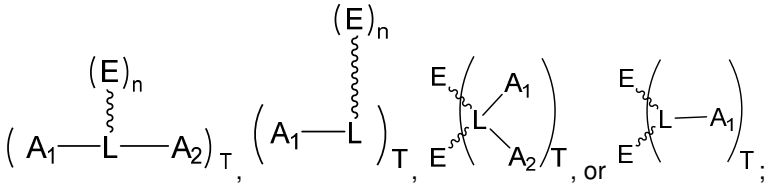
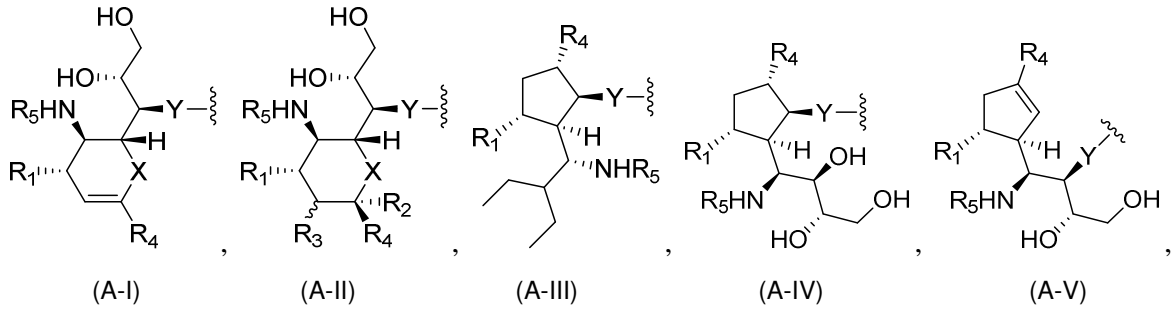
cells and further enhancing the antiviral activity of the conjugates. The albumin or albumin-binding peptide may extend the half-life of the conjugate, for example, by binding of albumin to the recycling neonatal Fc receptor. Such compositions are useful in methods for the inhibition of viral growth and in methods for the treatment of viral infections, such as those caused by an influenza virus A, influenza virus B and influenza virus C.

In a first example, the disclosure features a conjugate described by any one of formulas (D-I), (M-I), (1), or (2):

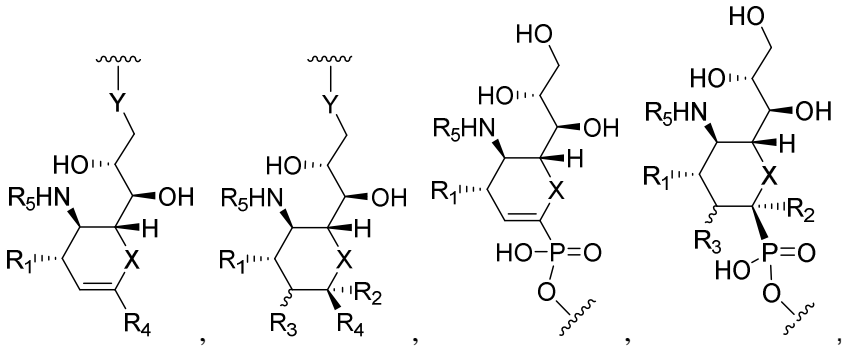


(D-I) (M-I) (1) (2)

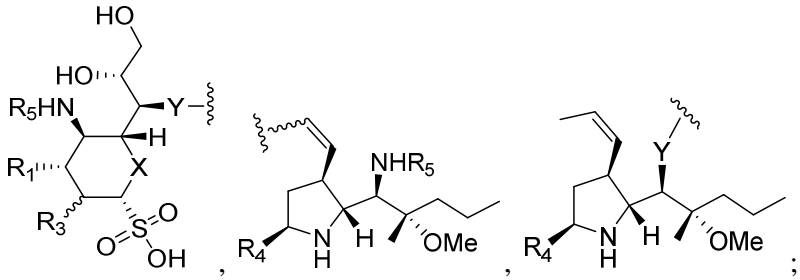
wherein each A_1 and each A_2 is independently selected from any one of formulas (A-I)-(A-XII):



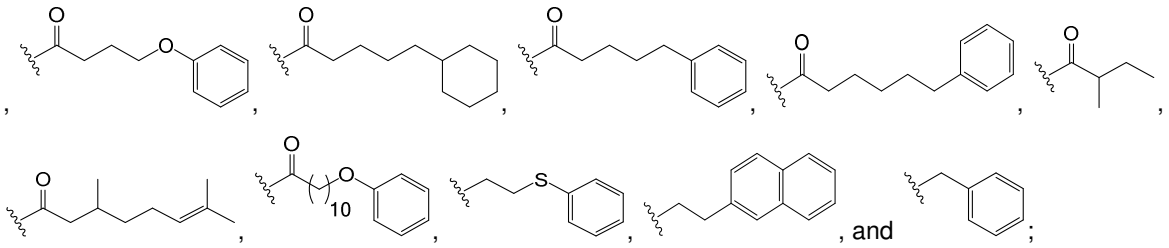
(A-I) (A-II) (A-III) (A-IV) (A-V)



(A-VI) (A-VII) (A-VIII) (A-IX)



(A-X) (A-XI) (A-XII)



R_7 is selected from H, C1-C20 alkyl, C3-C20 cycloalkyl, C3-C20 heterocycloalkyl; C5-C15 aryl, and C2-C15 heteroaryl; R_8 is selected from C3-C20 heterocycloalkyl, C5-C15 aryl, and C2-C15 heteroaryl;

n is 1 or 2;

each E comprises an Fc domain monomer, an albumin protein, an albumin protein-binding peptide, or an Fc-binding peptide;

L is a linker covalently attached to E and to each Y of each A_1 or each A_1 and A_2;

T is an integer from 1 to 20, and

each squiggly line in formulas (D-I), (M-I), (1), or (2) indicates that L is covalently attached to each E;

or a pharmaceutically acceptable salt thereof.

In some examples, n is 1 and each E includes an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138), an albumin protein (e.g., an albumin protein having the sequence of any one of SEQ ID NOs: 139-141), an albumin protein-binding peptide, or an Fc-binding peptide;

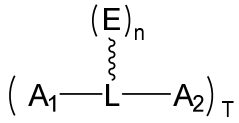
In some examples, n is 2 and each E includes an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138), wherein the Fc domain monomers dimerize to form and Fc domain;

L is a linker covalently attached to each E and to each Y or each A_1 and/or A_2;

T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), and each squiggly line in formulas (D-I), (M-I), (1), or (2) indicates that L is covalently attached (e.g., by way of a covalent bond or linker) to each E; or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1-L or each A_1-L-A_2 may be independently selected (e.g., independently selected from any of the A_1-L or A_1-L-A_2 structures described herein).

In preferred examples, n is 2 and each E includes an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138). In a conjugate having two Fc domain monomers (e.g., a conjugate of formula (1), formula (2), formula (D-I) where n equals 2, or (M-I) where n equals 2), the Fc domain monomers dimerize to form an Fc domain.

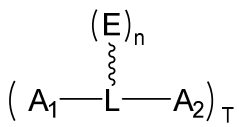
In another example, the disclosure features a conjugate described by formula (D-I):



(D-I)

wherein each E includes an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138); L in each A_1-L-A_2 is a linker covalently attached to a sulfur atom of a hinge cysteine in E and to each of A_1 and A_2; n is 1 or 2 (e.g., when n is 2, the two Fc domain monomers dimerize to form and Fc domain); T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), and the squiggly line connected to the E indicates that each A_1-L-A_2 is covalently attached (e.g., by way of a covalent bond or linker) to a sulfur atom of a hinge cysteine in E, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1-L-A_2 may be independently selected (e.g., independently selected from any of the A_1-L-A_2 structures described herein).

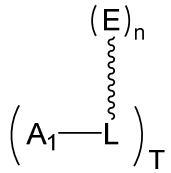
In another example, the disclosure features a conjugate described by formula (D-I):



(D-I)

wherein each E includes an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138); L in each A_1- L-A_2 is a linker covalently attached to a nitrogen atom of a surface exposed lysine in E and to each of A_1 and A_2; n is 1 or 2 (e.g., when n is 2, the two Fc domain monomers dimerize to form and Fc domain); T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), and the squiggly line connected to the E indicates that each A_1-L-A_2 is covalently attached (e.g., by way of a covalent bond or linker) to the nitrogen atom of a surface exposed lysine in E, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1-L-A_2 may be independently selected (e.g., independently selected from any of the A_1-L-A_2 structures described herein). In some examples, each of A_1 and A_2 may be independently selected from any one of formulas (A-I), (A-II), (A-VI), or (A-VII). In other examples, each of A_1 and A_2 may be independently selected from formula (A-I).

In another example, the disclosure features a conjugate described by formula (M-I):

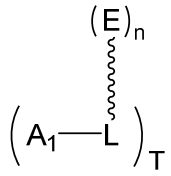


(M-I)

wherein each E includes an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138); L in each L-A_1 is a linker covalently attached to a sulfur atom of a hinge

cysteine in E and to A_1; n is 1 or 2 (e.g., when n is 2, the two Fc domain monomers dimerize to form and Fc domain); T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20); and the squiggly line connected to E indicates that each L-A_1 is covalently attached (e.g., by way of a covalent bond or linker) to the sulfur atom of the hinge cysteine in E, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1 may be independently selected from any structure described by formula (A-I)-(A-XII). In some examples, each A_1 may be independently selected from any one of formulas (A-I), (A-II), (A-VI), or (A-VII). In other examples, each A_1 may be independently selected from formula (A-I).

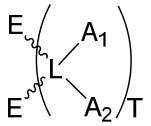
In another example, the disclosure features a conjugate described by formula (M-I):



(M-I)

wherein each E includes an Fc domain monomer(e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138); L in each L-A_1 is a linker covalently attached to a nitrogen atom of a surface exposed lysine in E and to A_1; n is 1 or 2 (e.g., when n is 2, the two Fc domain monomers dimerize to form and Fc domain); T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), the squiggly line connected to E indicates that each L-A_1 is covalently attached (e.g., by way of a covalent bond or linker) to the nitrogen atom of a surface exposed lysine in E, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1 may be independently selected from any structure described by formula (A-I)-(A-XII). In some examples, each A_1 may be independently selected from any one of formulas (A-I), (A-II), (A-VI), or (A-VII). In other examples, each A_1 may be independently selected from formula (A-I).

In one example, the disclosure features a conjugate described by formula (1):

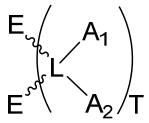


(1)

wherein each A_1 and each A_2 is independently selected from any one of formulas (A-I)-(A-XII);
each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138); L in each A_1-L-A_2 is a linker covalently attached to a sulfur atom of a hinge cysteine in each E and to each of A_1 and A_2; T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), and the two squiggly lines connected to the two Es indicate that each A_1-L-A_2 is covalently attached (e.g., by way of a covalent bond or a linker) to a pair of sulfur atoms of two hinge cysteines in the two Es, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1-L-A_2 may be

independently selected (e.g., independently selected from any of the A_1-L-A_2 structures described herein). In some examples, each of A_1 and A_2 may be independently selected from any one of formulas (A-I), (A-II), (A-VI), or (A-VII). In other examples, each of A_1 A_2 may be independently selected from formula (A-I).

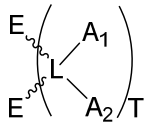
In another example, the disclosure features a conjugate described by formula (1):



(1)

wherein each A_1 and each A_2 is independently selected from any one of formulas (A-I)-(A-V); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138); L in each A_1-L-A_2 is a linker covalently attached to a sulfur atom of a hinge cysteine in each E and to each of A_1 and A_2; T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), and the two squiggly lines connected to the two Es indicate that each A_1-L-A_2 is covalently attached (e.g., by way of a covalent bond or a linker) to a pair of sulfur atoms of two hinge cysteines in the two Es, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1-L-A_2 may be independently selected (e.g., independently selected from any of the A_1-L-A_2 structures described herein).

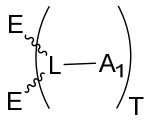
In another example, the disclosure features a conjugate described by formula (1):



(1)

wherein each A_1 and each A_2 is independently selected from any one of formulas (A-VI)-(A-IX); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138); L in each A_1-L-A_2 is a linker covalently attached to a sulfur atom of a hinge cysteine in each E and to each of A_1 and A_2; T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), and the two squiggly lines connected to the two Es indicate that each A_1-L-A_2 is covalently attached (e.g., by way of a covalent bond or a linker) to a pair of sulfur atoms of two hinge cysteines in the two Es, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1-L-A_2 may be independently selected (e.g., independently selected from any of the A_1-L-A_2 structures described herein).

In another example, the disclosure features a conjugate described by formula (2):

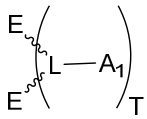


(2)

wherein each A_1 is independently selected from any one of formulas (A-I)-(A-XII); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-

138); L in each L-A_1 is a linker covalently attached to a sulfur atom in a hinge cysteine in E and to A_1; T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), and the two squiggly lines connected to the two sulfur atoms indicate that each L-A_1 is covalently (e.g., by way of a covalent bond or a linker) attached to a pair of sulfur atoms of two hinge cysteines in the two Es, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1 may be independently selected from any one of formulas (A-I)-(A-XII). In some examples, each of A_1 and A_2 may be independently selected from any one of formulas (A-I), (A-II), (A-VI), or (A-VII). In other examples, each of A_1 A_2 may be independently selected from formula (A-I).

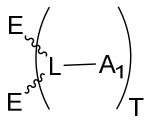
In another example, the disclosure features a conjugate described by formula (2):



(2)

wherein each A_1 is independently selected from any one of formulas (A-I)-(A-V); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138); L in each L-A_1 is a linker covalently attached to a sulfur atom in a hinge cysteine in E and to A_1; T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), and the two squiggly lines connected to the two sulfur atoms indicate that each L-A_1 is covalently attached (e.g., by way of a covalent bond or a linker) to a pair of sulfur atoms of two hinge cysteines in the two Es, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1 may be independently selected from any one of formulas (A-I)-(A-V).

In another example, the disclosure features a conjugate described by formula (2):



(2)

wherein each A_1 is independently selected from any one of formulas (A-VI)-(A-IX); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138); L in each L-A_1 is a linker covalently attached to a sulfur atom in a hinge cysteine in E and to A_1; T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), and the two squiggly lines connected to the two sulfur atoms indicate that each L-A_1 is covalently attached (e.g., by way of a covalent bond or a linker) to a pair of sulfur atoms of two hinge cysteines in the two Es, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1 may be independently selected from any one of formulas (A-VI)-(A-IX).

In some examples, each E includes an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138.

In some examples, at least one of the pair of sulfur atoms is the sulfur atom corresponding to (e.g., the sulfur atom of) a hinge cysteine of SEQ ID NO: 10 or SEQ ID NO: 11, i.e., Cys10, Cys13, Cys16, or Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11. In some examples, the pair of sulfur atoms are the sulfur atoms corresponding to (e.g., the sulfur atoms of) Cys10 and Cys13 in SEQ ID NO: 10 or SEQ ID NO: 11, Cys10 and Cys16 in SEQ ID NO: 10 or SEQ ID NO: 11, Cys 30 and Cys18 in SEQ ID NO: 10 or SEQ ID NO: 11, Cys13 and Cys 36 in SEQ ID NO: 10 or SEQ ID NO: 11, Cys13 and Cys 38 in SEQ ID NO: 10 or SEQ ID NO: 11, and/or Cys 36 and Cys 38 in SEQ ID NO: 10 or SEQ ID NO: 11.

In some examples, when T is 2, the pair of sulfur atoms are (e.g., the sulfur atoms corresponding to) Cys10 and Cys13 in SEQ ID NO: 10 or SEQ ID NO: 11 or Cys 36 and Cys 38 in SEQ ID NO: 10 or SEQ ID NO: 11.

In some examples, the pair of sulfur atoms include one sulfur atom of a cysteine from each E, i.e., L-A along with the sulfur atoms to which it is attached forms a bridge between two Fc domains (e.g., two Fc domains comprising the sequence of SEQ ID NO: 10 or SEQ ID NO: 11). In some examples, the pair of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E. In some examples, the pair of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E. In some examples, the pair of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E. In some examples, the pair of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E.

In some examples, when T is 2, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E. In some examples, when T is 2, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E. In some examples, when T is 2, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E.

In some examples, when T is 2, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E. In some examples, when T is 2, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E.

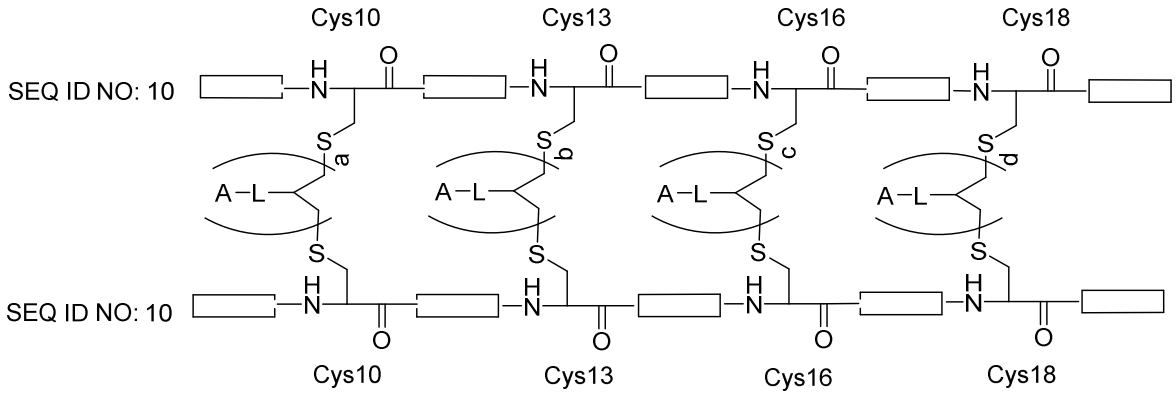
In some examples, when T is 2, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E.

In some examples, when T is 3, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E; the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E; and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E. In some examples, when T is 3, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E; the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E; and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E. In some examples, when T is 3, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E; the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E; and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E. In some examples, when

T is 3, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E; the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E; and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E.

In some examples, when T is 3, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E; the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E; the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys16 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E; and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys18 of SEQ ID NO: 10 or SEQ ID NO: 11 from another E.

In some examples, the conjugate has the structure:



wherein each of a, b, c, and d is, independently, 0 or 1 and wherein when a, b, c, or d is 0, the two sulfur atoms form a disulfide bond.

In some examples, a is 1 and b, c, and d are 0. In some examples, a and b are 1 and c and d are 0. In some examples, a and c are 1 and b and d are 0. In some examples, a and d are 1 and b and c are 0. In some examples, a, b, and c are 1 and d is 0. In some examples, a, b, and d are 1 and c is 0. In some examples, a, c, and d are 1 and b is 0. In some examples, b and c are 1 and a and d are 0. In some examples, b and d are 1 and a and c are 0. In some examples, b, c, and d are 1 and a is 0. In some examples, c and d are 1 and a and b are 0. In some examples, a, b, c, and d are 1.

In some examples, each E comprises the sequence

MVRSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR

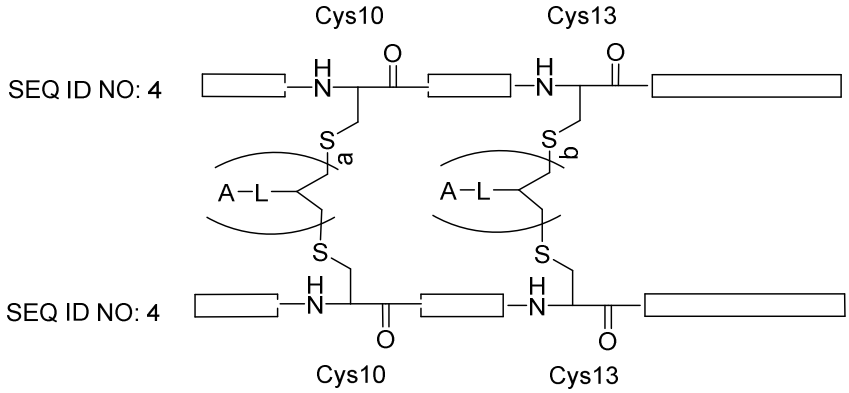
EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 4).

In some examples, each E comprises the sequence
MVRSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 33).

In some examples, at least one of the pair of sulfur atoms is the sulfur atom corresponding to (e.g., the sulfur atom of) a hinge cysteine of SEQ ID NO: 4 or SEQ ID NO: 33, i.e., Cys10 and/or Cys13. In some examples, the pair of sulfur atoms are the sulfur atoms corresponding to (e.g., the sulfur atoms of) Cys10 and Cys13 in SEQ ID NO: 4 or SEQ ID NO: 33.

In some examples, the pair of sulfur atoms include one sulfur atom of a cysteine from each E, i.e., L-A along with the sulfur atoms to which it is attached forms a bridge between two Fc domains (e.g., two Fc domains comprising the sequence of SEQ ID NO: 4 or SEQ ID NO: 33). In some examples, the pair of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 4 or SEQ ID NO: 33 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 4 or SEQ ID NO: 33 from another E. In some examples, the pair of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 4 or SEQ ID NO: 33 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 4 or SEQ ID NO: 33 from another E. In some examples, when T is 2, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 4 or SEQ ID NO: 33 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 4 or SEQ ID NO: 33 from another E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 4 or SEQ ID NO: 33 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 4 or SEQ ID NO: 33 from another E.

In some examples, the conjugate has the structure:



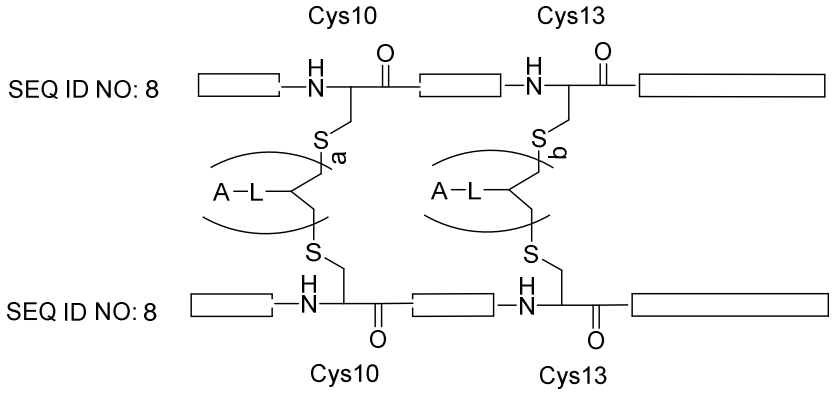
wherein each of a and b is, independently, 0 or 1 and wherein when a or b is 0, the two sulfur atoms form a disulfide bond. In some examples, a is 1 and b is 0. In some examples, a is 0 and b is 1. In some examples, a and b are 1.

In some examples, at least one of the pair of sulfur atoms is the sulfur atom corresponding to (e.g., the sulfur atom of) a hinge cysteine of SEQ ID NO: 8, i.e., Cys10 and/or Cys13. In some

examples, the pair of sulfur atoms are the sulfur atoms corresponding to (e.g., the sulfur atoms of) Cys10 and Cys13 in SEQ ID NO: 8.

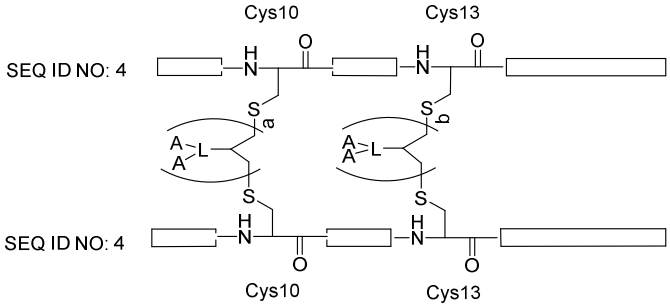
In some examples, the pair of sulfur atoms include one sulfur atom of a cysteine from each E, i.e., L-A along with the sulfur atoms to which it is attached forms a bridge between two Fc domains (e.g., two Fc domains comprising the sequence of SEQ ID NO: 8). In some examples, the pair of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 8 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 8 from another E. In some examples, the pair of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 8 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 8 from another E. In some examples, when T is 2, the pairs of sulfur atoms are the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 8 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys10 of SEQ ID NO: 8 from another E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 8 from one E and the sulfur atom corresponding to (e.g., the sulfur atom of) Cys13 of SEQ ID NO: 8 from another E.

In some examples, the conjugate has the structure:



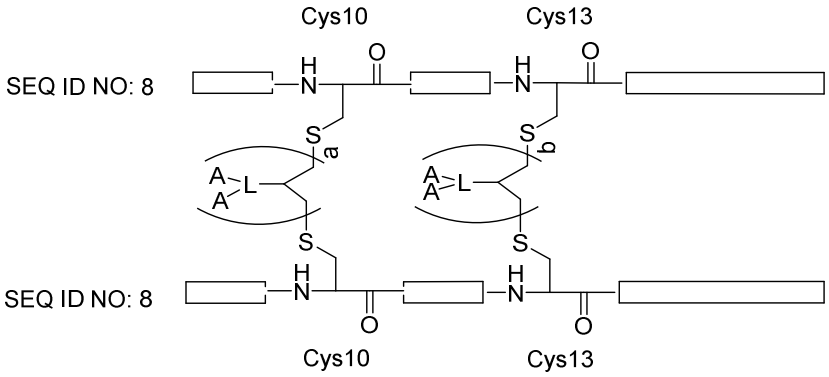
wherein each of a and b is, independently, 0 or 1 and wherein when a or b is 0, the two sulfur atoms form a disulfide bond. In some examples, a is 1 and b is 0. In some examples, a is 0 and b is 1. In some examples, a and b are 1.

In some examples, the conjugate has the structure:



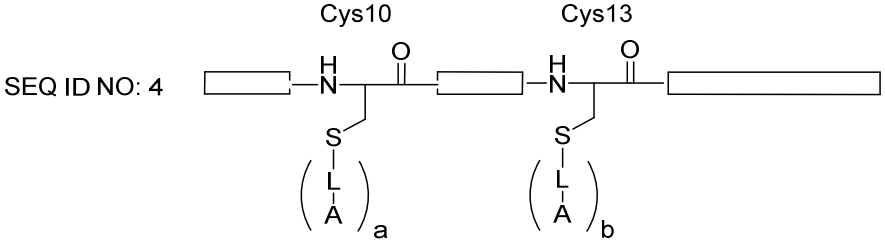
wherein each of a and b is, independently, 0 or 1 and wherein when a or b is 0, the two sulfur atoms form a disulfide bond. In some examples, a is 1 and b is 0. In some examples, a is 0 and b is 1. In some examples, a and b are 1.

In some examples, the conjugate has the structure:



wherein each of a and b is, independently, 0 or 1 and wherein when a or b is 0, the two sulfur atoms form a disulfide bond. In some examples, a is 1 and b is 0. In some examples, a is 0 and b is 1. In some examples, a and b are 1.

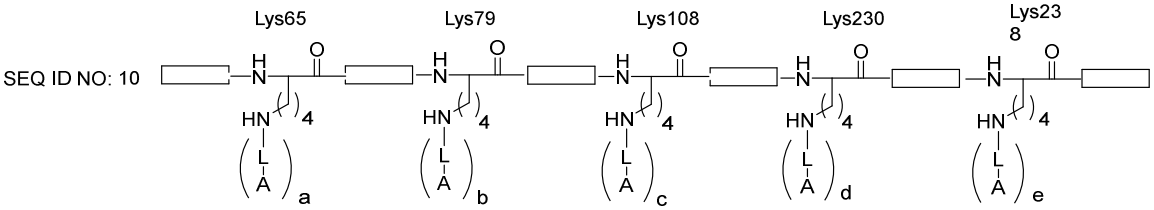
In some examples, the conjugate has the structure:



wherein each of a and b is, independently, 0 or 1 and wherein when a or b is 0, the sulfur atoms is a thiol. In some examples, a is 1 and b is 0. In some examples, a is 0 and b is 1. In some examples, a and b are 1.

In some examples, the nitrogen atom is the nitrogen of a surface exposed lysine, e.g., the nitrogen atom corresponding to (e.g., the nitrogen atom of) Lys35, Lys63, Lys77, Lys79, Lys106, Lys123, Lys129, Lys181, Lys203, Lys228, or Lys236 of SEQ ID NO: 10 or SEQ ID NO: 11. In some examples, the nitrogen atom is the nitrogen atom corresponding to (e.g., the nitrogen atom of) Lys65, Lys79, Lys108, Lys230, and/or Lys238 of SEQ ID NO: 10 or SEQ ID NO: 11.

In some examples, the conjugate has the structure:

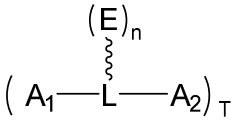


wherein each of a, b, c, d, and e is, independently, 0 or 1 and wherein when a, b, c, d, or e is 0, the two nitrogen atom is NH_2. In some examples, a is 1 and b, c, d, and e are 0. In some examples, b is 1 and a, c, d, and e are 0. In some examples, c is 1 and a, b, d, and e are 0. In some examples, d is 1 and a, b, c, and e are 0. In some examples, e is 1 and a, b, c, and d are 0. In some examples, a and b are 1 and c, d, and e are 0. In some examples, a and c are 1 and b, d, and e are 0. In some examples, a and d are 1 and b, c, and e are 0. In some examples, a and e are 1

and b, c, and d are 0. In some examples, b and c are 1 and a, d, and e are 0. In some examples, b and d are 1 and a, c, and e are 0. In some examples, b and e are 1 and a, c, and d are 0. In some examples, c and d are 1 and a, b, and e are 0. In some examples, c and e are 1 and a, b, and d are 0. In some examples, d and e are 1 and a, b, and c are 0. In some examples, a, b, and c are 1 and d and e are 0. In some examples, a, b, and d are 1 and c and e are 0. In some examples, a, b, and e are 1 and c and d are 0. In some examples, a, c, and d are 1 and b and e are 0. In some examples, a, c, and e are 1 and b and d are 0. In some examples, a, d, and e are 1 and b and c are 0. In some examples, b, c, and d are 1 and a and e are 0. In some examples, b, d, and e are 1 and a and c are 0. In some examples, c, d, and e are 1 and a and b are 0.

In some examples of any of the conjugates described herein, the conjugate forms a homodimer including an Fc domain. In some examples of the conjugates described herein, E homodimerizes with another E to form an Fc domain.

In another example, the disclosure features a conjugate described by (D-I):

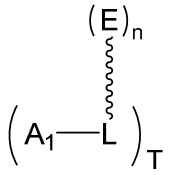


(D-I)

wherein E includes an albumin protein (e.g., an albumin protein having the sequence of any one of SEQ ID NOs: 139-141), an albumin protein-binding peptide, or an Fc-binding peptide; L in each A_1-L-A_2 is a linker independently covalently attached to a sulfur atom of a surface exposed cysteine or a nitrogen atom of a surface exposed lysine in E and to each of A_1 and A_2; n is 1; T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), and the squiggly line connected to the E indicates that each A_1-L-A_2 is independently covalently attached to the sulfur atom of a solvent-exposed cysteine or the nitrogen atom of a solvent-exposed lysine in E, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1-L-A_2 may be independently selected (e.g., independently selected from any of the A_1-L-A_2 structures described herein). In some examples, each of A_1 A_2 may be independently selected from any one of formulas (A-I), (A-II), (A-VI), or (A-VII). In other examples, each of A_1 A_2 may be independently selected from formula (A-I).

In a preferred example of the above, x is 2.

In another example, the disclosure features a conjugate described by formula (M-I):



(M-I)

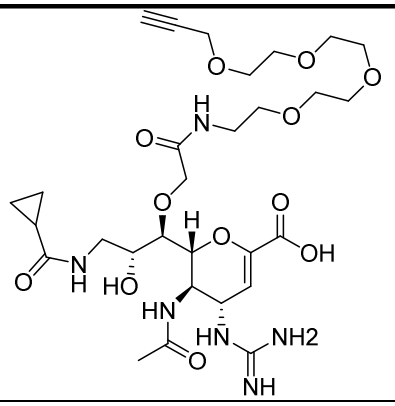
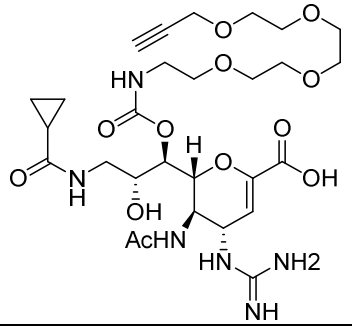
wherein E includes an albumin protein (e.g., an albumin protein having the sequence of any one of SEQ ID NOs: 139-141), an albumin protein-binding peptide, or an Fc-binding peptide; L in each L-A_1 is a linker independently covalently attached to a sulfur atom of a surface exposed cysteine or a nitrogen atom of a

surface exposed lysine in E and to A_1; n is 1; T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20); and the squiggly line connected to E indicates that each L-A_1 is independently covalently attached to the sulfur atom of the solvent-exposed cysteine or the nitrogen atom of the solvent-exposed lysine in E, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1 may be independently selected from any structure described by formula (A-I)-(A-XII). In some examples, each A_1 may be independently selected from any one of formulas (A-I), (A-II), (A-VI), or (A-VII). In other examples, each A_1 may be independently selected from formula (A-I). In a preferred example of the above, x is 2.

In some examples, each E includes an albumin protein having the sequence of any one of SEQ ID NOs: 139-141.

In some examples, T is 1 and L-A_1 is covalently attached to the sulfur atom corresponding to Cys34 of SEQ ID NO: 139.

Intermediates of Table 1a may be conjugated to an Fc domain or Fc domain monomer (e.g., by way of a linker) by any suitable methods known to those of skill in the art, including any of the methods described or exemplified herein. In some examples, the conjugate (e.g., a conjugate described by any one of formulas (1), (2), (D-I)-(D-XI), or (M-I)-(M-XI)) includes E, wherein E is an Fc domain monomer or an Fc domain (e.g., an Fc domain monomer or an Fc domain, each Fc domain monomer having, independently, the sequence of any one of SEQ ID NOs: 1-138). In preferred examples, one or more nitrogen atoms of one or more surface exposed lysine residues of E or one or more sulfur atoms of one or more surface exposed cysteines in E is covalently conjugated to a linker (e.g., a PEG_2-PEG_{20} linker). The linker conjugated to E may be functionalized such that it may react to form a covalent bond with any of the Ints described herein (e.g., an Int of Table 1a). In preferred examples, E is conjugated to a linker functionalized with an azido group and the Int (e.g., an Int of Table 1a) is functionalized with an alkyne group. Conjugation (e.g., by click chemistry) of the linker-azido of E and linker-alkyne of the Int forms a conjugate of the disclosure, for example a conjugate described by formula (5). In yet other examples, E is conjugated to a linker functionalized with an alkyne group and the Int (e.g., an Int of Table 1a) is functionalized with an azido group. Conjugation (e.g., by click chemistry; see, e.g., FIG. 103) of the linker-alkyne of E and linker-azido of the Int forms a conjugate of the disclosure, for example a conjugate described by any one of formulas (1), (2), (D-I)-(D-XI), or (M-I)-(M-XI).

Int-91	
Int-92	

In another example, the disclosure features conjugates of Table 1b. Each conjugate of Table 1b corresponds to a conjugate of either formula (M-I) or formula (D-I), as indicated. Conjugates of Table 1b include conjugates formed by the covalent reaction of an Int of Table 1a with a linker which is in turn conjugated to E (e.g., an Fc domain monomer, an albumin protein, an albumin protein-binding peptide, or an Fc-binding peptide). In some examples, the reactive moiety of the Int (e.g., the alkyne or azido group) reacts with a corresponding reactive group (e.g., an alkyne or azido group) of a linker (represented by L') covalently attached to E, such that an Int of Table 1a is covalently attached to E. As represented in Table 1b, L' corresponds to the remainder of L as defined in (M-1) or (D-I) (e.g., L' is a linker that covalently joins the Int and E). For example, L' may include a triazole (formed by the click chemistry reaction between the Int and a linker conjugated to E) and a linker (e.g., a PEG_2-PEG_{20} linker) which in turn is conjugated to an amino acid side chain of E (see, e.g., FIG. 103).

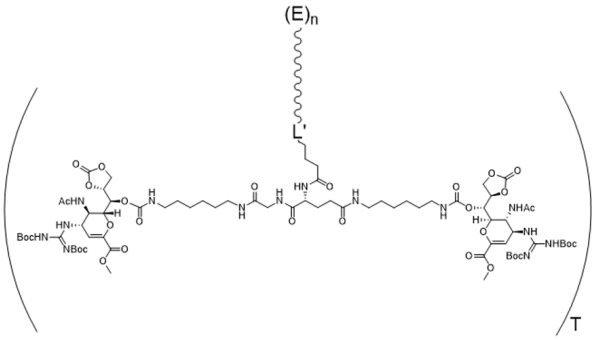
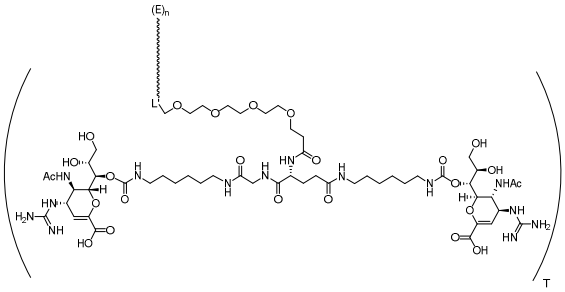
In some examples the conjugate of Table 1b, n is 1 or 2. When n is 1, each E includes an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138), an albumin protein (e.g., an albumin protein having a sequence of any one of SEQ ID NOs: 139-141), an albumin protein-binding peptide, or an Fc-binding peptide. When n is 2, each E includes an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138), and the Fc domain monomers dimerize to form an Fc domain.

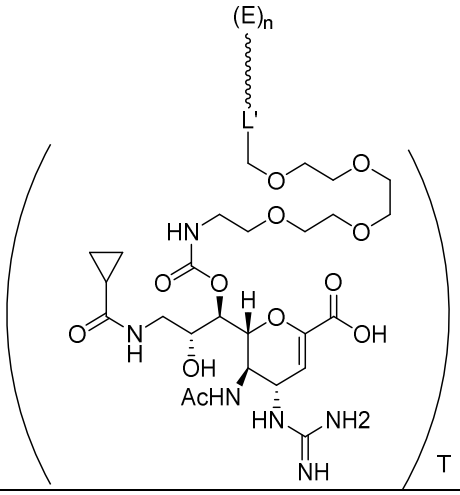
In some examples of any conjugate of Table 1b, T is an integer from 1 to 20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20). The disclosure also provides a population of any of the conjugates of Table 2 wherein the average value of T is 1 to 20 (e.g., the average value of T is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5). In some examples, the average value of T is 1, 2, 3, 4, 5, 6,

7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20. In certain examples, the average T is 1 to 10 (e.g., 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5, 9, 9.5, or 10). In certain examples, the average T is 1 to 5 (e.g., 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, or 5). In some example, the average T is 5 to 10 (e.g., 5, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10). In some examples, the average T is 2.5 to 7.5 (e.g., 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7, 7.1, 7.2, 7.3, 7.4, or 7.5).

The squiggly line in the conjugates of Table 1b indicates that each L'-Int is covalently attached to an amino acid side chain in E (e.g., the nitrogen atom of a surface exposed lysine or the sulfur atom of a surface exposed cysteine in E), or a pharmaceutically acceptable salt thereof.

Table 1b: Conjugates Corresponding to Intermediates of Table 1a

Corresponding Intermediate of Table 1a	**Described by Formula**	**Conjugate Structure**
Int-1	(D-I)	
Int-2	(D-I)	

Int-92	(M-I)	

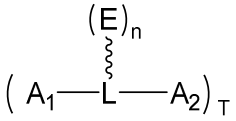
In some examples, each E includes an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138. In other examples, each E includes an Fc domain monomer having a sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64. In other examples, each E includes an Fc domain monomer having the amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64. In other examples, each E includes an Fc domain monomer having a sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 67 or SEQ ID NO: 68. In other examples, each E includes an Fc domain monomer having the amino acid sequence of SEQ ID NO: 67 or SEQ ID NO: 68. In other examples, each E includes an Fc domain monomer having a sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 72 or SEQ ID NO: 73. In other examples, each E includes an Fc domain monomer having the amino acid sequence of SEQ ID NO: 72 or SEQ ID NO: 73. In other examples, each E includes an Fc domain monomer having a sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 76 or SEQ ID NO: 77. In other examples, each E includes an Fc domain monomer having the amino acid sequence of SEQ ID NO: 76 or SEQ ID NO: 77. In other examples, each E includes an Fc domain monomer having a sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 82. In other examples, each E includes an Fc domain monomer having the amino acid sequence of SEQ ID NO: 81 or SEQ ID NO: 82. In other examples, each E includes an Fc domain monomer having a sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 85 or SEQ ID NO: 86. In other examples, each E includes an Fc domain monomer having the amino acid sequence of SEQ ID NO: 85 or SEQ ID NO: 86.

In another example, the disclosure features a conjugate including (i) a first moiety, A_1; (ii) a second moiety, A_2; (iii) an Fc domain monomer or an Fc domain; and (iv) a linker covalently attached to A_1 and A_2, and to the Fc domain monomer or the Fc domain; wherein each A_1 and each A_2 is independently selected from any one of formulas (A-I)-(A-XII). In some examples, each of A_1 and A_2 may be independently selected from any one of formulas (A-I), (A-II), (A-VI), or (A-VII). In other examples, each of A_1 and A_2 may be independently selected from formula (A-I). In a preferred example of the above, x is 2.

In another example, the disclosure features a conjugate including (i) a first moiety, Int; (ii) an Fc domain monomer or an Fc domain; and (iv) a linker covalently attached to Int, and to the Fc domain monomer or the Fc domain; wherein each Int is independently selected from any one of the intermediates of Table 1a.

In another example, the disclosure features a conjugate including (i) a first moiety, A_1; (ii) a second moiety, A_2; (iii) an albumin protein, an albumin protein-binding peptide, or an Fc-binding peptide; and (iv) a linker covalently attached to A_1 and A_2, and to the albumin protein, the albumin protein-binding peptide, or the Fc-binding peptide; wherein each A_1 and each A_2 is independently selected from any one of formulas (A-I)-(A-XII). In some examples, each of A_1 and A_2 may be independently selected from any one of formulas (A-I), (A-II), (A-VI), or (A-VII). In other examples, each of A_1 and A_2 may be independently selected from formula (A-I). In a preferred example of the above, x is 2.

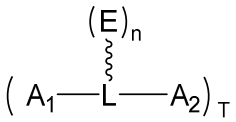
In another example, the disclosure features a conjugate described by formula (D-I):



(D-I)

wherein each A_1 and each A_2 is independently selected from any one of formulas (A-I)-(A-XII); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138), an albumin protein (e.g., an albumin protein having the sequence of any one of SEQ ID NOs: 139-141), an albumin protein-binding peptide, or an Fc-binding peptide; n is 1 or 2; T is an integer from 1 to 20 (e.g., T is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20); and L is a linker covalently attached to each of E, A_1, and A_2, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1-L-A_2 may be independently selected (e.g., independently selected from any of the A_1-L-A_2 structures described herein). In some examples, each of A_1 and A_2 may be independently selected from any one of formulas (A-I), (A-II), (A-VI), or (A-VII). In other examples, each of A_1 and A_2 may be independently selected from formula (A-I).

In another example, the disclosure features a conjugate described by formula (D-I):

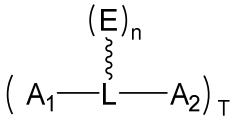


(D-I)

wherein each A_1 and each A_2 is independently selected from any one of formulas (A-I)-(A-V); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138), an albumin protein (e.g., an albumin protein having the sequence of any one of SEQ ID NOs: 139-141), an albumin protein-binding peptide, or an Fc-binding peptide; n is 1 or 2; T is an integer from 1 to 20 (e.g., T is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20); and L is a linker covalently attached to each of E, A_1, and A_2, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1-L-A_2

may be independently selected (e.g., independently selected from any of the A_1-L-A_2 structures described herein).

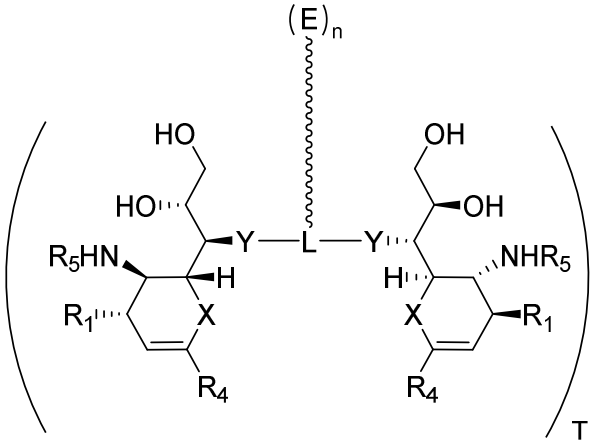
In another example, the disclosure features a conjugate described by formula (D-I):



(D-I)

wherein each A_1 and each A_2 is independently selected from any one of formulas (A-VI)-(A-IX); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138), an albumin protein (e.g., an albumin protein having the sequence of any one of SEQ ID NOs: 139-141), an albumin protein-binding peptide, or an Fc-binding peptide; n is 1 or 2; T is an integer from 1 to 20 (e.g., T is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20); and L is a linker covalently attached to each of E, A_1, and A_2, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1-L-A_2 may be independently selected (e.g., independently selected from any of the A_1-L-A_2 structures described herein).

