

**IMMUNE STIMULATING ANTI-HBSAG ANTIBODY CONJUGATES,
PHARMACEUTICAL COMPOSITIONS, AND THERAPEUTIC APPLICATIONS**

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit of the priority of International Application No. PCT/CN2023/143278, filed December 29, 2023, under 35 U.S.C. 119(a); the disclosure of which is incorporated herein by reference in its entirety.

FIELD

[0002] Provided herein are immune stimulating anti-HBsAg antibody conjugates and pharmaceutical compositions thereof. Also provided herein are methods of their use for treating, preventing, or ameliorating one or more symptoms of an HBV infection.

REFERENCE TO A SEQUENCE LISTING

[0003] The present specification is being filed with a Sequence Listing entitled 296A001WO01_SEQLIST_ST26.XML of 75,601 bytes in size and created December 25, 2024; the content of which is incorporated herein by reference in its entirety.

BACKGROUND

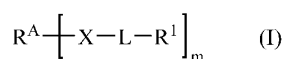
[0004] Hepatitis B virus (HBV) infection remains a significant global health threat, with an estimated 296 million people chronically infected and 820,000 deaths worldwide in 2019. Chisari *et al.*, *Pathol. Biol. (Paris)* **2010**, 58, 258-66; Martyn *et al.*, *eLife* **2023**, 12, e81070; Forbes *et al.*, *Expert Rev. Ant-Infect. Ther.* **2023**, 21, 847-62; Jeng *et al.*, *Lancet* **2023**, 401, 1039-52. People with chronic HBV infection are at an increased risk of developing hepatic fibrosis, hepatic cirrhosis, and hepatocellular carcinoma (HCC). Chisari *et al.*, *Pathol. Biol. (Paris)* **2010**, 58, 258-66; Martyn *et al.*, *eLife* **2023**, 12, e81070.

[0005] As of today, there is no cure for HBV infection. Chisari *et al.*, *Pathol. Biol. (Paris)* **2010**, 58, 258-66; Martyn *et al.*, *eLife* **2023**, 12, e81070; Forbes *et al.*, *Expert Rev. Ant-Infect. Ther.* **2023**, 21, 847-62; Jeng *et al.*, *Lancet* **2023**, 401, 1039-52. Current therapies,

pegylated interferon (Peg-IFN) and nucleos(t)ide analogues (NAs), can prevent development of cirrhosis and hepatocellular carcinoma, but do not eradicate the virus and rarely clear hepatitis B surface antigen (HBsAg), a serological marker for an HBV infection. Forbes *et al.*, *Expert Rev. Ant-Infect. Ther.* **2023**, *21*, 847-62; Jeng *et al.*, *Lancet* **2023**, *401*, 1039-52. Therefore, there is an unmet need for an effective therapy for HBV infection, especially chronic HBV infection. Martyn *et al.*, *eLife* **2023**, *12*, e81070; Forbes *et al.*, *Expert Rev. Ant-Infect. Ther.* **2023**, *21*, 847-62.

SUMMARY OF THE DISCLOSURE

[0006] Provided herein is a compound of Formula (I):



or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein:

each L is independently a linker;

each X is independently (i) a bond or $-S-$; or (ii) heteroarylene or heterocyclylene, each optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q;

each R^1 is independently an immunostimulator;

R^A is an antibody or an antigen-binding fragment thereof, which binds specifically to a hepatitis B surface antigen; and

m is an integer of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16;

wherein each Q is independently selected from: (a) deuterium, cyano, halo, imino, nitro, and oxo; (b) C_{1-6} alkyl, C_{1-6} heteroalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, and heterocyclyl, each of which is further optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q^a ; and (c) $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^bR^c$, $-C(O)SR^a$, $-C(NR^a)NR^bR^c$, $-C(S)R^a$, $-C(S)OR^a$, $-C(S)NR^bR^c$, $-OR^a$, $-OC(O)R^a$, $-OC(O)OR^a$, $-OC(O)NR^bR^c$, $-OC(O)SR^a$, $-OC(NR^a)NR^bR^c$, $-OC(S)R^a$, $-OC(S)OR^a$, $-OC(S)NR^bR^c$, $-OP(O)(OR^a)OR^d$, $-OS(O)R^a$, $-OS(O)_2R^a$, $-OS(O)NR^bR^c$, $-OS(O)_2NR^bR^c$, $-NR^bR^c$, $-NR^aC(O)R^d$, $-NR^aC(O)OR^d$, $-NR^aC(O)NR^bR^c$, $-NR^aC(O)SR^d$,

$-\text{NR}^a\text{C}(\text{NR}^d)\text{NR}^b\text{R}^c$, $-\text{NR}^a\text{C}(\text{S})\text{R}^d$, $-\text{NR}^a\text{C}(\text{S})\text{OR}^d$, $-\text{NR}^a\text{C}(\text{S})\text{NR}^b\text{R}^c$, $-\text{NR}^a\text{S}(\text{O})\text{R}^d$, $-\text{NR}^a\text{S}(\text{O})_2\text{R}^d$, $-\text{NR}^a\text{S}(\text{O})\text{NR}^b\text{R}^c$, $-\text{NR}^a\text{S}(\text{O})_2\text{NR}^b\text{R}^c$, $-\text{SR}^a$, $-\text{S}(\text{O})\text{R}^a$, $-\text{S}(\text{O})_2\text{R}^a$, $-\text{S}(\text{O})\text{NR}^b\text{R}^c$, and $-\text{S}(\text{O})_2\text{NR}^b\text{R}^c$, wherein each R^a , R^b , R^c , and R^d is independently (i) hydrogen or deuterium; (ii) C_{1-6} alkyl, C_{1-6} heteroalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or heterocyclyl, each of which is optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q^a ; or (iii) R^b and R^c together with the N atom to which they are attached form heterocyclyl, optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q^a ;

wherein each Q^a is independently selected from: (a) deuterium, cyano, halo, nitro, imino, and oxo; (b) C_{1-6} alkyl, C_{1-6} heteroalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, and heterocyclyl; and (c) $-\text{C}(\text{O})\text{R}^e$, $-\text{C}(\text{O})\text{OR}^e$, $-\text{C}(\text{O})\text{NR}^f\text{R}^g$, $-\text{C}(\text{O})\text{SR}^e$, $-\text{C}(\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{C}(\text{S})\text{R}^e$, $-\text{C}(\text{S})\text{OR}^e$, $-\text{C}(\text{S})\text{NR}^f\text{R}^g$, $-\text{OR}^e$, $-\text{OC}(\text{O})\text{R}^e$, $-\text{OC}(\text{O})\text{OR}^e$, $-\text{OC}(\text{O})\text{NR}^f\text{R}^g$, $-\text{OC}(\text{O})\text{SR}^e$, $-\text{OC}(\text{NR}^e)\text{NR}^f\text{R}^g$, $-\text{OC}(\text{S})\text{R}^e$, $-\text{OC}(\text{S})\text{OR}^e$, $-\text{OC}(\text{S})\text{NR}^f\text{R}^g$, $-\text{OS}(\text{O})\text{R}^e$, $-\text{OS}(\text{O})_2\text{R}^e$, $-\text{OS}(\text{O})\text{NR}^f\text{R}^g$, $-\text{OS}(\text{O})_2\text{NR}^f\text{R}^g$, $-\text{NR}^f\text{R}^g$, $-\text{NR}^e\text{C}(\text{O})\text{R}^h$, $-\text{NR}^e\text{C}(\text{O})\text{OR}^f$, $-\text{NR}^e\text{C}(\text{O})\text{NR}^f\text{R}^g$, $-\text{NR}^e\text{C}(\text{O})\text{SR}^f$, $-\text{NR}^e\text{C}(\text{NR}^h)\text{NR}^f\text{R}^g$, $-\text{NR}^e\text{C}(\text{S})\text{R}^h$, $-\text{NR}^e\text{C}(\text{S})\text{OR}^f$, $-\text{NR}^e\text{C}(\text{S})\text{NR}^f\text{R}^g$, $-\text{NR}^e\text{S}(\text{O})\text{R}^h$, $-\text{NR}^e\text{S}(\text{O})_2\text{R}^h$, $-\text{NR}^e\text{S}(\text{O})\text{NR}^f\text{R}^g$, $-\text{NR}^e\text{S}(\text{O})_2\text{NR}^f\text{R}^g$, $-\text{SR}^e$, $-\text{S}(\text{O})\text{R}^e$, $-\text{S}(\text{O})_2\text{R}^e$, $-\text{S}(\text{O})\text{NR}^f\text{R}^g$, and $-\text{S}(\text{O})_2\text{NR}^f\text{R}^g$; wherein each R^e , R^f , R^g , and R^h is independently (i) hydrogen or deuterium; (ii) C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or heterocyclyl; or (iii) R^f and R^g together with the N atom to which they are attached form heterocyclyl.

[0007] Also provided herein is a pharmaceutical composition comprising a compound of Formula (I), or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; and a pharmaceutically acceptable excipient.

[0008] Additionally provided herein is a method of treating, preventing, or ameliorating one or more symptoms of a hepatitis B virus (HBV) infection in a subject, comprising administering to the subject in need thereof a therapeutically effective amount of a compound of Formula (I), or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] FIG. 1 shows an SDS-PAGE analysis of anti-HBsAg antibody/CpG oligonucleotide conjugates under reduced conditions, where mAnti-HBsAg 1 (SEQ ID NOs: 8 and 9), **AOC-A1**, **AOC-A2**, **AOC-B1**, **AOC-A3**, **AOC-A4**, **AOC-A5**, **AOC-A6**, **AOC-A7**, and markers are in Lanes 1 to 10, respectively.

[0010] FIG. 2 shows a strong anion exchange chromatography (SAX-HPLC) analysis of anti-HBsAg antibody/CpG oligonucleotide conjugate **AOC-A1**.

[0011] FIG. 3 shows the antiviral efficacies of mAnti-HBsAg 1 (SEQ ID NOs: 8 and 9), and anti-HBsAg antibody/CpG oligonucleotide conjugate **AOC-A1** as measured by plasma HBsAg levels in an AAV-HBV mouse model.

[0012] FIG. 4 shows the antiviral efficacies of mAnti-HBsAg 1 (SEQ ID NOs: 8 and 9), and anti-HBsAg antibody/CpG oligonucleotide conjugate **AOC-A1** as measured by plasma anti-HBs levels in an AAV-HBV mouse model.

[0013] FIG. 5 shows the antiviral efficacies of mAnti-HBsAg 1 (SEQ ID NOs: 8 and 9), and anti-HBsAg antibody/CpG oligonucleotide conjugate **AOC-A1** as measured by plasma ALT levels in an AAV-HBV mouse model.

[0014] FIG. 6 shows the antiviral efficacies of mAnti-HBsAg 1 (SEQ ID NOs: 8 and 9), and anti-HBsAg antibody/CpG oligonucleotide conjugate **AOC-A1** as measured by hepatic HBcAg levels in an AAV-HBV mouse model.

[0015] FIG. 7 shows the antiviral efficacies of immune stimulating anti-HBsAg antibody conjugates **AOC-A1** to **AOC-A7**, **AOC-A9**, **AOC-B1**, **AOC-C1**, and **ISAC-A1** as measured by plasma HBsAg levels in an AAV-HBV mouse model.

[0016] FIG. 8 shows the antiviral efficacies of immune stimulating anti-HBsAg antibody conjugates **AOC-A1** to **AOC-A7**, **AOC-A9**, **AOC-B1**, **AOC-C1**, and **ISAC-A1** as measured by plasma anti-HBs levels in an AAV-HBV mouse model.

[0017] FIG. 9 shows the antiviral efficacies of immune stimulating anti-HBcAg antibody

conjugates **AOC-A1** to **AOC-A7**, **AOC-A9**, **AOC-B1**, **AOC-C1**, and **ISAC-A1** as measured by hepatic HBcAg levels in an AAV-HBV mouse model.

[0018] FIG. 10 shows the antiviral efficacies of anti-HBsAg antibody/CpG oligonucleotide conjugates **AOC-A4**, **AOC-A10**, **AOC-B3**, **AOC-B4**, **AOC-C1**, and **AOC-C2** as measured by plasma HBsAg levels in an AAV-HBV mouse model.

[0019] FIG. 11 shows the antiviral efficacies of anti-HBsAg antibody/CpG oligonucleotide conjugates **AOC-A4**, **AOC-A10**, **AOC-B3**, **AOC-B4**, **AOC-C1**, and **AOC-C2** as measured by plasma anti-HBs levels in an AAV-HBV mouse model.

[0020] FIG. 12 shows the antiviral efficacies of anti-HBsAg antibody/CpG oligonucleotide conjugates **AOC-A4**, **AOC-A10**, **AOC-B3**, **AOC-B4**, **AOC-C1**, and **AOC-C2** as measured by hepatic HBcAg levels in an AAV-HBV mouse model.

[0021] FIG. 13 shows the antiviral efficacies of immune stimulating anti-HBsAg antibody conjugates **AOC-B8**, **AOC-D1**, and **ISAC-A2** as measured by plasma HBsAg levels in an AAV-HBV mouse model.

[0022] FIG. 14 shows the effects of hAnti-HBsAg 1 (SEQ ID NOs: 10 and 11), hAnti-HBsAg 2 (SEQ ID NOs: 21 and 22), and hAnti-HBsAg 3 (SEQ ID NOs: 33 and 34) on the interaction of a biotinylated hAnti-HBsAg 1 (SEQ ID NOs: 10 and 11) with HBsAg (SEQ ID NO: 56) in a competitive ELISA.

DETAILED DESCRIPTION

[0023] To facilitate understanding of the disclosure set forth herein, a number of terms are defined below.

[0024] Generally, the nomenclature used herein and the laboratory procedures in organic chemistry, medicinal chemistry, biochemistry, biology, immunology, and pharmacology described herein are those well-known and commonly employed in the art. Unless defined otherwise, all technical and scientific terms used herein generally have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs.

[0025] The term “subject” refers to an animal, including, but not limited to, a primate (*e.g.*, human), cow, pig, sheep, goat, horse, dog, cat, rabbit, rat, or mouse. The terms “subject” and “patient” are used interchangeably herein in reference, for example, to a mammalian subject, such as a human subject. In one embodiment, the subject is a human.

[0026] The terms “treat,” “treating,” and “treatment” are meant to include alleviating or abrogating a disorder, disease, or condition, or one or more of the symptoms associated with the disorder, disease, or condition; or alleviating or eradicating the cause(s) of the disorder, disease, or condition itself.

[0027] The terms “prevent,” “preventing,” and “prevention” are meant to include a method of delaying and/or precluding the onset of a disorder, disease, or condition, and/or its attendant symptoms; barring a subject from acquiring a disorder, disease, or condition; or reducing a subject’s risk of acquiring a disorder, disease, or condition.

[0028] The terms “alleviate” and “alleviating” refer to easing or reducing one or more symptoms (*e.g.*, pain) of a disorder, disease, or condition. The terms can also refer to reducing adverse effects associated with an active ingredient. Sometimes, the beneficial effects that a subject derives from a prophylactic or therapeutic agent do not result in a cure of the disorder, disease, or condition.

[0029] The term “contacting” or “contact” is meant to refer to bringing together of a therapeutic agent and a biological molecule (*e.g.*, a protein, enzyme, RNA, or DNA), cell, or tissue such that a physiological and/or chemical effect takes place as a result of such contact. Contacting can take place *in vitro*, *ex vivo*, or *in vivo*. In one embodiment, a therapeutic agent is contacted with a biological molecule *in vitro* to determine the effect of the therapeutic agent on the biological molecule. In another embodiment, a therapeutic agent is contacted with a cell in cell culture (*in vitro*) to determine the effect of the therapeutic agent on the cell. In yet another embodiment, the contacting of a therapeutic agent with a biological molecule, cell, or tissue includes the administration of a therapeutic agent to a subject having the biological molecule, cell, or tissue to be contacted.

[0030] The term “therapeutically effective amount” or “effective amount” is meant to

include the amount of a compound that, when administered, is sufficient to prevent development of, or alleviate to some extent, one or more of the symptoms of the disorder, disease, or condition being treated. The term “therapeutically effective amount” or “effective amount” also refers to the amount of a compound that is sufficient to elicit a biological or medical response of a biological molecule (*e.g.*, a protein, enzyme, RNA, or DNA), cell, tissue, system, animal, or human, which is being sought by a researcher, veterinarian, medical doctor, or clinician.

[0031] The term “HBsAg” refers to a hepatitis B virus envelope protein, including HBV envelope proteins S, M, and L, which are also known as S-HBsAg, M-HBsAg, and L-HBsAg, respectively. S-HBsAg, M-HBsAg, and L-HBsAg share the same C terminus (also known as the S domain) of 226 amino acids in length, which corresponds to S-HBsAg and is critical for viral assembly and infectivity. Salisse and Sureau, *J. Virol.* **2009**, 83, 9321-8.

[0032] The term “pharmaceutically acceptable carrier,” “pharmaceutically acceptable excipient,” “physiologically acceptable carrier,” or “physiologically acceptable excipient” refers to a pharmaceutically acceptable material, composition, or vehicle, such as a liquid or solid filler, diluent, solvent, or encapsulating material. In one embodiment, each component is “pharmaceutically acceptable” in the sense of being compatible with the other ingredients of a pharmaceutical formulation, and suitable for use in contact with the tissue or organ of a subject (*e.g.*, a human or an animal) without excessive toxicity, irritation, allergic response, immunogenicity, or other problems or complications, and commensurate with a reasonable benefit/risk ratio. *See, e.g., Remington: The Science and Practice of Pharmacy*, 22nd ed.; Allen Ed.; Pharmaceutical Press: London, 2012; *Handbook of Pharmaceutical Excipients*, 8th ed.; Sheskey *et al.*, Eds.; Pharmaceutical Press: London, 2017; *Handbook of Pharmaceutical Additives*, 3rd ed.; Ash and Ash Eds.; Synapse Information Resources: 2007; *Pharmaceutical Preformulation and Formulation*, 2nd ed.; Gibson Ed.; Drugs and the Pharmaceutical Sciences 199; Informa Healthcare: New York, NY, 2009.

[0033] The term “about” or “approximately” means an acceptable error for a particular value as determined by one of ordinary skill in the art, which depends in part on how the value is measured or determined. In certain embodiments, the term “about” or “approximately” means within 1, 2, or 3 standard deviations. In certain embodiments, the term “about” or

- 8 -

[0036] The terms “alkylene” and “alkanediyl” are used interchangeably herein in reference to a linear or branched saturated divalent hydrocarbon radical, wherein the alkanediyl is optionally substituted with one or more substituents Q as described herein. For example, C₁₋₆ alkanediyl refers to a linear saturated divalent hydrocarbon radical of 1 to 6 carbon atoms or a branched saturated divalent hydrocarbon radical of 3 to 6 carbon atoms. In certain embodiments, the alkanediyl is a linear saturated divalent hydrocarbon radical that has 1 to 30 (C₁₋₃₀), 1 to 20 (C₁₋₂₀), 1 to 15 (C₁₋₁₅), 1 to 10 (C₁₋₁₀), or 1 to 6 (C₁₋₆) carbon atoms, or branched saturated divalent hydrocarbon radical of 3 to 30 (C₃₋₃₀), 3 to 20 (C₃₋₂₀), 3 to 15 (C₃₋₁₅), 3 to 10 (C₃₋₁₀), or 3 to 6 (C₃₋₆) carbon atoms. As used herein, linear C₁₋₆ and branched C₃₋₆ alkanediyl groups are also referred as “lower alkanediyl.” Examples of alkanediyl groups include, but are not limited to, methanediyl, ethanediyl (including all isomeric forms, *e.g.*, ethane-1,1-diyl and ethane-1,2-diyl), propanediyl (including all isomeric forms, *e.g.*, propane-1,1-diyl, propane-1,2-diyl, and propane-1,3-diyl), butanediyl (including all isomeric forms, *e.g.*, butane-1,1-diyl, butane-1,2-diyl, butane-1,3-diyl, and butane-1,4-diyl), pentanediyl (including all isomeric forms, *e.g.*, pentane-1,1-diyl, pentane-1,2-diyl, pentane-1,3-diyl, and pentane-1,5-diyl), and hexanediyl (including all isomeric forms, *e.g.*, hexane-1,1-diyl, hexane-1,2-diyl, hexane-1,3-diyl, and hexane-1,6-diyl). Examples of substituted alkanediyl groups include, but are not limited to, -C(O)CH₂-, -C(O)(CH₂)₂-, -C(O)(CH₂)₃-, -C(O)(CH₂)₄-, -C(O)(CH₂)₅-, -C(O)(CH₂)₆-, -C(O)(CH₂)₇-, -C(O)(CH₂)₈-, -C(O)(CH₂)₉-, -C(O)(CH₂)₁₀-, -C(O)CH₂C(O)-, -C(O)(CH₂)₂C(O)-, -C(O)(CH₂)₃C(O)-, -C(O)(CH₂)₄C(O)-, or -C(O)(CH₂)₅C(O)-.

[0037] The terms “heteroalkylene” and “heteroalkanediyl” are used interchangeably herein in reference to a linear or branched saturated divalent hydrocarbon radical that contains one or more heteroatoms in its main chain, each independently selected from O, S, N, and N. The heteroalkylene is optionally substituted with one or more substituents Q as described herein. For example, C₁₋₆ heteroalkylene refers to a linear saturated divalent hydrocarbon radical of 1 to 6 carbon atoms or a branched saturated divalent hydrocarbon radical of 3 to 6 carbon atoms. In certain embodiments, the heteroalkylene is a linear saturated divalent hydrocarbon radical that has 1 to 20 (C₁₋₂₀), 1 to 15 (C₁₋₁₅), 1 to 10 (C₁₋₁₀), or 1 to 6 (C₁₋₆) carbon atoms, or branched saturated divalent hydrocarbon radical of 3 to 20 (C₃₋₂₀), 3 to 15 (C₃₋₁₅), 3 to 10 (C₃₋₁₀), or 3 to 6 (C₃₋₆) carbon atoms. As used herein, linear C₁₋₆ and branched C₃₋₆ heteroalkylene groups are also referred as “lower heteroalkylene.” Examples of heteroalkylene groups include, but are not

limited to, $-\text{CH}_2\text{O}-$, $-(\text{CH}_2)_2\text{O}-$, $-(\text{CH}_2)_3\text{O}-$, $-(\text{CH}_2)_4\text{O}-$, $-(\text{CH}_2)_5\text{O}-$, $-(\text{CH}_2)_6\text{O}-$, $-(\text{CH}_2)_7\text{O}-$, $-(\text{CH}_2)_8\text{O}-$, $-(\text{CH}_2)_9\text{O}-$, $-(\text{CH}_2)_{10}\text{O}-$, $-\text{CH}_2\text{OCH}_2-$, $-\text{CH}_2\text{CH}_2\text{O}-$, $-(\text{CH}_2\text{CH}_2\text{O})_2-$, $-(\text{CH}_2\text{CH}_2\text{O})_3-$, $-(\text{CH}_2\text{CH}_2\text{O})_4-$, $-(\text{CH}_2\text{CH}_2\text{O})_5-$, $-\text{CH}_2\text{NH}-$, $-\text{CH}_2\text{NHCH}_2-$, $-\text{CH}_2\text{CH}_2\text{NH}-$, $-\text{CH}_2\text{S}-$, $-\text{CH}_2\text{SCH}_2-$, and $-\text{CH}_2\text{CH}_2\text{S}-$. Examples of substituted heteroalkylene groups include, but are not limited to, $-\text{C}(\text{O})\text{CH}_2\text{O}-$, $-\text{C}(\text{O})(\text{CH}_2)_2\text{O}-$, $-\text{C}(\text{O})(\text{CH}_2)_3\text{O}-$, $-\text{C}(\text{O})(\text{CH}_2)_4\text{O}-$, $-\text{C}(\text{O})(\text{CH}_2)_5\text{O}-$, $-\text{C}(\text{O})(\text{CH}_2)_6\text{O}-$, $-\text{C}(\text{O})(\text{CH}_2)_7\text{O}-$, $-\text{C}(\text{O})(\text{CH}_2)_8\text{O}-$, $-\text{C}(\text{O})(\text{CH}_2)_9\text{O}-$, $-\text{C}(\text{O})(\text{CH}_2)_{10}\text{O}-$, $-\text{C}(\text{O})\text{CH}_2\text{OCH}_2\text{CH}_2\text{O}-$, $-\text{C}(\text{O})\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_2-$, $-\text{C}(\text{O})\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_3-$, $-\text{C}(\text{O})\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_4-$, $-\text{C}(\text{O})\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_5-$, $-\text{CH}_2\text{NHC}(\text{O})\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{C}(\text{O})\text{NH}-$, $-\text{CH}_2\text{CH}_2\text{OP}(\text{O})(\text{O}^-)\text{O}-$, or $-\text{CH}_2\text{CH}_2\text{OP}(\text{S})(\text{O}^-)\text{O}-$, $-\text{CH}_2\text{CH}_2\text{OP}(\text{O})(\text{O}^-)-$, and $-\text{CH}_2\text{CH}_2\text{OP}(\text{S})(\text{O}^-)-$.

[0038] The term “alkenyl” refers to a linear or branched monovalent hydrocarbon radical, which contains one or more, in one embodiment, one, two, three, or four, in another embodiment, one, carbon-carbon double bond(s). The alkenyl is optionally substituted with one or more substituents Q as described herein. The term “alkenyl” embraces radicals having a “*cis*” or “*trans*” configuration or a mixture thereof, or alternatively, a “*Z*” or “*E*” configuration or a mixture thereof, as appreciated by those of ordinary skill in the art. For example, C₂₋₆ alkenyl refers to a linear unsaturated monovalent hydrocarbon radical of 2 to 6 carbon atoms or a branched unsaturated monovalent hydrocarbon radical of 3 to 6 carbon atoms. In certain embodiments, the alkenyl is a linear monovalent hydrocarbon radical of 2 to 20 (C₂₋₂₀), 2 to 15 (C₂₋₁₅), 2 to 10 (C₂₋₁₀), or 2 to 6 (C₂₋₆) carbon atoms, or a branched monovalent hydrocarbon radical of 3 to 20 (C₃₋₂₀), 3 to 15 (C₃₋₁₅), 3 to 10 (C₃₋₁₀), or 3 to 6 (C₃₋₆) carbon atoms. Examples of alkenyl groups include, but are not limited to, ethenyl, propenyl (including all isomeric forms, *e.g.*, propen-1-yl, propen-2-yl, and allyl), and butenyl (including all isomeric forms, *e.g.*, buten-1-yl, buten-2-yl, buten-3-yl, and 2-buten-1-yl).

[0039] The terms “alkenylene” and “alkenediyl” are used interchangeably herein in reference to a linear or branched divalent hydrocarbon radical, which contains one or more, in one embodiment, one, two, three, or four, in another embodiment, one, carbon-carbon double bond(s). The alkenediyl is optionally substituted with one or more substituents Q as described herein. The term “alkenediyl” embraces radicals having a “*cis*” or “*trans*” configuration or a mixture thereof, or alternatively, a “*Z*” or “*E*” configuration or a mixture thereof, as appreciated

by those of ordinary skill in the art. For example, C₂₋₆ alkenediyl refers to a linear unsaturated divalent hydrocarbon radical of 2 to 6 carbon atoms or a branched unsaturated divalent hydrocarbon radical of 3 to 6 carbon atoms. In certain embodiments, the alkenediyl is a linear divalent hydrocarbon radical of 2 to 30 (C₂₋₃₀), 2 to 20 (C₂₋₂₀), 2 to 15 (C₂₋₁₅), 2 to 10 (C₂₋₁₀), or 2 to 6 (C₂₋₆) carbon atoms, or a branched divalent hydrocarbon radical of 3 to 30 (C₃₋₃₀), 3 to 20 (C₃₋₂₀), 3 to 15 (C₃₋₁₅), 3 to 10 (C₃₋₁₀), or 3 to 6 (C₃₋₆) carbon atoms. Examples of alkenediyl groups include, but are not limited to, ethenediyl (including all isomeric forms, *e.g.*, ethene-1,1-diyl and ethene-1,2-diyl), propenediyl (including all isomeric forms, *e.g.*, 1-propene-1,1-diyl, 1-propene-1,2-diyl, and 1-propene-1,3-diyl), butenediyl (including all isomeric forms, *e.g.*, 1-butene-1,1-diyl, 1-butene-1,2-diyl, and 1-butene-1,4-diyl), pentenediyl (including all isomeric forms, *e.g.*, 1-pentene-1,1-diyl, 1-pentene-1,2-diyl, and 1-pentene-1,5-diyl), and hexenediyl (including all isomeric forms, *e.g.*, 1-hexene-1,1-diyl, 1-hexene-1,2-diyl, 1-hexene-1,3-diyl, 1-hexene-1,4-diyl, 1-hexene-1,5-diyl, and 1-hexene-1,6-diyl).

[0040] The terms “heteroalkenylene” and “heteroalkenediyl” are used interchangeably herein in reference to a linear or branched divalent hydrocarbon radical, which contains one or more, in one embodiment, one, two, three, or four, in another embodiment, one, carbon-carbon double bond(s), and which contains one or more heteroatoms each independently selected from O, S, and N in the hydrocarbon chain. The heteroalkenylene is optionally substituted with one or more substituents Q as described herein. The term “heteroalkenylene” embraces radicals having a “*cis*” or “*trans*” configuration or a mixture thereof, or alternatively, a “*Z*” or “*E*” configuration or a mixture thereof, as appreciated by those of ordinary skill in the art. For example, C₂₋₆ heteroalkenylene refers to a linear unsaturated divalent hydrocarbon radical of 2 to 6 carbon atoms or a branched unsaturated divalent hydrocarbon radical of 3 to 6 carbon atoms. In certain embodiments, the heteroalkenylene is a linear divalent hydrocarbon radical of 2 to 20 (C₂₋₂₀), 2 to 15 (C₂₋₁₅), 2 to 10 (C₂₋₁₀), or 2 to 6 (C₂₋₆) carbon atoms, or a branched divalent hydrocarbon radical of 3 to 20 (C₃₋₂₀), 3 to 15 (C₃₋₁₅), 3 to 10 (C₃₋₁₀), or 3 to 6 (C₃₋₆) carbon atoms. Examples of heteroalkenylene groups include, but are not limited to, -CH=CHO-, -CH=CHOCH₂-, -CH=CHCH₂O-, -CH=CHS-, -CH=CHSCH₂-, -CH=CHCH₂S-, or -CH=CHCH₂NH-.

[0041] The term “alkynyl” refers to a linear or branched monovalent hydrocarbon radical, which contains one or more, in one embodiment, one, two, three, or four, in another

embodiment, one, carbon-carbon triple bond(s). The alkynyl is optionally substituted with one or more substituents Q as described herein. For example, C₂₋₆ alkynyl refers to a linear unsaturated monovalent hydrocarbon radical of 2 to 6 carbon atoms or a branched unsaturated monovalent hydrocarbon radical of 4 to 6 carbon atoms. In certain embodiments, the alkynyl is a linear monovalent hydrocarbon radical of 2 to 20 (C₂₋₂₀), 2 to 15 (C₂₋₁₅), 2 to 10 (C₂₋₁₀), or 2 to 6 (C₂₋₆) carbon atoms, or a branched monovalent hydrocarbon radical of 4 to 20 (C₄₋₂₀), 4 to 15 (C₄₋₁₅), 4 to 10 (C₄₋₁₀), or 4 to 6 (C₄₋₆) carbon atoms. Examples of alkynyl groups include, but are not limited to, ethynyl ($-\text{C}\equiv\text{CH}$), propynyl (including all isomeric forms, *e.g.*, 1-propynyl ($-\text{C}\equiv\text{CCH}_3$) and propargyl ($-\text{CH}_2\text{C}\equiv\text{CH}$)), butynyl (including all isomeric forms, *e.g.*, 1-butyne-1-yl and 2-butyne-1-yl), pentynyl (including all isomeric forms, *e.g.*, 1-pentyne-1-yl and 1-methyl-2-butyne-1-yl), and hexynyl (including all isomeric forms, *e.g.*, 1-hexyne-1-yl and 2-hexyne-1-yl).

