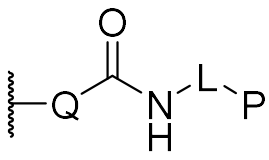
[0008] CpG ODNs may include, for example, oligodeoxynucleotides having poly-G tails with phosphorothioate backbones at 3'- and 5'-termini and a central palindromic sequence including a phosphate backbone and a CpG within its central palindrome sequence, or oligodeoxynucleotides having a fully phosphorothioate backbone, and a sequence at the 5' end for TLR9 activation, or oligodeoxynucleotides having a fully phosphorothioate backbone with a 3'-end sequence enabling formation of a duplex. However, CpG ODNs are often susceptible to degradation in serum and thus pharmacokinetics of CpG ODNs may be one of the limiting factors in their development as therapeutics. Also CpG ODNs often exhibit uneven tissue distribution in vivo, with primary sites of accumulation being in liver, kidney, and spleen. Such distribution can elicit off-target activity and local toxicity associated with PAMPs.

[0009] All references cited herein, including patent applications, patent publications, and scientific literature, are herein incorporated by reference in their entirety, as if each individual reference were specifically and individually indicated to be incorporated by reference.

SUMMARY

[0010] As demonstrated herein, conjugates were found to integrate TLR9 activation with blockade of CD47-SIRP-α interaction of myeloid cells, leading to anti-tumor immune responses engaging both the innate and adaptive immune systems. Without wishing to be bound to theory, it is thought that anti-SIRP-α antibody-CpG oligonucleotide conjugates can have the additional benefit of preferential tumor cell targeting in SIRP-α-expressing cancers.

[0011] In one aspect, provided herein is a conjugate comprising (i) an antibody or antigen-binding fragment thereof that specifically binds an extracellular domain of a human SIRP-α polypeptide and (ii) 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, 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);

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

R^{c1} is -H or methoxy;

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

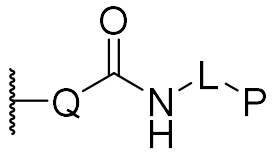
$R^{3'}$ is methoxy;

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

R^2 is -H or methyl; and

n is an integer from 0 to 2.

[0012] In another example, provided herein is a conjugate comprising (i) an antibody or antigen-binding fragment thereof that specifically binds an extracellular domain of a human SIRP-α polypeptide and (ii) one or more immunomodulating oligonucleotides (P); wherein the antibody or antigen-binding fragment is linked to one or more Q-tag peptides (Q); wherein the antibody or antigen-binding fragment thereof (Ab) comprises: (a) a heavy chain variable (VH) domain that comprises a CDR-H1 comprising the amino acid sequence of SNAMS (SEQ ID NO:56), a CDR-H2 comprising the amino acid sequence of GISAGGSDTYYPASVKG (SEQ ID NO:57), and a CDR-H3 comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:58), and (b) a light chain variable (VL) domain that comprises a CDR-L1 comprising the amino acid sequence of SGGSYSSYYYA (SEQ ID NO:59), a CDR-L2 comprising the amino acid sequence of SDDKRPS (SEQ ID NO:60), and a CDR-L3 comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:61); 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)

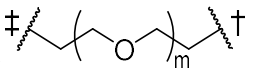


(A),

wherein:

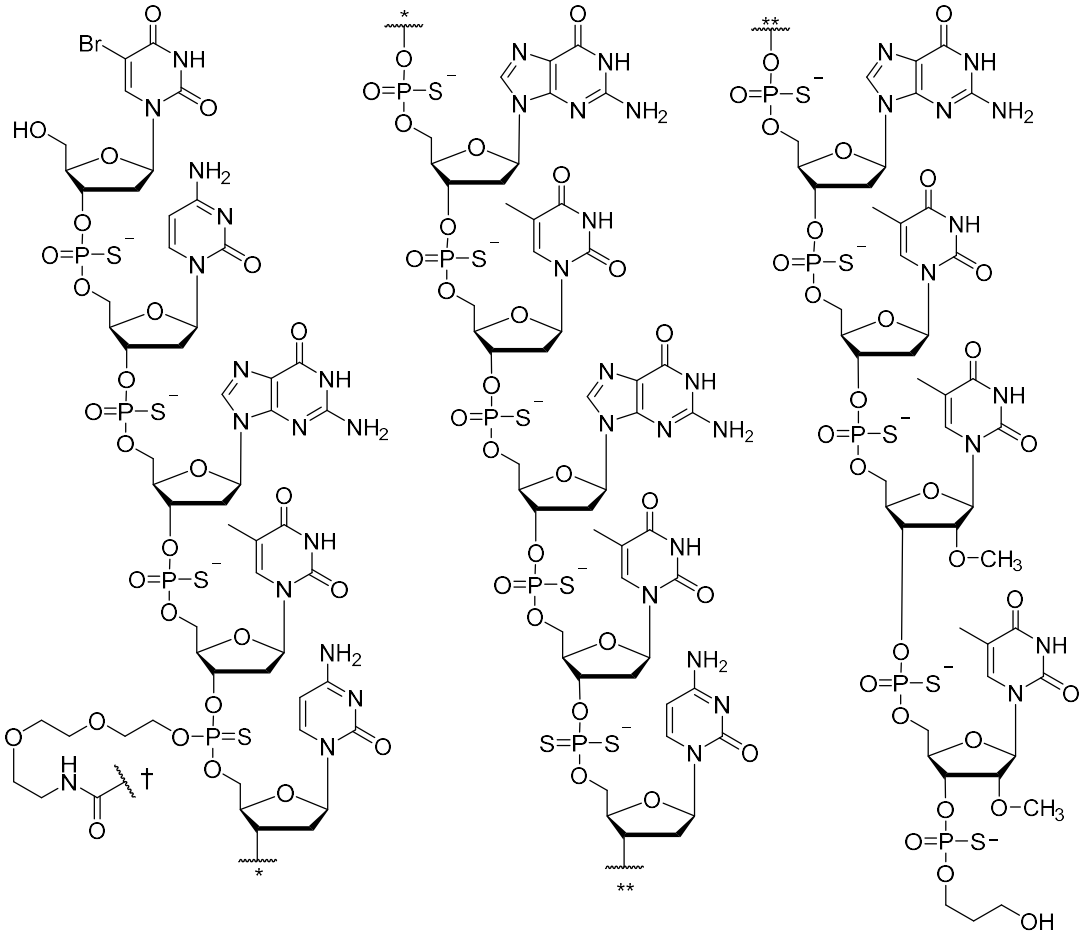
〰 indicates the point of attachment of each Q to the antibody or antigen-binding fragment thereof (Ab)