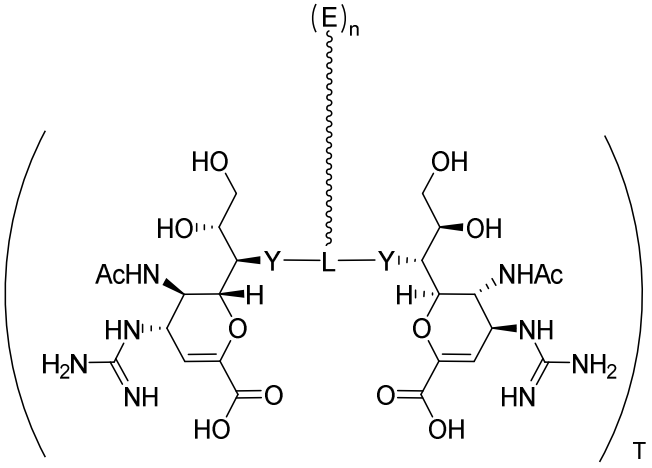
In some examples, the conjugate is described by formula (D-II):



(D-II)

or a pharmaceutically acceptable salt thereof.

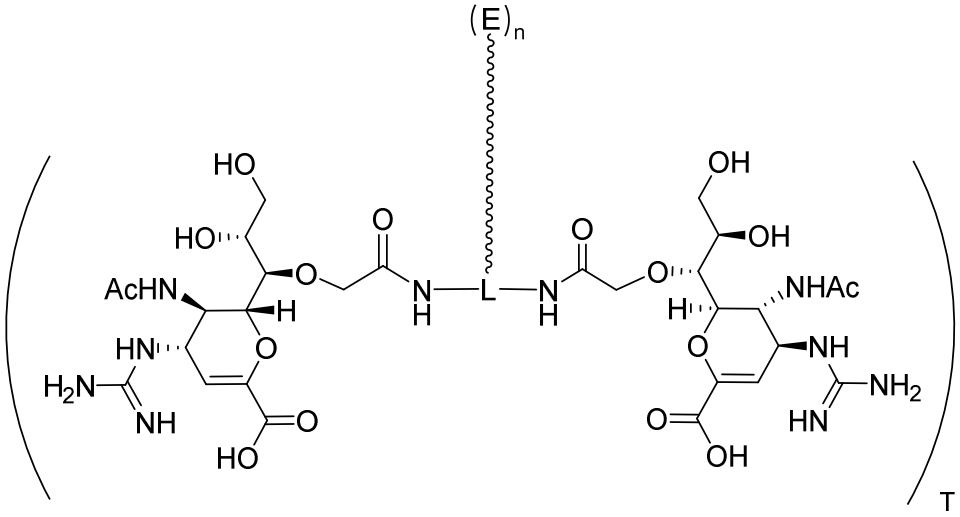
In some examples, the conjugate is described by formula (D-II-1):



(D-II-1)

or a pharmaceutically acceptable salt thereof.

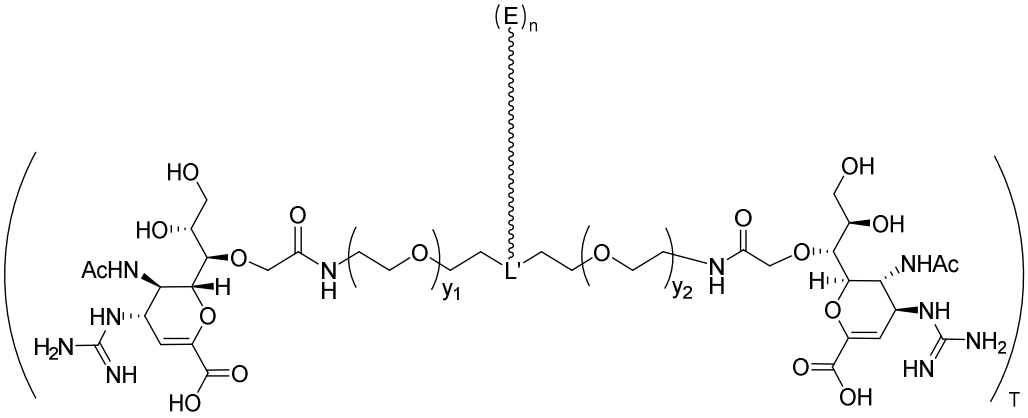
In some examples, the conjugate is described by formula (D-II-2):



(D-II-2)

or a pharmaceutically acceptable salt thereof.

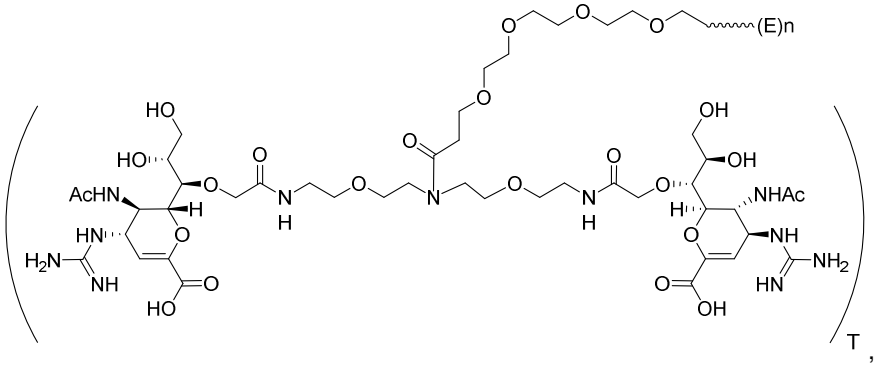
In some examples, the conjugate is described by formula (D-II-3):



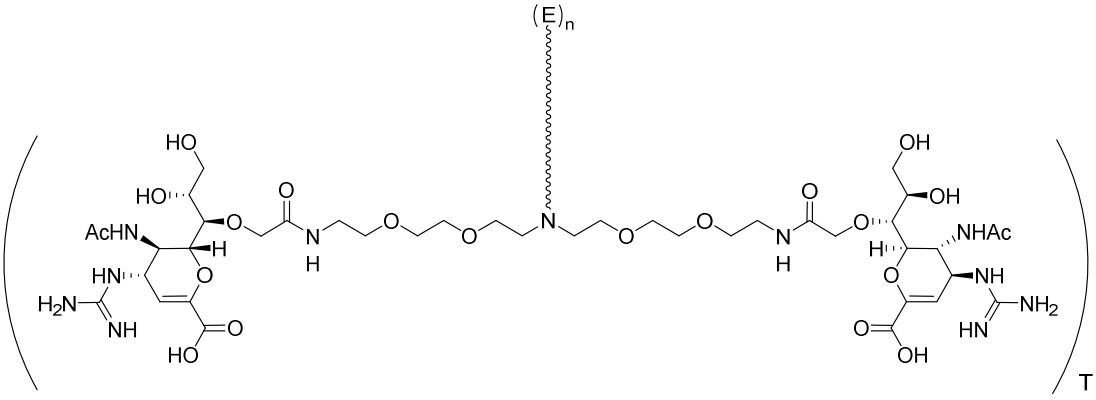
(D-II-3)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

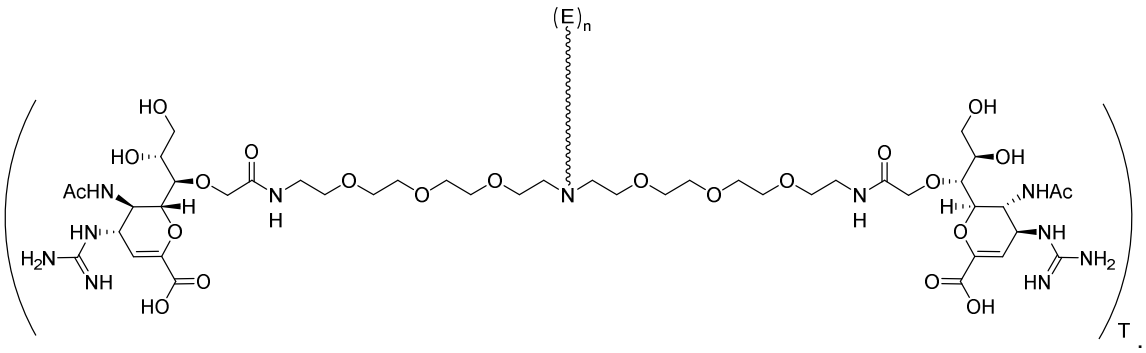
In some examples, the conjugate has the structure selected from:



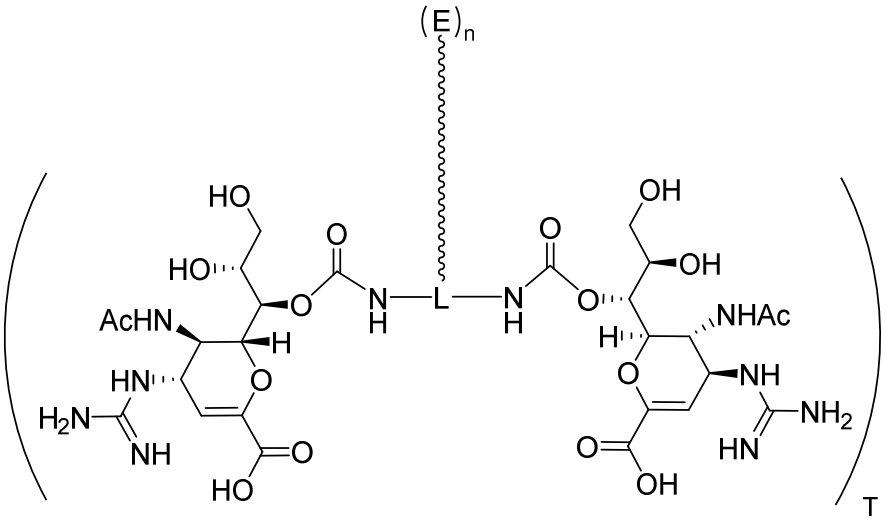
,



, or



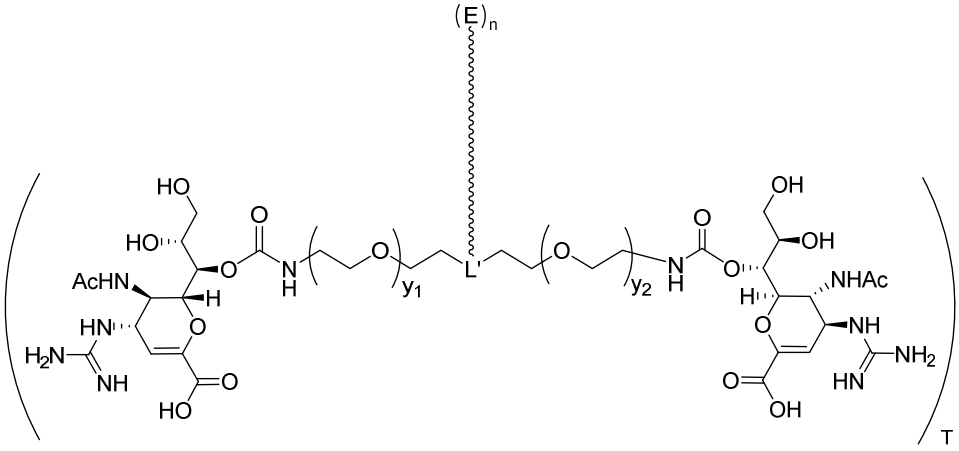
In some examples, the conjugate is described by formula (D-II-4):



(D-II-4)

or a pharmaceutically acceptable salt thereof.

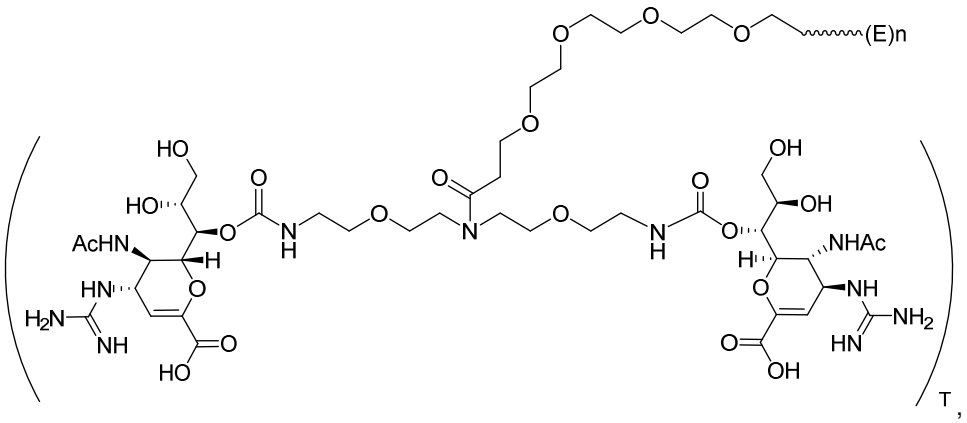
In some examples, the conjugate is described by formula (D-II-5):

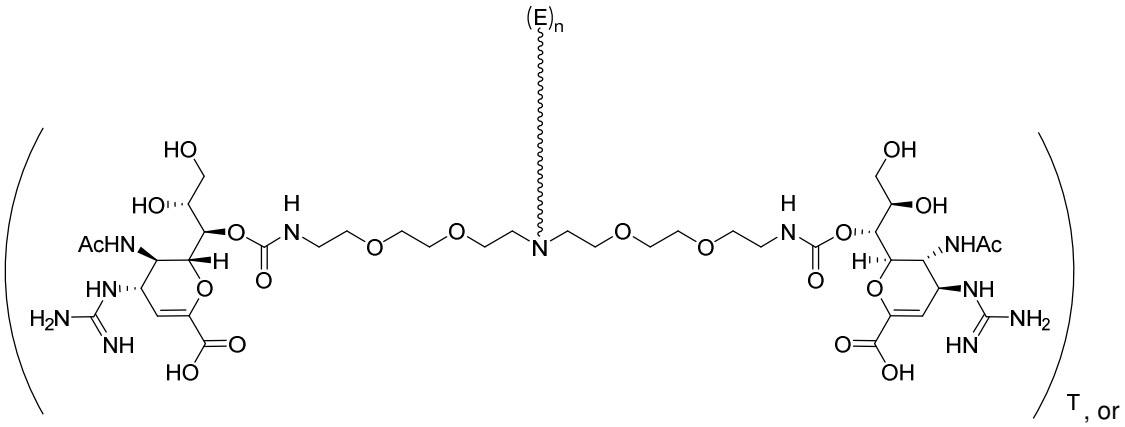


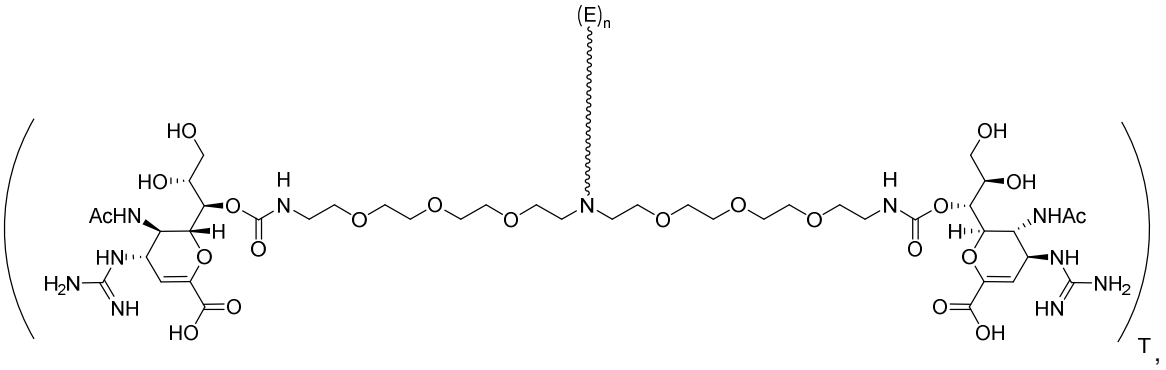
(D-II-5)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

In some examples, the conjugate has the structure selected from:

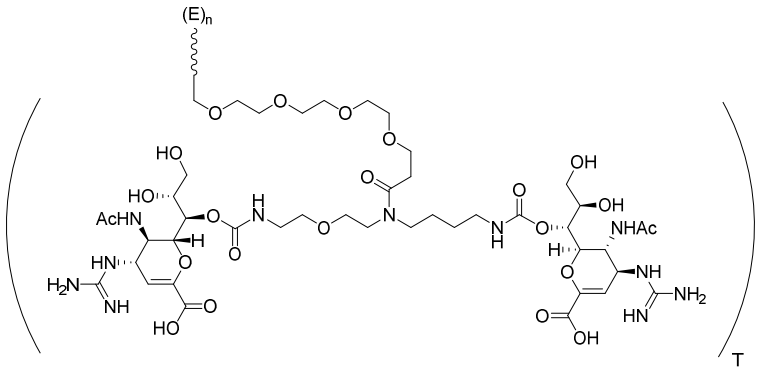




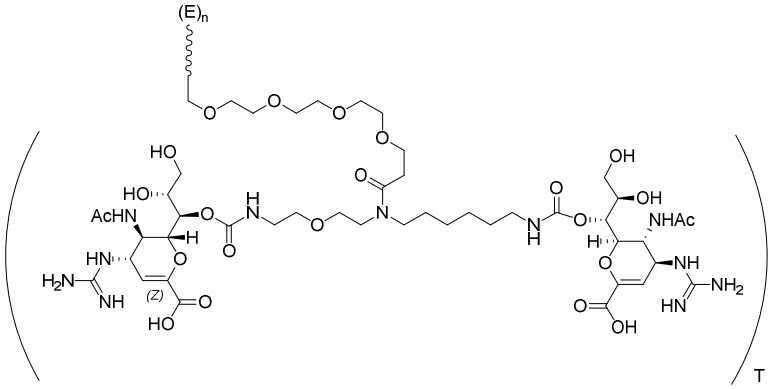


or a pharmaceutically acceptable salt thereof.

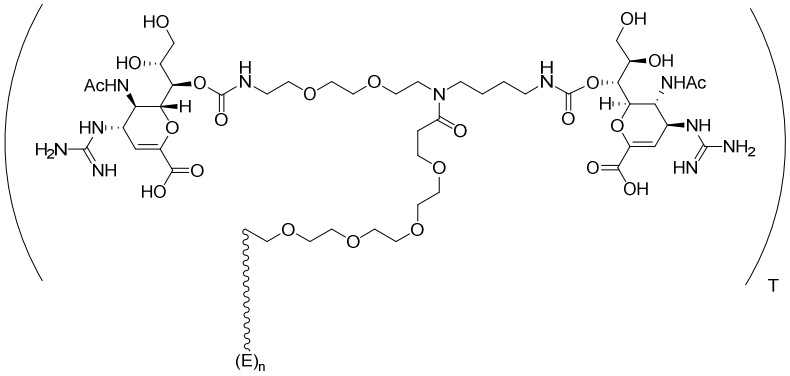
In some examples, the conjugate has the structure selected from:



T ,

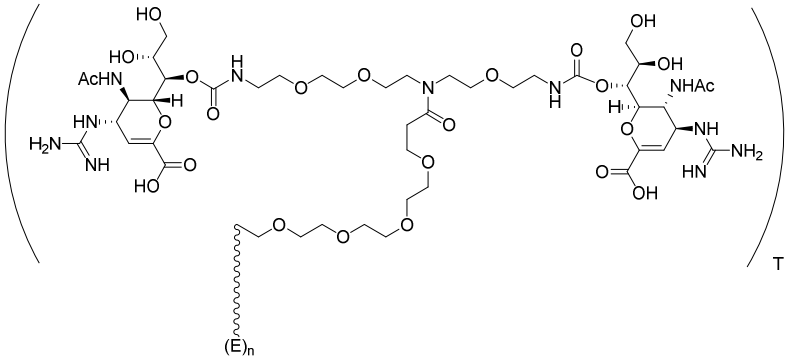


T ,



T

, or

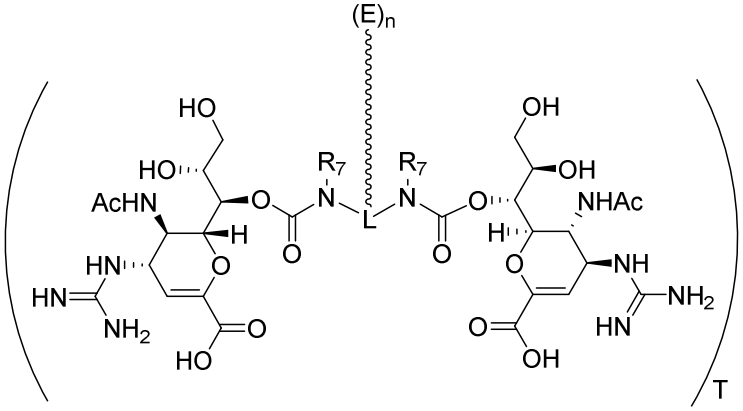


T

,

or a pharmaceutically acceptable salt thereof.

In one aspect, the present disclosure provides a conjugate described by formula (D-II-6):



(D-II-6)

wherein each E comprises an Fc domain monomer;

n is 1 or 2;

T is an integer from 1 to 20;

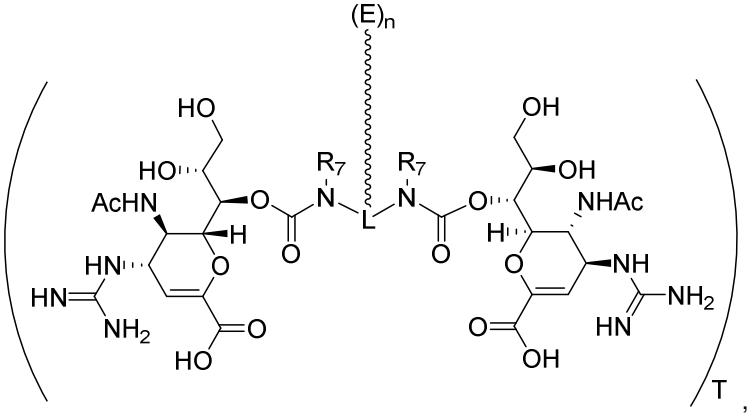
L is a linker;

R_7 is selected from C_1-C_{20} alkyl, C_3-C_{20} cycloalkyl, C_3-C_{20} heterocycloalkyl, C_5-C_{15} aryl, and C_2-C_{15} heteroaryl; and

the squiggly line indicates that L is covalently attached to E,

or a pharmaceutically acceptable salt thereof.

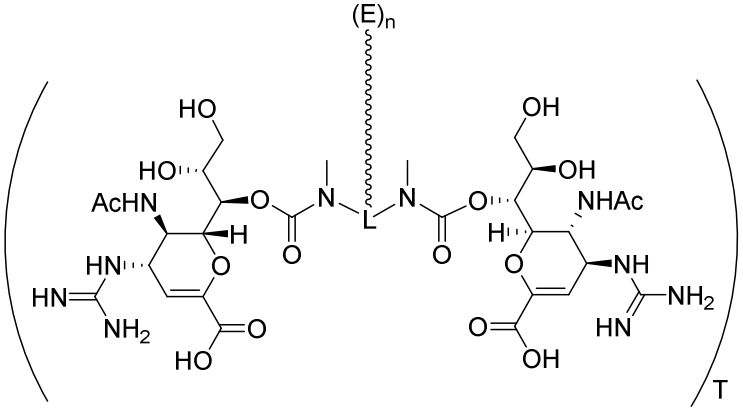
In some examples, the conjugate is described by formula (D-II-6):



(D-II-6)

wherein R_7 is selected from H, C1-C20 alkyl, C3-C20 cycloalkyl, C3-C20 heterocycloalkyl; C5-C15 aryl, and C2-C15 heteroaryl; or a pharmaceutically acceptable salt thereof. In some examples, R_7 is selected from C1-C20 alkyl (e.g., methyl, ethyl, propyl, or butyl).

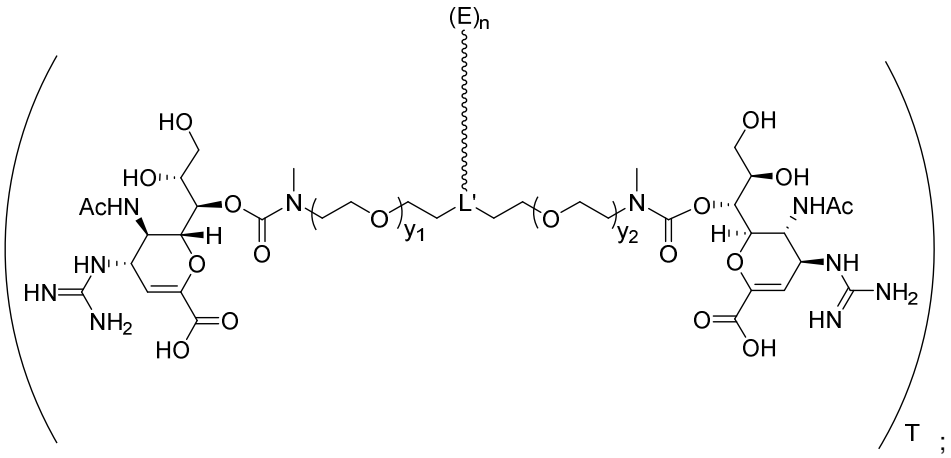
In some examples, the conjugate is described by formula (D-II-7):



(D-II-7)

or a pharmaceutically acceptable salt thereof.

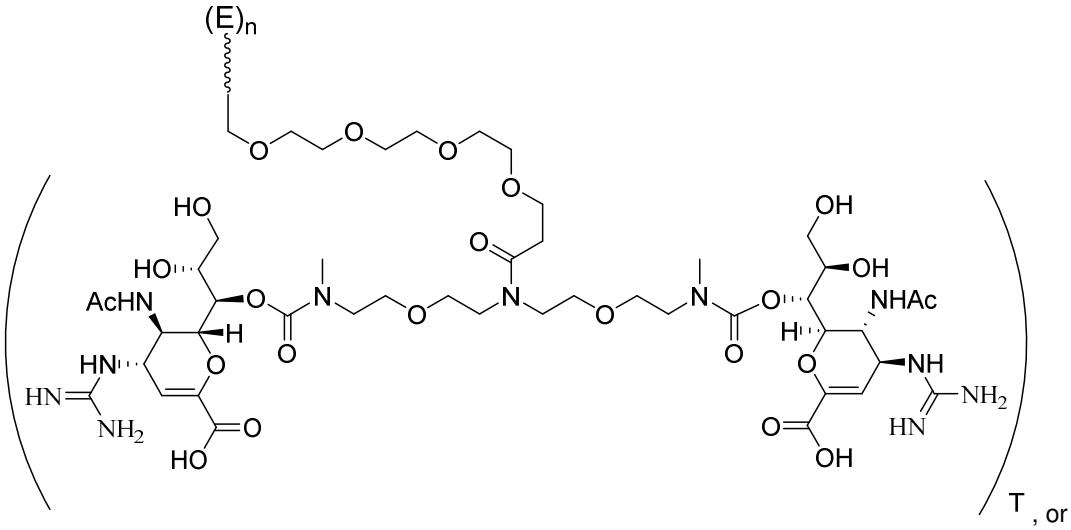
In some examples, the conjugate is described by formula (D-II-8):



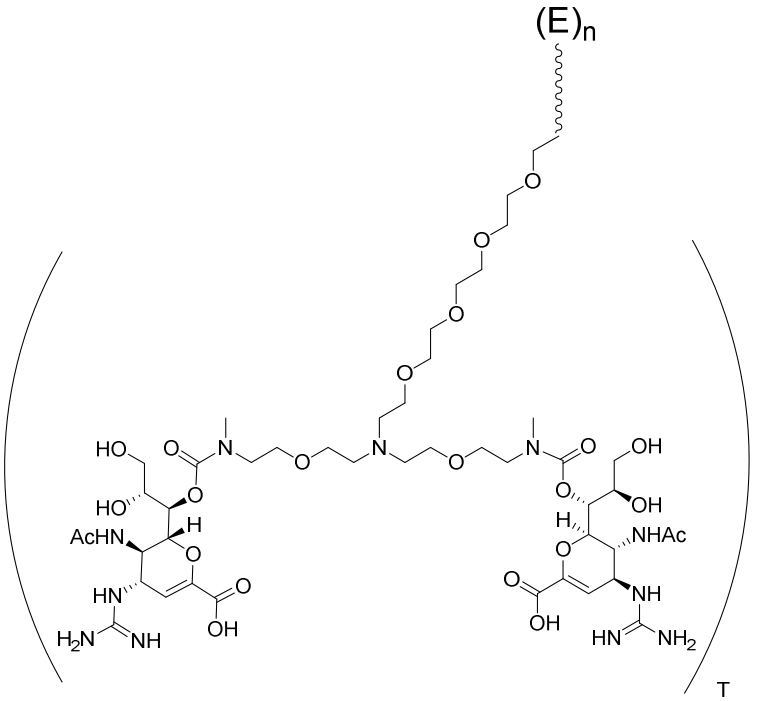
(D-II-8)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

In some examples, the conjugate has the structure



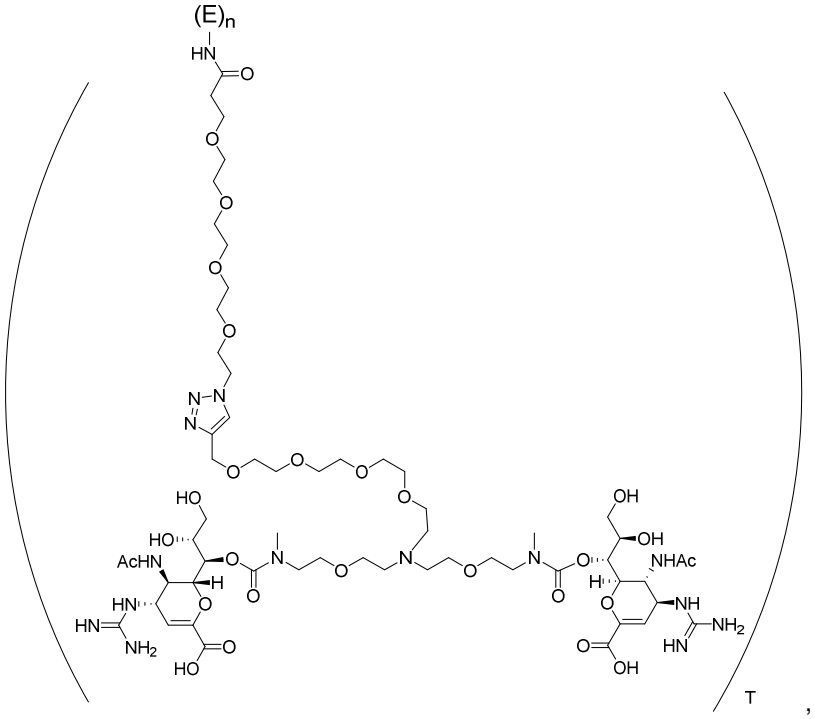
T , or



T ,

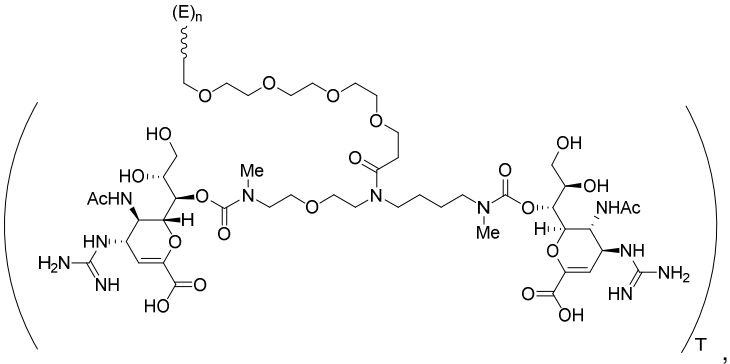
or a pharmaceutically acceptable salt thereof.

In some examples, the conjugate has the structure

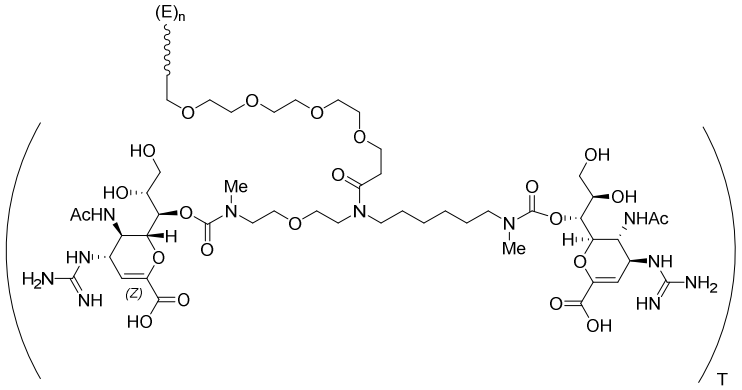


or a pharmaceutically acceptable salt thereof.

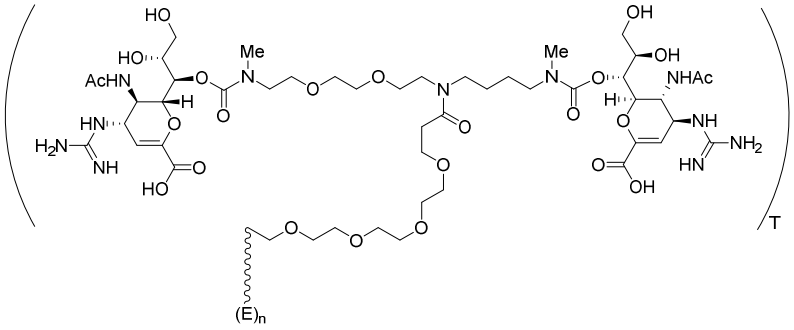
In some examples, the conjugate has the structure



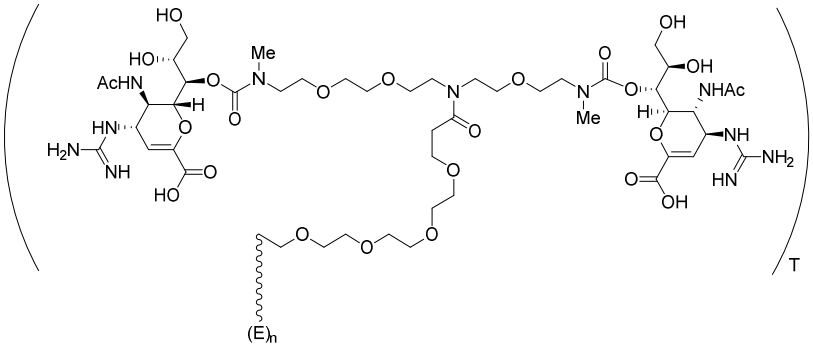
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,



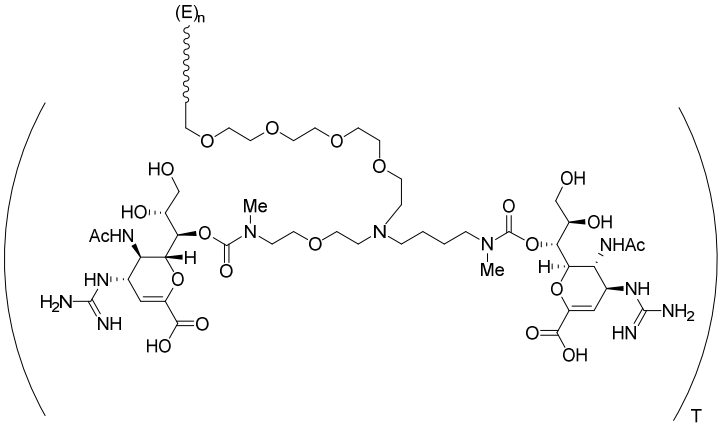
, or



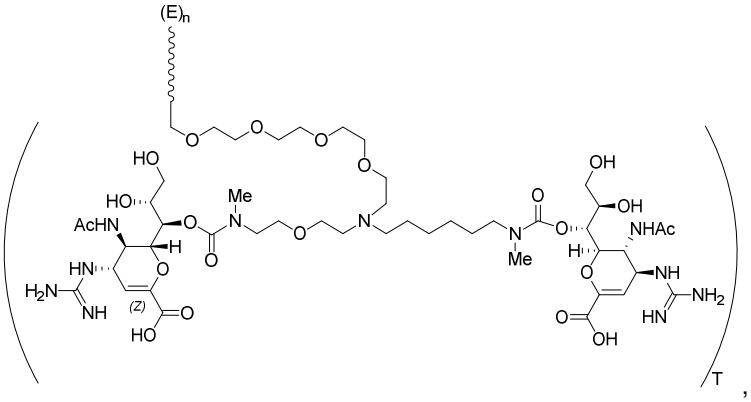
,

or a pharmaceutically acceptable salt thereof.

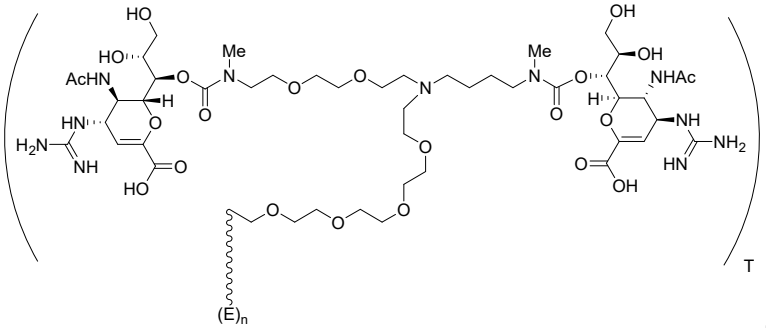
In some examples, the conjugate has the structure



T ,

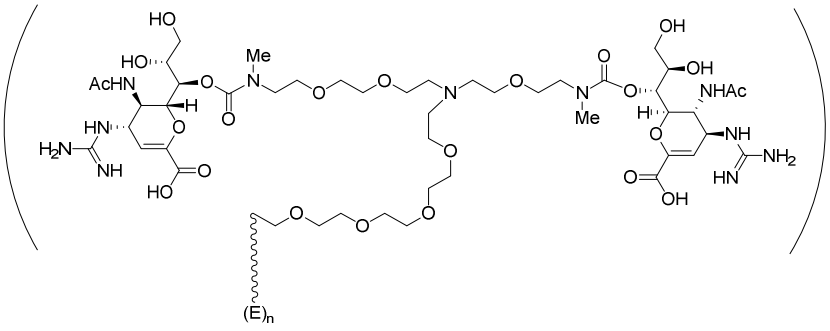


T ,



T

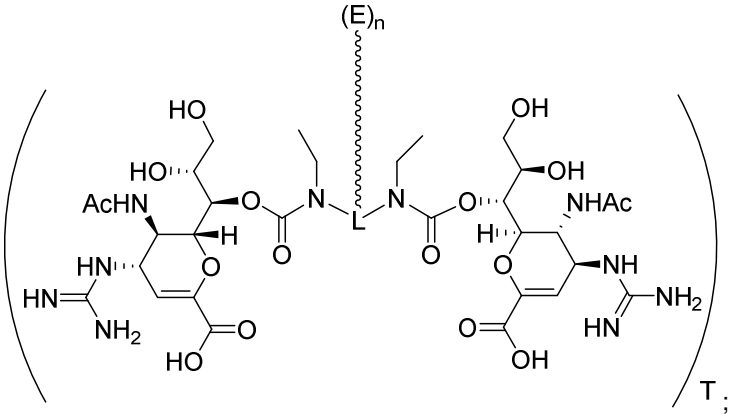
, or



,

or a pharmaceutically acceptable salt thereof.

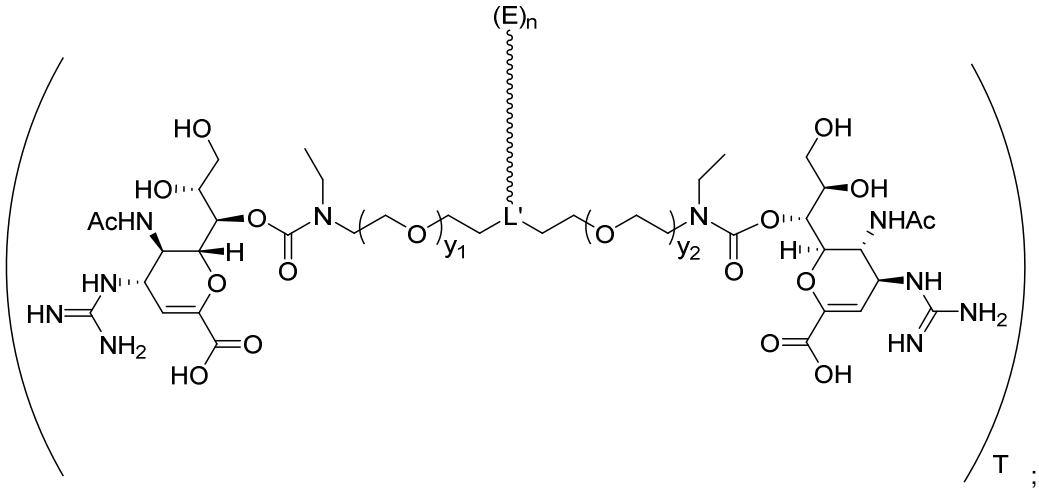
In some examples, the conjugate is described by formula (D-II-9):



(D-II-9)

or a pharmaceutically acceptable salt thereof.

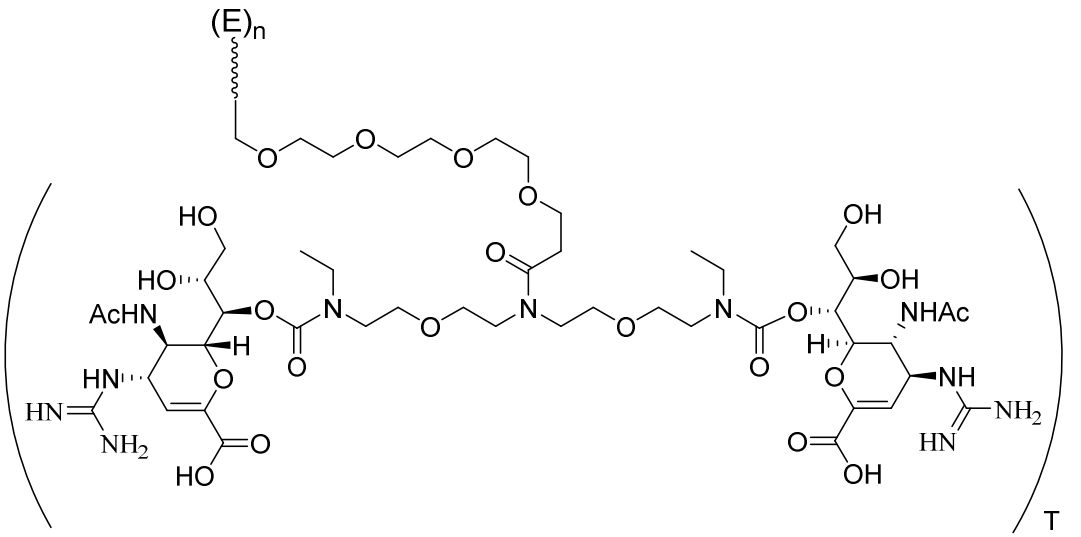
In some examples, the conjugate is described by formula (D-II-10):



(D-II-10)

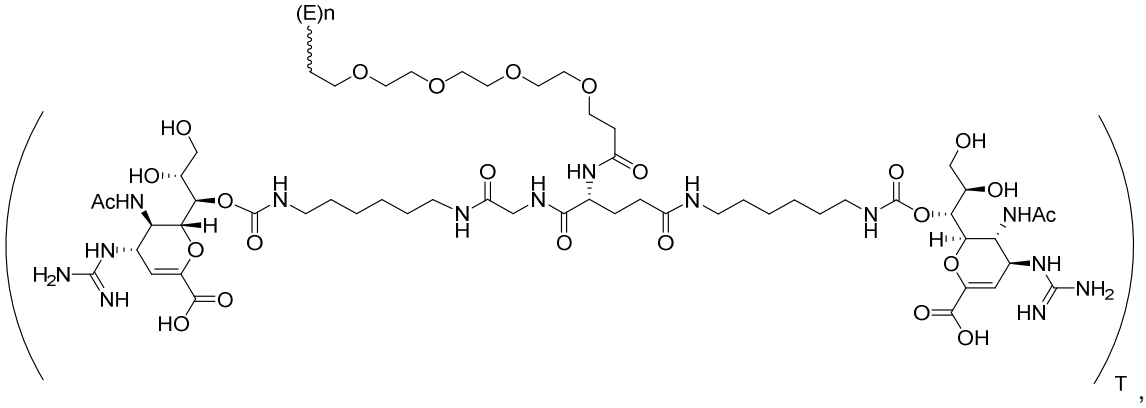
wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

In some examples, the conjugate has the structure



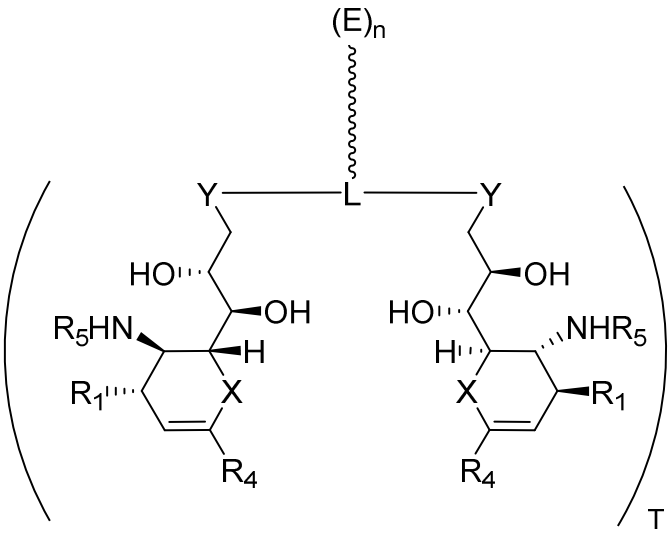
or a pharmaceutically acceptable salt thereof.

