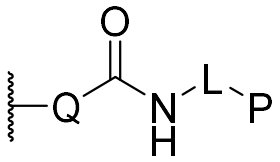
## ~~BRIEF~~ SUMMARY

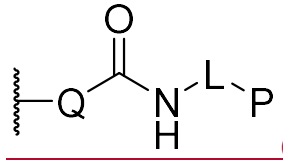
**[0009]** In one ~~aspect~~example, provided herein is a conjugate comprising an antibody or antigen-binding fragment thereof and one or more immunomodulating oligonucleotides (P), wherein each immunomodulating oligonucleotide is linked via an amide bond to a glutamine residue (Q) of the antibody or 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 ~~embodiment~~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 ~~embodiment~~examples, the glutamine residue is part of the antibody (*e.g.*, part of the Fc region, such as residue Q295). In some ~~embodiment~~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 ~~embodiment~~examples, 1-4 immunomodulating oligonucleotides are conjugated to the antibody. Exemplary linkers (L) are described herein. In some ~~embodiment~~examples, the linker comprises a polyethylene glycol moiety.

**[0009a]** In one aspect, 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):

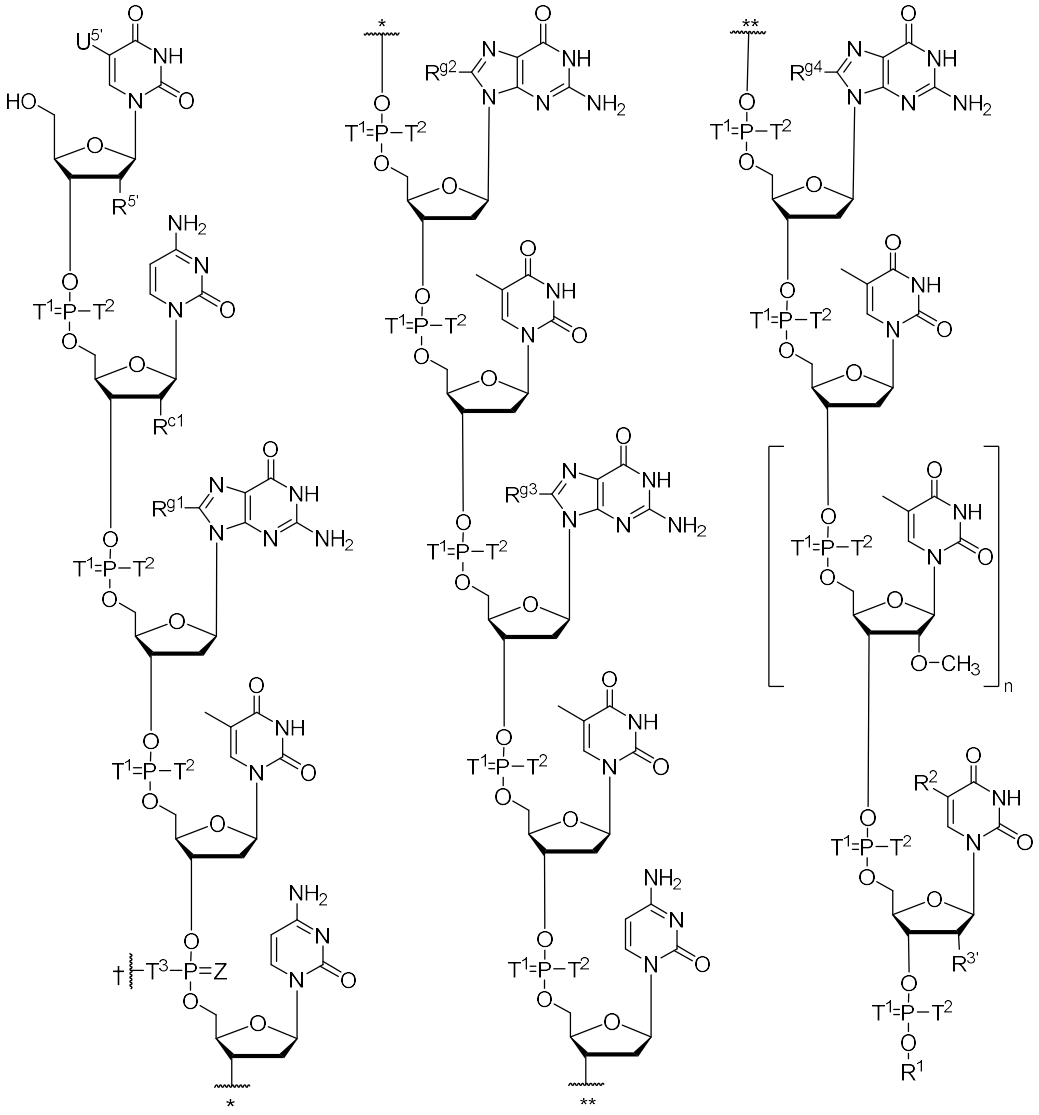


(A);

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



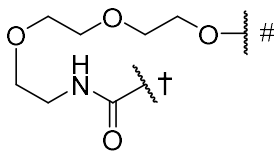
,

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;

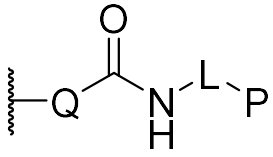
$R^{3'}$ is methoxy;

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

$R^2$ is -H or methyl; and

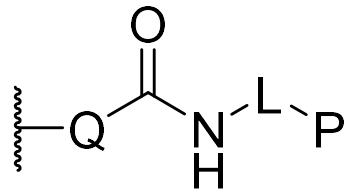
n is an integer from 0 to 2.

**[0010]** In one ~~aspect~~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 aspect, 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)

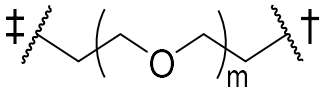



(A),

wherein:

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

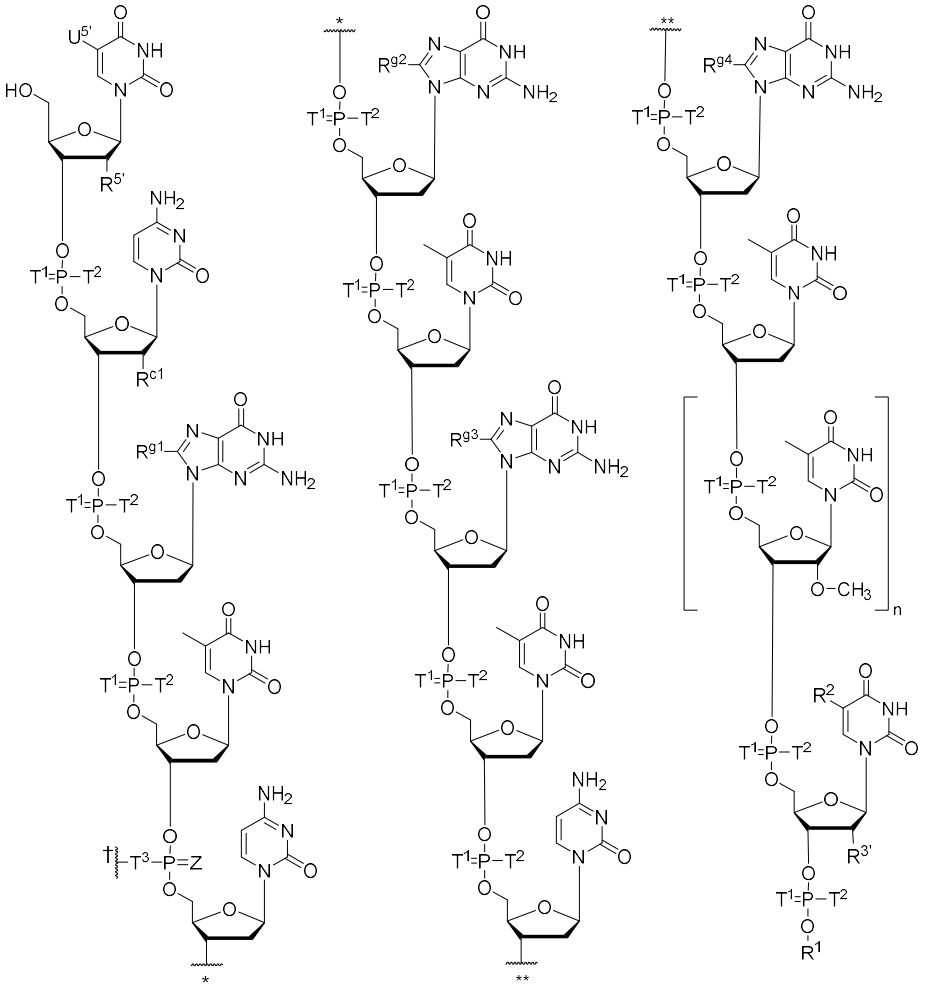
each Q independently comprises a Q-tag peptide sequence RPQGF (SEQ ID NO:47);

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

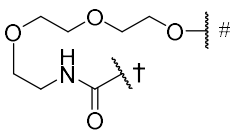


wherein ~~~ * and ~~~ ** indicate the points of attachment within the oligonucleotide, and wherein ~~~ † indicates the point of attachment to the linker L;

each $T^1$ is independently O or S;

each $T^2$ is $S^-$;

provided that each P comprises one or two pairs of geminal $T^1$ and $T^2$ wherein $T^1$ is S and $T^2$ is S, and the one or two pairs of geminal $T^1$ and $T^2$ are between nucleoside residues 2 and 3, between nucleoside residues 3 and 4, between nucleoside residues 5 and 6, between nucleoside residues 6 and 7, between nucleoside residues 7 and 8, between nucleoside residues 8 and 9, between nucleoside residues 9 and 10, or between nucleoside residues 10 and 11;

$T^3$ 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;

$R^{c1}$ 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.

**[0011]** In some ~~embodiment~~examples, the antibody is linked to 2 Q-tag peptides, and one of the Q-tag peptides is linked to an immunomodulating oligonucleotide. In some ~~embodiment~~examples, the antibody is linked to 2 Q-tag peptides, and each of the 2 Q-tag peptides is linked to an immunomodulating oligonucleotide. In some ~~embodiment~~examples, the antibody or fragment thereof is a monoclonal antibody or fragment thereof. In an additional ~~embodiment~~example of the present ~~aspect~~example, the antibody or fragment thereof is a Fab, F(ab')2, Fab'-SH, Fv, scFv, single domain, single heavy chain, or single light chain antibody or antibody fragment. In yet another ~~embodiment~~example ~~of this aspect~~ which may be combined with any of the preceding ~~embodiment~~examples, the antibody or fragment thereof is a humanized, human, or chimeric antibody or fragment thereof. In still further ~~embodiment~~examples ~~of the present aspect~~, the antibody or fragment thereof specifically binds a tumor associated antigen.

