the point of attachment of Q to the antibody (Ab);
wherein each heavy chain of the Ab comprises a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:65, and each light chain of the Ab comprises a light chain variable (VL) domain comprising an amino acid sequence selected from the group consisting of SEQ ID Nos:68, 73, and 87;
wherein the linker L is



,

wherein m is 24, and wherein ~~~ † indicates the point of attachment to the oligonucleotide P, and ~~~ ‡ indicates the point of attachment to the glutamine residue of the Q-tag; and
wherein the oligonucleotide P comprises the structure:

$U^{5'}$ is –H or halogen;

$R^{5'}$ is -H;

R^{c1} is -H;

R^{g1}, R^{g2}, R^{g3}, and R^{g4} are H;

$R^{3'}$ is methoxy;

R^1 is -$(CH_2)_3$-OH;

R^2 is -methyl; and

n is 1,

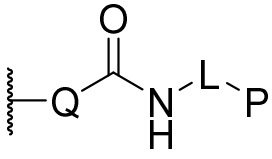
wherein Ab is an antibody or antigen-binding fragment thereof that binds a tumor associated antigen.

[0061] In some examples, the antibody or conjugate specifically binds an antigen expressed by the cancer or cancer-associated stroma.

[0062] In another example, also provided herein is a pharmaceutical composition comprising a conjugate as described herein. In still another example, provided herein is a pharmaceutical composition comprising an immunomodulating oligonucleotide as described herein. In still yet a further example, provided herein is a kit comprising a conjugate as described herein, and instructions for use of the conjugate.

[0062a] In one example, the present disclosure refers to a pharmaceutical composition comprising: (a) a conjugate disclosed herein; or (b) an immunomodulating oligonucleotide disclosed herein; and a pharmaceutically acceptable carrier.

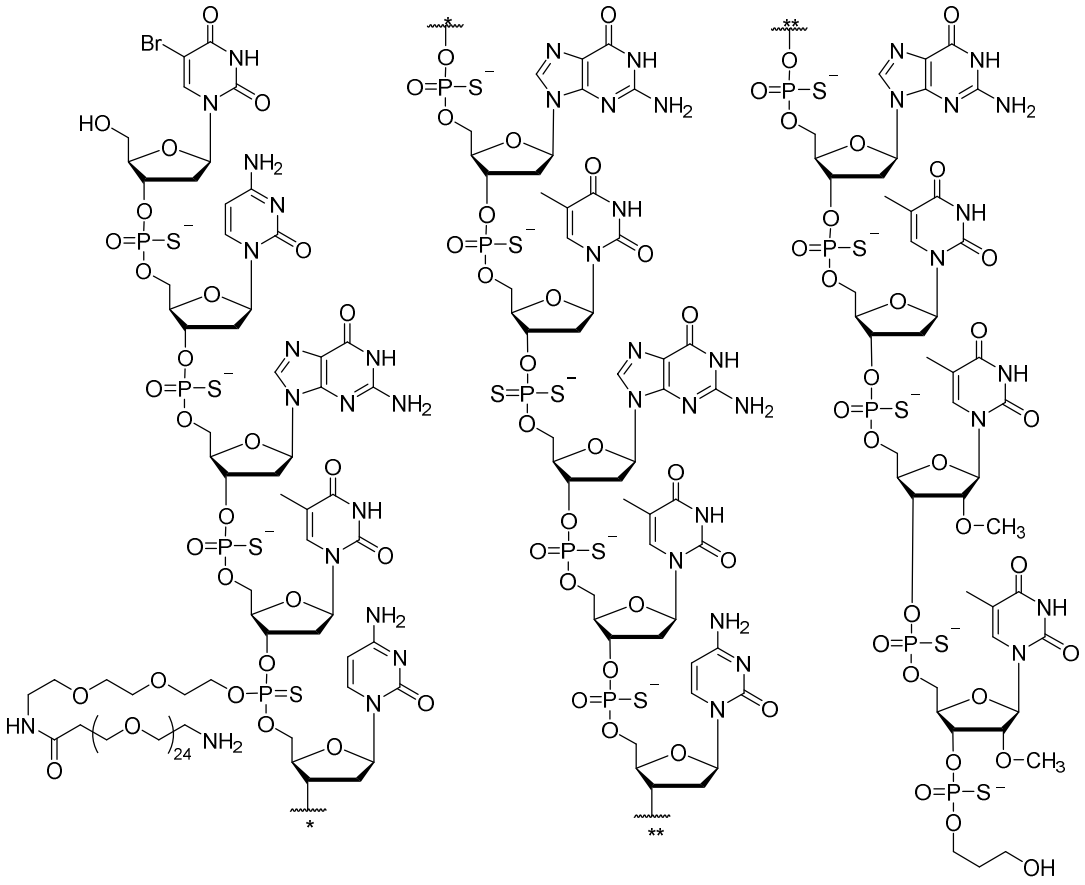
[0063] In still further examples, provided herein are methods for preparing the conjugates as described herein. In one example, provided herein is a method for preparing a conjugate that comprises an antibody or antigen-binding fragment thereof (Ab) and one or more immunomodulating oligonucleotides (P), wherein the antibody or antigen-binding fragment is linked to one or more Q-tag peptides (Q) comprising the amino acid sequence RPQGF (SEQ ID NO:47), wherein each immunomodulating oligonucleotide is linked to a Q-tag peptide via an amide bond with the glutamine residue of the Q-tag peptide and a linker (L) as shown in formula (A),



