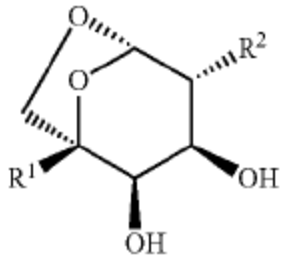
What is claimed is:

1. A compound of Formula (A)

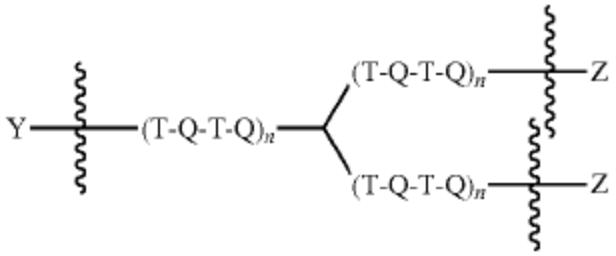
(A)



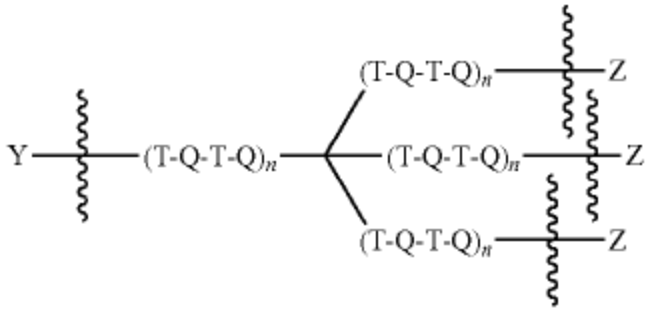
wherein

R^1 is Z—X—Y wherein X is a linker of any of structures L1-L10

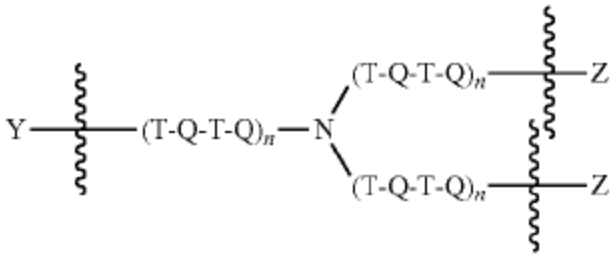
L1



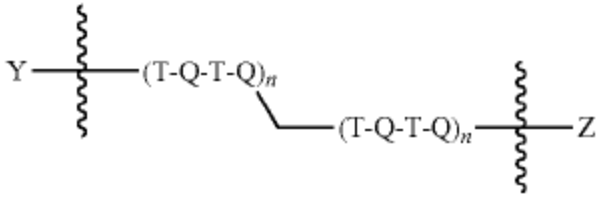
L2



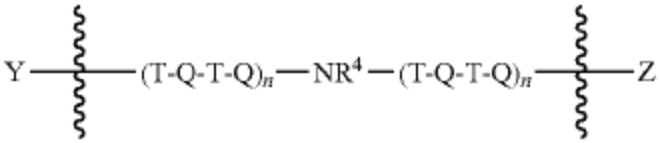
L3



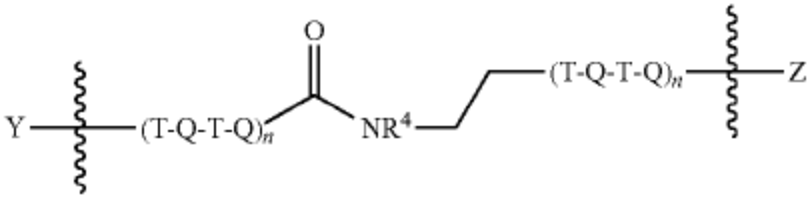
L4



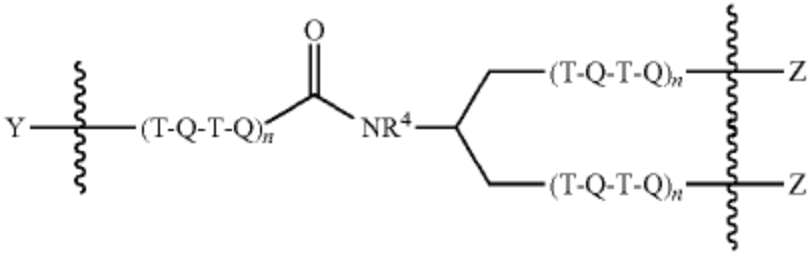
L5



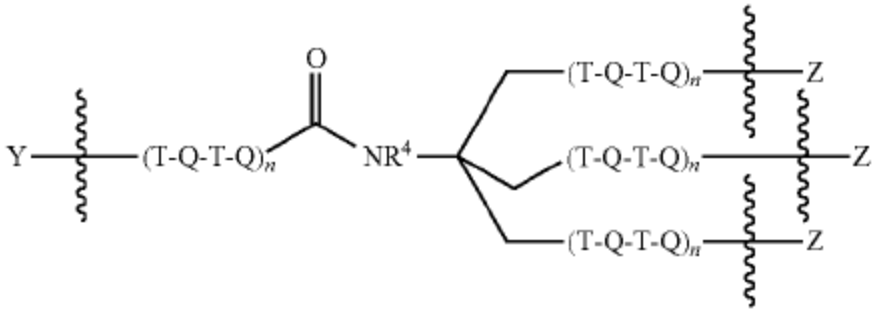
L6



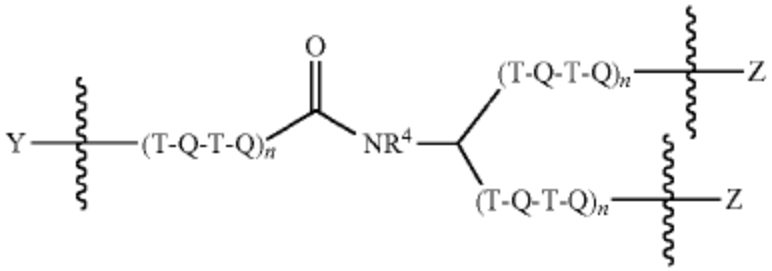
L7



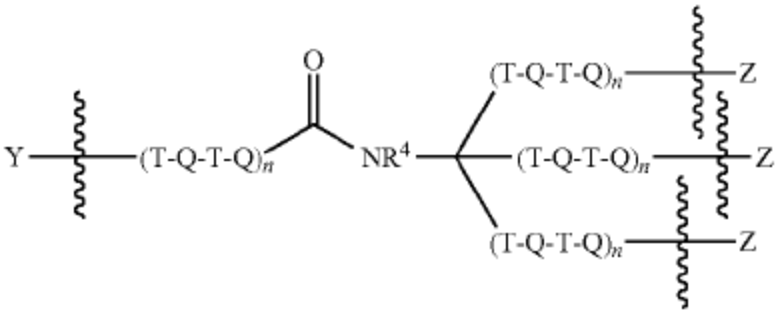
L8



L9



L10



wherein each T is independently absent or is alkylene, alkenylene, or alkynylene, wherein one or more —CH_2— groups of the alkylene, alkenylene, or alkynylene may each independently be replaced with a heteroatom group independently selected from —O—, —S—, and —$N(R^4)$— wherein the heteroatom groups are separated by at least 2 carbon atoms;

each Q is independently absent or is C(O), C(O)—NR^4, NR^4—C(O), O—C(O)—NR^4, NR^4—C(O)—O, —CH_2—, a heteroaryl, or a heteroatom group selected from O, S, S—S, S(O), $S(O)_2$, and NR^4, wherein at least two carbon atoms separate the heteroatom groups O, S, S—S, S(O), $S(O)_2$ and NR^4 from any other heteroatom group;

each R^4 is independently —H, —(C_1-C_{20})alkyl, or (C_3-C_6)cycloalkyl wherein one to six —CH_2— groups of the alkyl or cycloalkyl separated by at least two carbon atoms may be replaced with —O—, —S—, or —$N(R^4)$—, and —CH_3 of the alkyl may be replaced with a heteroatom group selected from —$N(R^4)2$, —OR^4, and —$S(R^4)$ wherein the heteroatom groups are separated by at least 2 carbon atoms; and wherein the alkyl and cycloalkyl may be substituted with halo atoms; and

each n is independently 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11,12,13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40, wherein if n is greater than 1, each T and each Q of each (T-Q-T-Q) is independently selected;