**[0012]** In still further ~~embodiment~~examples ~~of the present aspect~~, the antibody or fragment thereof specifically binds human CD22. In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises CDR-H1, CDR-H2, and CDR-H3 sequences from a VH domain sequence selected from the group consisting of:
EVQLVESGGGLVQPGGSLRLSCAASGFAFSIYDMSWVRQAPGKGLEWVAYISSGGGTT
YYPDTVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWGR
GTLVTVSS (SEQ ID NO: 64),
QVQLLESGGGVVQPGGSLRLSCAASGFAFSIYDMNWVRQAPGKGLEWVSAISSGGGTT
YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWG
RGTLVTVSS (SEQ ID NO: 65),
EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYEMNWVRQAPGKGLEWVSYISSSGSTIY
YADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWGR
GTLVTVSS (SEQ ID NO: 66), and
QVQLQESGPGLVKPSDTLSLTCTVSGFAFSIYDMSWIRQPPGKGLEWIAYISSGGGTTYY
NPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARHSGYGTHWGVLFAYWGRGTL
VTVSS (SEQ ID NO:67). In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises CDR-H1, CDR-H2, and CDR-H3 sequences from a VH domain shown in **Table 8**. In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises

a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the sequence of SEQ ID NO:113, a CDR-H2 comprising the sequence of SEQ ID NO:115, and a CDR-H3 comprising the sequence of SEQ ID NO:116; or a CDR-H1 comprising the sequence of SEQ ID NO:114, a CDR-H2 comprising the sequence of SEQ ID NO:189, and a CDR-H3 comprising the sequence of SEQ ID NO:116. In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the sequence of SEQ ID NO:113, a CDR-H2 comprising the sequence of SEQ ID NO:115, and a CDR-H3 comprising the sequence of SEQ ID NO:116, and the VL domain comprises a CDR-L1 comprising the sequence of SEQ ID NO:117, a CDR-L2 comprising the sequence of SEQ ID NO:119, and a CDR-L3 comprising the sequence of SEQ ID NO:120. In yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, and wherein the VH domain comprises an amino acid sequence selected from the group consisting of EVQLVESGGGLVQPGGSLRLSCAASGFAFSIYDMSWVRQAPGKGLEWVAYISSGGGTT YYPDTVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWGR GTLVTVSS (SEQ ID NO: 64), QVQLLESGGGVVQPGGSLRLSCAASGFAFSIYDMNWVRQAPGKGLEWVSAISSGGGTT YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWG RGTLVTVSS (SEQ ID NO: 65), EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYEMNWVRQAPGKGLEWVSYISSSGSTIY YADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWGR GTLVTVSS (SEQ ID NO: 66), and QVQLQESGPGLVKPSDTLSLTCTVSGFAFSIYDMSWIRQPPGKGLEWIAYISSGGGTTYY NPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARHSGYGTHWGVLFAYWGRGTL VTVSS (SEQ ID NO: 67). In yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the sequence of SEQ ID NO:65, and the VL domain comprises the sequence of SEQ ID NO:87. In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VL domain comprises CDR-L1, CDR-L2, and CDR-L3 sequences from a VL domain

sequence selected from the group consisting of:
DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS
RFSGSGSGTDFTLTISSLQPEDFATYFCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 68),
DIQMTQSPSSVSASVGDRVTITCRASQDIHGYLAWYQQKPGKAPKLLIYYTSSLQSGVPS
RFSGSGSGTDFTLTISSLQPEDFATYYCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 69),
DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSR
FSGSGSGTDFTLTISSLQPEDFATYYCQQGNTLPWTFGQGTKLEIK (SEQ ID NO:7 0),
EIVLTQSPATLSLSPGERATLSCRASQDIHGYLNWYQQKPGQAPRLLIYYTSILHSGIPAR
FSGSGPGTDFTLTISSLEPEDFAVYYCQQGNTLPWTFGGGTKLEIK (SEQ ID NO: 71), and
DIVMTQTPLSLSVTPGQPASISCRASQDIHGYLNWYQQKPGQSPQLLIYYTSILHSGVPDR
FSGSGSGTDFTLKISRVEAEDVGVYFCQQGNTLPWTFGGGTKLEIK (SEQ ID NO: 72). In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VL domain comprises CDR-L1, CDR-L2, and CDR-L3 sequences from a VL domain sequence selected from the group consisting of SEQ ID Nos: 68-91. In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VL domain comprises CDR-L1, CDR-L2, and CDR-L3 sequences from a VL domain shown in **Table 8**. In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VL domain comprises a CDR-L1 comprising the sequence of SEQ ID NO:117, a CDR-L2 comprising the sequence of SEQ ID NO:119, and a CDR-L3 comprising the sequence of SEQ ID NO:120; or a CDR-L1 comprising the sequence of SEQ ID NO:118, a CDR-L2 comprising the sequence of SEQ ID NO:177, and a CDR-L3 comprising the sequence of SEQ ID NO:120. In still further ~~embodiment~~examples ~~of the present aspect~~, the VL domain further comprises an amino acid substitution at residue N92. In certain ~~embodiment~~examples wherein the VL domain comprises an amino acid substitution at residue N92, the amino acid substitution at residue N92 is selected from the group consisting of N92A, N92L and N92S. In still further ~~embodiment~~examples ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VL domain an amino acid sequence selected from the group consisting of
DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPSRFS
GSGSGTDFTLTISSLQPEDFATYFCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 68),

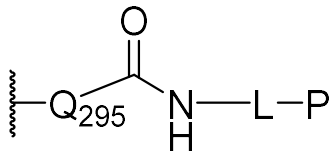
DIQMTQSPSSVSASVGDRVTITCRASQDIHGYLAWYQQKPGKAPKLLIYYTSSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 69), DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSR FSGSGSGTDFTLTISSLQPEDFATYYCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 70), EIVLTQSPATLSLSPGERATLSCRASQDIHGYLNWYQQKPGQAPRLLIYYTSILHSGIPAR FSGSGPGTDFTLTISSLEPEDFAVYYCQQGNTLPWTFGGGTKLEIK (SEQ ID NO: 71), and DIVMTQTPLSLSVTPGQPASISCRASQDIHGYLNWYQQKPGQSPQLLIYYTSILHSGVPDR FSGSGSGTDFTLKISRVEAEDVGVYFCQQGNTLPWTFGGGTKLEIK (SEQ ID NO: 72). In still further ~~embodiment~~examples ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence QVQLLESGGGVVQPGGSLRLSCAASGFAFSIYDMNWVRQAPGKGLEWVSAISSGGGTT YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWG RGTLVTVSS (SEQ ID NO: 65), and wherein the VL domain comprises an amino acid sequence selected from the group consisting of DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 68), DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQGATLPWTFGQGTKLEIK (SEQ ID NO: 73), DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQGLTLPWTFGQGTKLEIK (SEQ ID NO: 82), and DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQGSTLPWTFGQGTKLEIK (SEQ ID NO: 87).

**[0013]** In still further ~~embodiment~~examples, the antibody or fragment thereof specifically binds human Her2. In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises CDR-H1, CDR-H2, and CDR-H3 sequences from the VH domain sequence EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYA DSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ ID NO:168) and/or wherein the VL domain comprises CDR-L1, CDR-L2, and

CDR-L3 sequences from the VL domain sequence DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVP SRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:169). In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the sequence EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYT RYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGT LVTVSS (SEQ ID NO:168) and/or wherein the VL domain comprises the sequence DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVP SRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:169). In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises CDR-H1, CDR-H2, and CDR-H3 sequences from the VH domain sequence EVQLVESGGGLVQPGGSLRLSCAASGFTFTDYTMDWVRQAPGKGLEWVADVNPNSGGSIY NQRFKGRFTLSVDRSKNTLYLQMNSLRAEDTAVYYCARNLGPSFYFDYWGQGTLVTVSS (SEQ ID NO:170) and/or wherein the VL domain comprises CDR-L1, CDR-L2, and CDR-L3 sequences from the VL domain sequence DIQMTQSPSSLSASVGDRVTITCKASQDVSIGVAWYQQKPGKAPKLLIYSASYRYTGVPSRFS GSGSGTDFTLTISSLQPEDFATYYCQQYYIYPYTFGQGTKVEIK (SEQ ID NO:171). In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the sequence EVQLVESGGGLVQPGGSLRLSCAASGFTFTDYTMDWVRQAPGKGLEWVADVNPNSGGSIY NQRFKGRFTLSVDRSKNTLYLQMNSLRAEDTAVYYCARNLGPSFYFDYWGQGTLVTVSS (SEQ ID NO:170) and/or wherein the VL domain comprises the sequence DIQMTQSPSSLSASVGDRVTITCKASQDVSIGVAWYQQKPGKAPKLLIYSASYRYTGVPSRFS GSGSGTDFTLTISSLQPEDFATYYCQQYYIYPYTFGQGTKVEIK (SEQ ID NO:171). In some ~~embodiment~~examples, the anti-Her2 antibody is trastuzumab or pertuzumab

**[0014]** In still yet another ~~embodiment~~examples ~~of the present aspect~~ that can be combined with any of the preceding ~~aspect~~examples, the antibody comprises an Fc region. In certain ~~embodiment~~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 ~~embodiment~~examples, the Fc region is a wild-type human IgG1, IgG2, or IgG4 Fc region. In some ~~embodiment~~examples, the Fc region is a human Fc region comprising one or more amino acid substitutions that reduce one or more effector functions, as compared with the effector function(s) of a human Fc region that lacks the amino acid substitution(s). In still further ~~embodiment~~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 still yet another ~~embodiment~~example, the Fc region further comprises an N297A substitution, amino acid position numbering according to EU index. In some ~~embodiment~~examples, the antibody comprises an antibody heavy chain constant domain comprising an amino acid sequence selected from the group consisting of SEQ ID Nos:92-107 and 178. In certain ~~embodiment~~examples wherein the Fc region comprises an N297A substitution, the conjugate further comprises an immunomodulating oligonucleotide P attached to the Q295 residue of the Fc region as shown in the following formula

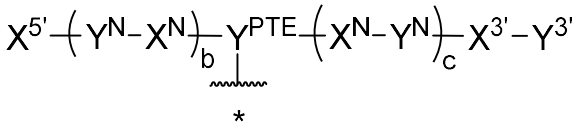



, wherein L is a linker moiety connected to Q295 via an amide bond. In yet other ~~embodiment~~examples, the Fc region further comprises a D265A substitution, amino acid position numbering according to EU index. In some ~~embodiment~~examples, the conjugate binds to human CD22 expressed on the surface of a B cell. In some ~~embodiment~~examples, the conjugate induces activation of TLR9.

**[0015]** In some ~~embodiment~~examples ~~of the present aspect~~, the antibody comprises a human lambda light chain. In other ~~embodiment~~examples ~~of the present aspect~~, the antibody comprises a human kappa light chain. In some ~~embodiment~~examples, the antibody comprises an antibody light chain constant domain comprising an amino acid sequence selected from the group consisting of SEQ ID Nos:108-110. In still further ~~embodiment~~examples which may be combined with any preceding ~~embodiment~~examples ~~of the present aspect~~, at least one Q-tag is attached to the heavy chain of the antibody. In certain ~~embodiment~~examples, at least one Q-tag is fused to the C-terminus of the heavy

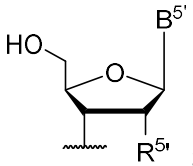
chain of the antibody. In other ~~embodiment~~examples, at least one Q-tag is attached to the light chain of the antibody. In still yet other ~~embodiment~~examples, 1 or 2 Q-tags is/are linked to the antibody or antigen-binding fragment. In still further ~~embodiment~~examples, the conjugate has a DAR of 1. In still further ~~embodiment~~examples, the conjugate has a DAR of 2.

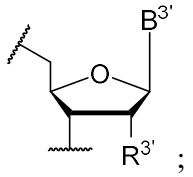
**[0016]** In still further ~~embodiment~~examples ~~of the present aspect~~, each immunomodulating oligonucleotide P is independently

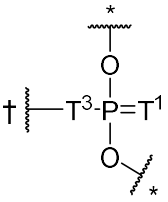


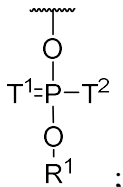
,

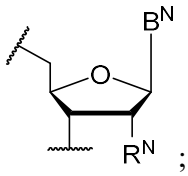
wherein
b and c are each independently an integer from 1 to 25; with the proviso that the sum of b and c is at least 5;
〰 * indicates the point of attachment of the immunomodulating oligonucleotide P to the rest of the conjugate;

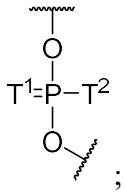
$X^{5'}$ is a 5' terminal nucleoside having the structure  ;

$X^{3'}$ is a 3' terminal nucleoside having the structure  ;

$Y^{PTE}$ is an internucleoside phosphotriester having the structure  , wherein * indicates the points of attachment to the rest of the oligonucleotide and 〰 † indicates the point of attachment to the linker L, or, if L is absent, 〰 † indicates the point of attachment to the Q tag peptide Q at the glutamine residue via an amide bond;

$Y^{3'}$ is a terminal phosphotriester having the structure  ;

each $X^N$ is independently a nucleoside having the structure ;

each $Y^N$ is independently an internucleoside linker having the structure ;

wherein each $B^N$ is independently a modified or unmodified nucleobase;

each $R^N$ is independently -H or -O-$C_{1-4}$-alkyl, wherein the $C_{1-4}$-alkyl of the -O-$C_{1-4}$-alkyl is further optionally substituted by -O-$C_1$-$C_4$-alkyl;

$B^{5'}$ and $B^{3'}$ are independently a modified or unmodified nucleobase;

$R^{5'}$ and $R^{3'}$ are independently -H or -O-$C_1$-$C_4$-alkyl, wherein the $C_{1-4}$-alkyl of the -O-$C_{1-4}$-alkyl is further optionally substituted by -O-$C_1$-$C_4$-alkyl;

each $T_1$ is independently O or S;

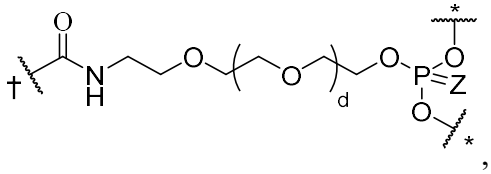
each $T_2$ is independently $O^-$ or $S^-$; and

$T_3$ is a group comprising an oligoethylene glycol moiety; and

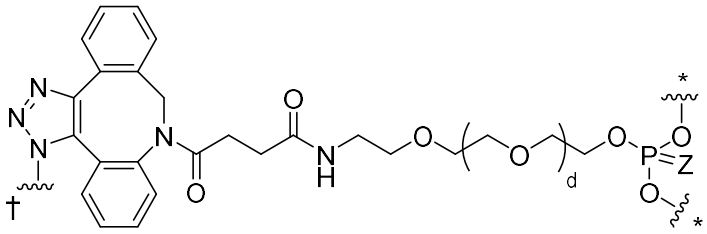
$R^1$ is $C_{1-4}$-alkylene-hydroxy.