In some examples, the conjugate has the structure of



or a pharmaceutically acceptable salt thereof.

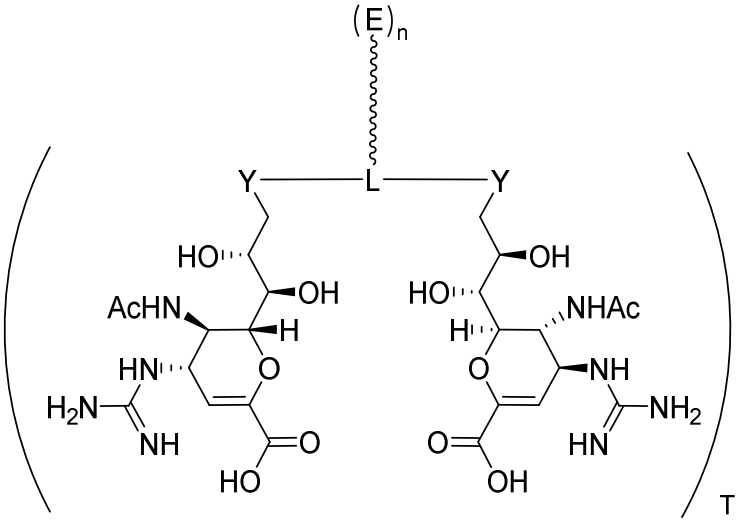
In some examples, the conjugate is described by formula (D-III):



(D-III)

or a pharmaceutically acceptable salt thereof.

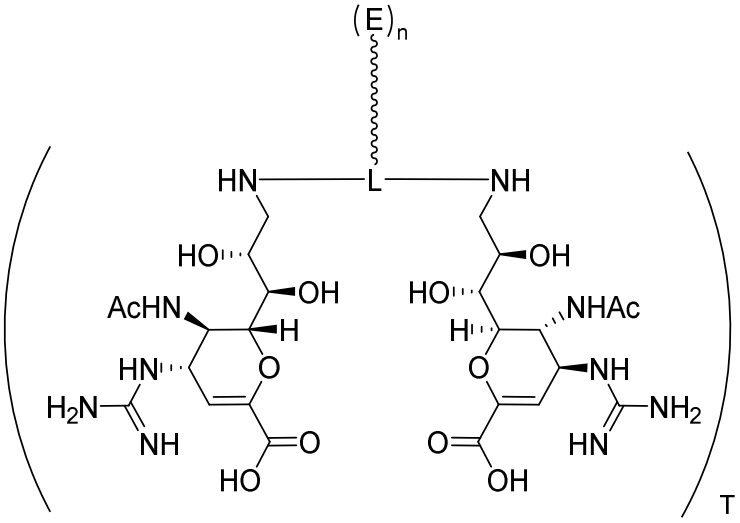
In some examples, the conjugate is described by formula (D-III-1):



(D-III-1)

or a pharmaceutically acceptable salt thereof.

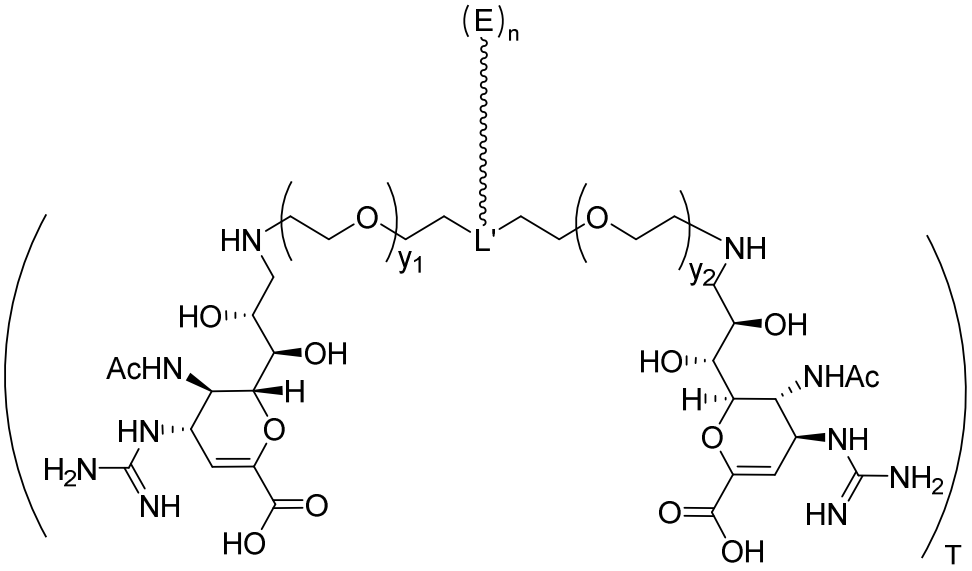
In some examples, the conjugate is described by formula (D-III-2):



(D-III-2)

or a pharmaceutically acceptable salt thereof.

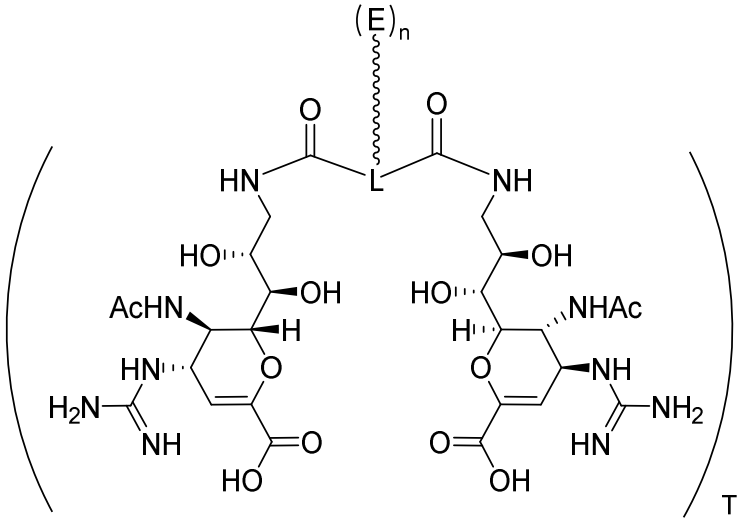
In some examples, the conjugate is described by formula (D-III-3):



(D-III-3)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

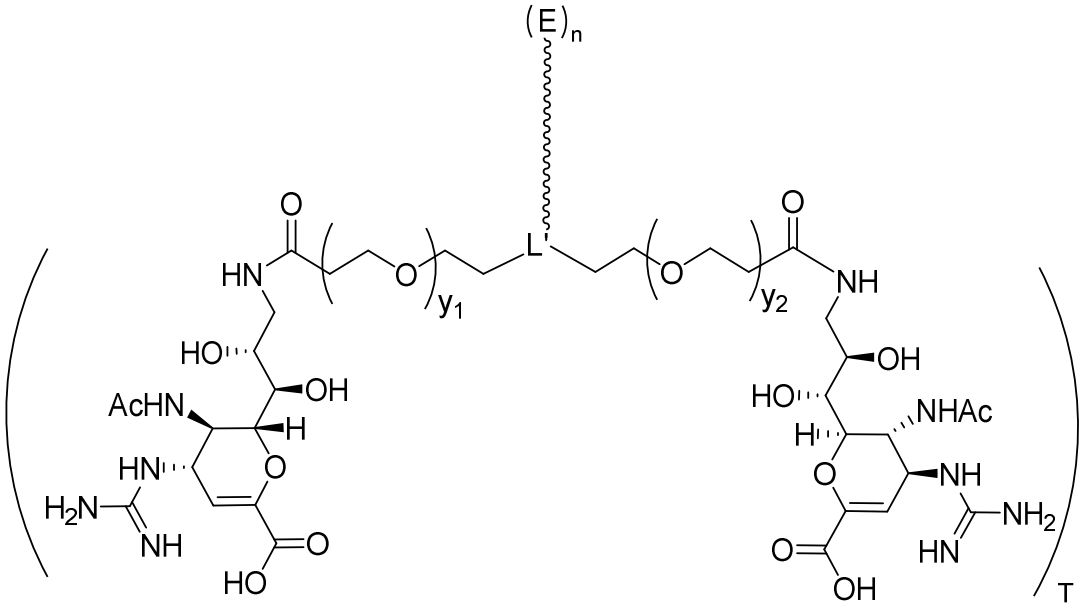
In some examples, the conjugate is described by formula (D-III-4):



(D-III-4)

or a pharmaceutically acceptable salt thereof.

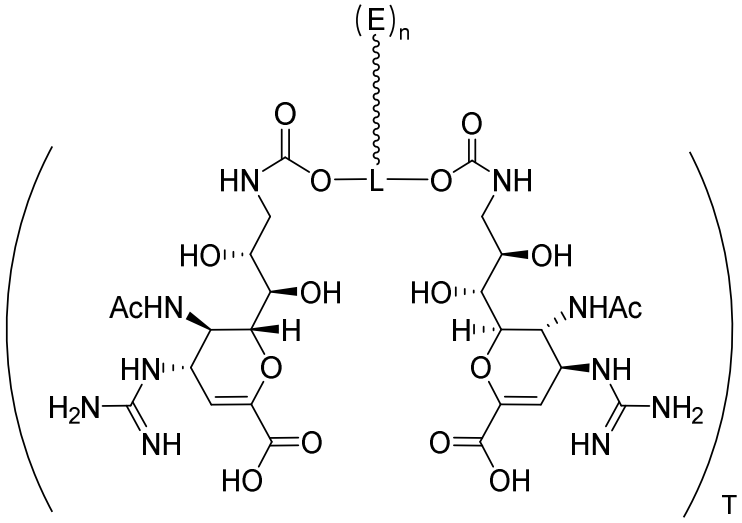
In some examples, the conjugate is described by formula (D-III-5):



(D-III-5)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

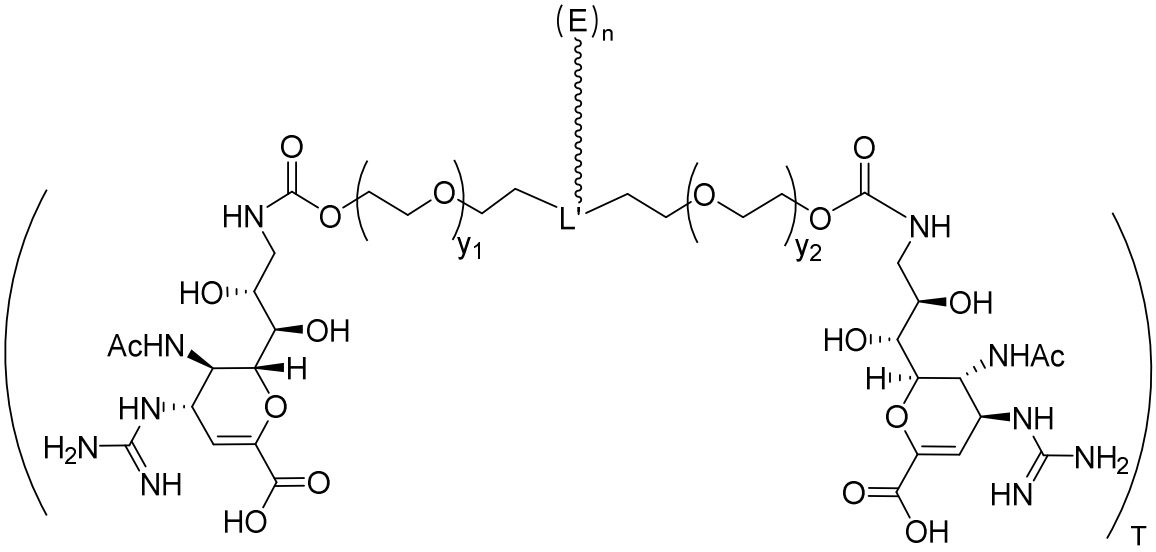
In some examples, the conjugate is described by formula (D-III-6):



(D-III-6)

or a pharmaceutically acceptable salt thereof.

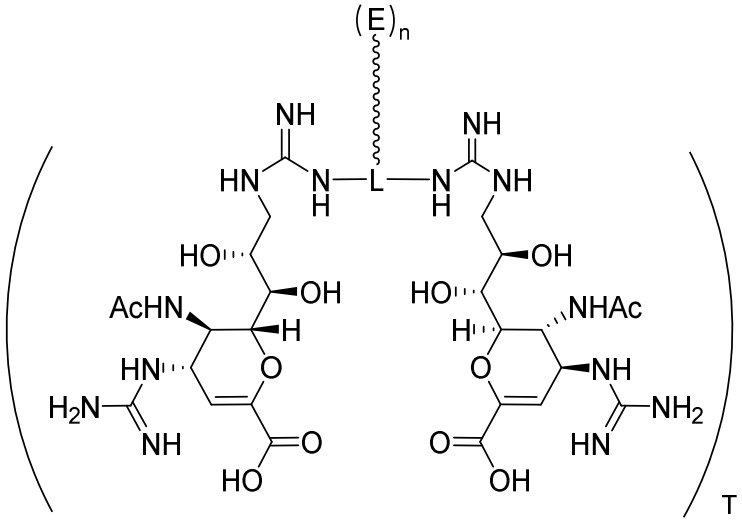
In some examples, the conjugate is described by formula (D-III-7):



(D-III-7)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

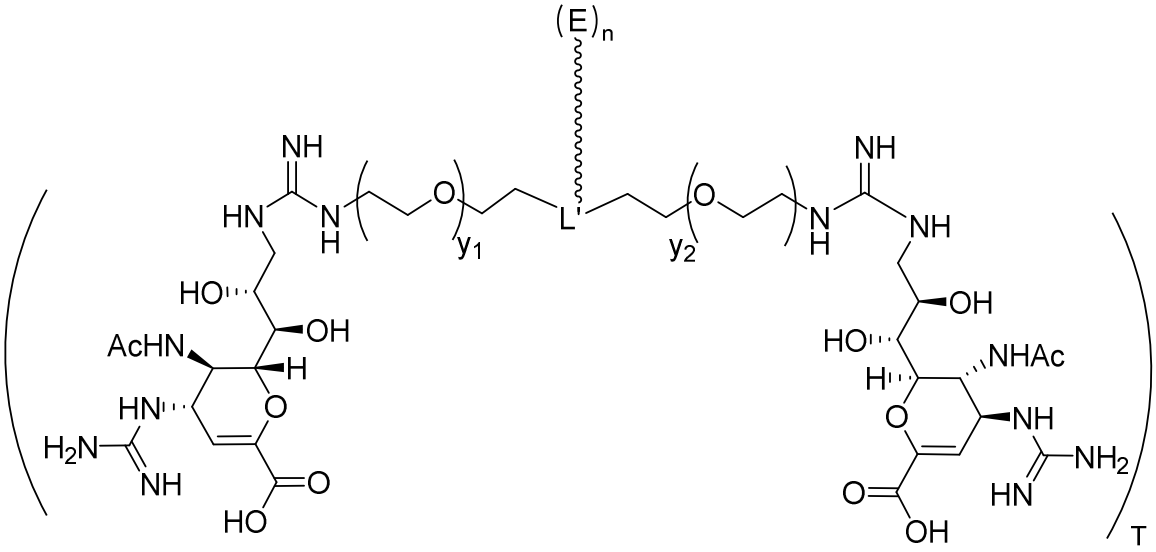
In some examples, the conjugate is described by formula (D-III-8):



(D-III-8)

or a pharmaceutically acceptable salt thereof.

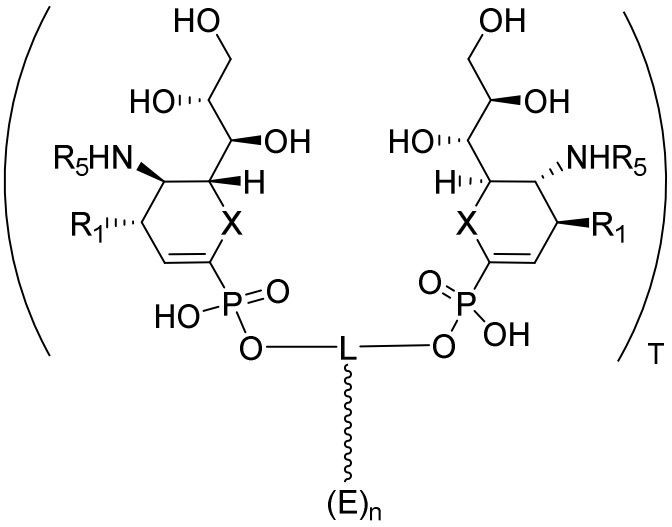
In some examples, the conjugate is described by formula (D-III-9):



(D-III-9)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

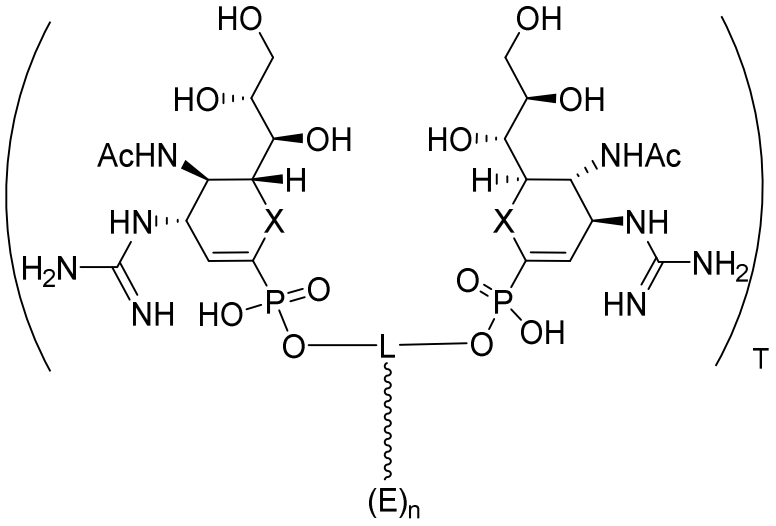
In some examples, the conjugate is described by formula (D-IV):



(D-IV)

or a pharmaceutically acceptable salt thereof.

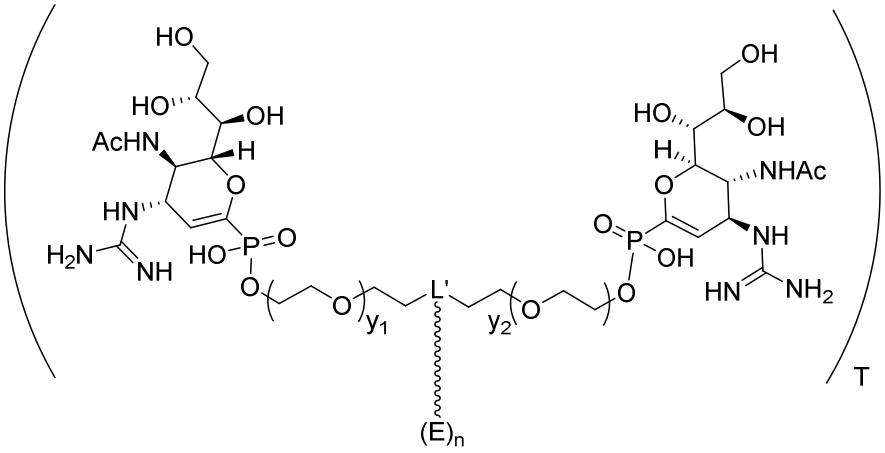
In some examples, the conjugate is described by formula (D-IV-1):



(D-IV-1)

or a pharmaceutically acceptable salt thereof.

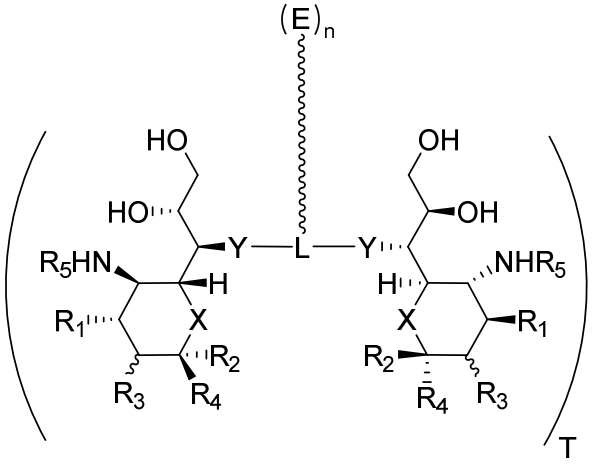
In some examples, the conjugate is described by formula (D-IV-2):



(D-IV-2)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

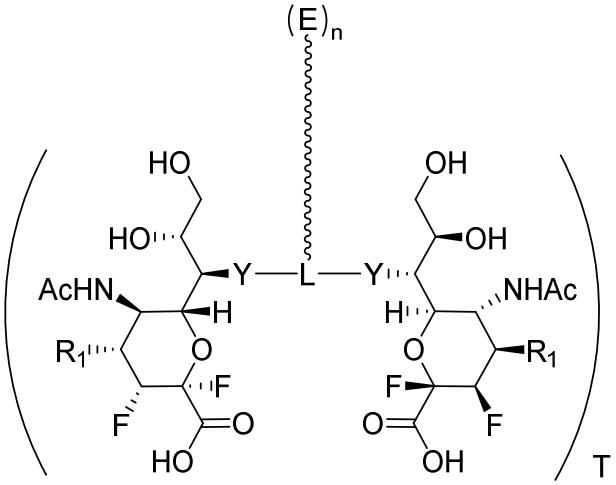
In some examples, the conjugate is described by formula (D-V):



(D-V)

or a pharmaceutically acceptable salt thereof.

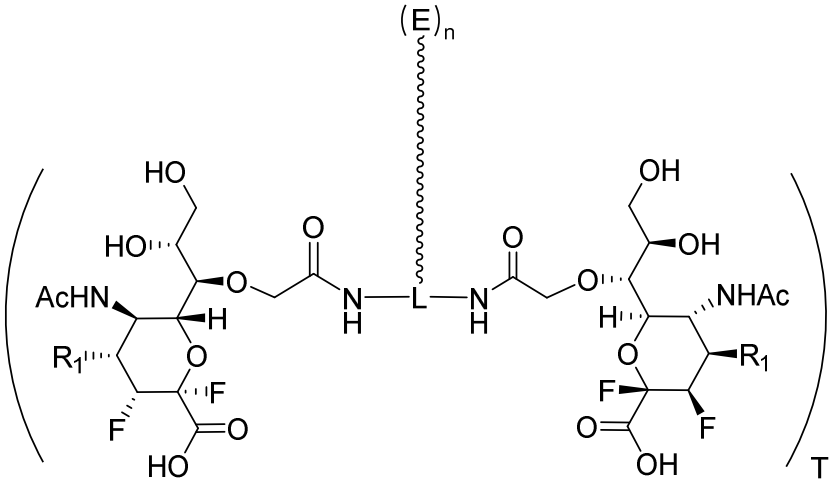
In some examples, the conjugate is described by formula (D-V-1):



(D-V-1)

or a pharmaceutically acceptable salt thereof.

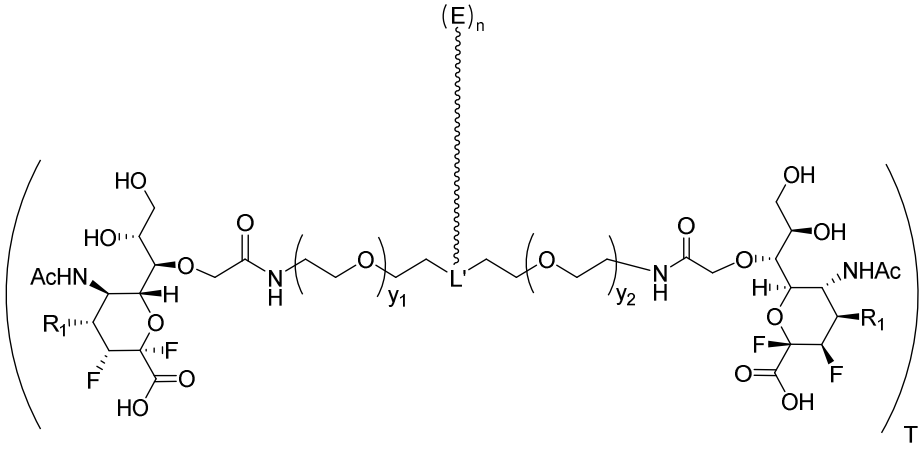
In some examples, the conjugate is described by formula (D-V-2):



(D-V-2)

or a pharmaceutically acceptable salt thereof.

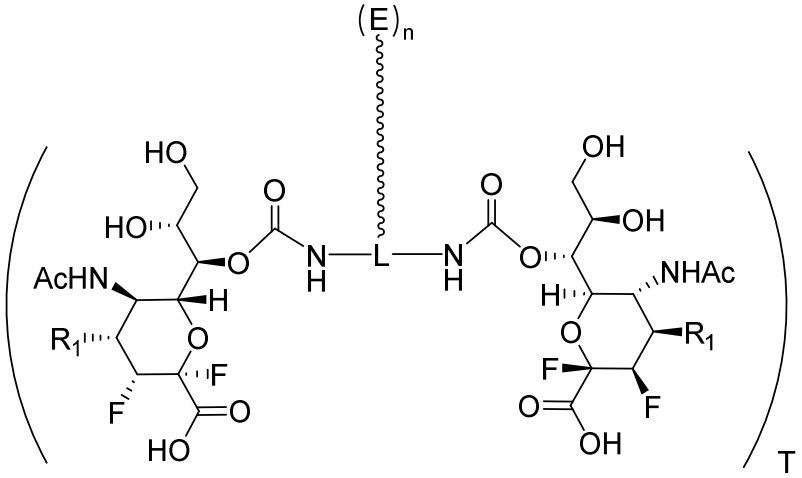
In some examples, the conjugate is described by formula (D-V-3):



(D-V-3)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom. In some examples, y_1 and y_2 are each 1, y_1 and y_2 are each 2, or y_1 and y_2 are each 3.

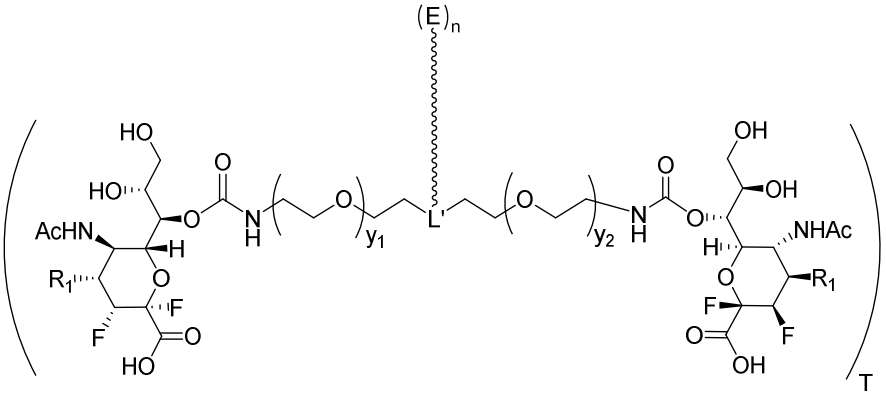
In some examples, the conjugate is described by formula (D-V-4):



(D-V-4)

or a pharmaceutically acceptable salt thereof.

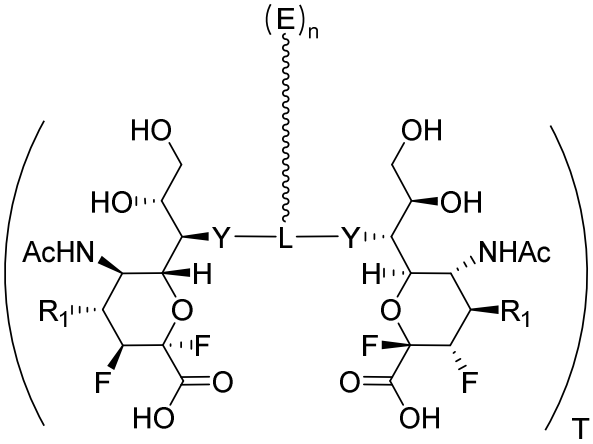
In some examples, the conjugate is described by formula (D-V-5):



(D-V-5)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom. In some examples, y_1 and y_2 are each 1, y_1 and y_2 are each 2, or y_1 and y_2 are each 3.

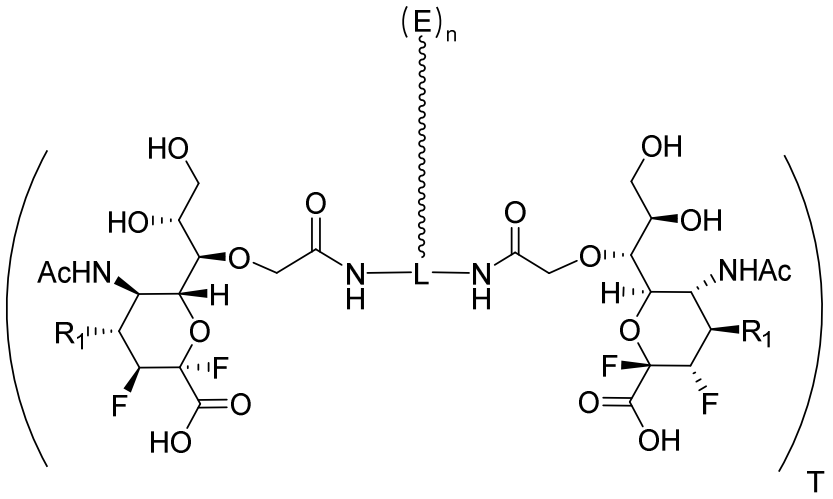
In some examples, the conjugate is described by formula (D-V-6):



(D-V-6)

or a pharmaceutically acceptable salt thereof.

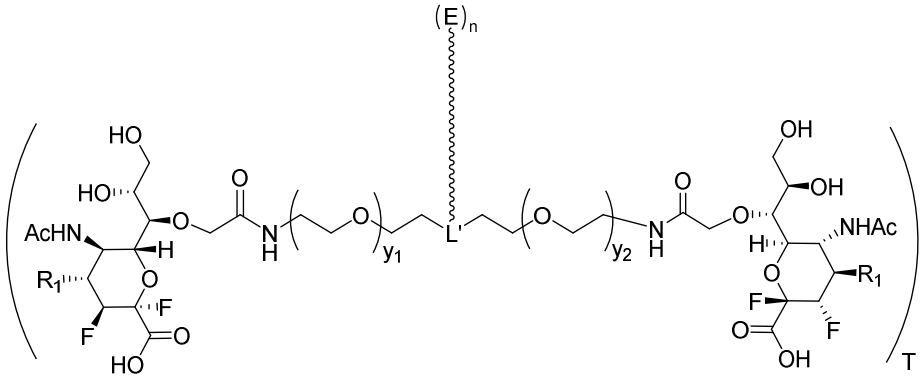
In some examples, the conjugate is described by formula (D-V-7):



(D-V-7)

or a pharmaceutically acceptable salt thereof.

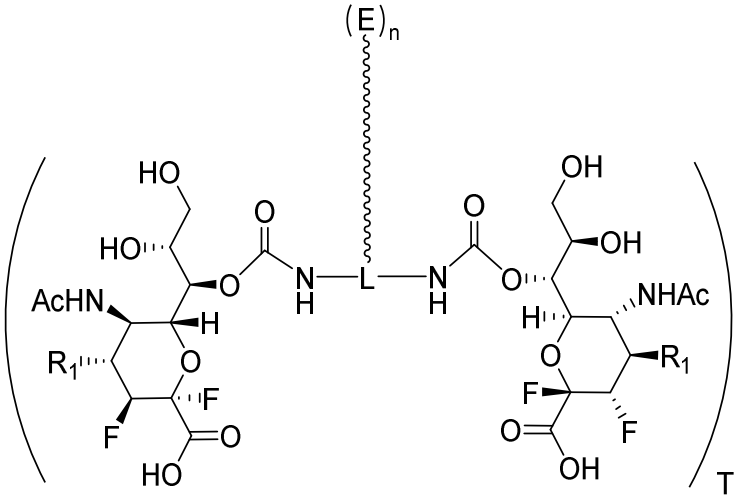
In some examples, the conjugate is described by formula (D-V-8):



(D-V-8)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom. In some examples, y_1 and y_2 are each 1, y_1 and y_2 are each 2, or y_1 and y_2 are each 3.

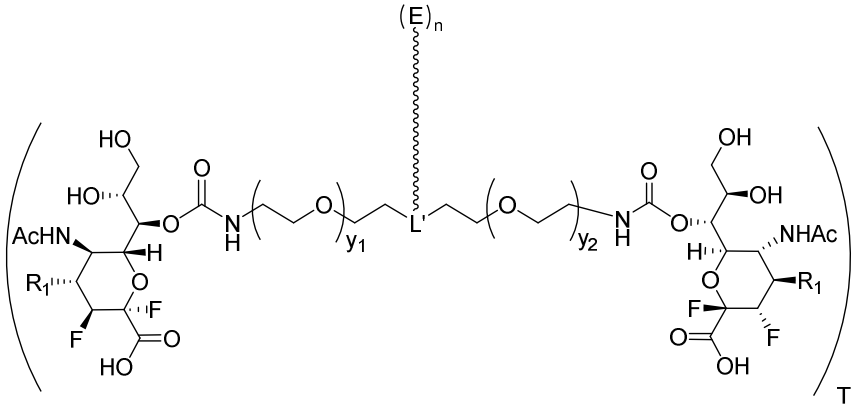
In some examples, the conjugate is described by formula (D-V-9):



(D-V-9)

or a pharmaceutically acceptable salt thereof.

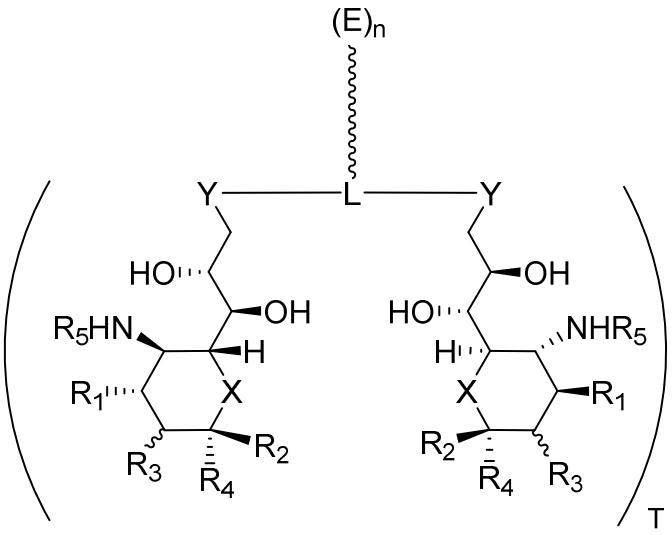
In some examples, the conjugate is described by formula (D-V-10):



(D-V-10)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom. In some examples, y_1 and y_2 are each 1, y_1 and y_2 are each 2, or y_1 and y_2 are each 3.

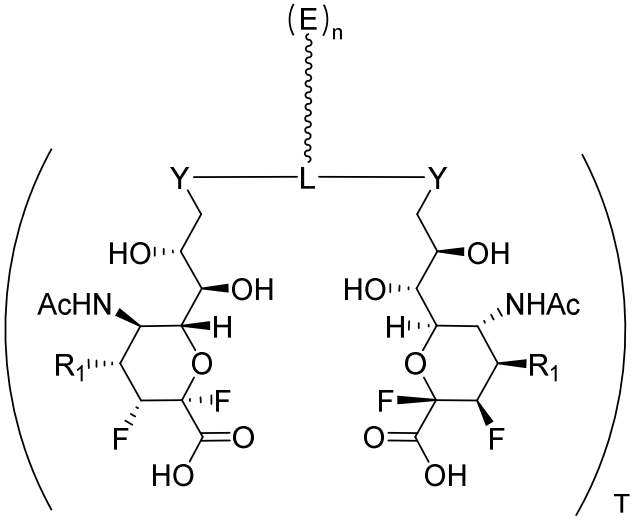
In some examples, the conjugate is described by formula (D-VI):



(D-VI)

or a pharmaceutically acceptable salt thereof.

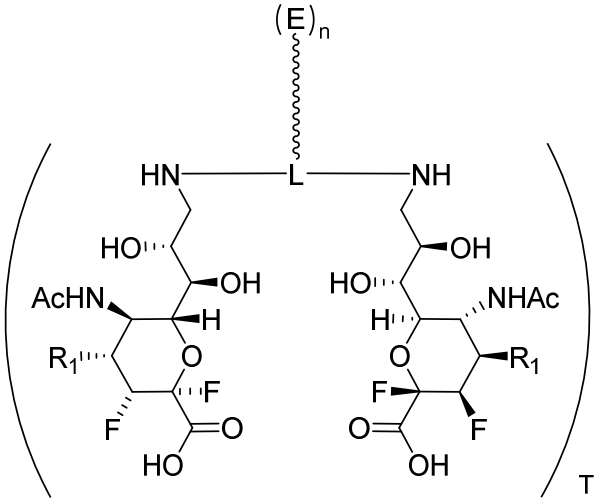
In some examples, the conjugate is described by formula (D-VI-1):



(D-VI-1)

or a pharmaceutically acceptable salt thereof.

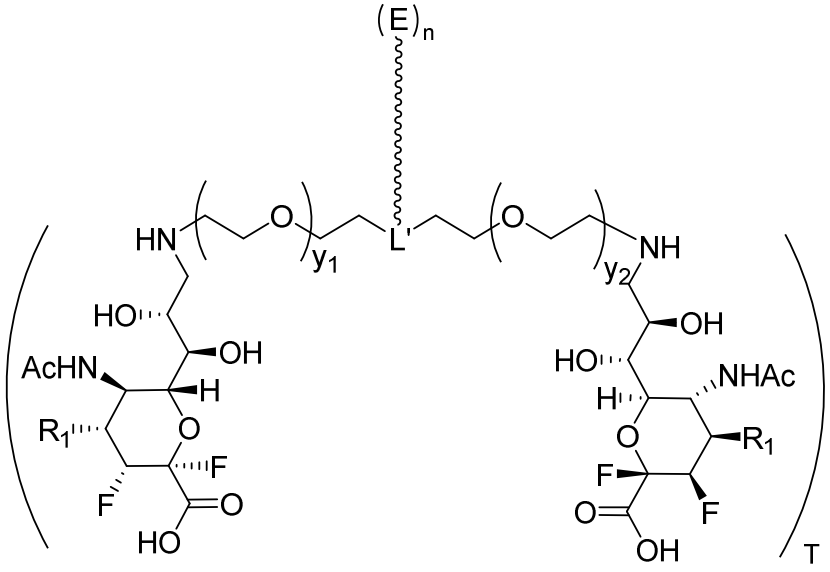
In some examples, the conjugate is described by formula (D-VI-2):



(D-VI-2)

or a pharmaceutically acceptable salt thereof.

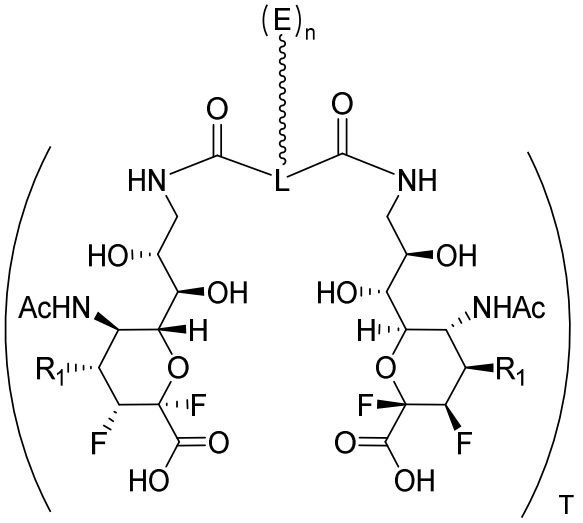
In some examples, the conjugate is described by formula (D-VI-3):



(D-VI-3)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom. In some examples, y_1 and y_2 are each 1, y_1 and y_2 are each 2, or y_1 and y_2 are each 3.

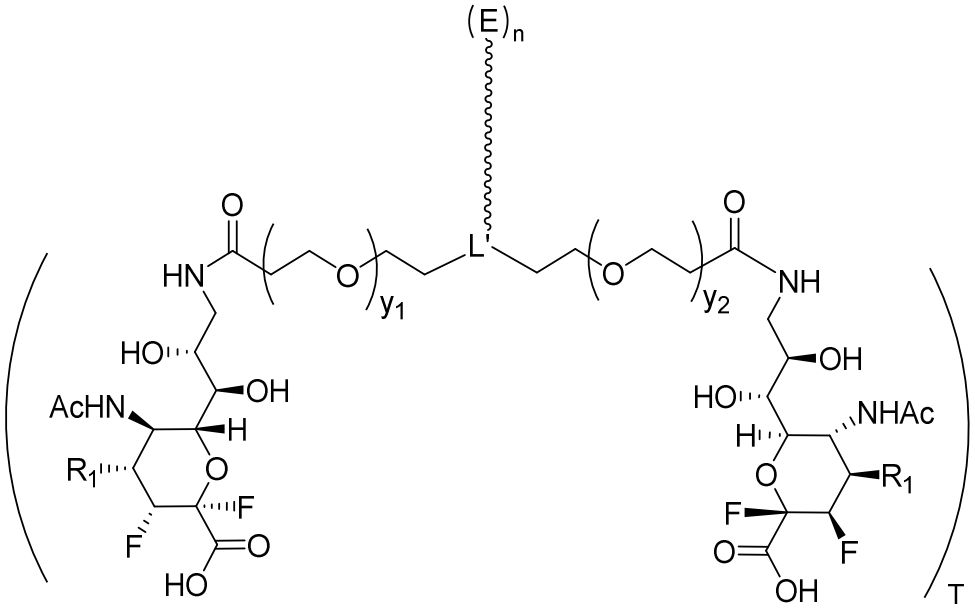
In some examples, the conjugate is described by formula (D-VI-4):



(D-VI-4)

or a pharmaceutically acceptable salt thereof.

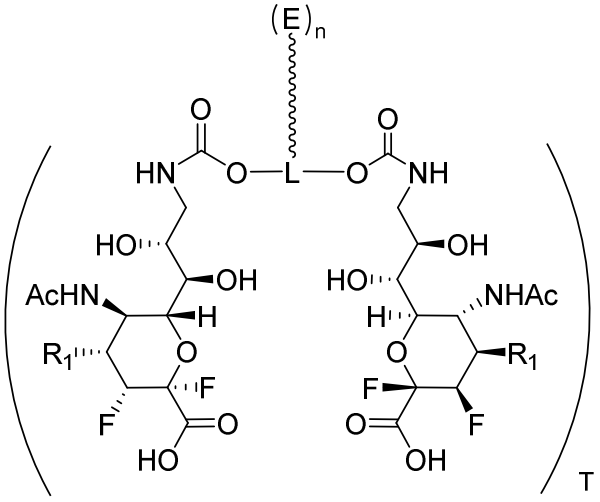
In some examples, the conjugate is described by formula (D-VI-5):



(D-VI-5)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom. In some examples, y_1 and y_2 are each 1, y_1 and y_2 are each 2, or y_1 and y_2 are each 3.

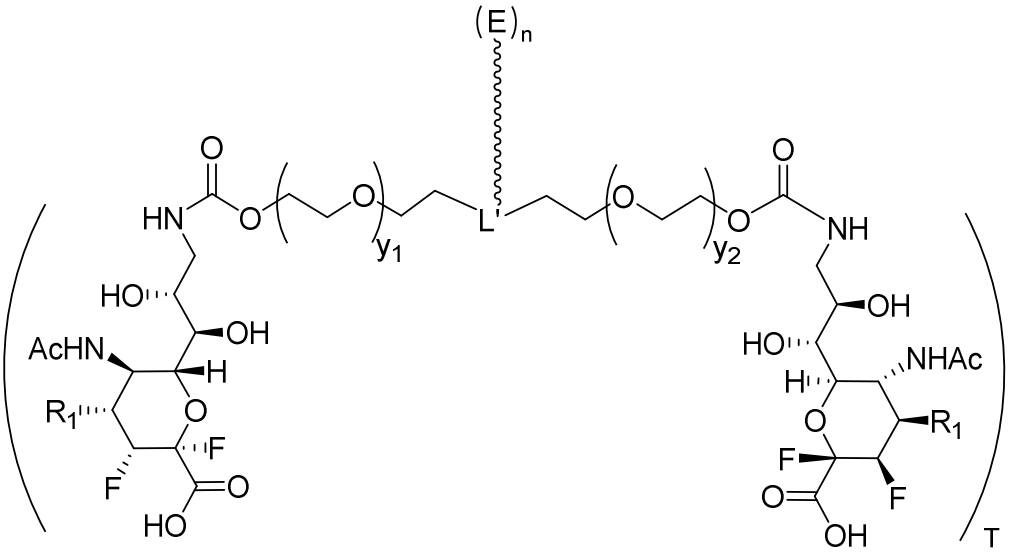
In some examples, the conjugate is described by formula (D-VI-6):



(D-VI-6)

or a pharmaceutically acceptable salt thereof.