(A),

wherein:

[0063a] In one example, the present disclosure refers to a method for preparing a conjugate that comprises an antibody (Ab) and an immunomodulating oligonucleotide (P), comprising: contacting the Ab with the oligonucleotide P in the presence of a transglutaminase; wherein the Ab comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides (Q) having at least one glutamine residue; wherein one Q-tag peptide is linked to the C-terminus of each of the two antibody heavy chains; and wherein the oligonucleotide P comprises the structure:



or

[0065] In still other examples, provided herein is an antibody or antigen binding fragment thereof that binds to CD22, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a VH domain sequence selected from the group consisting of SEQ ID Nos:64-67; and wherein the VL domain comprises a VL domain sequence selected from the group consisting of SEQ ID Nos:68-91. In still other examples, provided herein is an antibody or antigen binding fragment thereof that binds to CD22, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1, CDR-H2, and CDR-H3 from a VH domain shown in **Table 8**, and wherein the VL domain comprises a CDR-L1, CDR-L2, and CDR-L3 from a VL domain shown in **Table 8**. In some examples, the antibody is a Fab, F(ab')2, Fab'-SH, Fv, scFv, single domain, single heavy chain, or single light chain antibody or antibody fragment. In some examples, the antibody comprises an Fc region. In some examples, the Fc region is a human Fc region selected from the group consisting of an IgG1 Fc region, an IgG2 Fc region, and an IgG4 Fc region. In some examples, the Fc region is a wild-type human IgG1, IgG2, or IgG4 Fc region. In some examples, the Fc region is a human Fc region comprising one or more amino acid substitutions that reduce binding to C1q. In some examples, the Fc region is a human Fc region comprising one or more amino acid substitutions that reduce effector function, as compared with a human Fc region that lacks the amino acid substitution(s). In some examples, the Fc region is: (a) a human IgG1 Fc region comprising L234A, L235A, and/or G237A substitutions, amino acid position numbering according to EU index; (b) a human IgG2 Fc region comprising A330S and/or P331S substitutions, amino acid position numbering according to EU index; or (c) a human IgG4 Fc region comprising S228P and/or L235E substitutions, amino acid position numbering according to EU index. In some examples, the Fc region further comprises an N297A substitution, amino acid position numbering according to EU index. In some examples, the antibody further comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:92-110.

[0065a] In one example, the present disclosure refers to an antibody or antigen binding fragment thereof that binds to CD22, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a VH domain sequence selected from the group consisting of SEQ ID Nos:64-67; and wherein the VL domain comprises a VL domain sequence selected from the group consisting of SEQ ID Nos:68-91.

[0066] In still other examples, provided herein is an antibody that binds to human CD22, wherein the antibody comprises an antibody heavy chain and an antibody light chain, wherein the antibody heavy chain comprises the sequence of SEQ ID NO:179 or 180, and the antibody light chain comprises the sequence of SEQ ID NO:181 or 182. In some examples, the antibody heavy chain comprises the sequence of SEQ ID NO:179, and the antibody light chain comprises the

urothelial cancer, and gastric cancer. In some examples, the administration results in reduced growth, size, and/or volume of the cancer. In another example, provided herein is the conjugate, immunomodulating oligonucleotide, antibody, or pharmaceutical composition according to any one of the examples herein for use in a method of treating cancer, wherein the method comprises administering an effective amount of the conjugate, immunomodulating oligonucleotide, antibody, or pharmaceutical composition to an individual. In some examples, the cancer is a solid tumor. In some examples, the cancer is a liquid tumor. In some examples, the cancer is a B cell cancer. In some examples, the cancer is a lymphoma or leukemia. In some examples, the cancer is breast cancer, colorectal cancer, lung cancer, head and neck cancer, melanoma, lymphoma, or leukemia. In still other example, provided herein is a method for delivering the immunomodulating oligonucleotide according to any of the examples herein, comprising contacting the immunomodulating oligonucleotide with a cell. In some examples, the immunomodulating oligonucleotide is pegylated. In some examples, the immunomodulating oligonucleotide is formulated in a nanoparticle. In some examples, the immunomodulating oligonucleotide is conjugated to a polypeptide. In some examples, the antibody or conjugate specifically binds an antigen expressed by the cancer or cancer-associated stroma.

[0068a] In one example, the present disclosure refers to use of the conjugate disclosed herein, immunomodulating oligonucleotide disclosed herein, pharmaceutical composition disclosed herein, or antibody disclosed herein, in the manufacture of a medicament for treating cancer in an individual.

DESCRIPTION OF THE FIGURES

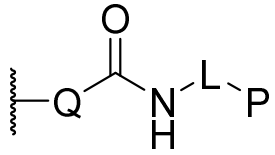
[0069] The present application can be understood by reference to the following description taken in conjunction with the accompanying figures.