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

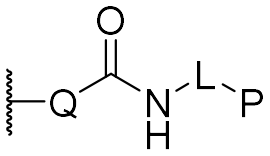
each P is independently an immunomodulating oligonucleotide comprising the structure



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

[0013] In another example, provided herein is a conjugate comprising (i) an antibody or antigen-binding fragment thereof that specifically binds an extracellular domain of a human SIRP-α polypeptide and (ii) one or more immunomodulating oligonucleotides (P); wherein the antibody or antigen-binding fragment is linked to one or more Q-tag peptides (Q); wherein the antibody or

comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:61); and wherein each immunomodulating oligonucleotide (P) 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):



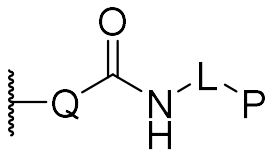
(A),

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

[0015] In another example, provided herein is a conjugate comprising an antibody or antigen-binding fragment thereof (Ab) that specifically binds an extracellular domain of a human SIRP-α polypeptide, wherein the antibody comprises two antibody light chains that each comprise a light chain variable (VL) domain that comprises a CDR-L1 comprising the amino acid sequence of SGGSYSSYYYA (SEQ ID NO:59), a CDR-L2 comprising the amino acid sequence of SDDKRPS (SEQ ID NO:60), and a CDR-L3 comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:61); two antibody heavy chains that each comprise a heavy chain variable (VH) domain that comprises a CDR-H1 comprising the amino acid sequence of SNAMS (SEQ ID NO:56), a CDR-H2 comprising the amino acid sequence of GISAGGSDTYYPASVKG (SEQ ID NO:57), and a CDR-H3 comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:58); and two Q-tag peptides comprising a peptide 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; 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) as shown in **FIG. 9A** or **FIG. 9B**.

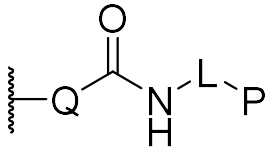
[0016] In another example, provided herein is a conjugate comprising (i) an antibody or antigen-binding fragment thereof that specifically binds an extracellular domain of a human SIRP-α polypeptide and (ii) one or more immunomodulating oligonucleotides (P), wherein the antibody or antigen-binding fragment thereof (Ab) comprises: (a) a heavy chain variable (VH) domain that comprises a CDR-H1 comprising the amino acid sequence of SNAMS (SEQ ID NO:56), a CDR-H2 comprising the amino acid sequence of GISAGGSDTYYPASVKG (SEQ ID NO:57), and a CDR-H3 comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:58), and (b) a light

chain variable (VL) domain that comprises a CDR-L1 comprising the amino acid sequence of SGGSYSSYYYA (SEQ ID NO:59), a CDR-L2 comprising the amino acid sequence of SDDKRPS (SEQ ID NO:60), and a CDR-L3 comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:61); wherein the antibody or antigen-binding fragment is linked to one or more Q-tag peptides (Q), wherein each immunomodulating oligonucleotide (P) 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):



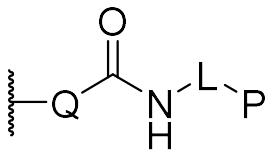
(A),

wherein 〰 indicates the point of attachment of each Q to the antibody or antigen-binding fragment thereof (Ab); and wherein the antibody heavy chain comprises an Fc region (*e.g.*, a human IgG1, IgG2, or IgG4 Fc region) comprising an N297A substitution, amino acid position numbering according to EU index. In another example, provided herein is a conjugate comprising (i) an antibody or antigen-binding fragment thereof that specifically binds an extracellular domain of a human SIRP-α polypeptide and (ii) one or more immunomodulating oligonucleotides (P); wherein the antibody or antigen-binding fragment is linked to one or more Q-tag peptides (Q); wherein the antibody or antigen-binding fragment thereof (Ab) comprises: (a) a heavy chain variable (VH) domain that comprises a CDR-H1 comprising the amino acid sequence of SNAMS (SEQ ID NO:56), a CDR-H2 comprising the amino acid sequence of GISAGGSDTYYPASVKG (SEQ ID NO:57), and a CDR-H3 comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:58), and (b) a light chain variable (VL) domain that comprises a CDR-L1 comprising the amino acid sequence of SGGSYSSYYYA (SEQ ID NO:59), a CDR-L2 comprising the amino acid sequence of SDDKRPS (SEQ ID NO:60), and a CDR-L3 comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:61); 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),

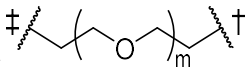
index. In another example, provided herein is a conjugate comprising (i) an antibody or antigen-binding fragment thereof that specifically binds an extracellular domain of a human SIRP-α polypeptide and (ii) one or more immunomodulating oligonucleotides (P); wherein the antibody or antigen-binding fragment is linked to one or more Q-tag peptides (Q); wherein the antibody or antigen-binding fragment thereof (Ab) comprises: (a) a heavy chain variable (VH) domain that comprises a CDR-H1 comprising the amino acid sequence of SNAMS (SEQ ID NO:56), a CDR-H2 comprising the amino acid sequence of GISAGGSDTYYPASVKG (SEQ ID NO:57), and a CDR-H3 comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:58), and (b) a light chain variable (VL) domain that comprises a CDR-L1 comprising the amino acid sequence of SGGSYSSYYYA (SEQ ID NO:59), a CDR-L2 comprising the amino acid sequence of SDDKRPS (SEQ ID NO:60), and a CDR-L3 comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:61); 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:

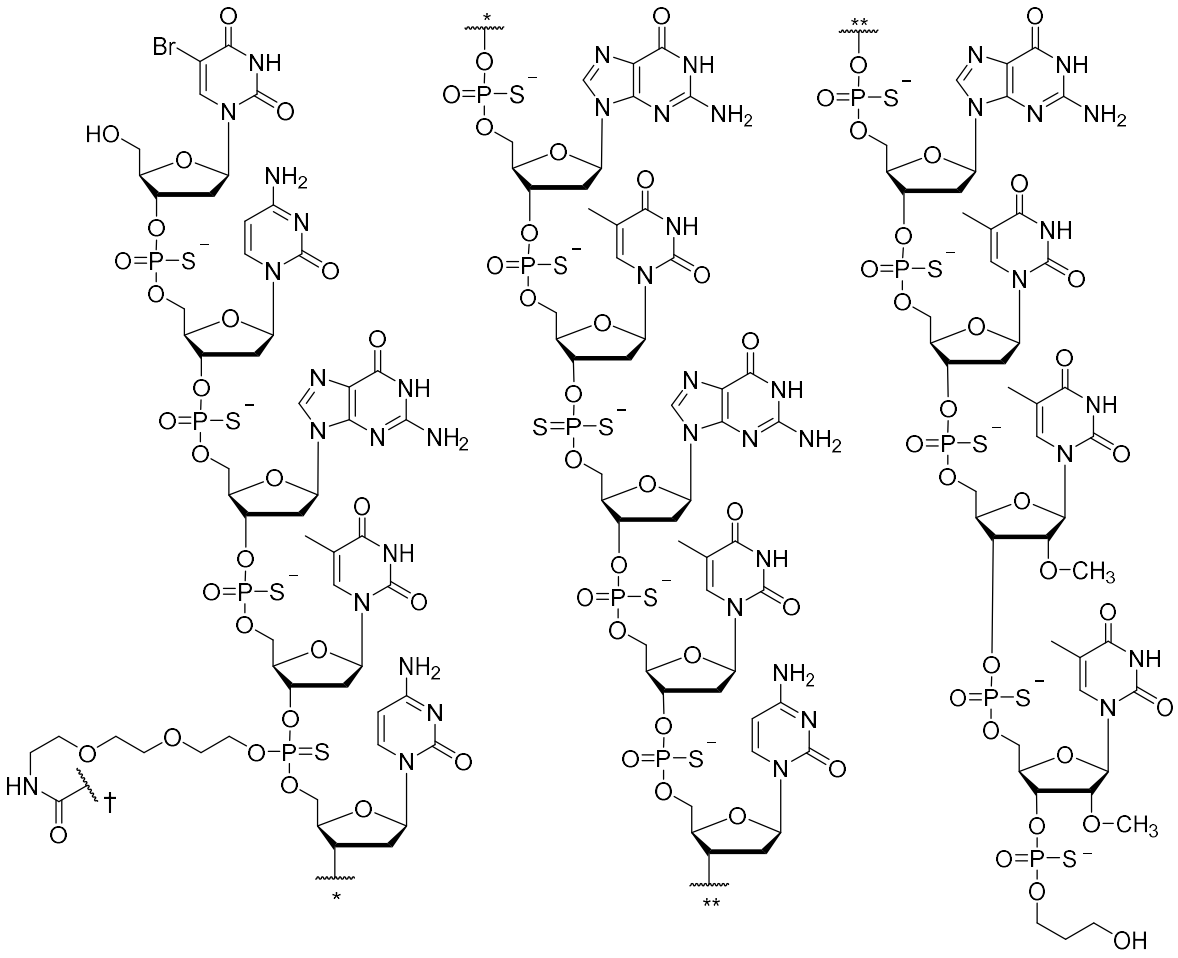
〰 indicates the point of attachment of each Q to the antibody or antigen-binding fragment thereof (Ab);

each 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;

wherein each P is independently an immunomodulating oligonucleotide comprising the structure



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

wherein the antibody heavy chain comprises an Fc region (*e.g.*, a human IgG1, IgG2, or IgG4 Fc region) comprising an N297A substitution, amino acid position numbering according to EU index. In another example, provided herein is a conjugate comprising an antibody or antigen-binding fragment thereof (Ab) that specifically binds an extracellular domain of a human SIRP-α polypeptide, wherein the antibody comprises two antibody light chains that each comprise a light chain variable (VL) domain that comprises a CDR-L1 comprising the amino acid sequence of SGGSYSSYYYA (SEQ ID NO:59), a CDR-L2 comprising the amino acid sequence of SDDKRPS (SEQ ID NO:60), and a CDR-L3 comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:61); two antibody heavy chains that each comprise a heavy chain variable (VH) domain that comprises a CDR-H1 comprising the amino acid sequence of SNAMS (SEQ ID NO:56), a CDR-H2 comprising the amino acid sequence of

GISAGGSDTYYPASVKG (SEQ ID NO:57), and a CDR-H3 comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:58); 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 or present in the Fc region of one of the antibody heavy chains; wherein the antibody heavy chain comprises an Fc region (*e.g.*, a human IgG1, IgG2, or IgG4 Fc region) comprising an N297A substitution, amino acid position numbering according to EU index; 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) as shown in **FIG. 9A** or **FIG. 9B**. In some examples, Q295 of the Fc region serves as the glutamine residue of the Q-tag peptide.