**[0017]** In certain ~~embodiment~~examples~~ of the present aspect~~, b is 3. In additional ~~embodiment~~examples~~ of the present aspect~~, (i) P comprises at least one modified nucleoside $X^N$; (ii) P has at least one modified internucleoside linker $Y^N$, wherein at least one of $T^1$ or $T^2$ is S; or (iii) both (i) and (ii). In some ~~embodiment~~examples, P has at least one phosphorodithioate or phosphorothioate internucleoside linker. In certain ~~embodiment~~examples, P comprises 0, 1, 2 or 3 phosphorodithioate internucleoside linkers. In still further ~~embodiment~~examples, P comprises a modified nucleoside selected from the group consisting of 2'-O-alkyl nucleoside, 2'-O-alkoxyalkyl nucleoside, 2'-deoxynucleoside and ribonucleoside. In certain ~~embodiment~~examples, the modified nucleoside is selected from the group consisting of 5-bromo-2'-O-methyluridine, 5-bromo-2'-deoxyuridine, 2'-O-methyluridine, 2'-deoxyuridine, 2'-O-methylthymidine, 2'-O-methylcytidine, 2'-O-(2-methoxyethyl)thymidine and 8-oxo-7,8-dihydro-2'-deoxyguanosine. In yet other ~~embodiment~~examples, $Y^{3'}$ or the $Y^N$ at the 3' position of $X^{5'}$ comprises an unsubstituted or substituted phosphorothioate.

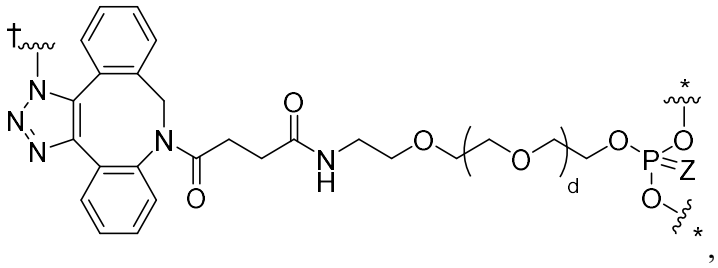
**[0018]** In yet other ~~embodiment~~examples~~ of the present aspect~~, $Y^{PTE}$ is:



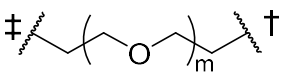
wherein Z is O or S; d is an integer from 0 to 95; the two ~~* on the right side of the structure indicate the points of attachment to the adjacent nucleosides $X^N$ in the oligonucleotide P, and the ~~† on the left side of the structure indicates the point of attachment to the linker L. In other ~~embodiment~~examples, $Y^{PTE}$ is:



or



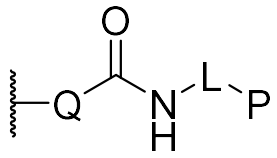
wherein Z is O or S; d is an integer from 0 to 95; the two ~~* on the right side of the structure indicate the points of attachment to the adjacent nucleosides $X^N$ in the oligonucleotide P, and the one † on the left side of the structure indicates the point of attachment to the linker L. In certain ~~embodiment~~examples, Z is S. In still further ~~embodiment~~examples, d is an integer from 1 to 25. In additional ~~embodiment~~examples which may be combined with any of the preceding ~~embodiment~~examples, the linker L comprises a polyethylene glycol moiety. In yet further ~~embodiment~~examples, the linker L is



, wherein m is an integer ranging from about 0 to about 50, and wherein ~~† indicates the point of attachment to $Y^{PTE}$, and ~~‡ indicates the point of attachment to the rest of the conjugate. In still further ~~embodiment~~examples, P comprises one or more CpG sites. In still another ~~embodiment~~example, P comprises at least 3 CpG sites. In yet other ~~embodiment~~examples, each P independently comprises an oligonucleotide sequence selected from the group consisting of the oligonucleotides of ***Table 9*** and ***Table 10***.

**[0019]** In some ~~embodiment~~examples, the conjugate comprises one or more, two or more, three or more, four or more, five or more, or ten or more Q-tag peptides. In some ~~embodiment~~examples, the conjugate comprises two Q-tag peptides. In some ~~embodiment~~examples, the conjugate comprises one or more, two or more, three or more, four or more, five or more, or ten or more immunomodulating oligonucleotides. In some ~~embodiment~~examples, the conjugate comprises one immunomodulating oligonucleotide. In certain ~~embodiment~~examples, the antibody is linked to 2 Q-tag peptides, and wherein one of the Q-tag peptides is linked to an immunomodulating oligonucleotide. In some ~~embodiment~~examples, 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 an immunomodulating oligonucleotide (P) via an amide bond with the glutamine residue of the Q-tag peptide and linker (L), *e.g.*, as shown in **FIG. 16**.

**[0020]** In yet another ~~aspect~~example, the present disclosure provides 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 at least one glutamine residue, 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 is independently a Q-tag peptide sequence having at least one glutamine residue;

each L is independently a bond or a linker moiety connected to Q via an amide bond with the glutamine residue; and

each P is independently an immunomodulating oligonucleotide of having the structure

$R^{5'}$ 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;

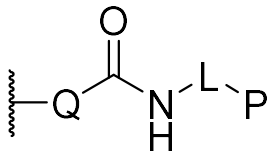
$R^{1}$ is $-(CH_2)_3$-OH;

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

n is an integer from 0 to 2.

In still further ~~embodiment~~examples ~~of the present aspect~~, the antibody or fragment thereof specifically binds a tumor associated antigen.

**[0021]** In yet another ~~aspect~~example, the present disclosure provides 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 at least one glutamine residue, 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 is independently a Q-tag peptide sequence having at least one glutamine residue;

each L is independently a bond or a linker moiety connected to Q via an amide bond with the glutamine residue; and

each P is independently an immunomodulating oligonucleotide of having the structure

$R^{c1}$ is -H or methoxy;

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

$R^{3'}$ is methoxy;

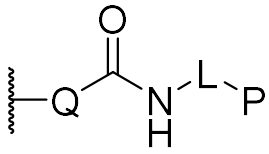
$R^1$ is $-(CH_2)_3$-OH;

$R^2$ is -H or methyl; and

n is an integer from 0 to 2.

In still further ~~embodiment~~examples ~~of the present aspect~~, the antibody or fragment thereof specifically binds a tumor associated antigen.

**[0022]** In another ~~aspect~~example, provided herein is 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)

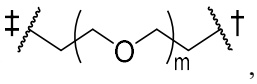


(A),

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;

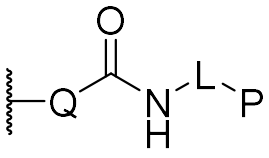
$R^1$ is $-(CH_2)_3$-OH;

$R^2$ is -H or methyl; and

n is an integer from 0 to 2,

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

**[0023]** In yet another ~~aspect~~example, the present disclosure provides 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)

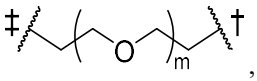


(A),

wherein:

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

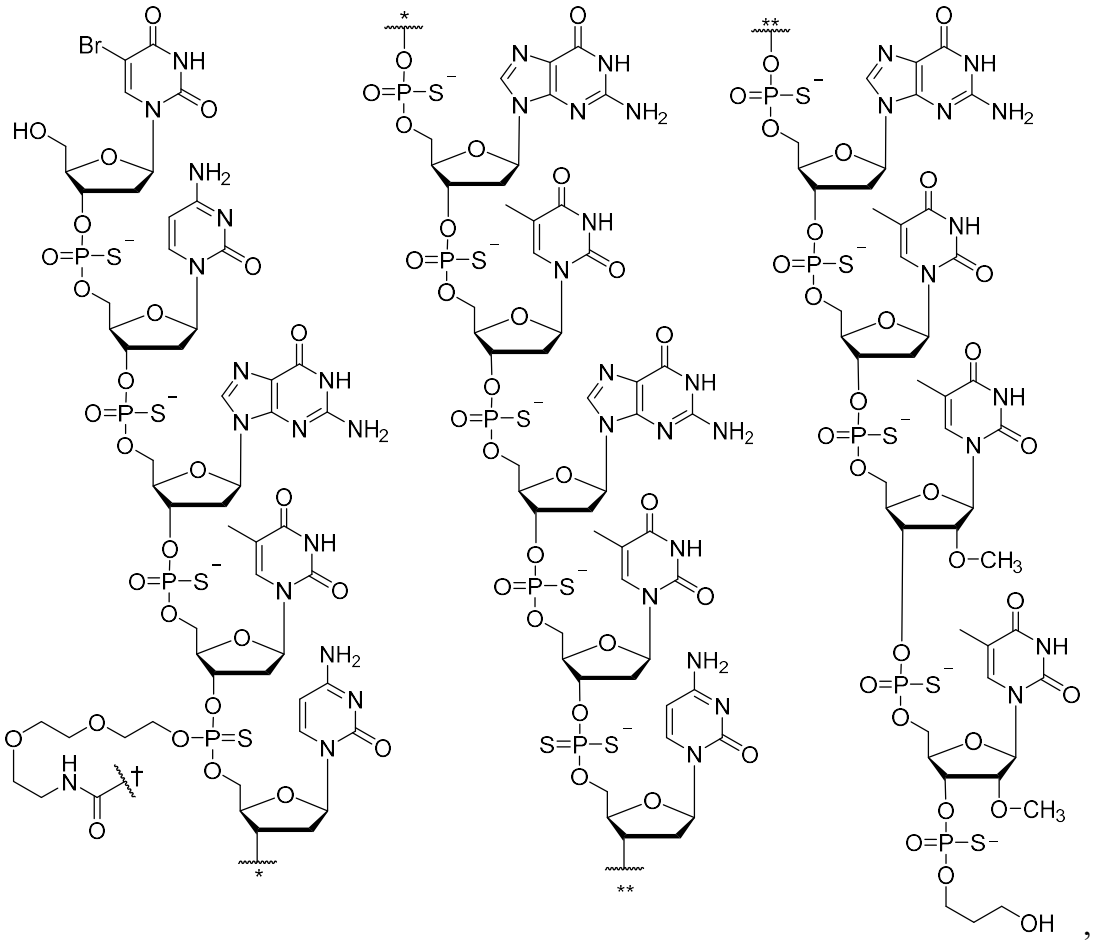
each Q independently comprises a Q-tag peptide sequence RPQGF (SEQ ID NO:47);

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



wherein ~~~ * and ~~~ ** indicate the points of attachment within the oligonucleotide; wherein Ab is an antibody or antigen-binding fragment thereof that binds a tumor associated antigen.