Y is an amino acid sequence, a nucleic acid sequence, or an oligomer, and

Z is absent or is —C≡C—, —CH═CH—, —CH_2—, —CH_2—O—, —C(O)—$N(R^4)$—, —CH_2—S—, —CH_2—S(O)—, —CH_2—$S(O)_2$—, —CH_2—$S(O)_2$—$N(R^4)$—, —C(O)—O—, —CH_2—$N(R^4)$—, —CH_2-$N(R^4)$—C(O)—, —CH_2—$N(R^4)$—$S(O)_2$—, —CH_2—$N(R^4)$—C(O)—O—, —CH_2—$N(R^4)$—C(O)—$N(R^4)$—, —CH_2—O—C(O)—, —CH_2—O—C(O)—$N(R^4)$—, —CH_2—O—C(O)—O—, or aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with R^5;

R^2 is —OH, —N_3, —$N(R^3)_2$, —$N(R^3)$—C(O)—R^3, —$N(R^3)$—C(O)—$N(R^3)_2$, —$N(R^3)$—C(O)—OR^3, tetrazole, or triazole, wherein the tetrazole and triazole are optionally substituted with R^3;

each R^3 is independently —H, —(C_1-C_5)alkyl, halo-substituted (C_1-C_5)alkyl, or (C_3-C_6)cycloalkyl, wherein a —CH_2— group of the alkyl or cycloalkyl may be replaced with a heteroatom group selected from —O—, —S—, and —$N(R^4)$— and —CH_3 of the alkyl may be replaced with a heteroatom group selected from —$N(R^4)_2$, —OR^4, and —$S(R^4)$ wherein the heteroatom groups are separated by at least 2 carbon atoms;

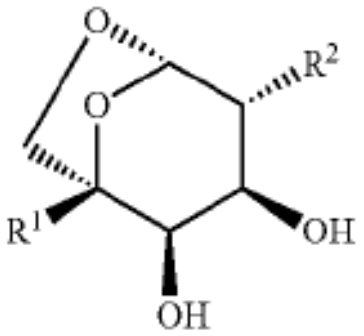
each R^4 is independently —H, —(C_1-C_{20})alkyl, or (C_3-C_6)cycloalkyl wherein one to six —CH_2— groups of the alkyl or cycloalkyl separated by at least two carbon atoms may be replaced with —O—, —S—, or —$N(R^4)$—, and —CH_3 of the alkyl may be replaced with a heteroatom group selected from —$N(R^4)_2$, —OR^4, and —$S(R^4)$ wherein the heteroatom groups are separated by at least 2 carbon atoms; and wherein the alkyl and cycloalkyl may be substituted with one to six halo atoms; and

each R^5 is independently —H, (C_3-C_{20})cycloalkyl or (C_1-C_{20})alkyl wherein one to six —CH_2— groups of the alkyl or cycloalkyl separated by at least two carbon atoms may be replaced with —O—, —S—, or —N(R^4)—, and —CH_3 of the alkyl may be replaced with a heteroatom group selected from —N(R^4)$_2$, —OW, and —S(R^4) wherein the heteroatom groups are separated by at least 2 carbon atoms; and wherein the alkyl and cycloalkyl may be substituted with one to six halo atoms;

or a pharmaceutically acceptable salt thereof.