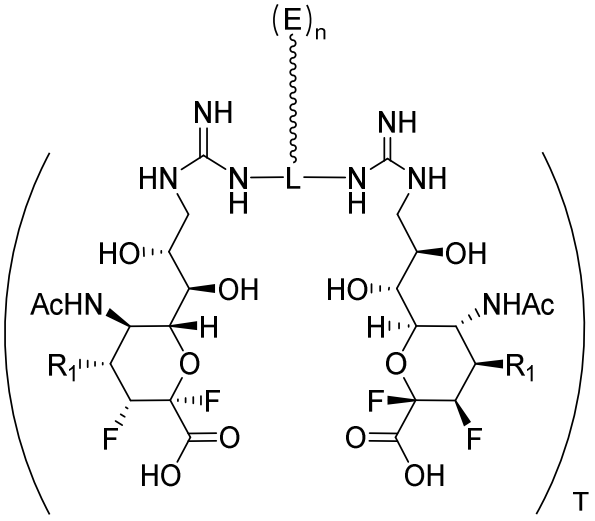
In some examples, the conjugate is described by formula (D-VI-7):



(D-VI-7)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom. In some examples, y_1 and y_2 are each 1, y_1 and y_2 are each 2, or y_1 and y_2 are each 3.

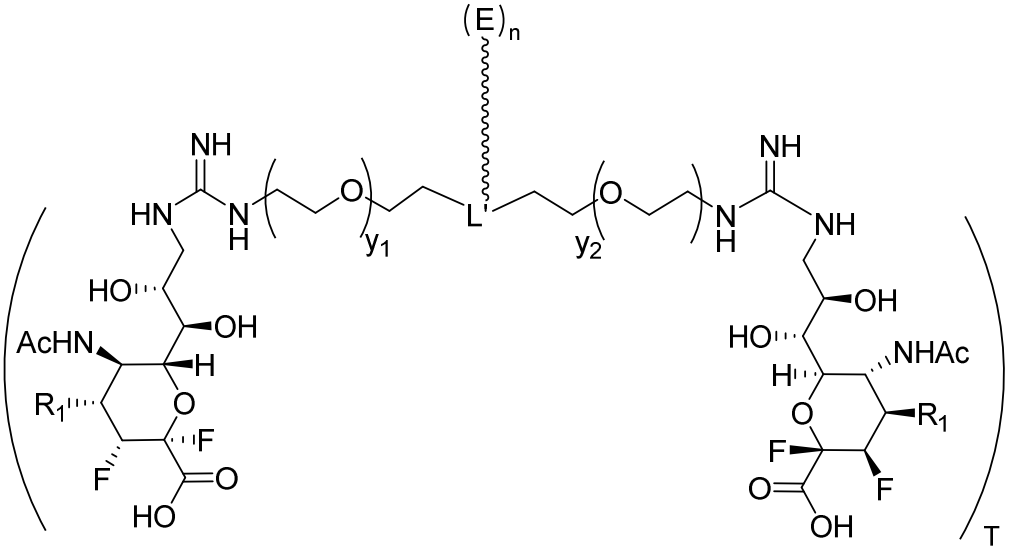
In some examples, the conjugate is described by formula (D-VI-8):



(D-VI-8)

or a pharmaceutically acceptable salt thereof.

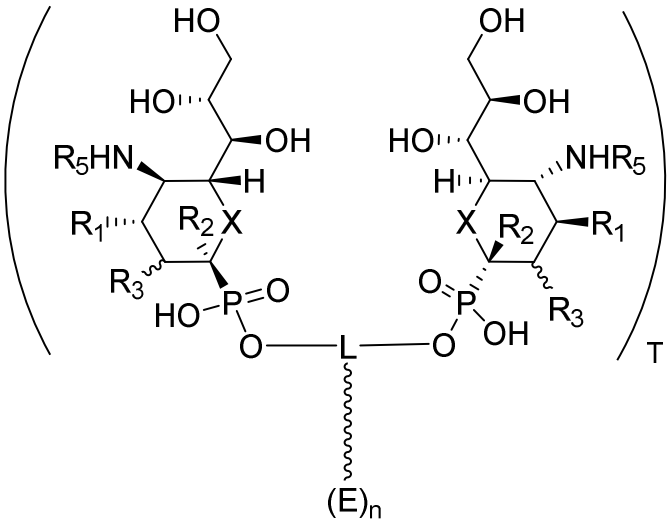
In some examples, the conjugate is described by formula (D-VI-9):



(D-VI-9)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom. In some examples, y_1 and y_2 are each 1, y_1 and y_2 are each 2, or y_1 and y_2 are each 3.

In some examples, the conjugate is described by formula (D-VII):

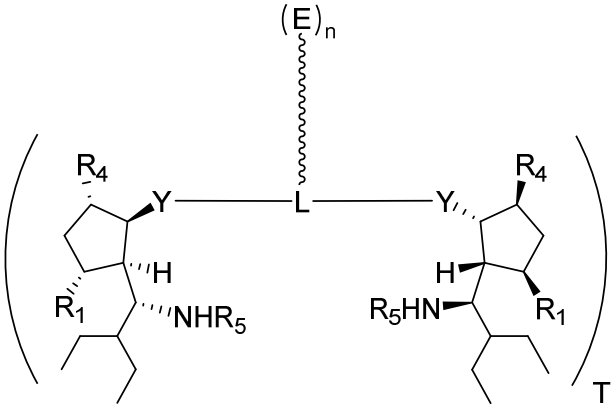


(D-VII)

or a pharmaceutically acceptable salt thereof.

In some examples or aspects described herein, R_1 is OH. In some examples or aspects described herein, R_1 is NH_2. In some examples or aspects described herein, R_1 is -NHC(=NH)NH_2.

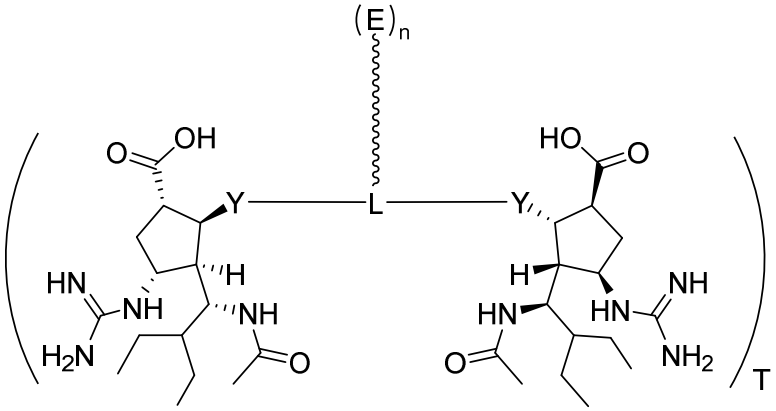
In some examples, the conjugate is described by formula (D-VIII):



(D-VIII)

or a pharmaceutically acceptable salt thereof.

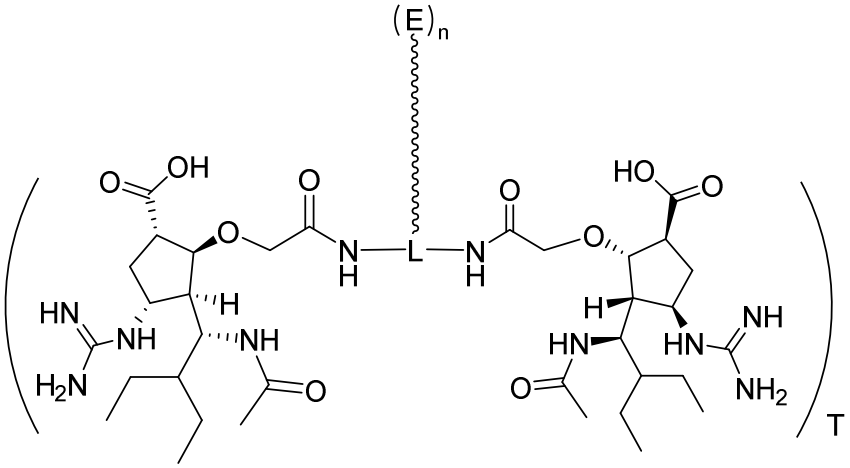
In some examples, the conjugate is described by formula (D-VIII-1):



(D-VIII-1)

or a pharmaceutically acceptable salt thereof.

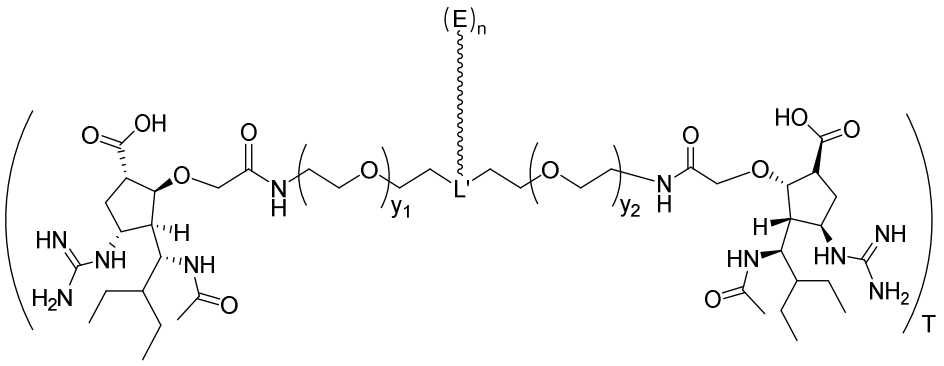
In some examples, the conjugate is described by formula (D-VIII-2):



(D-VIII-2)

or a pharmaceutically acceptable salt thereof.

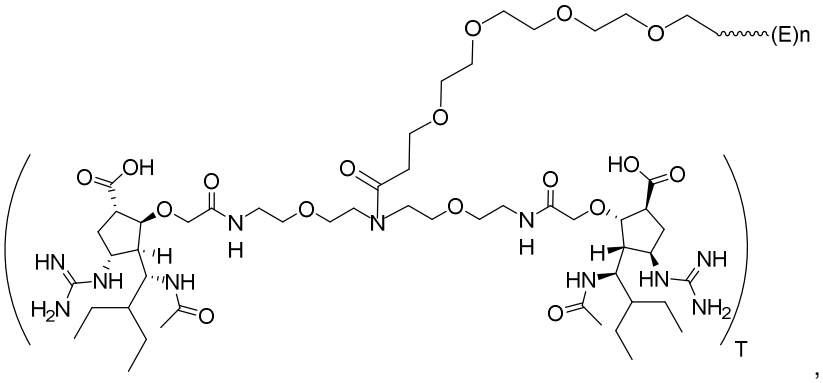
In some examples, the conjugate is described by formula (D-VIII-3):



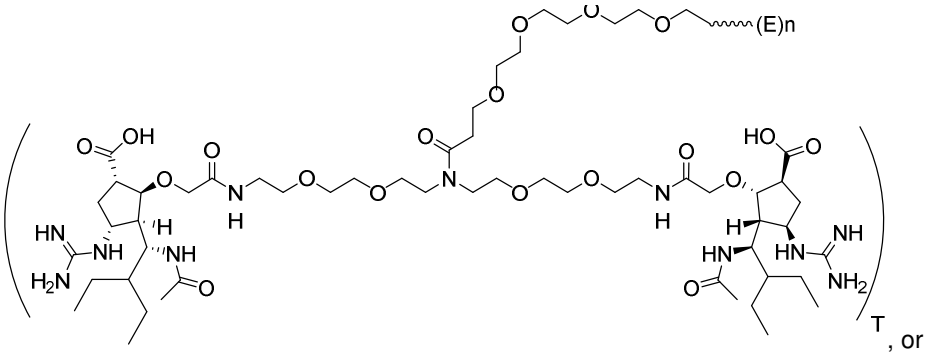
(D-VIII-3)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

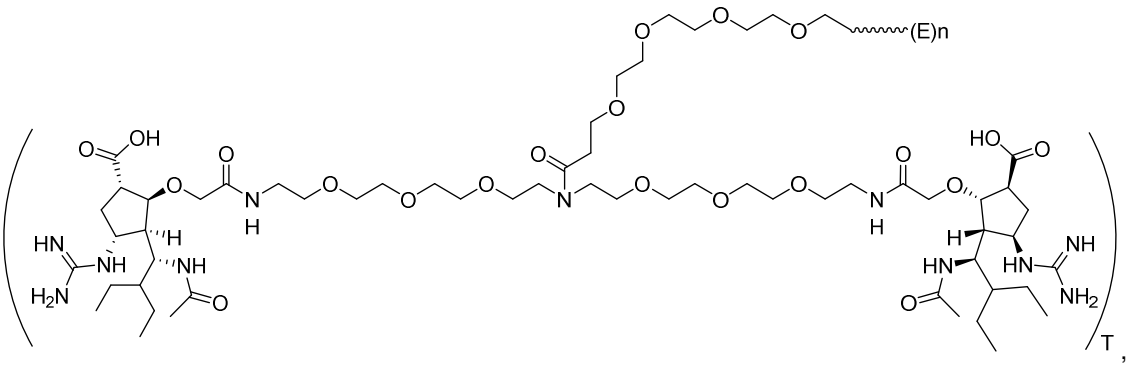
In some examples, the conjugate has the structure selected from



,

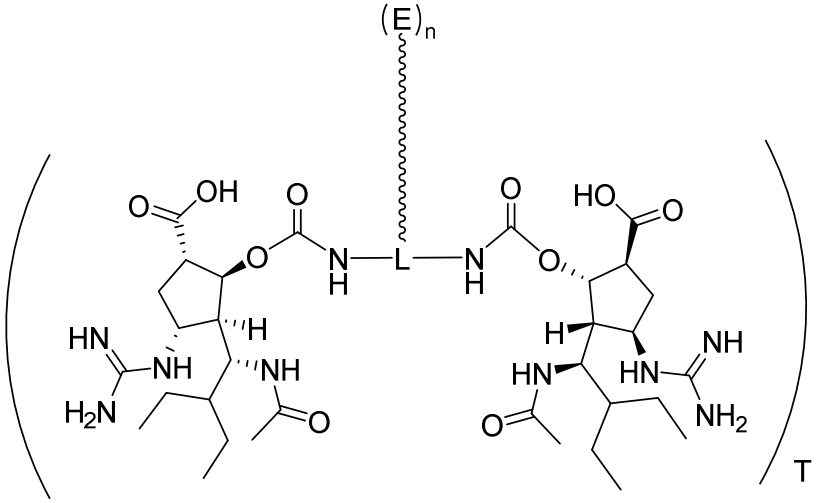


, or



or a pharmaceutically acceptable salt thereof.

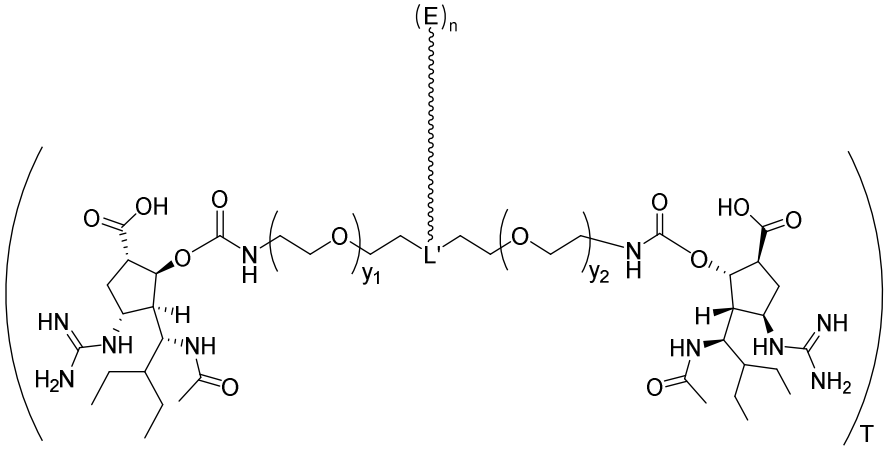
In some examples, the conjugate is described by formula (D-VIII-4):



(D-VIII-4)

or a pharmaceutically acceptable salt thereof.

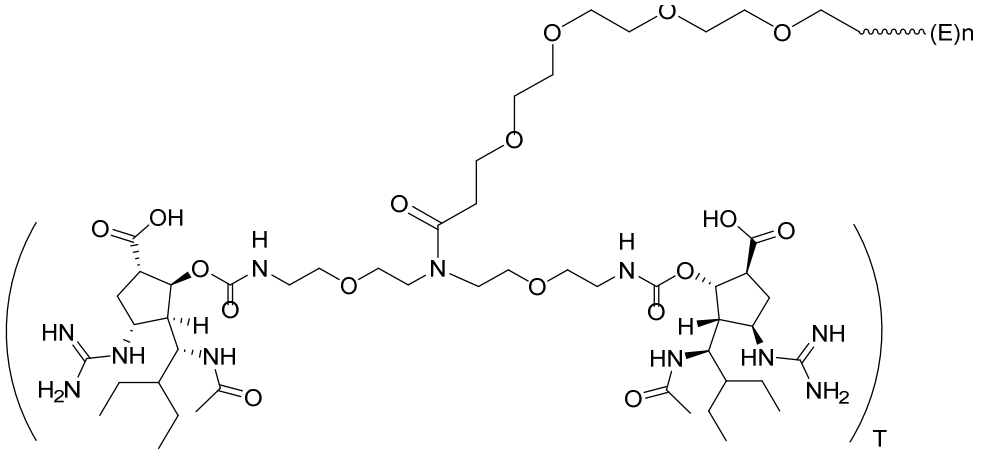
In some examples, the conjugate is described by formula (D-VIII-5):



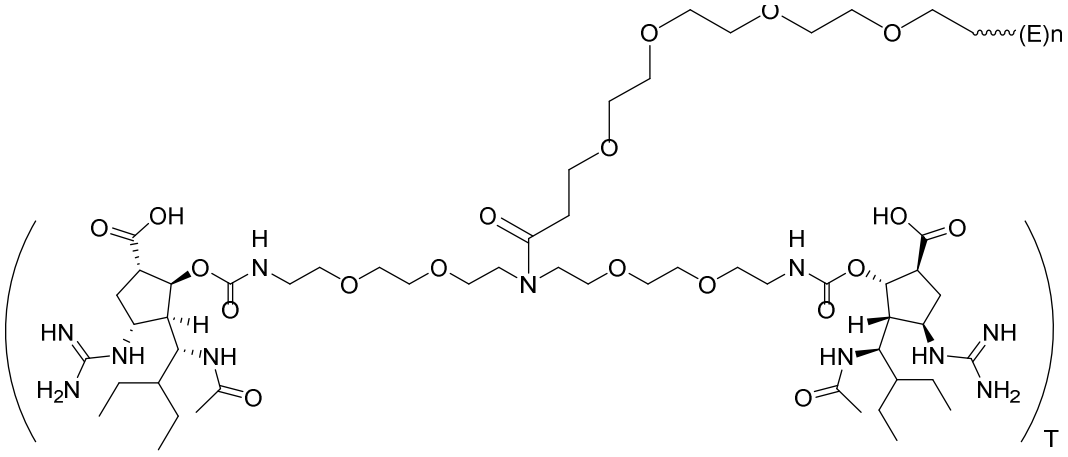
(D-VIII-5)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

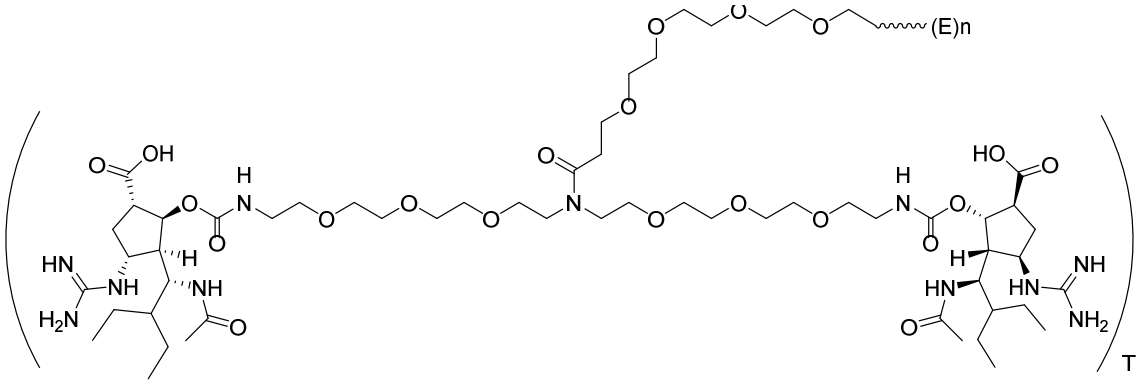
In some examples, the conjugate has the structure selected from:



,

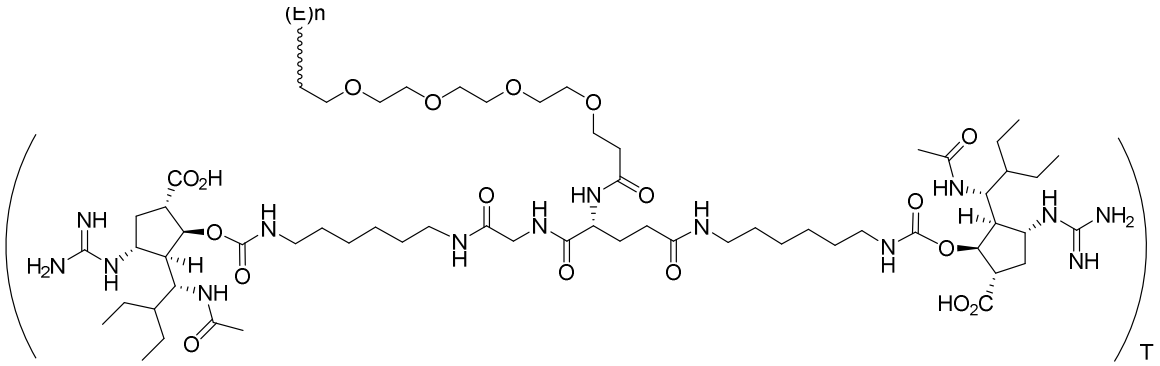


, or



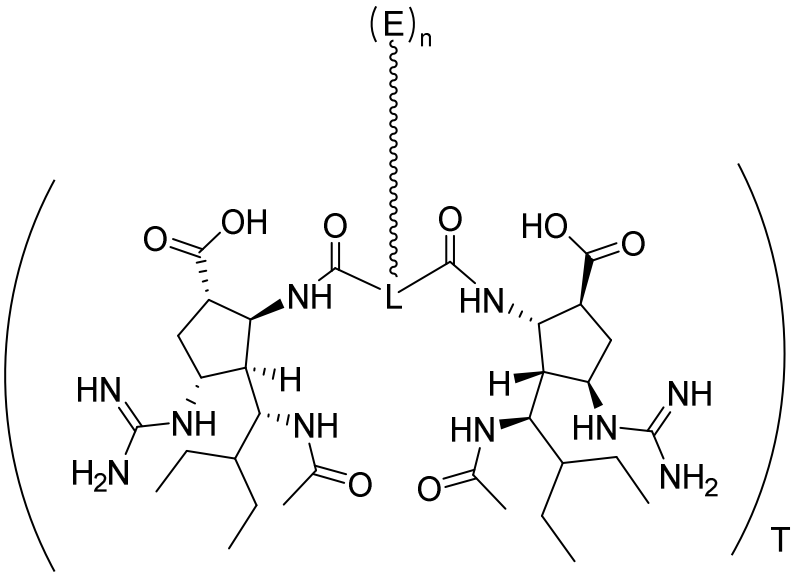
or a pharmaceutically acceptable salt thereof.

In some examples, the conjugate is described by the structure



or a pharmaceutically acceptable salt thereof.

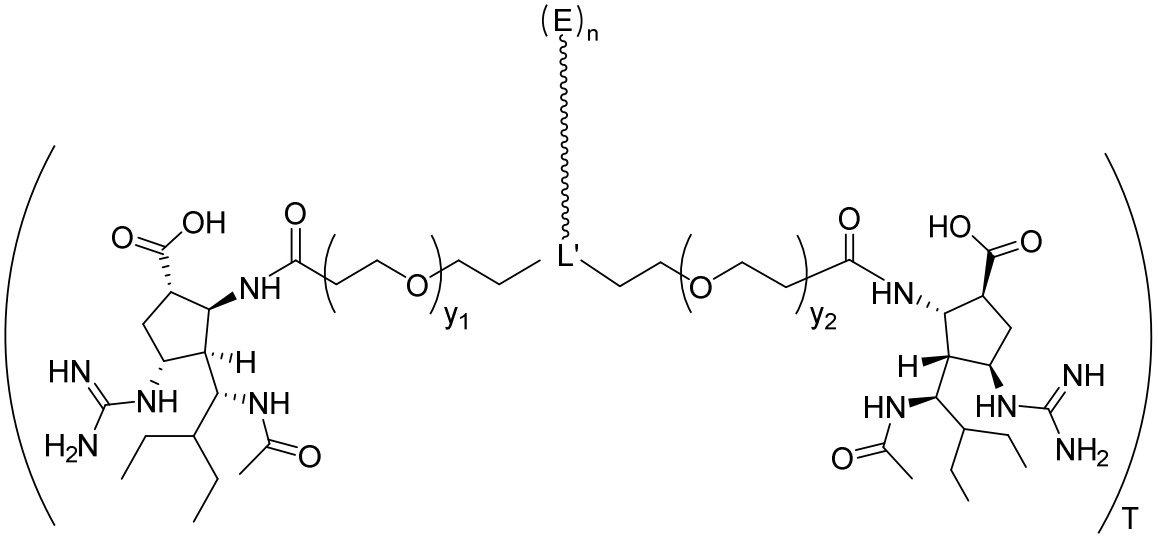
In some examples, the conjugate is described by formula (D-VIII-6):



(D-VIII-6)

or a pharmaceutically acceptable salt thereof.

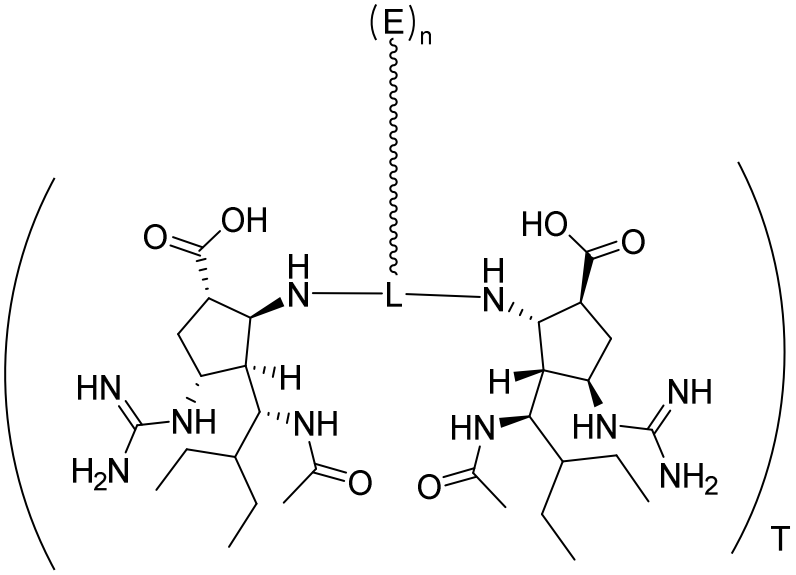
In some examples, the conjugate is described by formula (D-VIII-7):



(D-VIII-7)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

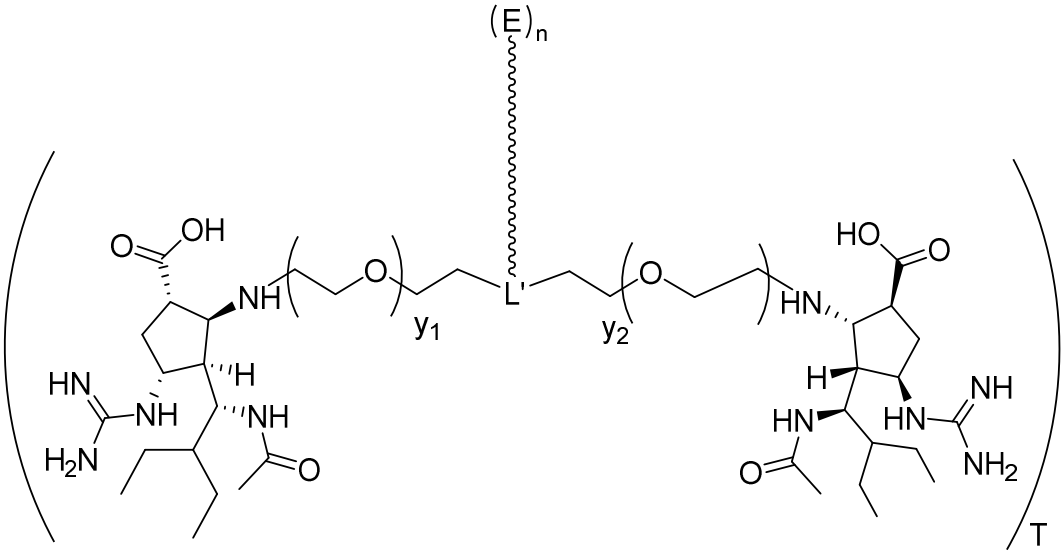
In some examples, the conjugate is described by formula (D-VIII-8):



(D-VIII-8)

or a pharmaceutically acceptable salt thereof.

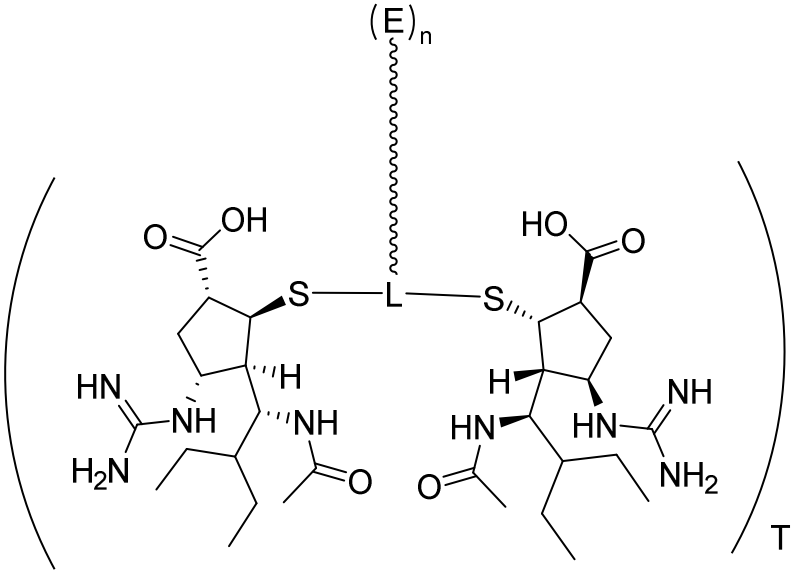
In some examples, the conjugate is described by formula (D-VIII-9):



(D-VIII-9)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

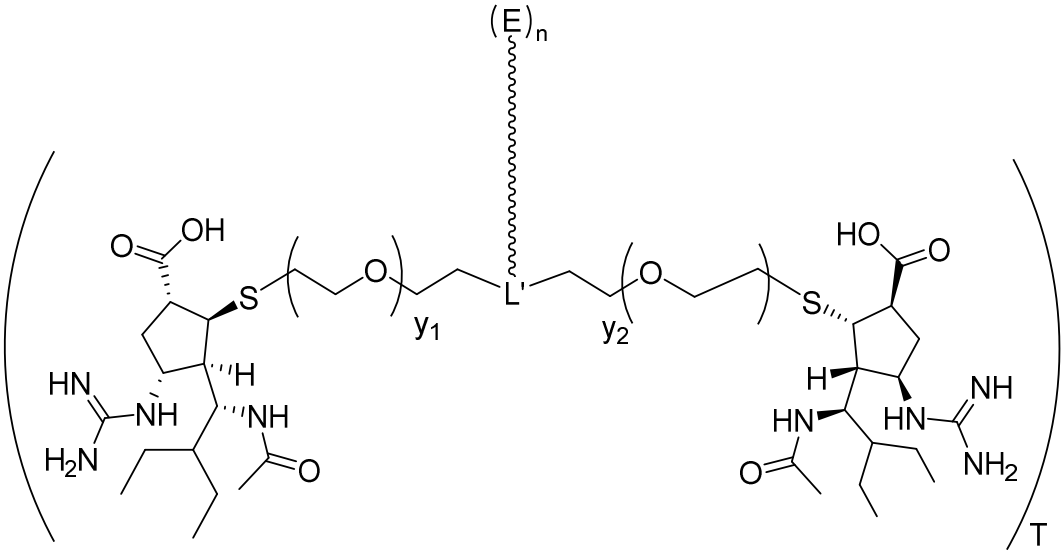
In some examples, the conjugate is described by formula (D-VIII-10):



(D-VIII-10)

or a pharmaceutically acceptable salt thereof.

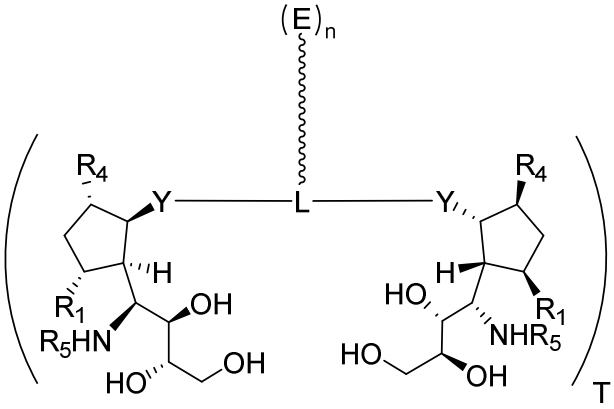
In some examples, the conjugate is described by formula (D-VIII-11):



(D-VIII-11)

wherein L' is the remainder of L, and y_1 and y_2 are each independently an integer from 1-20 (e.g., y_1 and y_2 are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof. In some examples, L' is a nitrogen atom.

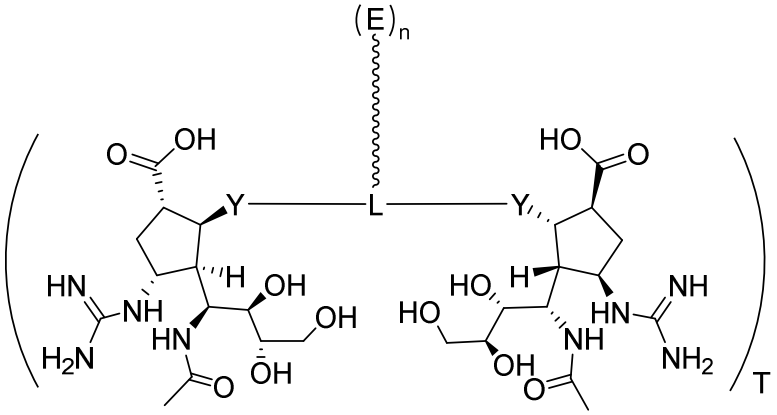
In some examples, the conjugate is described by formula (D-IX):



(D-IX)

or a pharmaceutically acceptable salt thereof.

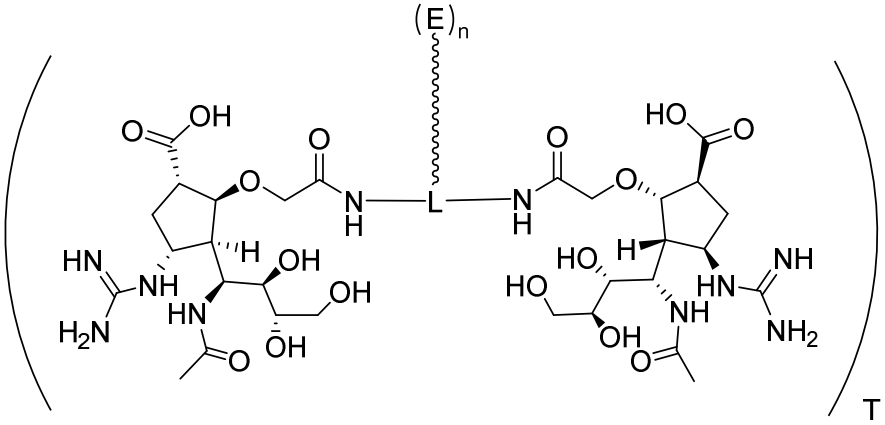
In some examples, the conjugate is described by formula (D-IX-1):



(D-IX-1)

or a pharmaceutically acceptable salt thereof.

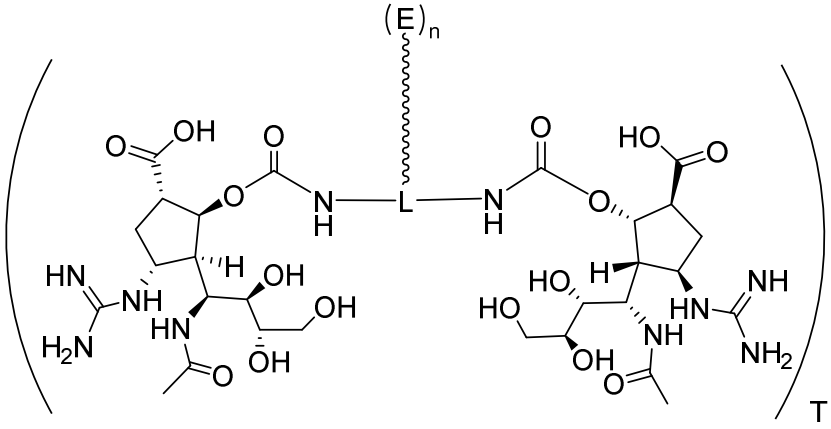
In some examples, the conjugate is described by formula (D-IX-2):



(D-IX-2)

or a pharmaceutically acceptable salt thereof.

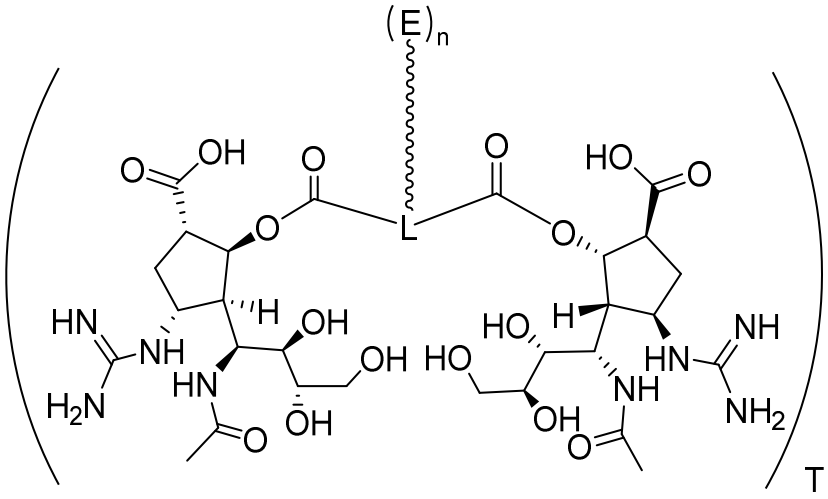
In some examples, the conjugate is described by formula (D-IX-3):



(D-IX-3)

or a pharmaceutically acceptable salt thereof.

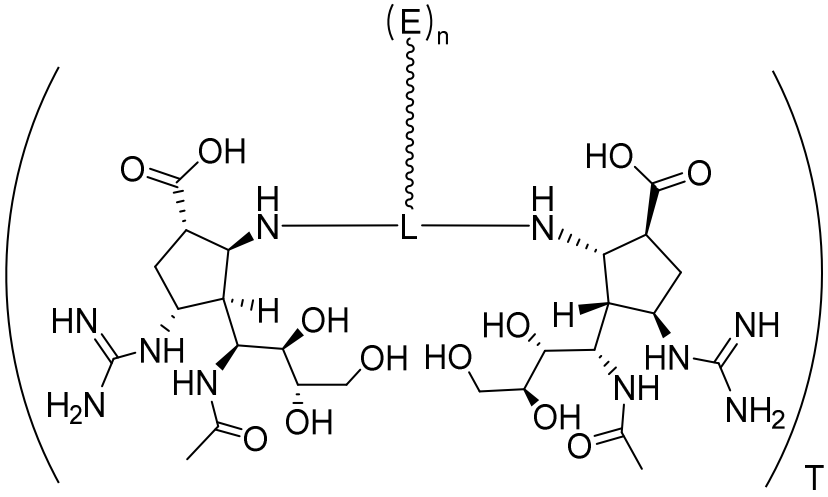
In some examples, the conjugate is described by formula (D-IX-4):



(D-IX-4)

or a pharmaceutically acceptable salt thereof.

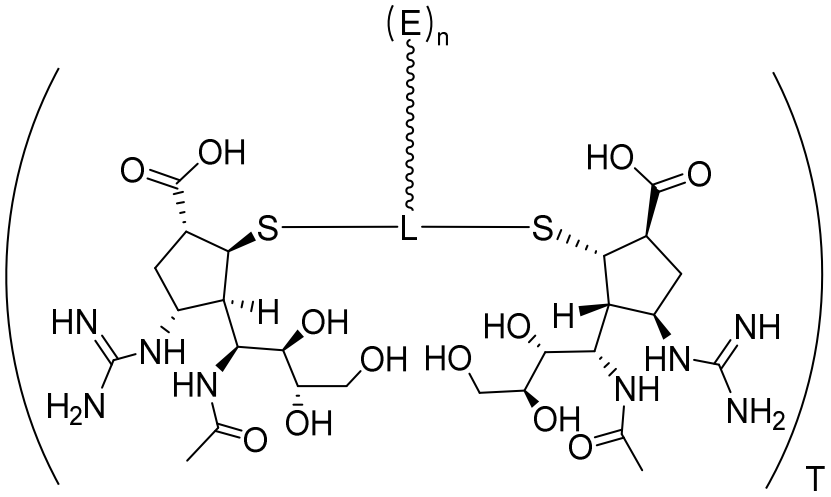
In some examples, the conjugate is described by formula (D-IX-5):



(D-IX-5)

or a pharmaceutically acceptable salt thereof.

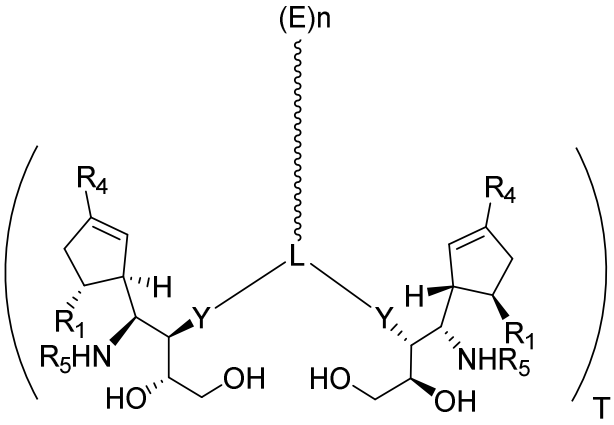
In some examples, the conjugate is described by formula (D-IX-6):



(D-IX-6)

or a pharmaceutically acceptable salt thereof.

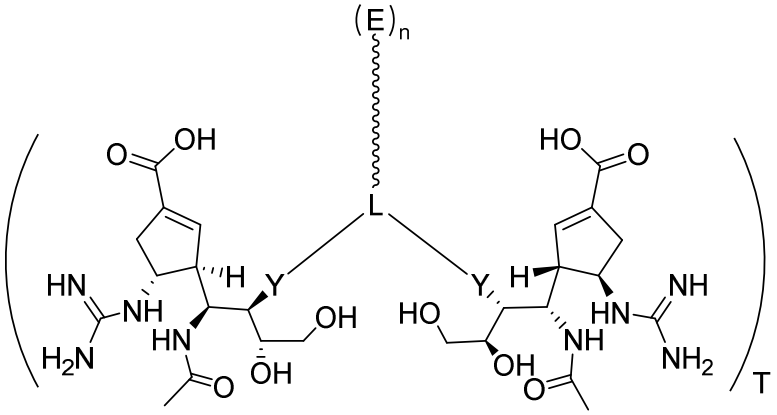
In some examples, the conjugate is described by formula (D-X):



(D-X)

or a pharmaceutically acceptable salt thereof.

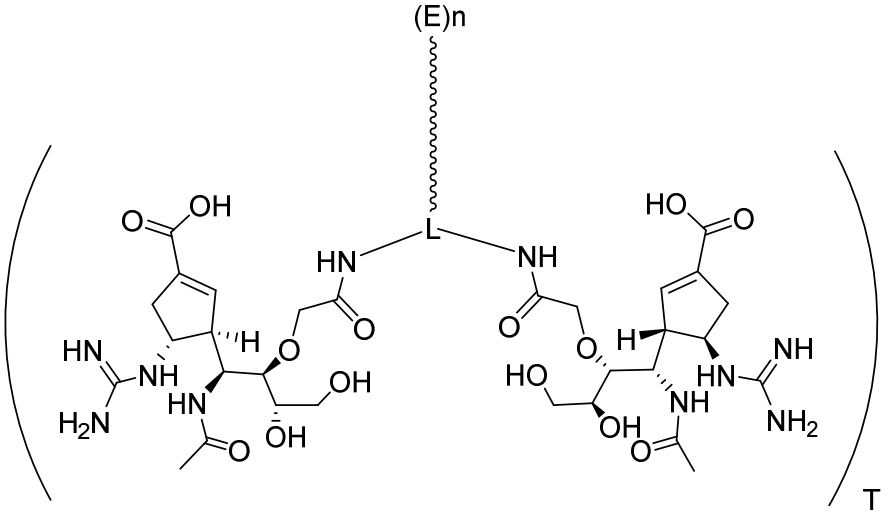
In some examples, the conjugate is described by formula (D-X-1):



(D-X-1)

or a pharmaceutically acceptable salt thereof.