**[0024]** In some ~~embodiment~~examples, the tumor associated antigen is expressed by a cancer cell. In some ~~embodiment~~examples, the tumor associated antigen is expressed by a cancer-associated stromal cell. In some ~~embodiment~~examples, the tumor associated antigen is selected from the group consisting of CD19, CD20, CD22, CD25, CD30, CD33, CD38, CD40, CD44, CD45R (B220), CD49, CD52, CD56, CD70, CD74, CD79a, CD79b, CD93, CD123, CD138, CD163, CD205, CD206, CD274, CD303, and CD304, folate receptor alpha, folate receptor beta, mesothelin, PSMA, Her-2, EGFR, CLDN18.2, 5T4, CD47, nectin 4, transferrin receptor, integrin, cripto, EphA2, AGS-5, AGS-16, CanAg, EpCAM, IL4 receptor, IL2 receptor, Lewis Y, GPNMB, DLL3, GCC, GPA33, tissue factor (TF), and Trop2. In some ~~embodiment~~examples, the cancer is breast cancer, colorectal cancer, lung cancer, head and neck cancer, melanoma, lymphoma, or leukemia.

**[0025]** In some ~~embodiment~~examples of the present ~~aspect~~example, the antibody or fragment thereof is a monoclonal antibody or fragment thereof. In some ~~embodiment~~examples, the antibody is linked to 2 Q-tag peptides, and wherein one of the Q-tag peptides is linked to an immunomodulating oligonucleotide. In additional ~~embodiment~~examples ~~of the present aspect~~, the antibody or fragment thereof is a Fab, F(ab')2, Fab'-SH, Fv, scFv, single domain, single heavy chain, or single light chain antibody or antibody fragment. In yet other ~~embodiment~~examples ~~of the present aspect~~, the antibody or fragment thereof is a humanized, human, or chimeric antibody or fragment thereof.

**[0026]** In still further ~~embodiment~~examples, the antibody or fragment thereof specifically binds human CD22. In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises CDR-H1, CDR-H2, and CDR-H3 sequences from a VH domain sequence selected from the group consisting of:
EVQLVESGGGLVQPGGSLRLSCAASGFAFSIYDMSWVRQAPGKGLEWVAYISSGGGTT
YYPDTVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWGR
GTLVTVSS (SEQ ID NO: 64),
QVQLLESGGGVVQPGGSLRLSCAASGFAFSIYDMNWVRQAPGKGLEWVSAISSGGGTT
YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWG
RGTLVTVSS (SEQ ID NO: 65),
EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYEMNWVRQAPGKGLEWVSYISSSGSTIY
YADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWGR
GTLVTVSS (SEQ ID NO: 66), and
QVQLQESGPGLVKPSDTLSLTCTVSGFAFSIYDMSWIRQPPGKGLEWIAYISSGGGTTYY
NPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARHSGYGTHWGVLFAYWGRGTL
VTVSS (SEQ ID NO:67). In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises CDR-H1, CDR-H2, and CDR-H3 sequences from a VH domain shown in **Table 8**. In yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, and wherein the VH domain comprises an amino acid sequence selected from the group consisting of
EVQLVESGGGLVQPGGSLRLSCAASGFAFSIYDMSWVRQAPGKGLEWVAYISSGGGTT
YYPDTVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWGR

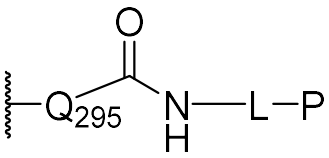
GTLVTVSS (SEQ ID NO: 64),
QVQLLESGGGVVQPGGSLRLSCAASGFAFSIYDMNWVRQAPGKGLEWVSAISSGGGTT
YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWG
RGTLVTVSS (SEQ ID NO: 65),
EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYEMNWVRQAPGKGLEWVSYISSSGSTIY
YADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWGR
GTLVTVSS (SEQ ID NO: 66), and
QVQLQESGPGLVKPSDTLSLTCTVSGFAFSIYDMSWIRQPPGKGLEWIAYISSGGGTTYY
NPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARHSGYGTHWGVLFAYWGRGTL
VTVSS (SEQ ID NO: 67). In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VL domain comprises CDR-L1, CDR-L2, and CDR-L3 sequences from a VL domain sequence selected from the group consisting of:
DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPSRFS
GSGSGTDFTLTISSLQPEDFATYFCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 68),
DIQMTQSPSSVSASVGDRVTITCRASQDIHGYLAWYQQKPGKAPKLLIYYTSSLQSGVPSRFS
GSGSGTDFTLTISSLQPEDFATYYCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 69),
DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFS
GSGSGTDFTLTISSLQPEDFATYYCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 70),
EIVLTQSPATLSLSPGERATLSCRASQDIHGYLNWYQQKPGQAPRLLIYYTSILHSGIPARFSG
SGPGTDFTLTISSLEPEDFAVYYCQQGNTLPWTFGGGTKLEIK (SEQ ID NO: 71), and
DIVMTQTPLSLSVTPGQPASISCRASQDIHGYLNWYQQKPGQSPQLLIYYTSILHSGVPDRFS
GSGSGTDFTLKISRVEAEDVGVYFCQQGNTLPWTFGGGTKLEIK (SEQ ID NO: 72). In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VL domain comprises CDR-L1, CDR-L2, and CDR-L3 sequences from a VL domain shown in **Table 8**. In still further ~~embodiment~~examples ~~of the present aspect~~, the VL domain further comprises an amino acid substitution at residue N92. In certain ~~embodiment~~examples wherein the VL domain comprises an amino acid substitution at residue N92, the amino acid substitution at residue N92 is selected from the group consisting of N92A, N92L and N92S. In still further ~~embodiment~~examples ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain,

wherein the VL domain an amino acid sequence selected from the group consisting of DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 68), DIQMTQSPSSVSASVGDRVTITCRASQDIHGYLAWYQQKPGKAPKLLIYYTSSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 69), DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSR FSGSGSGTDFTLTISSLQPEDFATYYCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 70), EIVLTQSPATLSLSPGERATLSCRASQDIHGYLNWYQQKPGQAPRLLIYYTSILHSGIPAR FSGSGPGTDFTLTISSLEPEDFAVYYCQQGNTLPWTFGGGTKLEIK (SEQ ID NO: 71), DIVMTQTPLSLSVTPGQPASISCRASQDIHGYLNWYQQKPGQSPQLLIYYTSILHSGVPDR FSGSGSGTDFTLKISRVEAEDVGVYFCQQGNTLPWTFGGGTKLEIK (SEQ ID NO: 72), DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQGATLPWTFGQGTKLEIK (SEQ ID NO: 73), and DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQGLTLPWTFGQGTKLEIK (SEQ ID NO: 82). In still further ~~embodiment~~examples ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence QVQLLESGGGVVQPGGSLRLSCAASGFAFSIYDMNWVRQAPGKGLEWVSAISSGGGTT YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWG RGTLVTVSS (SEQ ID NO: 65), and wherein the VL domain comprises an amino acid sequence selected from the group consisting of DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQGNTLPWTFGQGTKLEIK (SEQ ID NO: 68), DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQGATLPWTFGQGTKLEIK (SEQ ID NO: 73), DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQGLTLPWTFGQGTKLEIK (SEQ ID NO: 82), and

DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQGSTLPWTFGQGTKLEIK (SEQ ID NO: 87).

**[0027]** In still further ~~embodiment~~examples, the antibody or fragment thereof specifically binds human Her2. In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises CDR-H1, CDR-H2, and CDR-H3 sequences from the VH domain sequence EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYA DSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ ID NO:168) and/or wherein the VL domain comprises CDR-L1, CDR-L2, and CDR-L3 sequences from the VL domain sequence DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRF SGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:169). In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the sequence EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYA DSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS (SEQ ID NO:168) and/or wherein the VL domain comprises the sequence DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRF SGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:169). In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises CDR-H1, CDR-H2, and CDR-H3 sequences from the VH domain sequence EVQLVESGGGLVQPGGSLRLSCAASGFTFTDYTMDWVRQAPGKGLEWVADVNPNSGGSIY NQRFKGRFTLSVDRSKNTLYLQMNSLRAEDTAVYYCARNLGPSFYFDYWGQGTLVTVSS (SEQ ID NO:170) and/or wherein the VL domain comprises CDR-L1, CDR-L2, and CDR-L3 sequences from the VL domain sequence DIQMTQSPSSLSASVGDRVTITCKASQDVSIGVAWYQQKPGKAPKLLIYSASYRYTGVPSRFS GSGSGTDFTLTISSLQPEDFATYYCQQYYIYPYTFGQGTKVEIK (SEQ ID NO:171). In still yet another ~~embodiment~~example ~~of the present aspect~~, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the

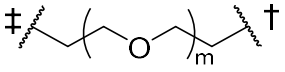
sequence EVQLVESGGGLVQPGGSLRLSCAASGFTFTDYTMDWVRQAPGKGLEWVADVNPNSGG SIYNQRFKGRFTLSVDRSKNTLYLQMNSLRAEDTAVYYCARNLGPSFYFDYWGQGTLV TVSS (SEQ ID NO:170) and/or wherein the VL domain comprises the sequence DIQMTQSPSSLSASVGDRVTITCKASQDVSIGVAWYQQKPGKAPKLLIYSASYRYTGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQYYIYPYTFGQGTKVEIK (SEQ ID NO:171). In some ~~embodiment~~examples, the anti-Her2 antibody is trastuzumab or pertuzumab.

**[0028]** In still yet another ~~embodiment~~examples ~~of the present aspect~~ that can be combined with any of the preceding ~~aspect~~examples, the antibody comprises an Fc region. In certain ~~embodiment~~examples, wherein 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 ~~embodiment~~examples, the Fc region is a wild-type human IgG1, IgG2, or IgG4 Fc region. In some ~~embodiment~~examples, the Fc region is a human Fc region comprising one or more amino acid substitutions that reduce one or more effector functions, as compared with the effector function(s) of a human Fc region that lacks the amino acid substitution(s). In still further ~~embodiment~~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 still yet another ~~embodiment~~example, the Fc region further comprises an N297A substitution, amino acid position numbering according to EU index. In certain ~~embodiment~~examples the Fc region further comprises an N297A substitution. In some ~~embodiment~~examples, the antibody comprises an antibody heavy chain constant domain comprising an amino acid sequence selected from the group consisting of SEQ ID Nos:92-107 and 178. In some ~~embodiment~~examples, the conjugate further comprises an immunomodulating oligonucleotide P attached to the Q295 residue of the Fc region as shown in the following formula 

, wherein L is a linker moiety connected to Q295 via an amide bond. In yet other ~~embodiment~~examples, the Fc region further comprises a D265A substitution, amino acid position numbering according to EU index. In

some ~~embodiment~~examples, the conjugate binds to human CD22 expressed on the surface of a B cell. In some ~~embodiment~~examples, the conjugate induces activation of TLR9.

**[0029]** In some ~~embodiment~~examples ~~of the present aspect~~, the antibody comprises a human lambda light chain. In other ~~embodiment~~examples ~~of the present aspect~~, the antibody comprises a human kappa light chain. In some ~~embodiment~~examples, the antibody comprises an antibody light chain constant domain comprising an amino acid sequence selected from the group consisting of SEQ ID Nos:108-110. In still further ~~embodiment~~examples which may be combined with any preceding ~~embodiment~~examples ~~of the present aspect~~, at least one Q-tag is attached to the heavy chain of the antibody. In certain ~~embodiment~~examples, at least one Q-tag is fused to the C-terminus of the heavy chain of the antibody. In other ~~embodiment~~examples, at least one Q-tag is attached to the light chain of the antibody. In certain ~~embodiment~~examples, the antibody comprises two heavy chains and two light chains, and at least one Q-tag is fused to the C-terminus of each heavy chain.

**[0030]** In still further ~~embodiment~~examples, at least one Q-tag is within the Fc domain. In additional ~~embodiment~~examples, each Q-tag independently comprises a peptide sequence having between 5 and 15 amino acid residues. In certain ~~embodiment~~examples ~~of the present aspect~~, the Q-tag is naturally occurring. In still further ~~embodiment~~examples, the peptide sequence of each Q-tag is independently selected from the group consisting of SEQ ID NOs: 39-55. In certain ~~embodiment~~examples, wherein the Q-tag comprises the peptide sequence RPQGF (SEQ ID NO:47). In still yet other ~~embodiment~~examples, 1 or 2 Q-tags is/are linked to the antibody or antigen-binding fragment. In yet other ~~embodiment~~examples, the conjugate has a DAR of 1. In yet other ~~embodiment~~examples, the conjugate has a DAR of 2. In additional ~~embodiment~~examples which may be combined with any of the preceding ~~embodiment~~examples, the linker L comprises a polyethylene glycol moiety. In yet further ~~embodiment~~examples, the linker L is 

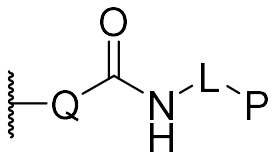
, wherein m is an integer ranging from about 0 to about 50, and wherein ~~wavy~~ † indicates the point of attachment to $Y^{PTE}$, and ~~wavy~~ ‡ indicates the point of attachment to the rest of the conjugate.