[0042] The terms “alkynylene” and “alkynediyl” are used interchangeably herein in reference to a linear or branched divalent hydrocarbon radical, which contains one or more, in one embodiment, one, two, three, or four, in another embodiment, one, carbon-carbon triple bond(s). The alkynediyl is optionally substituted with one or more substituents Q as described herein. For example, C₂₋₆ alkynediyl refers to a linear unsaturated divalent hydrocarbon radical of 2 to 6 carbon atoms or a branched unsaturated divalent hydrocarbon radical of 4 to 6 carbon atoms. In certain embodiments, the alkynediyl is a linear divalent hydrocarbon radical of 2 to 30 (C₂₋₃₀), 2 to 20 (C₂₋₂₀), 2 to 15 (C₂₋₁₅), 2 to 10 (C₂₋₁₀), or 2 to 6 (C₂₋₆) carbon atoms, or a branched divalent hydrocarbon radical of 4 to 30 (C₄₋₃₀), 4 to 20 (C₄₋₂₀), 4 to 15 (C₄₋₁₅), 4 to 10 (C₄₋₁₀), or 4 to 6 (C₄₋₆) carbon atoms. Examples of alkynediyl groups include, but are not limited to, ethynediyl, propynediyl (including all isomeric forms, *e.g.*, 1-propyne-1,3-diyl and 1-propyne-3,3-diyl), butynediyl (including all isomeric forms, *e.g.*, 1-butyne-1,3-diyl, 1-butyne-1,4-diyl, and 2-butyne-1,1-diyl), pentynediyl (including all isomeric forms, *e.g.*, 1-pentyne-1,3-diyl, 1-pentyne-1,4-diyl, and 2-pentyne-1,1-diyl), and hexynediyl (including all isomeric forms, *e.g.*, 1-hexyne-1,3-diyl, 1-hexyne-1,4-diyl, and 2-hexyne-1,1-diyl).

[0043] The terms “heteroalkynylene” and “heteroalkynediyl” are used interchangeably herein in reference to a linear or branched divalent hydrocarbon radical, which contains one or more, in one embodiment, one, two, three, or four, in another embodiment, one, carbon-carbon triple bond(s), and which contains one or more heteroatoms in its main chain, each independently

selected from O, S, and N. The heteroalkynylene is optionally substituted with one or more substituents Q as described herein. For example, C₂₋₆ heteroalkynylene refers to a linear unsaturated divalent hydrocarbon radical of 2 to 6 carbon atoms or a branched unsaturated divalent hydrocarbon radical of 4 to 6 carbon atoms. In certain embodiments, the heteroalkynylene is a linear divalent hydrocarbon radical of 2 to 30 (C₂₋₃₀), 2 to 20 (C₂₋₂₀), 2 to 15 (C₂₋₁₅), 2 to 10 (C₂₋₁₀), or 2 to 6 (C₂₋₆) carbon atoms, or a branched divalent hydrocarbon radical of 4 to 30 (C₄₋₃₀), 4 to 20 (C₄₋₂₀), 4 to 15 (C₄₋₁₅), 4 to 10 (C₄₋₁₀), or 4 to 6 (C₄₋₆) carbon atoms. Examples of heteroalkynylene groups include, but are not limited to, $-\text{C}\equiv\text{CCH}_2\text{O}-$, $-\text{C}\equiv\text{CCH}_2\text{S}-$, or $-\text{C}\equiv\text{CCH}_2\text{NH}-$.

[0044] The term “cycloalkyl” refers to a cyclic monovalent hydrocarbon radical, which is optionally substituted with one or more substituents Q as described herein. In one embodiment, the cycloalkyl is a saturated or unsaturated but non-aromatic, and/or bridged or non-bridged, and/or fused bicyclic group. In certain embodiments, the cycloalkyl has from 3 to 20 (C₃₋₂₀), from 3 to 15 (C₃₋₁₅), from 3 to 10 (C₃₋₁₀), or from 3 to 7 (C₃₋₇) carbon atoms. In one embodiment, the cycloalkyl is monocyclic. In another embodiment, the cycloalkyl is bicyclic. In yet another embodiment, the cycloalkyl is tricyclic. In still another embodiment, the cycloalkyl is polycyclic. Examples of cycloalkyl groups include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cyclohexadienyl, cycloheptyl, cycloheptenyl, bicyclo[1.1.1]pentyl, bicyclo[2.1.1]hexyl, bicyclo[2.2.1]heptyl, bicyclo[2.2.2]octyl, decalinyl, and adamantyl.

[0045] The terms “cycloalkylene” and “cycloalkanediyl” are used interchangeably herein in reference to a cyclic divalent hydrocarbon radical, which may be optionally substituted with one or more substituents Q as described herein. In one embodiment, cycloalkanediyl groups may be saturated or unsaturated but non-aromatic, and/or bridged, and/or non-bridged, and/or fused bicyclic groups. In certain embodiments, the cycloalkanediyl has from 3 to 30 (C₃₋₃₀), 3 to 20 (C₃₋₂₀), from 3 to 15 (C₃₋₁₅), from 3 to 10 (C₃₋₁₀), or from 3 to 7 (C₃₋₇) carbon atoms. Examples of cycloalkanediyl groups include, but are not limited to, cyclopropanediyl (including all isomeric forms, *e.g.*, cyclopropane-1,1-diyl and cyclopropane-1,2-diyl), cyclobutanediyl (including all isomeric forms, *e.g.*, cyclobutane-1,1-diyl, cyclobutane-1,2-diyl, and cyclobutane-1,3-diyl), cyclopentanedyl (including all isomeric forms, *e.g.*, cyclopentane-1,1-diyl, cyclo-

pentane-1,2-diyl, and cyclopentane-1,3-diyl), cyclohexanediyl (including all isomeric forms, *e.g.*, cyclohexane-1,1-diyl, cyclohexane-1,2-diyl, cyclohexane-1,3-diyl, and cyclohex-1,4-diyl), cycloheptanediyl (including all isomeric forms, *e.g.*, cycloheptane-1,1-diyl, cycloheptane-1,2-diyl, cycloheptane-1,3-diyl, and cycloheptane-1,4-diyl), decalinediyl (including all isomeric forms, *e.g.*, decaline-1,1-diyl, decaline-1,2-diyl, and decaline-1,8-diyl), and adamantdiyl (including all isomeric forms, *e.g.*, adamant-1,2-diyl, adamant-1,3-diyl, and adamant-1,8-diyl).

[0046] The term “aryl” refers to a monovalent monocyclic aromatic hydrocarbon radical and/or monovalent polycyclic aromatic hydrocarbon radical that contain at least one aromatic carbon ring. In certain embodiments, the aryl has from 6 to 20 (C₆₋₂₀), from 6 to 15 (C₆₋₁₅), or from 6 to 10 (C₆₋₁₀) ring carbon atoms. Examples of aryl groups include, but are not limited to, phenyl, naphthyl, fluorenyl, azuleny, anthryl, phenanthryl, pyrenyl, biphenyl, and terphenyl. The aryl also refers to bicyclic or tricyclic carbon rings, where one of the rings is aromatic and the others of which may be saturated, partially unsaturated, or aromatic, for example, dihydronaphthyl, indenyl, indanyl, or tetrahydronaphthyl (tetralinyl). In one embodiment, the aryl is monocyclic. In another embodiment, the aryl is bicyclic. In yet another embodiment, the aryl is tricyclic. In still another embodiment, the aryl is polycyclic. In certain embodiments, the aryl is optionally substituted with one or more substituents Q as described herein.

[0047] The terms “arylene” and “arenediyl” are used interchangeably herein in reference to a divalent monocyclic aromatic hydrocarbon radical or divalent polycyclic aromatic hydrocarbon radical that contains at least one aromatic hydrocarbon ring. In certain embodiments, the arylene has from 6 to 20 (C₆₋₂₀), from 6 to 15 (C₆₋₁₅), or from 6 to 10 (C₆₋₁₀) ring atoms. Examples of arylene groups include, but are not limited to, phenylene (including all isomeric forms, *e.g.*, phen-1,2-diyl, phen-1,3-diyl, and phen-1,4-diyl), naphthylene (including all isomeric forms, *e.g.*, naphth-1,2-diyl, naphth-1,3-diyl, and naphth-1,8-diyl), fluorenylene (including all isomeric forms, *e.g.*, fluoren-1,2-diyl, fluoren-1,3-diyl, and fluoren-1,8-diyl), azulenyne (including all isomeric forms, *e.g.*, azulen-1,2-diyl, azulen-1,3-diyl, and azulen-1,8-diyl), anthrylene (including all isomeric forms, *e.g.*, anthr-1,2-diyl, anthr-1,3-diyl, and anthr-1,8-diyl), phenanthrylene (including all isomeric forms, *e.g.*, phenanthr-1,2-diyl, phenanthr-1,3-diyl, and phenanthr-1,8-diyl), pyrenylene (including all isomeric forms, *e.g.*, pyren-1,2-diyl, pyren-1,3-diyl, and pyren-1,8-diyl), biphenylene (including all isomeric forms, *e.g.*, biphen-2,3-diyl,

biphen-3,4'-diyl, and biphen-4,4'-diyl), and terphenylene (including all isomeric forms, *e.g.*, terphen-2,3-diyl, terphen-3,4'-diyl, and terphen-4,4'-diyl). Arylene also refers to bicyclic or tricyclic carbon rings, where one of the rings is aromatic and the others of which may be saturated, partially unsaturated, or aromatic, for example, dihydronaphthylene (including all isomeric forms, *e.g.*, dihydronaphth-1,2-diyl and dihydronaphth-1,8-diyl), indenylene (including all isomeric forms, *e.g.*, inden-1,2-diyl, inden-1,5-diyl, and inden-1,7-diyl), indanylene (including all isomeric forms, *e.g.*, indan-1,2-diyl, indan-1,5-diyl, and indan-1,7-diyl), or tetrahydronaphthylene (tetralinylene) (including all isomeric forms, *e.g.*, tetrahydronaphth-1,2-diyl, tetrahydronaphth-1,5-diyl, and tetrahydronaphth-1,8-diyl). In certain embodiments, arylene is optionally substituted with one or more substituents Q as described herein.

[0048] The term “aralkyl” or “arylalkyl” refers to a monovalent alkyl group substituted with one or more aryl groups. In certain embodiments, the aralkyl has from 7 to 30 (C_{7-30}), from 7 to 20 (C_{7-20}), or from 7 to 16 (C_{7-16}) carbon atoms. Examples of aralkyl groups include, but are not limited to, benzyl, phenylethyl (including all isomeric forms, *e.g.*, 1-phenylethyl and 2-phenylethyl), and phenylpropyl (including all isomeric forms, *e.g.*, 1-phenylpropyl, 2-phenylpropyl, and 3-phenylpropyl). In certain embodiments, the aralkyl is optionally substituted with one or more substituents Q as described herein.

[0049] The term “aralkylene” or “arylalkylene” refers to a divalent alkyl group substituted with one or more aryl groups. In certain embodiments, the aralkylene has from 7 to 30 (C_{7-30}), from 7 to 20 (C_{7-20}), or from 7 to 16 (C_{7-16}) carbon atoms. Examples of aralkylene groups include, but are not limited to, benzylene (including all isomeric forms, *e.g.*, phenylmethdiyl), phenylethylene (including all isomeric forms, *e.g.*, 2-phenyl-ethan-1,1-diyl and 2-phenyl-ethan-1,2-diyl), and phenylpropylene (including all isomeric forms, *e.g.*, 3-phenylpropan-1,1-diyl, 3-phenylpropan-1,2-diyl, and 3-phenylpropan-1,3-diyl). In certain embodiments, the aralkylene is optionally substituted with one or more substituents Q as described herein.

[0050] The term “heteroaryl” refers to a monovalent monocyclic aromatic group or monovalent polycyclic aromatic group that contain at least one aromatic ring, wherein at least one aromatic ring contains one or more heteroatoms, each independently selected from O, S, and

N, in the ring. The heteroaryl is bonded to the rest of a molecule through the aromatic ring. Each ring of a heteroaryl group can contain one or two O atoms, one or two S atoms, and/or one to four N atoms; provided that the total number of heteroatoms in each ring is four or less and each ring contains at least one carbon atom. In certain embodiments, the heteroaryl has from 5 to 20, from 5 to 15, or from 5 to 10 ring atoms. In one embodiment, the heteroaryl is monocyclic. Examples of monocyclic heteroaryl groups include, but are not limited to, furanyl, imidazolyl, isothiazolyl, isoxazolyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridyl, pyrimidinyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl, tetrazolyl, triazinyl, and triazolyl. In another embodiment, the heteroaryl is bicyclic. Examples of bicyclic heteroaryl groups include, but are not limited to, benzofuranyl, benzimidazolyl, benzoisoxazolyl, benzopyranyl, benzothiadiazolyl, benzothiazolyl, benzothienyl, benzotriazolyl, benzoxazolyl, furopyridyl (including all isomeric forms, *e.g.*, furo[2,3-*b*]pyridinyl, furo[2,3-*c*]pyridinyl, furo[3,2-*b*]pyridinyl, furo[3,2-*c*]pyridinyl, furo[3,4-*b*]pyridinyl, and furo[3,4-*c*]pyridinyl), imidazopyridinyl (including all isomeric forms, *e.g.*, imidazo[1,2-*a*]pyridinyl, imidazo[4,5-*b*]pyridinyl, and imidazo[4,5-*c*]pyridinyl), imidazothiazolyl (including all isomeric forms, *e.g.*, imidazo[2,1-*b*]thiazolyl and imidazo[4,5-*d*]thiazolyl), indazolyl, indolizynyl, indolyl, isobenzofuranyl, isobenzothienyl (*i.e.*, benzo[*c*]thienyl), isoindolyl, isoquinolynyl, naphthyridinyl (including all isomeric forms, *e.g.*, 1,5-naphthyridinyl, 1,6-naphthyridinyl, 1,7-naphthyridinyl, and 1,8-naphthyridinyl), oxazolopyridinyl (including all isomeric forms, *e.g.*, oxazolo[4,5-*b*]pyridinyl, oxazolo[4,5-*c*]pyridinyl, oxazolo[5,4-*b*]pyridinyl, and oxazolo[5,4-*c*]pyridinyl), phthalazinyl, pteridinyl, purinyl, pyrrolopyridyl (including all isomeric forms, *e.g.*, pyrrolo[2,3-*b*]pyridinyl, pyrrolo[2,3-*c*]pyridinyl, pyrrolo[3,2-*b*]pyridinyl, and pyrrolo[3,2-*c*]pyridinyl), quinolynyl, quinoxalynyl, quinazolinyl, thiadiazolopyrimidinyl (including all isomeric forms, *e.g.*, [1,2,5]thiadiazolo[3,4-*d*]pyrimidinyl and [1,2,3]thiadiazolo[4,5-*d*]pyrimidinyl), and thienopyridyl (including all isomeric forms, *e.g.*, thieno[2,3-*b*]pyridinyl, thieno[2,3-*c*]pyridinyl, thieno[3,2-*b*]pyridinyl, and thieno[3,2-*c*]pyridinyl). In yet another embodiment, the heteroaryl is tricyclic. Examples of tricyclic heteroaryl groups include, but are not limited to, acridinyl, benzindolyl, carbazolyl, dibenzofuranyl, perimidinyl, phenanthrolinyl, phenanthridinyl (including all isomeric forms, *e.g.*, 1,5-phenanthrolinyl, 1,6-phenanthrolinyl, 1,7-phenanthrolinyl, 1,9-phenanthrolinyl, and 2,10-phenanthrolinyl), phenarsazinyl, phenazinyl, phenothiazinyl, phenoxazinyl, and xanthenyl. In certain embodiments, the heteroaryl is optionally substituted with one or more substituents Q as

described herein.

[0051] The terms “heteroarylene” and “heteroarenediyl” are used interchangeably herein in reference to a divalent monocyclic aromatic group or divalent polycyclic aromatic group that contains at least one aromatic ring, wherein at least one aromatic ring contains one or more heteroatoms in the ring, each of which is independently selected from O, S, and N. A heteroarylene group has at least one linkage to the rest of a molecule *via* its aromatic ring(s). Each ring of a heteroarylene group can contain one or two O atoms, one or two S atoms, and/or one to four N atoms, provided that the total number of heteroatoms in each ring is four or less and each ring contains at least one carbon atom. In certain embodiments, the heteroarylene has from 5 to 20, from 5 to 15, or from 5 to 10 ring atoms. Examples of monocyclic heteroarylene groups include, but are not limited to, furandiyl, imidazoldiyl, isothiazoldiyl, isoxazoldiyl, oxadiazoldiyl, oxazoldiyl, pyrazindiyl, pyrazoldiyl, pyridazindiyl, pyridindiyl, pyrimidindiyl, pyrroldiyl, thiadiazoldiyl, thiazoldiyl, thiendiyl, tetrazoldiyl, triazinediyl, and triazoldiyl. Examples of bicyclic heteroarylene groups include, but are not limited to, benzofurandiyl, benzimidazoldiyl, benzoisoxazoldiyl, benzopyrandiyl, benzothiadiazoldiyl, benzothiazoldiyl, benzothiendiyl, benzotriazoldiyl, benzoxazoldiyl, furopyridindiyl (including all isomeric forms, *e.g.*, furo[2,3-*b*]pyridindiyl, furo[2,3-*c*]pyridindiyl, furo[3,2-*b*]pyridindiyl, furo[3,2-*c*]pyridindiyl, furo[3,4-*b*]pyridindiyl, and furo[3,4-*c*]pyridindiyl), imidazopyridindiyl (including all isomeric forms, *e.g.*, imidazo[1,2-*a*]pyridindiyl, imidazo[4,5-*b*]pyridindiyl, and imidazo[4,5-*c*]pyridindiyl), imidazothiazoldiyl (including all isomeric forms, *e.g.*, imidazo[2,1-*b*]thiazoldiyl and imidazo[4,5-*d*]thiazoldiyl), indazoldiyl, indolizindiyl, indoldiyl, isobenzofurandiyl, isobenzothiendiyl (*i.e.*, benzo[*c*]thiendiyl), isoindoldiyl, isoquinolindiyl, naphthyridindiyl (including all isomeric forms, *e.g.*, 1,5-naphthyridindiyl, 1,6-naphthyridindiyl, 1,7-naphthyridindiyl, and 1,8-naphthyridindiyl), oxazolopyridindiyl (including all isomeric forms, *e.g.*, oxazolo[4,5-*b*]pyridindiyl, oxazolo[4,5-*c*]pyridindiyl, oxazolo[5,4-*b*]pyridindiyl, and oxazolo[5,4-*c*]pyridindiyl), phthalazindiyl, pteridindiyl, purindiyl, pyrrolopyridindiyl (including all isomeric forms, *e.g.*, pyrrolo[2,3-*b*]pyridindiyl, pyrrolo[2,3-*c*]pyridindiyl, pyrrolo[3,2-*b*]pyridindiyl, and pyrrolo[3,2-*c*]pyridindiyl), quinolindiyl, quinoxalindiyl, quinazolindiyl, thiadiazolopyrimidindiyl (including all isomeric forms, *e.g.*, [1,2,5]thiadiazolo[3,4-*d*]pyrimidindiyl and [1,2,3]thiadiazolo[4,5-*d*]pyrimidindiyl), and thienopyridindiyl (including all isomeric forms, *e.g.*, thieno[2,3-*b*]pyridindiyl, thieno[2,3-*c*]pyridindiyl, thieno[3,2-*b*]pyridindiyl, and thieno[3,2-*c*]pyridindiyl).

Examples of tricyclic heteroarylene groups include, but are not limited to, acridindiyl, benz-indoldiyl, carbazoldiyl, dibenzofurandiyl, perimidindiyl, phenanthrolindiyl (including all isomeric forms, *e.g.*, 1,5-phenanthrolindiyl, 1,6-phenanthrolindiyl, 1,7-phenanthrolindiyl, 1,9-phenanthrolindiyl, and 2,10-phenanthrolindiyl), phenanthridindiyl, phenarsazindiyl, phenazindiyl, phenothiazindiyl, phenoxazindiyl, and xanthendiyl. In certain embodiments, heteroarylene is optionally substituted with one or more substituents Q as described herein.

[0052] The term “heterocyclyl” or “heterocyclic” refers to a monovalent monocyclic non-aromatic ring system or monovalent polycyclic ring system that contains at least one non-aromatic ring, wherein one or more of the non-aromatic ring atoms are heteroatoms, each independently selected from O, S, and N; and the remaining ring atoms are carbon atoms. In certain embodiments, the heterocyclyl or heterocyclic group has from 3 to 20, from 3 to 15, from 3 to 10, from 3 to 8, from 4 to 7, or from 5 to 6 ring atoms. The heterocyclyl is bonded to the rest of a molecule through the non-aromatic ring. In certain embodiments, the heterocyclyl is a monocyclic, bicyclic, tricyclic, or tetracyclic ring system, which may be fused or bridged, and in which nitrogen or sulfur atoms may be optionally oxidized, nitrogen atoms may be optionally quaternized, and some rings may be partially or fully saturated, or aromatic. The heterocyclyl may be attached to the main structure at any heteroatom or carbon atom which results in the creation of a stable compound. Examples of heterocyclyls and heterocyclic groups include, but are not limited to, azepinyl, benzodioxanyl, benzodioxolyl, benzofuranonyl, chromanyl, decahydroisoquinolinyl, dihydrobenzofuranyl, dihydrobenzisothiazolyl, dihydrobenzisoxazinyl (including all isomeric forms, *e.g.*, 1,4-dihydrobenzo[*d*][1,3]oxazinyl, 3,4-dihydrobenzo[*c*][1,2]-oxazinyl, and 3,4-dihydrobenzo[*d*][1,2]oxazinyl), dihydrobenzothienyl, dihydroisobenzofuranyl, dihydrobenzo[*c*]thienyl, dihydrofuryl, dihydroisoindolyl, dihydropyranyl, dihydropyrazolyl, dihydropyrazinyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dioxolanyl, 1,4-dithianyl, furanonyl, imidazolidinyl, imidazolyl, indolyl, isochromanyl, isoindolyl, isothiazolidinyl, isoxazolidinyl, morpholinyl, octahydroindolyl, octahydroisoindolyl, oxazolidinonyl, oxazolidinyl, oxiranyl, piperazinyl, piperidinyl, 4-piperidonyl, pyrazolidinyl, pyrazolinyl, pyrrolidinyl, pyrrolinyl, quinuclidinyl, tetrahydrofuryl, tetrahydroisoquinolinyl, tetrahydropyranyl, tetrahydrothienyl, thiamorpholinyl, thiazolidinyl, thiochromanyl, tetrahydroquinolinyl, and 1,3,5-trithianyl. In certain embodiments, the heterocyclyl is optionally substituted with one or more substituents Q as described herein.

[0053] The term “heterocyclylene” refers to a divalent monocyclic non-aromatic ring system or divalent polycyclic ring system that contains at least one non-aromatic ring, wherein one or more of the non-aromatic ring atoms are heteroatoms independently selected from O, S, and N; and the remaining ring atoms are carbon atoms. Heterocyclylene groups are bonded to the rest of a molecule through the non-aromatic ring. In certain embodiments, the heterocyclylene group has from 3 to 20, from 3 to 15, from 3 to 10, from 3 to 8, from 4 to 7, or from 5 to 6 ring atoms. In certain embodiments, the heterocyclylene is a monocyclic, bicyclic, tricyclic, or tetracyclic ring system, which may be fused or bridged, and in which nitrogen or sulfur atoms may be optionally oxidized, nitrogen atoms may be optionally quaternized, and some rings may be partially or fully saturated, or aromatic. The heterocyclylene may be attached to the main structure at any heteroatom or carbon atom which results in the creation of a stable compound. Examples of such heterocyclylene groups include, but are not limited to, azepindiyl, benzodioxandiyl, benzodioxoldiyl, benzofuranondiyl, chromandiyl, decahydroisoquinolindiyl, dihydrobenzofurandiyl, dihydrobenzisothiazoldiyl, dihydrobenzisoxazindiyl (including all isomeric forms, *e.g.*, 1,4-dihydrobenzo[*d*][1,3]oxazindiyl, 3,4-dihydrobenzo[*c*][1,2]oxazindiyl, and 3,4-dihydrobenzo[*d*][1,2]oxazindiyl), dihydrobenzothiendiyl, dihydroisobenzofurandiyl, dihydrobenzo[*c*]thiendiyl, dihydrofurdiyl, dihydroisoindoldiyl, dihydropyrandiyl, dihydropyrazoldiyl, dihydropyrazindiyl, dihydropyridindiyl, dihydropyrimidindiyl, dihydropyrroldiyl, dioxolandiyl, 1,4-dithiandiyl, furanondiyl, imidazolidindiyl, imidazolindiyl, indolindiyl, isochromandiyl, isoindolindiyl, isothiazolidindiyl, isoxazolidindiyl, morpholindiyl, octahydroindoldiyl, octahydroisoindoldiyl, oxazolidinondiyl, oxazolidindiyl, oxirandiyl, piperazindiyl, piperidindiyl, 4-piperidondiyl, pyrazolidindiyl, pyrazolindiyl, pyrrolidindiyl, pyrrolindiyl, quinuclidindiyl, tetrahydrofurdiyl, tetrahydroisoquinolindiyl, tetrahydropyrandiyl, tetrahydrothiendiyl, thiamorpholindiyl, thiazolidindiyl, thiochromandiyl, tetrahydroquinolindiyl, and 1,3,5-trithiandiyl. In certain embodiments, the heterocyclylene is optionally substituted with one or more substituents Q as described herein.

[0054] The term “halogen,” “halide,” or “halo” refers to fluoro, chloro, bromo, and/or iodo.

[0055] The term “optionally substituted” is intended to mean that a group or substituent, such as an alkyl, heteroalkyl, alkylene, heteroalkylene, alkenyl, alkenylene, heteroalkenylene,

alkynyl, alkynylene, heteroalkynylene, cycloalkyl, cycloalkylene, aryl, arylene, aralkyl, aralkylene, heteroaryl, heteroarylene, heterocyclyl, or heterocyclylene group, may be substituted with one or more, in one embodiment, one, two, three, or four, substituents Q, each of which is independently selected from, *e.g.*, (a) deuterium (–D), cyano (–CN), halo, imino (=NH), nitro (–NO₂), and oxo (=O); (b) C₁₋₆ alkyl, C₁₋₆ heteroalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₄ aryl, C₇₋₁₅ aralkyl, heteroaryl, and heterocyclyl, each of which is further optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q^a; and (c) –C(O)R^a, –C(O)OR^a, –C(O)NR^bR^c, –C(O)SR^a, –C(NR^a)NR^bR^c, –C(S)R^a, –C(S)OR^a, –C(S)NR^bR^c, –OR^a, –OC(O)R^a, –OC(O)OR^a, –OC(O)NR^bR^c, –OC(O)SR^a, –OC(NR^a)NR^bR^c, –OC(S)R^a, –OC(S)OR^a, –OC(S)NR^bR^c, –OP(O)(OR^a)OR^d, –OS(O)R^a, –OS(O)₂R^a, –OS(O)NR^bR^c, –OS(O)₂NR^bR^c, –NR^bR^c, –NR^aC(O)R^d, –NR^aC(O)OR^d, –NR^aC(O)NR^bR^c, –NR^aC(O)SR^d, –NR^aC(NR^d)NR^bR^c, –NR^aC(S)R^d, –NR^aC(S)OR^d, –NR^aC(S)NR^bR^c, –NR^aS(O)R^d, –NR^aS(O)₂R^d, –NR^aS(O)NR^bR^c, –NR^aS(O)₂NR^bR^c, –SR^a, –S(O)R^a, –S(O)₂R^a, –S(O)NR^bR^c, and –S(O)₂NR^bR^c, wherein each R^a, R^b, R^c, and R^d is independently (i) hydrogen or deuterium; (ii) C₁₋₆ alkyl, C₁₋₆ heteroalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₄ aryl, C₇₋₁₅ aralkyl, heteroaryl, or heterocyclyl, each of which is optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q^a; or (iii) R^b and R^c together with the N atom to which they are attached form heterocyclyl optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q^a. As used herein, all groups that can be substituted are “optionally substituted.”

[0056] In one embodiment, each Q^a is independently selected from: (a) deuterium, cyano, halo, imino, nitro, and oxo; (b) C₁₋₆ alkyl, C₁₋₆ heteroalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₄ aryl, C₇₋₁₅ aralkyl, heteroaryl, and heterocyclyl; and (c) –C(O)R^e, –C(O)OR^e, –C(O)NR^fR^g, –C(O)SR^e, –C(NR^e)NR^fR^g, –C(S)R^e, –C(S)OR^e, –C(S)NR^fR^g, –OR^e, –OC(O)R^e, –OC(O)OR^e, –OC(O)NR^fR^g, –OC(O)SR^e, –OC(NR^e)NR^fR^g, –OC(S)R^e, –OC(S)OR^e, –OC(S)NR^fR^g, –OS(O)R^e, –OS(O)₂R^e, –OS(O)NR^fR^g, –OS(O)₂NR^fR^g, –NR^fR^g, –NR^eC(O)R^h, –NR^eC(O)OR^f, –NR^eC(O)NR^fR^g, –NR^eC(O)SR^f, –NR^eC(NR^h)NR^fR^g, –NR^eC(S)R^h, –NR^eC(S)OR^f, –NR^eC(S)NR^fR^g, –NR^eS(O)R^h, –NR^eS(O)₂R^h, –NR^eS(O)NR^fR^g, –NR^eS(O)₂NR^fR^g, –SR^e, –S(O)R^e, –S(O)₂R^e, –S(O)NR^fR^g, and –S(O)₂NR^fR^g; wherein each R^e, R^f, R^g, and R^h is independently (i) hydrogen or deuterium; (ii) C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₄ aryl, C₇₋₁₅ aralkyl, heteroaryl, or heterocyclyl; or (iii) R^f and R^g

together with the N atom to which they are attached form heterocyclyl.

[0057] In certain embodiments, “optically active” and “enantiomerically active” refer to a collection of molecules, which has an enantiomeric excess of no less than about 80%, no less than about 90%, no less than about 91%, no less than about 92%, no less than about 93%, no less than about 94%, no less than about 95%, no less than about 96%, no less than about 97%, no less than about 98%, no less than about 99%, no less than about 99.5%, or no less than about 99.8%. In certain embodiments, an optically active compound comprises about 95% or more of one enantiomer and about 5% or less of the other enantiomer based on the total weight of the enantiomeric mixture in question. In certain embodiments, an optically active compound comprises about 98% or more of one enantiomer and about 2% or less of the other enantiomer based on the total weight of the enantiomeric mixture in question. In certain embodiments, an optically active compound comprises about 99% or more of one enantiomer and about 1% or less of the other enantiomer based on the total weight of the enantiomeric mixture in question.

[0058] In describing an optically active compound, the prefixes *R* and *S* are used to denote the absolute configuration of the compound about its chiral center(s). The (+) and (-) are used to denote the optical rotation of the compound, that is, the direction in which a plane of polarized light is rotated by the optically active compound. The (-) prefix indicates that the compound is levorotatory, that is, the compound rotates the plane of polarized light to the left or counterclockwise. The (+) prefix indicates that the compound is dextrorotatory, that is, the compound rotates the plane of polarized light to the right or clockwise. However, the sign of optical rotation, (+) and (-), is not related to the absolute configuration of the compound, *R* and *S*.