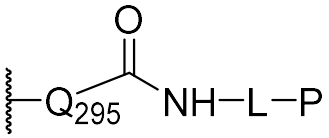
[0017] In another example, provided herein is a conjugate comprising an antibody (Ab) that specifically binds an extracellular domain of a human SIRP-α polypeptide, at least one Q tag peptide sequence comprising a glutamine residue, and at least one immunomodulatory oligonucleotide (P), wherein the antibody or antigen-binding fragment thereof (Ab) comprises: (a) a heavy chain variable (VH) domain that comprises a CDR-H1 comprising the amino acid sequence of SNAMS (SEQ ID NO:56), a CDR-H2 comprising the amino acid sequence of GISAGGSDTYYPASVKG (SEQ ID NO:57), and a CDR-H3 comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:58), and (b) a light chain variable (VL) domain that comprises a CDR-L1 comprising the amino acid sequence of SGGSYSSYYYA (SEQ ID NO:59), a CDR-L2 comprising the amino acid sequence of SDDKRPS (SEQ ID NO:60), and a CDR-L3 comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:61); wherein the Q-tag peptide sequence is naturally occurring or synthetic; wherein each immunomodulatory oligonucleotide is linked to a Q-tag via an amide bond with the glutamine residue and linker (L); and wherein at least one Q-tag peptide sequence is selected from the group consisting of SEQ ID NOs: 39-55.

[0018] In some examples described herein, the VH domain comprises the amino acid sequence of
EVQLVESGGGVVQPGGSLRLSCAASGFTFSSNAMSWVRQAPGKGLEWVAGISAGGSDT
YYPASVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARETWNHLFDYWGQGTLVT
VSS (SEQ ID NO:62). In some examples, the VH domain comprises the amino acid sequence of
EVQLVESGGGVVQPGGSLRLSCAASGFTFSSNAMSWVRQAPGKGLEWVAGISAGGSDT
YYPASVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARETWNHLFDYWGQGTLVT

VSS (SEQ ID NO:62), and the VL domain comprises the amino acid sequence of SYELTQPPSVSVSPGQTARITCSGGSYSSYYYAWYQQKPGQAPVTLIYSDDKRPSNIPER FSGSSSGTTVTLTISGVQAEDEADYYCGGYDQSSYTNPFGGGTQLTVL (SEQ ID NO:63). In some examples, the VH domain comprises the amino acid sequence of EVQLVESGGGVVQPGGSLRLSCAASGFTFSSNAMSWVRQAPGKGLEWVAGISAGGSDT YYPASVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARETWNHLFDYWGQGTLVT VSS (SEQ ID NO:62), and the VL domain comprises the amino acid sequence of SYELTQPPSVSVSPGQTARITCSGGSYSSYYYAWYQQKPGQAPVTLIYSDDKRPSNIPER FSGSSSGTTVTLTISGVQAEDEADYYCGGYDQSSYTNPFGGGTKLTVL (SEQ ID NO:64). In some examples, the VH domain comprises the amino acid sequence of EVQLVESGGGVVQPGGSLRLSCAASGFTFSSNAMSWVRQAPGKGLEWVAGISAGGSDT YYPASVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARETWNHLFDYWGQGTLVT VSS (SEQ ID NO:62), and the VL domain comprises the amino acid sequence of SYELTQPPSVSVSPGQTARITCSGGSYSSYYYAWYQQKPGQAPVTLIYSDDKRPSNIPER FSGSSSGTTVTLTISGVQAEDEADYYCGGYDQSSYTNPFGGGTELTVL (SEQ ID NO:65).

[0019] In some examples described herein, the antibody is a monoclonal antibody. In some examples, the antibody is a Fab, F(ab')2, Fab'-SH, Fv, or scFv antibody or antibody fragment. In some examples, the antibody is a humanized, human, or chimeric antibody or fragment thereof. In some examples, the antibody comprises an antibody heavy chain comprising a VH domain of the present disclosure and an Fc region. In some examples, the antibody heavy chain comprises a human IgG1, human IgG2, or human IgG4 Fc region. In some examples, the antibody heavy chain comprises a human IgG1 Fc region comprising L234A, L235A, and/or G237A substitutions, amino acid position numbering according to EU index. In some examples, the antibody heavy chain comprises a wild-type human IgG1 Fc region. In some examples, the antibody heavy chain comprises a human IgG1 Fc region comprising an N297A substitution, amino acid position numbering according to EU index. In some examples, the antibody heavy chain comprises a human IgG1 Fc region comprising a D265A substitution, amino acid position numbering according to EU index. In some examples, the antibody heavy chain comprises a wild-type human IgG2 Fc region. In some examples, the antibody heavy chain comprises a human IgG2 Fc region comprising an N297A substitution, amino acid position numbering

according to EU index. In some examples, the antibody heavy chain comprises a human IgG4 Fc region comprising an S228P substitution, amino acid position numbering according to EU index. In some examples, the Fc region comprises an N297A substitution, amino acid position numbering according to EU index. In some examples, the conjugate further comprises an immunomodulating oligonucleotide P attached to the Q295 of the Fc region residue as shown in the following formula



wherein L is a linker moiety connected to Q295 of the Fc region via an amide bond.

[0020] In some examples described herein, the antibody comprises an antibody heavy chain, with C-terminal Q-tag peptide, comprising the amino acid sequence EVQLVESGGGVVQPGGSLRLSCAASGFTFSSNAMSWVRQAPGKGLEWVAGISAGGSDT YYPASVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARETWNHLFDYWGQGTLVT VSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQ EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDK SRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGRPQGFGPP (SEQ ID NO:66). In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence EVQLVESGGGVVQPGGSLRLSCAASGFTFSSNAMSWVRQAPGKGLEWVAGISAGGSDT YYPASVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARETWNHLFDYWGQGTLVT VSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQ EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSRLTVDK

SRWQEGNVFSCSVMHEALHNHYTQKSLSLSLG (SEQ ID NO:87). In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence of SEQ ID NO:87 and a Q-tag sequence of the present disclosure. In some examples, the antibody comprises an antibody heavy chain, with C-terminal Q-tag peptide, comprising the amino acid sequence
EVQLVESGGGVVQPGGSLRLSCAASGFTFSSNAMSWVRQAPGKGLEWVAGISAGGSDT
YYPASVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARETWNHLFDYWGQGTLVT
VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEA
AGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGRPQGFGPP (SEQ ID NO:67). In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence
EVQLVESGGGVVQPGGSLRLSCAASGFTFSSNAMSWVRQAPGKGLEWVAGISAGGSDT
YYPASVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARETWNHLFDYWGQGTLVT
VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEA
AGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:88). In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence of SEQ ID NO:88 and a Q-tag sequence of the present disclosure. In some examples, the antibody comprises an antibody heavy chain, with C-terminal Q-tag peptide, comprising the amino acid sequence
EVQLVESGGGVVQPGGSLRLSCAASGFTFSSNAMSWVRQAPGKGLEWVAGISAGGSDT
YYPASVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARETWNHLFDYWGQGTLVT
VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL

LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGRPQGFGPP (SEQ ID NO:68). In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence
EVQLVESGGGVVQPGGSLRLSCAASGFTFSSNAMSWVRQAPGKGLEWVAGISAGGSDT
YYPASVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARETWNHLFDYWGQGTLVT
VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL
QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL
LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:89). In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence of SEQ ID NO:89 and a Q-tag sequence of the present disclosure.

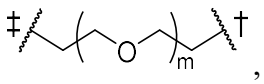
[0021] In some examples described herein, the antibody comprises an antibody light chain comprising the VL domain and a light chain constant (CL) domain comprising the amino acid sequence
GQPKANPTVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADGSPVKAGVETTKPS
KQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS (SEQ ID NO:69). In some examples, the antibody comprises an antibody light chain comprising the VL domain and a light chain constant (CL) domain comprising the amino acid sequence
GQPKANPTVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADGSPVKAGVETTKPS
KQSSDKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS (SEQ ID NO:70). In some examples, the antibody comprises an antibody light chain comprising the VL domain and a light chain constant (CL) domain comprising the amino acid sequence
GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPS
KQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS (SEQ ID NO:71). In some examples, the antibody comprises an antibody light chain comprising an amino acid sequence selected from the group consisting of SEQ ID Nos:72-80. In some examples, the

antibody comprises an antibody heavy chain, with C-terminal Q-tag peptide, comprising the amino acid sequence of SEQ ID NO:68 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:79. In some examples, the antibody comprises an antibody heavy chain, with C-terminal Q-tag peptide, comprising the amino acid sequence of SEQ ID NO:67 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:79. In some examples, the antibody comprises an antibody heavy chain, with C-terminal Q-tag peptide, comprising the amino acid sequence of SEQ ID NO:66 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:79. In some examples, the antibody comprises an antibody heavy chain, with C-terminal Q-tag peptide, comprising the amino acid sequence of SEQ ID NO:68 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:75. In some examples, the antibody comprises an antibody heavy chain, with C-terminal Q-tag peptide, comprising the amino acid sequence of SEQ ID NO:67 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:75. In some examples, the antibody comprises an antibody heavy chain, with C-terminal Q-tag peptide, comprising the amino acid sequence of SEQ ID NO:66 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:75. In some examples, the antibody comprises an antibody heavy chain, with C-terminal Q-tag peptide, comprising the amino acid sequence of SEQ ID NO:68 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:73. In some examples, the antibody comprises an antibody heavy chain, with C-terminal Q-tag peptide, comprising the amino acid sequence of SEQ ID NO:67 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:73. In some examples, the antibody comprises an antibody heavy chain, with C-terminal Q-tag peptide, comprising the amino acid sequence of SEQ ID NO:66 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:73. In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence of SEQ ID NO:88 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:79. In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence of SEQ ID NO:87 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:79. In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence of SEQ ID NO:89 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:75. In some examples, the antibody comprises an antibody heavy chain comprising the amino acid

sequence of SEQ ID NO:88 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:75. In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence of SEQ ID NO:87 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:75. In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence of SEQ ID NO:89 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:73. In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence of SEQ ID NO:88 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:73. In some examples, the antibody comprises an antibody heavy chain comprising the amino acid sequence of SEQ ID NO:87 and an antibody light chain comprising the amino acid sequence of SEQ ID NO:73. In some examples, the antibody heavy and/or light chain further comprises a Q-tag peptide sequence of the present disclosure.

[0022] In some examples described herein, each of the one or more Q-tag peptides (Q) comprises a peptide sequence having between 5 and 15 amino acid residues. In some examples, each of the one or more Q-tag peptides is naturally occurring. In some examples, each of the one or more Q-tag peptides comprises a sequence independently selected from the group consisting of SEQ ID NOs: 39-55. In some examples, each of the one or more Q-tag peptides comprises the peptide sequence RPQGF (SEQ ID NO:47), RPQGFPP (SEQ ID NO:48), or RPQGFGPP (SEQ ID NO:49). In some examples, each of the one or more Q-tag peptides comprises the peptide sequence RPQGF (SEQ ID NO:47). In some examples, the at least one Q-tag peptide sequence comprises the peptide sequence RPQGF (SEQ ID NO:47), RPQGFPP (SEQ ID NO:48), or RPQGFGPP (SEQ ID NO:49). In some examples, the at least one Q-tag peptide sequence comprises the peptide sequence RPQGFGPP (SEQ ID NO:49). In some examples, the antibody comprises two antibody heavy chains and two antibody light chains, and wherein one or both heavy chains further comprises a Q-tag. In some examples, the Q-tag is fused to the C-terminus of one or both of the heavy chains. In some examples, the Q-tag is within the Fc domain. In some examples, the antibody comprises two antibody heavy chains and two antibody light chains, and wherein one or both light chains further comprises a Q-tag. In some examples, the conjugate induces activation of TLR9. In some examples, 1 or 2 Q-tags is/are linked to the antibody. In some examples, the conjugate has a DAR of 1 or 2.