**[0031]** In some ~~embodiment~~examples, Z is S. In still further ~~embodiment~~examples, the oligonucleotide comprises at least one pair of geminal $T^1$ and $T^2$ wherein $T^1$ is S and $T^2$ is $S^-$. In certain ~~embodiment~~examples, the oligonucleotide comprises at least two pairs of geminal $T^1$ and $T^2$ wherein $T^1$ is S and $T^2$ is $S^-$. In still further ~~embodiment~~examples, which may be combined with any of the preceding ~~embodiment~~examples, $R^{5'}$ is H. In other ~~embodiment~~examples, $R^{5'}$ is methoxy. In some ~~embodiment~~examples, $R^{c1}$ is H. In

yet other ~~embodiment~~examples, $R^{c1}$ is methoxy. In still further ~~embodiment~~examples, $R^2$ is methyl. In still other ~~embodiment~~examples, $R^2$ is H. In additional ~~embodiment~~examples, m is an integer from 20 to 25. In some ~~embodiment~~examples of the present ~~aspect~~example, each P independently comprises an oligonucleotide sequence selected from the group consisting of the oligonucleotides of ***Table 10***.

**[0032]** In some ~~embodiment~~examples, the conjugate comprises one or more, two or more, three or more, four or more, five or more, or ten or more Q-tag peptides. In some ~~embodiment~~examples, the conjugate comprises two Q-tag peptides. In some ~~embodiment~~examples, the conjugate comprises one or more, two or more, three or more, four or more, five or more, or ten or more immunomodulating oligonucleotides. In some ~~embodiment~~examples, the conjugate comprises one immunomodulating oligonucleotide. In other ~~embodiment~~examples, the antibody is linked to 2 Q-tag peptides, and wherein one of the Q-tag peptides is linked to an immunomodulating oligonucleotide. In some ~~embodiment~~examples, 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 at least one of the Q-tag peptides is linked to an immunomodulating oligonucleotide (P) via an amide bond with the glutamine residue of the Q-tag peptide and linker (L), *e.g.*, as shown in **FIGS. 16A-16D**. In certain ~~embodiment~~examples, the two Q-tag peptides comprise the peptide sequence RPQGF (SEQ ID NO:47). In other ~~embodiment~~examples, the two Q-tag peptides comprise a Q295 residue exposed by N297A mutation (of the Fc region). In still other ~~embodiment~~examples, the conjugate has a DAR of 1 or 2.

**[0033]** In yet another ~~aspect~~example, provided herein is 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:

wherein Ab comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises CDR-H1, CDR-H2, and CDR-H3 sequences from a VH domain sequence

QVQLLESGGGVVQPGGSLRLSCAASGFAFSIYDMNWVRQAPGKGLEWVSAISSGGGTT YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSGYGTHWGVLFAYWG RGTLVTVSS (SEQ ID NO: 65) or a VH domain shown in **Table 8**;

wherein the VL domain comprises CDR-L1, CDR-L2, and CDR-L3 sequences from a VL domain sequence:
DIQMTQSPSSLSASVGDRVTITCRASQDIHGYLNWYQQKPGKAPKLLIYYTSILHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQGNTLPWTFGQGTKLEIK (SEQ ID NO:68) or a VL domain shown in **Table 8**.

**[0034]** In some ~~embodiment~~examples ~~of the present aspect~~, the VL domain further comprises an amino acid substitution N92A. In other ~~embodiment~~examples, the VL domain further comprises an amino acid substitution N92L. In still other ~~embodiment~~examples, the VL domain further comprises an amino acid substitution N92S.

**[0035]** In other ~~embodiment~~examples ~~of the present aspect~~, each Q tag is independently selected from the group consisting of RPQGF (SEQ ID NO:47), RPQGFPP (SEQ ID NO:48), and RPQGFGPP (SEQ ID NO:49). In certain ~~embodiment~~examples, each Q tag is RPQGFGPP (SEQ ID NO:49). In some ~~embodiment~~examples, 1 or 2 Q-tags are linked to the antibody or antigen-binding fragment. In other ~~embodiment~~examples, the Q-tag is linked to the C-terminus of the heavy chain of the antibody. In still further ~~embodiment~~examples, the antibody comprises a human IgG1 Fc region comprising L234A, L235A, and/or G237A substitutions, amino acid position numbering according to EU index. In yet other ~~embodiment~~examples, m is an integer from about 20 to about 25. In certain ~~embodiment~~examples, m is 24. In yet further ~~embodiment~~examples, the conjugate has a DAR of 1. In yet further ~~embodiment~~examples, the conjugate has a DAR of 2. In still other ~~embodiment~~examples, the conjugate binds to human CD22 expressed on the surface of a B cell.

**[0036]** In another ~~aspect~~example, provided herein is 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

**[0037]** In some ~~embodiment~~examples ~~of the present aspect~~, the VL domain further comprises an amino acid substitution N92A. In other ~~embodiment~~examples, the VL domain further comprises an amino acid substitution N92L. In still other ~~embodiment~~examples, the VL domain further comprises an amino acid substitution N92S.

**[0038]** In other ~~embodiment~~examples ~~of the present aspect~~, each Q tag is independently selected from the group consisting of RPQGF (SEQ ID NO:47), RPQGFPP (SEQ ID NO:48), and RPQGFGPP. In certain ~~embodiment~~examples, each Q tag is RPQGFGPP (SEQ ID NO:49). In some ~~embodiment~~examples, 1 or 2 Q-tags are linked to the antibody or antigen-binding fragment. In other ~~embodiment~~examples, the Q-tag is linked to the C-terminus of the heavy chain of the antibody. In still further ~~embodiment~~examples, the antibody comprises a human IgG1 Fc region comprising L234A, L235A, and/or G237A substitutions, amino acid position numbering according to EU index. In yet other ~~embodiment~~examples, m is an integer from about 20 to about 25. In certain ~~embodiment~~examples, m is 24. In yet further ~~embodiment~~examples, the conjugate has a DAR of 1. In yet further ~~embodiment~~examples, the conjugate has a DAR of 2. In still other ~~embodiment~~examples, the conjugate binds to human CD22 expressed on the surface of a B cell.

**[0039]** In still yet another ~~aspect~~example, the present disclosure also provides an immunomodulating oligonucleotide of Formula (C):

$R^{c1}$ is -H or methoxy;

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

$R^{3'}$ is methoxy;

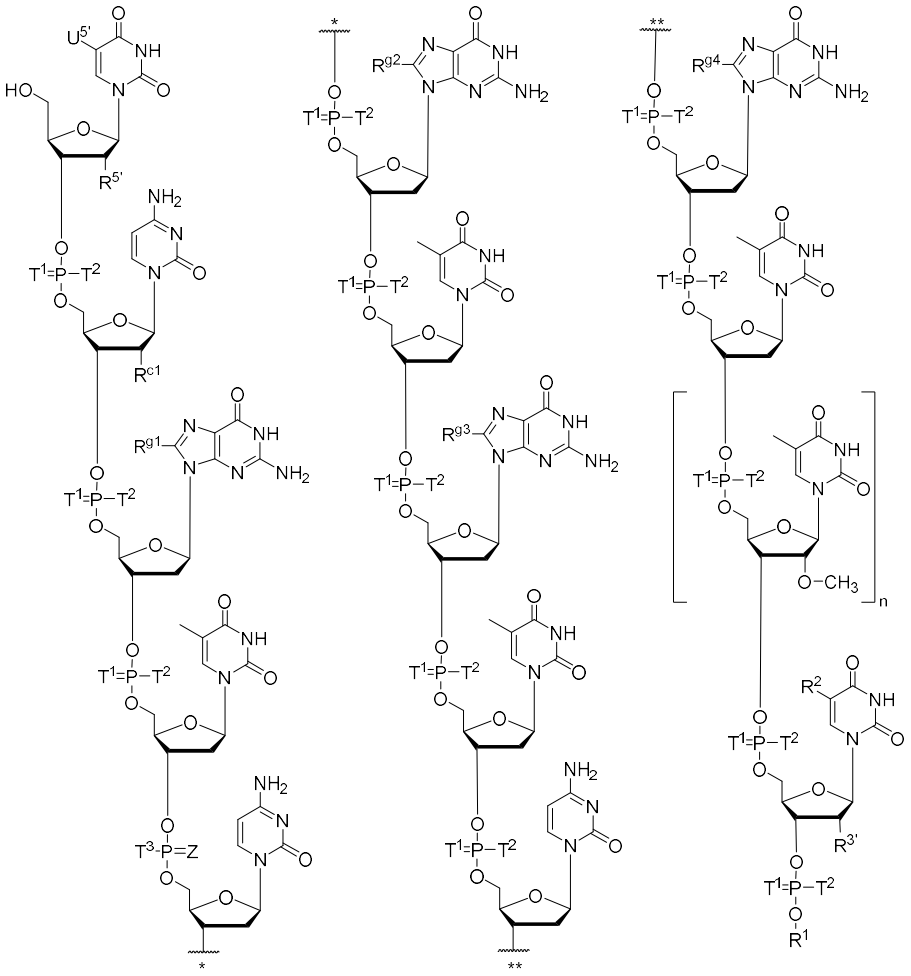
$R^1$ is $-(CH_2)_3$-OH;

$R^2$ is -H or methyl; and

n is an integer from 0 to 2,

or a pharmaceutically acceptable salt thereof.

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



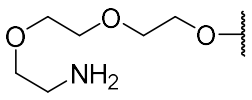
(C),

wherein

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

each $T^1$ is independently O or S;

each $T^2$ is $S^-$;



$T^3$ is a group , wherein m is an integer from 0 to 50 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;

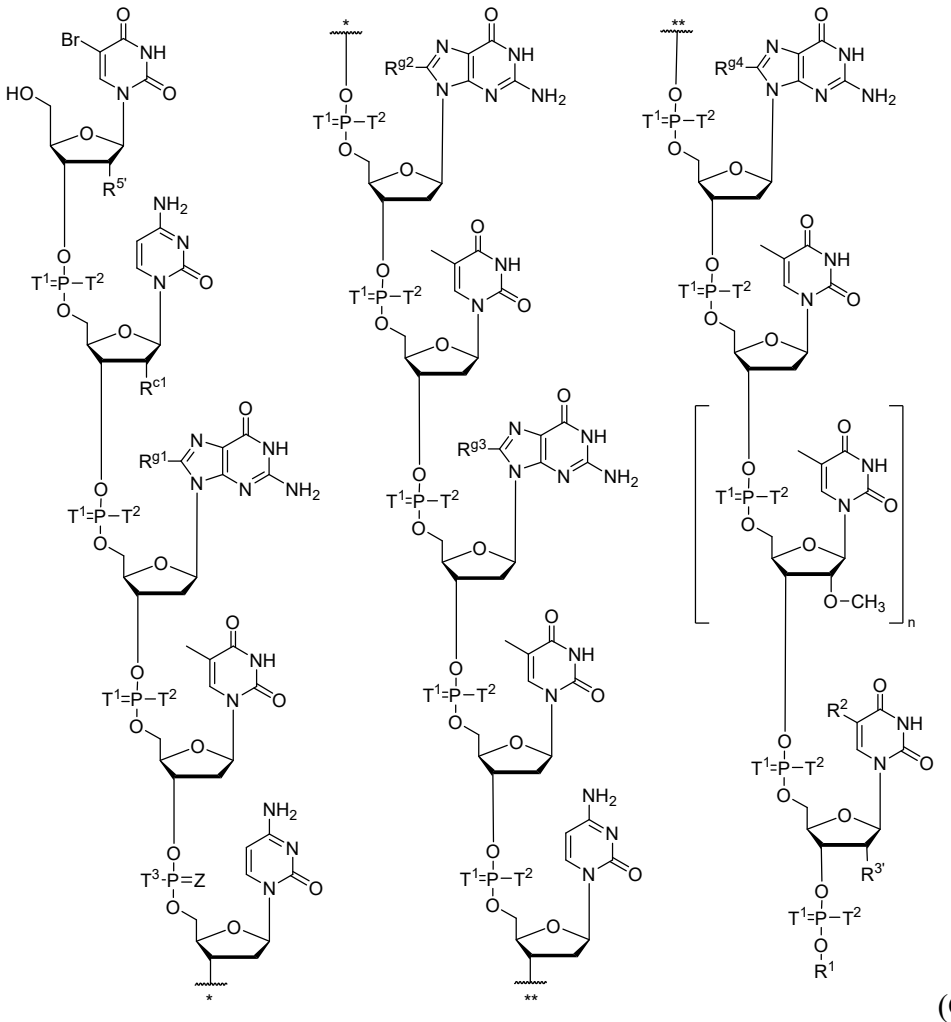
$R^1$ is $-(CH_2)_3$-OH;

$R^2$ is -H or methyl; and

n is an integer from 0 to 2,

or a pharmaceutically acceptable salt thereof.