[0070] **FIGS. 1A and 1B** depict the activity of immunomodulating oligonucleotides alone in human PBMCs based upon observed increased expression of (a) HLADR and (b) CD40.

[0071] **FIGS. 2A-2D** show the effect of immunomodulating polynucleotides and their antibody conjugates on increasing B cells numbers and activation. **FIG. 2A** depicts the observed effect on B cell numbers by the various immunomodulating polypeptides alone. **FIGS. 2B-2C** depict the observed activation of B cells (via detection of CD40 expression) produced by the immunomodulating polynucleotides alone. **FIG. 2D** depicts the observed activity of antibody-oligonucleotide conjugates with RFB4 (anti-CD22) (DAR1).

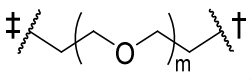
CLAIMS

1. A conjugate comprising an antibody (Ab) that specifically binds human CD22 and an immunomodulating oligonucleotide (P), wherein the anti-CD22 Ab comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides (Q) having at least one glutamine residue, wherein one Q-tag peptide is linked to the C-terminus of each of the two antibody heavy chains, and wherein the peptide sequence of each Q-tag is independently selected from the group consisting of SEQ ID NOs: 39-55; wherein one of the two Q-tag peptides is linked to the immunomodulating oligonucleotide via an amide bond with the glutamine residue of the Q-tag peptide and a linker (L) as shown in Formula (A):



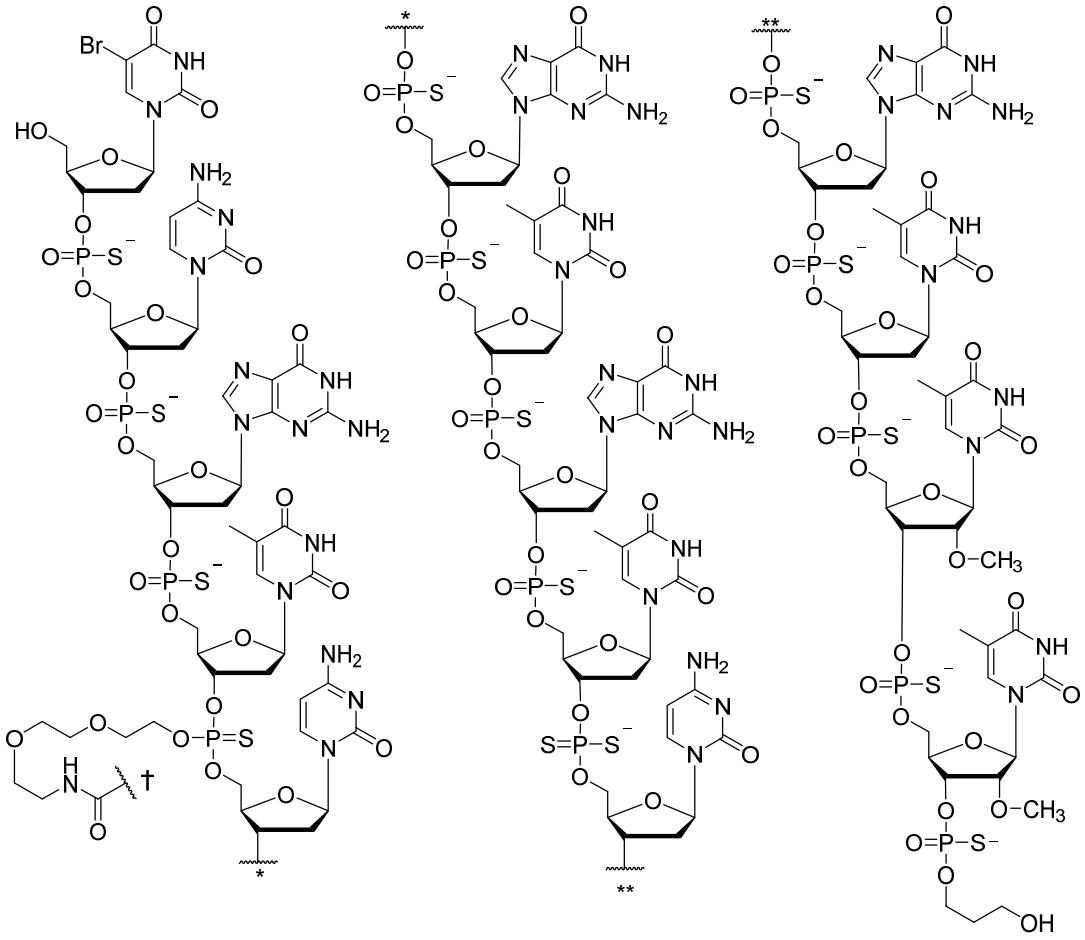
(A);

wherein ~~~ indicates the point of attachment of Q to the antibody (Ab);
wherein each heavy chain of the Ab comprises a heavy chain variable (VH) domain comprising the amino acid sequence of SEQ ID NO:65, and each light chain of the Ab comprises a light chain variable (VL) domain comprising an amino acid sequence selected from the group consisting of SEQ ID Nos:68, 73, and 87;
wherein the linker L is