[0059] The terms “substantially pure” and “substantially homogeneous” mean, when referred to a substance, sufficiently homogeneous to appear free of readily detectable impurities as determined by a standard analytical method used by one of ordinary skill in the art, including, but not limited to, thin layer chromatography (TLC), gel electrophoresis, high performance liquid chromatography (HPLC), gas chromatography (GC), nuclear magnetic resonance (NMR), and mass spectrometry (MS); or sufficiently pure such that further purification would not detectably alter the physical, chemical, biological, and/or pharmacological properties, such as enzymatic and biological activities, of the substance. In certain embodiments, “substantially

pure” or “substantially homogeneous” refers to a collection of molecules, wherein at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or at least about 99.5% by weight of the molecules are a single compound, including a single enantiomer, a racemic mixture, or a mixture of enantiomers, as determined by standard analytical methods. As used herein, when an atom at a particular position in an isotopically enriched molecule is designated as a particular less prevalent isotope, a molecule that contains other than the designated isotope at the specified position is an impurity with respect to the isotopically enriched compound. Thus, for a deuterated compound that has an atom at a particular position designated as deuterium, a compound that contains a protium at the same position is an impurity.

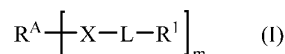
[0060] The term “solvate” refers to a complex or aggregate formed by one or more molecules of a solute, *e.g.*, a compound provided herein, and one or more molecules of a solvent, which are present in stoichiometric or non-stoichiometric amount. Suitable solvents include, but are not limited to, water, methanol, ethanol, *n*-propanol, isopropanol, and acetic acid. In certain embodiments, the solvent is pharmaceutically acceptable. In one embodiment, the complex or aggregate is in a crystalline form. In another embodiment, the complex or aggregate is in a noncrystalline form. Where the solvent is water, the solvate is a hydrate. Examples of hydrates include, but are not limited to, a hemihydrate, monohydrate, dihydrate, trihydrate, tetrahydrate, and pentahydrate.

[0061] For a divalent group described herein, no orientation is implied by the direction in which the divalent group is presented. For example, unless a particular orientation is specified, the formula --C(O)NH-- represents both --C(O)NH-- and --NHC(O)-- .

[0062] The phrase “a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof” has the same meaning as the phrase “(i) a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers of the compound referenced therein; (ii) a pharmaceutically acceptable salt, solvate, or hydrate of the compound referenced therein; or (iii) a pharmaceutically acceptable salt, solvate, or hydrate of a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers of the compound referenced therein.”

Compounds

[0063] In one embodiment, provided herein is a compound of Formula (I):



or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein:

each L is independently a linker;

each X is independently (i) a bond or $-S-$; or (ii) heteroarylene or heterocyclylene, each optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q;

each R^1 is independently an immunostimulator;

R^A is an antibody or an antigen-binding fragment thereof, which binds specifically to a hepatitis B surface antigen; and

m is an integer of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16;

wherein each Q is independently selected from: (a) deuterium, cyano, halo, imino, nitro, and oxo; (b) C_{1-6} alkyl, C_{1-6} heteroalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, and heterocyclyl, each of which is further optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q^a ; and (c) $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^bR^c$, $-C(O)SR^a$, $-C(NR^a)NR^bR^c$, $-C(S)R^a$, $-C(S)OR^a$, $-C(S)NR^bR^c$, $-OR^a$, $-OC(O)R^a$, $-OC(O)OR^a$, $-OC(O)NR^bR^c$, $-OC(O)SR^a$, $-OC(NR^a)NR^bR^c$, $-OC(S)R^a$, $-OC(S)OR^a$, $-OC(S)NR^bR^c$, $-OP(O)(OR^a)OR^d$, $-OS(O)R^a$, $-OS(O)_2R^a$, $-OS(O)NR^bR^c$, $-OS(O)_2NR^bR^c$, $-NR^bR^c$, $-NR^aC(O)R^d$, $-NR^aC(O)OR^d$, $-NR^aC(O)NR^bR^c$, $-NR^aC(O)SR^d$, $-NR^aC(NR^d)NR^bR^c$, $-NR^aC(S)R^d$, $-NR^aC(S)OR^d$, $-NR^aC(S)NR^bR^c$, $-NR^aS(O)R^d$, $-NR^aS(O)_2R^d$, $-NR^aS(O)NR^bR^c$, $-NR^aS(O)_2NR^bR^c$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-S(O)NR^bR^c$, and $-S(O)_2NR^bR^c$, wherein each R^a , R^b , R^c , and R^d is independently (i) hydrogen or deuterium; (ii) C_{1-6} alkyl, C_{1-6} heteroalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or heterocyclyl, each of which is optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q^a ; or (iii) R^b and R^c together with the N atom to which they are attached form heterocyclyl, optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q^a ;

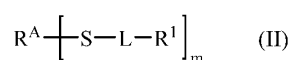
wherein each Q^a is independently selected from: (a) deuterium, cyano, halo, nitro, imino, and oxo; (b) C₁₋₆ alkyl, C₁₋₆ heteroalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₄ aryl, C₇₋₁₅ aralkyl, heteroaryl, and heterocyclyl; and (c) -C(O)R^e, -C(O)OR^e, -C(O)NR^fR^g, -C(O)SR^e, -C(NR^e)NR^fR^g, -C(S)R^e, -C(S)OR^e, -C(S)NR^fR^g, -OR^e, -OC(O)R^e, -OC(O)OR^e, -OC(O)NR^fR^g, -OC(O)SR^e, -OC(NR^e)NR^fR^g, -OC(S)R^e, -OC(S)OR^e, -OC(S)NR^fR^g, -OS(O)R^e, -OS(O)₂R^e, -OS(O)NR^fR^g, -OS(O)₂NR^fR^g, -NR^fR^g, -NR^eC(O)R^h, -NR^eC(O)OR^f, -NR^eC(O)NR^fR^g, -NR^eC(O)SR^f, -NR^eC(NR^h)NR^fR^g, -NR^eC(S)R^h, -NR^eC(S)OR^f, -NR^eC(S)NR^fR^g, -NR^eS(O)R^h, -NR^eS(O)₂R^h, -NR^eS(O)NR^fR^g, -NR^eS(O)₂NR^fR^g, -SR^e, -S(O)R^e, -S(O)₂R^e, -S(O)NR^fR^g, and -S(O)₂NR^fR^g, wherein each R^e, R^f, R^g, and R^h is independently (i) hydrogen or deuterium; (ii) C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₄ aryl, C₇₋₁₅ aralkyl, heteroaryl, or heterocyclyl; or (iii) R^f and R^g together with the N atom to which they are attached form heterocyclyl.

[0064] In certain embodiments, each X is a bond. In certain embodiments, each X is -S-. In certain embodiments, each X is independently heteroarylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently monocyclic heteroarylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently 5- or 6-membered heteroarylene, each optionally substituted with one or more substituents Q. In certain embodiments, each X is independently 5-membered heteroarylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently 6-membered heteroarylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently bicyclic heteroarylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently 5,5-, 5,6-, or 6,6-membered heteroarylene, each optionally substituted with one or more substituents Q. In certain embodiments, each X is independently 5,5-membered heteroarylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently 5,6-membered heteroarylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently 6,6-membered heteroarylene, optionally substituted with one or more substituents Q.

[0065] In certain embodiments, each X is independently heterocyclylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently

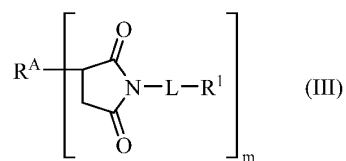
monocyclic heterocyclylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently 3-, 4-, 5-, 6-, or 7-membered heterocyclylene, each optionally substituted with one or more substituents Q. In certain embodiments, each X is independently 3-membered heterocyclylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently 4-membered heterocyclylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently 5-membered heterocyclylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently pyrrolidindiyl, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently pyrrolidin1,3-diyl, optionally substituted with one or more substituents Q. In certain embodiments, each X is 2,5-dioxy-pyrrolidin-1,3-diyl. In certain embodiments, each X is independently 6-membered heterocyclylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently 7-membered heterocyclylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently bicyclic heterocyclylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently bridged, fused, or spiro heterocyclylene, each optionally substituted with one or more substituents Q. In certain embodiments, each X is independently bridged heterocyclylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently fused heterocyclylene, optionally substituted with one or more substituents Q. In certain embodiments, each X is independently spiro heterocyclylene, optionally substituted with one or more substituents Q.

[0066] In another embodiment, provided is a compound of Formula (II):



or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein each L is independently connected covalently to a thiol group of a cysteine residue of R^A via a disulfide bond; and wherein each R^1 , R^A , L, and m is as defined herein.

[0067] In yet another embodiment, provided is a compound of Formula (III):



or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein each L is independently connected covalently to a thiol group of a cysteine residue of R^A via a 2,5-dioxypyrrolidin-1,3-diyl group; and wherein each R^1 , R^A , L, and m is as defined herein.

[0068] In one embodiment, each L is independently a cleavable linker. In another embodiment, each L is independently a non-cleavable linker.

[0069] In certain embodiments, each L is independently a cleavable linker that is sensitive to an acidic pH. In certain embodiments, each L is independently a cleavable linker comprising a reducible disulfide. In certain embodiments, each L is independently a linker cleavable by glutathione. In certain embodiments, each L is independently a linker cleavable by an enzyme. In certain embodiments, each L is independently a linker cleavable by a protease. In certain embodiments, each L is independently a linker cleavable by a lysosomal protease. In certain embodiments, each L is independently a linker cleavable by cathepsin B. In certain embodiments, each L is independently a linker cleavable by a glycosidase. In certain embodiments, each L is independently a linker cleavable by a β -glycosidase. In certain embodiments, each L is independently a linker cleavable by a galactosidase. In certain embodiments, each L is independently a linker cleavable by a β -galactosidase. In certain embodiments, each L is independently a linker cleavable by a glucuronidase. In certain embodiments, each L is independently a linker cleavable by a β -glucuronidase. In certain embodiments, each L is independently a linker cleavable by a phosphatase. Exemplary linkers suitable for a compound provided herein include, but are not limited to, those disclosed in Beck *et al.*, *Nat. Rev. Drug Discov.* **2017**, *16*, 317-37; Bargh *et al.*, *Chem. Soc. Rev.* **2019**, *48*, 4361-74; the disclosure of each of which is incorporated herein by reference in its entirety.

[0070] In certain embodiments, each L is independently C_{1-50} alkylene, C_{1-50} heteroalkylene, C_{2-50} alkenylene, C_{2-50} heteroalkenylene, C_{2-50} alkynylene, C_{2-50}

heteroalkynylene, C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene, each of which is optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₅₀ alkylene, C₁₋₅₀ heteroalkylene, C₂₋₅₀ alkenylene, C₂₋₅₀ heteroalkenylene, C₂₋₅₀ alkynylene, or C₂₋₅₀ heteroalkynylene, each of which is optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₅₀ alkylene or C₁₋₅₀ heteroalkylene, each of which is optionally substituted with one or more substituents Q.

[0071] In certain embodiments, each L is independently C₁₋₅₀ alkylene, optionally substituted with one or substituents Q. In certain embodiments, each L is independently C₁₋₄₀ alkylene, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₃₀ alkylene, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ alkylene, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₂₋₁₆ alkylene, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₂₋₁₂ alkylene, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₂₋₆ alkylene, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ alkylene, optionally substituted with one or two oxo. In certain embodiments, each L is independently C₂₋₁₆ alkylene, optionally substituted with one or two oxo. In certain embodiments, each L is independently C₂₋₁₂ alkylene, optionally substituted with one or two oxo. In certain embodiments, each L is independently C₂₋₆ alkylene, optionally substituted with one or two oxo. In certain embodiments, each L is independently $-(CH_2)_p-$, optionally substituted with one or two oxo; wherein p is an integer of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16. In certain embodiments, each L is independently $-(CH_2)_p-$, optionally substituted with one or two oxo; wherein p is an integer of 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12. In certain embodiments, each L is independently $-(CH_2)_p-$, optionally substituted with one or two oxo; wherein p is an integer of 2, 3, 4, 5, or 6.

[0072] In certain embodiments, each L is independently C₁₋₅₀ heteroalkylene, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₄₀ heteroalkylene, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₃₀ heteroalkylene, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene,

optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₂₋₁₆ heteroalkylene, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₂₋₁₂ heteroalkylene, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₂₋₆ heteroalkylene, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, optionally substituted with one, two, or three oxo. In certain embodiments, each L is independently C₂₋₁₆ heteroalkylene, optionally substituted with one, two, or three oxo. In certain embodiments, each L is independently C₂₋₁₂ heteroalkylene, optionally substituted with one, two, or three oxo. In certain embodiments, each L is independently C₂₋₆ heteroalkylene, optionally substituted with one, two, or three oxo.

[0073] In certain embodiments, each L is independently C₂₋₅₀ heteroalkylene comprising an ethyleneoxy (–CH₂CH₂O–) group, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₂₋₄₀ heteroalkylene comprising an ethyleneoxy group, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₂₋₃₀ heteroalkylene comprising an ethyleneoxy group, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₂₋₂₀ heteroalkylene comprising an ethyleneoxy group, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₂₋₁₄ heteroalkylene comprising an ethyleneoxy group, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₂₋₁₀ heteroalkylene comprising an ethyleneoxy group, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₂₋₆ heteroalkylene comprising an ethyleneoxy group, optionally substituted with one or more substituents Q.

[0074] In certain embodiments, each L is independently C₃₋₅₀ heteroalkylene comprising a propyleneoxy (–CH₂CH₂CH₂O–) group, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₃₋₄₀ heteroalkylene comprising a propyleneoxy group, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₃₋₃₀ heteroalkylene comprising a propyleneoxy group, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₃₋₂₀ heteroalkylene comprising a propyleneoxy group, optionally substituted with

one or more substituents Q. In certain embodiments, each L is independently C₃₋₁₄ heteroalkylene comprising a propyleneoxy group, optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₃₋₁₀ heteroalkylene comprising a propyleneoxy group, optionally substituted with one or more substituents Q.

[0075] In certain embodiments, each L is independently C₁₋₅₀ alkylene, C₁₋₅₀ heteroalkylene, C₂₋₅₀ alkenylene, C₂₋₅₀ heteroalkenylene, C₂₋₅₀ alkynylene, or C₂₋₅₀ heteroalkynylene, wherein one or more methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the alkylene, heteroalkylene, alkenylene, heteroalkenylene, alkynylene, heteroalkynylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₅₀ alkylene or C₁₋₅₀ heteroalkylene, wherein one or more methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the alkylene, heteroalkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q.

[0076] In certain embodiments, each L is independently C₁₋₅₀ alkylene, wherein one or more methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the alkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₄₀ alkylene, wherein one or more methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the alkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₃₀ alkylene, wherein one or more methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the alkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain

embodiments, each L is independently C₁₋₂₀ alkylene, wherein one or more methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the alkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q.

[0077] In certain embodiments, each L is independently C₁₋₅₀ alkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the alkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₄₀ alkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the alkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₃₀ alkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the alkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the alkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexanediyl, phendiyl, triazoldiyl, 2,5-dioxopyrrolidindiyl, or piperazindiyl. In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexanediyl, phendiyl, triazoldiyl, or 2,5-dioxopyrrolidindiyl. In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein one, two, three, or four

methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, 2,5-dioxopyrrolidin-1,3-diyl, or piperazin-1,4-diyl. In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, or 2,5-dioxopyrrolidin-1,3-diyl.

[0078] In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein one or two methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the alkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein one or two methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexanediyl, phendiyl, triazoldiyl, 2,5-dioxopyrrolidindiyl, or piperazindiyl. In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein one or two methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexanediyl, phendiyl, triazoldiyl, or 2,5-dioxopyrrolidindiyl. In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein one or two methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, 2,5-dioxopyrrolidin-1,3-diyl, or piperazin-1,4-diyl. In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein one or two methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, or 2,5-dioxopyrrolidin-1,3-diyl.

[0079] In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein a methylene group is replaced by a divalent group; wherein the divalent group is C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the alkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ alkylene,

wherein a methylene group is replaced by a divalent group; wherein the divalent group is cyclohexanediyl, phendiyl, triazoldiyl, 2,5-dioxopyrrolidindiyl, or piperazindiyl. In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein a methylene group is replaced by a divalent group; wherein the divalent group is cyclohexanediyl, phendiyl, triazoldiyl, or 2,5-dioxopyrrolidindiyl. In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein a methylene group is replaced by a divalent group; wherein each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, 2,5-dioxopyrrolidin-1,3-diyl, or piperazin-1,4-diyl. In certain embodiments, each L is independently C₁₋₂₀ alkylene, wherein a methylene group is replaced by a divalent group; wherein each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, or 2,5-dioxopyrrolidin-1,3-diyl.

[0080] In certain embodiments, each L is independently C₁₋₅₀ heteroalkylene, wherein one or more methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the heteroalkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₄₀ heteroalkylene, wherein one or more methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the heteroalkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₃₀ heteroalkylene, wherein one or more methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the heteroalkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein one or more methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the heteroalkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q.

[0081] In certain embodiments, each L is independently C₁₋₅₀ heteroalkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the heteroalkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₄₀ heteroalkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the heteroalkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₃₀ heteroalkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the heteroalkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the heteroalkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexanediyl, phendiyl, triazoldiyl, 2,5-dioxopyrrolidindiyl, or piperazindiyl. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexanediyl, phendiyl, triazoldiyl, or 2,5-dioxopyrrolidindiyl. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein one, two, three, or four methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, 2,5-dioxopyrrolidin-1,3-diyl, or piperazin-1,4-diyl. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein one, two, three, or four methylene groups are each independently

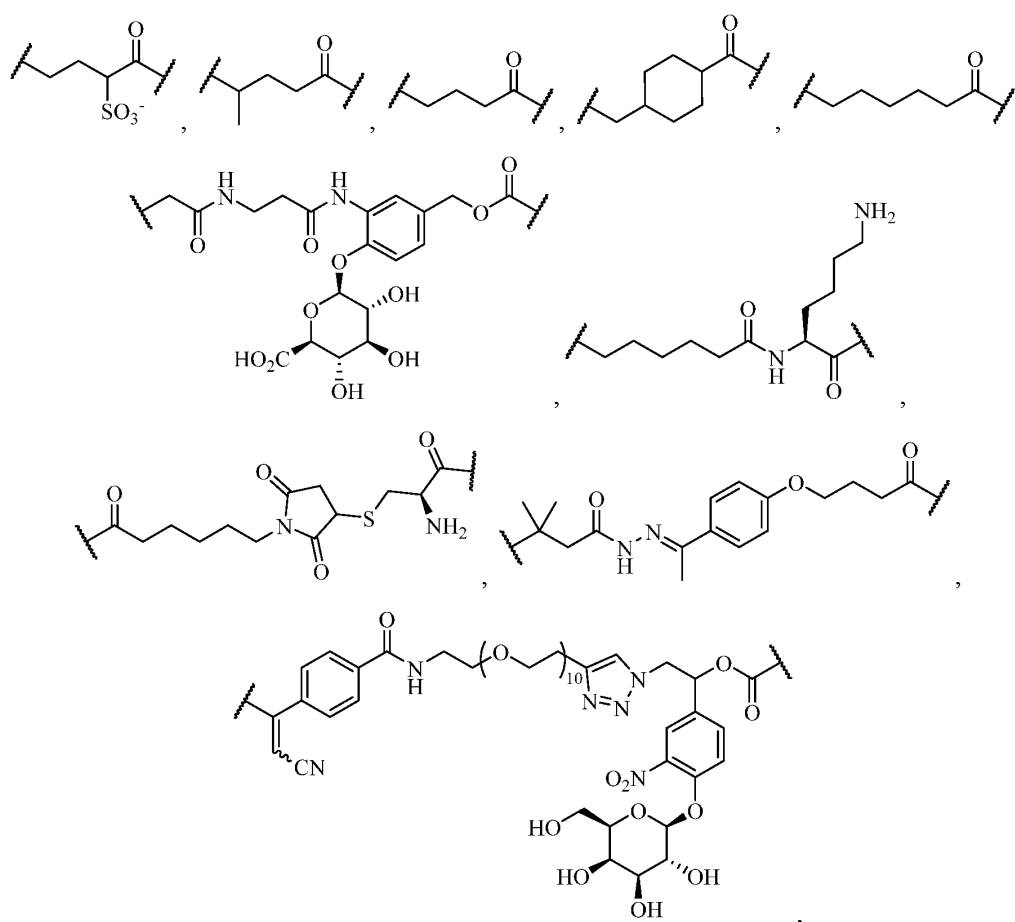
replaced by a divalent group; wherein each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, or 2,5-dioxopyrrolidin-1,3-diyl.

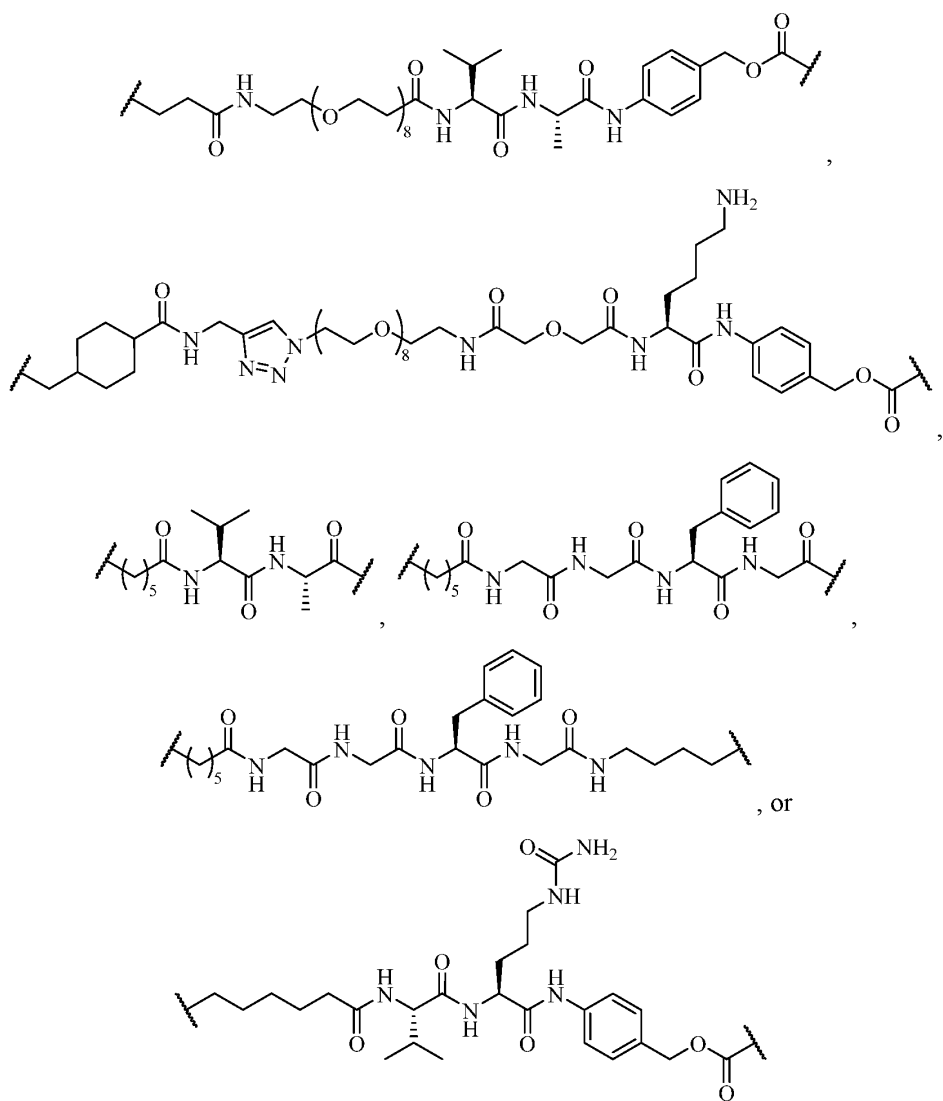
[0082] In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein one or two methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the heteroalkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein one or two methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexanediyl, phendiyl, triazoldiyl, 2,5-dioxopyrrolidindiyl, or piperazindiyl. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein one or two methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexanediyl, phendiyl, triazoldiyl, or 2,5-dioxopyrrolidindiyl. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein one or two methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, 2,5-dioxopyrrolidin-1,3-diyl, or piperazin-1,4-diyl. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein one or two methylene groups are each independently replaced by a divalent group; wherein each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, or 2,5-dioxopyrrolidin-1,3-diyl.

[0083] In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein a methylene group is replaced by a divalent group; wherein the divalent group is C₃₋₁₀ cycloalkylene, C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein the heteroalkylene, cycloalkylene, arylene, heteroarylene, and heterocyclylene are each optionally substituted with one or more substituents Q. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein a methylene group is replaced by a divalent group; wherein the divalent group is cyclohexanediyl, phendiyl, triazoldiyl, 2,5-dioxopyrrolidindiyl, or piperazindiyl. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein a methylene group is replaced by a divalent group; wherein the divalent group is cyclohexanediyl, phendiyl,

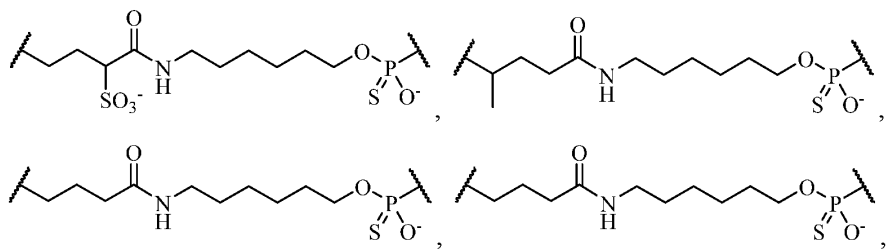
triazoldiyl, or 2,5-dioxopyrrolidindiyl. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein a methylene group is replaced by a divalent group; wherein each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, or 2,5-dioxopyrrolidin-1,3-diyl. In certain embodiments, each L is independently C₁₋₂₀ heteroalkylene, wherein a methylene group is replaced by a divalent group; wherein each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, dioxopyrrolidin-1,3-diyl, or piperazin-1,4-diyl.

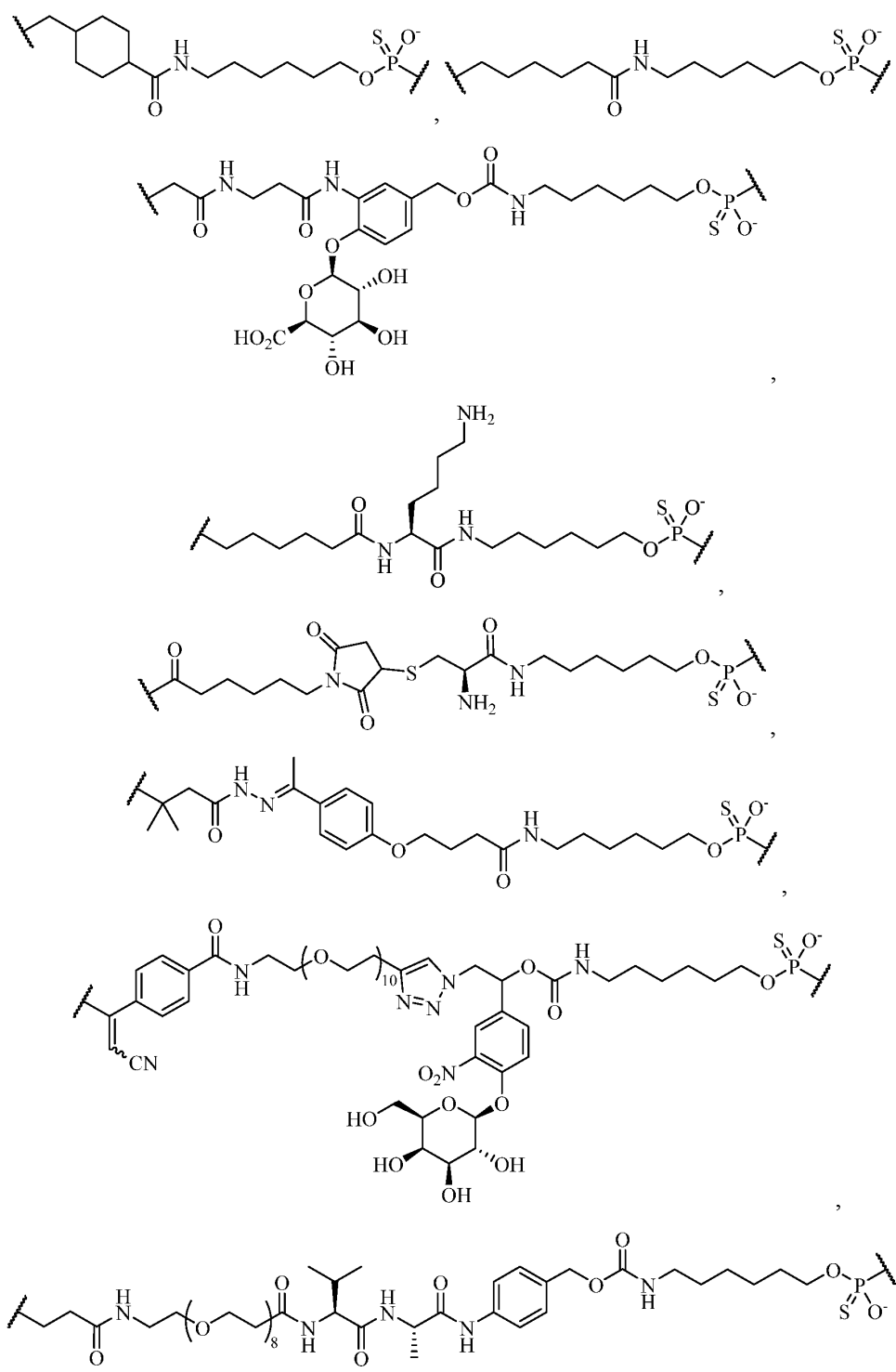
[0084] In certain embodiments, each L is independently:

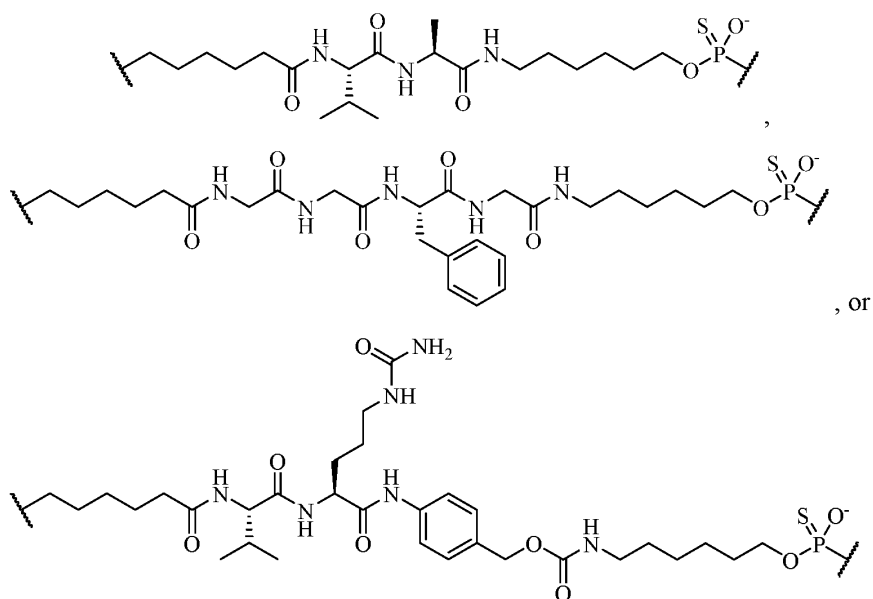




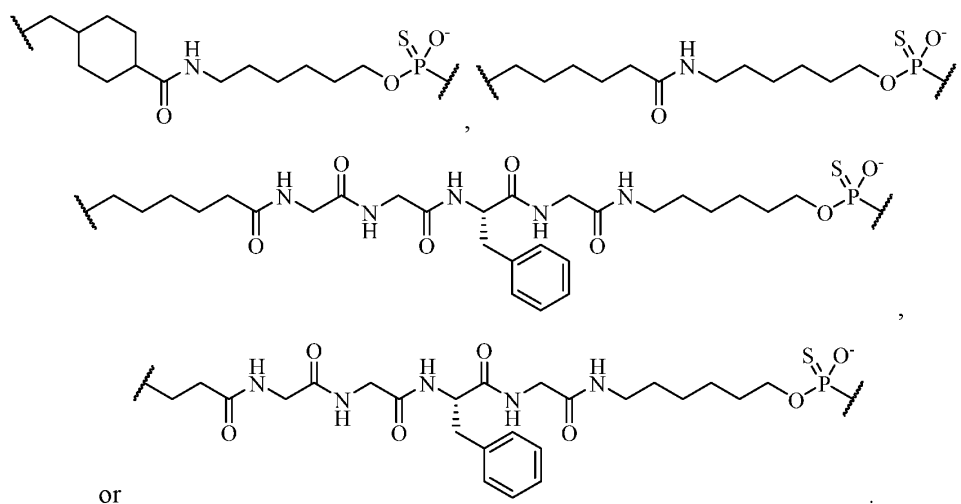
[0085] In certain embodiments, each L is independently:



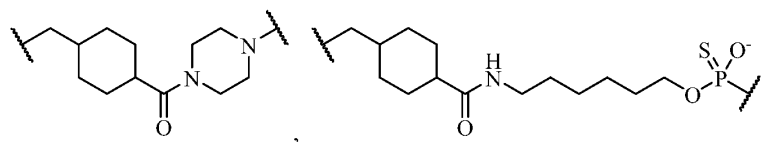


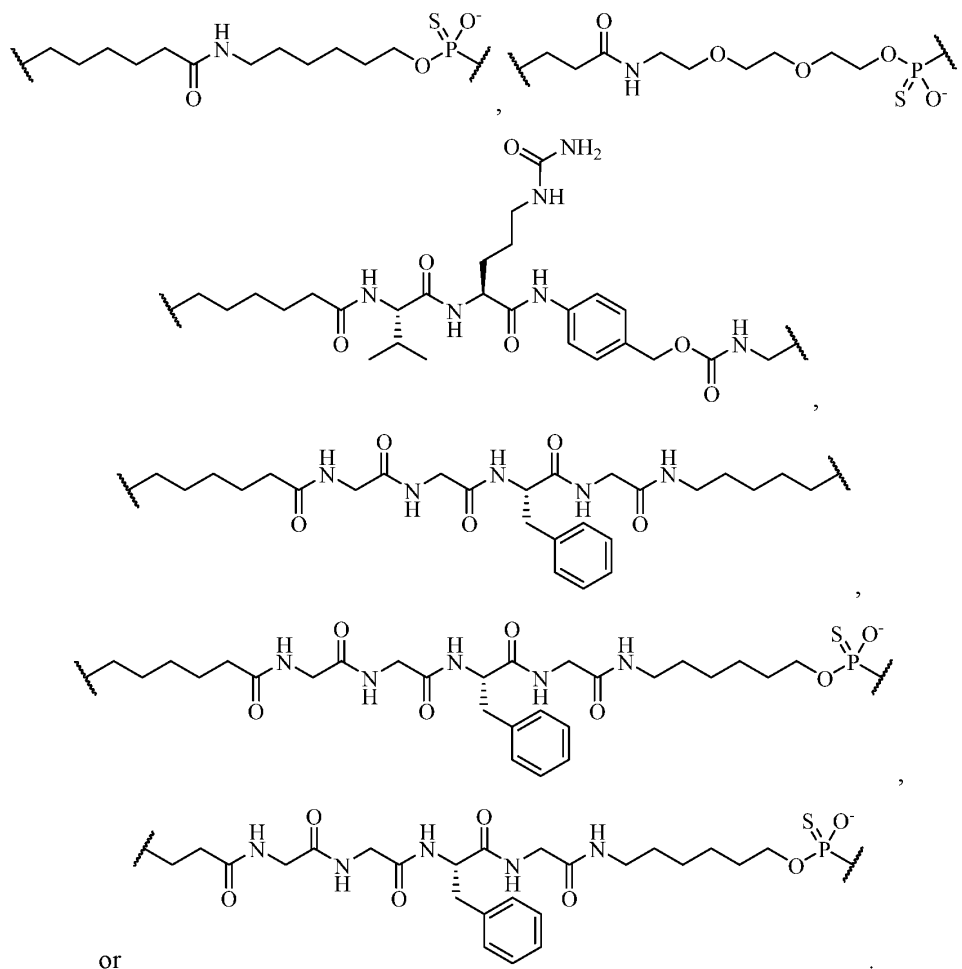


[0086] In certain embodiments, each L is independently:

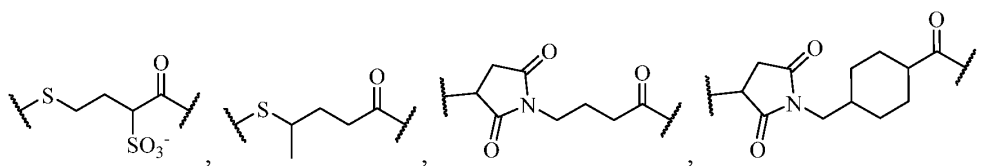


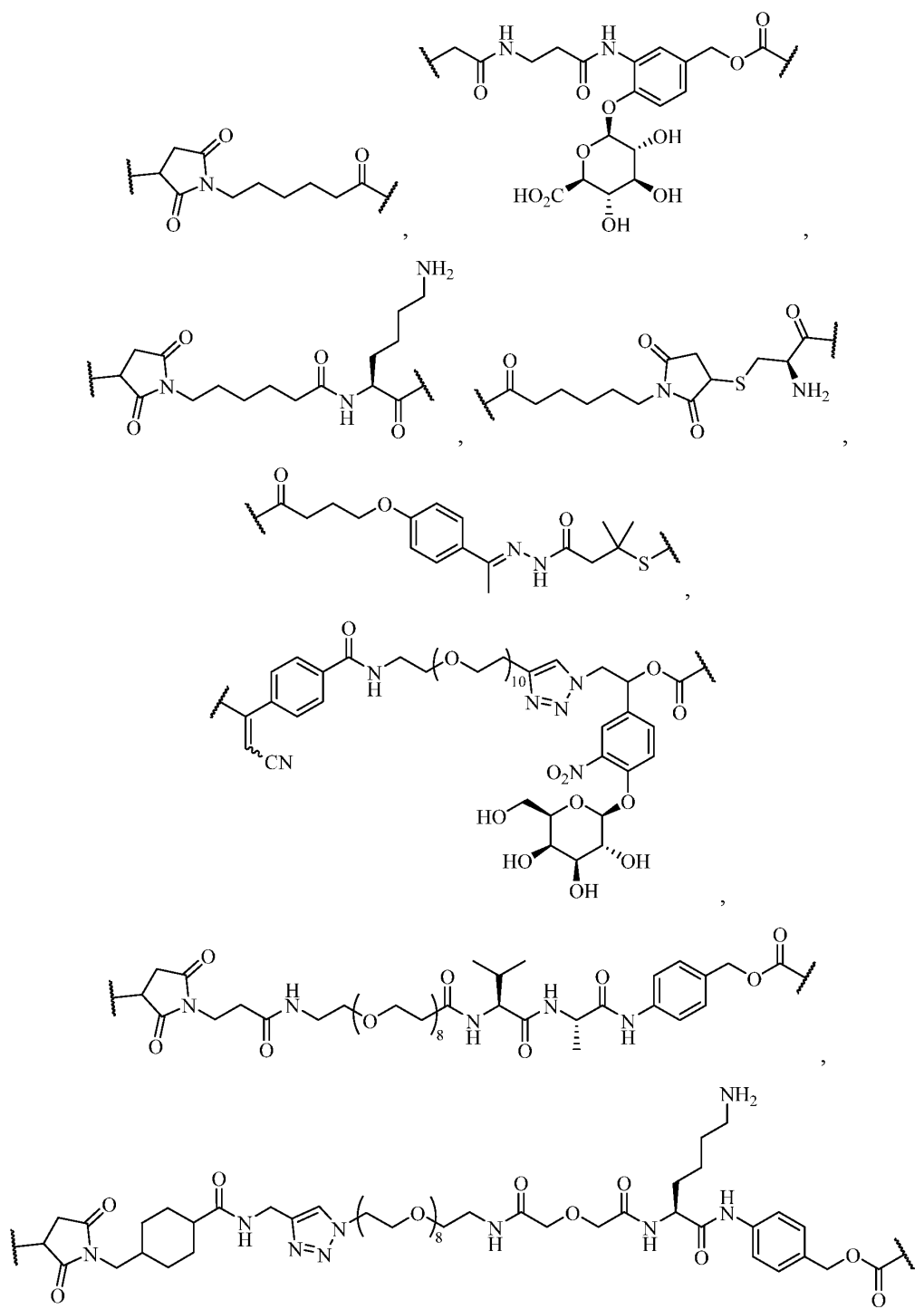
[0087] In certain embodiments, each L is independently:

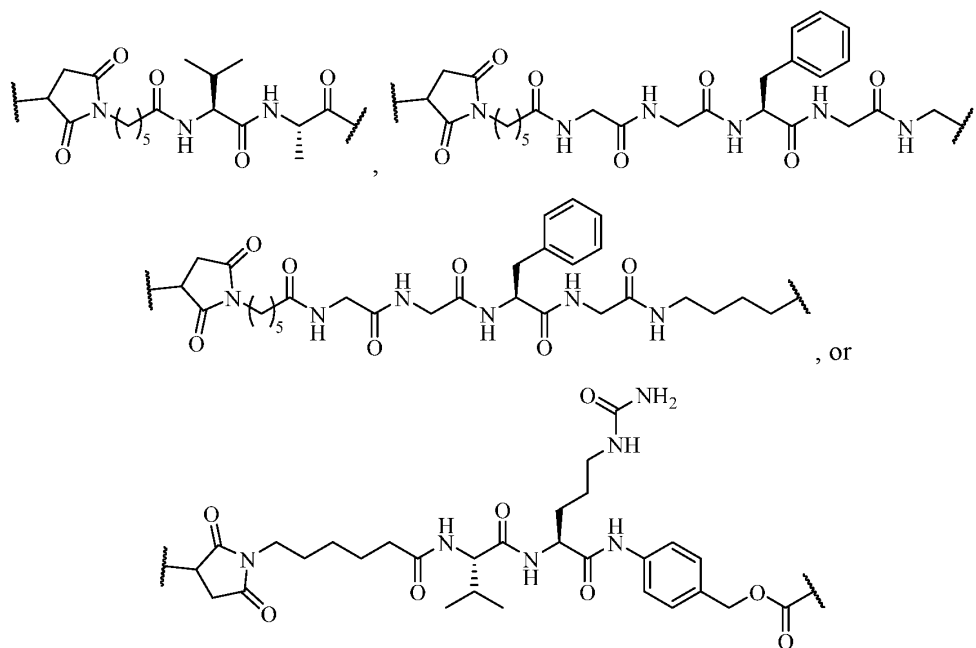




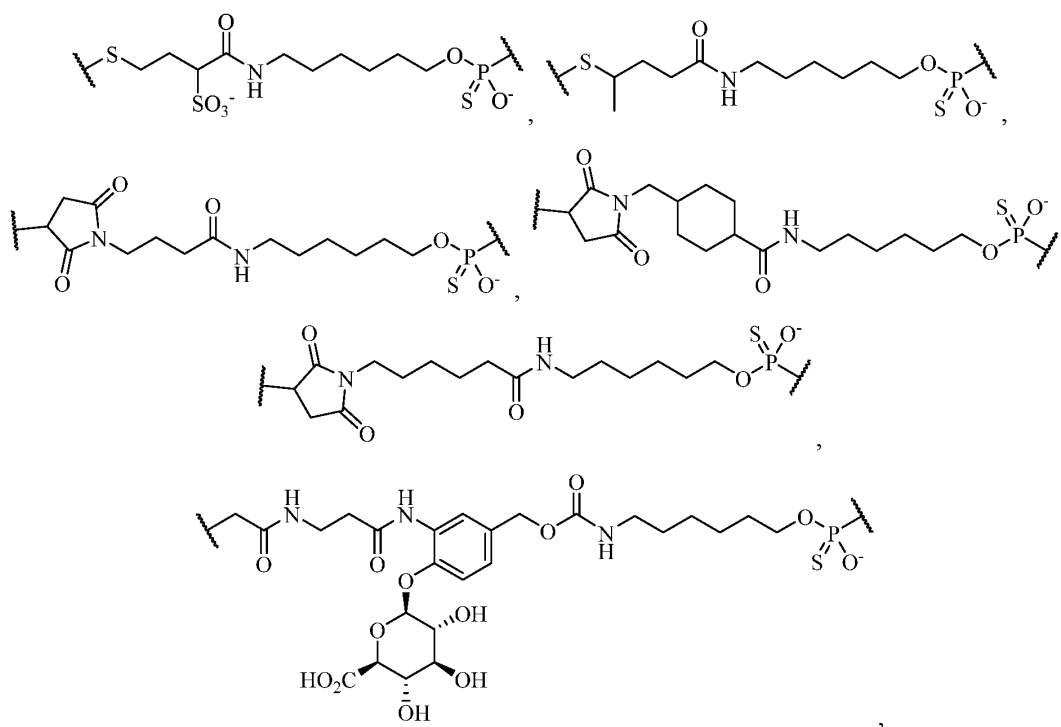
[0088] In certain embodiments, each L is independently:

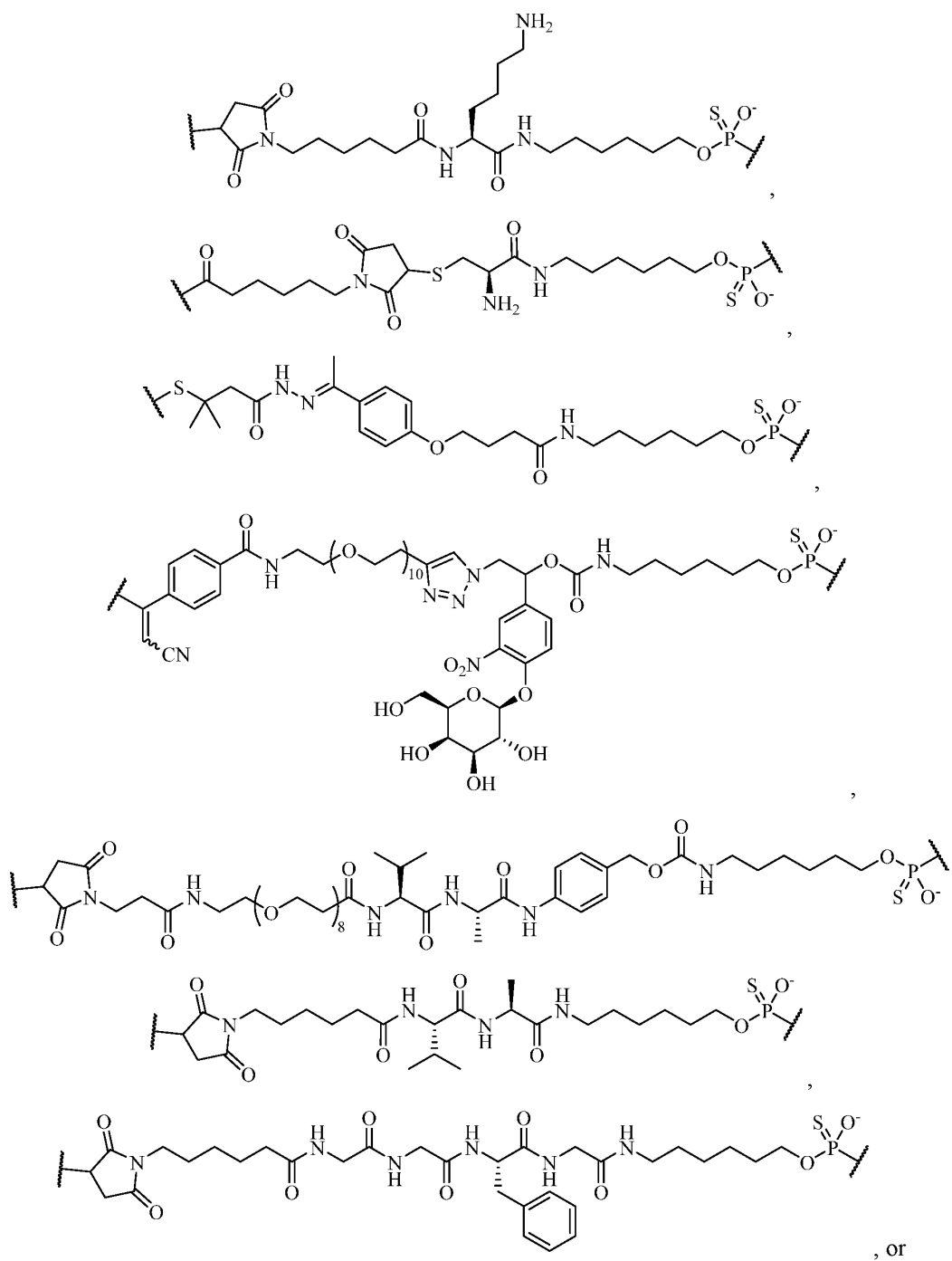


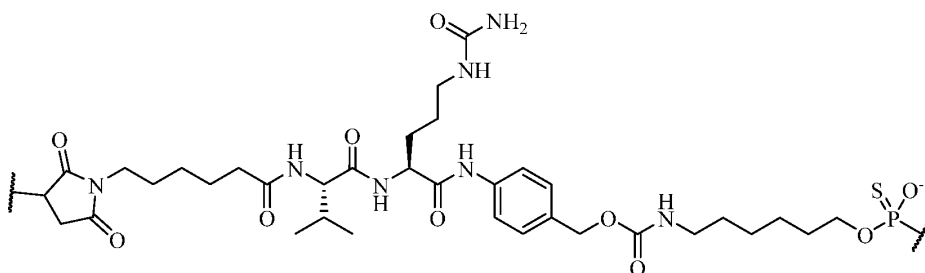




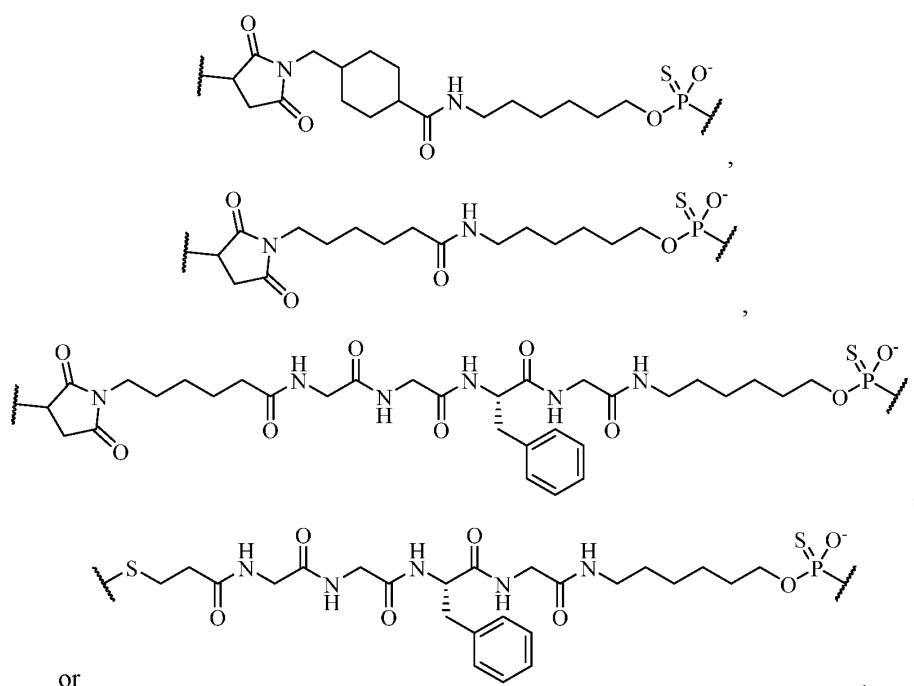
[0089] In certain embodiments, each L is independently:



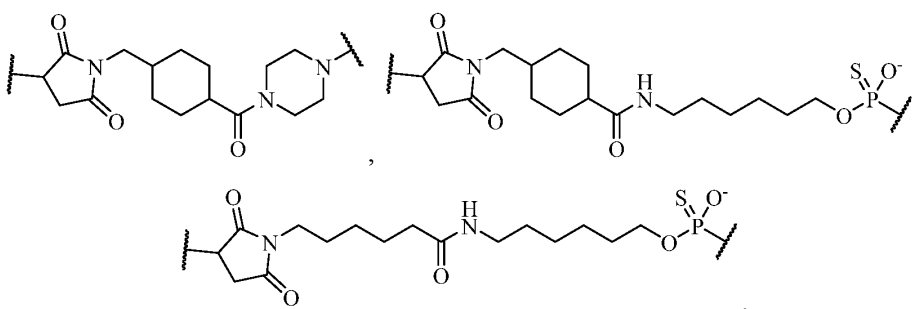


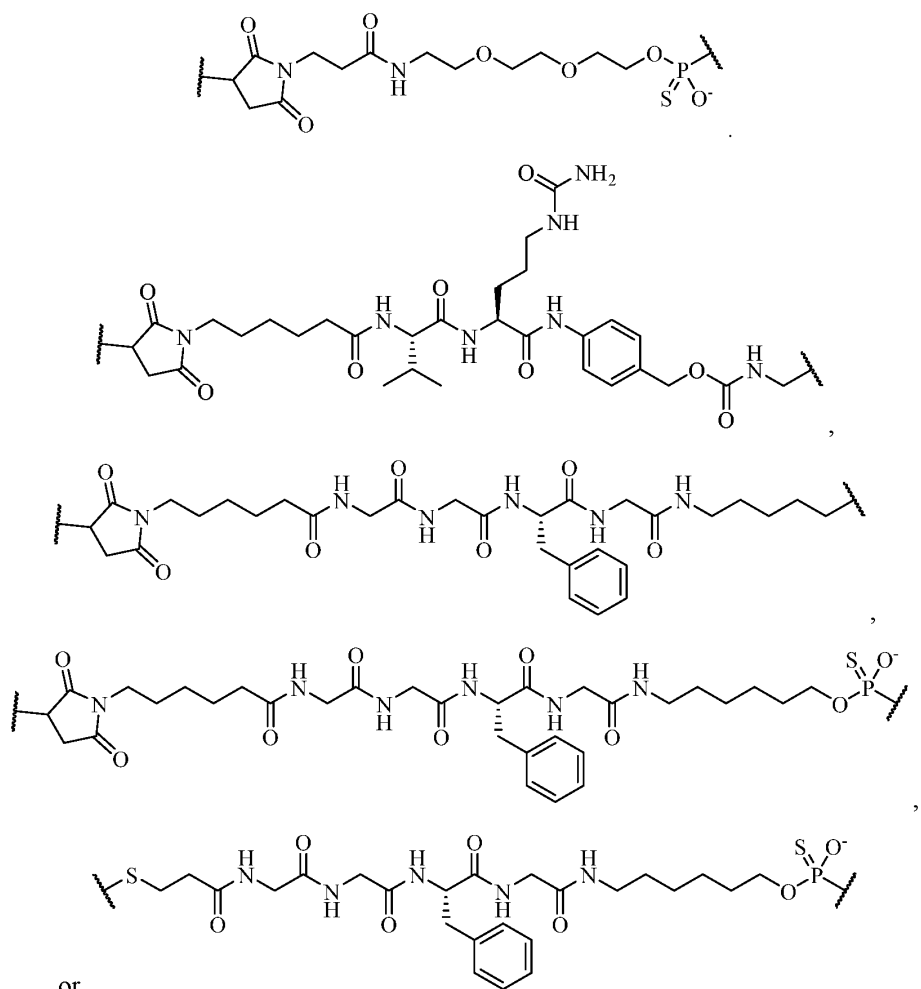


[0090] In certain embodiments, each L is independently:

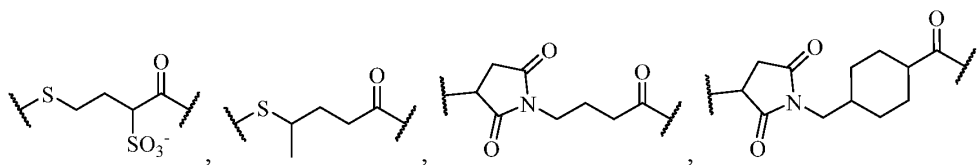


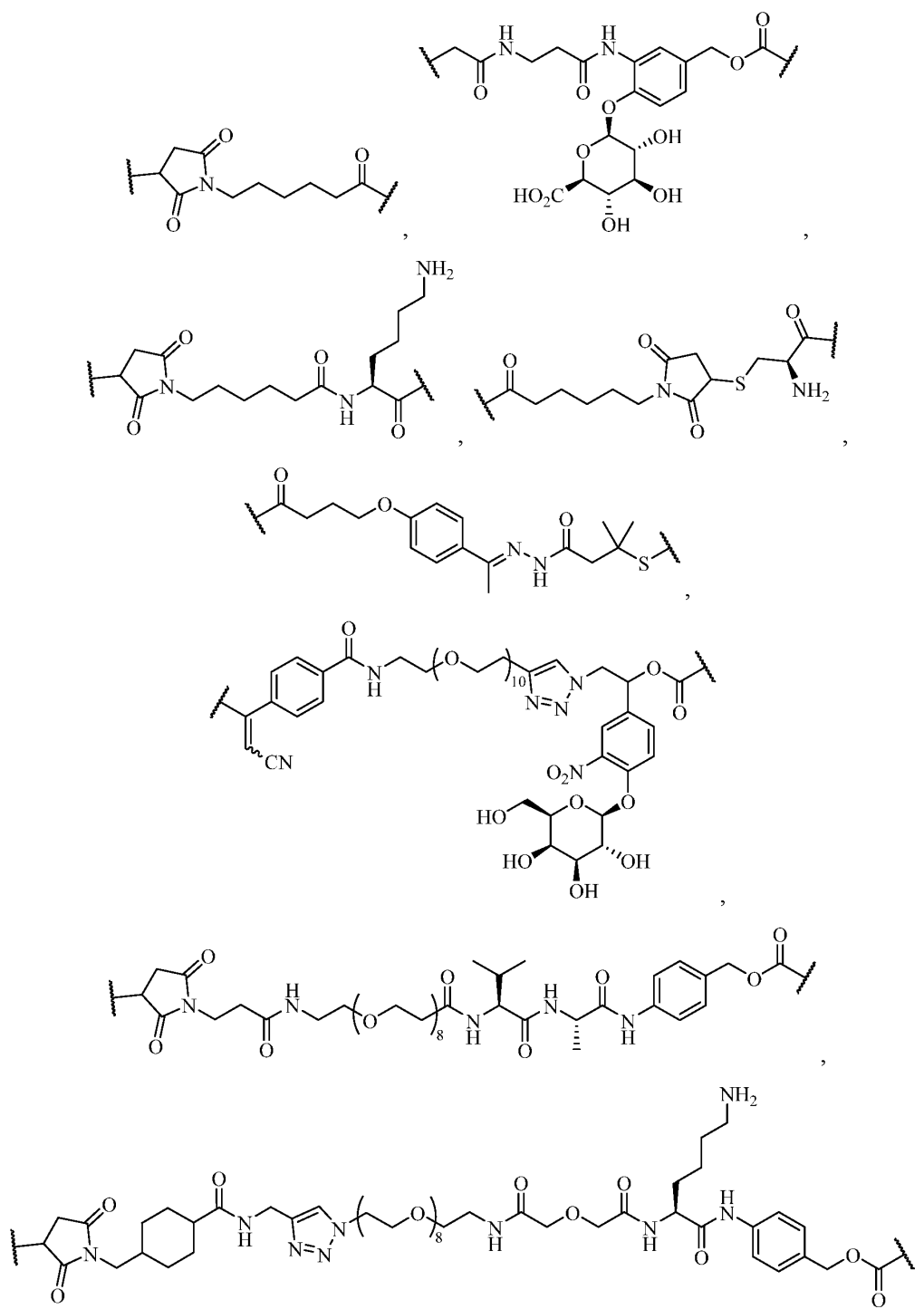
[0091] In certain embodiments, each L is independently:

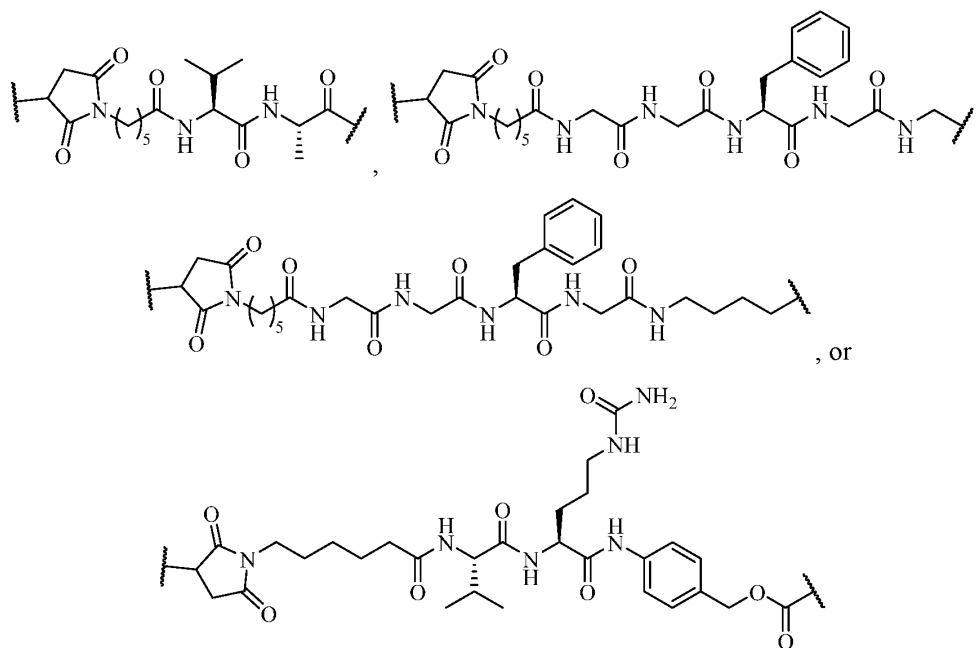




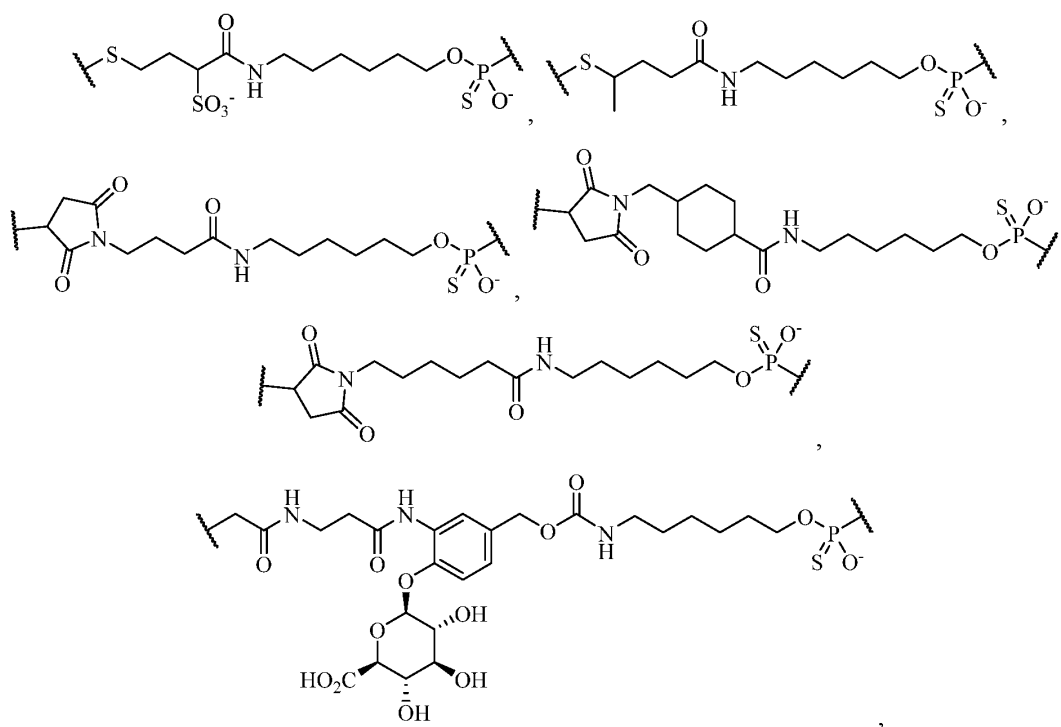
[0092] In certain embodiments, each X-L moiety is independently:

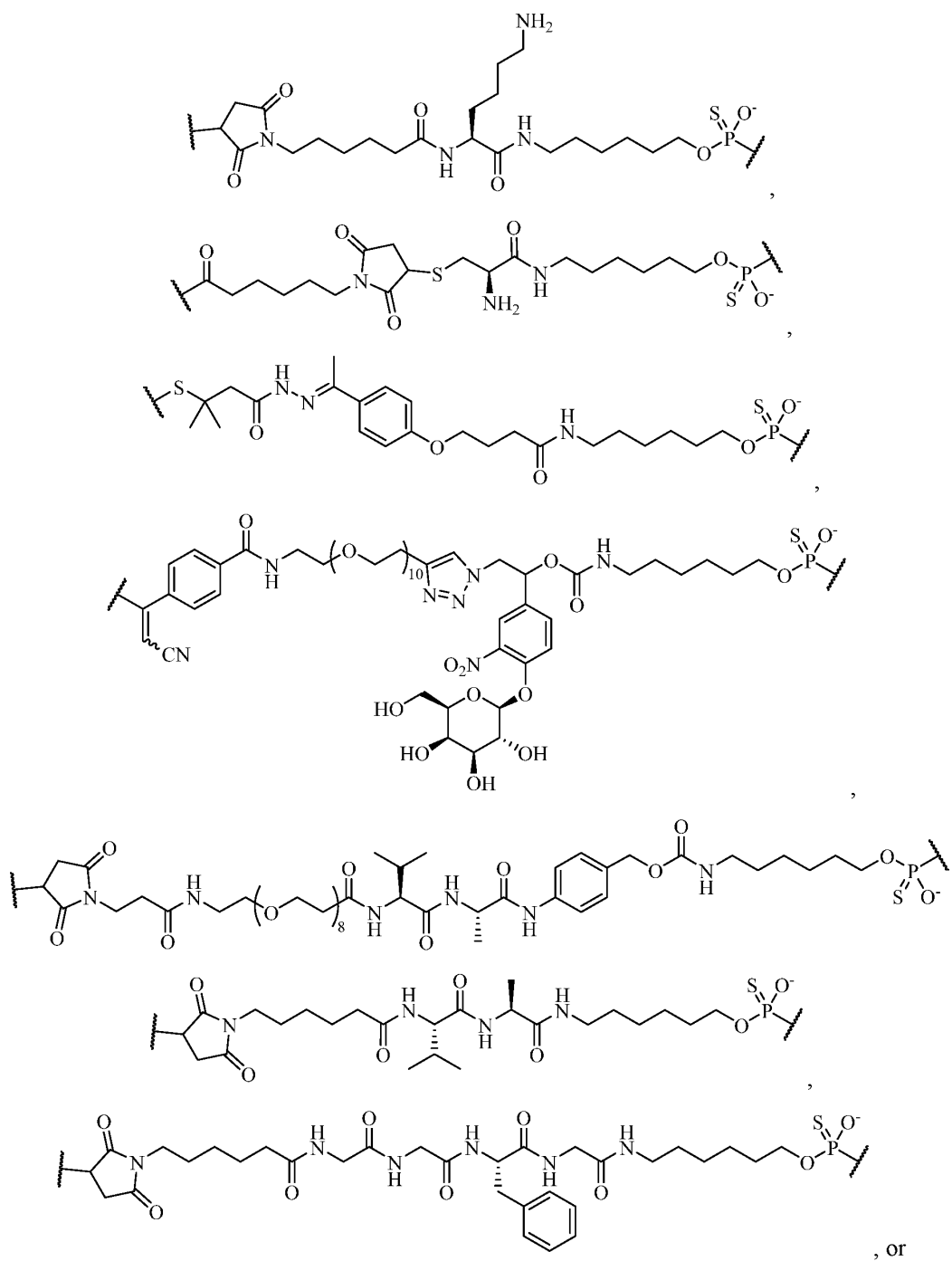


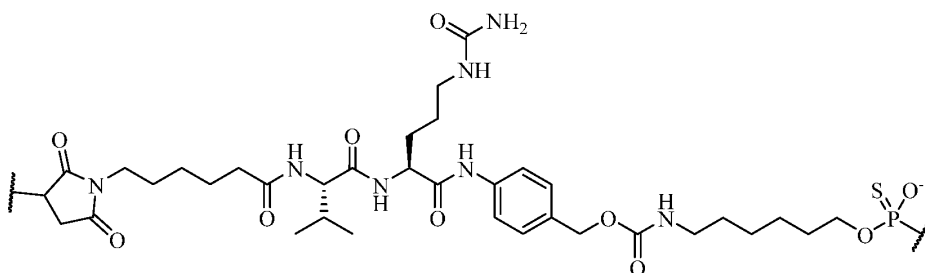




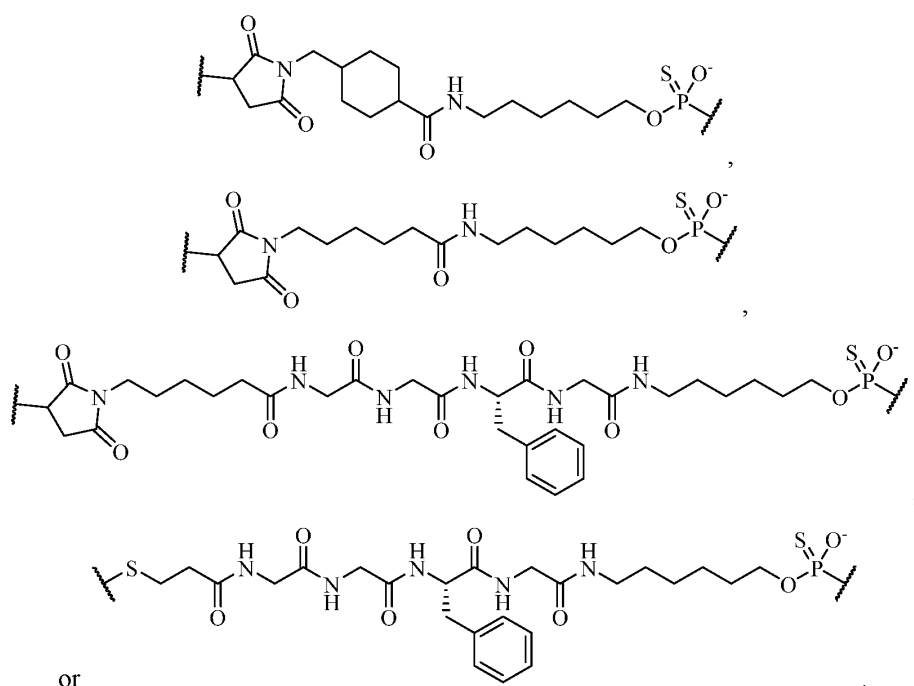
[0093] In certain embodiments, each X-L moiety is independently:



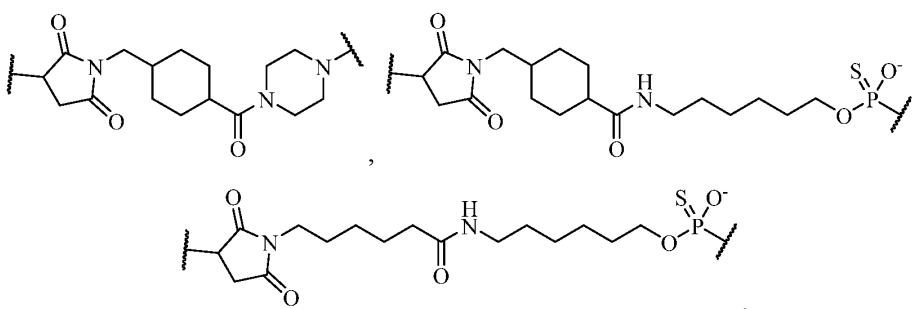


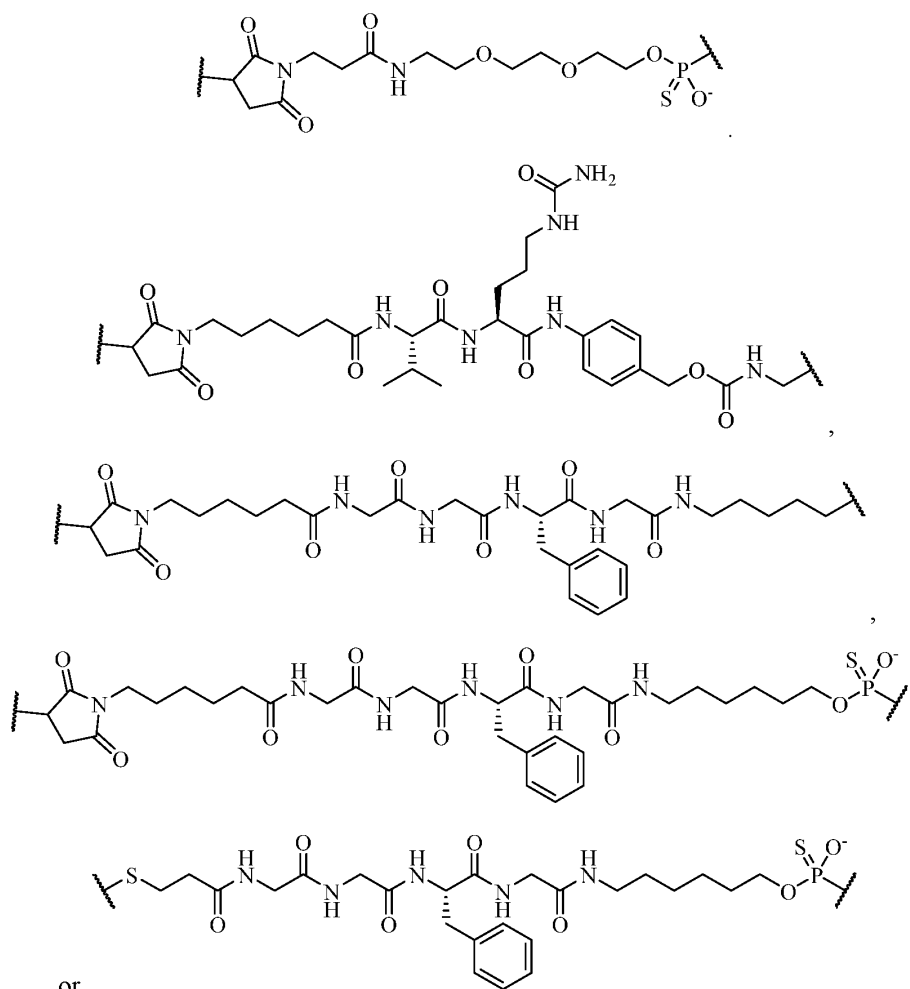


[0094] In certain embodiments, each X-L moiety is independently:

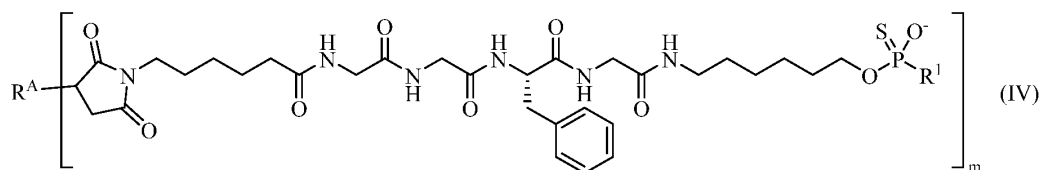


[0095] In certain embodiments, each X-L moiety is independently:





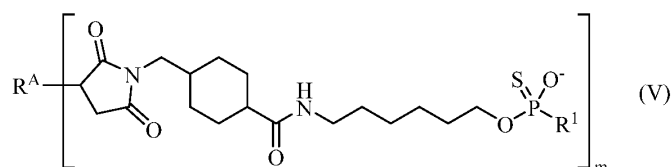
[0096] In one embodiment, provided herein is a compound of Formula (IV):



or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein each R^1 , R^A , and m is as defined herein. In certain embodiments, each linker is independently connected covalently to a thiol group of a cysteine residue of R^A via a 2,5-

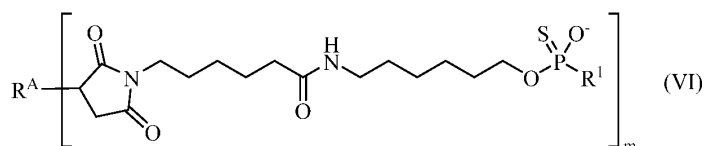
dioxypyrrolidin-1,3-diyl group. When R^1 is an immunostimulatory oligonucleotide, in certain embodiments, each linker is independently connected covalently to a 3'- or 5'-terminus of R^1 ; in certain embodiments, each linker is independently connected covalently to a 3'-terminus of R^1 ; in certain embodiments, each linker is independently connected covalently to a 5'-terminus of R^1 .

[0097] In another embodiment, provided herein is a compound of Formula (V):



or a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein each R^1 , R^A , and m is as defined herein. In certain embodiments, each linker is independently connected covalently to a thiol group of a cysteine residue of R^A *via* a 2,5-dioxypyrrolidin-1,3-diyl group. When R^1 is an immunostimulatory oligonucleotide, in certain embodiments, each linker is independently connected covalently to a 3'- or 5'-terminus of R^1 ; in certain embodiments, each linker is independently connected covalently to a 3'-terminus of R^1 ; in certain embodiments, each linker is independently connected covalently to a 5'-terminus of R^1 .

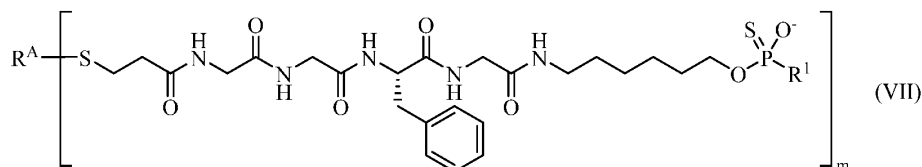
[0098] In yet another embodiment, provided herein is a compound of Formula (VI):



or a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein each R^1 , R^A , and m is as defined herein. In certain embodiments, each linker is independently connected covalently to a thiol group of a cysteine residue of R^A *via* a 2,5-dioxypyrrolidin-1,3-diyl group. When R^1 is an immunostimulatory oligonucleotide, in certain embodiments, each linker is independently connected covalently to a 3'- or 5'-terminus of R^1 ; in certain embodiments, each linker is independently connected covalently to a 3'-terminus of R^1 .

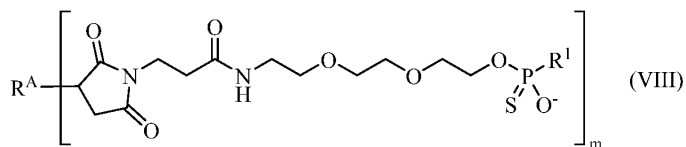
of R^1 ; in certain embodiments, each linker is independently connected covalently to a 5'-terminus of R^1 .

[0099] In yet another embodiment, provided herein is a compound of Formula (VII):



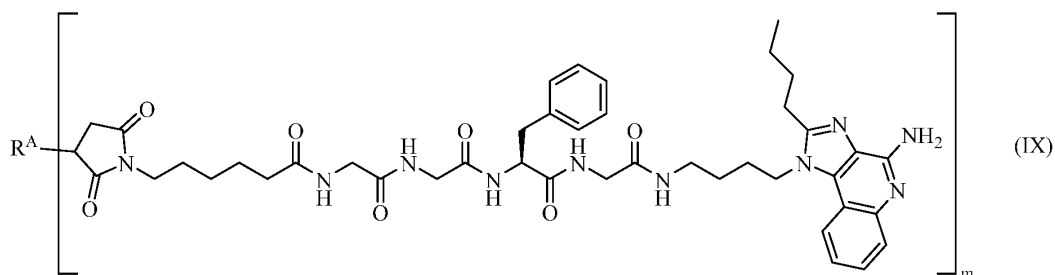
or a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein each R^1 , R^A , and m is as defined herein. In certain embodiments, each linker is independently connected covalently to a thiol group of a cysteine residue of R^A *via* a disulfide bond. When R^1 is an immunostimulatory oligonucleotide, in certain embodiments, each linker is independently connected covalently to a 3'- or 5'-terminus of R^1 ; in certain embodiments, each linker is independently connected covalently to a 3'-terminus of R^1 ; in certain embodiments, each linker is independently connected covalently to a 5'-terminus of R^1 .

[00100] In yet another embodiment, provided herein is a compound of Formula (VIII):



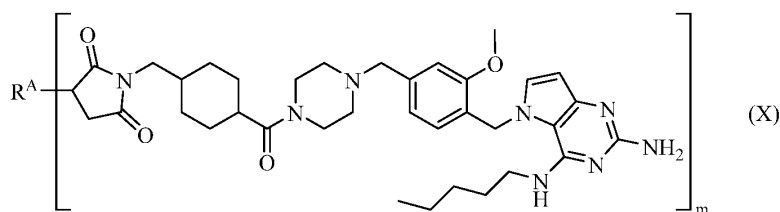
or a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein each R^1 , R^A , and m is as defined herein. In certain embodiments, each linker is independently connected covalently to a thiol group of a cysteine residue of R^A *via* a 2,5-dioxypyrrolidin-1,3-diyl group. When R^1 is an immunostimulatory oligonucleotide, in certain embodiments, each linker is independently connected covalently to a 3'- or 5'-terminus of R^1 ; in certain embodiments, each linker is independently connected covalently to a 3'-terminus of R^1 ; in certain embodiments, each linker is independently connected covalently to a 5'-terminus of R^1 .

[00101] In yet another embodiment, provided herein is a compound of Formula (IX):



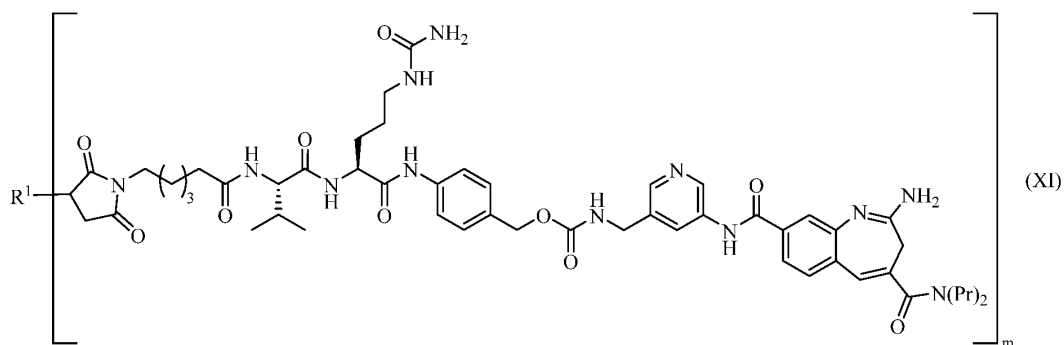
or a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein R^A and m are each as defined herein. In certain embodiments, each linker is independently connected covalently to a thiol group of a cysteine residue of R^A *via* a 2,5-dioxypyrrolidin-1,3-diyl group.

[00102] In yet another embodiment, provided herein is a compound of Formula (X):



or a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein R^A and m are each as defined herein. In certain embodiments, each linker is independently connected covalently to a thiol group of a cysteine residue of R^A *via* a 2,5-dioxypyrrolidin-1,3-diyl group.

[00103] In still another embodiment, provided herein is a compound of Formula (XI):



or a diastereomer, a mixture of two or more diastereomers, a tautomer, a mixture of two or more tautomers, or an isotopic variant thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein R^A and m are each as defined herein. In certain embodiments, each linker is independently connected covalently to a thiol group of a cysteine residue of R^A *via* a 2,5-dioxypyrrolidin-1,3-diyl group.

[00104] In certain embodiments, R^A is an antibody or an antigen-binding fragment thereof, which binds specifically to S-HBsAg, M-HBsAg, or L-HBsAg. In certain embodiments, R^A is an antibody or an antigen-binding fragment thereof, which binds specifically to S-HBsAg. In certain embodiments, R^A is an antibody or an antigen-binding fragment thereof, which binds specifically to M-HBsAg. In certain embodiments, R^A is an antibody or an antigen-binding fragment thereof, which binds specifically to L-HBsAg. In certain embodiments, R^A is an antibody or an antigen-binding fragment thereof, which binds specifically to an S domain. In certain embodiments, R^A is an antibody or an antigen-binding fragment thereof, which binds specifically to a hepatitis B surface antigen comprising the amino acid sequence of SEQ ID NO: 56. In certain embodiments, R^A is an antibody or an antigen-binding fragment thereof, which binds specifically to a hepatitis B surface antigen that comprises an amino acid sequence having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 56.

[00105] In certain embodiments, R^A is a full length or intact monoclonal antibody. In certain embodiments, R^A is a single-chain variable fragment (scFv), Fab, Fab', F(ab)₂, F(ab')₂, Fv, diabody, triabody, tetrabody, or minibody. In certain embodiments, R^A is an scFv. In certain embodiments, R^A is a Fab. In certain embodiments, R^A is a Fab'. In certain embodiments, R^A is a F(ab)₂. In certain embodiments, R^A is a F(ab')₂. In certain embodiments, R^A is a Fv. In certain embodiments, R^A is a diabody. In certain embodiments, R^A is a triabody. In certain embodiments, R^A is a tetrabody. In certain embodiments, R^A is a minibody.

[00106] In certain embodiments, R^A is a monoclonal antibody or an antigen-binding fragment thereof. In certain embodiments, R^A is an afucosylated antibody or an antigen-binding fragment thereof. In certain embodiments, R^A is a human, humanized, or chimeric antibody, or

an antigen-binding fragment thereof. In certain embodiments, R^A is a human antibody or an antigen-binding fragment thereof. In certain embodiments, R^A is a humanized antibody or an antigen-binding fragment thereof. In certain embodiments, R^A is a chimeric antibody or an antigen-binding fragment thereof.

[00107] In one embodiment, R^A is an IgA, IgD, IgE, IgG, or IgM antibody, or an antigen-binding fragment thereof. In another embodiment, R^A is an IgA antibody or an antigen-binding fragment thereof. In yet another embodiment, R^A is an IgD antibody or an antigen-binding fragment thereof. In yet another embodiment, R^A is an IgE antibody or an antigen-binding fragment thereof. In yet another embodiment, R^A is an IgG antibody or an antigen-binding fragment thereof. In still another embodiment, R^A is an IgM antibody or an antigen-binding fragment thereof.

[00108] In one embodiment, R^A is an IgA1, IgA2, IgG1, IgG2, IgG3, or IgG4 antibody, or an antigen-binding fragment thereof. In another embodiment, R^A is an IgA1 or IgA2, or an antigen-binding fragment thereof. In yet another embodiment, R^A is an IgA1 or an antigen-binding fragment thereof. In yet another embodiment, R^A is an IgA2 or an antigen-binding fragment thereof. In yet another embodiment, R^A is an IgG1, IgG2, IgG3, or IgG4 antibody, or an antigen-binding fragment thereof. In yet another embodiment, R^A is an IgG1 antibody or an antigen-binding fragment thereof. In yet another embodiment, R^A is an IgG2 antibody or an antigen-binding fragment thereof. In yet another embodiment, R^A is an IgG3 antibody or an antigen-binding fragment thereof. In still another embodiment, R^A is an IgG4 antibody or an antigen-binding fragment thereof.

[00109] In one embodiment, R^A is a recombinant antibody or an antigen-binding fragment thereof. In another embodiment, R^A is a purified antibody or an antigen-binding fragment thereof. In yet another embodiment, R^A is an isolated antibody or an antigen-binding fragment thereof.

[00110] In one embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a light chain complementarity determining region 1 (CDRL1) having the amino acid sequence of SEQ ID NO: 1; (ii) a light chain complementarity determining region 2 (CDRL2) having the amino acid sequence of AAS; (iii) a light chain complementarity

determining region 3 (CDRL3) having the amino acid sequence of SEQ ID NO: 2; (iv) a heavy chain complementarity determining region 1 (CDRH1) having the amino acid sequence of SEQ ID NO: 3; (v) a heavy chain complementarity determining region 2 (CDRH2) having the amino acid sequence of SEQ ID NO: 4; and (vi) a heavy chain complementarity determining region 3 (CDRH3) having the amino acid sequence of SEQ ID NO: 5. In another embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a CDRL1 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 1; (ii) a CDRL2 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of AAS; (iii) a CDRL3 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 2; (iv) a CDRH1 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 3; (v) a CDRH2 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 4; and (vi) a CDRH3 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 5. In certain embodiments, the CDRs described herein are defined according to the IMGT or Kabat numbering system. In certain embodiments, the CDRs described herein are defined according to the IMGT numbering system. In certain embodiments, the CDRs described herein are defined according to the Kabat numbering system.

[00111] In another embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a light chain variable region having the amino acid sequence of SEQ ID NO: 6; and (ii) a heavy chain variable region having the amino acid sequence of SEQ ID NO: 7. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 6. In certain embodiments, R^A is an antibody comprising a heavy chain variable region

having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 7.

[00112] In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 6; and a heavy chain variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 7. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 6; and a heavy chain variable region having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 7. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 6; and a heavy chain variable region having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 7. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 6; and a heavy chain variable region having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 7. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 6; and a heavy chain variable region having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 7. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 6; and a heavy chain variable region having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 7. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 6; and a heavy chain variable region having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 7.

[00113] In yet another embodiment, R^A is an antibody or an antigen-binding fragment thereof, wherein the antibody comprises (i) a light chain having the amino acid sequence of SEQ ID NO: 10; and (ii) a heavy chain having the amino acid sequence of SEQ ID NO: 11. In certain embodiments, R^A is an antibody comprising a light chain having at least about 80%, at least

about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 10. In certain embodiments, R^A is an antibody comprising a heavy chain having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 11.

[00114] In certain embodiments, R^A is an antibody comprising a light chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a heavy chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 11. In certain embodiments, R^A is an antibody comprising a light chain having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a heavy chain having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 11. In certain embodiments, R^A is an antibody comprising a light chain having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a heavy chain having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 11. In certain embodiments, R^A is an antibody comprising a light chain having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a heavy chain having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 11. In certain embodiments, R^A is an antibody comprising a light chain having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a heavy chain having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 11. In certain embodiments, R^A is an antibody comprising a light chain having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a heavy chain having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 11. In certain embodiments, R^A is an antibody comprising a light chain having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a heavy chain having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 11.

[00115] In one embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a CDRL1 having the amino acid sequence of SEQ ID NO: 12; (ii) a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; (iii) a CDRL3 having the amino acid sequence of SEQ ID NO: 14; (iv) a CDRH1 having the amino acid sequence of SEQ ID

NO: 15; (v) a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and (vi) a CDRH3 having the amino acid sequence of SEQ ID NO: 18. In another embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a CDRL1 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 12; (ii) a CDRL2 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of EVK or SEQ ID NO: 13; (iii) a CDRL3 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 14; (iv) a CDRH1 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 15; (v) a CDRH2 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 16 or 17; and (vi) a CDRH3 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 18. In certain embodiments, the CDRs described herein are defined according to the IMGT or Kabat numbering system. In certain embodiments, the CDRs described herein are defined according to the IMGT numbering system. In certain embodiments, the CDRs described herein are defined according to the Kabat numbering system.

[00116] In another embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a light chain variable region having the amino acid sequence of SEQ ID NO: 19; and (ii) a heavy chain variable region having the amino acid sequence of SEQ ID NO: 20. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 19. In certain embodiments, R^A is an antibody comprising a heavy chain variable region having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 20.

[00117] In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 19; and a heavy chain variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 20. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 19; and a heavy chain variable region having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 20. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 19; and a heavy chain variable region having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 20. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 19; and a heavy chain variable region having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 20. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 19; and a heavy chain variable region having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 20. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 19; and a heavy chain variable region having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 20. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 19; and a heavy chain variable region having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 20.

[00118] In yet another embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a light chain having the amino acid sequence of SEQ ID NO: 21; and (ii) a heavy chain having the amino acid sequence of SEQ ID NO: 22. In certain embodiments, R^A is an antibody comprising a light chain having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 21. In certain embodiments, R^A is an antibody comprising a heavy chain having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99%

sequence identity to the amino acid sequence of SEQ ID NO: 22.

[00119] In certain embodiments, R^A is an antibody comprising a light chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 21; and a heavy chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 22. In certain embodiments, R^A is an antibody comprising a light chain having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 21; and a heavy chain having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 22. In certain embodiments, R^A is an antibody comprising a light chain having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 21; and a heavy chain having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 22. In certain embodiments, R^A is an antibody comprising a light chain having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 21; and a heavy chain having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 22. In certain embodiments, R^A is an antibody comprising a light chain having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 21; and a heavy chain having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 22. In certain embodiments, R^A is an antibody comprising a light chain having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 21; and a heavy chain having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 22. In certain embodiments, R^A is an antibody comprising a light chain having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 21; and a heavy chain having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 22.

[00120] In one embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a CDRL1 having the amino acid sequence of SEQ ID NO: 23; (ii) a CDRL2 having the amino acid sequence of SEQ ID NO: 24; (iii) a CDRL3 having the amino acid sequence of SEQ ID NO: 25; (iv) a CDRH1 having the amino acid sequence of SEQ ID NO: 26; (v) a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and (vi) a CDRH3 having the amino acid sequence of SEQ ID NO: 28. In another embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a CDRL1 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at

least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 23; (ii) a CDRL2 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 24; (iii) a CDRL3 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 25; (iv) a CDRH1 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 26; (v) a CDRH2 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 27; and (vi) a CDRH3 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 28. In certain embodiments, the CDRs described herein are defined according to the IMGT or Kabat numbering system. In certain embodiments, the CDRs described herein are defined according to the IMGT numbering system. In certain embodiments, the CDRs described herein are defined according to the Kabat numbering system.

[00121] In another embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a light chain variable region having the amino acid sequence of SEQ ID NO: 29; and (ii) a heavy chain variable region having the amino acid sequence of SEQ ID NO: 30. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 29. In certain embodiments, R^A is an antibody comprising a heavy chain variable region having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 30.

[00122] In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 29; and a heavy chain variable region having at least about 80% sequence identity to the amino

acid sequence of SEQ ID NO: 30. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 29; and a heavy chain variable region having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 30. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 29; and a heavy chain variable region having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 30. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 29; and a heavy chain variable region having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 30. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 29; and a heavy chain variable region having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 30. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 29; and a heavy chain variable region having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 30. In certain embodiments, R^A is an antibody comprising a light chain variable region having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 29; and a heavy chain variable region having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 30.

[00123] In yet another embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a light chain having the amino acid sequence of SEQ ID NO: 33; and (ii) a heavy chain having the amino acid sequence of SEQ ID NO: 34. In certain embodiments, R^A is an antibody comprising a light chain having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 33. In certain embodiments, R^A is an antibody comprising a heavy chain having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 34.