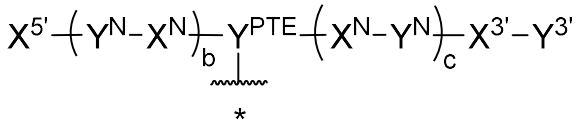
[0023] In some examples, the linker L comprises a polyethylene glycol moiety. In some examples, the linker L is



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wherein m is an integer ranging from about 0 to about 50, and wherein ~~~ † indicates the point of attachment to T^3, and ~~~ ‡ indicates the point of attachment to the rest of the conjugate. In some examples, Z is S. In some examples, the oligonucleotide P comprises at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S^-. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 1. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 2. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 3. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 5. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 6. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 7. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 8. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 9. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 10. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 11. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 12. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 13. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 14. In some examples, the at least one pair of geminal T^1 and T^2 wherein T^1 is S and T^2 is S is located at the 3'-position of nucleoside residue 15. In some examples, the oligonucleotide P comprises at least two pairs of geminal T^1 and T^2 wherein T^1 is S and T^2 is S^-. In some examples, $R^{5'}$ is H. In some examples,

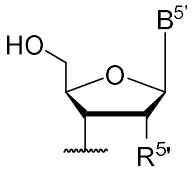
$R^{5'}$ is methoxy. In some examples, R^{c1} is H. In some examples, R^{c1} is methoxy. In some examples, R^2 is methyl. In some examples, R^2 is H. In some examples, $U^{5'}$ is bromo. In some examples, $U^{5'}$ is –H. In some examples, m is an integer from 20 to 25. In some examples, m is 24. In some examples, each P independently comprises an oligonucleotide selected from Table 2, Table 14, and Table 15. In some examples, each linker (L) and an each immunomodulating oligonucleotide (P) independently comprises an oligonucleotide selected from Table 2, Table 16 and Table 17. In some examples, each P independently comprises an oligonucleotide selected from SEQ ID NOS: 1-38 and 129-166. In some examples, each immunomodulating oligonucleotide P is independently

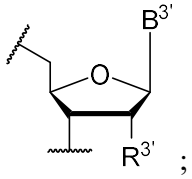


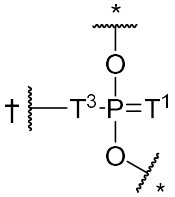
wherein

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;

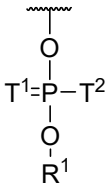
〰 * indicates the point of attachment of the immunomodulating oligonucleotide P to the rest of the conjugate;

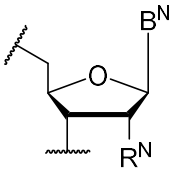
$X^{5'}$ is a 5' terminal nucleoside comprising the structure  ;

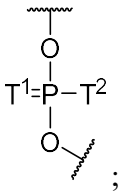
$X^{3'}$ is a 3' terminal nucleoside comprising the structure  ;

Y^{PTE} is an internucleoside phosphotriester comprising 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 at the glutamine residue via an amide bond;

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

each X^N is independently a nucleoside comprising the structure ;

each Y^N is independently an internucleoside linker comprising 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 optionally further 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 optionally further substituted by -O-C_{1-4}-alkyl;

each T_1 is independently O or S;

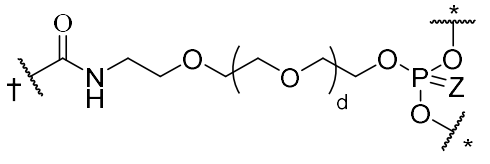
each T_2 is independently O^- or S^-; and

T_3 is a group comprising an oligoethylene glycol moiety; and

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

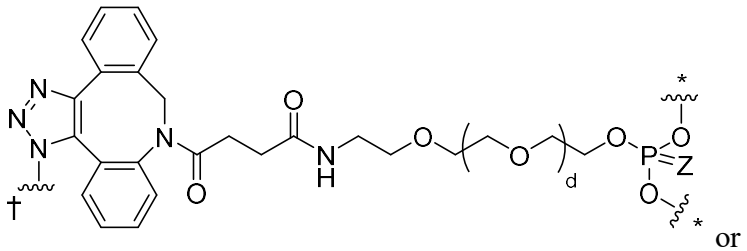
[0024] In some examples according to any of the examples described herein, b is 3. In some examples, (i) P comprises at least one modified nucleoside X^N; (ii)P comprises at least one modified internucleoside linker Y^N, wherein at least one of T^1 or T^2 is S; or (iii) both (i) and (ii). In some examples, P comprises at least one phosphorodithioate or phosphorothioate internucleoside linker. In some examples, P comprises 0, 1, 2, or 3 phosphorodithioate internucleoside linkers. In some 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 some 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 some examples, $X^{5'}$ is a 5-bromo-2'-O-methyluridine, 5-bromo-2'-deoxyuridine, 2'-O-methyluridine or 2'-deoxyuridine. In some examples, $Y^{3'}$ or the Y^N at the 3' position of $X^{5'}$ comprises an unsubstituted or substituted phosphorothioate. In some examples, Y^{PTE} is

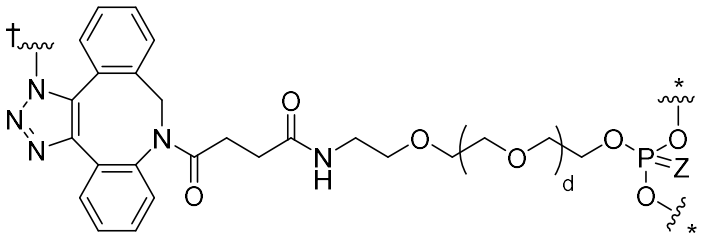


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wherein Z is O or S; d is an integer from 0 to 95; the two 〰 * on the right side of the structure indicate the points of attachment to the adjacent nucleosides X^N in the oligonucleotide P, and the 〰 † on the left side of the structure indicates the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

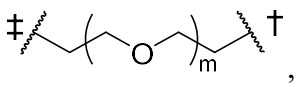


or



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 some examples, Z is S. In some examples, d is an integer from 1 to 25. In some

examples, the linker L comprises a polyethylene glycol moiety. In some examples, the linker L is



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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 some examples, P comprises one or more CpG sites. In some 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).