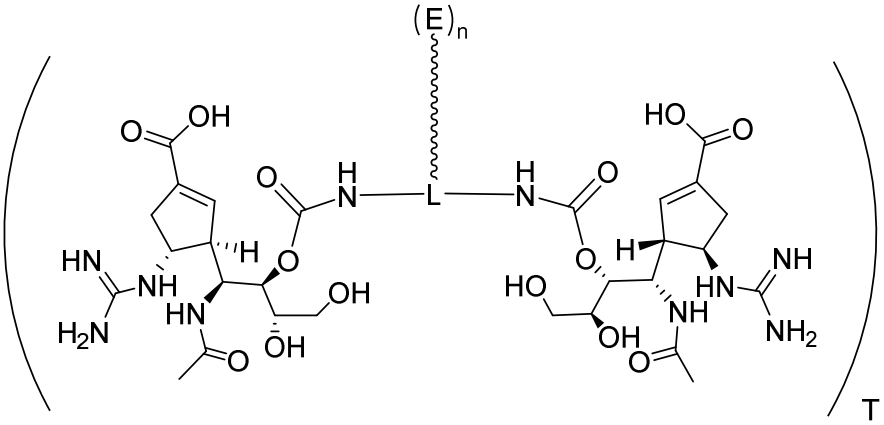
In some examples, the conjugate is described by formula (D-X-2):



(D-X-2)

or a pharmaceutically acceptable salt thereof.

In some examples, the conjugate is described by formula (D-X-3):



(D-X-3)

or a pharmaceutically acceptable salt thereof.

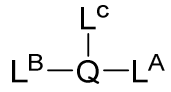
In some examples or aspects described herein, L or L' includes one or more optionally substituted C1-C20 alkylene, optionally substituted C1-C20 heteroalkylene, optionally substituted C2-C20 alkenylene, optionally substituted C2-C20 heteroalkenylene, optionally substituted C2-C20 alkynylene, optionally substituted C2-C20 heteroalkynylene, optionally substituted C3-C20 cycloalkylene, optionally substituted C3-C20 heterocycloalkylene, optionally substituted C4-C20 cycloalkenylene, optionally substituted C4-C20 heterocycloalkenylene, optionally substituted C8-C20 cycloalkynylene, optionally substituted C8-C20 heterocycloalkynylene, optionally substituted C5-C15 arylene, optionally substituted C2-C15 heteroarylene, O, S, NR^i, P, carbonyl, thiocarbonyl, sulfonyl, phosphate, phosphoryl, or imino, wherein R^i is H, optionally substituted C1-C20 alkyl, optionally substituted C1-C20 heteroalkyl, optionally substituted C2-C20 alkenyl, optionally substituted C2-C20 heteroalkenyl, optionally substituted C2-C20 alkynyl, optionally substituted C2-C20 heteroalkynyl, optionally substituted C3-C20 cycloalkyl, optionally substituted C3-C20 heterocycloalkyl, optionally substituted C4-C20 cycloalkenyl, optionally substituted C4-C20 heterocycloalkenyl, optionally substituted C8-C20 cycloalkynyl, optionally substituted C8-C20 heterocycloalkynyl, optionally substituted C5-C15 aryl, or optionally substituted C2-C15 heteroaryl.

In some examples or aspects described herein, the backbone of L or L' consists of one or more optionally substituted C1-C20 alkylene, optionally substituted C1-C20 heteroalkylene, optionally substituted C2-C20 alkenylene, optionally substituted C2-C20 heteroalkenylene, optionally substituted C2-C20 alkynylene, optionally substituted C2-C20 heteroalkynylene, optionally substituted C3-C20 cycloalkylene, optionally substituted C3-C20 heterocycloalkylene, optionally substituted C4-C20 cycloalkenylene, optionally substituted C4-C20 heterocycloalkenylene, optionally substituted C8-C20 cycloalkynylene, optionally substituted C8-C20 heterocycloalkynylene, optionally substituted C5-C15 arylene, optionally substituted C2-C15 heteroarylene, O, S, NR^i, P, carbonyl, thiocarbonyl, sulfonyl, phosphate, phosphoryl, or imino, wherein R^i is H, optionally substituted C1-C20 alkyl, optionally substituted C1-C20 heteroalkyl, optionally substituted C2-C20 alkenyl, optionally substituted C2-C20 heteroalkenyl, optionally substituted C2-C20 alkynyl, optionally substituted C2-C20 heteroalkynyl, optionally substituted C3-C20 cycloalkyl, optionally substituted C3-C20 heterocycloalkyl, optionally

substituted C4-C20 cycloalkenyl, optionally substituted C4-C20 heterocycloalkenyl, optionally substituted C8-C20 cycloalkynyl, optionally substituted C8-C20 heterocycloalkynyl, optionally substituted C5-C15 aryl, or optionally substituted C2-C15 heteroaryl.

In some examples or aspects described herein, L or L' is oxo substituted. In some examples, the backbone of L or L' comprises no more than 250 atoms. In some examples, L or L' is capable of forming an amide, a carbamate, a sulfonyl, or a urea linkage. In some examples L or L' is a bond. In some examples, L or L' is an atom.

In some examples or aspects described herein, each L is described by formula (D-L-I):



(D-L-I)

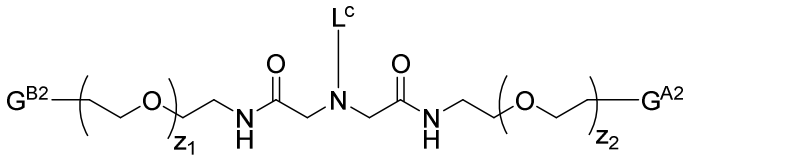
wherein L^A is described by formula G^{A1}-$(Z^{A1})_{g1}$-$(Y^{A1})_{h1}$-$(Z^{A2})_{i1}$-$(Y^{A2})_{j1}$-$(Z^{A3})_{k1}$-$(Y^{A3})_{l1}$-$(Z^{A4})_{m1}$-$(Y^{A4})_{n1}$-$(Z^{A5})_{o1}$-G^{A2}; L^B is described by formula G^{B1}-$(Z^{B1})_{g2}$-$(Y^{B1})_{h2}$-$(Z^{B2})_{i2}$-$(Y^{B2})_{j2}$-$(Z^{B3})_{k2}$-$(Y^{B3})_{l2}$-$(Z^{B4})_{m2}$-$(Y^{B4})_{n2}$-$(Z^{B5})_{o2}$-G^{B2}; L^C is described by formula G^{C1}-$(Z^{C1})_{g3}$-$(Y^{C1})_{h3}$-$(Z^{C2})_{i3}$-$(Y^{C2})_{j3}$-$(Z^{C3})_{k3}$-$(Y^{C3})_{l3}$-$(Z^{C4})_{m3}$-$(Y^{C4})_{n3}$-$(Z^{C5})_{o3}$-G^{C2}; G^{A1} is a bond attached to Q; G^{A2} is a bond attached to A1; G^{B1} is a bond attached to Q); G^{B2} is a bond attached to A2; G^{C1} is a bond attached to Q; G^{C2} is a bond attached to E or a functional group capable of reacting with a functional group conjugated to E (e.g., maleimide and cysteine, amine and activated carboxylic acid, thiol and maleimide, activated sulfonic acid and amine, isocyanate and amine, azide and alkyne, and alkene and tetrazine); each of Z^{A1}, Z^{A2}, Z^{A3}, Z^{A4}, Z^{A5}, Z^{B1}, Z^{B2}, Z^{B3}, Z^{B4}, Z^{B5}, Z^{C1}, Z^{C2}, Z^{C3}, Z^{C4}, and Z^{C5} is, independently, optionally substituted C1-C20 alkylene, optionally substituted C1-C20 heteroalkylene, optionally substituted C2-C20 alkenylene, optionally substituted C2-C20 heteroalkenylene, optionally substituted C2-C20 alkynylene, optionally substituted C2-C20 heteroalkynylene, optionally substituted C3-C20 cycloalkylene, optionally substituted C3-C20 heterocycloalkylene, optionally substituted C4-C20 cycloalkenylene, optionally substituted C4-C20 heterocycloalkenylene, optionally substituted C8-C20 cycloalkynylene, optionally substituted C8-C20 heterocycloalkynylene, optionally substituted C5-C15 arylene, or optionally substituted C2-C15 heteroarylene; each of Y^{A1}, Y^{A2}, Y^{A3}, Y^{A4}, Y^{B1}, Y^{B2}, Y^{B3}, Y^{B4}, Y^{C1}, Y^{C2}, Y^{C3}, and Y^{C4} is, independently, O, S, NR^i, P, carbonyl, thiocarbonyl, sulfonyl, phosphate, phosphoryl, or imino; R^i is H, optionally substituted C1-C20 alkyl, optionally substituted C1-C20 heteroalkyl, optionally substituted C2-C20 alkenyl, optionally substituted C2-C20 heteroalkenyl, optionally substituted C2-C20 alkynyl, optionally substituted C2-C20 heteroalkynyl, optionally substituted C3-C20 cycloalkyl, optionally substituted C3-C20 heterocycloalkyl, optionally substituted C4-C20 cycloalkenyl, optionally substituted C4-C20 heterocycloalkenyl, optionally substituted C8-C20 cycloalkynyl, optionally substituted C8-C20 heterocycloalkynyl, optionally substituted C5-C15 aryl, or optionally substituted C2-C15 heteroaryl; each of g1, h1, i1, j1, k1, l1, m1, n1, o1, g2, h2, i2, j2, k2, l2, m2, n2, o2, g3, h3, i3, j3, k3, l3, m3, n3, and o3 is, independently, 0 or 1; Q is a nitrogen atom, optionally substituted C1-C20 alkylene, optionally substituted C1-C20 heteroalkylene, optionally substituted C2-C20 alkenylene, optionally substituted C2-C20 heteroalkenylene, optionally substituted C2-C20 alkynylene, optionally substituted C2-C20 heteroalkynylene, optionally substituted C3-C20 cycloalkylene, optionally substituted C3-C20 heterocycloalkylene, optionally substituted C4-C20

cycloalkenylene, optionally substituted C4-C20 heterocycloalkenylene, optionally substituted C8-C20 cycloalkynylene, optionally substituted C8-C20 heterocycloalkynylene, optionally substituted C5-C15 arylene, or optionally substituted C2-C15 heteroarylene.

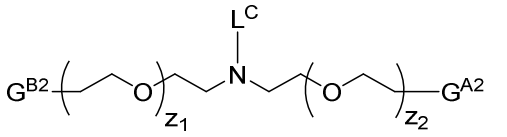
In some examples, L^C may have two points of attachment to the Fc domain, Fc-binding peptide, albumin protein, or albumin protein-binding peptide (e.g., two G^{C2}).

In some examples or aspects described herein, L includes a polyethylene glycol (PEG) linker. A PEG linker includes a linker having the repeating unit structure $(-CH_2CH_2O-)_n$, wherein n is an integer from 2 to 100. A polyethylene glycol linker may covalently join a neuraminidase inhibitor and E (e.g., in a conjugate of any one of formulas (M-I)-(M-XI)). A polyethylene glycol linker may covalently join a first neuraminidase inhibitor and a second neuraminidase inhibitor (e.g., in a conjugate of any one of formulas (D-I)-(D-XI)). A polyethylene glycol linker may covalently join a neuraminidase inhibitor dimer and E (e.g., in a conjugate of any one of formulas (D-I)-(D-XI)). A polyethylene glycol linker may be selected any one of PEG_2 to PEG_{100} (e.g., PEG_2, PEG_3, PEG_4, PEG_5, PEG_5-PEG_{10}, PEG_{10}-PEG_{20}, PEG_{20}-PEG_{30}, PEG_{30}-PEG_{40}, PEG_{50}-PEG_{60}, PEG_{60}-PEG_{70}, PEG_{70}-PEG_{80}, PEG_{80}-PEG_{90}, PEG_{90}-PEG_{100}). In some examples, L^c includes a PEG linker, where L^C is covalently attached to each of Q and E.

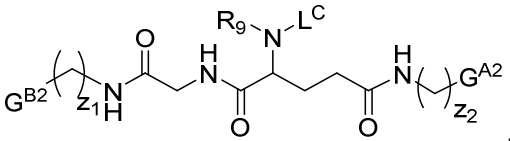
In some examples, L is



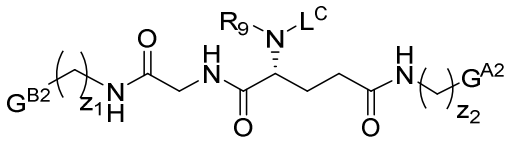
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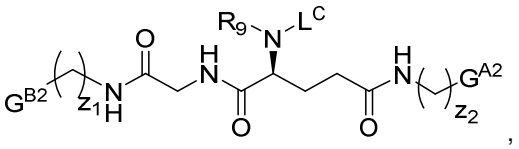
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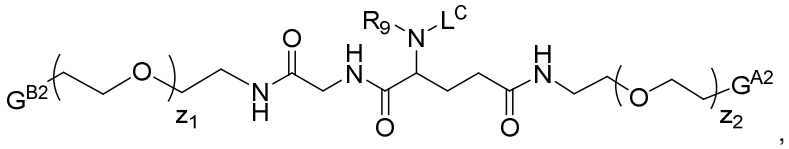
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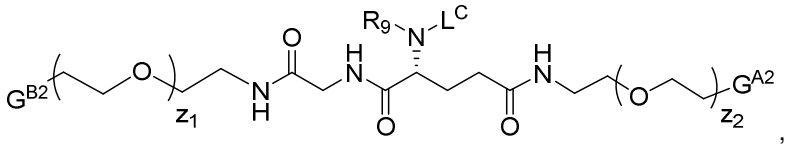
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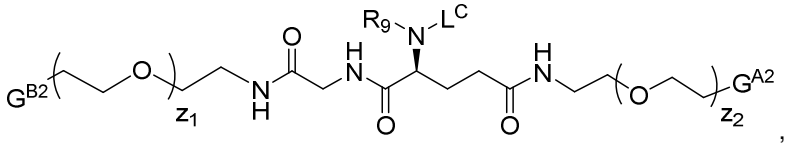
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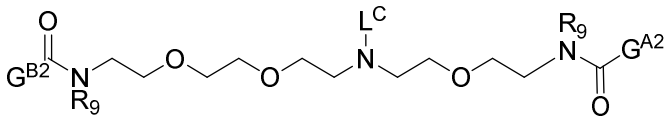
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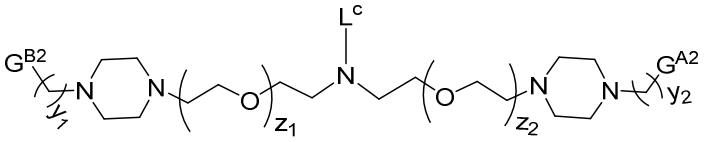


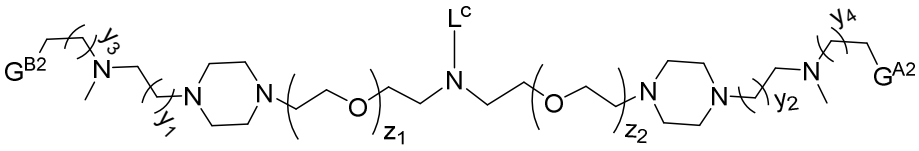
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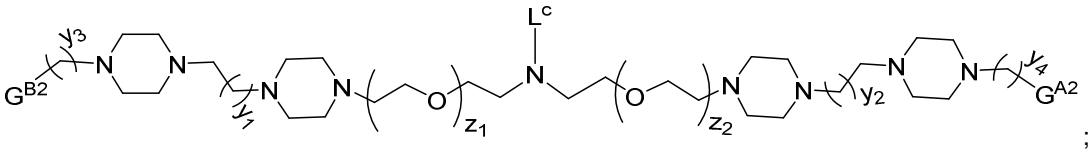


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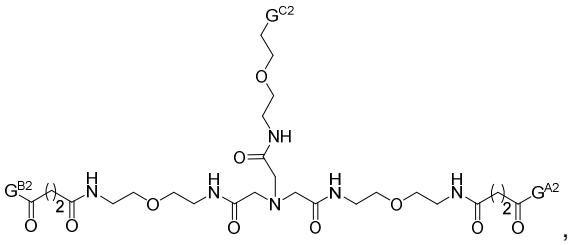

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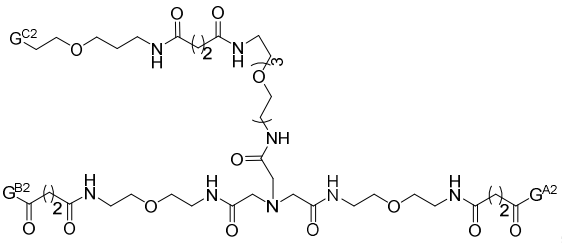

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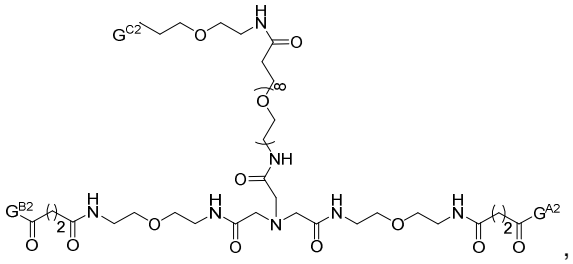

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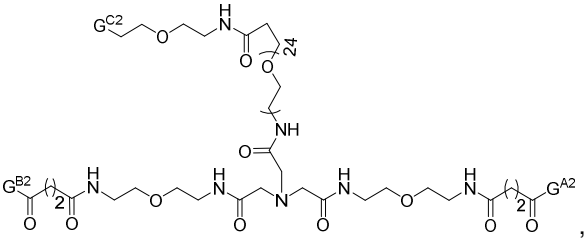
wherein z_1 and z_2 are each, independently, and integer from 1 to 20; and R_9 is selected from H, C1-C20 alkyl, C3-C20 cycloalkyl, C3-C20 heterocycloalkyl; C5-C15 aryl, and C2-C15 heteroaryl.

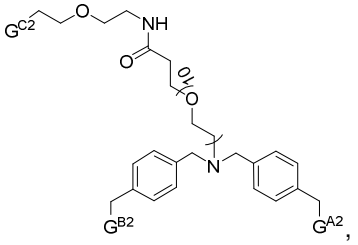
In some examples, L is

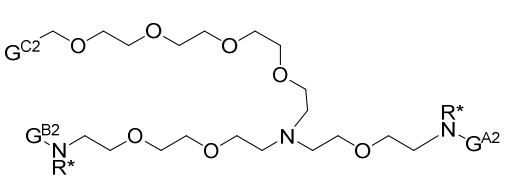
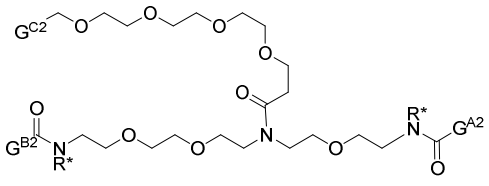
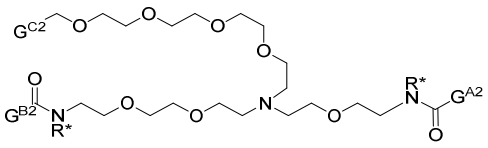

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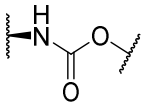

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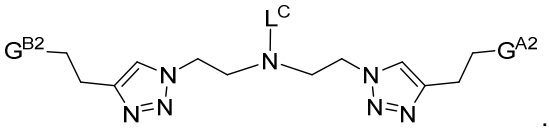

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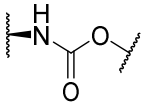

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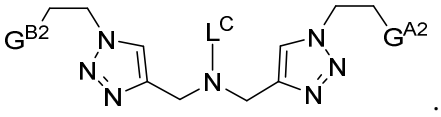


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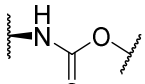
wherein R* is a bond or includes one or more of optionally substituted C1-C20 alkylene, optionally substituted C1-C20 heteroalkylene, optionally substituted C2-C20 alkenylene, optionally substituted C2-C20 heteroalkenylene, optionally substituted C2-C20 alkynylene, optionally substituted C2-C20 heteroalkynylene, optionally substituted C3-C20 cycloalkylene, optionally substituted C3-C20 heterocycloalkylene, optionally substituted C4-C20 cycloalkenylene, optionally substituted C4-C20 heterocycloalkenylene, optionally substituted C8-C20 cycloalkynylene, optionally substituted C8-C20 heterocycloalkynylene, optionally substituted C5-C15 arylene, optionally substituted C2-C15 heteroarylene, O, S, NR^i, P, carbonyl, thiocarbonyl, sulfonyl, phosphate, and imino, and wherein R^i is H, optionally substituted C1-C20 alkyl, optionally substituted C1-C20 heteroalkyl, optionally substituted C2-C20 alkenyl, optionally substituted C2-C20 heteroalkenyl, optionally substituted C2-C20 alkynyl, optionally substituted C2-C20 heteroalkynyl, optionally substituted C3-C20 cycloalkyl, optionally substituted C3-C20 heterocycloalkyl, optionally substituted C4-C20 cycloalkenyl, optionally substituted C4-C20 heterocycloalkenyl, optionally substituted C8-C20 cycloalkynyl, optionally substituted C8-C20 heterocycloalkynyl, optionally substituted C5-C15 aryl, or optionally substituted C2-C15 heteroaryl.

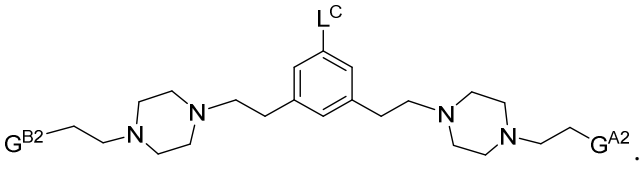
In some examples, Y is:  (-NH(C=O)O-) and L is:

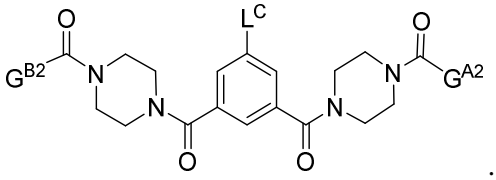

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In some examples, Y is:  (-NH(C=O)O-) and L is:

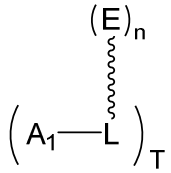

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In some examples, Y is:  (-NH(C=O)O-) and L is:



In some example, Y is:  (-O-) and L is: .

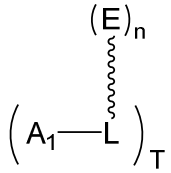
In another example, the disclosure features a conjugate described by formula (M-I):



(M-I)

wherein each A_1 is independently selected from any one of formulas (A-I)-(A-XII); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138), an albumin protein (e.g., an albumin protein having the sequence of any one of SEQ ID NOs: 139-141), an albumin protein-binding peptide, or an Fc-binding peptide; n is 1 or 2; T is an integer from 1 to 20 (e.g., T is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20); and L is a linker covalently attached to each of E and A_1, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1 may be independently selected from any one of formulas (A-I)-(A-XII). In some examples, each A_1 may be independently selected from any one of formulas (A-I), (A-II), (A-VI), or (A-VII). In other examples, each A_1 may be independently selected from formula (A-I).

In another example, the disclosure features a conjugate described by formula (M-I):

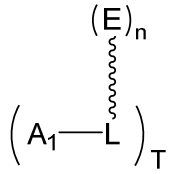


(M-I)

wherein each A_1 is independently selected from any one of formulas (A-I)-(A-V); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138), an albumin protein (e.g., an albumin protein having the sequence of any one of SEQ ID NOs: 139-141),

an albumin protein-binding peptide, or an Fc-binding peptide; n is 1 or 2; T is an integer from 1 to 20 (e.g., T is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20); and L is a linker covalently attached to each of E and A_1, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1 may be independently selected from any one of formulas (A-I)-(A-V).

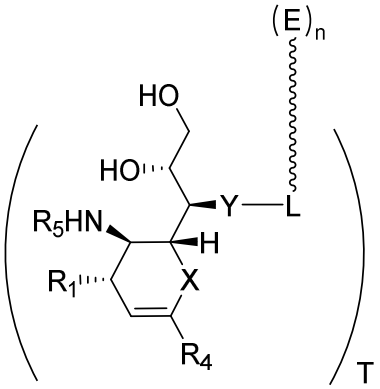
In another example, the disclosure features a conjugate described by formula (M-I):



(M-I)

wherein each A_1 is independently selected from any one of formulas (A-VI)-(A-IX); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138), an albumin protein (e.g., an albumin protein having the sequence of any one of SEQ ID NOs: 139-141), an albumin protein-binding peptide, or an Fc-binding peptide; n is 1 or 2; T is an integer from 1 to 20 (e.g., T is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20); and L is a linker covalently attached to each of E and A_1, or a pharmaceutically acceptable salt thereof. When T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1 may be independently selected from any one of formulas (A-VI)-(A-IX).

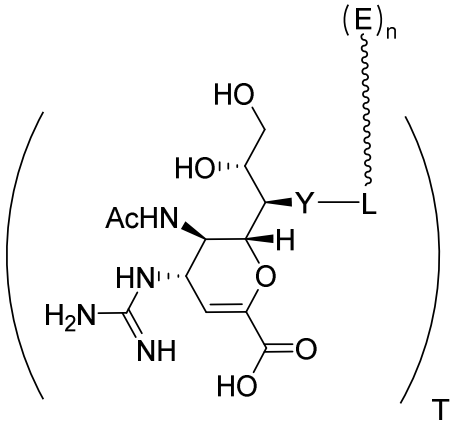
In some examples, the conjugate is described by formula (M-II):



(M-II)

or a pharmaceutically acceptable salt thereof.

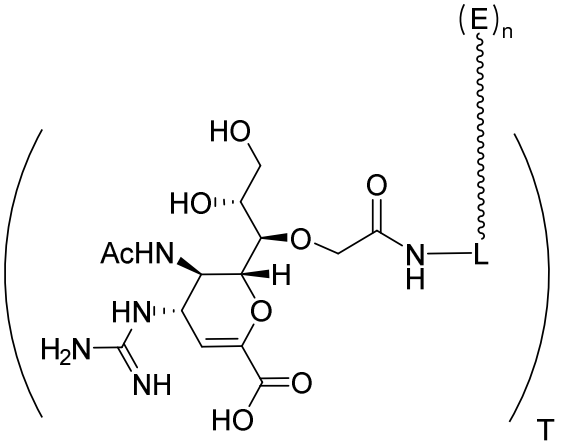
In some examples, the conjugate is described by formula (M-II-1):



(M-II-1)

or a pharmaceutically acceptable salt thereof.

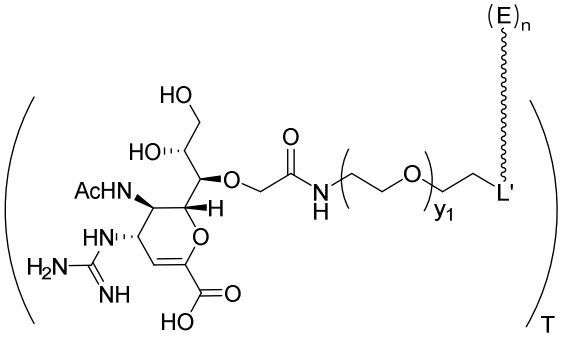
In some examples, the conjugate is described by formula (M-II-2):



(M-II-2)

or a pharmaceutically acceptable salt thereof.

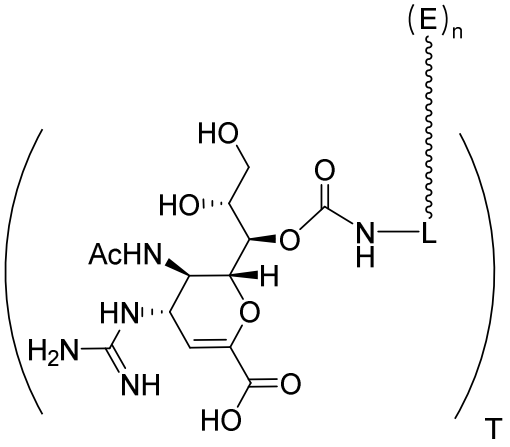
In some examples, the conjugate is described by formula (M-II-3):



(M-II-3)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

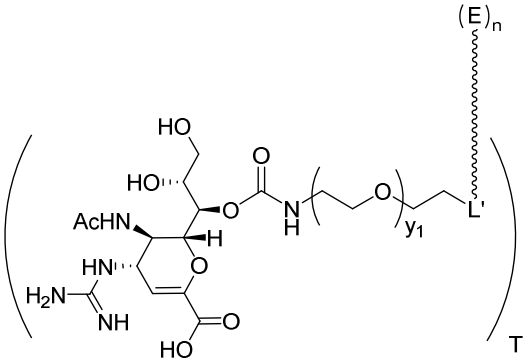
In some examples, the conjugate is described by formula (M-II-4):



(M-II-4)

or a pharmaceutically acceptable salt thereof.

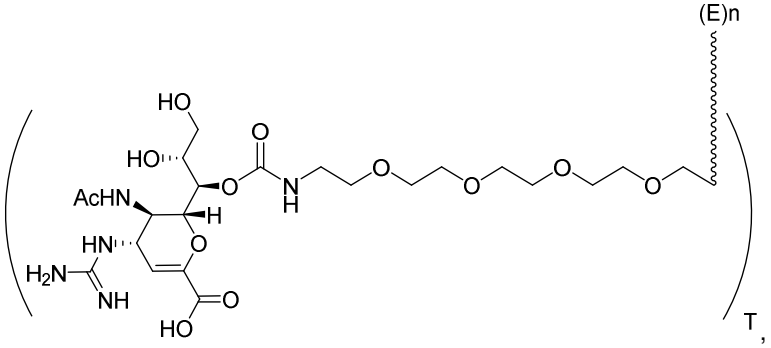
In some examples, the conjugate is described by formula (M-II-5):



(M-II-5)

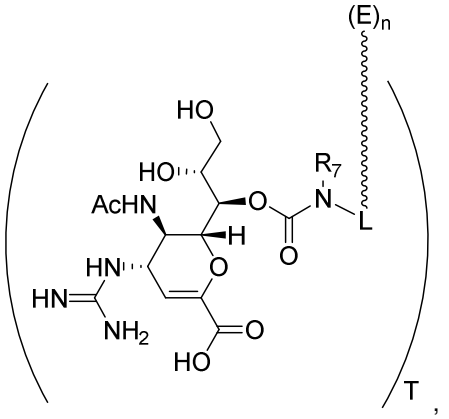
wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

In some examples, the conjugate has the structure



or a pharmaceutically acceptable salt thereof.

In another aspect, the present disclosure provides a conjugate described by formula (M-II-6):

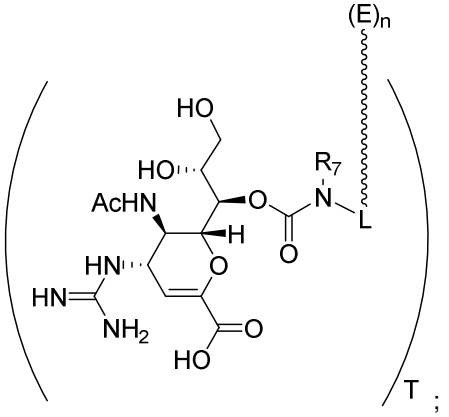


(M-II-6)

wherein R_7 is selected from C_1-C_{20} alkyl, C_3-C_{20} cycloalkyl, C_3-C_{20} heterocycloalkyl, C_5-C_{15} aryl, and C_2-C_{15} heteroaryl,

or a pharmaceutically acceptable salt thereof.

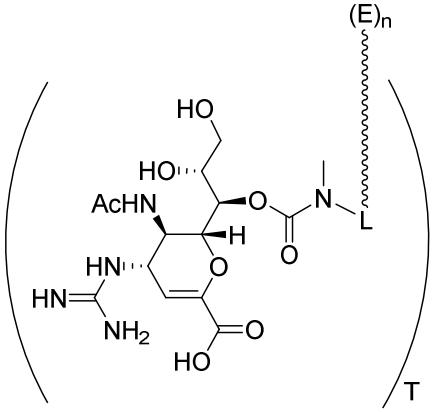
In some examples, the conjugate is described by formula (M-II-6):



(M-II-6)

wherein R_7 is selected from H, C1-C20 alkyl, C3-C20 cycloalkyl, C3-C20 heterocycloalkyl; C5-C15 aryl, and C2-C15 heteroaryl; or a pharmaceutically acceptable salt thereof. In some examples, R_7 is selected from C1-C20 alkyl (e.g., methyl, ethyl, propyl, or butyl).

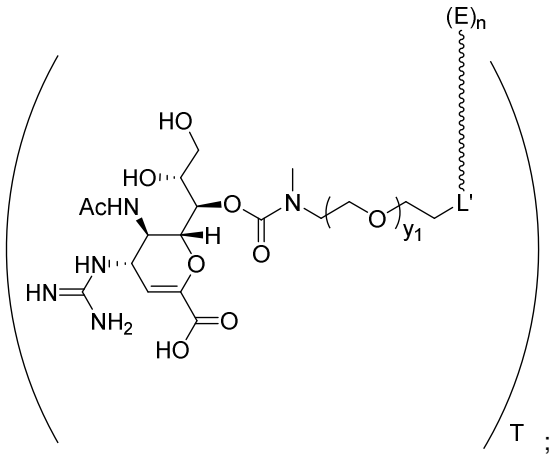
In some examples, the conjugate is described by formula (M-II-7):



(M-II-7)

or a pharmaceutically acceptable salt thereof.

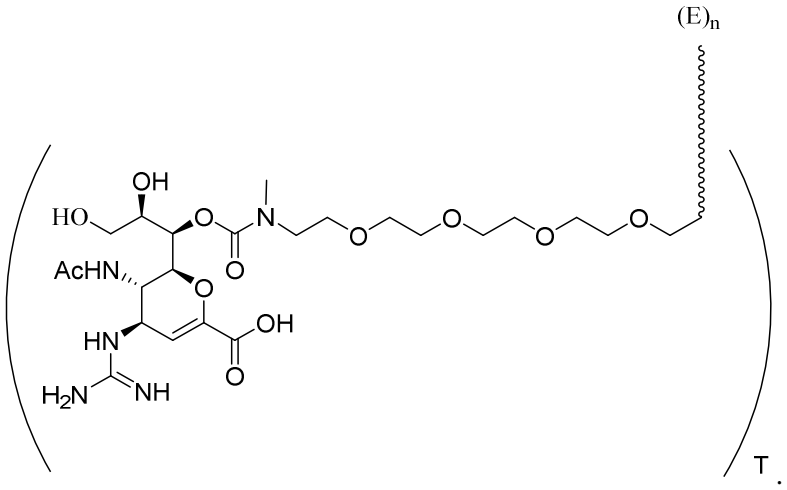
In some examples, the conjugate is described by formula (M-II-8):



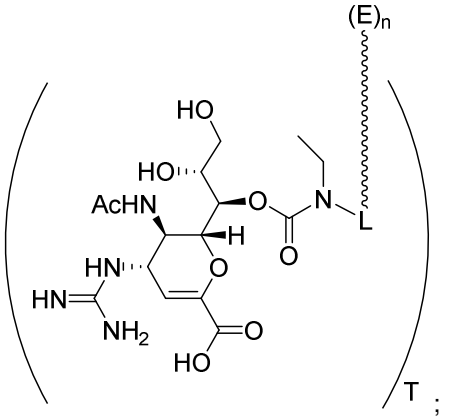
(M-II-8)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

In some examples, the conjugate has the structure:



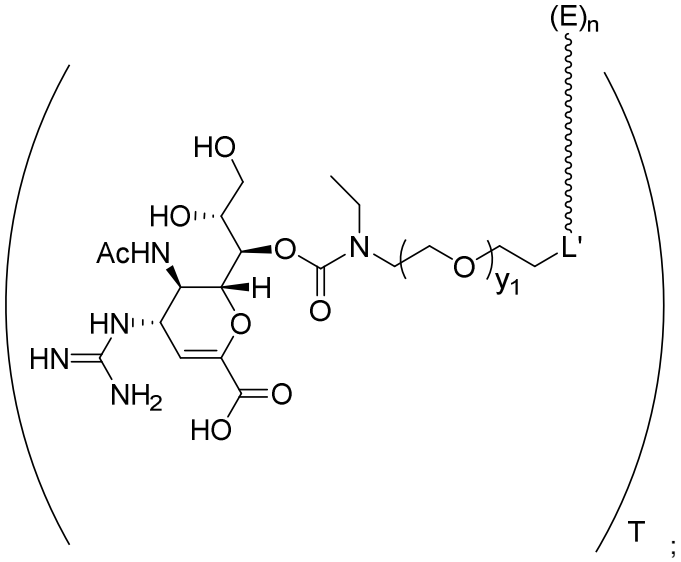
In some examples, the conjugate is described by formula (M-II-9):



(M-II-9)

or a pharmaceutically acceptable salt thereof.

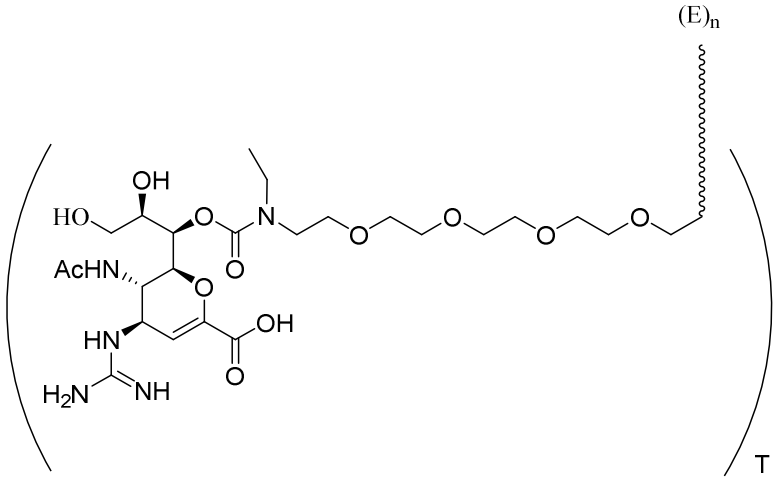
In some examples, the conjugate is described by formula (M-II-10):



(M-II-10)

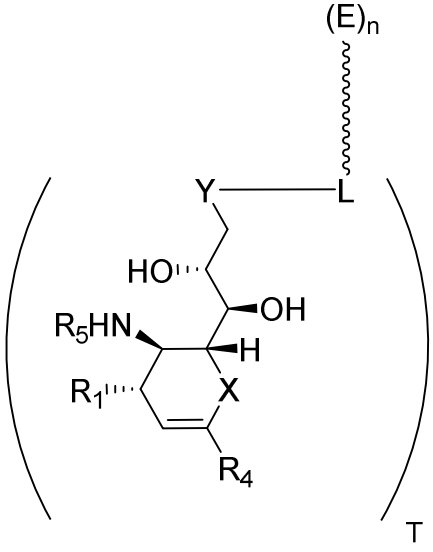
wherein L' is the remainder of L, and y1 is an integer from 1-20 (e.g., y1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

In some examples, the conjugate has the structure



or a pharmaceutically acceptable salt thereof.

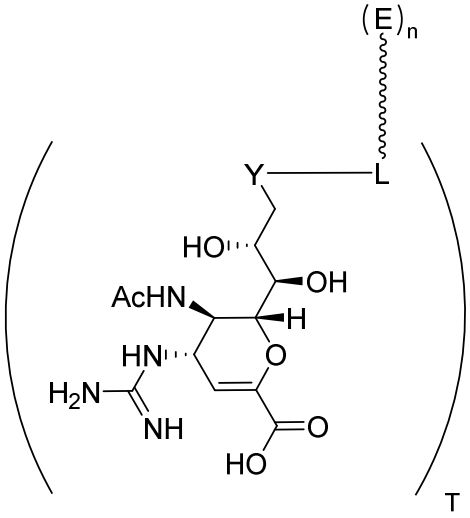
In some examples, the conjugate is described by formula (M-III):



(M-III)

or a pharmaceutically acceptable salt thereof.

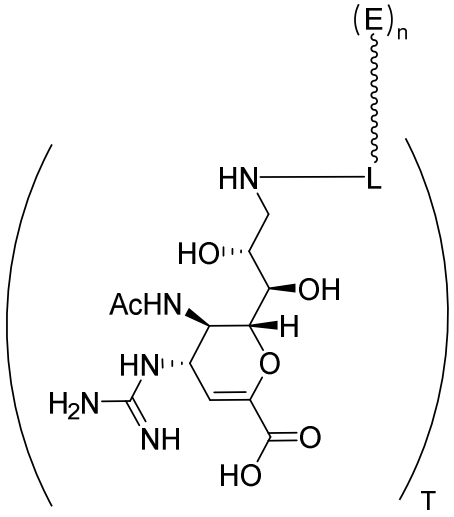
In some examples, the conjugate is described by formula (M-III-1):



(M-III-1)

or a pharmaceutically acceptable salt thereof.

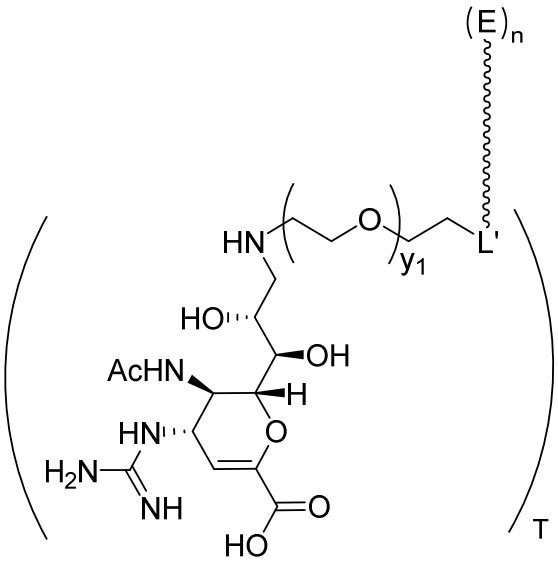
In some examples, the conjugate is described by formula (M-III-2):



(M-III-2)

or a pharmaceutically acceptable salt thereof.

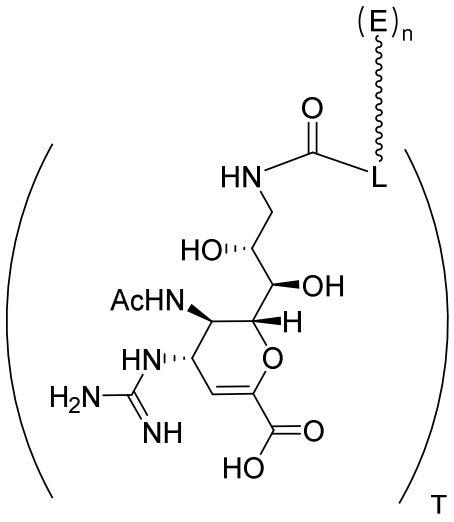
In some examples, the conjugate is described by formula (M-III-3):



(M-III-3)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

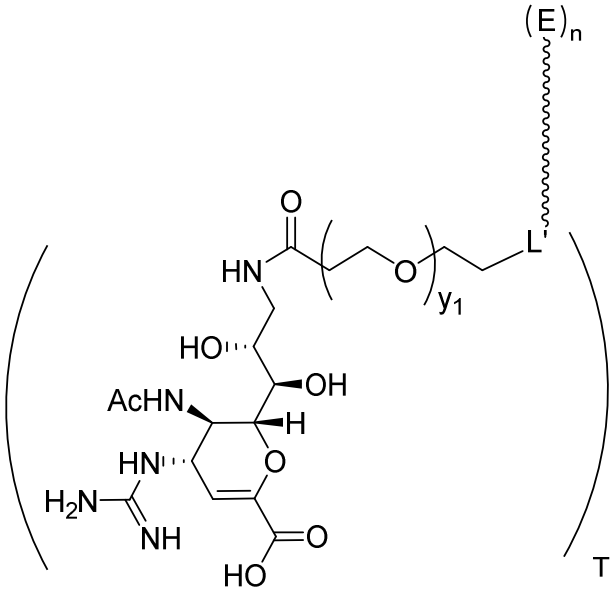
In some examples, the conjugate is described by formula (M-III-4):



(M-III-4)

or a pharmaceutically acceptable salt thereof.

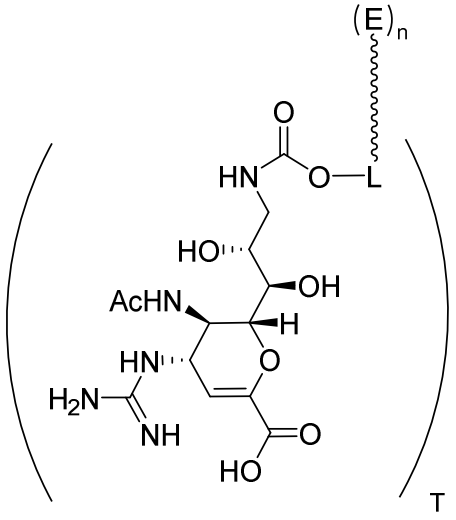
In some examples, the conjugate is described by formula (M-III-5):



(M-III-5)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

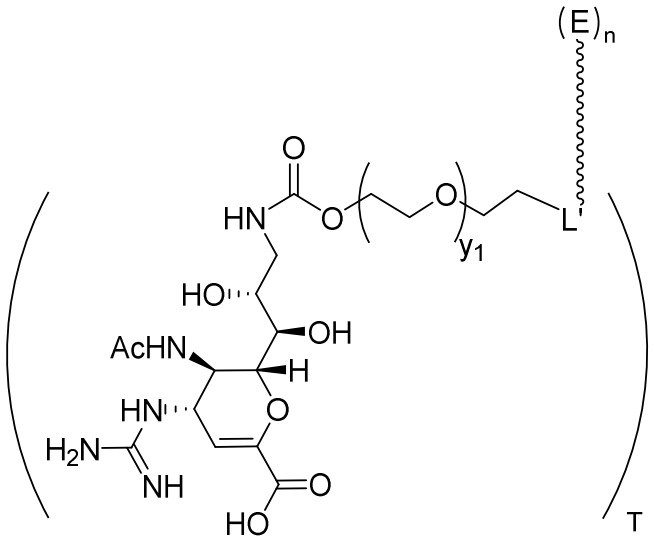
In some examples, the conjugate is described by formula (M-III-6):



(M-III-6)

or a pharmaceutically acceptable salt thereof.