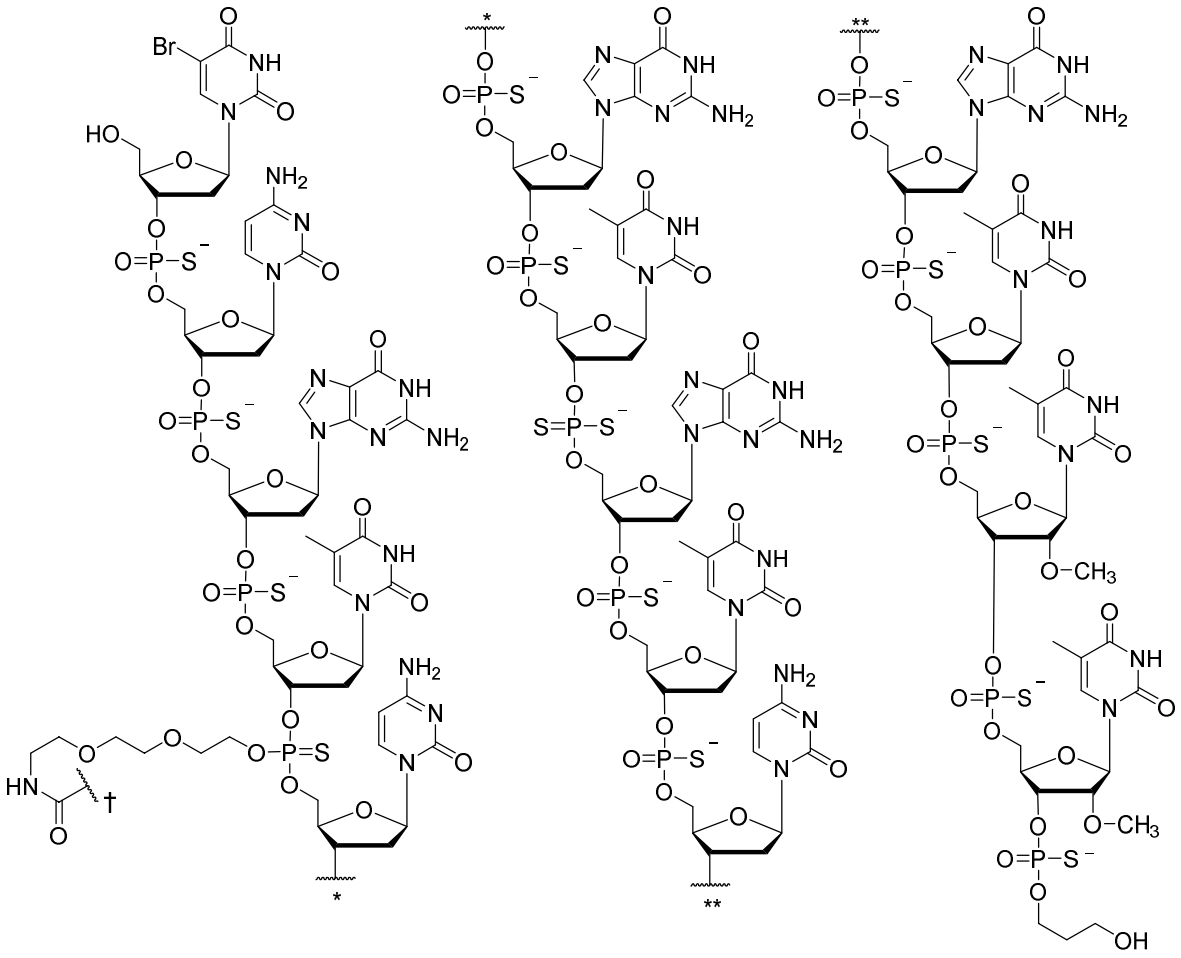


,

wherein m is 24, and wherein ~~~ † indicates the point of attachment to the oligonucleotide P, and ~~~ ‡ indicates the point of attachment to the glutamine residue of the Q-tag; and
wherein the oligonucleotide P comprises the structure



or



or a pharmaceutically acceptable salt thereof,

wherein ~~~ * and ~~~ ** indicate the points of attachment within the oligonucleotide, and wherein ~~~ † indicates the point of attachment to the linker L.

2. The conjugate of claim 1, wherein each heavy chain of the antibody comprises a VH domain that comprises the amino acid sequence QVQLLESGGGVVQPGGSLRLSCAASGFAFSIYDMNWVRQAPGKGLEWVSAISSGGGTTYYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWGRGTLVTVSS (SEQ ID NO: 65), and wherein each light chain of the antibody comprises a VL domain that comprises the amino acid sequence DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPSRFSGSGSGTDFTLTISSLQPEDFATYFCQQGSTLPWTFGQGTKLEIK (SEQ ID NO: 87).