[00124] In certain embodiments, R^A is an antibody comprising a light chain having at least

about 80% sequence identity to the amino acid sequence of SEQ ID NO: 33; and a heavy chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 34. In certain embodiments, R^A is an antibody comprising a light chain having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 33; and a heavy chain having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 34. In certain embodiments, R^A is an antibody comprising a light chain having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 33; and a heavy chain having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 34. In certain embodiments, R^A is an antibody comprising a light chain having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 33; and a heavy chain having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 34. In certain embodiments, R^A is an antibody comprising a light chain having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 33; and a heavy chain having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 34. In certain embodiments, R^A is an antibody comprising a light chain having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 33; and a heavy chain having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 34. In certain embodiments, R^A is an antibody comprising a light chain having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 33; and a heavy chain having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 34.

[00125] In one embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a CDRL1 having the amino acid sequence of SEQ ID NO: 35; (ii) a CDRL2 having the amino acid sequence of AAS; (iii) a CDRL3 having the amino acid sequence of SEQ ID NO: 36; (iv) a CDRH1 having the amino acid sequence of SEQ ID NO: 37; (v) a CDRH2 having the amino acid sequence of SEQ ID NO: 38; and (vi) a CDRH3 having the amino acid sequence of SEQ ID NO: 39. In another embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a CDRL1 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 35; (ii) a CDRL2 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of AAS; (iii)

a CDRL3 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 36; (iv) a CDRH1 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 37; (v) a CDRH2 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 38; and (vi) a CDRH3 having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, or at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 39. In certain embodiments, the CDRs described herein are defined according to the IMGT or Kabat numbering system. In certain embodiments, the CDRs described herein are defined according to the IMGT numbering system. In certain embodiments, the CDRs described herein are defined according to the Kabat numbering system.

[00126] In yet another embodiment, R^A is an antibody or an antigen-binding fragment thereof, wherein the antibody comprises (i) a light chain having the amino acid sequence of SEQ ID NO: 40; and (ii) a heavy chain having the amino acid sequence of SEQ ID NO: 41. In certain embodiments, R^A is an antibody comprising a light chain having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 40. In certain embodiments, R^A is an antibody comprising a heavy chain having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 41.

[00127] In certain embodiments, R^A is an antibody comprising a light chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 40; and a heavy chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 41. In certain embodiments, R^A is an antibody comprising a light chain having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 40; and a heavy chain having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 41. In certain embodiments, R^A is an antibody comprising a light chain having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 40; and a heavy chain having at least about

90% sequence identity to the amino acid sequence of SEQ ID NO: 41. In certain embodiments, R^A is an antibody comprising a light chain having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 40; and a heavy chain having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 41. In certain embodiments, R^A is an antibody comprising a light chain having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 40; and a heavy chain having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 41. In certain embodiments, R^A is an antibody comprising a light chain having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 40; and a heavy chain having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 41. In certain embodiments, R^A is an antibody comprising a light chain having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 40; and a heavy chain having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 41.

[00128] In yet another embodiment, R^A is an antibody or an antigen-binding fragment thereof, comprising (i) a light chain having the amino acid sequence of SEQ ID NO: 42; and (ii) a heavy chain having the amino acid sequence of SEQ ID NO: 43. In certain embodiments, R^A is an antibody comprising a light chain having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 42. In certain embodiments, R^A is an antibody comprising a heavy chain having at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97%, at least about 98%, at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 43.

[00129] In certain embodiments, R^A is an antibody comprising a light chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 42; and a heavy chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 43. In certain embodiments, R^A is an antibody comprising a light chain having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 42; and a heavy chain having at least about 85% sequence identity to the amino acid sequence of SEQ ID NO: 43. In certain embodiments, R^A is an antibody comprising a light chain having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 42; and a heavy chain having at least about

90% sequence identity to the amino acid sequence of SEQ ID NO: 43. In certain embodiments, R^A is an antibody comprising a light chain having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 42; and a heavy chain having at least about 95% sequence identity to the amino acid sequence of SEQ ID NO: 43. In certain embodiments, R^A is an antibody comprising a light chain having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 42; and a heavy chain having at least about 97% sequence identity to the amino acid sequence of SEQ ID NO: 43. In certain embodiments, R^A is an antibody comprising a light chain having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 42; and a heavy chain having at least about 98% sequence identity to the amino acid sequence of SEQ ID NO: 43. In certain embodiments, R^A is an antibody comprising a light chain having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 42; and a heavy chain having at least about 99% sequence identity to the amino acid sequence of SEQ ID NO: 43.

[00130] Additional exemplary antibodies and antigen-binding fragments thereof suitable for a compound provided herein include, but are not limited to, those disclosed in WO 2021/042000 A1 and US 10,689,434 B2, the disclosure of each of which is incorporated herein by reference in its entirety.

[00131] In certain embodiments, R¹ is a retinoic acid-inducible gene 1 (RIG-I) agonist, a stimulator of interferon gene (STING) agonist, or a toll-like receptor (TLR) agonist. In certain embodiments, R¹ is an RIG-I agonist. In certain embodiments, R¹ is a STING agonist.

[00132] In certain embodiments, R¹ is a TLR agonist. In certain embodiments, R¹ is a TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, TLR11, TLR12, or TLR13 agonist. In certain embodiments, R¹ is a TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, or TLR10 agonist. In certain embodiments, R¹ is a TLR3, TLR7, TLR8, or TLR9 agonist. In certain embodiments, R¹ is a TLR3 agonist. In certain embodiments, R¹ is a TLR7 agonist. In certain embodiments, R¹ is a TLR8 agonist. In certain embodiments, R¹ is a TLR9 agonist.

[00133] In certain embodiments, R¹ is a synthetic TLR agonist. In certain embodiments, R¹ is a synthetic TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10,

TLR11, TLR12, or TLR13 agonist. In certain embodiments, R^1 is a synthetic TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, or TLR10 agonist. In certain embodiments, R^1 is a synthetic TLR3, TLR7, TLR8, or TLR9 agonist. In certain embodiments, R^1 is a synthetic TLR3 agonist. In certain embodiments, R^1 is a synthetic TLR7 agonist. In certain embodiments, R^1 is a synthetic TLR8 agonist. In certain embodiments, R^1 is a synthetic TLR9 agonist.

[00134] In certain embodiments, R^1 is an immunostimulatory oligonucleotide. In certain embodiments, R^1 is a single-stranded oligonucleotide. In certain embodiments, each R^1 is independently a single-stranded oligonucleotide comprising from about 10 to about 50, from about 15 to about 40, or from about 15 to about 30 nucleotides. In certain embodiments, each R^1 is independently a single-stranded oligonucleotide comprising from about 10 to about 50 nucleotides. In certain embodiments, each R^1 is independently a single-stranded oligonucleotide comprising from about 15 to about 40 nucleotides. In certain embodiments, each R^1 is independently a single-stranded oligonucleotide comprising from about 15 to about 30 nucleotides. In certain embodiments, each R^1 is independently a single-stranded oligonucleotide comprising about 15, about 16, about 17, about 18, about 19, about 20, about 21, about 22, about 23, about 24, about 25, about 26, about 27, about 28, about 29, or about 30 nucleotides.

[00135] In certain embodiments, R^1 is a single-stranded CpG oligodeoxynucleotide. In certain embodiments, each R^1 is independently a single-stranded CpG oligodeoxynucleotide comprising from about 10 to about 50, from about 15 to about 40, from about 15 to about 30, or from about 20 to about 30 deoxyribonucleotides. In certain embodiments, each R^1 is independently a single-stranded oligodeoxynucleotide comprising from about 10 to about 50 deoxyribonucleotides. In certain embodiments, each R^1 is independently a single-stranded oligodeoxynucleotide comprising from about 15 to about 40 deoxyribonucleotides. In certain embodiments, each R^1 is independently a single-stranded oligodeoxynucleotide comprising from about 15 to about 30 deoxyribonucleotides. In certain embodiments, each R^1 is independently a single-stranded oligodeoxynucleotide comprising from about 20 to about 30 deoxyribonucleotides. In certain embodiments, each R^1 is independently a single-stranded oligodeoxynucleotide comprising about 20, about 21, about 22, about 23, about 24, about 25, about 26, about 27, about 28, about 29, or about 30 deoxyribonucleotides.

[00136] In certain embodiments, R^1 is a single-stranded oligodeoxynucleotide comprising one or more unmethylated CpG dideoxynucleotide motifs. In certain embodiments, R^1 comprises from about 1 to about 20 or from about 1 to about 10 unmethylated CpG dideoxynucleotide motifs. In certain embodiments, R^1 comprises from about 1 to about 20 unmethylated CpG dideoxynucleotide motifs. In certain embodiments, R^1 comprises from about 1 to about 10 unmethylated CpG dideoxynucleotide motifs. In certain embodiments, R^1 comprises about 1, about 2, about 3, about 4, about 5, about 6, about 7, about 8, about 9, or about 10 unmethylated CpG dideoxynucleotide motifs.

[00137] In certain embodiments, each deoxynucleotide in the single-stranded oligodeoxynucleotide is independently a natural deoxynucleotide or modified deoxynucleotide. In certain embodiments, a natural nucleotide includes deoxyadenosine (dA), deoxycytidine (dC), deoxyguanosine (dG), and deoxythymine (dT). In certain embodiments, a modified deoxynucleotide is a deoxynucleotide with a modification on its nucleobase, a modification on its sugar, and/or a modification on its phosphate linkage group. Examples of modified deoxynucleotide include, but are not limited to, 2'-fluoroadenosine (fA), 2'-fluorocytidine (fC), 2'-fluoroguanosine (fG), 2'-fluorouridine (fU), 2'-*O*-methyladenosine (mA), 2'-*O*-methylcytidine (mC), 2'-*O*-methylguanosine (mG), or 2'-*O*-methyluridine (mU). In certain embodiments, each deoxynucleotide in the single-stranded oligodeoxynucleotide is independently adenosine, cytidine, guanosine, inosine, uridine, deoxyadenosine, deoxycytidine, deoxyguanosine, deoxyinosine, deoxythymine, 2'-fluoroadenosine, 2'-fluorocytidine, 2'-fluoroguanosine, 2'-fluorouridine, 2'-deoxyadenosine, 2'-deoxycytidine, 2'-deoxyguanosine, 2'-deoxyinosine, 2'-deoxythymidine, 2'-*O*-methyladenosine, 2'-*O*-methylcytidine, 2'-*O*-methylguanosine, 2'-*O*-methyluridine, 2'-deoxy-5-bromouridine or 5-methyl-2'-methoxyuridine. In certain embodiments, each deoxynucleotide in the single-stranded oligodeoxynucleotide is independently adenosine, cytidine, guanosine, uridine, deoxyadenosine, deoxycytidine, deoxyguanosine, deoxythymine, 2'-fluoroadenosine, 2'-fluorocytidine, 2'-fluoroguanosine, 2'-fluorouridine, 2'-deoxyadenosine, 2'-deoxycytidine, 2'-deoxyguanosine, 2'-deoxythymidine, 2'-*O*-methyladenosine, 2'-*O*-methylcytidine, 2'-*O*-methylguanosine, or 2'-*O*-methyluridine. In certain embodiments, each deoxynucleotide in the single-stranded oligodeoxynucleotide is independently deoxyadenosine, deoxycytidine, deoxyguanosine, deoxyinosine, deoxythymine, 2'-fluoroadenosine, 2'-fluorocytidine, 2'-fluoroguanosine, 2'-fluorouridine, 2'-deoxyadenosine,

2'-deoxycytidine, 2'-deoxyguanosine, 2'-deoxythymidine, 2'-*O*-methyladenosine, 2'-*O*-methylcytidine, 2'-*O*-methylguanosine, 2'-*O*-methyluridine, 2'-deoxy-5-bromouridine or 5-methyl-2'-methoxyuridine. In certain embodiments, each deoxynucleotide in the single-stranded oligodeoxynucleotide is independently deoxyadenosine, deoxycytidine, deoxyguanosine, deoxythymine, 2'-fluoroadenosine, 2'-fluorocytidine, 2'-fluoroguanosine, 2'-fluorouridine, 2'-deoxyadenosine, 2'-deoxycytidine, 2'-deoxyguanosine, 2'-deoxythymidine, 2'-*O*-methyladenosine, 2'-*O*-methylcytidine, 2'-*O*-methylguanosine, or 2'-*O*-methyluridine.

[00138] In certain embodiments, the single-stranded oligonucleotide has one or more phosphate linkage groups replaced with methylphosphate, phosphoramidate, phosphorothioate, phosphorodithioate, phosphotriester, or diphosphate. In certain embodiments, the single-stranded oligonucleotide has one or more phosphate linkage groups replaced with phosphorothioate or phosphorodithioate. In certain embodiments, the single-stranded oligonucleotide has all phosphate linkage groups replaced with phosphorothioate or phosphorodithioate. In certain embodiments, the single-stranded oligonucleotide has all phosphate linkage groups replaced with phosphorothioate.

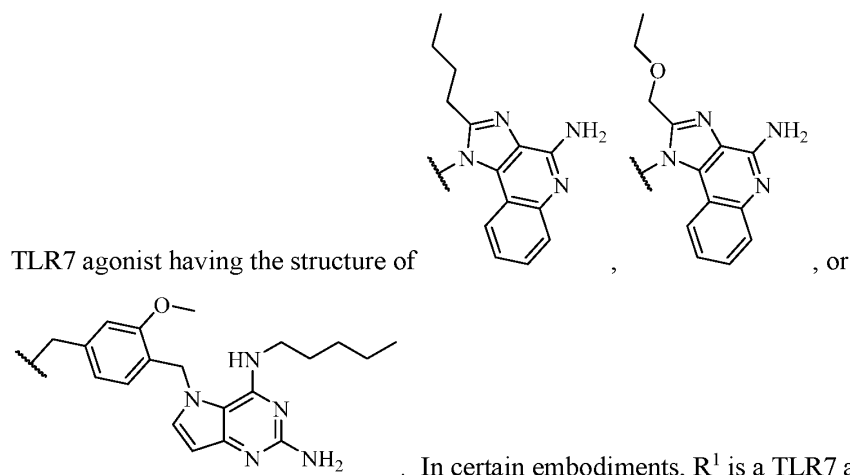
[00139] In certain embodiments, R¹ is a TLR9 agonist of Class A. In certain embodiments, R¹ is a TLR9 agonist of Class B. In certain embodiments, R¹ is a TLR9 agonist of Class C. In certain embodiments, R¹ is a TLR9 agonist of Class P.

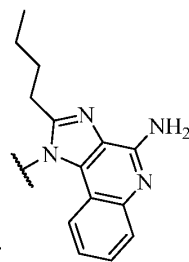
[00140] In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of any one of SEQ ID NOs: 44 to 55. In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of any one of SEQ ID NOs: 44 to 54. In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 44. In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 45. In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 46. In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 47. In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 48. In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 49. In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 50. In certain embodiments, R¹ is a TLR9 agonist comprising the

nucleotide sequence of SEQ ID NO: 51. In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 52. In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 53. In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 54. In certain embodiments, R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 55.

[00141] In certain embodiments, R¹ is CpG 1018, CpG 1826, CpG 2006/7909, CpG 2007, CpG 2216, CpG 2336, CpG 2395, CpG BW006, CpG D-SL01, CpG D-SL03, CpG M362, or T-CpG. In certain embodiments, R¹ is CpG 1018, CpG 1826, CpG 2006/7909, CpG 2007, CpG 2216, CpG 2336, CpG 2395, CpG BW006, CpG D-SL01, CpG D-SL03, or CpG M362. In certain embodiments, R¹ is CpG 1018. In certain embodiments, R¹ is CpG 1826. In certain embodiments, R¹ is CpG 2006. In certain embodiments, R¹ is CpG 2007. In certain embodiments, R¹ is CpG 2216. In certain embodiments, R¹ is CpG 2336. In certain embodiments, R¹ is CpG 2395. In certain embodiments, R¹ is CpG BW006. In certain embodiments, R¹ is CpG D-SL01. In certain embodiments, R¹ is CpG D-SL03. In certain embodiments, R¹ is CpG M362. In certain embodiments, R¹ is T-CpG.

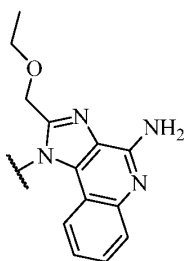
[00142] In certain embodiments, R¹ is a TLR7 agonist. In certain embodiments, R¹ is a



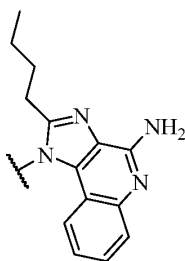


embodiments, R¹ is a TLR7 agonist having the structure of

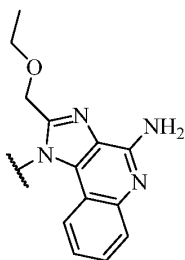
or



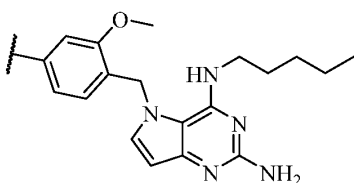
. In certain embodiments, R¹ is a TLR7 agonist having the structure of



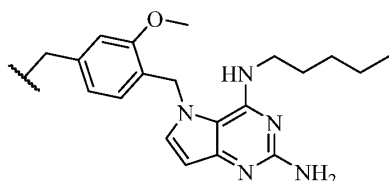
. In certain embodiments, R¹ is a TLR7 agonist having the structure of



. In certain embodiments, R¹ is a TLR7 agonist comprising the structure of

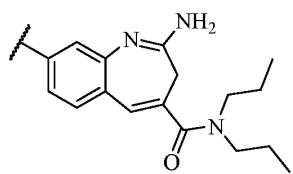


. In certain embodiments, R¹ is a TLR7 agonist having the



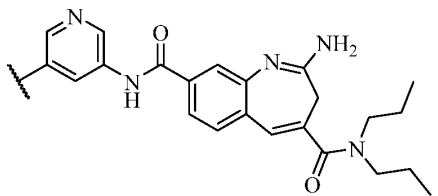
structure of

[00143] In certain embodiments, R^1 is a TLR8 agonist. In certain embodiments, R^1 is a



TLR8 agonist comprising the structure of

R^1 is a TLR8 agonist. In certain embodiments, R^1 is a TLR8 agonist having the structure of



[00144] In certain embodiments, m is an integer of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12. In certain embodiments, m is an integer of 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10. In certain embodiments, m is an integer of 1, 2, 3, 4, 5, 6, 7, or 8. In certain embodiments, m is an integer of 1. In certain embodiments, m is an integer of 2. In certain embodiments, m is an integer of 3. In certain embodiments, m is an integer of 4. In certain embodiments, m is an integer of 5. In certain embodiments, m is an integer of 6. In certain embodiments, m is an integer of 7. In certain embodiments, m is an integer of 8. In certain embodiments, m is an integer of 9. In certain embodiments, m is an integer of 10. In certain embodiments, m is an integer of 11. In certain embodiments, m is an integer of 12. In certain embodiments, m is an integer of 13. In certain embodiments, m is an integer of 14. In certain embodiments, m is an integer of 15. In certain embodiments, m is an integer of 16.

[00145] In certain embodiments, the compound provided herein in a composition (*e.g.*, a pharmaceutical composition) has a drug-antibody ratio (DAR) ranging from about 0.5 to about 12, from about 1 to about 10, or from about 2 to about 8. In certain embodiments, the compound

provided herein in a composition (*e.g.*, a pharmaceutical composition) has a DAR ranging from about 0.5 to about 12. In certain embodiments, the compound provided herein in a composition (*e.g.*, a pharmaceutical composition) has a DAR ranging from about 1 to about 10. In certain embodiments, the compound provided herein in a composition (*e.g.*, a pharmaceutical composition) has a DAR ranging from about 2 to about 8. In certain embodiments, the compound provided herein in a composition (*e.g.*, a pharmaceutical composition) has a DAR of about 2, about 2.5, about 3, about 3.5, about 4, about 4.5, about 5, about 5.5, about 6, about 6.5, about 7, about 7.5, or about 8.

[00146] All combinations of the embodiments provided herein for the groups, R^1 , R^A , L, X, and m in the formulae described herein, including Formulae (I) to (XI), are within the scope of this disclosure.

[00147] In one embodiment, provided herein is an antibody-oligonucleotide conjugate of any one of Formulae (I) to (VIII); wherein each R^1 is independently a single-stranded CpG oligonucleotide of any one of SEQ ID NOs: 44 to 55 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising:

- (i) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (ii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 12; (b) a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 14; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 15; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 18;
- (iii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 23; (b) a CDRL2 having the amino acid sequence of SEQ ID NO: 24; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 25; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 26; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 28; or

- (iv) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 35; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 36; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 37; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 38; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 39.

[00148] In another embodiment, provided herein is an antibody-oligonucleotide conjugate of any one of Formulae (I) to (VIII); wherein each R¹ is independently a single-stranded CpG oligonucleotide of any one of SEQ ID NOs: 44 to 55 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising:

- (i) a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (ii) a light chain variable region of SEQ ID NO: 19 and a heavy chain variable region of SEQ ID NO: 20;
- (iii) a light chain variable region of SEQ ID NO: 29 and a heavy chain variable region of SEQ ID NO: 30; or
- (iv) a light chain variable region of SEQ ID NO: 40 and a heavy chain variable region of SEQ ID NO: 41.

[00149] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of any one of Formulae (I) to (VIII); wherein each R¹ is independently a single-stranded CpG oligonucleotide of any one of SEQ ID NOs: 44 to 55 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising:

- (i) a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11;
- (ii) a light chain of SEQ ID NO: 21 and a heavy chain of SEQ ID NO: 22;
- (iii) a light chain of SEQ ID NO: 33 and a heavy chain of SEQ ID NO: 34; or
- (iv) a light chain of SEQ ID NO: 42 and a heavy chain of SEQ ID NO: 43.

[00150] In one embodiment, provided herein is an antibody-oligonucleotide conjugate of any one of Formulae (IV) to (VIII); wherein each R¹ is independently a single-stranded CpG oligonucleotide of SEQ ID NO: 44, 45, 46, 53, or 55 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising:

- (i) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (ii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 12; (b) a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 14; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 15; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 18;
- (iii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 23; (b) a CDRL2 having the amino acid sequence of SEQ ID NO: 24; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 25; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 26; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 28; or
- (iv) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 35; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 36; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 37; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 38; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 39.

[00151] In another embodiment, provided herein is an antibody-oligonucleotide conjugate of any one of Formulae (IV) to (VIII); wherein each R¹ is independently a single-stranded CpG oligonucleotide of SEQ ID NO: 44, 45, 46, 53, or 55 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising:

- (i) a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (ii) a light chain variable region of SEQ ID NO: 19 and a heavy chain variable region of SEQ ID NO: 20;
- (iii) a light chain variable region of SEQ ID NO: 29 and a heavy chain variable region of SEQ ID NO: 30; or
- (iv) a light chain variable region of SEQ ID NO: 40 and a heavy chain variable region of SEQ

ID NO: 41.

[00152] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of any one of Formulae (IV) to (VIII); wherein each R¹ is independently a single-stranded CpG oligonucleotide of SEQ ID NO: 44, 45, 46, 53, or 55 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising:

- (i) a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11;
- (ii) a light chain of SEQ ID NO: 21 and a heavy chain of SEQ ID NO: 22;
- (iii) a light chain of SEQ ID NO: 33 and a heavy chain of SEQ ID NO: 34; or
- (iv) a light chain of SEQ ID NO: 42 and a heavy chain of SEQ ID NO: 43.

[00153] In one embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (IV); wherein each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 44, 45, 46, 53, or 55 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising:

- (i) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (ii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 12; (b) a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 14; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 15; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 18;
- (iii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 23; (b) a CDRL2 having the amino acid sequence of SEQ ID NO: 24; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 25; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 26; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 28; or
- (iv) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 35; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ

ID NO: 36; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 37; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 38; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 39.

[00154] In another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (IV); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 44, 45, 46, or 53 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising:

- (i) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (ii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 12; (b) a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 14; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 15; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 18; or
- (iii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 23; (b) a CDRL2 having the amino acid sequence of SEQ ID NO: 24; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 25; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 26; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 28.

[00155] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (IV); wherein:

- (i) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid

- sequence of SEQ ID NO: 5;
- (ii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
 - (iii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 44 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
 - (iv) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
 - (v) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 53 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
 - (vi) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1

- having the amino acid sequence of SEQ ID NO: 12; (b) a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 14; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 15; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 18;
- (vii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 23; (b) a CDRL2 having the amino acid sequence of SEQ ID NO: 24; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 25; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 26; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 28; or
- (viii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5.

[00156] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (IV); wherein:

- (i) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (ii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid

- sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (iii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 44 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (iv) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (v) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 53 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (vi) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 12; (b) a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 14; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 15; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and (f) a CDRH3

having the amino acid sequence of SEQ ID NO: 18; or

- (vii) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 23; (b) a CDRL2 having the amino acid sequence of SEQ ID NO: 24; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 25; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 26; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 28.

[00157] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (IV); wherein:

- (i) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (ii) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (iii) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 44 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (iv) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (v) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 53 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (vi) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 19 and a heavy chain variable region of SEQ ID NO: 20;
- (vii) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 29 and a heavy chain variable region of SEQ ID NO: 30;

or

- (viii) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7.

[00158] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (IV); wherein:

- (i) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (ii) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (iii) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 44 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (iv) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (v) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 53 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (vi) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 19 and a heavy chain variable region of SEQ ID NO: 20;

or

- (vii) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 29 and a heavy chain variable region of SEQ ID NO: 30.

[00159] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (IV); wherein:

- (i) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 8 and a heavy chain of SEQ ID NO: 9;
- (ii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 8 and a heavy chain of SEQ ID NO: 9;
- (iii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 44 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 8 and a heavy chain of SEQ ID NO: 9;
- (iv) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 8 and a heavy chain of SEQ ID NO: 9;
- (v) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 53 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 8 and a heavy chain of SEQ ID NO: 9;
- (vi) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 21 and a heavy chain of SEQ ID NO: 22;
- (vii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 31 and a heavy chain of SEQ ID NO: 32;
- (viii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11; or
- (ix) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11.

[00160] In still another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (IV); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 8 and a heavy chain of SEQ ID NO: 9.

[00161] In one embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VI); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 or 46 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising:

- (i) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (ii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 12; (b) a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 14; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 15; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 18;
- (iii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 23; (b) a CDRL2 having the amino acid sequence of SEQ ID NO: 24; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 25; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 26; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 28; or
- (iv) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 35; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 36; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 37; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 38; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 39.

[00162] In another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VI); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 or 46 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of

SEQ ID NO: 5.

[00163] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VI); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 or 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5.

[00164] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VI); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 or 46 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5.

[00165] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VI); wherein:

- (i) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (ii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (iii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7;
- (iv) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus

connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 19 and a heavy chain variable region of SEQ ID NO: 20; or.

- (v) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 29 and a heavy chain variable region of SEQ ID NO: 30.

[00166] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VI); wherein:

- (i) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7; or
- (ii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7.

[00167] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VI); wherein:

- (i) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 8 and a heavy chain of SEQ ID NO: 9;
- (ii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 8 and a heavy chain of SEQ ID NO: 9;
- (iii) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11;
- (iv) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 8 and a heavy chain of SEQ ID NO: 9;
- (v) each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of

- SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11;
- (vi) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 21 and a heavy chain of SEQ ID NO: 22;
 - (vii) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 33 and a heavy chain of SEQ ID NO: 34; or
 - (viii) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 42 and a heavy chain of SEQ ID NO: 43.

[00168] In still another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VI); wherein:

- (i) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 46 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 8 and a heavy chain of SEQ ID NO: 9; or
- (ii) each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11.

[00169] In one embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VII); wherein each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 or 46 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising:

- (i) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (ii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 12; (b) a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 14; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 15; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 16; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 17.

- NO: 15; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 18;
- (iii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 23; (b) a CDRL2 having the amino acid sequence of SEQ ID NO: 24; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 25; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 26; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 28; or
- (iv) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 35; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 36; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 37; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 38; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 39.

[00170] In another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VII); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'- or 5'-terminus connected to R^A via the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5.

[00171] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VII); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A via the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5.

[00172] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VII); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ

ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5.

[00173] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VII); wherein each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7.

[00174] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VII); wherein each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7.

[00175] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VII); wherein each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7.

[00176] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VII); wherein each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11.

[00177] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VII); wherein each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody

comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11.

[00178] In still another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VII); wherein each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11.

[00179] In one embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VIII); wherein each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 45 or 55 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising:

- (i) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (ii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 12; (b) a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 14; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 15; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 18;
- (iii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 23; (b) a CDRL2 having the amino acid sequence of SEQ ID NO: 24; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 25; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 26; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 28; or
- (iv) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 35; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 36; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 37; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 38; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 39.

[00180] In another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VIII); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 55 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5.

[00181] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VIII); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 55 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5.

[00182] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VIII); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 55 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5.

[00183] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VIII); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 55 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7.

[00184] In yet another embodiment, provided herein is an antibody-oligonucleotide

conjugate of Formula (VIII); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 55 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7.

[00185] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VIII); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 55 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7.

[00186] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VIII); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 55 with its 3'- or 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11.

[00187] In yet another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VIII); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 55 with its 3'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11.

[00188] In still another embodiment, provided herein is an antibody-oligonucleotide conjugate of Formula (VIII); wherein each R^1 is a single-stranded CpG oligonucleotide of SEQ ID NO: 55 with its 5'-terminus connected to R^A *via* the X-L moiety; and R^A is an antibody comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11.

[00189] In one embodiment, provided herein is an antibody-immunostimulator conjugate of any one of Formulae (I) to (III) and (IX) to (XI); wherein R^A is an antibody comprising:

- (i) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;

- (ii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 12; (b) a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 14; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 15; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 18;
- (iii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 23; (b) a CDRL2 having the amino acid sequence of SEQ ID NO: 24; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 25; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 26; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 28; or
- (iv) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 35; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 36; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 37; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 38; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 39.

[00190] In one embodiment, provided herein is an antibody-immunostimulator conjugate of Formula (IX); wherein R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5. In another embodiment, provided herein is an antibody-immunostimulator conjugate of Formula (IX); wherein R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7. In yet another embodiment, provided herein is an antibody-immunostimulator conjugate of Formula (IX); wherein R^A is an antibody comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11.

[00191] In one embodiment, provided herein is an antibody-immunostimulator conjugate of Formula (X); wherein R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence

of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5. In another embodiment, provided herein is an antibody-immunostimulator conjugate of Formula (X); wherein R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7. In yet another embodiment, provided herein is an antibody-immunostimulator conjugate of Formula (X); wherein R^A is an antibody comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11.

[00192] In one embodiment, provided herein is an antibody-immunostimulator conjugate of Formula (XI); wherein R^A is an antibody comprising (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5. In another embodiment, provided herein is an antibody-immunostimulator conjugate of Formula (XI); wherein R^A is an antibody comprising a light chain variable region of SEQ ID NO: 6 and a heavy chain variable region of SEQ ID NO: 7. In yet another embodiment, provided herein is an antibody-immunostimulator conjugate of Formula (X); wherein R^A is an antibody comprising a light chain of SEQ ID NO: 10 and a heavy chain of SEQ ID NO: 11.

[00193] In one embodiment, provided herein is one of antibody-immunostimulator conjugates **AOC-A1** to **AOC-A10**, **AOC-B1** to **AOC-B8**, **AOC-C1**, **AOC-C2**, **AOC-D1**, and **ISAC-A1** to **ISAC-A3**.

[00194] In certain embodiments, a compound provided herein is isolated or purified. In certain embodiments, a compound provided herein has a purity of at least about 90%, at least about 95%, at least about 98%, at least about 99%, or at least about 99.5% by weight.