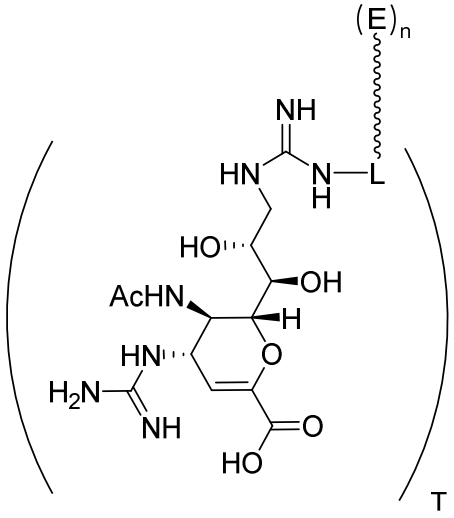
In some examples, the conjugate is described by formula (M-III-7):



(M-III-7)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

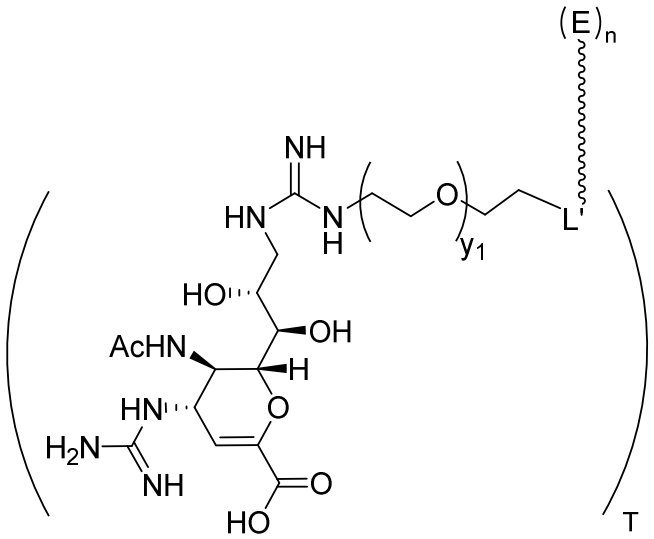
In some examples, the conjugate is described by formula (M-III-8):



(M-III-8)

or a pharmaceutically acceptable salt thereof.

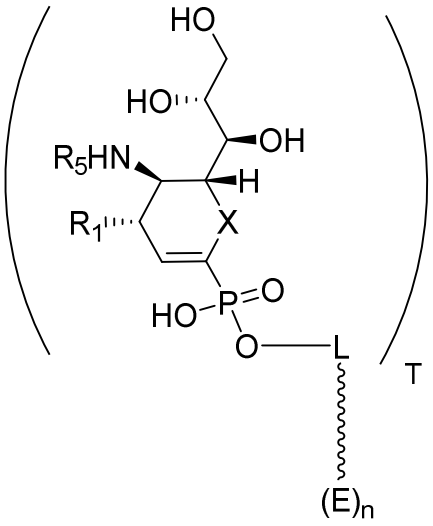
In some examples, the conjugate is described by formula (M-III-9):



(M-III-9)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

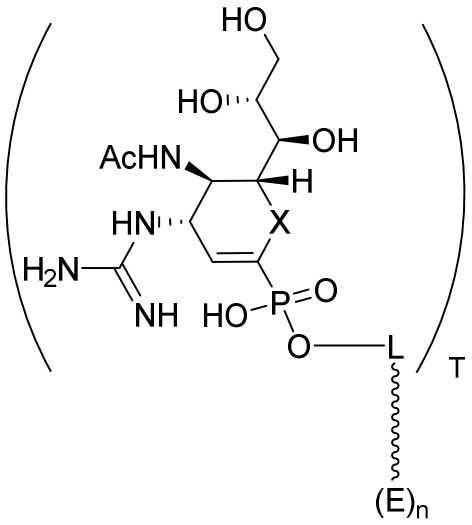
In some examples, the conjugate is described by formula (M-IV):



(M-IV)

or a pharmaceutically acceptable salt thereof.

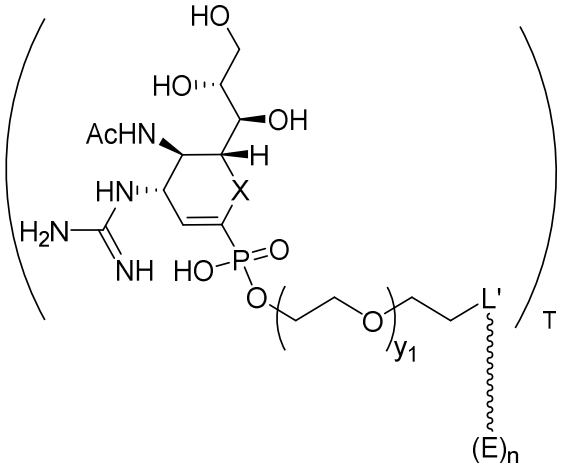
In some examples, the conjugate is described by formula (M-IV-1):



(M-IV-1)

or a pharmaceutically acceptable salt thereof.

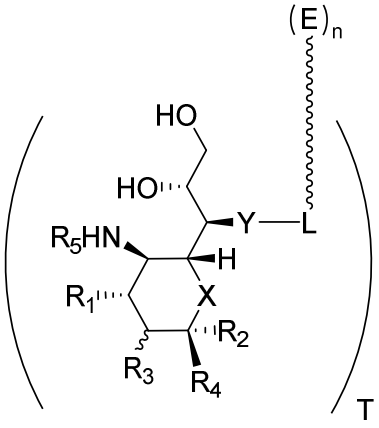
In some examples, the conjugate is described by formula (M-IV-2):



(M-IV-2)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

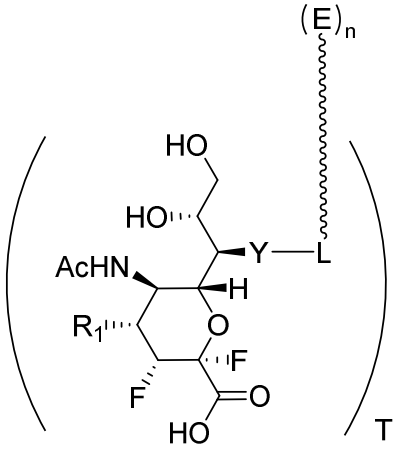
In some examples, the conjugate is described by formula (M-V):



(M-V)

or a pharmaceutically acceptable salt thereof.

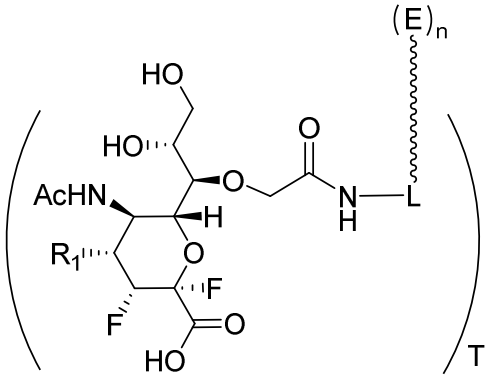
In some examples, the conjugate is described by formula (M-V-1):



(M-V-1)

or a pharmaceutically acceptable salt thereof.

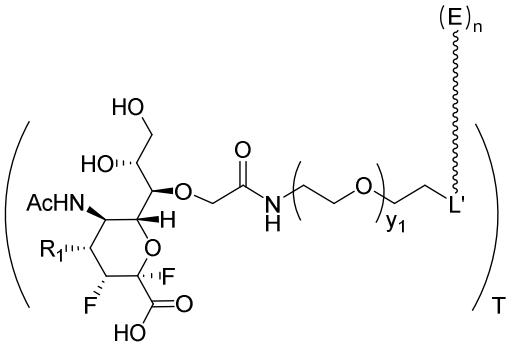
In some examples, the conjugate is described by formula (M-V-2):



(M-V-2)

or a pharmaceutically acceptable salt thereof.

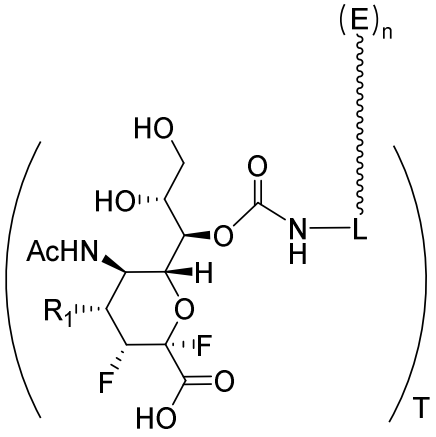
In some examples, the conjugate is described by formula (M-V-3):



(M-V-3)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

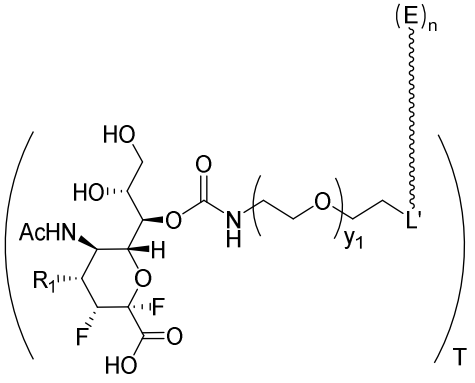
In some examples, the conjugate is described by formula (M-V-4):



(M-V-4)

or a pharmaceutically acceptable salt thereof.

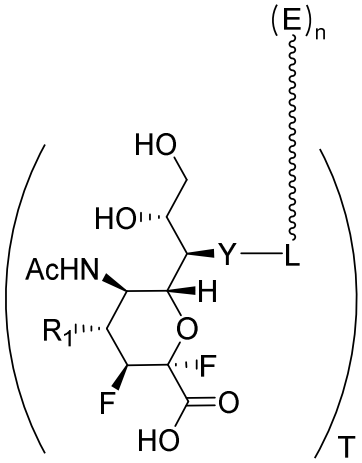
In some examples, the conjugate is described by formula (M-V-5):



(M-V-5)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

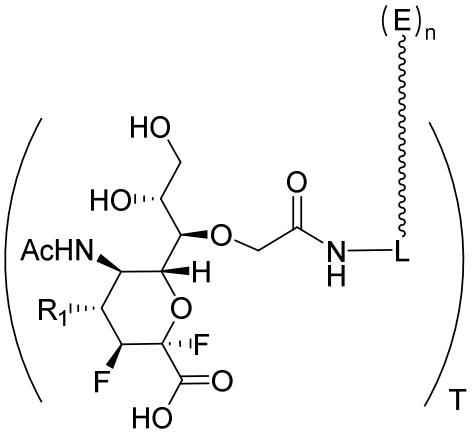
In some examples, the conjugate is described by formula (M-V-6):



(M-V-6)

or a pharmaceutically acceptable salt thereof.

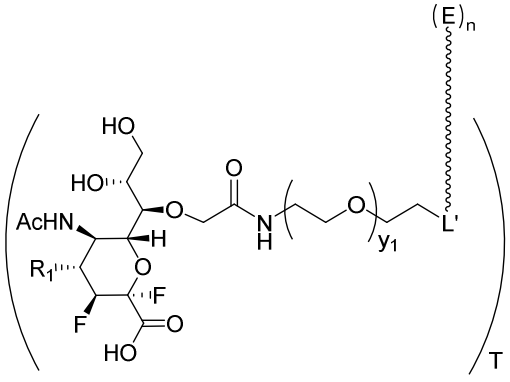
In some examples, the conjugate is described by formula (M-V-7):



(M-V-7)

or a pharmaceutically acceptable salt thereof.

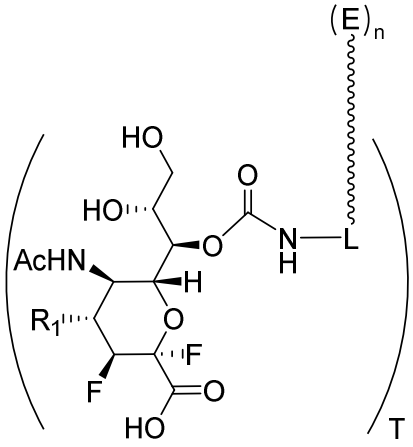
In some examples, the conjugate is described by formula (M-V-8):



(M-V-8)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

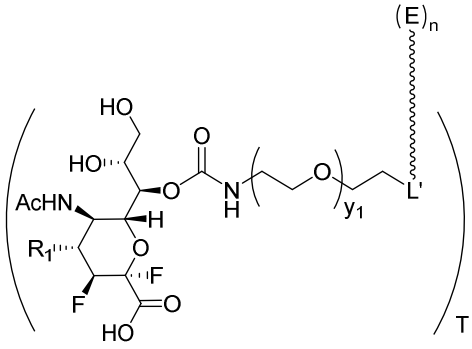
In some examples, the conjugate is described by formula (M-V-9):



(M-V-9)

or a pharmaceutically acceptable salt thereof.

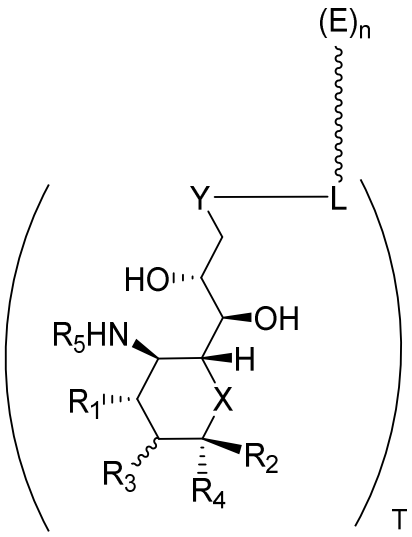
In some examples, the conjugate is described by formula (M-V-10):



(M-V-10)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

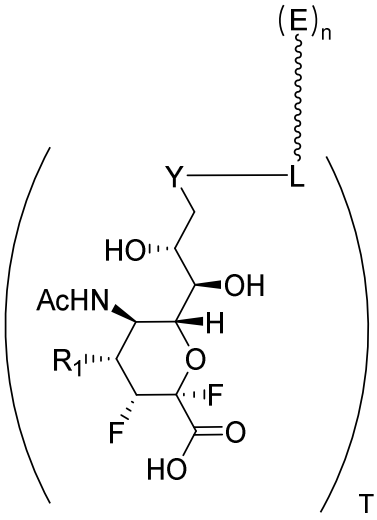
In some examples, the conjugate is described by formula (M-VI):



(M-VI)

or a pharmaceutically acceptable salt thereof.

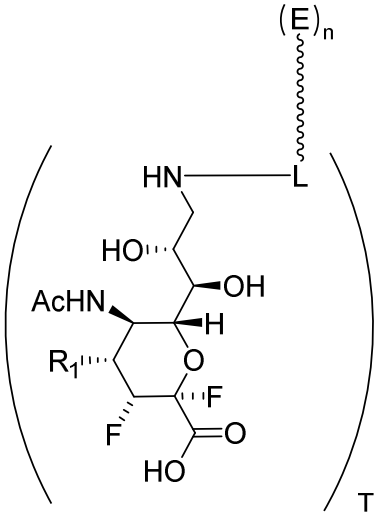
In some examples, the conjugate is described by formula (M-VI-1):



(M-VI-1)

or a pharmaceutically acceptable salt thereof.

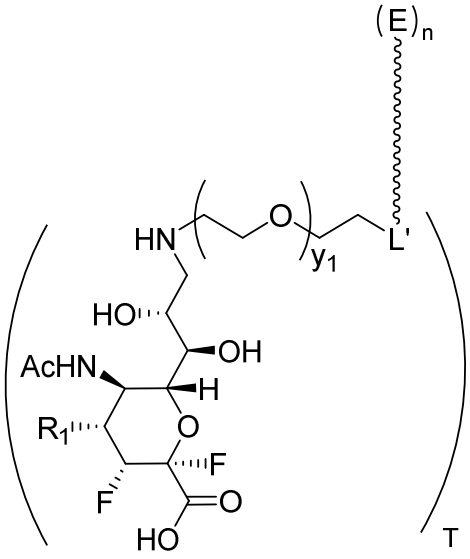
In some examples, the conjugate is described by formula (M-VI-2):



(M-VI-2)

or a pharmaceutically acceptable salt thereof.

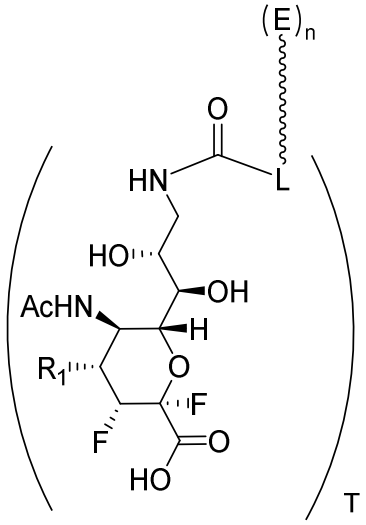
In some examples, the conjugate is described by formula (M-VI-3):



(M-VI-3)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

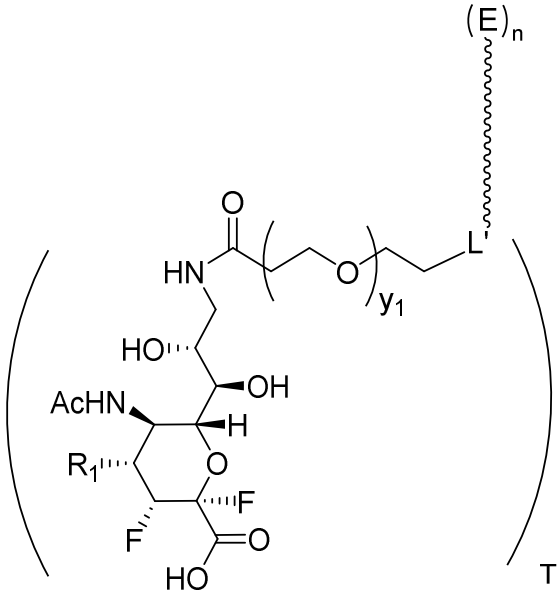
In some examples, the conjugate is described by formula (M-VI-4):



(M-VI-4)

or a pharmaceutically acceptable salt thereof.

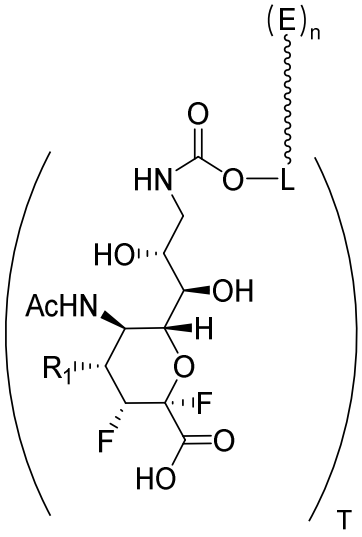
In some examples, the conjugate is described by formula (M-VI-5):



(M-VI-5)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

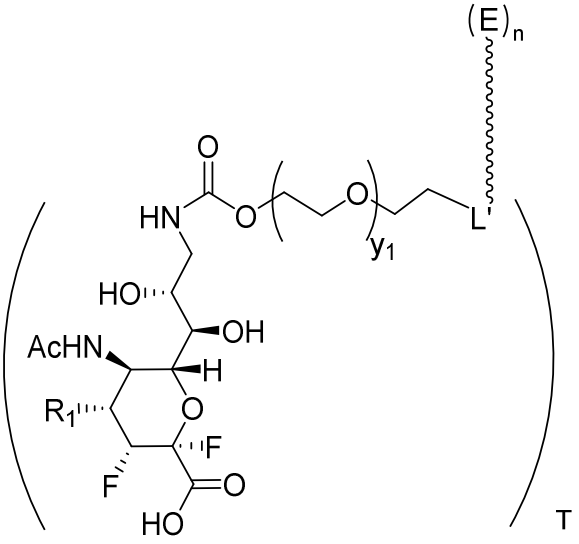
In some examples, the conjugate is described by formula (M-VI-6):



(M-VI-6)

or a pharmaceutically acceptable salt thereof.

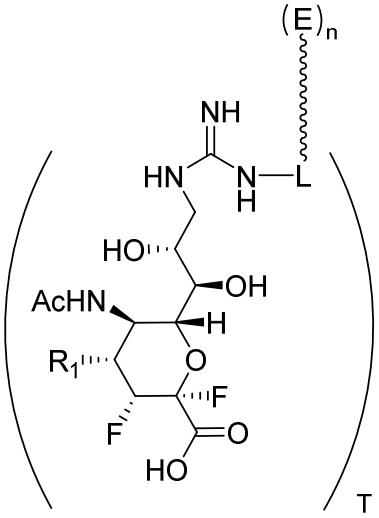
In some examples, the conjugate is described by formula (M-VI-7):



(M-VI-7)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

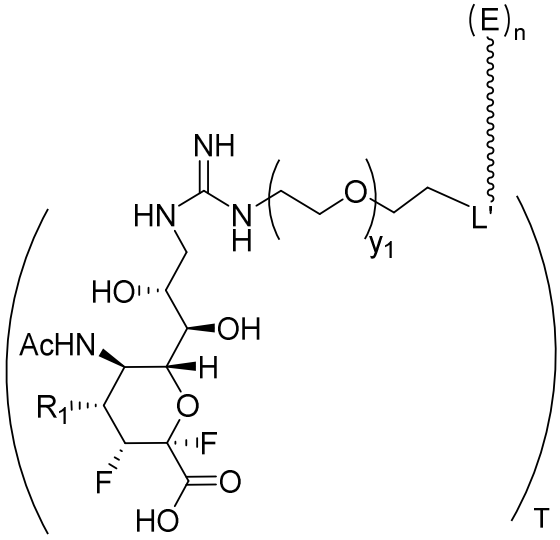
In some examples, the conjugate is described by formula (M-VI-8):



(M-VI-8)

or a pharmaceutically acceptable salt thereof.

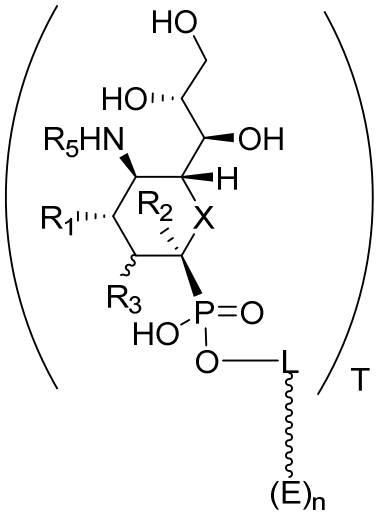
In some examples, the conjugate is described by formula (M-VI-9):



(M-VI-9)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

In some examples, the conjugate is described by formula (M-VII):

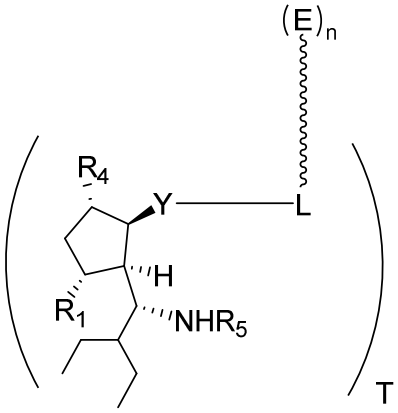


(M-VII)

or a pharmaceutically acceptable salt thereof.

In some examples or aspects described herein, R_1 is OH. In some examples or aspects described herein, R_1 is NH_2. In some examples or aspects described herein, R_1 is -NHC(=NH)NH_2.

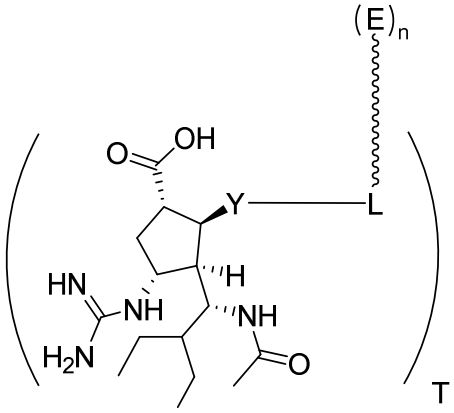
In some examples, the conjugate is described by formula (M-VIII):



(M-VIII)

or a pharmaceutically acceptable salt thereof.

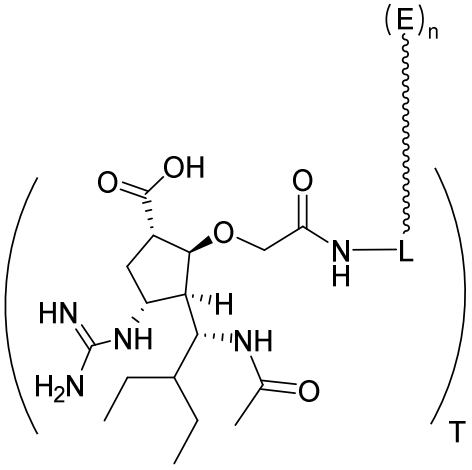
In some examples, the conjugate is described by formula (M-VIII-1):



(M-VIII-1)

or a pharmaceutically acceptable salt thereof.

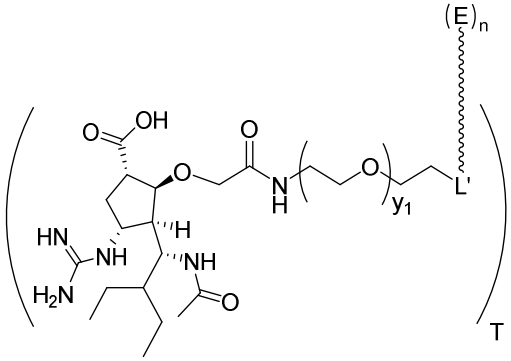
In some examples, the conjugate is described by (M-VIII-2):



(M-VIII-2)

or a pharmaceutically acceptable salt thereof.

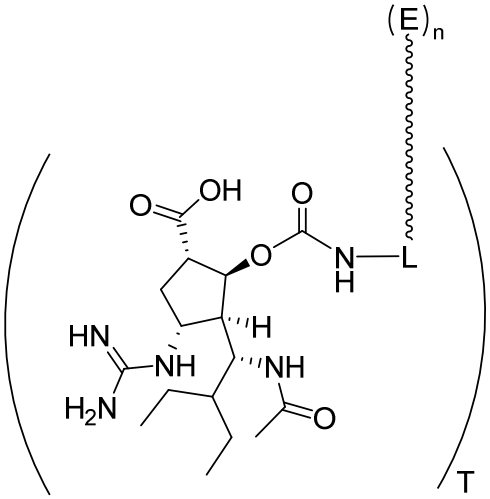
In some examples, the conjugate is described by formula (M-VIII-3):



(M-VIII-3)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

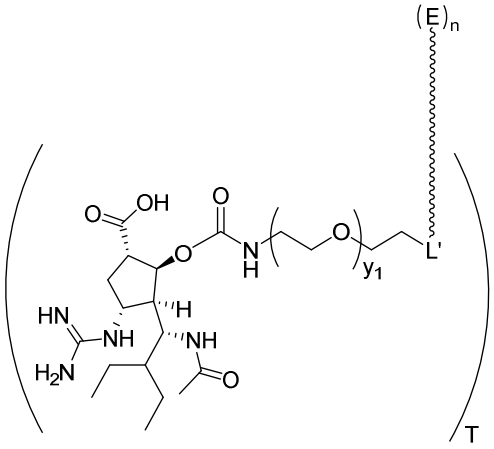
In some examples, the conjugate is described by formula (M-VIII-4):



(M-VIII-4)

or a pharmaceutically acceptable salt thereof.

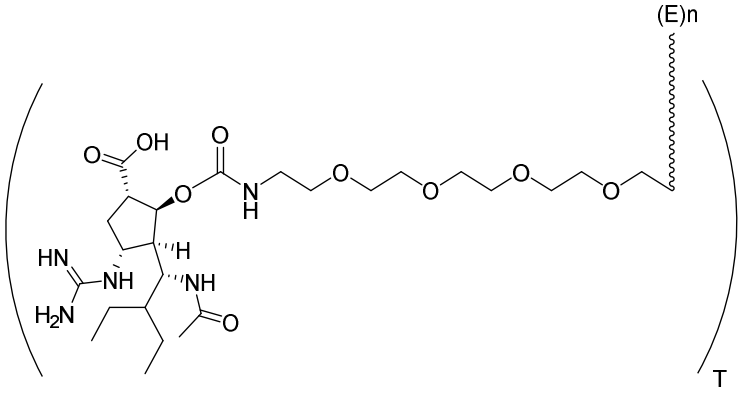
In some examples, the conjugate is described by formula (M-VIII-5):



(M-VIII-5)

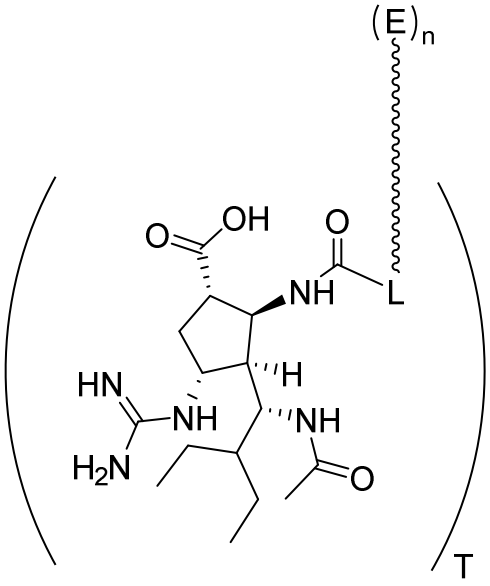
wherein L' is the remainder of L, and y_1 is an integer from 1-20, or a pharmaceutically acceptable salt thereof.

In some examples, the conjugate has the structure of



or a pharmaceutically acceptable salt thereof.

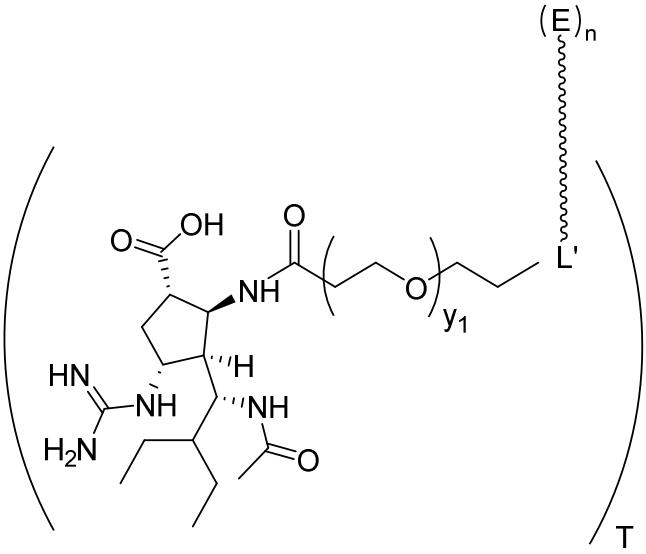
In some examples, the conjugate is described by formula (M-VIII-6):



(M-VIII-6)

or a pharmaceutically acceptable salt thereof.

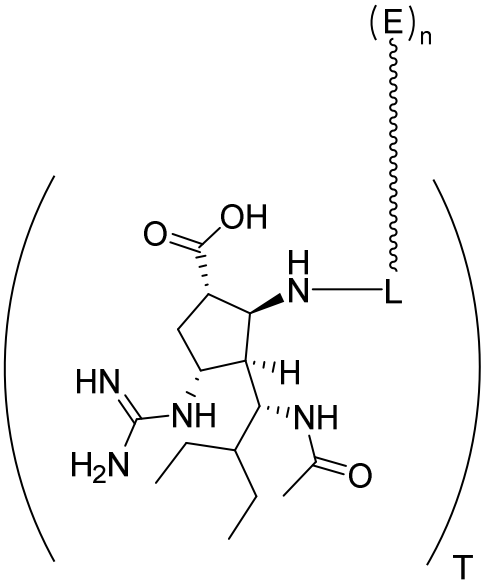
In some examples, the conjugate is described by formula (M-VIII-7):



(M-VIII-7)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

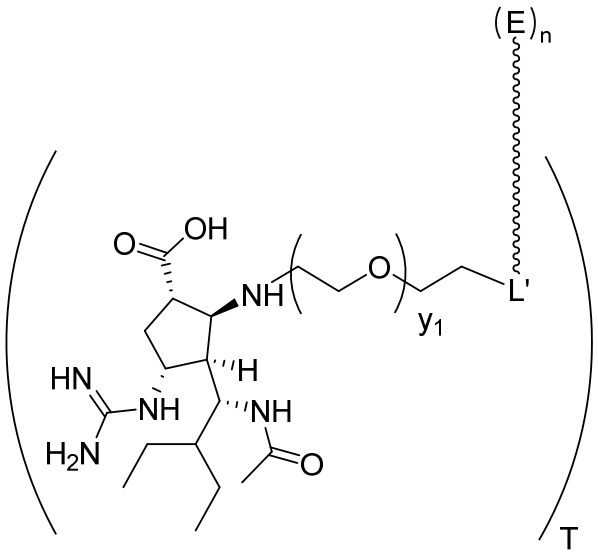
In some examples, the conjugate is described by formula (M-VIII-8):



(M-VIII-8)

or a pharmaceutically acceptable salt thereof.

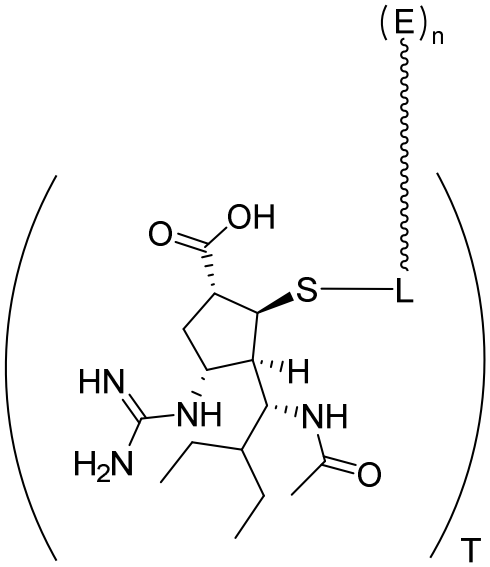
In some examples, the conjugate is described by formula (M-VIII-9):



(M-VIII-9)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

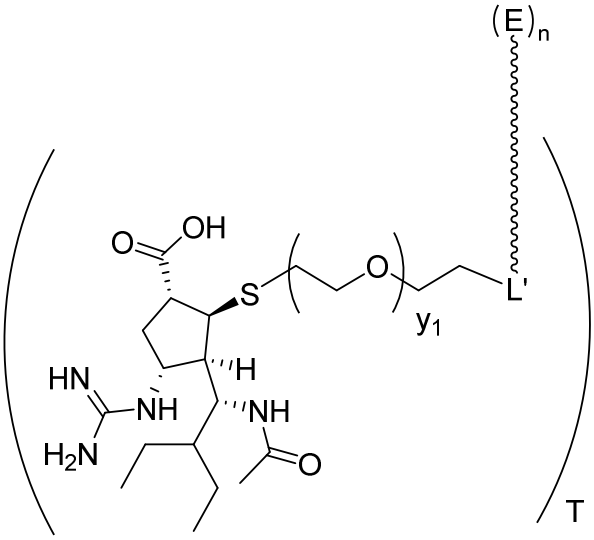
In some examples, the conjugate is described by formula (M-VIII-10):



(M-VIII-10)

or a pharmaceutically acceptable salt thereof.

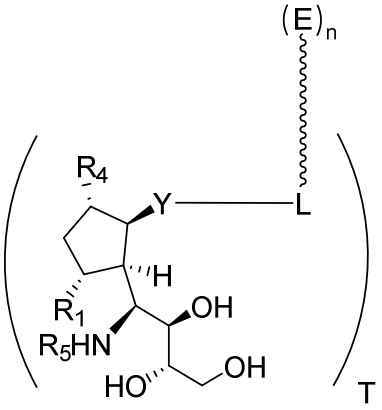
In some examples, the conjugate is described by formula (M-VIII-11):



(M-VIII-11)

wherein L' is the remainder of L, and y_1 is an integer from 1-20 (e.g., y_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

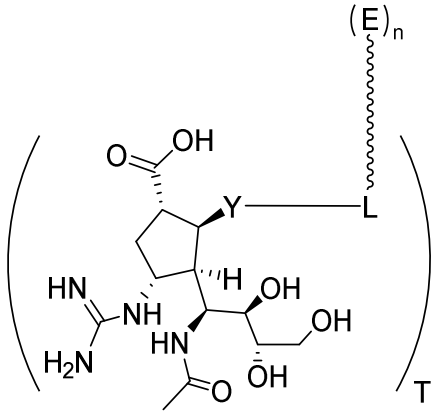
In some examples, the conjugate is described by formula (M-IX):



(M-IX)

or a pharmaceutically acceptable salt thereof.

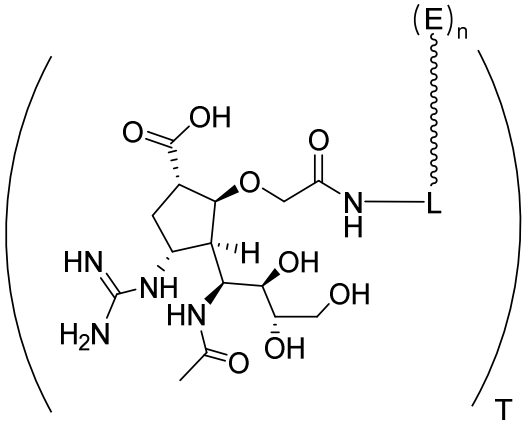
In some examples, the conjugate is described by formula (M-IX-1):



(M-IX-1)

or a pharmaceutically acceptable salt thereof.

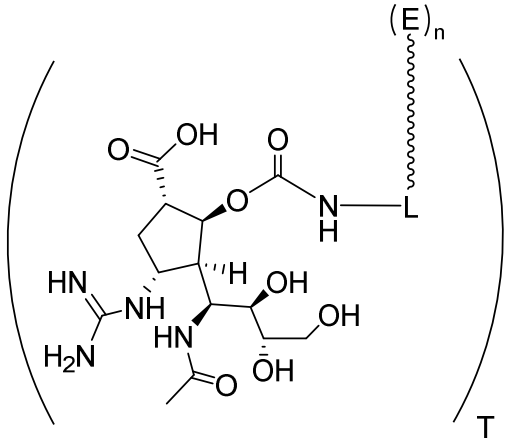
In some examples, the conjugate is described by formula (M-IX-2):



(M-IX-2)

or a pharmaceutically acceptable salt thereof.

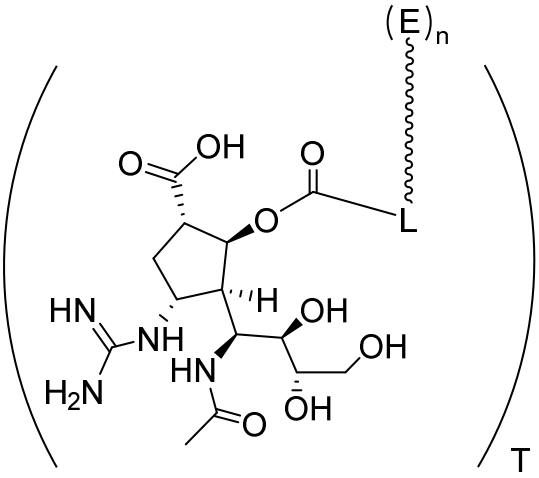
In some examples, the conjugate is described by formula (M-IX-3):



(M-IX-3)

or a pharmaceutically acceptable salt thereof.

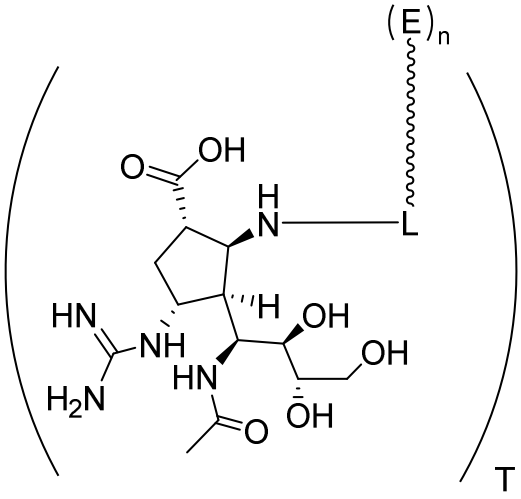
In some examples, the conjugate is described by formula (M-IX-4):



(M-IX-4)

or a pharmaceutically acceptable salt thereof.

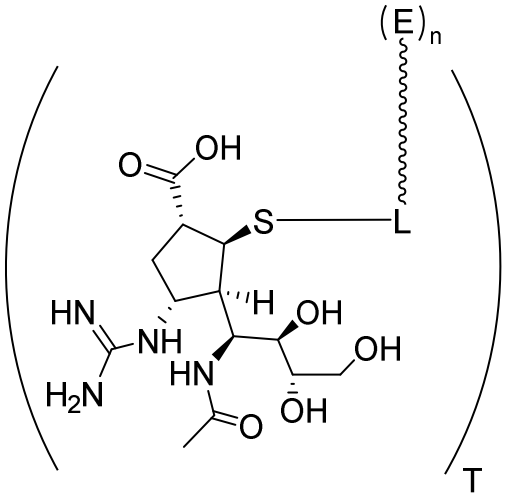
In some examples, the conjugate is described by formula (M-IX-5):



(M-IX-5)

or a pharmaceutically acceptable salt thereof.

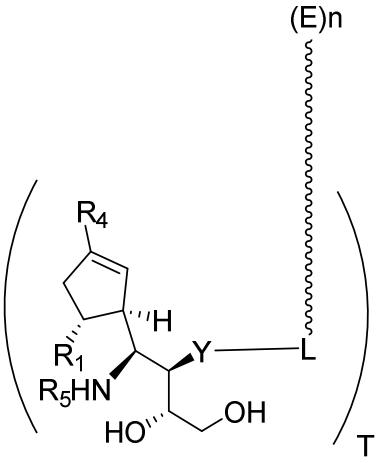
In some examples, the conjugate is described by formula (M-IX-6):



(M-IX-6)

or a pharmaceutically acceptable salt thereof.

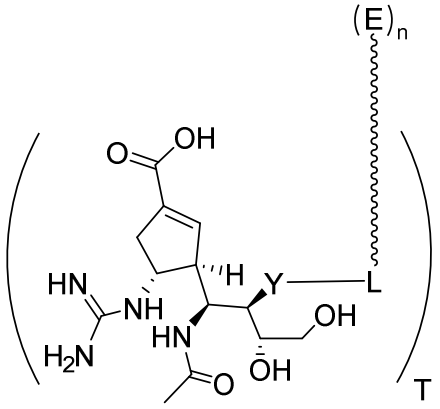
In some examples, the conjugate is described by formula (M-X):



(M-X)

or a pharmaceutically acceptable salt thereof.

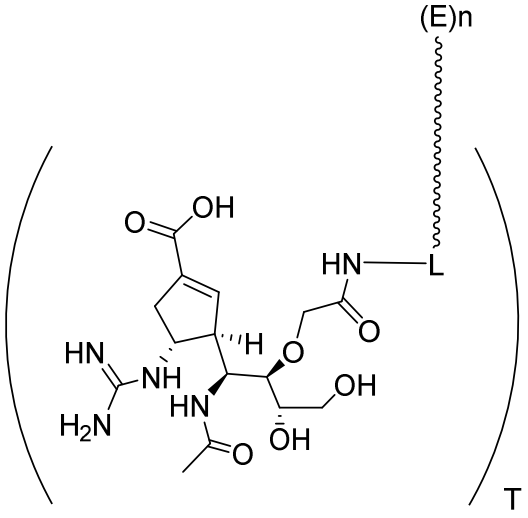
In some examples, the conjugate is described by formula (M-X-1):



(M-X-1)

or a pharmaceutically acceptable salt thereof.

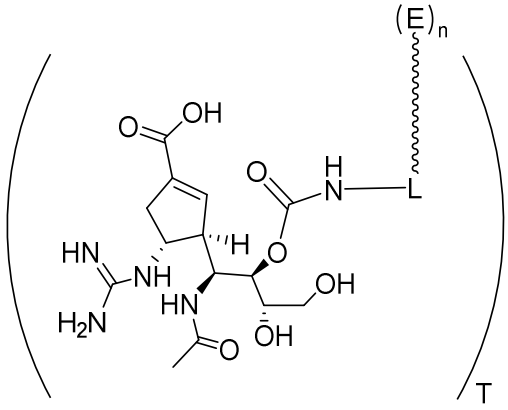
In some examples, the conjugate is described by formula (M-X-2):



(M-X-2)

or a pharmaceutically acceptable salt thereof.

In some examples, the conjugate is described by formula (M-X-3):



(M-X-3)

or a pharmaceutically acceptable salt thereof.