3. The conjugate of claim 1, wherein each heavy chain of the antibody comprises a VH domain that comprises the amino acid sequence QVQLLESGGGVVQPGGSLRLSCAASGFAFSIYDMNWVRQAPGKGLEWVSAISSGGGTTY YADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWGRG TLVTVSS (SEQ ID NO: 65), and wherein each light chain of the antibody comprises a VL domain that comprises the amino acid sequence DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPSR FSGSGSGTDFTLTISSLQPEDFATYFCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 68).

4. The conjugate of claim 1, wherein each heavy chain of the antibody comprises a VH domain that comprises the amino acid sequence QVQLLESGGGVVQPGGSLRLSCAASGFAFSIYDMNWVRQAPGKGLEWVSAISSGGGTTY YADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWGRG TLVTVSS (SEQ ID NO: 65), and wherein each light chain of the antibody comprises a VL domain that comprises the amino acid sequence DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPSR FSGSGSGTDFTLTISSLQPEDFATYFCQQGATLPWTFGQGTKLEIK (SEQ ID NO: 73).

5. The conjugate of any one of claims 1 to 4, wherein each Q-tag independently comprises RPQGF (SEQ ID NO:47), RPQGFPP (SEQ ID NO:48), or RPQGFGPP (SEQ ID NO:49)**.**

6. The conjugate of any one of claims 1 to 5, wherein each Q-tag comprises RPQGFGPP (SEQ ID NO:49).

7. The conjugate of claim 1, wherein the peptide sequence of each Q-tag comprises RPQGF (SEQ ID NO:47), and wherein:

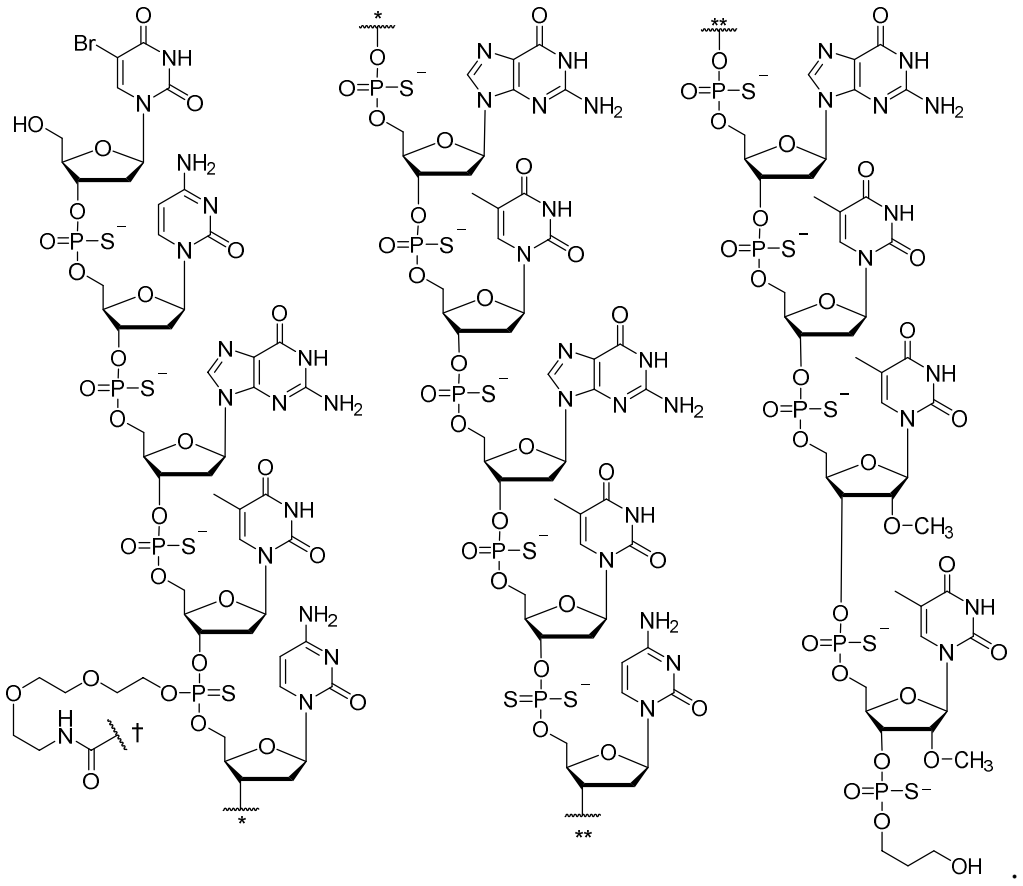
(a) each heavy chain of the antibody comprises a heavy chain comprising the sequence of SEQ ID NO:179, and each light chain of the antibody comprises the sequence of SEQ ID NO:181;

(b) each heavy chain of the antibody comprises a heavy chain comprising the sequence of SEQ ID NO:180, and each light chain of the antibody comprises the sequence of SEQ ID NO:181;

(c) each heavy chain of the antibody comprises a heavy chain comprising the sequence of SEQ ID NO:179, and each light chain of the antibody comprises the sequence of SEQ ID NO:182; or