[00195] The compounds provided herein are intended to encompass all possible stereoisomers unless a particular stereochemistry is specified. Where a compound provided herein contains an alkenyl group, the compound may exist as one or mixture of geometric *cis/trans* (or *Z/E*) isomers. Where structural isomers are interconvertible, the compound may exist as a single tautomer or a mixture of tautomers. This can take the form of proton

tautomerism in the compound that contains, for example, an imino, keto, or oxime group; or so-called valence tautomerism in the compound that contains an aromatic moiety. It follows that a single compound may exhibit more than one type of isomerism.

[00196] A compound provided herein can be enantiomerically pure, such as a single enantiomer or a single diastereomer, or be stereoisomeric mixtures, such as a mixture of enantiomers, *e.g.*, a racemic mixture of two enantiomers; or a mixture of two or more diastereomers. As such, one of ordinary skill in the art will recognize that administration of a compound in its (*R*) form is equivalent, for the compound that undergoes epimerization *in vivo*, to administration of the compound in its (*S*) form. Conventional techniques for the preparation/isolation of individual enantiomers include synthesis from a suitable optically pure precursor, asymmetric synthesis from achiral starting materials, or resolution of an enantiomeric mixture, for example, chiral chromatography, recrystallization, resolution, diastereomeric salt formation, or derivatization into diastereomeric adducts followed by separation.

[00197] When a compound provided herein contains an acidic or basic moiety, it can also be provided as a pharmaceutically acceptable salt. *See*, Berge *et al.*, *J. Pharm. Sci.* **1977**, *66*, 1-19; *Handbook of Pharmaceutical Salts: Properties, Selection, and Use*, 2nd ed.; Stahl and Wermuth Eds.; John Wiley & Sons, 2011. In certain embodiments, a pharmaceutically acceptable salt of a compound provided herein is a solvate. In certain embodiments, a pharmaceutically acceptable salt of a compound provided herein is a hydrate.

[00198] Suitable acids for use in the preparation of pharmaceutically acceptable salts of a compound provided herein include, but are not limited to, acetic acid, 2,2-dichloroacetic acid, acylated amino acids, adipic acid, alginic acid, ascorbic acid, L-aspartic acid, benzenesulfonic acid, benzoic acid, 4-acetamidobenzoic acid, boric acid, (+)-camphoric acid, camphorsulfonic acid, (+)-(1*S*)-camphor-10-sulfonic acid, capric acid, caproic acid, caprylic acid, cinnamic acid, citric acid, cyclamic acid, cyclohexanesulfamic acid, dodecylsulfuric acid, ethane-1,2-disulfonic acid, ethanesulfonic acid, 2-hydroxy-ethanesulfonic acid, formic acid, fumaric acid, galactaric acid, gentisic acid, glucoheptonic acid, D-gluconic acid, D-glucuronic acid, L-glutamic acid, α -oxoglutaric acid, glycolic acid, hippuric acid, hydrobromic acid, hydrochloric acid, hydroiodic acid, (+)-L-lactic acid, ($\pm$)-DL-lactic acid, lactobionic acid, lauric acid, maleic acid, (-)-L-malic

acid, malonic acid, (±)-DL-mandelic acid, methanesulfonic acid, naphthalene-2-sulfonic acid, naphthalene-1,5-disulfonic acid, 1-hydroxy-2-naphthoic acid, nicotinic acid, nitric acid, oleic acid, orotic acid, oxalic acid, palmitic acid, pamoic acid, perchloric acid, phosphoric acid, L-pyroglutamic acid, saccharic acid, salicylic acid, 4-amino-salicylic acid, sebacic acid, stearic acid, succinic acid, sulfuric acid, tannic acid, (+)-L-tartaric acid, thiocyanic acid, *p*-toluenesulfonic acid, undecylenic acid, and valeric acid.

[00199] Suitable bases for use in the preparation of pharmaceutically acceptable salts of a compound provided herein include, but are not limited to, inorganic bases, such as magnesium hydroxide, calcium hydroxide, potassium hydroxide, zinc hydroxide, or sodium hydroxide; and organic bases, such as primary, secondary, tertiary, and quaternary, aliphatic and aromatic amines, including, but not limited to, L-arginine, benethamine, benzathine, choline, deanol, diethanolamine, diethylamine, dimethylamine, dipropylamine, diisopropylamine, 2-(diethylamino)-ethanol, ethanolamine, ethylamine, ethylenediamine, isopropylamine, *N*-methyl-glucamine, hydrabamine, 1*H*-imidazole, L-lysine, morpholine, 4-(2-hydroxyethyl)-morpholine, methylamine, piperidine, piperazine, propylamine, pyrrolidine, 1-(2-hydroxyethyl)-pyrrolidine, pyridine, quinuclidine, quinoline, isoquinoline, triethanolamine, trimethylamine, triethylamine, *N*-methyl-D-glucamine, 2-amino-2-(hydroxymethyl)-1,3-propanediol, and tromethamine.

Pharmaceutical Compositions

[00200] In one embodiment, provided herein is a pharmaceutical composition, comprising a compound provided herein, *e.g.*, a compound of Formula (I), or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; and a pharmaceutically acceptable excipient.

[00201] In one embodiment, the pharmaceutical composition provided herein is formulated in a dosage form for parenteral administration. In another embodiment, the pharmaceutical composition provided herein is formulated in a dosage form for intravenous administration. In yet another embodiment, the pharmaceutical composition provided herein is formulated in a dosage form for intramuscular administration. In still another embodiment, the pharmaceutical composition provided herein is formulated in a dosage form for subcutaneous

administration.

[00202] The pharmaceutical composition provided herein can be provided in a unit-dosage form or multiple-dosage form. A unit-dosage form, as used herein, refers to physically discrete unit suitable for administration to a subject, and packaged individually as is known in the art. Each unit-dose contains a predetermined quantity of an active ingredient(s) (*e.g.*, a compound provided herein) sufficient to produce the desired therapeutic effect, in association with the required pharmaceutical excipient(s). Examples of a unit-dosage form include, but are not limited to, an ampoule and syringe. A unit-dosage form may be administered in fractions or multiples thereof. A multiple-dosage form is a plurality of identical unit-dosage forms packaged in a single container to be administered in a segregated unit-dosage form. Examples of a multiple-dosage form include, are not limited to, a vial or bottle of pints or gallons.

[00203] The pharmaceutical composition provided herein can be administered at once or multiple times at intervals of time. It is understood that the precise dosage and duration of treatment may vary with the age, weight, and condition of the subject being treated, and may be determined empirically using known testing protocols or by extrapolation from *in vivo* or *in vitro* test or diagnostic data. It is further understood that for any particular individual, specific dosage regimens should be adjusted over time according to the subject's need and the professional judgment of the person administering or supervising the administration of the pharmaceutical composition.

Methods of Use

[00204] In one embodiment, provided herein is a method of treating, preventing, or ameliorating one or more symptoms of an HBV infection in a subject, comprising administering to the subject in need thereof a therapeutically effective amount of a compound of Formula (I), or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

[00205] In certain embodiments, the HBV infection is an acute HBV infection. In certain embodiments, the HBV infection is a chronic HBV infection.

[00206] In certain embodiments, the subject is a mammal. In certain embodiments, the

subject is a human.

[00207] In certain embodiments, the therapeutically effective amount of a compound provided herein is ranging from about 0.1 mg/kg every four weeks to about 20 mg/kg every week, from about 0.2 mg/kg every four weeks to about 10 mg/kg every week, from about 0.5 mg/kg every four weeks to about 5 mg/kg every week, or from about 1 mg/kg every four weeks to about 2 mg/kg every week.

[00208] In one embodiment, the therapeutically effective amount of a compound provided herein is ranging from about 0.1 mg/kg every four weeks to about 20 mg/kg every week. In another embodiment, the therapeutically effective amount of a compound provided herein is ranging from about 0.2 mg/kg every four weeks to about 10 mg/kg every week. In yet another embodiment, the therapeutically effective amount of a compound provided herein is ranging from about 0.5 mg/kg every four weeks to about 5 mg/kg every week. In yet another embodiment, the therapeutically effective amount of a compound provided herein is ranging from about 1 mg/kg every four weeks to about 2 mg/kg every week. In still another embodiment, the therapeutically effective amount of a compound provided herein is about 1, about 1.5, about 2, about 2.5, about 3, about 3.5, about 4, about 4.5, or about 5 mg/kg every three weeks.

[00209] Depending on the disorder, disease, or condition to be treated and the subject's condition, a compound provided herein may be administered by parenteral (*e.g.*, intramuscular, intraperitoneal, intravenous, CIV, intracisternal injection or infusion, subcutaneous injection, or implant) routes of administration. A compound provided herein may be formulated in suitable dosage unit with a pharmaceutically acceptable excipient, carrier, adjuvant, or vehicle, appropriate for the route of administration.

[00210] In one embodiment, a compound provided herein is administered parenterally. In another embodiment, a compound provided herein is administered intravenously. In yet another embodiment, a compound provided herein is administered intramuscularly. In still another embodiment, a compound provided herein is administered subcutaneously.

[00211] A compound provided herein can be delivered as a single dose such as, *e.g.*, a

single bolus injection, or over time such as, *e.g.*, continuous infusion over time or divided bolus doses over time. A compound provided herein can be administered repetitively if necessary, for example, until the subject experiences stable disease or regression, or until the patient experiences disease progression or unacceptable toxicity.

[00212] A compound provided herein can be administered once a week, once every two weeks, once every three weeks, once every four weeks, once every five weeks, or once every six weeks. In one embodiment, a compound provided herein is administered once a week. In another embodiment, a compound provided herein is administered once every two weeks. In yet another embodiment, a compound provided herein is administered once every two weeks. In yet another embodiment, a compound provided herein is administered once every three weeks. In yet another embodiment, a compound provided herein is administered once every four weeks. In yet another embodiment, a compound provided herein is administered once every five weeks. In yet another embodiment, a compound provided herein is administered once every six weeks.

[00213] A compound provided herein can also be provided as an article of manufacture using packaging materials well known to those of skill in the art. *See, e.g.*, U.S. Pat. Nos. 5,525,907; 5,052,558; and 5,055,252. Examples of pharmaceutical packaging materials include, but are not limited to, blister packs, bottles, tubes, inhalers, pumps, bags, vials, containers, syringes, and any packaging material suitable for a selected formulation and intended mode of administration and treatment.

[00214] In certain embodiments, provided herein is a kit which, when used by a medical practitioner, can simplify the administration of an appropriate amount of a compound provided herein as an active ingredient to a subject. In certain embodiments, the kit provided herein includes a container and a dosage form of a compound provided herein.

[00215] Kits provided herein can further include pharmaceutically acceptable vehicles that can be used to administer one or more active ingredients. For example, if an active ingredient is provided in a solid form that must be reconstituted for parenteral administration, the kit can comprise a sealed container of a suitable vehicle in which the active ingredient can be dissolved to form a particulate-free sterile solution that is suitable for parenteral administration. Examples of pharmaceutically acceptable vehicles include, but are not limited to: aqueous vehicles,

including, but not limited to, water for injection USP, sodium chloride injection, Ringer's injection, dextrose injection, dextrose and sodium chloride injection, and lactated Ringer's injection; water-miscible vehicles, including, but not limited to, ethyl alcohol, polyethylene glycol, and polypropylene glycol; and non-aqueous vehicles, including, but not limited to, corn oil, cottonseed oil, peanut oil, sesame oil, ethyl oleate, isopropyl myristate, and benzyl benzoate.

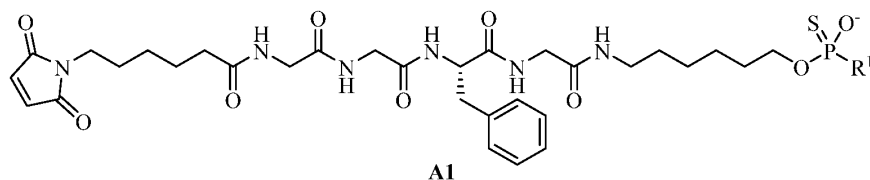
[00216] The disclosure will be further understood by the following non-limiting examples.

EXAMPLES

[00217] As used herein, the symbols and conventions used in these processes, schemes and examples, regardless of whether a particular abbreviation is specifically defined, are consistent with those used in the contemporary scientific literature, for example, the Journal of the American Chemical Society, the Journal of Medicinal Chemistry, or the Journal of Biological Chemistry. Specifically, but without limitation, the following abbreviations may be used in the examples and throughout the specification: g (grams); mg (milligrams); mL (milliliters); μ L (microliters); mM (millimolar); μ M (micromolar); mmol (millimoles); h (hour or hours); min (minute or minutes); Su (succinimido); TCEP (tris(2-carboxyethyl)phosphine); TEAA (triethylammonium acetate); HPLC (high-performance liquid chromatography); prep-HPLC (preparative HPLC); SDS-PAGE (sodium dodecylsulfate polyacrylamide gel electrophoresis); and SAX-HPLC (strong anion exchange chromatography HPLC).

[00218] For all of the following examples, standard work-up and purification methods known to those skilled in the art can be utilized. Unless otherwise indicated, all temperatures are expressed in $^{\circ}$ C (degrees Centigrade). All reactions are conducted at room temperature unless otherwise specified. Synthetic methodologies illustrated herein are intended to exemplify the applicable chemistry through the use of specific examples and are not indicative of the scope of the disclosure.

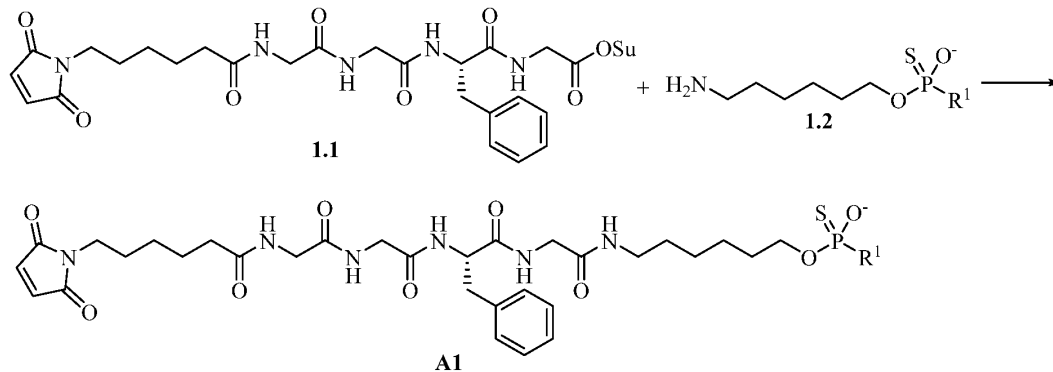
Example 1

Preparation of Functionalized CpG Oligodeoxynucleotide **A1**

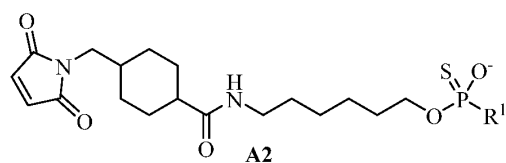
[00219] Compound **A1** was synthesized as shown in Scheme 1, wherein R^1 is a CpG oligodeoxynucleotide having the nucleotide sequence of SEQ ID NO: 44, 45, 46, or 53; and wherein CpG oligodeoxynucleotides **1.2** was prepared by solid-phase oligonucleotide synthesis.

[00220] A mixture of compound **1.1** (5 mmol) and oligodeoxynucleotide **1.2** (1 mmol) in a phosphate buffer (50 mL) at pH 8 was stirred at 35 °C for 120 min. The reaction mixture was then diluted with TEAA. The resulting precipitates were collected and purified by reverse-phase prep-HPLC, followed by ultrafiltration and lyophilization to afford compound **A1**.

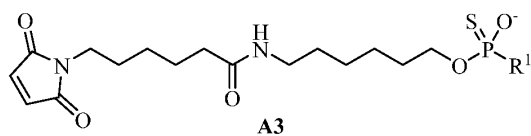
Scheme 1



[00221] Functionalized CpG oligodeoxynucleotide **A2** is prepared similarly, wherein R^1 is a CpG oligodeoxynucleotide having the nucleotide sequence of SEQ ID NO: 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, or 55.

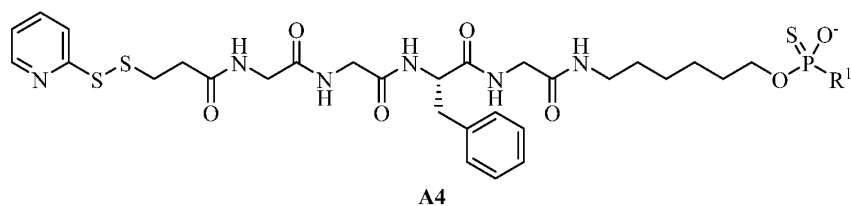


[00222] Functionalized CpG oligodeoxynucleotide **A3** was prepared similarly, wherein R¹ is a CpG oligodeoxynucleotide having the nucleotide sequence of SEQ ID NO: 45 or 46.



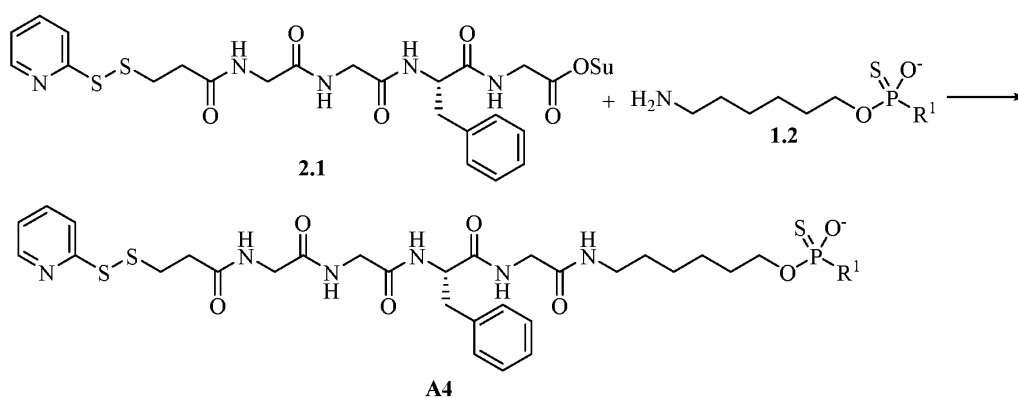
Example 2

Preparation of Functionalized CpG Oligodeoxynucleotide **A4**



[00223] Compound **A4** was synthesized as shown in Scheme 2, wherein R¹ is a CpG oligodeoxynucleotide having the nucleotide sequence of SEQ ID NO: 45.

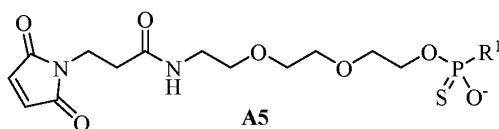
Scheme 2



[00224] A mixture of oligodeoxynucleotide **1.2** (1 mmol) and compound **2.1** (5 mmol) and in a phosphate buffer (50 mL) at pH 8 was stirred at 35 °C for 120 min. The reaction mixture was then diluted with TEAA. The resulting precipitates were collected and purified by reverse-phase prep-HPLC, followed by ultrafiltration and lyophilization to afford compound **A4**.

Example 3

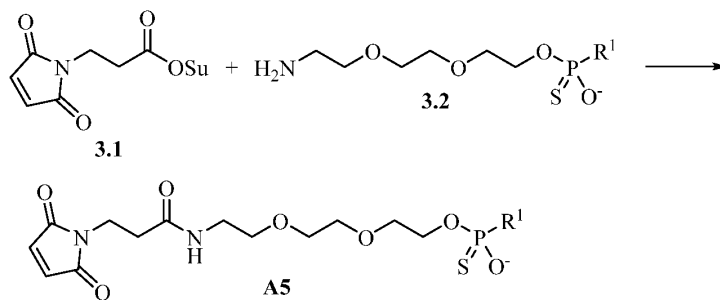
Preparation of Functionalized CpG Oligodeoxynucleotide **A5**



[00225] Compound **A5** was synthesized as shown in Scheme 3, wherein R¹ is a CpG oligodeoxynucleotide having the nucleotide sequence of SEQ ID NO: 55.

[00226] To a solution of oligodeoxynucleotide **3.2** (0.1 g/mL) in a PBS buffer (pH 8) was added compound **3.1** (3-5 equiv.) in the same volume of DMF. After incubating at 35 °C for 2 h, the reaction mixture was precipitated and purified by prep-HPLC (TEAA system). The fraction was freeze-dried, salt exchanged, desalted by ultrafiltration, and lyophilized to afford compound **A5**.

Scheme 3



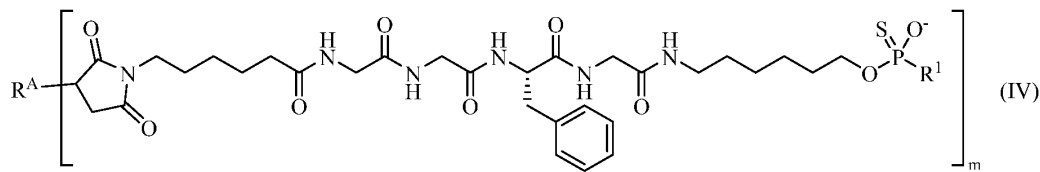
Example 4

Preparation of Anti-HBsAg/CpG Oligonucleotide Conjugates

[00227] A monoclonal anti-HBsAg antibody was buffer exchanged into a 20 mM sodium phosphate buffered saline solution and further diluted to 2-10 mg/mL in the same buffer. Eight

molar equivalences of TCEP were added to reduce the interchain disulfide bonds of the anti-HBsAg antibody at pH 4-6. Six molar equivalents of a functionalized CpG oligodeoxynucleotide (*e.g.*, **A1**, **A3**, or **A5**) (10 mg/mL) were added to the reduced anti-HBsAg antibody solution and incubated for 1-12 h at room temperature. Excess TCEP and functionalized CpG oligodeoxynucleotide were removed *via* a gel filtration chromatography or ultrafiltration to afford an anti-HBsAg/CpG oligonucleotide conjugate, which was analyzed by SDS-PAGE (FIG. 1) to determine its drug-to-antibody ratio (DAR). The anti-HBsAg/CpG oligonucleotide conjugates were analyzed by SAX-HPLC as shown in FIG. 2 for anti-HBsAg/CpG oligonucleotide conjugate **AOC-A1**. The results are summarized in Tables 1 to 3, wherein each anti-HBsAg/CpG oligonucleotide conjugate was determined to have a DAR of about 4.

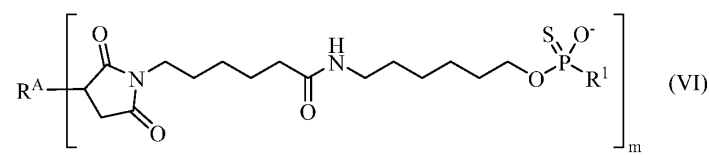
TABLE 1. Anti-HBsAg/CpG Oligonucleotide Conjugates



Conjugate	R ^A	R ¹		m
		Sequence	Connection	
AOC-A1	mAnti-HBsAg 1 (SEQ ID NOs: 8 & 9)	SEQ ID NO: 46	3'-Terminus	about 4
AOC-A2	mAnti-HBsAg 1 (SEQ ID NOs: 8 & 9)	SEQ ID NO: 46	5'-Terminus	about 4
AOC-A3	mAnti-HBsAg 1 (SEQ ID NOs: 8 & 9)	SEQ ID NO: 44	3'-Terminus	about 4
AOC-A4	mAnti-HBsAg 1 (SEQ ID NOs: 8 & 9)	SEQ ID NO: 45	3'-Terminus	about 4
AOC-A5	mAnti-HBsAg 1 (SEQ ID NOs: 8 & 9)	SEQ ID NO: 53	3'-Terminus	about 4
AOC-A6	hAnti-HBsAg 2 (SEQ ID NOs: 21 & 22)	SEQ ID NO: 46	3'-Terminus	about 4
AOC-A7	mAnti-HBsAg 3 (SEQ ID NOs: 31 & 32)	SEQ ID NO: 46	3'-Terminus	about 4

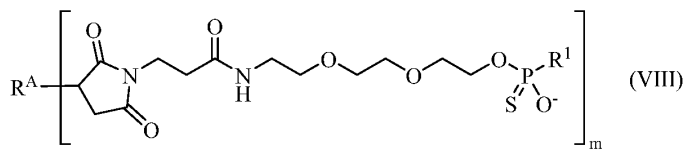
Conjugate	R ^A	R ¹		m
		Sequence	Connection	
AOC-A8	hAnti-HBsAg 1 (SEQ ID NOs: 10 & 11)	SEQ ID NO: 45	3'-Terminus	about 4
AOC-A9	hAnti-HBsAg 1 (SEQ ID NOs: 10 & 11)	SEQ ID NO: 46	3'-Terminus	about 4
AOC-A10	mAnti-HBsAg 1 (SEQ ID NOs: 8 & 9)	SEQ ID NO: 45	5'-Terminus	about 4

TABLE 2. Anti-HBsAg/CpG Oligonucleotide Conjugates



Conjugate	R ^A	R ¹		m
		Sequence	Connection	
AOC-B1	mAnti-HBsAg 1 (SEQ ID NOs: 8 & 9)	SEQ ID NO: 46	3'-Terminus	about 4
AOC-B2	hAnti-HBsAg 1 (SEQ ID NOs: 10 & 11)	SEQ ID NO: 45	3'-Terminus	about 4
AOC-B3	mAnti-HBsAg 1 (SEQ ID NOs: 8 & 9)	SEQ ID NO: 45	3'-Terminus	about 4
AOC-B4	mAnti-HBsAg 1 (SEQ ID NOs: 8 & 9)	SEQ ID NO: 45	5'-Terminus	about 4
AOC-B5	hAnti-HBsAg 1 (SEQ ID NOs: 10 & 11)	SEQ ID NO: 45	5'-Terminus	about 4
AOC-B6	hAnti-HBsAg 2 (SEQ ID NOs: 21 & 22)	SEQ ID NO: 45	5'-Terminus	about 4
AOC-B7	hAnti-HBsAg 3 (SEQ ID NOs: 33 & 34)	SEQ ID NO: 45	5'-Terminus	about 4
AOC-B8	hAnti-HBsAg 4 (SEQ ID NOs: 42 & 43)	SEQ ID NO: 45	5'-Terminus	about 4

TABLE 3. Anti-HBsAg/CpG Oligonucleotide Conjugate



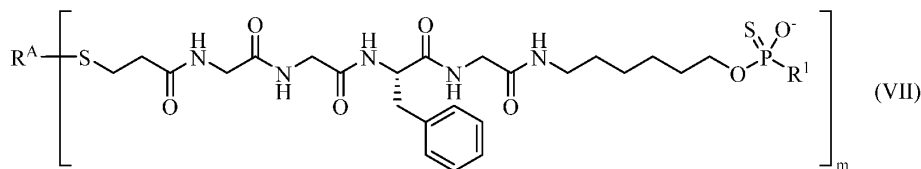
Conjugate	R ^A	R ¹		m
		Sequence	Connection	
AOC-D1	hAnti-HBsAg 1 (SEQ ID NOs: 10 & 11)	SEQ ID NO: 55	5'-Terminus	about 4

Example 5

Preparation of Anti-HBsAg/CpG Oligonucleotide Conjugates

[00228] A monoclonal anti-HBsAg antibody was buffer exchanged into a 20 mM sodium phosphate buffered saline solution and further diluted to 2-10 mg/mL in the same buffer. Eight molar equivalences of TCEP were added to reduce the interchain disulfide bonds of the anti-HBsAg antibody at pH 4-6. Excess TCEP was then removed *via* a gel filtration chromatography or ultrafiltration. Six molar equivalents of a functionalized CpG oligodeoxynucleotide (*e.g.*, **A4**) (10 mg/mL) were added to the reduced antibody solution and incubated for 1-12 h at room temperature. Excess functionalized CpG oligodeoxynucleotide was removed *via* a gel filtration chromatography or ultrafiltration to afford an anti-HBsAg/CpG oligonucleotide conjugate, which was analyzed by SDS-PAGE to determine its drug-to-antibody ratio (DAR). The result is summarized in Table 4, wherein each anti-HBsAg/CpG oligonucleotide conjugate was determined to have a DAR of about 4.

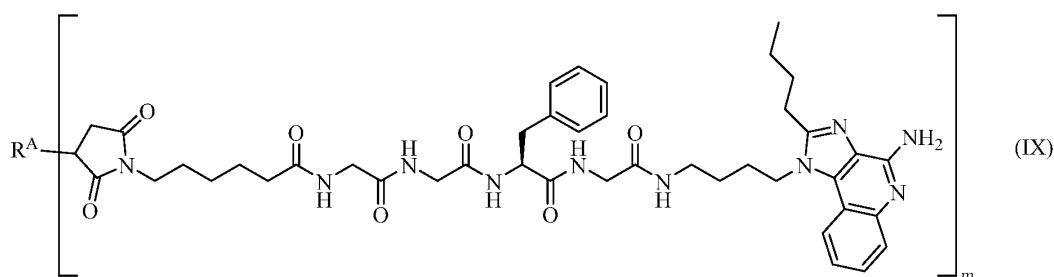
TABLE 4. Anti-HBsAg/CpG Oligonucleotide Conjugate



Conjugate	R ^A	R ¹		m
		Sequence	Connection	
AOC-C1	mAnti-HBsAg 1 (SEQ ID NOs: 8 & 9)	SEQ ID NO: 45	3'-Terminus	about 4
AOC-C2	mAnti-HBsAg 1 (SEQ ID NOs: 8 & 9)	SEQ ID NO: 45	5'-Terminus	about 4

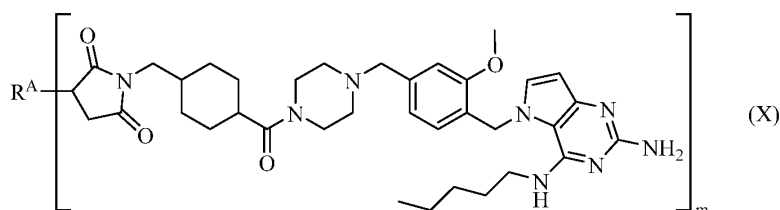
Example 6

Preparation of Anti-HBsAg/TLR-7 Agonist Conjugate ISAC-A1



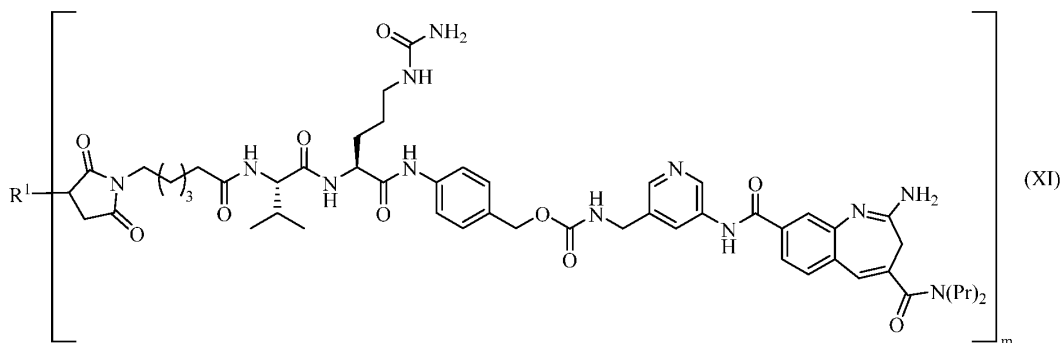
[00229] Monoclonal anti-HBsAg 1 (SEQ ID NOS: 8 and 9) was buffer exchanged into a 20 mM sodium phosphate and 0.5 M EDTA buffered saline solution, and further diluted to 2-10 mg/mL in the same buffer. Six molar equivalences of TCEP were added to reduce the interchain disulfide bonds of the anti-HBsAg at pH 4-6. Six molar equivalents of functionalized TLR-7 agonist, (*S*)-*N*-(16-(4-amino-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)-7-benzyl-2,5,8,11-tetraoxo-3,6,9,12-tetraazahexadecyl)-6-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)hexanamide (10 mg/mL) were added to the reduced anti-HBsAg solution and incubated for 1-12 h at room temperature. Excess TCEP and functionalized TLR-7 agonist were removed *via* a gel filtration chromatography or ultrafiltration to afford anti-HBsAg/TLR-7 agonist conjugate **ISAC-A1** (*m* = about 4), which was determined by HIC-HPLC or mass spectrometry to have a DAR of about 4.