**[0040]** In some ~~embodiment~~examples, the present disclosure also provides an immunomodulating oligonucleotide of Formula (C'):



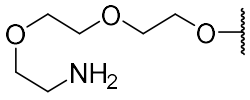
(C')

wherein

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

each $T^1$ is independently O or S;

each $T^2$ is $S^-$;

$T^3$ is a group , wherein m is an integer from 0 to 50 and wherein 〰 indicates the point of attachment to the rest of the oligonucleotide;

Z is O or S;

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

$R^{c1}$ is -H or methoxy;

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

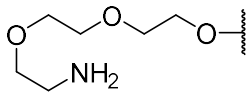
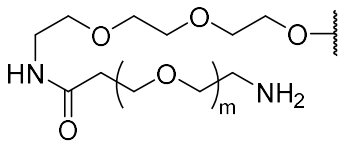
$R^{3'}$ is methoxy;

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

$R^2$ is -H or methyl; and

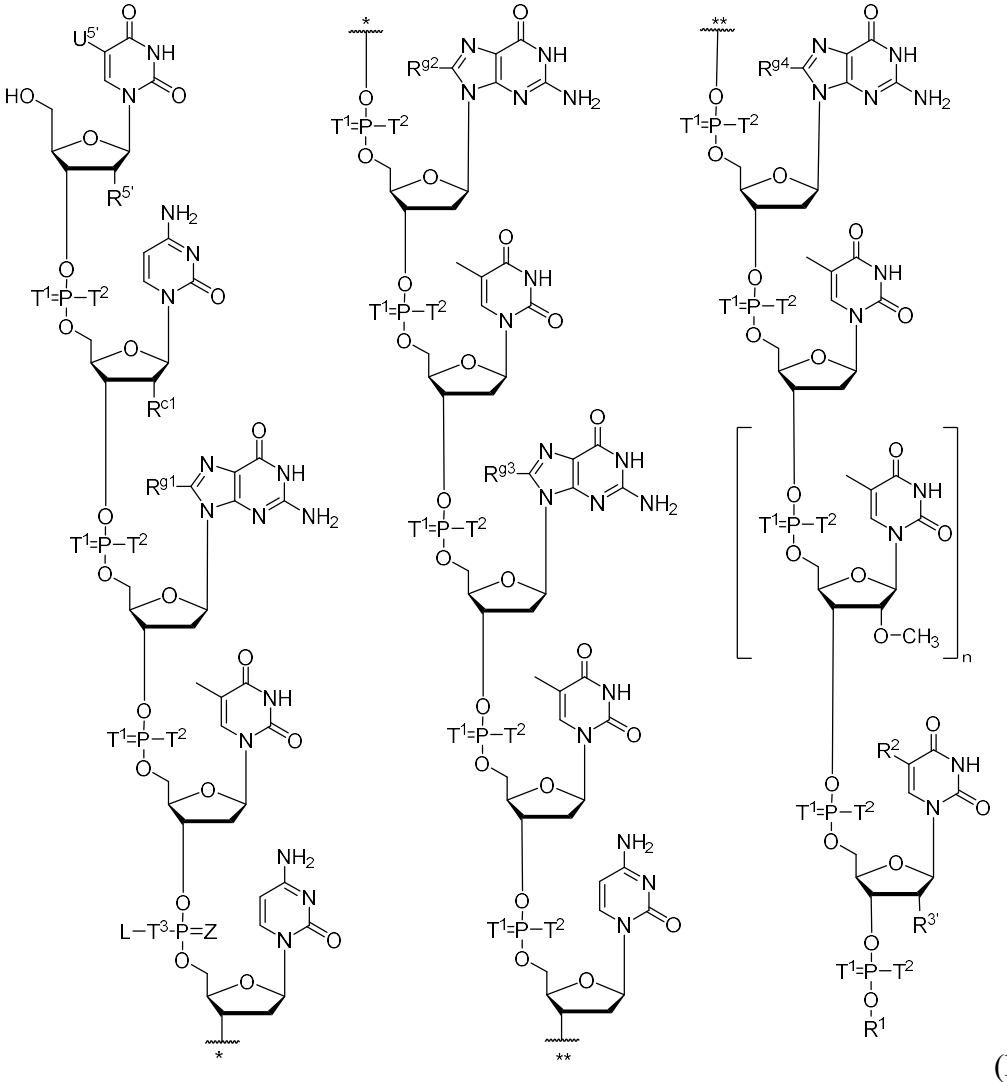
n is an integer from 0 to 2.

**[0041]** In some ~~embodiment~~examples ~~of the present aspect~~, Z is S. In additional ~~embodiment~~examples, the oligonucleotide comprises at least one pair of geminal $T^1$ and $T^2$ wherein $T^1$ is S and $T^2$ is $S^-$. In certain ~~embodiment~~examples, the oligonucleotide comprises at least two pairs of geminal $T^1$ and $T^2$ wherein $T^1$ is S and $T^2$ is $S^-$.

**[0042]** In some ~~embodiment~~examples, $R^{5'}$ is H. In other ~~embodiment~~examples, $R^{5'}$ is methoxy. In some ~~embodiment~~examples, $R^{c1}$ is H. In yet other ~~embodiment~~examples, $R^{c1}$ is methoxy. In still further ~~embodiment~~examples, $R^2$ is methyl. In still other ~~embodiment~~examples, $R^2$ is H. In yet other additional ~~embodiment~~examples, which may be combined with any of the preceding ~~embodiment~~examples, $T^3$ is . In still other ~~embodiment~~examples, $T^3$ is . In certain ~~embodiment~~examples, m is an integer from 20 to 25.

**[0043]** In still further ~~embodiment~~examples ~~of the present aspect~~, the oligonucleotide is selected from the group consisting of the oligonucleotides of ***Table 10.***

**[0044]** In still yet another ~~aspect~~example, provided herein is an immunomodulating oligonucleotide of formula (D):



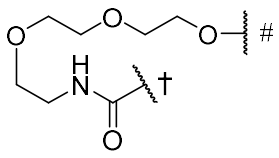
(D),

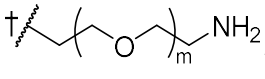
wherein

~~wave~~ * and ~~wave~~ ** indicate the points of attachment within the oligonucleotide;

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;

L is a group  wherein m is an integer from 0 to 50 and wherein 〰 † indicates the point of attachment to the rest of the oligonucleotide via $T^3$;

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;

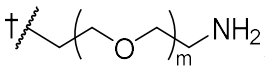
$R^{3'}$ is methoxy;

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

$R^2$ is -H or methyl; and

n is an integer from 0 to 2.

**[0045]** In some ~~embodiment~~examples, provided herein is an immunomodulating oligonucleotide of formula (D'):

L is a group  wherein m is an integer from 0 to 50 and wherein ⁓ † indicates the point of attachment to the rest of the oligonucleotide via $T^3$;

Z is O or S;

$R^{5'}$ 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.

**[0046]** In some ~~embodiment~~examples ~~of the present aspect~~, Z is S. In additional ~~embodiment~~examples, the oligonucleotide comprises at least one pair of geminal $T^1$ and $T^2$ wherein $T^1$ is S and $T^2$ is $S^-$. In certain ~~embodiment~~examples, the oligonucleotide comprises at least two pairs of geminal $T^1$ and $T^2$ wherein $T^1$ is S and $T^2$ is $S^-$.

**[0047]** In some ~~embodiment~~examples, $R^{5'}$ is H. In other ~~embodiment~~examples, $R^{5'}$ is methoxy. In some ~~embodiment~~examples, $R^{c1}$ is H. In yet other ~~embodiment~~examples, $R^{c1}$ is methoxy. In still further ~~embodiment~~examples, $R^2$ is methyl. In still other ~~embodiment~~examples, $R^2$ is H. In certain ~~embodiment~~examples, m is an integer from 20 to 25.

**[0048]** In still further ~~embodiment~~examples ~~of the present aspect~~, the oligonucleotide is selected from the group consisting of the oligonucleotides of ***Table 12.***

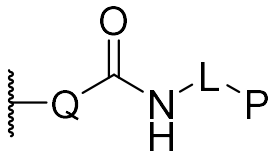
**[0049]** In yet another ~~aspect~~example, provided herein is an immunomodulating oligonucleotide selected from the group consisting of the oligonucleotides of ***Table 10*** and ***Table 12***.

**[0050]** In still yet another ~~aspect~~example, the present disclosure provides 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 the immunomodulatory oligonucleotide is linked to the Q-tag via an amide bond with the glutamine residue, wherein the Q-tag peptide sequence is selected from the group

consisting of SEQ ID NOs: 39-55. In some ~~embodiment~~examples ~~of the present aspect~~, immunomodulatory oligonucleotide has a sequence selected from the group consisting of the oligonucleotides of ***Table 10*** and ***Table 12***. In further ~~embodiment~~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 aspect, 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 ~~aspect~~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):

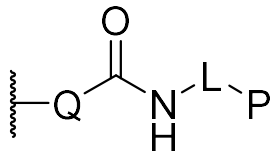


(A),

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

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

**[0053]** In yet another ~~aspect~~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):

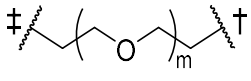


(A),

wherein ~~~ indicates the point of attachment of each Q to the antibody (Ab).

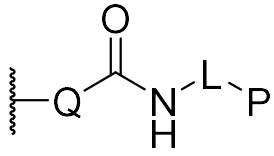
**[0054]** In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-CD22 antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence 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:35. In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-CD22 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 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:94, 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:35. In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-CD22 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 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:94, wherein the two antibody light chains comprise a VL domain comprising the sequence of SEQ ID NO:73 and a constant region comprising the sequence of SEQ ID NO:108, and wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:34. In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-CD22 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 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:73 and a constant region comprising the sequence of SEQ ID NO:108, and wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:34. In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-CD22 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 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:73 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 yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-CD22 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 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 ~~embodiment~~examples, the linker comprises the linker moiety 

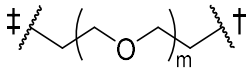
, wherein m is an integer 24, and wherein 〰 † indicates the point of attachment to P, and 〰 ‡ indicates the point of attachment to the rest of the conjugate connected to Q via an amide bond with the glutamine residue.