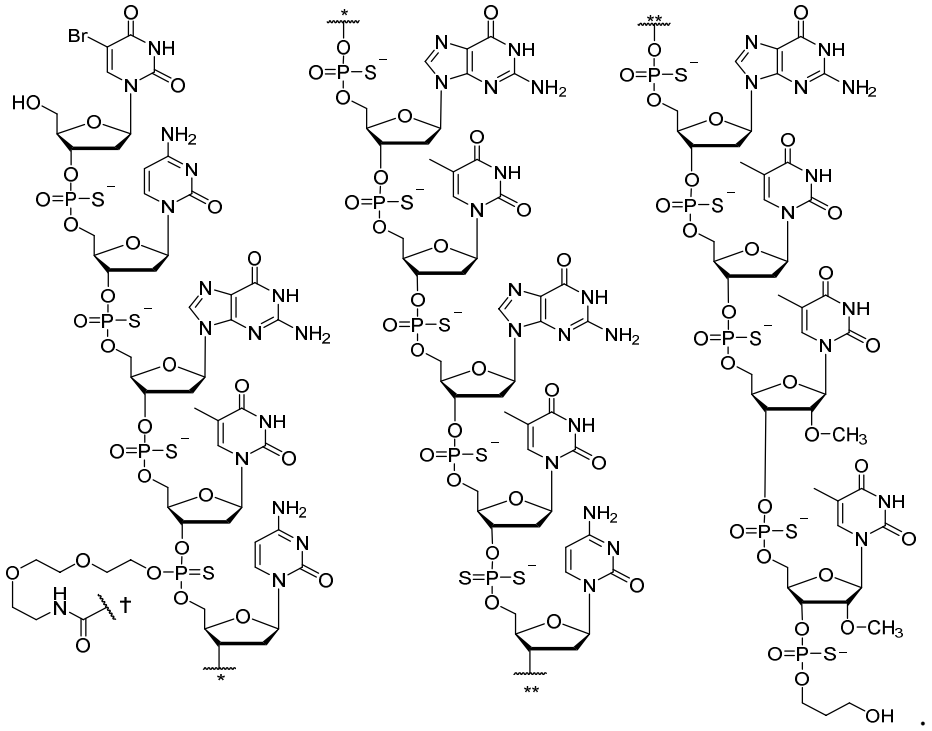
(d) each heavy chain of the antibody comprises a heavy chain comprising the sequence of SEQ ID NO:180, and each light chain of the antibody comprises the sequence of SEQ ID NO:182.

8. The conjugate of claim 1, wherein each of the two Q-tag peptides comprises the amino acid sequence RPQGFGPP (SEQ ID NO:49), each heavy chain of the Ab including Q comprises the amino acid sequence of SEQ ID NO:180, each light chain of the Ab comprises the amino acid sequence of SEQ ID NO:182, and the oligonucleotide P comprises the structure:

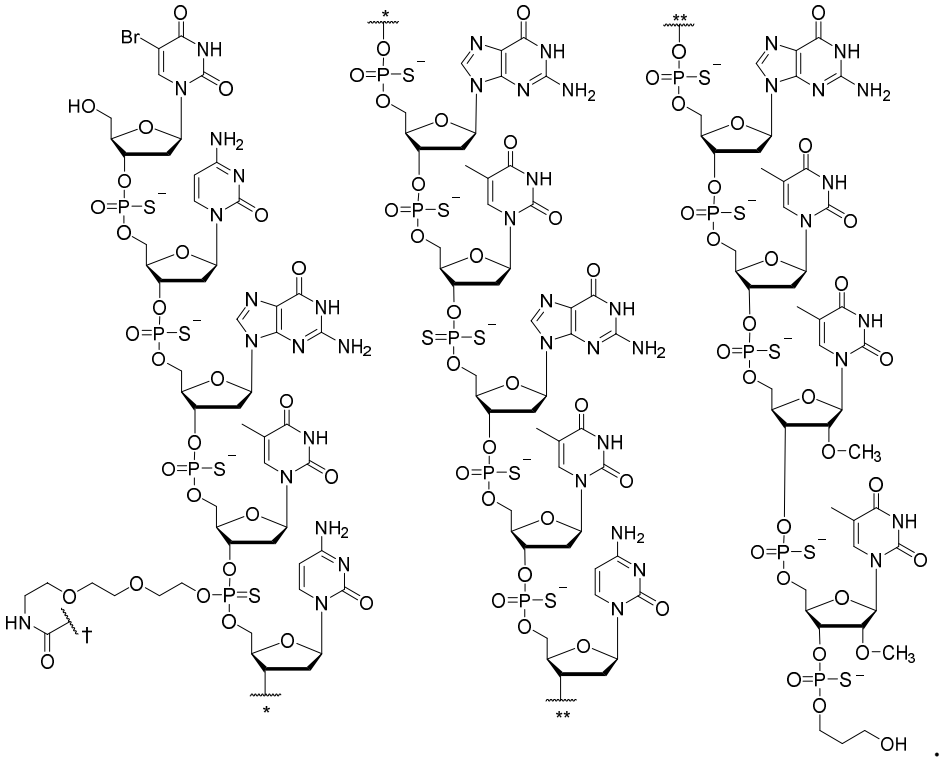


9. The conjugate of claim 1, wherein each of the two Q-tag peptides comprises the amino acid sequence RPQGFGPP (SEQ ID NO:49), each heavy chain of the Ab including Q comprises