In some examples or aspects described herein, L or L' comprises one or more optionally substituted C1-C20 alkylene, optionally substituted C1-C20 heteroalkylene, optionally substituted C2-C20 alkenylene, optionally substituted C2-C20 heteroalkenylene, optionally substituted C2-C20 alkynylene, optionally substituted C2-C20 heteroalkynylene, optionally substituted C3-C20 cycloalkylene, optionally substituted C3-C20 heterocycloalkylene, optionally substituted C4-C20 cycloalkenylene, optionally substituted C4-C20 heterocycloalkenylene, optionally substituted C8-C20 cycloalkynylene, optionally substituted C8-C20 heterocycloalkynylene, optionally substituted C5-C15 arylene, optionally substituted C2-C15 heteroarylene, O, S, NR^i, P, carbonyl, thiocarbonyl, sulfonyl, phosphate, phosphoryl, or imino, wherein R^i is H, optionally substituted C1-C20 alkyl, optionally substituted C1-C20 heteroalkyl, optionally substituted C2-C20 alkenyl, optionally substituted C2-C20 heteroalkenyl, optionally substituted C2-C20 alkynyl, optionally substituted C2-C20 heteroalkynyl, optionally substituted C3-C20 cycloalkyl, optionally substituted C3-C20 heterocycloalkyl, optionally substituted C4-C20 cycloalkenyl, optionally substituted C4-C20 heterocycloalkenyl, optionally substituted C8-C20 cycloalkynyl, optionally substituted C8-C20 heterocycloalkynyl, optionally substituted C5-C15 aryl, or optionally substituted C2-C15 heteroaryl.

In some examples or aspects described herein, the backbone of L or L' consists of one or more optionally substituted C1-C20 alkylene, optionally substituted C1-C20 heteroalkylene, optionally substituted C2-C20 alkenylene, optionally substituted C2-C20 heteroalkenylene, optionally substituted C2-C20 alkynylene, optionally substituted C2-C20 heteroalkynylene, optionally substituted C3-C20 cycloalkylene, optionally substituted C3-C20 heterocycloalkylene, optionally substituted C4-C20 cycloalkenylene, optionally substituted C4-C20 heterocycloalkenylene, optionally substituted C8-C20 cycloalkynylene, optionally substituted C8-C20 heterocycloalkynylene, optionally substituted C5-C15 arylene, optionally substituted C2-C15 heteroarylene, O, S, NR^i, P, carbonyl, thiocarbonyl, sulfonyl, phosphate, phosphoryl, or imino, wherein R^i is H, optionally substituted C1-C20 alkyl, optionally substituted C1-C20 heteroalkyl, optionally substituted C2-C20 alkenyl, optionally substituted C2-C20 heteroalkenyl, optionally substituted C2-C20 alkynyl, optionally substituted C2-C20 heteroalkynyl, optionally substituted C3-C20 cycloalkyl, optionally substituted C3-C20 heterocycloalkyl, optionally

substituted C4-C20 cycloalkenyl, optionally substituted C4-C20 heterocycloalkenyl, optionally substituted C8-C20 cycloalkynyl, optionally substituted C8-C20 heterocycloalkynyl, optionally substituted C5-C15 aryl, or optionally substituted C2-C15 heteroaryl.

In some examples or aspects described herein, L or L' is oxo substituted. In some examples, the backbone of L or L' comprises no more than 250 atoms. In some examples, L or L' is capable of forming an amide, a carbamate, a sulfonyl, or a urea linkage. In some examples, L or L' is a bond. In some examples, L or L' is an atom. In some examples, L' is a nitrogen atom.

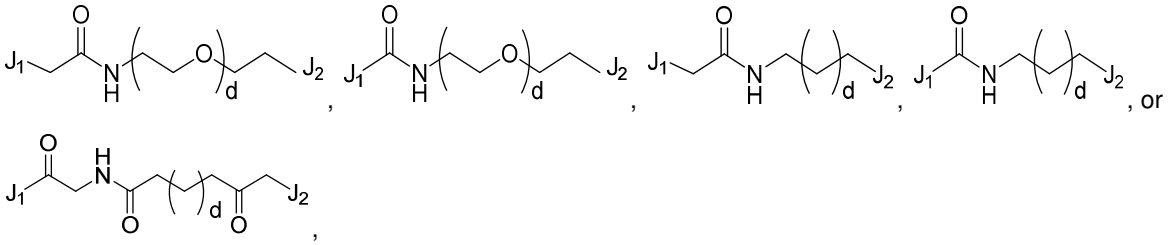
In some examples, each L is described by formula (M-L-1):

$$J^1\text{-}(Q^1)_g\text{-}(T^1)_h\text{-}(Q^2)_i\text{-}(T^2)_j\text{-}(Q^3)_k\text{-}(T^3)_l\text{-}(Q^4)_m\text{-}(T^4)_n\text{-}(Q^5)_o\text{-}J^2$$

wherein: J^1 is a bond attached to A1; J^2 is a bond attached to E or a functional group capable of reacting with a functional group conjugated to E (e.g., maleimide and cysteine, amine and activated carboxylic acid, thiol and maleimide, activated sulfonic acid and amine, isocyanate and amine, azide and alkyne, and alkene and tetrazine); each of Q^1, Q^2, Q^3, Q^4, and Q^5 is, independently, optionally substituted C1-C20 alkylene, optionally substituted C1-C20 heteroalkylene, optionally substituted C2-C20 alkenylene, optionally substituted C2-C20 heteroalkenylene, optionally substituted C2-C20 alkynylene, optionally substituted C2-C20 heteroalkynylene, optionally substituted C3-C20 cycloalkylene, optionally substituted C3-C20 heterocycloalkylene, optionally substituted C4-C20 cycloalkenylene, optionally substituted C4-C20 heterocycloalkenylene, optionally substituted C8-C20 cycloalkynylene, optionally substituted C8-C20 heterocycloalkynylene, optionally substituted C5-C15 arylene, or optionally substituted C2-C15 heteroarylene; each of T^1, T^2, T^3, T^4 is, independently, O, S, NR^i, P, carbonyl, thiocarbonyl, sulfonyl, phosphate, phosphoryl, or imino; R^i is H, optionally substituted C1-C20 alkyl, optionally substituted C1-C20 heteroalkyl, optionally substituted C2-C20 alkenyl, optionally substituted C2-C20 heteroalkenyl, optionally substituted C2-C20 alkynyl, optionally substituted C2-C20 heteroalkynyl, optionally substituted C3-C20 cycloalkyl, optionally substituted C3-C20 heterocycloalkyl, optionally substituted C4-C20 cycloalkenyl, optionally substituted C4-C20 heterocycloalkenyl, optionally substituted C8-C20 cycloalkynyl, optionally substituted C8-C20 heterocycloalkynyl, optionally substituted C5-C15 aryl, or optionally substituted C2-C15 heteroaryl; and each of g, h, i, j, k, l, m, n, and o is, independently, 0 or 1; or a pharmaceutically acceptable salt thereof.

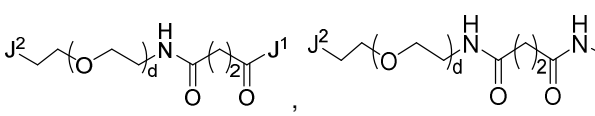
In some examples, J^2 may have two points of attachment to the Fc domain, Fc-binding peptide, albumin protein, or albumin protein-binding peptide (e.g., two J^2).

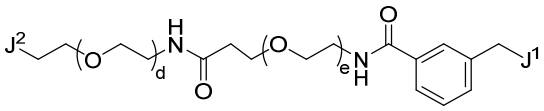
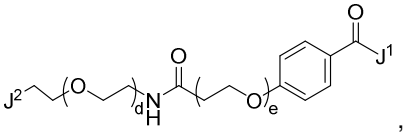
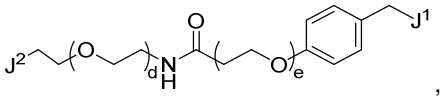
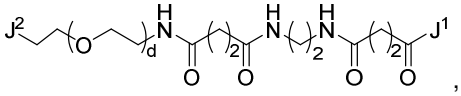
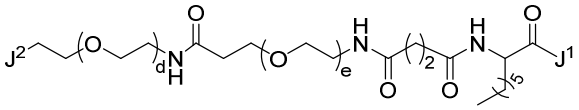
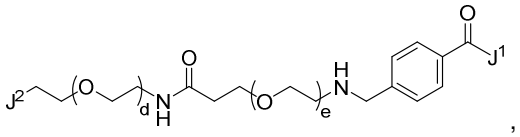
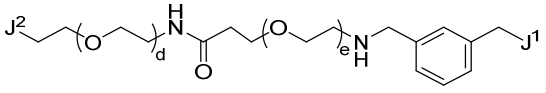
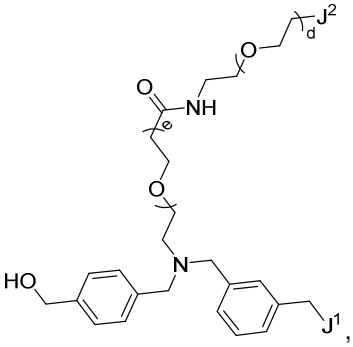
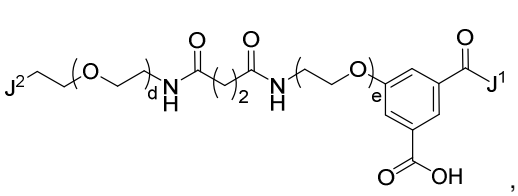
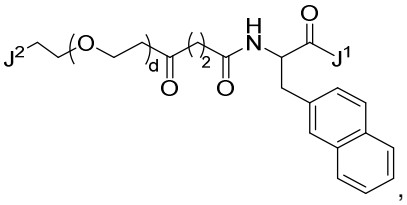
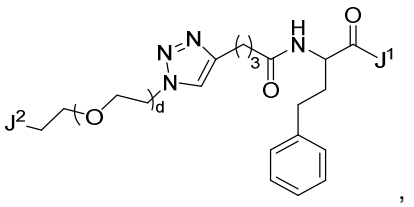
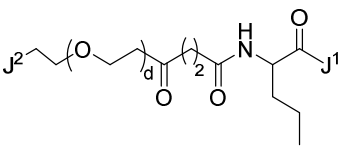
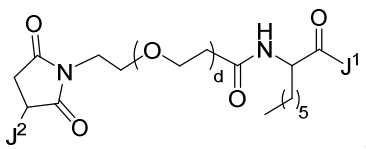
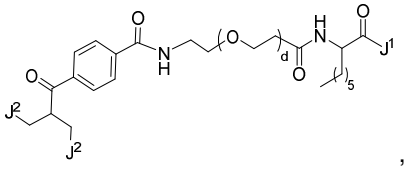
In some examples, L is



wherein d is an integer from 1 to 20 (e.g., d is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20).

In some examples, L is


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wherein each of d and e is, independently, an integer from 1 to 26; or a pharmaceutically acceptable salt thereof.

In some examples or aspects described herein, L includes a polyethylene glycol (PEG) linker. A PEG linker includes a linker having the repeating unit structure $(-CH_2CH_2O-)_n$, wherein n

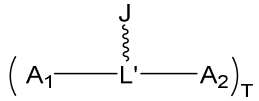
is an integer from 2 to 100. A polyethylene glycol linker may covalently join a neuraminidase inhibitor and E (e.g., in a conjugate of any one of formulas (M-I)-(M-XI)). A polyethylene glycol linker may covalently join a first neuraminidase inhibitor and a second neuraminidase inhibitor (e.g., in a conjugate of any one of formulas (D-I)-(D-XI)). A polyethylene glycol linker may covalently join a neuraminidase inhibitor dimer and E (e.g., in a conjugate of any one of formulas (D-I)-(D-XI)). A polyethylene glycol linker may be selected any one of PEG_2 to PEG_{100} (e.g., PEG_2, PEG_3, PEG_4, PEG_5, PEG_5-PEG_{10}, PEG_{10}-PEG_{20}, PEG_{20}-PEG_{30}, PEG_{30}-PEG_{40}, PEG_{50}-PEG_{60}, PEG_{60}-PEG_{70}, PEG_{70}-PEG_{80}, PEG_{80}-PEG_{90}, PEG_{90}-PEG_{100}). In some examples, L^c includes a PEG linker, where L^C is covalently attached to each of Q and E.

In some examples or aspects described herein, R_1 is -NHC(=NH)NH_2. In some examples or aspects described herein, R_2 is -F. In some examples or aspects described herein, R_3 is -F. In some examples or aspects described herein, R_4 is $–CO_2H$. In some examples or aspects described herein, R_5 is $–COCH_3$.

In some examples or aspects described herein, L is covalently attached to the nitrogen atom of a surface exposed lysine of E or L is covalently attached to the sulfur atom of a surface exposed cysteine of E.

In some examples or aspects described herein, E is an Fc domain monomer. In some examples, n is 2 and each E dimerizes to form an Fc domain.

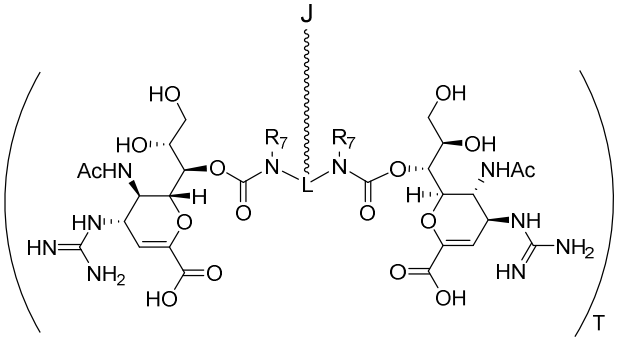
In some examples, n is 2, each E is an Fc domain monomer, each E dimerizes to form an Fc domain, and the conjugate is described by formula (D-I-1):



(D-I-1)

wherein J is an Fc domain; and T is an integer from 1 to 20 (e.g., T is 1 ,2 ,3 ,4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

In one aspect, the present disclosure provides a conjugate described by the structure:



wherein J is an Fc domain comprising two Fc domain monomers;

T is an integer from 1 to 20,

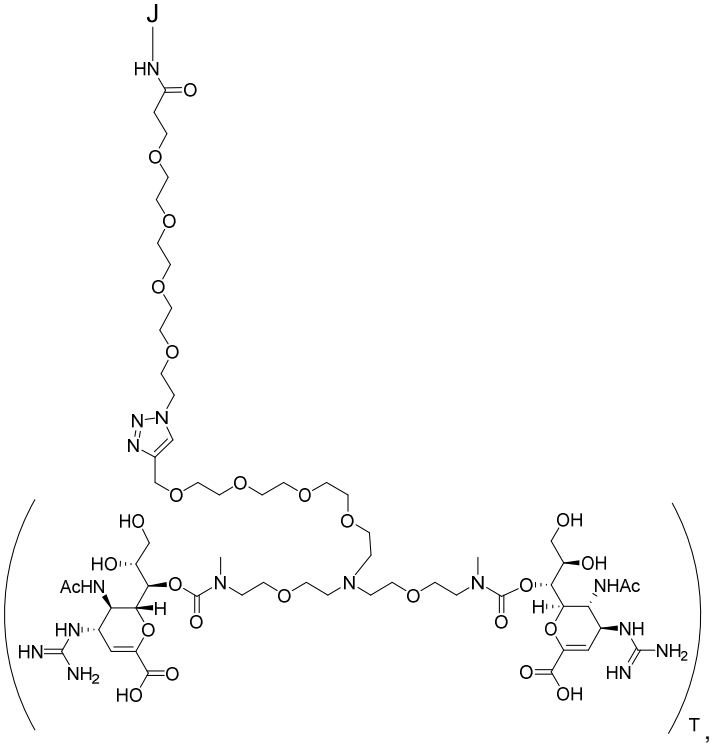
L is a linker;

R_7 is selected from C_1-C_{20} alkyl, C_3-C_{20} cycloalkyl, C_3-C_{20} heterocycloalkyl, C_5-C_{15} aryl, and C_2-C_{15} heteroaryl; and

the squiggly line indicates that L is covalently attached to J,

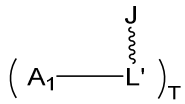
or a pharmaceutically acceptable salt thereof.

In some examples, the conjugate has the structure of



or a pharmaceutically acceptable salt thereof.

In some examples, n is 2, each E is an Fc domain monomer, each E dimerizes to form an Fc domain, and the conjugate is described by formula (M-I-1):



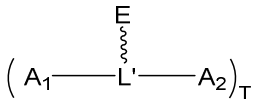
(M-I-1)

wherein J is an Fc domain; and T is an integer from 1 to 20 (e.g., T is 1 ,2 ,3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), or a pharmaceutically acceptable salt thereof.

In some examples or aspects described herein, E has the sequence of any one of SEQ ID NOs: 1-138.

In some examples or aspects described herein, E is an albumin protein, an albumin protein-binding peptide, or an Fc-binding peptide. In some examples, where E is an albumin protein, an albumin protein-binding peptide, or an Fc-binding peptide, n is 1.

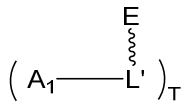
In some examples, n is 1, E is an albumin protein, an albumin protein-binding peptide, or an Fc-binding peptide and the conjugate is described by formula (D-I-2):



(D-I-2)

wherein E is an albumin protein, an albumin protein-binding peptide, or Fc-binding peptide; and T is an integer from 1 to 20, or a pharmaceutically acceptable salt thereof.

In some examples, n is 1, E is an albumin protein, an albumin protein-binding peptide, or an Fc-binding peptide, and the conjugate is described by formula (M-I-2):



(M-I-2)

wherein E is an albumin protein, an albumin protein-binding peptide, or an Fc-binding peptide; and T is an integer from 1 to 20, or a pharmaceutically acceptable salt thereof.

In some examples or aspects described herein, E is an albumin protein having the sequence of any one of SEQ ID NOs: 139-141.

In some examples or aspects described herein, T is 1, 2, 3, 4, or 5.

In one aspect, the present disclosure provides a population of conjugates disclosed herein, wherein the average value of T is 1 to 10. In another example, the disclosure provides a population of conjugates having the structure of any of the conjugates described herein (e.g., a population of conjugates having the formula of any one of formulas (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I)), wherein the average value of T is 1 to 20 (e.g., the average value of T is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5). In some examples, the average value of T is about 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5, 9, 9.5, 10, 10.5, 11, 11.5, 12, 12.5, 13, 13.5, 14, 14.5, 15, 15.5, 16, 16.5, 17, 17.5, 18, 18.5, 19, 19.5, or 20.

In some examples or aspects described herein, when T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1-L-A_2 may be independently selected (e.g., independently selected from any of the A_1-L-A_2 structures described herein). In some examples, E may be conjugated to 2, 3, 4, 5, 6, 7, 8, 9, 10, or more different A_1-L-A_2 moieties. In some examples, E is conjugated to a first A_1-L-A_2 moiety, and a second A_1-L-A_2, moiety. In some examples, A_1 and A_2 of the first A_1-L-A_2 moiety are independently selected from any one of formulas (A-III)-(A-V), and A_1 and A_2 of the second A_1-L-A_2 moiety are independently selected from any one of formulas (A-I), (A-II), (A-VI), (A-VII), (A-VIII), and (A-IX).

In some examples, each of the first A_1-L-A_2 moieties is conjugated specifically to a lysine residue of E (e.g., the nitrogen atom of a surface exposed lysine residue of E), and each of the second A_1-L-A_2 moieties is conjugated specifically to a cysteine residue of E (e.g., the sulfur atom of a surface exposed cysteine residue of E). In some examples, each of the first A_1-L-A_2 moieties is conjugated specifically to a cysteine residue of E (e.g., the sulfur atom of a surface exposed cysteine residue of E), and each of the second A_1-L-A_2 moieties is conjugated specifically to a lysine residue of E (e.g., the nitrogen atom of a surface exposed lysine residue of E).

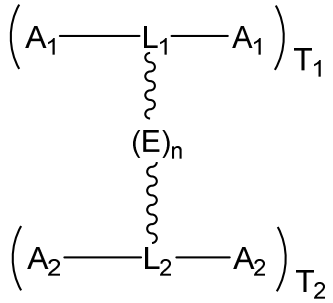
In some examples, the number of first A_1-L-A_2 moieties conjugated to E is an integer from 1 to 10 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10). In some examples, the number of second A_1-L-A_2 moieties conjugated to E is an integer from 1 to 10 (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10).

In some examples or aspects described herein, when T is greater than 1 (e.g., T is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20), each A_1-L may be independently selected (e.g., independently selected from any of the A_1-L structures described herein). In some examples, E may be conjugated to 2, 3, 4, 5, 6, 7, 8, 9, 10, or more different A_1-L moieties. In some examples, E is conjugated to a first A_1-L moiety, and a second A_1-L, moiety. In some examples, A_1 of the first A_1-L moiety is selected from any one of formulas (A-III)-(A-V),
and A_1 of the second A_1-L moiety is selected from any one of formulas (A-I), (A-II), (A-VI), (A-VII), (A-VIII), or (A-IX).

In some examples, each of the first A_1-L moieties is conjugated specifically to a lysine residue of E (e.g., the nitrogen atom of a surface exposed lysine residue of E), and each of the second A_1-L moieties is conjugated specifically to a cysteine residue of E (e.g., the sulfur atom of a surface exposed cysteine residue of E). In some examples, each of the first A_1-L moieties is conjugated specifically to a cysteine residue of E (e.g., the sulfur atom of a surface exposed cysteine residue of E), and each of the second A_1-L moieties is conjugated specifically to a lysine residue of E (e.g., the nitrogen atom of a surface exposed lysine residue of E).

In some examples, the number of first A_1-L moieties conjugated to E is an integer from 1 to 10 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10). In some examples, the number of second A_1-L moieties conjugated to E is an integer from 1 to 10 (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10).

In another example, the disclosure features a conjugate described by formula (D'-I):

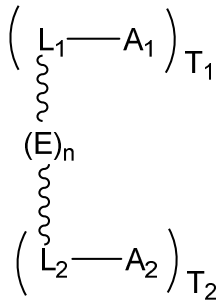


(D'-I)

wherein each A_1 is independently selected from any one of formulas (A-III)-(A-V); wherein each A_2 is independently selected from any one of formulas (A-I), (A-II), (A-VI), (A-VII), (A-VIII), and (A-IX); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138), an albumin protein (e.g., an albumin protein having the sequence of any one of SEQ ID NOs: 139-141), an albumin protein-binding peptide, or an Fc-binding peptide; n is 1 or 2; T_1 is an integer from 1 to 10 (e.g., T_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10); L_1 is a linker covalently conjugated to E and to each A_1; T_1 is an integer from 1 to 10 (e.g., T_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10); L_2 is a linker covalently conjugated to E and each A_2; T_2 is an integer from 1 to 10 (e.g., T_2 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10), or a pharmaceutically acceptable salt thereof.

In some examples, each A_1-L-A_1 is conjugated specifically to a lysine residue of E (e.g., the nitrogen atom of a surface exposed lysine residue of E), and each the A_2-L-A_2 is conjugated specifically to a cysteine residue of E (e.g., the sulfur atom of a surface exposed cysteine residue of E). In some examples, each A_1-L-A_1 moiety is conjugated specifically a cysteine residue of E (e.g., the sulfur atom of a surface exposed cysteine residue of E), and each A_2-L-A_2 moiety is conjugated specifically to a lysine residue of E (e.g., the nitrogen atom of a surface exposed lysine residue of E).

In another example, the disclosure features a conjugate described by formula (M'-I):



(M'-I)

wherein each A_1 is independently selected from any one (M-IX)of formulas (A-III)-(A-V); wherein each A_2 is independently selected from any one of formulas (A-I), (A-II), (A-VI), (A-VII), (A-VIII), and (A-IX); each E comprises an Fc domain monomer (e.g., an Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138), an albumin protein (e.g., an albumin protein having the sequence of any one of SEQ ID NOs: 139-141), an albumin protein-binding peptide, or an Fc-binding peptide; n is 1 or 2; T_1 is an integer from 1 to 10 (e.g., T_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10); L_1 is a linker covalently conjugated to E and A_1; T_1 is an integer from 1 to 10 (e.g., T_1 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10); L_2 is a linker covalently conjugated to E and A_2; T_2 is an integer from 1 to 10 (e.g., T_2 is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10), or a pharmaceutically acceptable salt thereof.

In some examples, each A_1-L is conjugated specifically to a lysine residue of E (e.g., the nitrogen atom of a surface exposed lysine residue of E), and each the A_2-L is conjugated specifically to a cysteine residue of E (e.g., the sulfur atom of a surface exposed cysteine residue of E). In some examples, each A_1-L moiety is conjugated specifically a cysteine residue of E (e.g., the sulfur atom of a surface exposed cysteine residue of E), and each A_2-L moiety is conjugated specifically to a lysine residue of E (e.g., the nitrogen atom of a surface exposed lysine residue of E).

In one aspect, the present disclosure provides a pharmaceutical composition comprising the conjugate or the population of conjugates disclosed herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient. In another example, the disclosure provides a pharmaceutical composition comprising any of the conjugates described herein (e.g., a conjugate of any one of formulas (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I)), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

In one aspect, the present disclosure provides use of the conjugate disclosed herein, the population of conjugates disclosed herein, or the pharmaceutical composition disclosed herein in the manufacture of a medicament for the treatment of a subject having a viral infection or presumed to have a viral infection. In another example, the disclosure provides a method for the treatment of a subject having a viral infection or presumed to have a viral infection, the method comprising administering to the subject an effective amount of any of the conjugates or compositions described herein (e.g., a conjugate of any one of formulas (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I)).

In one aspect, the present disclosure provides use of the conjugate disclosed herein, the population of conjugates disclosed herein, or the pharmaceutical composition disclosed herein in the manufacture of a medicament for the prophylactic treatment of a viral infection in a subject in need thereof. In another example, the disclosure provides a method for the prophylactic treatment of a viral infection in a subject in need thereof, the method comprising administering to the subject an effective

amount of any of the conjugates or compositions described herein (e.g., a conjugate of any one of formulas (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I)).

In some examples, the viral infection is caused by influenza virus or parainfluenza virus. In some examples, the viral infection is influenza virus A, B, or C, or parainfluenza virus.

In some examples, the subject is immunocompromised.

In some examples, the subject has been diagnosed with humoral immune deficiency, T cell deficiency, neutropenia, asplenia, or complement deficiency.

In some examples, the subject is being treated or is about to be treated with an immunosuppressive therapy.

In some examples, the subject has been diagnosed with a disease which causes immunosuppression. In some examples, the disease is cancer or acquired immunodeficiency syndrome. In some examples, the cancer is leukemia, lymphoma, or multiple myeloma.

In some examples, the subject has undergone or is about to undergo hematopoietic stem cell transplantation.

In some examples, the subject has undergone or is about to undergo an organ transplant.

In some examples, the subject has or is at risk of developing a secondary infection. In some examples, the secondary infection is a bacterial infection (e.g., methicillin-resistant *Staphylococcus aureus* (MRSA), *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, and/or *Haemophilus influenzae*), a viral infection, or a fungal infection. In particular examples, the secondary infection is MRSA. In certain examples, the secondary infection is *S. pneumoniae*. In some examples, the secondary infection is a respiratory infection (e.g., an infection of the respiratory tract). In some examples, the secondary infection is associated with (e.g., causes) pneumonia (e.g., bacterial or viral pneumonia). In some examples, the subject has or is at risk of developing pneumonia.

In one aspect, the present disclosure provides use of the conjugate disclosed herein, the population of conjugates disclosed herein, or the pharmaceutical composition disclosed herein in the manufacture of a medicament for preventing a secondary infection in a subject diagnosed with an influenza infection. In another example, the disclosure features a method of preventing a secondary infection in a subject diagnosed with an influenza infection, wherein the method includes administering to the subject a conjugate or composition described herein. In some examples, the method includes administering to the subject conjugate 45 or a pharmaceutical composition including conjugate 45. In some examples, administering a conjugate or composition of the present disclosure to a subject diagnosed with an influenza infection decreases the likelihood of developing a secondary infection, e.g., by 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 200%, 300%, 400%, 500% or more (e.g., as compared to a subject suffering from influenza not treated with the conjugate or composition). For example, administering a conjugate or composition of the present disclosure to a subject diagnosed with an influenza infection decreases the likelihood of developing a secondary bacterial infection (e.g., MRSA, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, and/or *Haemophilus influenzae), e.g.,* by 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 200%, 300%, 400%, 500% or more. In some examples, the conjugate or composition is administered intramuscularly, intravenously, intradermally, intraarterially, intraperitoneally, intralesionally, intracranially, intraarticularly, intraprostatically, intrapleurally, intratracheally, intranasally, intravitreally, intravaginally, intrarectally, topically, intratumorally, peritoneally, subcutaneously, subconjunctival, intravesicularlly, mucosally, intrapericardially, intraumbilically, intraocularally, orally, locally, by inhalation, by injection, or by infusion.

In some examples, the subject is treated with a second therapeutic agent. In some examples, the second therapeutic agent is an antiviral agent. In some examples, the antiviral agent is selected from pimovidir, oseltamivir, zanamivir, peramivir, laninamivir, amantadine, or rimantadine. In particular examples, the second therapeutic agent is pimovidir. In some examples, the second therapeutic agent is a viral vaccine. In some examples, the viral vaccine elicits an immune response in the subject against influenza virus A, B, or C, or parainfluenza virus.

In some examples, the conjugate is administered in combination with an antiviral agent, where the antiviral agent is baloxavir. In certain examples, the conjugate is described by formula (D-II-6). In other examples, the conjugate is described by formula (D-II-7). In certain examples, each E includes an Fc domain that has an amino acid sequence at least 95% identical to the sequence of any one of SEQ ID Nos: 63-138. In particular examples, each E includes an Fc domain that has an amino acid sequence at least 95% identical to the sequence of any one of SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 85, or SEQ ID NO: 86. In particular examples, each E includes an Fc domain that has the amino acid sequence of any one of SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 85, or SEQ ID NO: 86. In preferred examples, the conjugate is conjugate 45 (e.g., conjugate 45a or 45b) or conjugate 46.

In certain examples, the conjugate and baloxavir are administered sequentially. In other examples, the conjugate and baloxavir are administered simultaneously.

In another aspect, the present disclosure provides the conjugate disclosed herein, the population of conjugates disclosed herein, or the pharmaceutical composition disclosed herein for use in treating or preventing a viral infection in a subject, wherein the subject is to be administered a second therapeutic agent. In one example, the disclosure provides a method for treating or preventing a viral infection in subject by administering to the subject: a) an effective amount of a conjugate or composition of any one of claims 1-215; and b) a second therapeutic agent. In certain examples, the conjugate is administered to the subject after the subject has a viral infection, is presumed to have a viral infection, or has been exposed to a virus. In some examples, the conjugate is administered to the subject prophylactically. In certain examples, the second therapeutic agent is administered to the subject after the subject has a viral infection, is presumed to have a viral infection, or has been exposed to the virus. In some examples, the second therapeutic agent is administered to the subject prophylactically. In some examples, the second therapeutic agent is administered within 30 days, within 14 days, within 7 days, within 2 days, or within 24 hours days of the conjugate. In particular examples, the second therapeutic agent is administered within 2 days of the conjugate. In certain examples, the second therapeutic agent is an antiviral agent (e.g., pimovidir, oseltamivir, zanamivir, peramivir, laninamivir, amantadine, baloxavir marboxil, baloxavir acid, rimantadine, or a pharmaceutically acceptable salt thereof). In particular examples, the antiviral agent is baloxavir marboxil, baloxavir acid, or a pharmaceutically acceptable salt thereof. In certain examples, the baloxavir marboxil is administered in an amount between 20 mg and 90 mg (e.g., between 25 mg and 50 mg, between 45 mg and 70 mg, or between 65 and 90 mg). In some examples, the baloxavir marboxil is administered orally. In certain examples, the baloxavir marboxil is administered as a single dose. In other examples, the baloxavir marboxil is administered as more than one dose. In particular examples, the baloxavir marboxil is administered in an amount between 20 mg and 40 mg. In other examples,

the baloxavir marboxil is administered in an amount between 30 and 80 mg. In certain examples, conjugate is described by formula (D-II-6). In other examples, the conjugate is described by formula (D-II-7). In certain examples, each E has a sequence at least 95% identical to the sequence of any one of SEQ ID Nos: 63-138. In particular examples, each E includes an Fc domain that has an amino acid sequence at least 95% identical to the sequence of any one of SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 85, or SEQ ID NO: 86. In particular examples, each E includes an Fc domain that has the amino acid sequence of any one of SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 85, or SEQ ID NO: 86. In certain examples, the conjugate is conjugate 45 (e.g., conjugate 45a or conjugate 45b) or conjugate 46. In particular examples, the conjugate is administered intramuscularly, intravenously, intradermally, intraarterially, intraperitoneally, intralesionally, intracranially, intraarticularly, intraprostatically, intrapleurally, intratracheally, intranasally, intravitreally, intravaginally, intrarectally, topically, intratumorally, peritoneally, subcutaneously, subconjunctival, intravesicularlly, mucosally, intrapericardially, intraumbilically, intraocularally, orally, locally, by inhalation, by injection, or by infusion. In some examples, the conjugate is administered intravenously. In some examples, the conjugate is administered intramuscularly. In some examples, the viral infection is caused by an influenza virus or a parainfluenza virus. In certain examples, the virus is influenza virus A, B, or C, or parainfluenza virus.

In some examples, an Fc-domain-containing composition may be substituted for an Fc domain and an Fc-domain-monomer-containing composition may be substituted for an Fc domain monomer in any one of formulas (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I) (e.g., any one of formulas (1), (2), (3), (4), (5), (D-I), (D-II), (D-II-1), (D-II-2), (D-II-3), (D-II-4), (D-II-5), (D-II-6), (D-II-7), (D-II-8), (D-II-9), (D-II-10), (D-III), (D-III-1), (D-III-2), (D-III-3), (D-III-4), (D-III-5), (D-III-6), (D-III-7), (D-III-8), (D-III-9), (D-IV), (D-IV-1), (D-IV-2), (D-V), (D-V-1), (D-V-2), (D-V-3), (D-V-4), (D-V-5), (D-V-6), (D-V-7), (D-V-8), (D-V-9), (D-V-10), (D-VI), (D-VI-1), (D-VI-2), (D-VI-3), (D-VI-4), (D-VI-5), (D-VI-6), (D-VI-7), (D-VI-8), (D-VI-9), (D-VII), (D-VIII), (D-VIII-1), (D-VIII-2), (D-VIII-3), (D-VIII-4), (D-VIII-5), (D-VIII-6), (D-VIII-7), (D-VIII-8), (D-VIII-9), (D-VIII-10), (D-VIII-11), (D-IX), (D-IX-1), (D-IX-2), (D-IX-3), (D-IX-4), (D-IX-5), (D-IX-6), (D-X), (D-X-1), (D-X-2), (D-X-3), (D-XI), (D-XI-1), (D'-I), (M-I), (M-II), (M-II-1), (M-II-2), (M-II-3), (M-II-4), (M-II-5), (M-II-6), (M-II-7), (M-II-8), (M-II-9), (M-II-10), (M-III), (M-III-1), (M-III-2), (M-III-3), (M-III-4), (M-III-5), (M-III-6), (M-III-7), (M-III-8), (M-III-9), (M-IV), (M-IV-1), (M-IV-2), (M-V), (M-V-1), (M-V-2), (M-V-3), (M-V-4), (M-V-5), (M-V-6), (M-V-7), (M-V-8), (M-V-9), (M-V-10), (M-VI), (M-VI-1), (M-VI-2), (M-VI-3), (M-VI-4), (M-VI-5), (M-VI-6), (M-VI-7), (M-VI-8), (M-VI-9), (M-VII), (M-VIII), (M-VIII-1), (M-VIII-2), (M-VIII-3), (M-VIII-4), (M-VIII-5), (M-VIII-6), (M-VIII-7), (M-VIII-8), (M-VIII-9), (M-VIII-10), (M-VIII-11), (M-IX), (M-IX-1), (M-IX-2), (M-IX-3), (M-IX-4), (M-IX-5), (M-IX-6), (M-X), (M-X-1), (M-X-2), (M-X-3), (M-XI), (M-XI-1), or (M'-I)). In any of the formulas described herein (e.g., any one of formulas (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I)), when n is 1, E is an Fc-domain-monomer-containing composition. In any of the formulas described herein (e.g., any one of formulas (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I)), when n is 2, E is an Fc-domain-containing composition.

In certain examples, the Fc-domain-containing composition is an antibody or an antibody fragment. An antibody may include any form of immunoglobulin, heavy chain antibody, light chain antibody, LRR-based antibody, or other protein scaffold with antibody-like properties, as well as any other immunological binding moiety known in the art, including antibody fragments (e.g., a Fab, Fab', Fab'2, F(ab')2, Fd, Fv, Feb, scFv, or SMIP). The subunit structures and three-dimensional configurations of different classes of antibodies are known in the art. An antibody fragment may include a binding moiety that includes a portion derived from or having significant homology to an antibody, such as the antigen-determining region of an antibody. Exemplary antibody fragments include Fab, Fab', Fab'2, F(ab')2, Fd, Fv, Feb, scFv, and SMIP.

In particular examples, the antibody or antibody fragment is a human, mouse, camelid (e.g., llama, alpaca, or camel), goat, sheep, rabbit, chicken, guinea pig, hamster, horse, or rat antibody or antibody fragment. In specific examples, the antibody is an IgG, IgA, IgD, IgE, IgM, or intrabody. In certain examples, the antibody fragment includes an scFv, sdAb, dAb, Fab, Fab', Fab'2, F(ab')2, Fd, Fv, Feb, or SMIP.

In some examples, the Fc-domain-containing composition (e.g., an antibody or antibody fragment) confers binding specificity to a one or more targets (e.g., an antigen).

In some examples, the one or more targets (e.g., an antigen) bound by the Fc-domain-containing composition (e.g., an antibody or antibody fragment) is a viral (e.g., influenza) protein such as neuraminidase or hemagglutinin. In some examples, the antibody or antibody fragment recognizes a viral surface antigen. In some examples, the antibody or antibody fragment targets hemagglutinin. Hemagglutinin-targeting antibodies include monoclonal antibodies, such as CR6261, CR8020, MEDI8852, MHAA4549A, and VIS410. In some examples, the antibody or antibody fragment is a broadly neutralizing antibody or antibody fragment targeting influenza hemagglutinin (e.g., an antibody or antibody fragment described in Wu et al., J. Mol. Biol. 429:2694–2709 (2017)). In some examples the antibody or antibody fragment targets a viral matrix protein (e.g., matrix 2 protein). TCN032 is a matrix 2 protein targeting monoclonal antibody.

In some examples, the Fc-domain-containing composition (e.g., an antibody or antibody fragment) includes one or more single-domain antibodies (sdAbs). In some examples the Fc-domain-containing composition is an antibody or antibody fragment including a sdAb with influenza A reactivity, such as a sdAb that binds to hemagglutinin of influenza A (e.g., SD36 or SD38, described in Laursen et al. Science. 362:598-602 (2018)). In some examples the Fc-domain-containing composition is an antibody or antibody fragment including a sdAb with influenza B reactivity, such as a sdAb that binds to hemagglutinin of influenza B (e.g., SD83 or SD84, described in Laursen et al. Science. 362:598-602 (2018)).

In some examples the Fc-domain-containing composition is a multidomain antibody (MDAb) or multidomain antibody fragment including 2 or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9 or 10 or more) sdAbs. In some examples, the MDAb or fragment thereof includes one or more sdABs that binds to hemagglutinin of influenza A, and one or more sdAbs that binds to hemagglutinin of influenza B. In some examples, the MDAb is JNJ-7445 (also known as MD3606), which is described in Laursen et al. Science. 362:598-602 (2018). In brief, JNJ-7445 is an MDAb that includes two sdAbs that bind to

hemagglutinin of influenza A (SD36 and SD38) and two sdAbs that bind to hemagglutinin of influenza B (SD83 and SD84), which are linked to an Fc domain (IgG1). The sdAbs were produced by immunizing llamas with influenza vaccine and H7 and H2 recombinant hemagglutinin.

In another example, the disclosure includes a conjugate described by any one of formulas (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I) (e.g., any one of formulas (1), (2), (3), (4), (5), (D-I), (D-II), (D-II-1), (D-II-2), (D-II-3), (D-II-4), (D-II-5), (D-II-6), (D-II-7), (D-II-8), (D-II-9), (D-II-10), (D-III), (D-III-1), (D-III-2), (D-III-3), (D-III-4), (D-III-5), (D-III-6), (D-III-7), (D-III-8), (D-III-9), (D-IV), (D-IV-1), (D-IV-2), (D-V), (D-V-1), (D-V-2), (D-V-3), (D-V-4), (D-V-5), (D-V-6), (D-V-7), (D-V-8), (D-V-9), (D-V-10), (D-VI), (D-VI-1), (D-VI-2), (D-VI-3), (D-VI-4), (D-VI-5), (D-VI-6), (D-VI-7), (D-VI-8), (D-VI-9), (D-VII), (D-VIII), (D-VIII-1), (D-VIII-2), (D-VIII-3), (D-VIII-4), (D-VIII-5), (D-VIII-6), (D-VIII-7), (D-VIII-8), (D-VIII-9), (D-VIII-10), (D-VIII-11), (D-IX), (D-IX-1), (D-IX-2), (D-IX-3), (D-IX-4), (D-IX-5), (D-IX-6), (D-X), (D-X-1), (D-X-2), (D-X-3), (D-XI), (D-XI-1), (D'-I), (M-I), (M-II), (M-II-1), (M-II-2), (M-II-3), (M-II-4), (M-II-5), (M-II-6), (M-II-7), (M-II-8), (M-II-9), (M-II-10), (M-III), (M-III-1), (M-III-2), (M-III-3), (M-III-4), (M-III-5), (M-III-6), (M-III-7), (M-III-8), (M-III-9), (M-IV), (M-IV-1), (M-IV-2), (M-V), (M-V-1), (M-V-2), (M-V-3), (M-V-4), (M-V-5), (M-V-6), (M-V-7), (M-V-8), (M-V-9), (M-V-10), (M-VI), (M-VI-1), (M-VI-2), (M-VI-3), (M-VI-4), (M-VI-5), (M-VI-6), (M-VI-7), (M-VI-8), (M-VI-9), (M-VII), (M-VIII), (M-VIII-1), (M-VIII-2), (M-VIII-3), (M-VIII-4), (M-VIII-5), (M-VIII-6), (M-VIII-7), (M-VIII-8), (M-VIII-9), (M-VIII-10), (M-VIII-11), (M-IX), (M-IX-1), (M-IX-2), (M-IX-3), (M-IX-4), (M-IX-5), (M-IX-6), (M-X), (M-X-1), (M-X-2), (M-X-3), or (M'-I)), where E is an antibody or antibody fragment. In preferred examples, where E is an antibody or antibody fragment, n is 1. In some examples, the antibody or antibody fragment includes any antibody or antibody fragment described herein, such as a monoclonal antibody that binds to viral hemagglutinin (e.g., CR6261, CR8020, MEDI8852, MHAA4549A, or VIS410); a broadly neutralizing antibody or antibody fragment targeting viral hemagglutinin (e.g., antibodies or antibody fragments described in Wu et al., J. Mol. Biol. 429:2694–2709 (2017)); a sdAb targeting viral hemagglutinin (e.g., SD36, SD38, SD83, or SD84); or a MDAb or fragment thereof targeting viral hemagglutinin (e.g., JNJ-7445).

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 1. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 1.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 2. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 2.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 3. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 3.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 4. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 4.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 5. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 6. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 6.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 7. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 7.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 8. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 8.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 9. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 9.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 10. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 11. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 11.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 12. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 12.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 13. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 13.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 14. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 14.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 15. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 15.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 16. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 16.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 17. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 17.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 18. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 18.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 19. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 19.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 20. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 20.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 21. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 21.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 22. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 22.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 23. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 23.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 24. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 24.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 25. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 25.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 26. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 26.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 27. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 27.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 28. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 28.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 29. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 29.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 30. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 30.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 31. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 31.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 32. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 32.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 33. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 33.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 34. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 34.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 35. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 35.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 36. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 36.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 37. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 37.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 38. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 38.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 39. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 39.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 40. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 40.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 41. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 41.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 42. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 42.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 43. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 43.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 44. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 45.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 46. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 46.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 47. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 47.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 48. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 48.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 49. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 49.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 50. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 50.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 51. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 51.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 52. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 52.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 53. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 53.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 54. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 54.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 55. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 55.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 56. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 56.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 57. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 57.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 58. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 58.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 59. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 59.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 60. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 60.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 61. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 61.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 62. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 62.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 63. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 63.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 64. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 64.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 65. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 65.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 66. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 66.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 67. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 67.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 68. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 68.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 69. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 69.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 70. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 70.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 71. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 71.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 72. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 72.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 73. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 73.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 74. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 74.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 75. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 75.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 76. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 76.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 77. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 77.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 78. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 78.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 79. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 79.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 80. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 80.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 81. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 81.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 82. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 82.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 83. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 83.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 84. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 84.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 85. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 85.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 86. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 86.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 87. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 87.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 88. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 88.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 89. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 89.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 90. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 90.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 91. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 91.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 92. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 92.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 93. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 93.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 94. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 94.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 95. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 95.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 96. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 96.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 97. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 97.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 98. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 98.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 99. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 99.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 100. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 100.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 101. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 101.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 102. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 102.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 103. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 103.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 104. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 104.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 105. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 105.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 106. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 106.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 107. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 107.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 108. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 108.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 109. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 109.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 110. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 110.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 111. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 111.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 112. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 112.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 113. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 113.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 114. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 114.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 115. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 115.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 116. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 116.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 117. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 117.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 118. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 118.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 119. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 119.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 120. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 120.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 121. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 121.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 122. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 122.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 123. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 123.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 124. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 124.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 125. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 125.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 126. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 126.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 127. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 127.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 128. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 128.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 129. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 129.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 130. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 130.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 131. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 131.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 132. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 132.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 133. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 133.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 134. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 134.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 135. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 135.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 136. In some examples, E includes an amino acid sequence that is at

least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 136.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 137. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 137.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 138. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 138.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 139. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 139.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 140. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 140.