2. A compound of Formula (A)

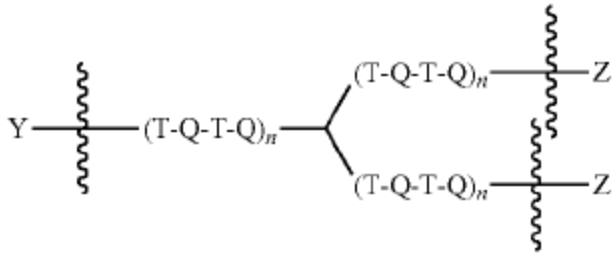
(A)



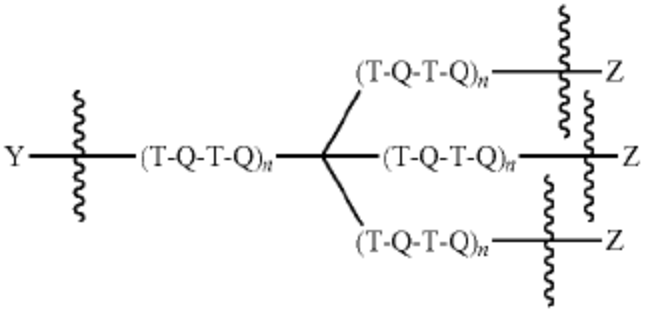
wherein

R^1 is —Z—X—Y, —Z—Y, or —X—Y wherein X is a linker of any of structures L1-L10

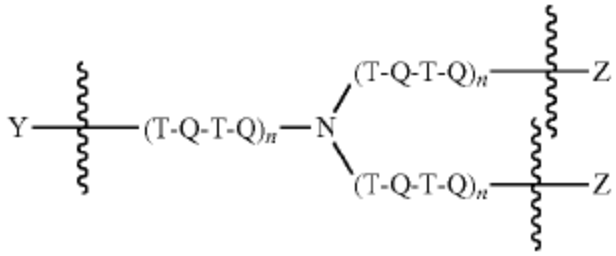
L1


Y
(T-Q-T-Q)n
(T-Q-T-Q)n
Z
(T-Q-T-Q)n
Z

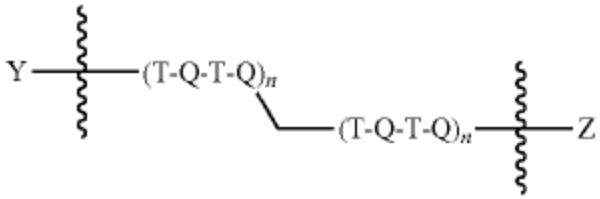
L2


Y
(T-Q-T-Q)n
(T-Q-T-Q)n
Z
(T-Q-T-Q)n
Z
(T-Q-T-Q)n
Z

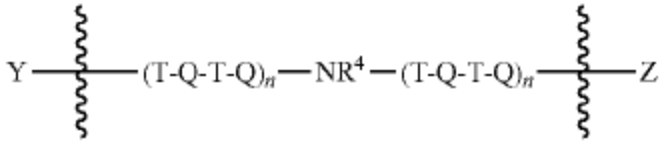
L3


Y
(T-Q-T-Q)n
N
(T-Q-T-Q)n
Z
(T-Q-T-Q)n
Z

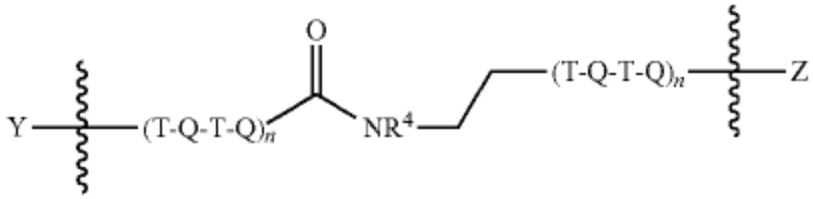
L4


Y
(T-Q-T-Q)n
(T-Q-T-Q)n
Z

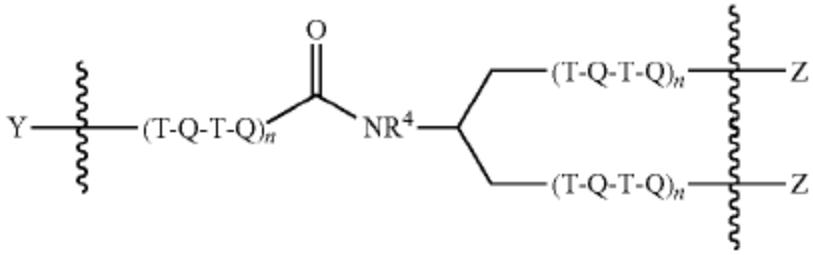
L5


Y
(T-Q-T-Q)n
NR4
(T-Q-T-Q)n
Z

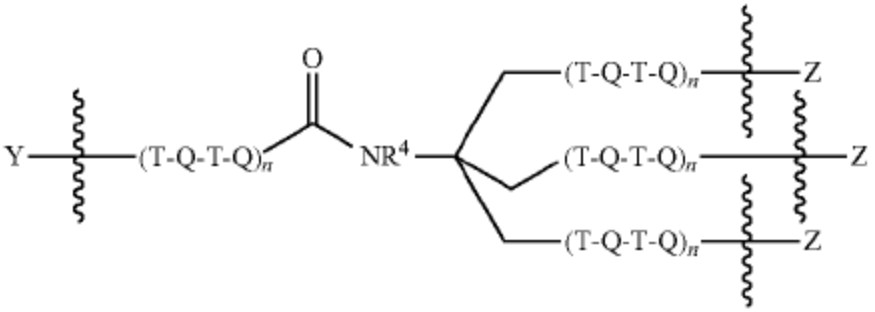
L6



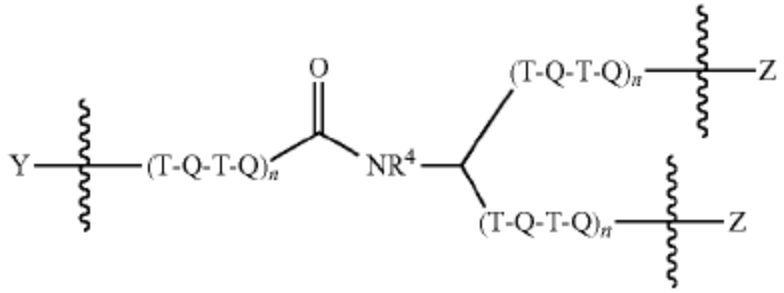
L7



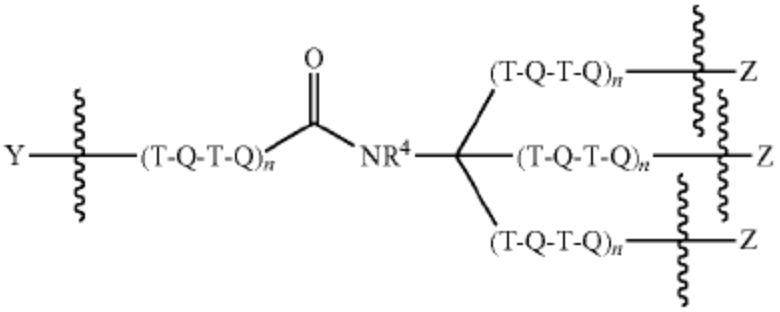
L8



L9



L10



wherein each T is independently absent or is alkylene, alkenylene, or alkynylene, wherein one or more —CH_2— groups of the alkylene, alkenylene, or alkynylene may each independently be replaced with a heteroatom group independently selected from —O—, —S—, and —$N(R^4)$— wherein the heteroatom groups are separated by at least 2 carbon atoms;

each Q is independently absent or is C(O), C(O)—NR^4, NR^4—C(O), O—C(O)—NR^4, NR^4—C(O)—O, —CH_2—, a heteroaryl, or a heteroatom group selected from O, S, S—S, S(O), $S(O)_2$, and NR^4, wherein at least two carbon atoms separate the heteroatom groups O, S, S—S, S(O), $S(O)_2$ and NR^4 from any other heteroatom group;

each R^4 is independently —H, —(C_1-C_{20})alkyl, or (C_3-C_6)cycloalkyl wherein one to six —CH_2— groups of the alkyl or cycloalkyl separated by at least two carbon atoms may be replaced with —O—, —S—, or —$N(R^4)$—, and —CH_3 of the alkyl may be replaced with a heteroatom group selected from —$N(R^4)$2, —OW, and —$S(R^4)$ wherein the heteroatom groups are separated by at least 2 carbon atoms; and wherein the alkyl and cycloalkyl may be substituted with halo atoms; and

each n is independently 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11,12,13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40, wherein if n is greater than 1, each T and each Q of each (T-Q-T-Q) is independently selected;