**[0054a]** In one aspect, 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):



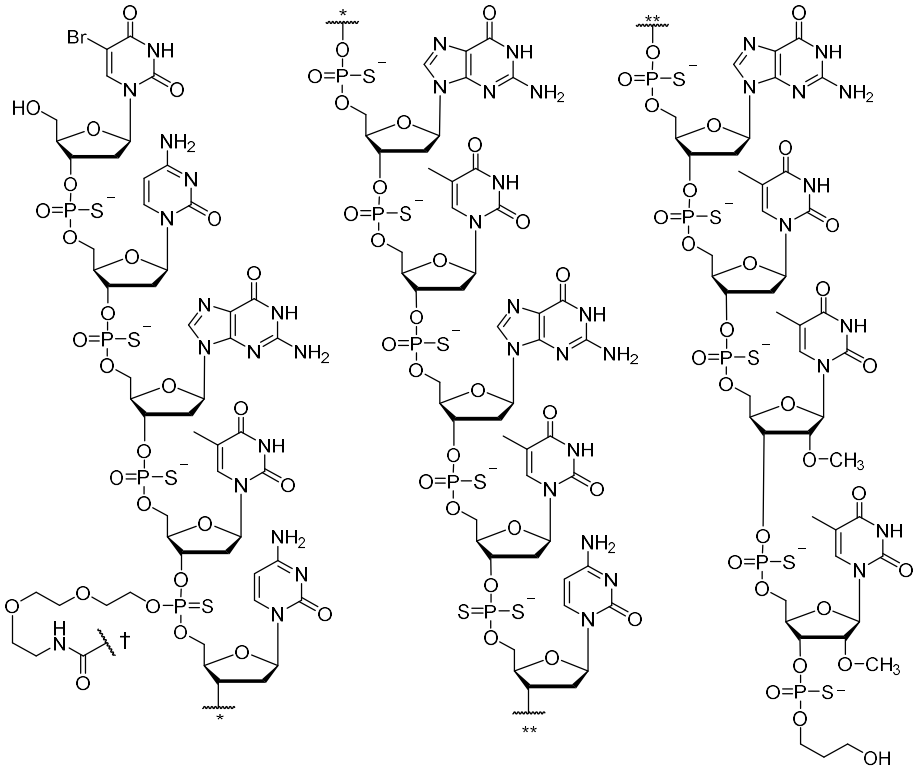
(A),

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

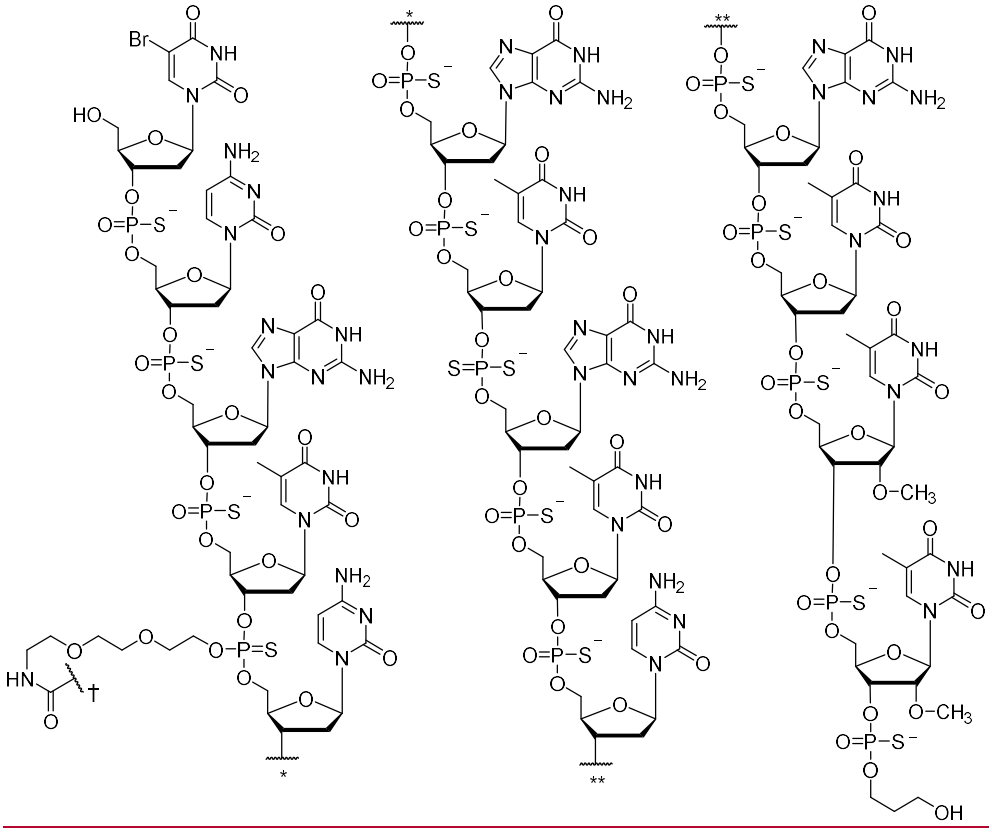


,

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:



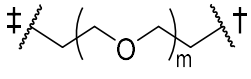
or



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.

**[0055]** In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-Her2 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 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:168 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:169 and a constant region comprising the sequence of SEQ ID NO:108, and wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:35. In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-Her2 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 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

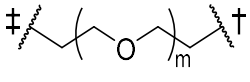
bond with the glutamine residue of the Q-tag peptide and a linker (L), wherein the two antibody heavy chains comprise a VH domain comprising the sequence of SEQ ID NO:168 and a constant region comprising the sequence of SEQ ID NO:104, wherein the two antibody light chains comprise a VL domain comprising the sequence of SEQ ID NO:169 and a constant region comprising the sequence of SEQ ID NO:108, and wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:35. In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-Her2 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 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:168 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:169 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 yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-Her2 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 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:170 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:171 and a constant region comprising the sequence of SEQ ID NO:108, and wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:35. In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-Her2 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 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:170 and a constant region comprising the sequence of SEQ ID NO:104, wherein the two antibody light chains comprise a VL domain comprising the sequence of SEQ ID NO:171 and a constant region comprising the sequence of SEQ ID NO:108, and wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:35. In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-Her2 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 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:170 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:171 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 ~~embodiment~~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.

**[0056]** In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-CD22 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 antibody light chains comprises the amino acid sequence of SEQ ID NO:182; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:179; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:35; and wherein at least 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). In yet another ~~aspect~~example,

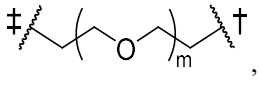
provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:182; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:180; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:35; and wherein at least 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). In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-CD22 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 antibody light chains comprises the amino acid sequence of SEQ ID NO:181; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:180; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:34; and wherein at least 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). In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-CD22 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 antibody light chains comprises the amino acid sequence of SEQ ID NO:181; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:179; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:34; and wherein at least 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). In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-CD22 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 antibody light chains comprises the amino acid sequence of SEQ ID NO:181; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:179; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:163; and wherein at least 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). In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-CD22 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 antibody light chains comprises the amino acid sequence of SEQ ID NO:182; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:179; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:163; and wherein at least 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). In some ~~embodiment~~examples, one of the two Q-tag peptides is linked to the immunomodulating oligonucleotide. In some ~~embodiment~~examples, the conjugate comprises two immunomodulating oligonucleotides, wherein each of the two Q-tag peptides is linked to one of the two immunomodulating oligonucleotides. In some ~~embodiment~~examples, the conjugate has a DAR of 1. In some ~~embodiment~~examples, the conjugate has a DAR of 2. In some ~~embodiment~~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.

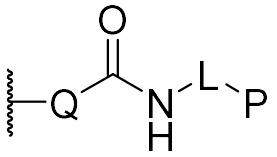
**[0057]** In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-Her2 antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:185; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:184; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:35; and wherein at least 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). In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-Her2 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 antibody light chains comprises the amino acid sequence of SEQ ID NO:185; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:183; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:35; and wherein at least 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). In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-

Her2 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 antibody light chains comprises the amino acid sequence of SEQ ID NO:185; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:184; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:163; and wherein at least 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). In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-Her2 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 antibody light chains comprises the amino acid sequence of SEQ ID NO:188; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:187; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:35; and wherein at least 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). In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-Her2 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 antibody light chains comprises the amino acid sequence of SEQ ID NO:188; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:186; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:35; and wherein at least 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). In yet another ~~aspect~~example, provided herein is a conjugate comprising an anti-Her2 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 antibody light chains comprises the amino acid sequence of SEQ ID NO:188; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:187; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:163; and wherein at least 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). In some ~~embodiment~~examples, one of the two Q-tag peptides is linked to the immunomodulating oligonucleotide. In some ~~embodiment~~examples, the conjugate comprises two

immunomodulating oligonucleotides, wherein each of the two Q-tag peptides is linked to one of the two immunomodulating oligonucleotides. In some ~~embodiment~~examples, the conjugate has a DAR of 1. In some ~~embodiment~~examples, the conjugate has a DAR of 2. In some ~~embodiment~~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.

**[0058]** In yet another ~~aspect~~example, provided herein is a conjugate that comprises an antibody (Ab) and one or more immunomodulating oligonucleotides (P), wherein the antibody is linked to one or more Q-tag peptides (Q) comprising at least one glutamine residue, 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:

wherein ~~~ indicates the point of attachment of Q to the antibody (Ab);

the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides;

each of the Q-tag peptides is linked to the C-terminus of one of the antibody heavy chains;

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;

each Q is independently a Q-tag peptide sequence having at least one glutamine residue;

each L is independently a bond or a linker moiety connected to Q via an amide bond with the glutamine residue; and

each P is independently an immunomodulating oligonucleotide having the structure

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

$R^{c1}$ is -H or methoxy;

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

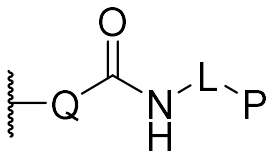
$R^{3'}$ is methoxy;

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

$R^2$ is -H or methyl; and

n is an integer from 0 to 2.

**[0059]** In yet another ~~aspect~~example, provided herein is a conjugate that comprises an antibody (Ab) and one or more immunomodulating oligonucleotides (P), wherein the antibody is linked to one or more Q-tag peptides (Q) comprising at least one glutamine residue, 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:

wherein 〰 indicates the point of attachment of Q to the antibody (Ab);

the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides;

each of the Q-tag peptides is linked to the C-terminus of one of the antibody heavy chains;

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;

each Q is independently a Q-tag peptide sequence having at least one glutamine residue;

each L is independently a bond or a linker moiety 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;

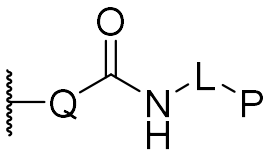
$R^{3'}$ is methoxy;

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

$R^2$ is -H or methyl; and

n is an integer from 0 to 2.

**[0060]** In still another ~~aspect~~example, provided herein is 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)

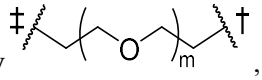


(A),

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

$U^{5'}$ 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,

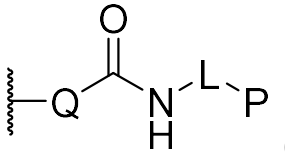
wherein Ab is an antibody or antigen-binding fragment thereof that binds a tumor associated antigen.

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

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

**[0062a]** In one aspect, 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.

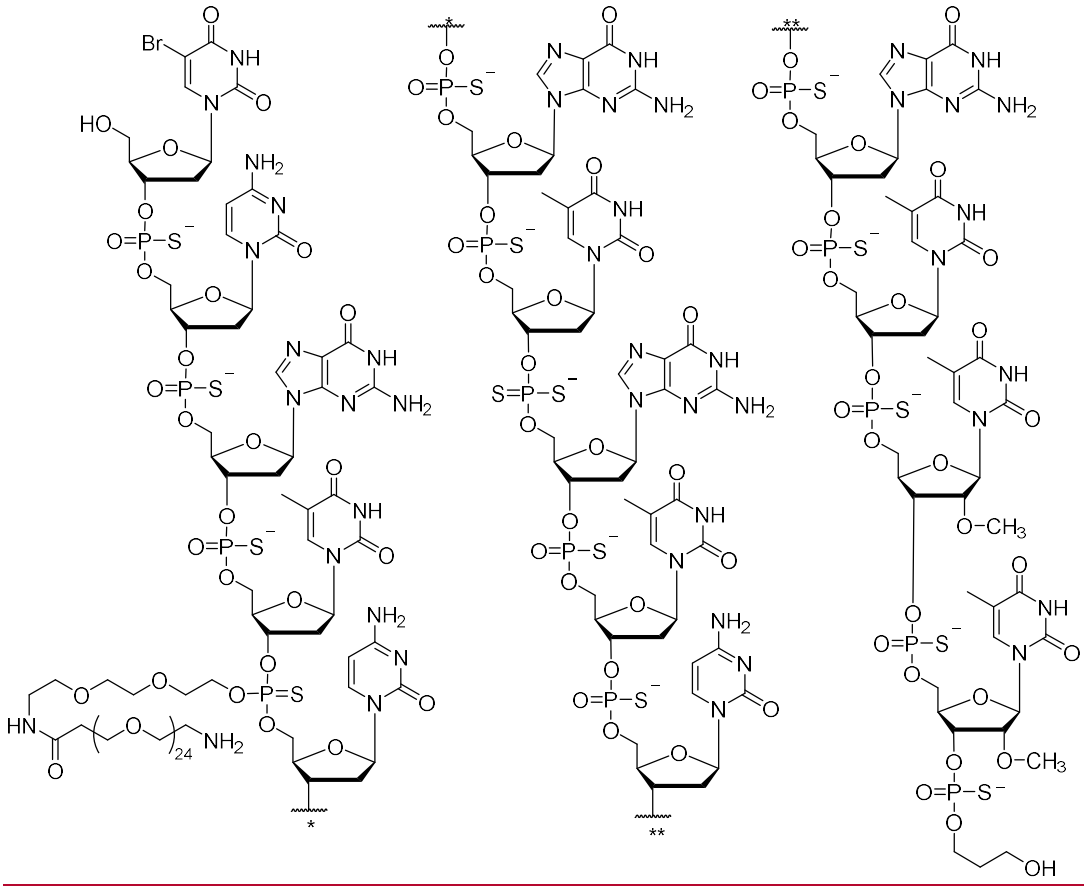
**[0063]** In still further ~~aspect~~example, provided herein are methods for preparing the conjugates as described herein. In one ~~aspect~~example, provided herein is a method for preparing a conjugate that comprises an antibody or antigen-binding fragment thereof (Ab) and one or more immunomodulating 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),