In some examples or aspects described herein, E (e.g., each E) includes the amino acid sequence of SEQ ID NO: 145. In some examples, E includes an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 141.

In some examples or aspects described herein, wherein E includes an Fc domain monomer, the Fc domain monomer (e.g., the Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138) includes a triple mutation corresponding to M252Y/S254T/T256E (YTE). As used herein, an amino acid "corresponding to" a particular amino acid residue (e.g., of a particular SEQ ID NO.) should be understood to include any amino acid residue that one of skill in the art would understand to align to the particular residue (e.g., of the particular sequence). For example, any one of SEQ ID NOs: 1-138 may be mutated to include a YTE mutation.

In some examples or aspects described herein, wherein E includes an Fc domain monomer, the Fc domain monomer (e.g., the Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138) includes a double mutant corresponding to M428L/N434S (LS). As used herein, an amino acid "corresponding to" a particular amino acid residue (e.g., of a particular SEQ ID NO.) should be understood to include any amino acid residue that one of skill in the art would understand to align to the particular residue (e.g., of the particular sequence). For example, any one of SEQ ID NOs: 1-138 may be mutated to include a LS mutation.

In some examples or aspects described herein, wherein E includes an Fc domain monomer, the Fc domain monomer (e.g., the Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138) includes a mutant corresponding to N434H. As used herein, an amino acid "corresponding to" a particular amino acid residue (e.g., of a particular SEQ ID NO.) should be understood to include any amino acid residue that one of skill in the art would understand to align to the particular residue (e.g., of the particular sequence). For example, any one of SEQ ID NOs: 1-138 may be mutated to include an N434H mutation.

In some examples or aspects described herein, wherein E includes an Fc domain monomer, the Fc domain monomer (e.g., the Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138) includes a mutant corresponding to C220S. As used herein, an amino acid "corresponding to" a particular amino acid residue (e.g., of a particular SEQ ID NO.) should be understood to include any amino acid residue that one of skill in the art would understand to align to the particular residue (e.g., of the particular sequence). For example, any one of SEQ ID NOs: 1-138 may be mutated to include a C220S mutation.

In some examples or aspects described herein, the Fc domain monomer (e.g., the Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-95) includes a triple mutation corresponding to V309D/Q311H/N434S (DHS). As used herein, an amino acid "corresponding to" a particular amino acid residue (e.g., of a particular SEQ ID NO.) should be understood to include any amino acid residue that one of skill in the art would understand to align to the particular residue (e.g., of the particular sequence). For example, any one of SEQ ID NOs: 1-95 may be mutated to include a DHS mutation.

In some examples or aspects described herein, wherein E includes an Fc domain monomer, the Fc domain monomer (e.g., the Fc domain monomer having the sequence of any one of SEQ ID NOs: 1-138) is a fragment of the Fc domain monomer (e.g., a fragment of at least 25 (e.g., 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50 or more), at least 50 (e.g., 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75 or more), at least 75 (e.g., 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100 or more) consecutive amino acids in length from SEQ ID NOs: 1-138.

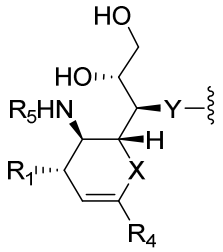
In some examples or aspects described herein (e.g., a conjugate of any one of formulas (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I)), one or more nitrogen atoms of one or more surface exposed lysine residues of E or one or more sulfur atoms of one or more surface exposed cysteines in E is covalently conjugated to a linker (e.g., a PEG_2-PEG_{20} linker). The linker conjugated to E may be functionalized such that it may reacts to form a covalent bond with the L of any A_1-L or any A_2-L-A_1 described herein. In preferred examples, E is conjugated to a linker functionalized with an azido group and the L of A_1-L or any A_2-L-A_1 is functionalized with an alkyne group. Conjugation (e.g., by click chemistry) of the linker-azido of E and linker-alkyne of A_1-L or A_2-L-A_1 forms a conjugate of the disclosure, for example a conjugate described by any one of formulas (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I). In yet other examples, E is conjugated to a linker functionalized with an alkyne group and L of any A_1-L or of any A_2-L-A_1 is functionalized with an azido group. Conjugation (e.g., by click chemistry, see,

e.g., FIG. 103) of the linker-alkyne of E and linker-azido of A_1-L or A_2-L-A_1 forms a conjugate of the disclosure, for example a conjugate described by formula (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I).

In some examples or aspects described herein, the squiggly line of any one of formulas (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I) may represent a covalent bond between E and the L of A_1-L or A_2-L-A_1.

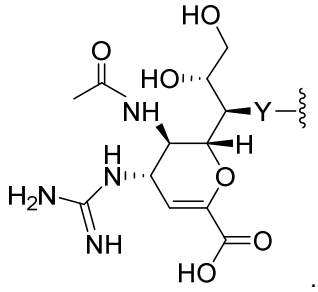
In some examples or aspects described herein, the squiggly line of any one of formulas (1)-(5), (D-I)-(D-XI), (D'-I), (M-I)-(M-XI), or (M'-I) may represent that one or more amino acid side chains of E (e.g., one or more nitrogen atoms of one or more surface exposed lysine residues of E or one or more sulfur atoms of one or more surface exposed cysteines in E) have been conjugated to a linker (e.g., a PEG_2-PEG_{20} linker) wherein the linker has been functionalized with a reactive moiety, such that the reactive moiety forms a covalent bond with the L of any A_1-L or any A_2-L-A_1 described herein (e.g., by click chemistry between an azido functionalized linker and an alkyne functionalized linker, as described above; see, e.g., FIG. 103).

In some examples or aspects described herein, A_1 and/or A_2 have the structure described by (A-I):



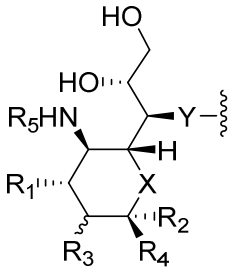
(A-I).

In preferred examples, wherein A_1 and/or A_2 have the structure described by (A-I): R_1 is -NHC(=NH)NH_2, R_4 is -CO_2H, R_5 is -$COCH_3$, and/or X is -O-. In preferred examples, A_1 and/or A_2 have the structure of zanamivir described by:



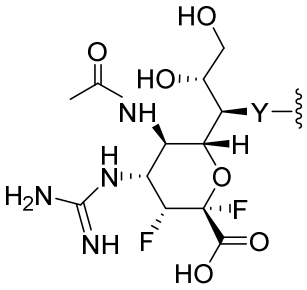
.

In some examples or aspects described herein, A_1 and/or A_2 have the structure described by (A-II):

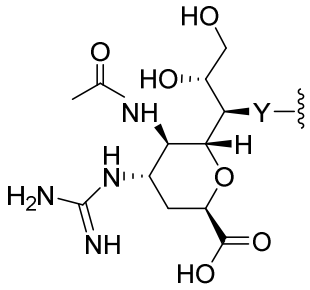


(A-II).

In preferred examples, wherein A_1 and/or A_2 have the structure described by (A-II): R_1 is -$NHC(=NH)NH_2$, R_2 is H or F, R_3 is H or F, R_4 is -CO_2H, R_5 is -$COCH_3$, and/or X is -O-. In preferred examples, A_1 and/or A_2 have the structure described by:

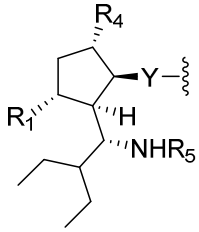


or



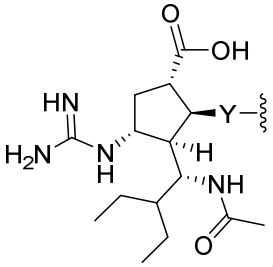
.

In some examples or aspects described herein, A_1 and/or A_2 have the structure described by (A-III):



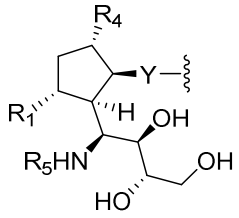
(A-III).

In preferred examples, wherein A_1 and/or A_2 have the structure described by (A-III): R_1 is -$NHC(=NH)NH_2$, R_4 is -CO_2H, and/or R_5 is -$COCH_3$. In preferred examples, A_1 and/or A_2 have the structure of peramivir described by:



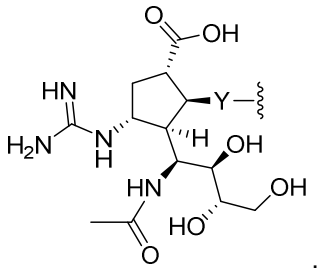
.

In some examples or aspects described herein, A_1 and/or A_2 have the structure described by (A-IV):



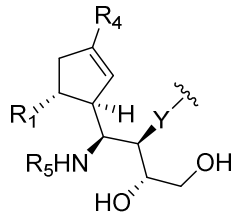
(A-IV).

In preferred examples, wherein A_1 and/or A_2 have the structure described by (A-IV): R_1 is -$NHC(=NH)NH_2$, R_4 is -CO_2H, and/or R_5 is -$COCH_3$. In preferred examples, A_1 and/or A_2 have the structure described by:



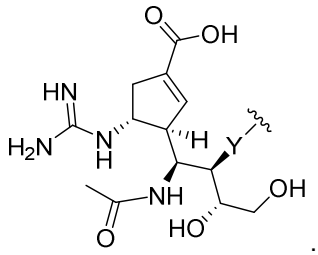
.

In some examples or aspects described herein, A_1 and/or A_2 have the structure described by (A-V):



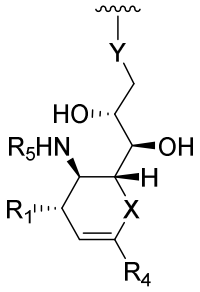
(A-V).

In preferred examples, wherein A_1 and/or A_2 have the structure described by (A-V): R_1 is -$NHC(=NH)NH_2$, R_4 is -CO_2H, and/or R_5 is -$COCH_3$. In preferred examples, A_1 and/or A_2 have the structure described by:



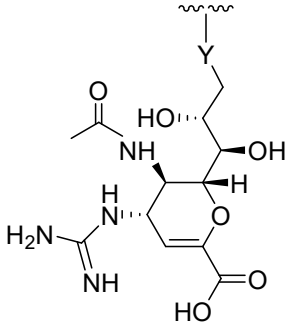
.

In some examples or aspects described herein, A_1 and/or A_2 have the structure described by (A-VI):



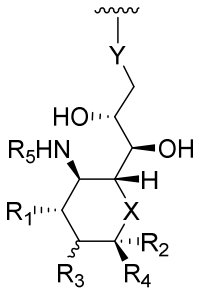
(A-VI).

In preferred examples, wherein A_1 and/or A_2 have the structure described by (A-VI): R_1 is -$NHC(=NH)NH_2$, R_4 is -CO_2H, R_5 is -$COCH_3$, and/or X is -O-. In preferred examples, A_1 and/or A_2 have the structure of zanamivir described by:



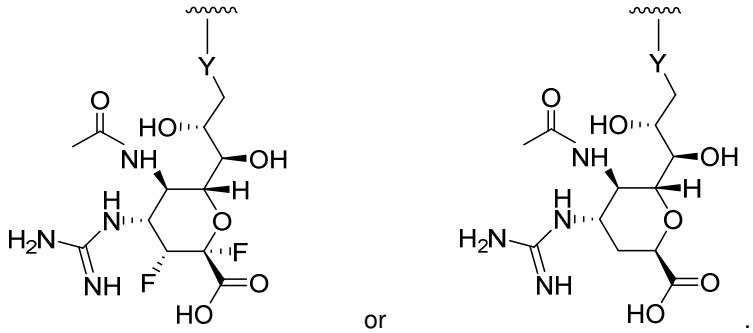
.

In some examples or aspects described herein, A_1 and/or A_2 have the structure described by (A-VII):



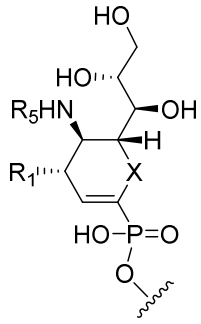
(A-VII).

In preferred examples, wherein A_1 and/or A_2 have the structure described by (A-VII): R_1 is -$NHC(=NH)NH_2$, R_2 is H or F, R_3 is H or F, R_4 is -CO_2H, R_5 is -$COCH_3$, and/or X is -O-. In preferred examples, A_1 and/or A_2 have the structure described by:



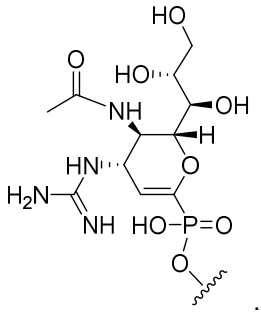
or .

In some examples or aspects described herein, A_1 and/or A_2 have the structure described by (A-VIII):



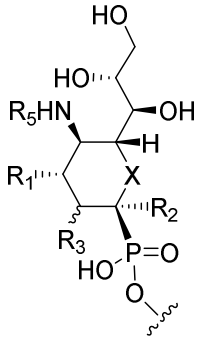
(A-VIII).

In preferred examples, wherein A_1 and/or A_2 have the structure described by (A-VIII): R_1 is -$NHC(=NH)NH_2$, R_5 is -$COCH_3$, and/or X is -O-. In preferred examples, A_1 and/or A_2 have the structure described by:



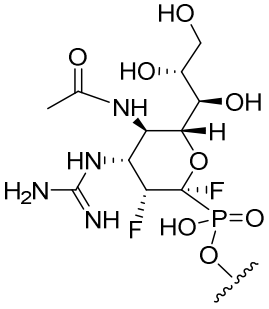
.

In some examples or aspects described herein, A_1 and/or A_2 have the structure described by (A-IX):

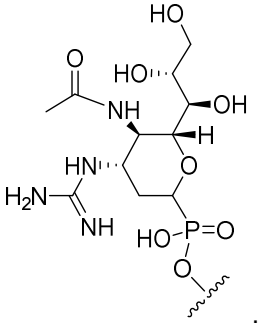


(A-IX).

In preferred examples, wherein A_1 and/or A_2 have the structure described by (A-IX): R_1 is -$NHC(=NH)NH_2$, R_2 is H or F, R_3 is H or F, R_5 is -$COCH_3$, and/or X is -O-. In preferred examples, A_1 and/or A_2 have the structure described by:

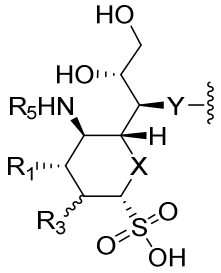


or



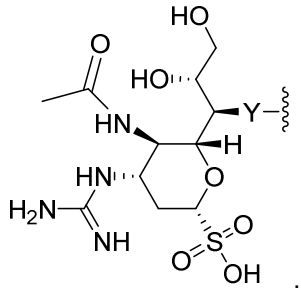
.

In some examples or aspects described herein, A_1 and/or A_2 have the structure described by (A-X):



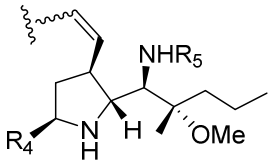
(A-X).

In preferred examples, wherein A_1 and/or A_2 have the structure described by (A-X): R_1 is -$NHC(=NH)NH_2$, R_3 is H, R_5 is -$COCH_3$, and/or X is -O-. In preferred examples, A_1 and/or A_2 have the structure of sulfozanamivir described by:



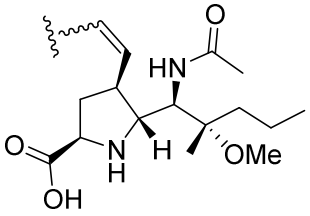
.

In some examples or aspects described herein, A_1 and/or A_2 have the structure described by (A-XI):



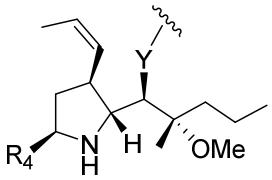
(A-XI).

In preferred examples, wherein A_1 and/or A_2 have the structure described by (A-XI): R_4 is -CO_2H, and/or R_5 is -$COCH_3$. In preferred examples, the alkene is (E), (Z), or a racemic mixture of (E)/(Z). In preferred examples, A_1 and/or A_2 have the structure of A-315675 (Abbott) described by:



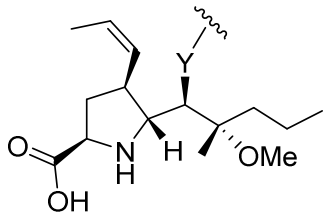
.

In some examples or aspects described herein, A_1 and/or A_2 have the structure described by (A-XII):



(A-XII).

In preferred examples, wherein A_1 and/or A_2 have the structure described by (A-XII): R_4 is -CO_2H. In preferred examples, A_1 and/or A_2 have the structure of A-315675 (Abbott) described by:



.

In some examples, the conjugate is conjugate 1, or any regioisomer thereof, and the drug-to-antibody ratio (DAR) (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 1, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 2, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 2, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 3, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 3, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 4, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 4, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 5, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 5, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 6, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 6, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 7, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another

example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 7, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 8, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 8, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 9, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 9, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 10, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 10, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 11, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3,

4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 11, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 12, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 12, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 13, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 13, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 14, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 14, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1

to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 15, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 15, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 16, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 16, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 17, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 17, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 18, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1,

9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 18, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 19, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 19, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 20, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 20, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 21, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 21, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 22, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 22, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 23, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 23, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 24, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 24, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 25, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another

example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 25, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 26, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 26, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 27, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 27, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 28, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 28, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 29, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3,

4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 29, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 30, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 30, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 31, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 31, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 32, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 32, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1

to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 33, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 33 wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 34, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 34, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 35, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 35, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 36, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1,

9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 36, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 37, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 37, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 38, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 38, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 39, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 39, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 40, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 40, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 41, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 41, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 42, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 42, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 43, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another

example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 43, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 44, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 44, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 45 (e.g., conjugate 45a or conjugate 45b), or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 45 (e.g., conjugate 45a or conjugate 45b), wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

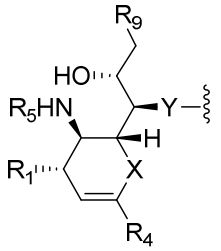
In some examples, the conjugate is conjugate 46, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 46, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples, the conjugate is conjugate 47, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3,

4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 47, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

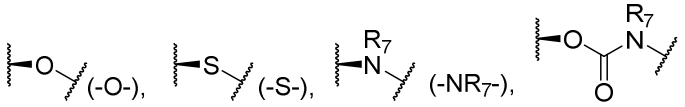
In some examples, the conjugate is conjugate 48, or any regioisomer thereof, and the DAR (e.g., T) is between 0.5 and 10.0, e.g., about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8.0, 7.9, 8, 8.1, 8.2, 8.3, 8.4, 8.5, 8.6, 8.7, 8.8, 8.9, 9.0, 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, or 10.0. In some examples the DAR is between 0.5 and 2.0, between 2.0 and 4.0, between 4.0 and 6.0, between 6.0 and 8.0, or between 8.0 and 10.0. In another example, the disclosure provides a population of conjugates, each conjugate having the structure of conjugate 48, wherein the average DAR (e.g., T) of the population of conjugates is 1 to 2, 1 to 3, 1 to 4, 1 to 5, 5 to 10, 10 to 15, 15 to 20, 1.5 to 3.5, 2.5 to 4.5, 3.5 to 5.5, 4.5 to 6.5, 5.5 to 7.5, 6.5 to 8.5, 7.5 to 9.5, or 8.5 to 10.5.

In some examples or aspects described herein, the disclosure features a conjugate described by any one of formulas (D-I), (M-I), (1), or (2): wherein each A_1 and each A_2 is independently selected from any one of formulas (A-XIII):



(A-XIII)

wherein R_1 is selected from -OH, $-NH_2$, $-NHC(=NH)NH_2$, and $-NHC(=NH)NHR_6$; R_4 is selected from $-CO_2H$, $-P(=O)(OH)_2$, $-SO_3H$; R_5 is selected from $-COCH_3$, $-COCF_3$, $-SO_2CH_3$; X is selected from -O- and -S-; Y is selected from



R_9 is selected from -H, a halogen (e.g., Cl or F), -OR_{10}, -NHC(=O)R_7, optionally substituted C1-C20 alkyl, C3-C20 cycloalkyl, C3-C20 heterocycloalkyl; C5-C15 aryl, and C2-C15 heteroaryl;

R_{10} is selected from C1-C20 alkyl, C3-C20 cycloalkyl, C3-C20 heterocycloalkyl; C5-C15 aryl, and C2-C15 heteroaryl;

n is 1 or 2;

each E comprises an Fc domain monomer, an albumin protein, an albumin protein-binding peptide, or an Fc-binding peptide;

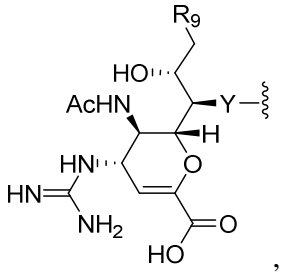
L is a linker covalently attached to E and to each Y of each A_1 or each A_1 and A_2;

T is an integer from 1 to 20, and

each squiggly line in formulas (D-I), (M-I), (1), or (2) indicates that L is covalently attached to each E;

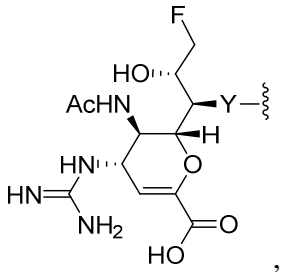
or a pharmaceutically acceptable salt thereof.

In some examples, each A_1 and each A_2 is described by formula (A-XIII-1):

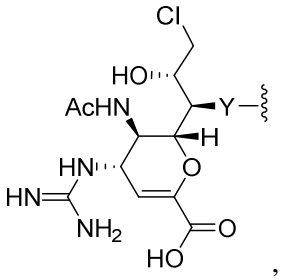


(A-XIII-1)

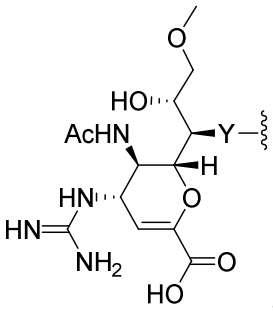
In some examples, each A_1 and each A_2 is independently selected from any one of formulas (A-XIII-1a)-(A-XIII-1d):



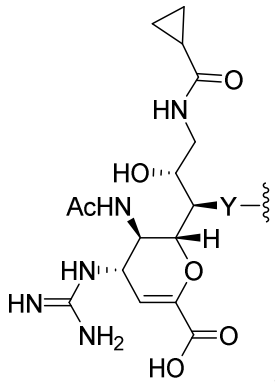
(A-XIII-1a)



(A-XIII-1b)

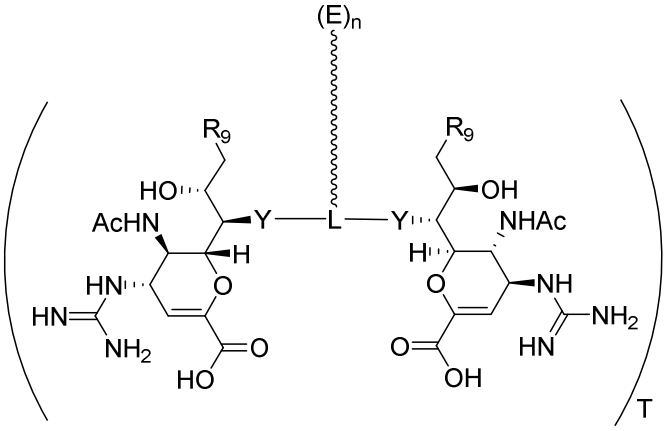


(A-XIII-1c)



(A-XIII-1d)

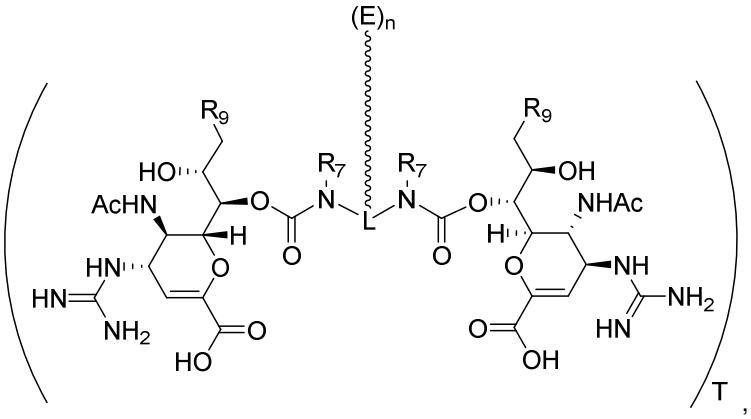
In some examples, the conjugate is described by formula (D-XI):



(D-XI)

or a pharmaceutically acceptable salt thereof.

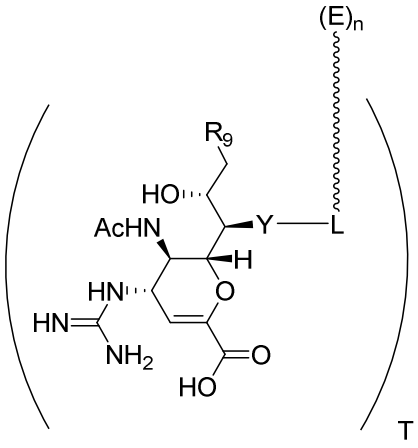
In some examples, the conjugate is described by formula (D-XI-1):



(D-XI-1)

wherein R_7 is selected from H, C1-C20 alkyl, C3-C20 cycloalkyl, C3-C20 heterocycloalkyl; C5-C15 aryl, and C2-C15 heteroaryl; or a pharmaceutically acceptable salt thereof.

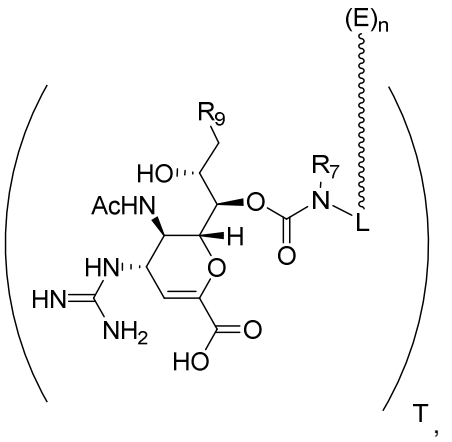
In some examples, the conjugate is described by formula (M-XI):



(M-XI)

or a pharmaceutically acceptable salt thereof.

In some examples, the conjugate is described by formula (M-XI-1):



(M-XI-1)

wherein R_7 is selected from H, C1-C20 alkyl, C3-C20 cycloalkyl, C3-C20 heterocycloalkyl; C5-C15 aryl, and C2-C15 heteroaryl; or a pharmaceutically acceptable salt thereof.

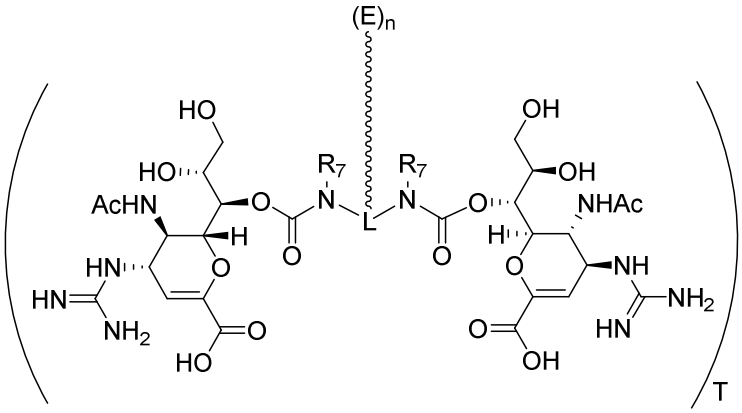
Definitions

To facilitate the understanding of this invention, a number of terms are defined below. Terms defined herein have meanings as commonly understood by a person of ordinary skill in the areas relevant to the present invention. Terms such as "a", "an," and "the" are not intended to refer to only a singular entity, but include the general class of which a specific example may be used for illustration. The terminology herein is used to describe specific embodiments of the invention, but their usage does not delimit the invention, except as outlined in the claims.

The term “neuraminidase inhibitor” or ““viral neuraminidase inhibitor,” as used herein, refers to compounds that decreases the activity of the enzyme influenza virus neuraminidase (e.g., from influenza virus A, B, or C). A neuraminidase inhibitor may be identified by methods known to those of skill in the art, for example, by reduction of viral replication in an influenza viral plaque reduction assay, e.g., at

CLAIMS

1. A conjugate described by formula (D-II-6):



(D-II-6)

wherein each E comprises an Fc domain monomer;

n is 1 or 2;

T is an integer from 1 to 20;

L is a linker;

R_7 is selected from C_1-C_{20} alkyl, C_3-C_{20} cycloalkyl, C_3-C_{20} heterocycloalkyl, C_5-C_{15} aryl, and C_2-C_{15} heteroaryl; and

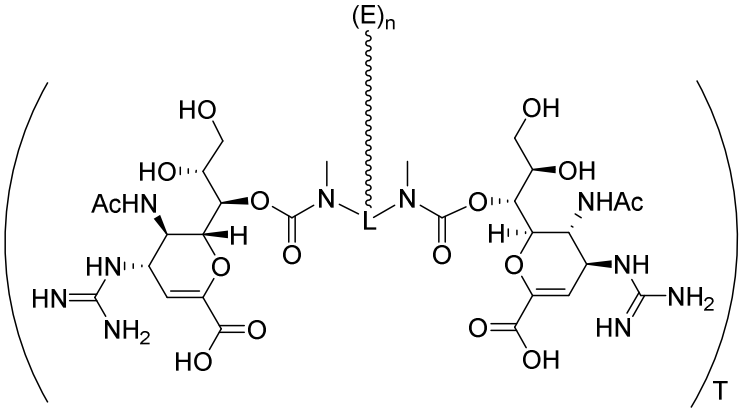
the squiggly line indicates that L is covalently attached to E,

or a pharmaceutically acceptable salt thereof.

2. The conjugate of claim 1, wherein R_7 is C_1-C_{20} alkyl.

3. The conjugate of claim 1 or 2, wherein R_7 is methyl, ethyl, propyl, or butyl.

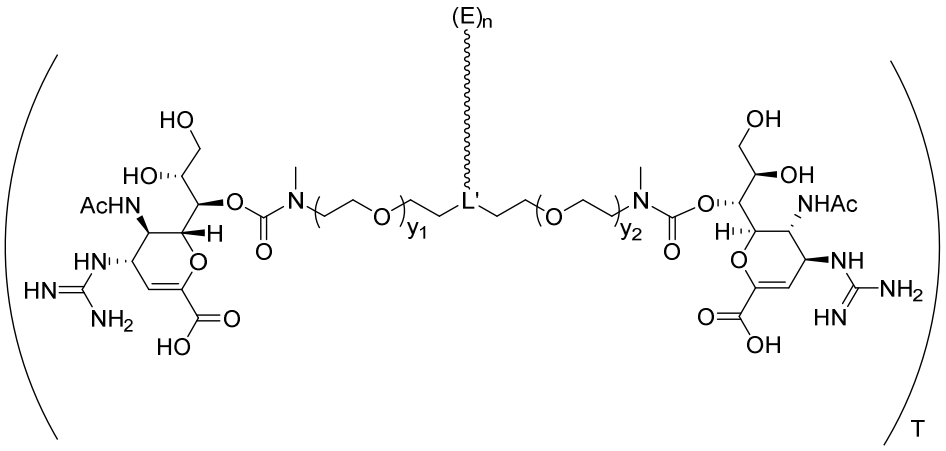
4. The conjugate of any one of claims 1 to 3, wherein the conjugate is described by formula (D-II-7):



(D-II-7)

or a pharmaceutically acceptable salt thereof.

5. The conjugate of claim 4, wherein the conjugate is described by formula (D-II-8):



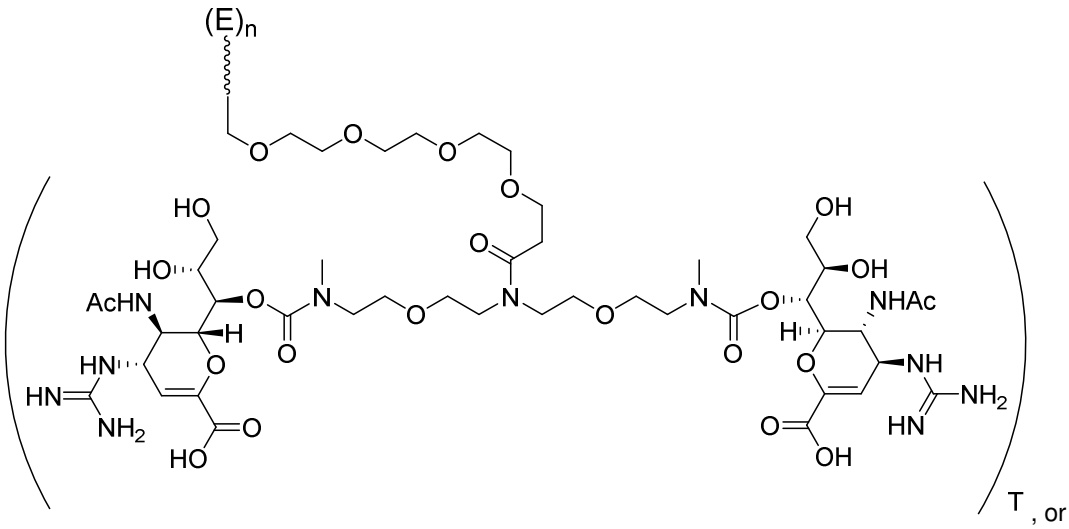
(D-II-8)

wherein L' is the remainder of L, and

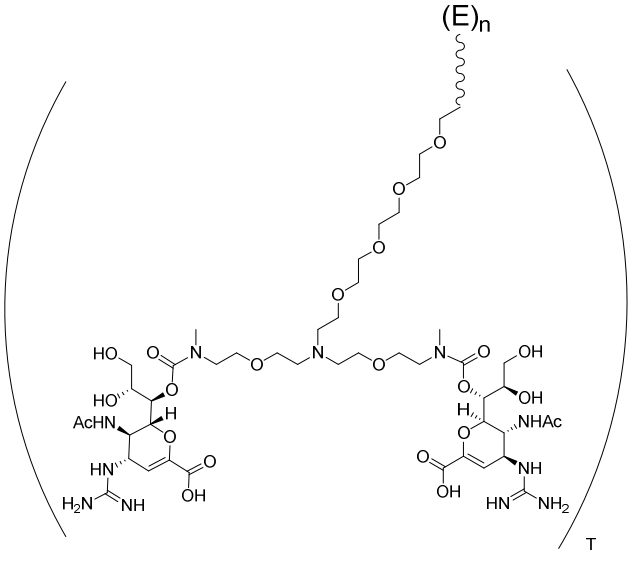
y_1 and y_2 are each independently an integer from 1-20,

or a pharmaceutically acceptable salt thereof.

6. The conjugate of claim 5, wherein the conjugate has the structure of:



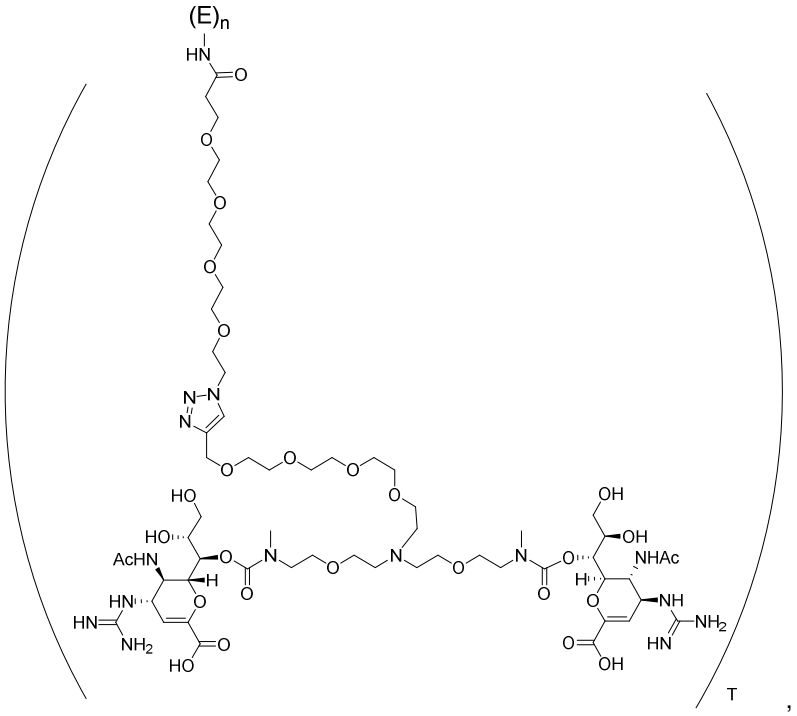
, or



,

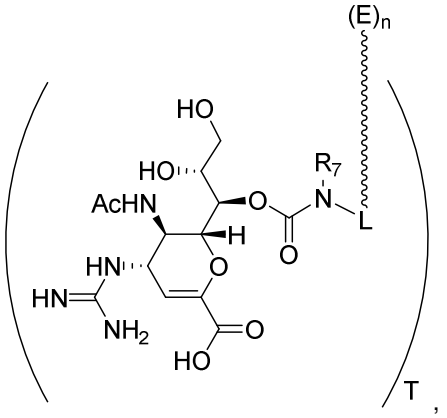
or a pharmaceutically acceptable salt thereof.

7. The conjugate of claim 6, wherein the conjugate has the structure of:



or a pharmaceutically acceptable salt thereof.

8. A conjugate described by formula (M-II-6):



(M-II-6)

wherein R_7 is selected from C_1-C_{20} alkyl, C_3-C_{20} cycloalkyl, C_3-C_{20} heterocycloalkyl, C_5-C_{15} aryl, and C_2-C_{15} heteroaryl,

or a pharmaceutically acceptable salt thereof.

9. The conjugate of claim 8, wherein R_7 is C_1-C_{20} alkyl.

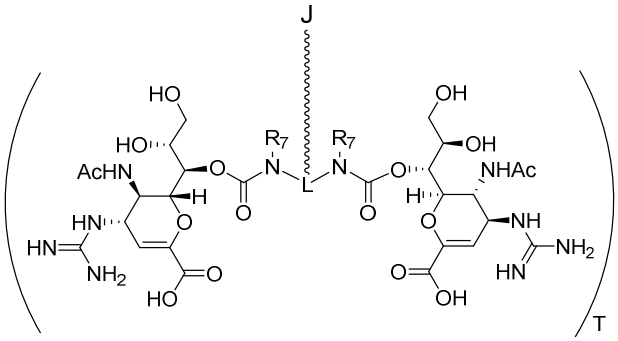
10. The conjugate of claim 8 or 9, wherein R_7 is methyl, ethyl, propyl, or butyl.

11. The conjugate of any one of claims 1 to 10, wherein the squiggly line indicates that L is covalently attached to a nitrogen atom of a solvent-exposed lysine of E.

12. The conjugate of any one of claims 1 to 10, wherein the squiggly line indicates that L is covalently attached to a sulfur atom of a solvent-exposed cysteine of E.

13. The conjugate of any one of claims 1 to 12, wherein n is 2, and the two Es dimerize with each other to form an Fc domain.

14. A conjugate described by the structure:



wherein J is an Fc domain comprising two Fc domain monomers;

T is an integer from 1 to 20,

L is a linker;

R_7 is selected from C_1-C_{20} alkyl, C_3-C_{20} cycloalkyl, C_3-C_{20} heterocycloalkyl, C_5-C_{15} aryl, and C_2-C_{15} heteroaryl; and

the squiggly line indicates that L is covalently attached to J,

or a pharmaceutically acceptable salt thereof.

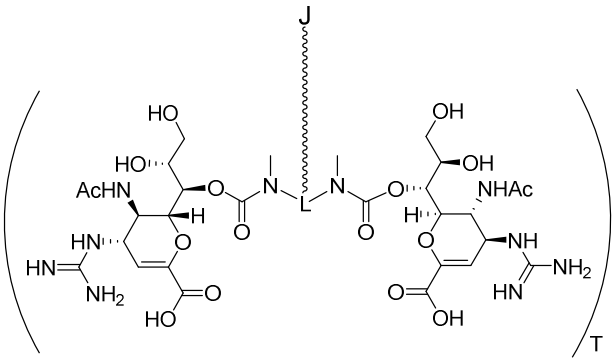
15. The conjugate of claim 14, wherein the squiggly line indicates that L is covalently attached to a nitrogen atom of a solvent-exposed lysine of J.

16. The conjugate of claim 14, wherein the squiggly line indicates that L is covalently attached to a sulfur atom of a solvent-exposed cysteine of J.

17. The conjugate of any one of claims 14 to 16 wherein R_7 is C_1-C_{20} alkyl.

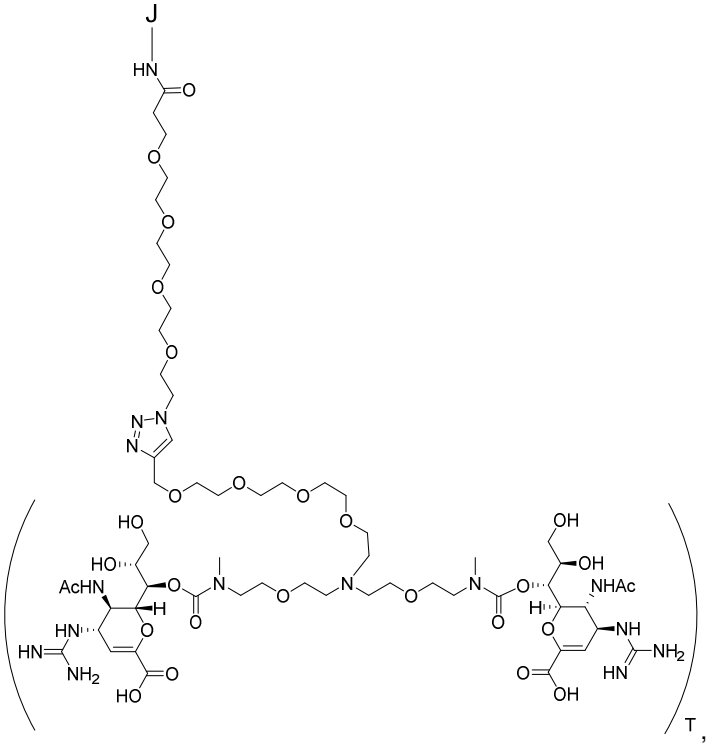
18. The conjugate of claim 17, wherein R_7 is methyl, ethyl, propyl, or butyl.

19. The conjugate of any one of claims 14 to 18, wherein the conjugate has the structure of:



or a pharmaceutically acceptable salt thereof.

20. The conjugate of claim 19, wherein the conjugate has the structure of:



or a pharmaceutically acceptable salt thereof.

21. The conjugate of any one of claims 1 to 20, wherein each Fc domain monomer comprises an amino acid sequence independently selected from any one of SEQ ID NOs: 1-138.

22. The conjugate of claim 21, wherein each Fc domain monomer comprises an amino acid sequence independently selected from any one of SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 94, and SEQ ID NO: 95.

23. The conjugate of claim 22, wherein each Fc domain monomer comprises the amino acid sequence of SEQ ID NO: 72.

24. The conjugate of claim 22, wherein each Fc domain monomer comprises the amino acid sequence of SEQ ID NO: 73.

25. The conjugate of claim 22, wherein each Fc domain monomer comprises the amino acid sequence of SEQ ID NO: 76.

26. The conjugate of claim 22, wherein each Fc domain monomer comprises the amino acid sequence of SEQ ID NO: 77.

27. The conjugate of any one of claims 1 to 26, wherein T is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

28. A population of conjugates of any one of claims 1 to 27, wherein the average value of T is 1 to 10.

29. A pharmaceutical composition comprising the conjugate or the population of conjugates of any one of claims 1 to 28, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

30. Use of the conjugate of any one of claims 1-27, the population of conjugates of claim 28, or the pharmaceutical composition of claim 29 in the manufacture of a medicament for the treatment of a subject having a viral infection or presumed to have a viral infection.

31. Use of the conjugate of any one of claims 1-27, the population of conjugates of claim 28, or the pharmaceutical composition of claim 29 in the manufacture of a medicament for the prophylactic treatment of a viral infection in a subject in need thereof.

32. The use of claim 30 or 31, wherein the viral infection is caused by an influenza virus or a parainfluenza virus.

33. The use of claim 32, wherein the influenza virus is influenza virus A, B, or C.

34. Use of the conjugate of any one of claims 1-27, the population of conjugates of claim 28, or the pharmaceutical composition of claim 29 in the manufacture of a medicament for preventing a secondary infection in a subject diagnosed with an influenza infection.

35. The use of any one of claims 30 to 34, wherein the subject is to be treated with a second therapeutic agent.

36. The conjugate of any one of claims 1-27, the population of conjugates of claim 28, or the pharmaceutical composition of claim 29 for use in treating or preventing a viral infection in a subject, wherein the subject is to be administered a second therapeutic agent.

37. The use of claim 35 or the conjugate, population of conjugates, or pharmaceutical composition for use of claim 36, wherein the second therapeutic agent is an antiviral agent.

38. The use or the conjugate, population of conjugates, or pharmaceutical composition for use of claim 37, wherein the antiviral agent is pimovidir, oseltamivir, zanamivir, peramivir, laninamivir, amantadine, baloxavir marboxil, baloxavir acid, rimantadine, or a pharmaceutically acceptable salt thereof.

39. The use or the conjugate, population of conjugates, or pharmaceutical composition for use of any one of claims 36 to 38, wherein the viral infection is caused by an influenza virus or a parainfluenza virus.