Y is an amino acid sequence, a nucleic acid sequence, or an oligomer, and

Z is —C≡C—, —CH═CH—, —CH_2—, —CH_2—O—, —C(O)—$N(R^4)$—, —CH_2—S—, —CH_2—S(O)—, —CH_2—$S(O)_2$—, —CH_2—$S(O)_2$—$N(R^4)$—, —C(O)—O—, —CH_2—$N(R^4)$—, —CH_2-$N(R^4)$—C(O)—, —CH_2—$N(R^4)$—$S(O)_2$—, —CH_2—$N(R^4)$—C(O)—O—, —CH_2—$N(R^4)$—C(O)—$N(R^4)$—, —CH_2—O—C(O)—, —CH_2—O—C(O)—$N(R^4)$—,

—CH_2—O—C(O)—O—, or aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with R^5;

R^2 is —OH, —N_3, —$N(R^3)_2$, —$N(R^3)$—C(O)—R^3, —$N(R^3)$—C(O)—$N(R^3)_2$, —$N(R^3)$—C(O)—OR^3, —$N(R^3)$—$S(O)_2$—R^3, tetrazole, or triazole, wherein the tetrazole and triazole are optionally substituted with R^3;

each R^3 is independently —H, —(C_1-C_5)alkyl, halo-substituted (C_1-C_5)alkyl, or (C_3-C_6)cycloalkyl, wherein one or more —CH_2— groups of the alkyl or cycloalkyl may each be replaced with a heteroatom group independently selected from —O—, —S—, and —$N(R^4)$— and —CH_3 of the alkyl may be replaced with a heteroatom group selected from —$N(R^4)_2$, —OR^4, and —$S(R^4)$ wherein the heteroatom groups are separated by at least 2 carbon atoms;

each R^4 is independently —H, —(C_1-C_{20})alkyl, or (C_3-C_6)cycloalkyl wherein one to six —CH_2— groups of the alkyl or cycloalkyl separated by at least two carbon atoms may each be replaced with a heteroatom independently selected from —O—, —S—, or —$N(R^4)$—, and —CH_3 of the alkyl may be replaced with a heteroatom group selected from —$N(R^4)_2$, —OR^4, and —$S(R^4)$ wherein the heteroatom groups are separated by at least 2 carbon atoms; and wherein the alkyl and cycloalkyl may be substituted with halo atoms;

each R^5 is independently —H, (C_3-C_{20})cycloalkyl or (C_1-C_{60})alkyl wherein one to six —CH_2— groups of the cycloalkyl or one to 20 —CH_2— groups of the alkyl

may each be replaced with heteroatoms independently selected from —O—, —S—, and —N(R^4)— wherein the heteroatoms are separated by at least two carbon atoms, and —CH_3 of the alkyl may be replaced with a heteroatom group selected from —N(R^4)$_2$, —OR^4, and —S(R^4) wherein the heteroatom groups are separated by at least 2 carbon atoms; and wherein the alkyl and cycloalkyl may be substituted with halo atoms;

or a pharmaceutically acceptable salt thereof.

3. The compound of claim **1** or **2** or a pharmaceutically acceptable salt thereof, wherein R^1 is —X—Y and R^2 is —NH—C(O)—CH_3.

4. The compound of claim **1** or **2** or a pharmaceutically acceptable salt thereof, wherein Y is an siRNA sequence.

5. The compound of claim **1** or **2** or a pharmaceutically acceptable salt thereof, wherein the compound of Formula (A) is capable of binding to a receptor present on a hepatocyte.

6. The compound of claim **5** or a pharmaceutically acceptable salt thereof, wherein the receptor present on a hepatocyte is an asialoglycoprotein receptor.

7. A pharmaceutical composition comprising (i) a compound of claim **5** or a pharmaceutically acceptable salt thereof; and (ii) a pharmaceutically acceptable excipient, diluent, or carrier.

8. The composition of claim **7** wherein said compound or said therapeutically acceptable salt thereof is present in a therapeutically effective amount.