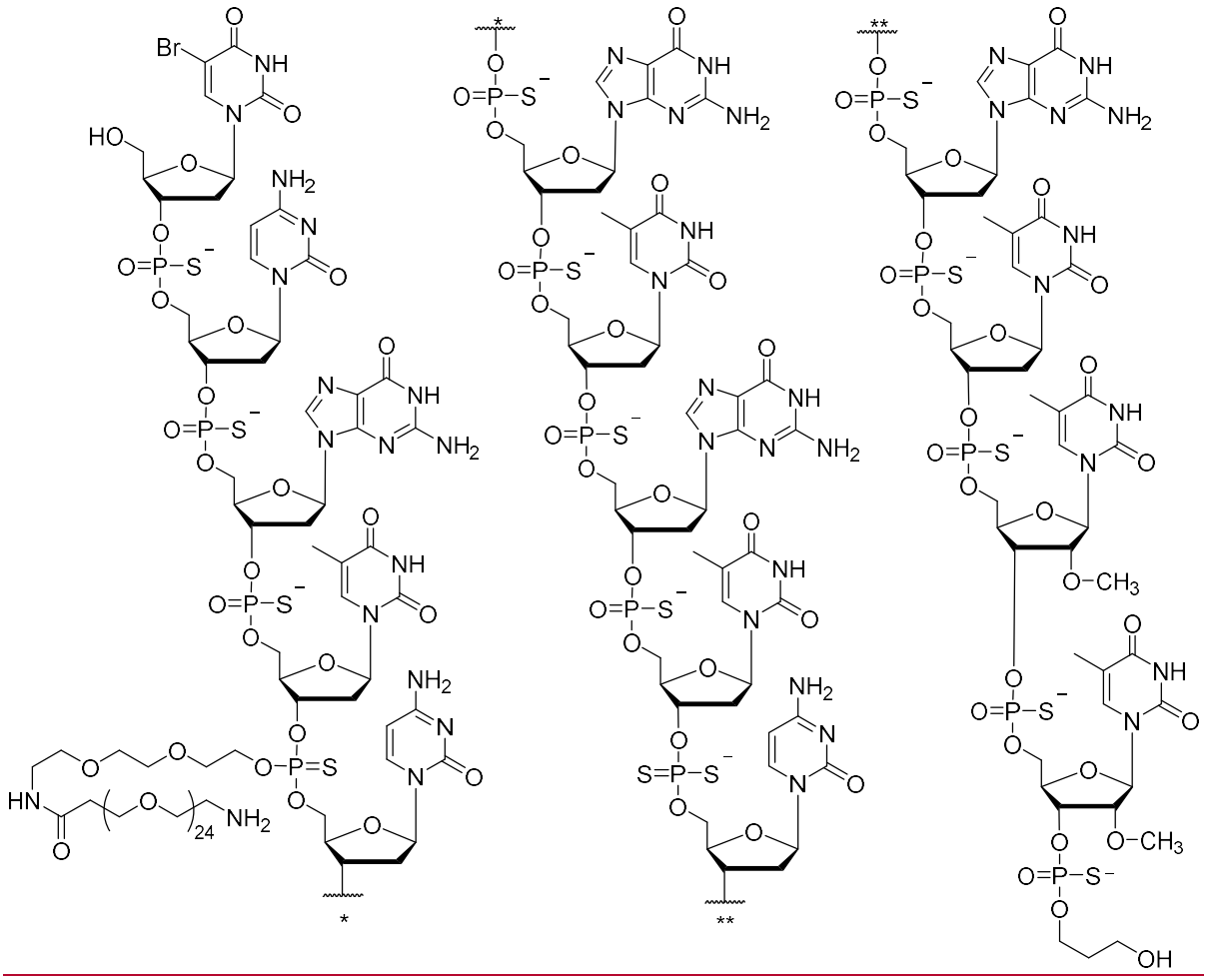
(A),

wherein:

**[0063a]** In one aspect, 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:

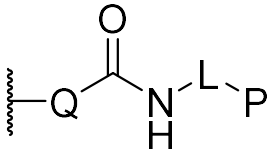


or



or a pharmaceutically acceptable salt thereof, wherein ~~~ * and ~~~ ** indicate the points of attachment within the oligonucleotide.

**[0064]** In another ~~aspect~~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 at least one glutamine residue, 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:

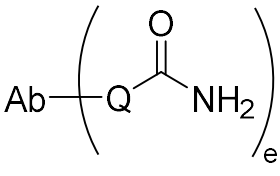
〰 indicates the point of attachment of each Q to the antibody or antigen-binding fragment thereof (Ab);

each Q is independently a Q-tag peptide having at least one glutamine residue;

each L is independently a bond or a linker moiety connected to Q via an amide bond with the glutamine residue; and

each P is independently an immunomodulating oligonucleotide;

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, wherein each immunomodulating oligonucleotide P is independently an oligonucleotide of formula (C) as described herein or an oligonucleotide of formula (D) according to as described herein, in the presence of a transglutaminase. In some ~~embodiment~~examples ~~of the present aspects~~ of methods of preparing conjugates, each immunomodulating oligonucleotide is independently an oligonucleotide of formula (C) or formula (D) is selected from the group consisting of the oligonucleotides of ***Table 10*** and ***Table 12.***

**[0065]** In still other ~~aspect~~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 ~~aspect~~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 ~~embodiment~~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 ~~embodiment~~examples, the antibody comprises an Fc region. In some ~~embodiment~~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 ~~embodiment~~examples, the Fc region is a wild-type human IgG1, IgG2, or IgG4 Fc region. In some ~~embodiment~~examples, the Fc region is a human Fc region comprising one or more amino acid substitutions that reduce binding to C1q. In some ~~embodiment~~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 ~~embodiment~~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 ~~embodiment~~examples, the Fc region further comprises an N297A substitution, amino acid position numbering according to EU index. In some ~~embodiment~~examples, the antibody further comprises an amino acid sequence selected from the group consisting of SEQ ID Nos:92-110.

**[0065a]** In one aspect, 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 ~~aspect~~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 ~~embodiment~~examples, the antibody heavy chain comprises the sequence of SEQ ID NO:179, and the antibody light chain comprises the

sequence of SEQ ID NO:181. In some ~~embodiment~~examples, the antibody heavy chain comprises the sequence of SEQ ID NO:179, and the antibody light chain comprises the sequence of SEQ ID NO:182. In some ~~embodiment~~examples, the antibody heavy chain comprises the sequence of SEQ ID NO:180, and the antibody light chain comprises the sequence of SEQ ID NO:181. In some ~~embodiment~~examples, the antibody heavy chain comprises the sequence of SEQ ID NO:180, and the antibody light chain comprises the sequence of SEQ ID NO:182.

**[0067]** In still other ~~aspect~~examples, provided herein is an antibody that binds to human Her2, 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:183, 184, 186, or 187, and the antibody light chain comprises the sequence of SEQ ID NO:185 or 188. In some ~~embodiment~~examples, the antibody heavy chain comprises the sequence of SEQ ID NO:183, and the antibody light chain comprises the sequence of SEQ ID NO:185. In some ~~embodiment~~examples, the antibody heavy chain comprises the sequence of SEQ ID NO:184, and the antibody light chain comprises the sequence of SEQ ID NO:185. In some ~~embodiment~~examples, the antibody heavy chain comprises the sequence of SEQ ID NO:186, and the antibody light chain comprises the sequence of SEQ ID NO:185. In some ~~embodiment~~examples, the antibody heavy chain comprises the sequence of SEQ ID NO:187, and the antibody light chain comprises the sequence of SEQ ID NO:185. In some ~~embodiment~~examples, the antibody heavy chain comprises the sequence of SEQ ID NO:183, and the antibody light chain comprises the sequence of SEQ ID NO:188. In some ~~embodiment~~examples, the antibody heavy chain comprises the sequence of SEQ ID NO:184, and the antibody light chain comprises the sequence of SEQ ID NO:188. In some ~~embodiment~~examples, the antibody heavy chain comprises the sequence of SEQ ID NO:186, and the antibody light chain comprises the sequence of SEQ ID NO:188. In some ~~embodiment~~examples, the antibody heavy chain comprises the sequence of SEQ ID NO:187, and the antibody light chain comprises the sequence of SEQ ID NO:188.

**[0068]** In still other ~~aspect~~examples, provided herein is a pharmaceutical composition comprising the conjugate or antibody according to any one of the ~~embodiment~~examples herein and a pharmaceutically acceptable carrier. In still other ~~aspect~~example, provided herein is a pharmaceutical composition comprising the immunomodulating oligonucleotide according to any one of the ~~embodiment~~examples herein and a pharmaceutically acceptable carrier. In still other ~~aspect~~example, provided herein are methods for treatment of a disease or disorder. In one ~~aspect~~example, provided herein is a method of treating cancer, comprising administering to an individual an effective amount of the conjugate,

immunomodulating oligonucleotide, antibody, or pharmaceutical composition according to any one of the ~~embodiment~~examples herein. In one ~~aspect~~example, provided herein is a method for treating cancer, comprising administering to an individual an effective amount of: (a) an immune checkpoint inhibitor and (b) the conjugate according to any one of the ~~embodiment~~examples herein, or the pharmaceutical composition according to any one of the ~~embodiment~~examples herein; wherein the cancer is refractory or resistant to the immune checkpoint inhibitor when administered in the absence of the conjugate; and wherein the antibody or antigen-binding fragment thereof binds to human CD22. In some ~~embodiment~~examples, the immune checkpoint inhibitor is a PD-1 inhibitor or a PD-L1 inhibitor. In some ~~embodiment~~examples, the immune checkpoint inhibitor is an anti-PD-1 antibody or an anti-PD-L1 antibody. In some ~~embodiment~~examples, the administration results in reduced growth, size, and/or volume of the cancer. In one ~~aspect~~example, provided herein is a method for treating cancer, comprising administering to an individual an effective amount of the conjugate according to any one of the ~~embodiment~~examples herein, or the pharmaceutical composition according to any one of the ~~embodiment~~examples herein; wherein the administration results in B cell activation in the individual. In one ~~aspect~~example, provided herein is a method for treating cancer, comprising administering to an individual an effective amount of the conjugate according to any one of the ~~embodiment~~examples herein, or the pharmaceutical composition according to any one of the ~~embodiment~~examples herein; 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. In one ~~aspect~~example, provided herein is a method for treating cancer, comprising administering to an individual an effective amount of the conjugate according to any one of the ~~embodiment~~examples herein, or the pharmaceutical composition according to any one of the ~~embodiment~~examples herein; wherein the cancer is selected from the group consisting of acute lymphoblastic leukemia (ALL), hairy cell leukemia, and diffuse large B cell lymphoma (DLBCL). In one ~~aspect~~example, provided herein is a method for treating cancer, comprising administering to an individual an effective amount of the conjugate according to any one of the ~~embodiment~~examples herein, or the pharmaceutical composition according to any one of the ~~embodiment~~examples herein; wherein the cancer is selected from the group consisting of breast cancer,

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

**[0068a]** In one aspect, 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).