[0025] In another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:68; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:67; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ

ID NO:75; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:66; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:68; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:67; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:66; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate

comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:67; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:68; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:68; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:67; wherein the immunomodulating oligonucleotide and the linker

comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:66; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:68; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:67; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light

chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:66; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:68; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:67; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:66; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:68; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:67; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:66; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:89; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ

ID NO:35; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:88; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:35; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:87; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:35; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:89; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:35; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an

immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:88; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:35; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:87; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:35; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:88; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:35; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:89; wherein the

immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:35; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:89; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:34; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:88; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:34; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49;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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:87; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:34; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49;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

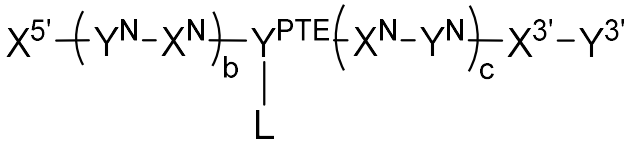
(L). In another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:89; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:34; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:88; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:34; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:87; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:34; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49;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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody

heavy chains comprises the amino acid sequence of SEQ ID NO:89; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:163; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:88; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:163; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:75; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:87; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:163; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:89; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:163; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:88; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:163; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:73; wherein each of the antibody heavy chains comprises the amino acid sequence of SEQ ID NO:87; wherein the immunomodulating oligonucleotide and the linker comprise the structure of SEQ ID NO:163; wherein each of the Q-tag peptides (Q) comprises the amino acid sequence of SEQ ID NO:49; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:79; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:66; 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 another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:79; wherein each of

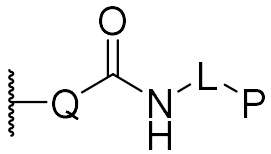
the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:67; wherein the immunomodulating oligonucleotide comprises the sequence of SEQ ID NO:35; and wherein at least one of the two Q-tag peptides is linked to the immunomodulating oligonucleotide via an amide bond with the glutamine residue of the Q-tag peptide and a linker (L). In another example, provided herein is a conjugate comprising an antibody (Ab) and an immunomodulating oligonucleotide (P), wherein the antibody comprises two antibody light chains, two antibody heavy chains, and two Q-tag peptides; wherein each of the antibody light chains comprises the amino acid sequence of SEQ ID NO:79; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:68; 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 some examples, the conjugate has a DAR of 1 or 2.

[0026] In another example, provided herein is a method for preparing a conjugate that comprises (i) an antibody or antigen-binding fragment thereof (Ab) that specifically binds human an extracellular domain of a human SIRP-α polypeptide and (ii) one or more immunomodulating oligonucleotides (P), comprising: contacting the Ab with the oligonucleotide P in the presence of a transglutaminase; 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 P independently comprises the following formula:



wherein $X^{5'}$ is a 5' terminal nucleoside; $X^{3'}$ is a 3' terminal nucleoside; Y^{PTE} is an internucleoside phosphotriester; $Y^{3'}$ is a terminal phosphotriester; each X^N is independently a nucleoside; each Y^N is independently an internucleoside linker; 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; and L is a linker moiety comprising a terminal amine; and wherein the antibody or antigen-binding fragment comprises: (a) a heavy chain variable (VH) domain that comprises a CDR-H1 comprising the

amino acid sequence of SNAMS (SEQ ID NO:56), a CDR-H2 comprising the amino acid sequence of GISAGGSDTYYPASVKG (SEQ ID NO:57), and a CDR-H3 comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:58), and (b) a light chain variable (VL) domain that comprises a CDR-L1 comprising the amino acid sequence of SGGSYSSYYYA (SEQ ID NO:59), a CDR-L2 comprising the amino acid sequence of SDDKRPS (SEQ ID NO:60), and a CDR-L3 comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:61). In another example, provided herein is a method for preparing a conjugate that comprises (i) an antibody or antigen-binding fragment thereof (Ab) that specifically binds human an extracellular domain of a human SIRP-α polypeptide and (ii) 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 the antibody or antigen-binding fragment comprises: (a) a heavy chain variable (VH) domain that comprises a CDR-H1 comprising the amino acid sequence of SNAMS (SEQ ID NO:56), a CDR-H2 comprising the amino acid sequence of GISAGGSDTYYPASVKG (SEQ ID NO:57), and a CDR-H3 comprising the amino acid sequence of ETWNHLFDY (SEQ ID NO:58), and (b) a light chain variable (VL) domain that comprises a CDR-L1 comprising the amino acid sequence of SGGSYSSYYYA (SEQ ID NO:59), a CDR-L2 comprising the amino acid sequence of SDDKRPS (SEQ ID NO:60), and a CDR-L3 comprising the amino acid sequence of GGYDQSSYTNP (SEQ ID NO:61); 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:

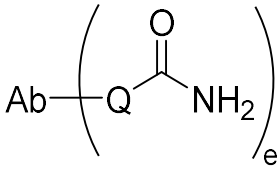
〰 indicates the point of attachment of each Q to the antibody or antigen-binding fragment thereof (Ab);

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

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

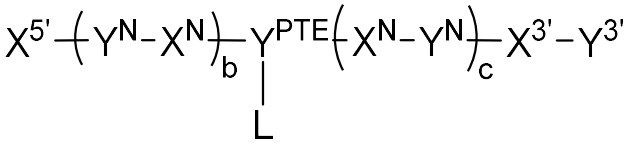
each P is independently an immunomodulating oligonucleotide;

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 P independently comprises the following formula:



,

wherein

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

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

Y^{PTE} is an internucleoside phosphotriester;

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

each X^N is independently a nucleoside;

each Y^N is independently an internucleoside linker;

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; and

L is a linker moiety comprising a terminal amine,

in the presence of a transglutaminase. In some examples, each immunomodulating oligonucleotide is independently an oligonucleotide of formula (C) or formula (D) is selected from the group consisting of the oligonucleotides of Table 15 and Table 17.