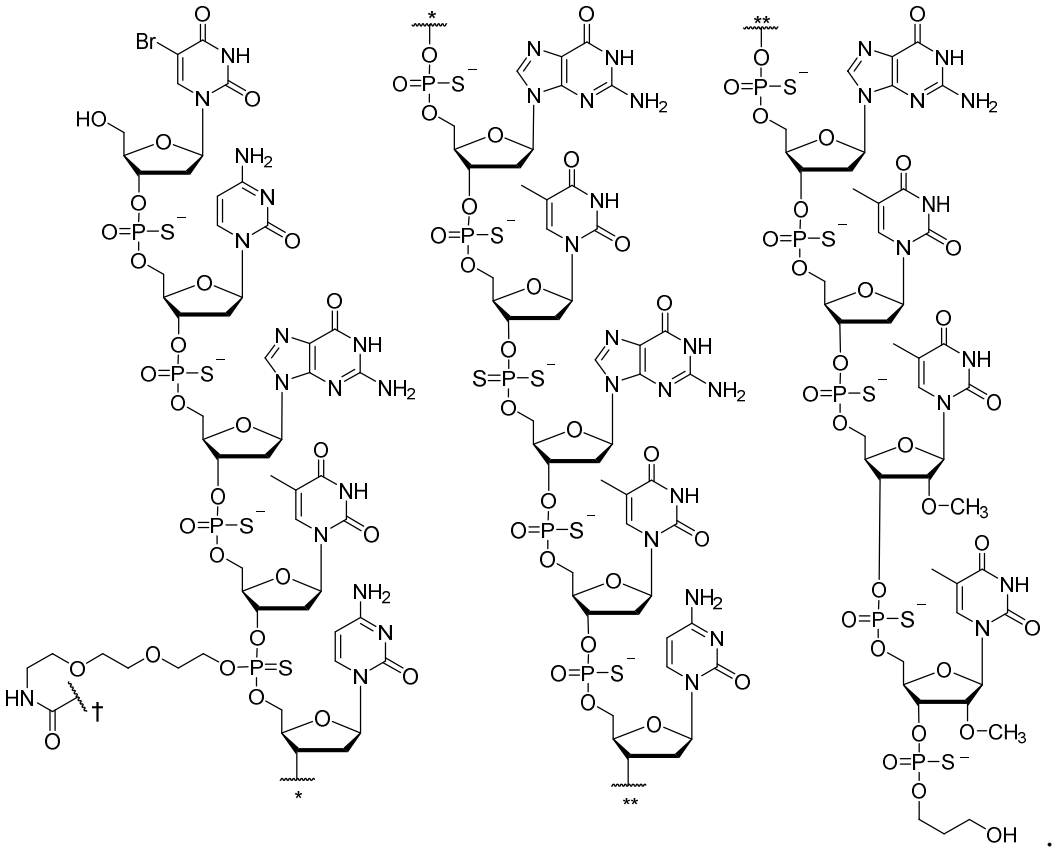
the amino acid sequence of SEQ ID NO:179, each light chain of the Ab comprises the amino acid sequence of SEQ ID NO:182, and the oligonucleotide P comprises the structure:



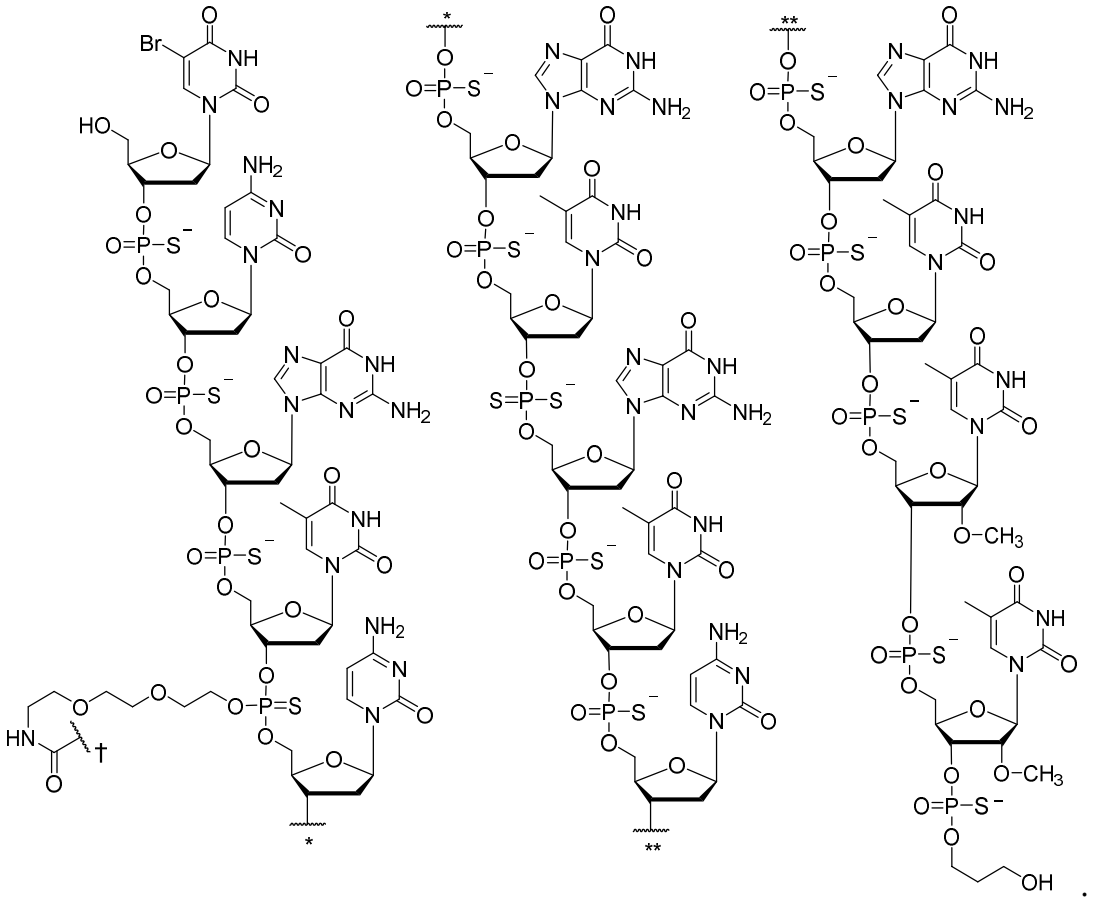
10. The conjugate of claim 1, wherein each of the two Q-tag peptides comprises the amino acid sequence RPQGFGPP (SEQ ID NO:49), each heavy chain of the Ab including Q comprises the amino acid sequence of SEQ ID NO:179, each light chain of the Ab comprises the amino acid sequence of SEQ ID NO:182, and the oligonucleotide P comprises the structure:



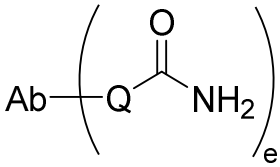
11. The conjugate of claim 1, wherein each of the two Q-tag peptides comprises the amino acid sequence RPQGFGPP (SEQ ID NO:49), each heavy chain of the Ab including Q comprises the amino acid sequence of SEQ ID NO:180, each light chain of the Ab comprises the amino acid sequence of SEQ ID NO:182, and the oligonucleotide P comprises the structure:



12. The conjugate of claim 1, wherein each of the two Q-tag peptides comprises the amino acid sequence RPQGFGPP (SEQ ID NO:49), each heavy chain of the Ab including Q comprises the amino acid sequence of SEQ ID NO:180, each light chain of the Ab comprises the amino acid sequence of SEQ ID NO:181, and the oligonucleotide P comprises the structure:



13. A method for preparing the conjugate of formula (A) of any one of claims 1-12 comprising contacting a compound of formula (B)



(B),

wherein Ab and Q are as defined for formula (A) above, and e is an integer from 1 to 20, with one or more immunomodulating oligonucleotides P in the presence of a transglutaminase; and wherein the peptide sequence of each Q-tag independently comprises RPQGF (SEQ ID NO:47), RPQGFPP (SEQ ID NO:48), or RPQGFGPP (SEQ ID NO:49).

14. An antibody or antigen binding fragment thereof that binds to CD22, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain the amino acid sequence of SEQ ID No:65; and wherein the VL domain comprises the VL domain sequence of SEQ ID No: 87.

15. The antibody of claim 14, wherein:
(a) the heavy chain comprises the amino acid sequence of SEQ ID NO:179, and the light chain comprises the amino acid sequence of SEQ ID NO:181; or

(b) the heavy chain comprises the amino acid sequence of SEQ ID NO:180, and the light chain comprises the amino acid sequence of SEQ ID NO:181.

16. A pharmaceutical composition comprising the conjugate according to any one of claims 1-12, or the antibody according to any one of claims 14-15, and pharmaceutically acceptable carrier.

17. Use of the conjugate according to any one of claims 1-12, antibody according to any one of claims 14-15, or pharmaceutical composition according to claim 16 for the manufacture of a medicament for treating cancer.

18. The use according to claim 17, wherein the cancer is selected from the group consisting of head and neck squamous cell carcinoma (HNSCC), non-small-cell lung carcinoma (NSCLC), renal cell carcinoma (RCC), gastric cancer, hepatocellular carcinoma (HCC), esophageal cancer, cervical cancer, cervical squamous cell carcinoma, Merkle cell carcinoma, endometrial cancer, ovarian cancer, pancreatic cancer, melanoma, cutaneous melanoma, sarcoma, colorectal cancer, breast cancer, small cell lung cancer (SCLC), cutaneous squamous cell carcinoma, and urothelial carcinoma.

19. The conjugate according to any one of claims 1-12, antibody according to any one of claims 14-15 or pharmaceutical composition according to claim 16 for use in therapy.