[0027] In some examples, each Q-tag peptide sequence comprises the peptide sequence RPQGFGPP (SEQ ID NO:49). In some examples, 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. In some examples, the conjugate has a DAR of 1 or 2. In some examples, the conjugate has a DAR of 1, and the method further comprises separating the conjugate having a DAR of 1 from free oligonucleotide, unconjugated antibody, and conjugates having a DAR of 2.

[0028] In another example, provided herein is a pharmaceutical composition comprising the conjugate of any one of the above examples and a pharmaceutically acceptable carrier.

[0028a] In one aspect, the present disclosure refers to a pharmaceutical composition comprising the conjugate disclosed herein and a pharmaceutically acceptable carrier.

[0029] In another 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 above examples or the pharmaceutical composition according to any one of the above examples. In another example, provided herein is the conjugate according to any one of the above examples or the pharmaceutical composition according to any one of the above examples for use in a method for treating cancer. In another example, provided herein are uses of the conjugate according to any one of the above examples or the pharmaceutical composition according to any one of the above examples in the manufacture of a medicament, *e.g.*, for use in treating cancer. In another example, provided herein is a method for activating myeloid cells, comprising administering to an individual in need thereof an effective amount of the conjugate according to any one of the above examples or the pharmaceutical composition according to any one of the above examples. In another example, provided herein is a method for inducing TLR9 signaling in myeloid cells, comprising administering to an individual in need thereof an effective amount of the conjugate according to any one of the above examples or the pharmaceutical composition according to any one of the above examples. In some examples, the individual has cancer. In some examples, the cancer is a liquid tumor. In other examples, the cancer is a solid tumor. In some examples, the cancer is lung cancer, squamous cell cancer, cholangiocarcinoma (*e.g.*, intrahepatic cholangiocarcinoma), brain tumors, glioblastoma, head and neck cancer, hepatocellular cancer, colorectal cancer, skin cancer, lung cancer, endometrial cancer, liver cancer, bladder cancer, gastric or stomach cancer, pancreatic cancer, cervical cancer, ovarian cancer, cancer of the urinary tract, urothelial cancer, breast cancer, peritoneal cancer, uterine cancer, salivary gland cancer, kidney or renal cancer, prostate cancer, vulval cancer, thyroid cancer, anal carcinoma, penile carcinoma, testis or testicular cancer, melanoma, multiple myeloma and B-cell lymphoma, non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia

(ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), Merkel cell carcinoma, hairy cell leukemia, or chronic myeloblastic leukemia (CML). In some examples, the cancer is known or predicted to be non-responsive to an inhibitor of PD-L1 or PD-1 (*e.g.*, when administered as a monotherapy, or when administered in the absence of an anti-SIRP-α antibody). In some examples, the individual does not achieve a significant therapeutic response to an inhibitor of PD-L1 or PD-1 (*e.g.*, an antibody that binds PD-L1 or PD-1). In some examples, prior to administration of the conjugate or composition, the individual has been treated with an inhibitor of PD-L1 or PD-1 (*e.g.*, an antibody that binds PD-L1 or PD-1). In some examples, the inhibitor of PD-L1 or PD-1 is pembrolizumab, nivolumab, cemiplimab-rwlc, atezolizumab, dostarlimab-gxly, durvalumab, or avelumab. In some examples, prior to administration of the conjugate or composition, the individual has been treated with an inhibitor of PD-L1 or PD-1 (*e.g.*, an antibody that binds PD-L1 or PD-1) and did not respond to said treatment with the inhibitor of PD-L1 or PD-1 (*e.g.*, when administered as a monotherapy, or when administered in the absence of an anti-SIRP-α antibody). In some examples, the cancer is melanoma or renal cancer, *e.g.,* that expresses or overexpresses SIRP-α. In some examples, cells of the cancer express human SIRP-α. In some examples, cells of the cancer do not express human SIRP-α. In some examples, the methods further comprise administering to the individual an additional therapeutic agent. In some examples, the additional therapeutic agent comprises an immunotherapy, chemotherapy, radiation therapy, cell-based therapy, anti-cancer vaccine, or anti-cancer agent. In some examples, the methods further comprise administering to the individual an inhibitor of PD-L1 or PD-1 (*e.g.*, an antibody that binds PD-L1 or PD-1). In some examples, the methods comprise administering to the individual an inhibitor of PD-L1 or PD-1, wherein: (a) the antibody of the conjugate 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:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:68; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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); (b) the antibody of the conjugate comprises two antibody light chains, two antibody heavy

wherein the immunomodulating oligonucleotide and the linker comprise the structure 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); (g) the antibody of the conjugate 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:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:68; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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); (h) the antibody of the conjugate 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:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:67; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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); or (i) the antibody of the conjugate 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:73; wherein each of the antibody heavy chains is linked to a C-terminal Q-tag peptide (Q) and comprises the amino acid sequence, with Q, of SEQ ID NO:66; wherein the immunomodulating oligonucleotide and the linker comprise the structure 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).

[0029a] In one aspect, the present disclosure refers to use of the conjugate disclosed herein or the pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating cancer in an individual.

[0029b] In one aspect, the present disclosure refers to a kit or article of manufacture comprising the conjugate disclosed herein.

[0030] It is to be understood that one, some, or all of the properties of the various examples described herein may be combined to form other examples of the present disclosure. These and other examples of the present disclosure will become apparent to one of skill in the art. These and other examples of the present disclosure are further described by the detailed description that follows.