Example 7

Preparation of Anti-HBsAg/TLR-7 Agonist Conjugate **ISAC-A2**

[00230] Anti-HBsAg/TLR-7 agonist conjugate **ISAC-A2** (m is about 4) was prepared from monoclonal anti-HBsAg 1 (SEQ ID NOs: 10 and 11) and functionalized TLR-7 agonist, 1-((4-(4-(4-((2-amino-4-(pentylamino)-5H-pyrrolo[3,2-*d*]pyrimidin-5-yl)methyl)-3-methoxybenzyl)piperazine-1-carbonyl)cyclohexyl)methyl)-1*H*-pyrrole-2,5-dione as described in Example 6. Anti-HBsAg/TLR-7 agonist conjugate **ISAC-A2** was determined by HIC-HPLC or mass spectrometry to have a DAR of about 4.

Example 8

Preparation of Anti-HBsAg/TLR-8 Agonist Conjugate **ISAC-A3**

[00231] Monoclonal anti-HBsAg 1 (SEQ ID NOS: 10 and 11) was buffer exchanged into a 20 mM sodium phosphate and 0.5 M EDTA buffered saline solution, and further diluted to 2-10 mg/mL in the same buffer. Six molar equivalences of TCEP were added to reduce the interchain disulfide bonds of the anti-HBsAg at pH 4-6. Six molar equivalents of functionalized TLR-8 agonist, 4-((*S*)-2-((*S*)-2-(6-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)-hexanamido)-3-methylbutanamido)-5-ureidopentanamido)benzyl ((5-(2-amino-4-(dipropyl-carbamoyl)-3*H*-

benzo[*b*]azepine-8-carboxamido)pyridin-3-yl)methyl)carbamate (10 mg/mL) were added to the reduced anti-HBsAg solution and incubated for 1-12 h at room temperature. Excess TCEP and functionalized TLR-8 agonist were removed *via* a gel filtration chromatography or ultrafiltration to afford anti-HBsAg/TLR-8 agonist conjugate **ISAC-A3** (m = about 4), which was determined by HIC-HPLC or mass spectrometry to have a DAR of about 4.

Example 9

Determination of the Binding Affinities of Anti-HBsAg/CpG Oligonucleotide Conjugates to Human HBsAg

[00232] The binding affinities of hAnti-HBsAg 1 and hAnti-HBsAg/CpG oligonucleotide conjugates **AOC-A8** and **AOC-B2** to a human HBsAg (SEQ ID NO: 56) were determined using an ELISA. Briefly, the human HBsAg was coated onto the wells of an ELISA plate at 4 °C overnight. Human hAnti-HBsAg 1, **AOC-A8**, and **AOC-B2** were added at the predetermined concentrations. After the ELISA plate was incubated at 25 °C for 1 h, a horseradish (HRP) solution was added to each well and the place was incubated at 25 °C for another 1 h. A TMB substrate was added. After the addition of a terminating solution, the ELISA plate was read with an ELISA plate reader at 450 nm. The binding affinities were calculated and the results are summarized in Table 5.

TABLE 5. Binding Affinities of Anti-HBsAg/CpG Oligonucleotide Conjugates

	Anti-HBsAg	CpG Oligonucleotide	Affinity (ng/mL)
hAnti-HBsAg 1	SEQ ID NOs: 10 & 11		19
AOC-A8	SEQ ID NOs: 10 & 11	SEQ ID NO: 45	21
AOC-B2	SEQ ID NOs: 10 & 11	SEQ ID NO: 45	22

Example 10

Antiviral Effects of Anti-HBsAg Antibody/TLR Conjugates on HBV-infected Cells

[00233] The hepatoma cells HepG2.2.15 with stable HBsAg expression were seeded in 96-well cell culture plates at a density of 8,000 cells per well and then cultured under 5% CO₂ at 37 °C overnight. On Day 1, the medium was discarded and PBMC was added to the 96-well plates containing HepG2.2.15 cells. Anti-HBsAg/TLR Agonist Conjugates **AOC-B5**, **AOC-B6**,

AOC-B7, **ISAC-A2**, **ISAC-A3**, and TLR9 agonist 2 (SEQ ID NO: 45), each in the amount of 100 μL , and a commercial human CD3/CD28 T cell activator as a positive control in the amount of 2 μL were each added separately to the wells of the 96-well plates. The final concentrations of each **AOC-B5**, **AOC-B6**, **AOC-B7**, and **ISAC-A2** were 120 $\mu\text{g/mL}$ (A), 12 $\mu\text{g/mL}$ (B), and 1.2 $\mu\text{g/mL}$ (C). The final concentrations of **ISAC-A3** were 780 $\mu\text{g/mL}$ (A), 78 $\mu\text{g/mL}$ (B), and 7.8 $\mu\text{g/mL}$ (C). The final concentration of TLR9 agonist 2 were 38 $\mu\text{g/mL}$ (A), 3.8 $\mu\text{g/mL}$ (B), and 0.38 $\mu\text{g/mL}$ (A). The medium (100 μL) was added to each well of the 96-well plates. On Day 7, the culture supernatant was collected and analyzed for HBsAg. The results are summarized in Table 6.

TABLE 6. Average HBsAg Inhibition (%) of Anti-HBsAg Antibody/TLR Agonist Conjugates in HBV-infected Cells

Compound	PBMC Donor 1			PBMC Donor 2		
	Conc. A	Conc. B	Conc. C	Conc. A	Conc. B	Conc. C
AOC-B5	100	95	80	100	93	74
AOC-B6	100	100	100	100	100	100
AOC-B7	100	94	76	100	94	81
ISAC-A2	99	92	70	98	86	92
ISAC-A3	86	86	91	82	74	86
TLR9 agonist 2	22	16	17	6	2	16
CD3/CD28 T cell activator	29	—	—	44	—	—

Example 11

Anti-HBV Effects of Anti-HBsAg/TLR Agonist Conjugates in AAV-HBV Mouse Model

[00234] C57BL/6 male mice were injected *via* the tail vein of each mouse with AAV8-HBV (genotype D) (1×10^{10} viral genome) in PBS (200 μL). Twenty eight days (Day 0) after the viral injection, the mice were randomized into three groups with four mice per group. mAnti-HBsAg 1 and mAnti-HBsAg/TLR agonist conjugate **AOC-A1** were administered intravenously at 15 mg/kg to the mice in Groups 1 and 2, respectively, on Day 0, 21, 42, 62, and 84. PBS (control) was administered intravenously to the mice in Group 3. Blood samples were collected from the mice in each group and analyzed for HBsAg, anti-HBs, ALT, and cytokine

levels. On Day 128, the mice were euthanized, and liver samples were collected and analyzed for hepatic HBcAg levels using an IHC method. The results are shown in FIGS. 3 to 6 and summarized in Table 7.

TABLE 7. Effects of mAnti-HBsAg/TLR Agonist Conjugate **AOC-A1** on Cytokine Levels

Cytokine	Time	AOC-A1	PBS
IFN α (pg/mL)	Day 1	45	36
	Day 3	106	38
	Day 42	39	38
TNF α (pg/mL)	Day 1	18	9.4
	Day 3	34	9.4
	Day 42	97	10
IFN γ (pg/mL)	Day 1	46	4.8
	Day 3	178	4.8
	Day 42	70	4.9
IL-6 (pg/mL)	Day 1	37	36
	Day 3	142	110
	Day 42	184	49
IL-1 β (pg/mL)	Day 1	5	5
	Day 3	7.6	5
	Day 42	5	5

[00235] Anti-HBsAg/TLR agonist conjugates **AOC-A1**, **AOC-A2**, **AOC-A3**, **AOC-A4**, **AOC-A5**, **AOC-A6**, **AOC-A7**, **AOC-A9**, **AOC-B1**, **AOC-C1**, and **ISAC-A1** were also evaluated for their anti-HBV activities. On Day 0, 21, 42, and 63, an anti-HBsAg conjugate was administered intravenously at 15 mg/kg to each mouse in a treatment group. PBS was administered intravenously to each mouse in a control group. Blood samples were collected from the mice and analyzed for HBsAg and anti-HBs levels. On Day 106, the mice were euthanized, and liver samples were collected and analyzed for hepatic HBcAg levels using an IHC method. The results are summarized in FIGS. 7 to 9.

[00236] Additionally, anti-HBsAg/TLR agonist conjugates **AOC-A4**, **AOC-A10**, **AOC-B3**, **AOC-B4**, **AOC-C1**, and **AOC-C2** were evaluated for their anti-HBV activities. On Day 0,

21, 42, and 63, an anti-HBsAg/TLR agonist conjugate was administered intravenously at 15 mg/kg to each mouse in a treatment group. PBS was administered intravenously to each mouse in a control group. Blood samples were collected from the mice and analyzed for HBsAg and anti-HBs levels. On Day 84, the mice were euthanized, and liver samples were collected and analyzed for hepatic HBcAg levels using an IHC method. The results are summarized in FIGS. 10 to 12.

[00237] Furthermore, anti-HBsAg/TLR agonist conjugates **AOC-B8**, **AOC-D1**, and **ISAC-A2**, as well as a CpG oligonucleotide (SEQ ID NO: 45) were evaluated for their anti-HBV activities. On Day 0, 21, and 42, anti-HBsAg/TLR agonist conjugates **AOC-B8** and **ISAC-A2** were administered intravenously at 15 mg/kg, anti-HBsAg/TLR agonist conjugate **AOC-D1** was administered intravenously at 5 mg/kg, and the CpG oligonucleotide was administered subcutaneously at 2.5 mg/kg. PBS was administered intravenously to each mouse in a control group. Blood samples were collected from the mice and analyzed for HBsAg. The results are summarized in FIG. 13.

Example 12

Epitope-Based Competitive ELISA

[00238] Anti-HBsAg antibodies, hAnti-HBsAg 1, hAnti-HBsAg 2, and hAnti-HBsAg 3, were evaluated in an epitope-based competitive ELISA. In the assay, each well of an ELISA plate was coated with HBsAg at 1 µg/mL. A mixture biotinylated hAnti-HBsAg 1 at 2 µg/mL with hAnti-HBsAg 1, hAnti-HBsAg 2, or hAnti-HBsAg 3 at predetermined concentrations was then added, followed by addition of streptavidin and a secondary streptavidin antibody. The results are shown in FIG. 14, which shows that there is no competition between hAnti-HBsAg 1 and hAnti-HBsAg 2, indicating that the two antibodies bind two distinct epitopes on HBsAg; but there is a competition between hAnti-HBsAg 1 and hAnti-HBsAg 3, suggesting that their epitopes likely overlap. The competitive ELISA results shown in FIG. 14, together with anti-HBV efficacy results shown in FIGS. 7 to 9, demonstrate that anti-HBsAg/CpG oligonucleotide conjugates targeting different HBsAg epitopes are efficacious in treating HBV infection.

[00239] Sequences described herein are provided in the sequence table below.

SEQUENCE TABLE

SEQ ID NO:	Description	Sequence
1	Anti-HBsAg 1 CDRL1 (Kabat)	SSISTD
	Anti-HBsAg 1 CDRL2 (Kabat)	AAS
2	Anti-HBsAg 1 CDRL3 (Kabat)	QQSYSTPLT
3	Anti-HBsAg 1 CDRH1 (Kabat)	GYTFTGY
4	Anti-HBsAg 1 CDRH2 (Kabat)	INPNSGGT
5	Anti-HBsAg 1 CDRH3 (Kabat)	ARDLWIERTEDYGMDV
6	Anti-HBsAg 1 Light Chain Variable Region	DIQLTQSPSSLSASVGDRVTITCRASSSISTDLNWWY QQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL LTISLQPEDFATYYCQQSYSTPLTFGGGKTKVDIKR
7	Anti-HBsAg 1 Heavy Chain Variable Region	QVQLVESGAIEVKKPGASVKVSCKASGYTFTGYYM HWVRQAPGQGLEWMGWINPNSGGTNYAQKFQGR VTMTRDTSISTAYMELSRRLSDDTAVYYCARDLWI ERTEDYGMDVWGKGTLLTVSS
8	mAnti-HBsAg 1 Light Chain	DIQLTQSPSSLSASVGDRVTITCRASSSISTDLNWWYQ QQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISLQPEDFATYYCQQSYSTPLTFGGGKTKVDIKRA DAAPTVISFPPSSEQLTSGGASVVCFLNNFYPKDIN VKWKIDGSEKQNGVLNSWTDQDSKDYSTYSMSSTL TLTKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC
9	mAnti-HBsAg 1 Heavy Chain	QVQLVESGAIEVKKPGASVKVSCKASGYTFTGYYM HWVRQAPGQGLEWMGWINPNSGGTNYAQKFQGR VTMTRDTSISTAYMELSRRLSDDTAVYYCARDLWI ERTEDYGMDVWGKGTLLTVSSAKTTPPSVYPLAP GSAAQTNSMVTGLCLVKGYFPEPVTVTWNSGSLSS GVHTFPAVLQSDLYTLSSSVTPSTWPSSETVTCNV AHPASSTKVDKIVPRDCGCKPCICTVPEVSSVFIFP PKPKDVLITLTPKVTCTVVDISKDDPEVQFSWFVD DVEVHTAQTQPREEQFNSTFRSVSELPIHQDWLN GKEFKCRVNSAAFPAPIEKTISKTKGRPKAPQVYTI PPPKEQMAKDKVSLTCMITDFFPEDITVEWQWNGQ PAENYKNTQPMIDTDGSYFVYSKLVQKSNWEAG NTFTCSVLHEGLHNHHTEKSLSHSPGK
10	hAnti-HBsAg 1 Light Chain	DIQLTQSPSSLSASVGDRVTITCRASSSISTDLNWWYQ QQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTL TISLQPEDFATYYCQQSYSTPLTFGGGKTKVDIKRT VAAPSVFIFPPSDEQLKSGTASVVCFLNNFYPREAK VQWKVDNALQSGNSQESVTEQDSKDYSTYSSTLT

SEQ ID NO:	Description	Sequence
		LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
11	hAnti-HBsAg 1 Heavy Chain	QVQLVESGAIEVKKPGASVKVSCASGYTFTGYYM HWVRQAPGQGLEWMGWINPNSGGTNYAQKFQGR VTMTRDTSISTAYMELSRLSDDTAVYYCARDLWI ERTEDYGMDVWGKGTLLTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPTVSWNSGALTSG VHTFPAVLQSSGLYSLSSVTPVSSSLGTQTYICNV NHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTTTPVLDSDGSFELYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG K
12	Anti-HBsAg 2 CDRL1 (Kabat)	KLGNKN
	Anti-HBsAg 2 CDRL2a (Kabat)	EVK
13	Anti-HBsAg 2 CDRL2b (Kabat)	VIYEVKYRP
14	Anti-HBsAg 2 CDRL3 (Kabat)	QTFDSTTVV
15	Anti-HBsAg 2 CDRH1 (Kabat)	GRIFRSFY
16	Anti-HBsAg 2 CDRH2a (Kabat)	NQDGSEK
17	Anti-HBsAg 2 CDRH2b (Kabat)	INQDGSEK
18	Anti-HBsAg 2 CDRH3 (Kabat)	AAWSGNSGGMDV
19	Anti-HBsAg 2 Light Chain Variable Region	SYELTQPPSVSVSPGQTVSIPCSGDKLGKNVAVF QHKPGQSPVLVIYEVKYRPSGIPERFSGNSGNTAT LTISGTQAMDEAAFYCQTFDSTTVVFGGGTRLTVL G
20	Anti-HBsAg 2 Heavy Chain Variable Region	ELQLVESGGGWVQPGGSQRLSCAASGRIFRSFYMS WVRQAPGKGLEWVATINQDGSEKLYVDSVKGRFT ISRDNANKSLFLQMNNLRVEDTAVYYCAAWSGNS GGMDVWGQGTTVSVSS
21	hAnti-HBsAg 2 Light Chain	SYELTQPPSVSVSPGQTVSIPCSGDKLGKNVAVF QHKPGQSPVLVIYEVKYRPSGIPERFSGNSGNTAT LTISGTQAMDEAAFYCQTFDSTTVVFGGGTRLTVL GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPG

SEQ ID NO:	Description	Sequence
		AVTVAWKADSSPVKAGVETTTTPSKQSNNKYAASS YLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTEC S
22	hAnti-HBsAg 2 Heavy Chain	ELQLVESGGGWVQPGGSQRLSCAASGRIFRSFYMS WVRQAPGKGLEWVATINQDGSEKLYVDSVKGRFT ISRDNAKNSLFLQMNNLRVEDTAVYYCAAWSGNS GGMDVWGQGTTVSVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKVEPKSCDKTHTCPPCPAPELLAGPSVFLF PPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNKEYKCKVSNKALPLPEEKTKAKGQPREPQ VYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVLHEALHSHYTQKSLSLSPGK
23	Anti-HBsAg 3 CDRL1 (Kabat)	RSSQSLVHSYGDTYLH
24	Anti-HBsAg 3 CDRL2 (Kabat)	KVSNRFS
25	Anti-HBsAg 3 CDRL3 (Kabat)	SQNTHPYPT
26	Anti-HBsAg 3 CDRH1 (Kabat)	YGYHWN
27	Anti-HBsAg 3 CDRH2 (Kabat)	YISYDGSVLYNPSEN
28	Anti-HBsAg 3 CDRH3 (Kabat)	GFDH
29	Anti-HBsAg 3 Light Chain Variable Region	DVVMTQSPLSLPVTLGEPASISCRSSQSLVHSYGDT YLHWYLQKPGQSPKLLIYKVSNNRFGVPDRFSGSG SGTDFTLKISRVEDTLGVYYCSQNTHPYPTFGGG TKLEIKR
30	Anti-HBsAg 3 Heavy Chain Variable Region	EVQLQESGPGLVKPSQTLSTCAVSGSSITYGYHW NWIRQFPGNKLEWIGYISYDGSVLYNPSEN RVIT RDTSKNQFFLKLSSVTAEDTAKYYCASGFDHWGQ GTTLTVSS
31	mAnti-HBsAg 3 Light Chain	DVVMTQSPLSLPVTLGEPASISCRSSQSLVHSYGDT YLHWYLQKPGQSPKLLIYKVSNNRFGVPDRFSGSG SGTDFTLKISRVEDTLGVYYCSQNTHPYPTFGGG TKLEIKRRADAAPTVISFPPSSEQLTSGGASVVCFLN NFYPKDINVKWKIDGSRQNGVLNSWTDQDSKDS TYSMSSTLTTLKDEYERHNSYTCEATHKTS TSPIVKSFNRNEC
32	mAnti-HBsAg 3 Heavy Chain	EVQLQESGPGLVKPSQTLSTCAVSGSSITYGYHW NWIRQFPGNKLEWIGYISYDGSVLYNPSEN RVIT

SEQ ID NO:	Description	Sequence
		RDTSKNQFFLKLSSVTAEDTAKYYCASGFDHWGQ GTTLTVSSAKTTPPSVYPLAPGSAAQTNSMVTLGC LVKGYFPEPVTWNSGSLSSGVHTFPAVLQSDLYTL SSSVTVPSSTWPSETVTCNV AHPASSTKV DKKIVPR DCGCKPCICTVPEVSSVFIFPPKPKDVL TITLTPKVT CVVVDISKDDPEVQFSWFVDDVEVHTAQTQPREE QFNSTFRSVSSELPIMHQDWLNGKEFKCRVNSAAF PAPIEKTISKTKGRPKAPQVYTIPPPKEQMAKDKVS LTCMITDFFPEDITVEWQWNGQPAENYKNTQPIMD TDGSYFVYSKLN VQSNWEAGNTFTCSVLHEGLHN HHTEKSLSHSPGK
33	hAnti-HBsAg 3 Light Chain	DVVMTQSPSLPVLTLGEPASISCRSSQSLVHSYGDT YLHWYLQKPGQSPKLLIYKVS NRFSGV PDRFSGSG SGTDFTLKISR VETEDLG VYYCSQNT HVPYTFGGG TKLEIKRTVAAPS VFIFPPSDEQLKSGTASV VCLLN NFYPREAKVQWKVDNALQSGNSQESVTEQDSKDS TYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVT KSFNRGEC
34	hAnti-HBsAg 3 Heavy Chain	EVQLQESGPGLVKPSQTLSTCAVSGSSITYGYHW NWIRQFPGNKLEWIGYISYDGSVLNPSLENRV TIT RDTSKNQFFLKLSSVTAEDTAKYYCASGFDHWGQ GTTLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCL VKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY SLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKRVE PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNA KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNAKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTTPVLDS DGSFFLYSKLTVDKSRWQQGNV FSCS VMHEALHNHYTQKSLSLSPGK
35	Anti-HBsAg 4 CDRL1 (Kabat)	QSISTY
	Anti-HBsAg 4 CDRL2 (Kabat)	AAS
36	Anti-HBsAg 4 CDRL3 (Kabat)	QQSYSTPLT
37	Anti-HBsAg 4 CDRH1 (Kabat)	GYTFTGY
38	Anti-HBsAg 4 CDRH2 (Kabat)	INPNSGGT
39	Anti-HBsAg 4 CDRH3 (Kabat)	ARDLWNDDVDYYGMDV
40	Anti-HBsAg 4 Light Chain Variable Region	DIQLTQSPSSLSASVGDRTITCRASQSISTYLNWY QQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFT LTISLQPEDFATYYCQQSYSTPLTFGGGT KVDIKR

SEQ ID NO:	Description	Sequence
41	Anti-HBsAg 4 Heavy Chain Variable Region	QVQLVESGAIEVKKPGASVKVSCASGYTFTGYYM HWVRQAPGQGLEWMGWINPNSGGTNYAQKFQGR VTMTRDTSISTAYMELSRLRSDDTAVYYCARDLW NDDVDYYGMDVWGKGLVTVSS
42	hAnti-HBsAg 4 Light Chain	DIQLTQSPSSLSASVGDRTITCRASQSISTYLNWY QQKPGKAPKLLIYAASLQSGVPSRFSGSGSGTDFT LTISLQPEDFATYYCQQSYSTPLTFGGGTKVDIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREA KVQWKVDNALQSGNSQESVTEQDSKDYSLSSLT TLISKADYEKHKVYACEVTHQGLSPVTKSFNRGEC
43	hAnti-HBsAg4 Heavy Chain	QVQLVESGAIEVKKPGASVKVSCASGYTFTGYYM HWVRQAPGQGLEWMGWINPNSGGTNYAQKFQGR VTMTRDTSISTAYMELSRLRSDDTAVYYCARDLW NDDVDYYGMDVWGKGLVTVSSASTKGPSVFPLA PSSKSTSGGTAALGCLVKDYFPEPTVSWNSGALT SGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYIC NVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVS VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA KGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSLK TVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLS PGK
44	TLR9 Agonist 1	dTsdGsdAsdCsdTsdGsdTsdGsdAsdAsdCsdGsdTsdTsdC sdGsdAsdGsdAsdTsdGsdA
45	TLR9 Agonist 2	dTsdCsdGsdTsdCsdGsdTsdTsdTsdTsdGsdTsdCsdGsdTs dTsdTsdTsdGsdTsdCsdGsdTsdT
46	TLR9 Agonist 3	dTsdCsdCsdAsdTsdGsdAsdCsdGsdTsdTsdCsdCsdTsdG sdAsdCsdGsdTsdT
47	TLR9 Agonist 4	dTsdCsdGsdAsdCsdGsdTsdTsdCsdGsdTsdCsdGsdTsdTs dCsdGsdTsdCsdGsdTsdTsdC
48	TLR9 Agonist 5	dTsdCsdGsdTsdCsdGsdTsdTsdGsdTsdCsdGsdTsdTsdTs dTsdGsdTsdCsdGsdTsdT
49	TLR9 Agonist 6	dTsdCsdGsdCsdGsdAsdCsdGsdTsdTsdCsdGsdCsdCsdC sdGsdAsdCsdGsdTsdTsdCsdGsdGsdTsdA
50	TLR9 Agonist 7	dGsdGsdGsdGsdGsdAsdCsdGsdAsdTsdCsdGsdTsdCsd GsdGsdGsdGsdGsdG
51	TLR9 Agonist 8	dGsdGsdGsdGsdAsdCsdGsdAsdCsdGsdTsdCsdGsdTsd GsdGsdGsdGsdGsdGsdG
52	TLR9 Agonist 9	dTsdCsdGsdTsdCsdGsdTsdTsdTsdTsdCsdGsdGsdCsdGs dCsdGsdCsdGsdCsdGsdG
53	TLR9 Agonist 10	dTsdCsdGsdTsdCsdGsdTsdCsdGsdTsdTsdCsdGsdAsdA sdCsdGsdAsdCsdGsdTsdTsdGsdAsdT

SEQ ID NO:	Description	Sequence
54	TLR9 Agonist 11	dTsdCsdGsdCsdGsdAsdAsdCsdGsdTsdTsdCsdGsdCsdCsdGsdCsdGsdTsdTsdCsdGsdAsdAsdCsdGsdCsdGsdG
55	TLR9 Agonist 12	br ³ dUsdCsdGsdIsdCsdGsdTsdGsdTSdCsdGsdTsm ³ Umsm ³ Um
56	S-HBsAg	MENVTSGLGPLLVLQAGFLLTRILTIPQSLDSWW TSLNFLGGTTVCLGQNSQSPTSNHSPTSCPPTCPGY RWMCLRRFIIFLFILLCLIFLLVLLDYQGMLPVCPL IPGSSTTGTPCRTCTTPAQGTSMYPPSCCCTKPSDG NCTCIPSSWAFGKFLWEWASARFSWLSLLVPFVQ WFGLSPTVWLSVIWMMWYWGPSLYSTLSPFLPL LPIFFCLWVYI

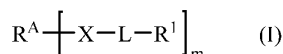
dA, dC, dG, dI, and dT represent 2'-deoxyadenosine, 2'-deoxycytidine, 2'-deoxyguanosine, 2'-deoxy-
inosine, and 2'-deoxythymidine, respectively.
S and s represent phosphonodithioate and phosphorothioate, respectively.
Br⁵dU and m⁵Um represent 2'-deoxy-5-bromouridine and 2'-O-methyl-5-methyluridine, respectively.

* * * * *

[00240] The examples set forth above are provided to give those of ordinary skill in the art with a complete disclosure and description of how to make and use the claimed embodiments and are not intended to limit the scope of what is disclosed herein. Modifications that are obvious to persons of skill in the art are intended to be within the scope of the following claims. All publications, patents, and patent applications cited in this specification are incorporated herein by reference as if each such publication, patent or patent application were specifically and individually indicated to be incorporated herein by reference.

What is claimed is:

1. A compound of Formula (I):



or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; wherein:

each L is independently a linker;

each X is independently (i) a bond or $-S-$; or (ii) heteroarylene or heterocyclylene, each optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q;

each R^1 is independently an immunostimulator;

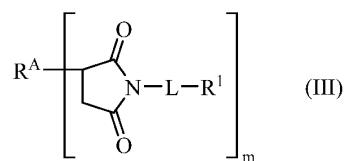
R^A is an antibody or an antigen-binding fragment thereof, which binds specifically to a hepatitis B surface antigen (HBsAg); and

m is an integer of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16;

wherein each Q is independently selected from: (a) deuterium, cyano, halo, imino, nitro, and oxo; (b) C_{1-6} alkyl, C_{1-6} heteroalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, and heterocyclyl, each of which is further optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q^a ; and (c) $-C(O)R^a$, $-C(O)OR^a$, $-C(O)NR^bR^c$, $-C(O)SR^a$, $-C(NR^a)NR^bR^c$, $-C(S)R^a$, $-C(S)OR^a$, $-C(S)NR^bR^c$, $-OR^a$, $-OC(O)R^a$, $-OC(O)OR^a$, $-OC(O)NR^bR^c$, $-OC(O)SR^a$, $-OC(NR^a)NR^bR^c$, $-OC(S)R^a$, $-OC(S)OR^a$, $-OC(S)NR^bR^c$, $-OP(O)(OR^a)OR^d$, $-OS(O)R^a$, $-OS(O)_2R^a$, $-OS(O)NR^bR^c$, $-OS(O)_2NR^bR^c$, $-NR^bR^c$, $-NR^aC(O)R^d$, $-NR^aC(O)OR^d$, $-NR^aC(O)NR^bR^c$, $-NR^aC(O)SR^d$, $-NR^aC(NR^d)NR^bR^c$, $-NR^aC(S)R^d$, $-NR^aC(S)OR^d$, $-NR^aC(S)NR^bR^c$, $-NR^aS(O)R^d$, $-NR^aS(O)_2R^d$, $-NR^aS(O)NR^bR^c$, $-NR^aS(O)_2NR^bR^c$, $-SR^a$, $-S(O)R^a$, $-S(O)_2R^a$, $-S(O)NR^bR^c$, and $-S(O)_2NR^bR^c$, wherein each R^a , R^b , R^c , and R^d is independently (i) hydrogen or deuterium; (ii) C_{1-6} alkyl, C_{1-6} heteroalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, C_{6-14} aryl, C_{7-15} aralkyl, heteroaryl, or heterocyclyl, each of which is optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q^a ; or (iii) R^b and R^c together with the N atom to which they are attached form heterocyclyl, optionally substituted with one or more, in one embodiment, one, two, three, or four, substituents Q^a ;

wherein each Q^a is independently selected from: (a) deuterium, cyano, halo, nitro, imino, and oxo; (b) C₁₋₆ alkyl, C₁₋₆ heteroalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₄ aryl, C₇₋₁₅ aralkyl, heteroaryl, and heterocyclyl; and (c) -C(O)R^e, -C(O)OR^e, -C(O)NR^fR^g, -C(O)SR^e, -C(NR^e)NR^fR^g, -C(S)R^e, -C(S)OR^e, -C(S)NR^fR^g, -OR^e, -OC(O)R^e, -OC(O)OR^e, -OC(O)NR^fR^g, -OC(O)SR^e, -OC(NR^e)NR^fR^g, -OC(S)R^e, -OC(S)OR^e, -OC(S)NR^fR^g, -OS(O)R^e, -OS(O)₂R^e, -OS(O)NR^fR^g, -OS(O)₂NR^fR^g, -NR^fR^g, -NR^eC(O)R^h, -NR^eC(O)OR^f, -NR^eC(O)NR^fR^g, -NR^eC(O)SR^f, -NR^eC(NR^h)NR^fR^g, -NR^eC(S)R^h, -NR^eC(S)OR^f, -NR^eC(S)NR^fR^g, -NR^eS(O)R^h, -NR^eS(O)₂R^h, -NR^eS(O)NR^fR^g, -NR^eS(O)₂NR^fR^g, -SR^e, -S(O)R^e, -S(O)₂R^e, -S(O)NR^fR^g, and -S(O)₂NR^fR^g, wherein each R^e, R^f, R^g, and R^h is independently (i) hydrogen or deuterium; (ii) C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₃₋₁₀ cycloalkyl, C₆₋₁₄ aryl, C₇₋₁₅ aralkyl, heteroaryl, or heterocyclyl; or (iii) R^f and R^g together with the N atom to which they are attached form heterocyclyl.

2. The compound of claim 1, wherein each X is a bond.
3. The compound of claim 1, wherein each X is independently heterocyclylene, optionally substituted with one or more substituents Q.
4. The compound of claim 1 or 3, wherein each X is independently monocyclic heterocyclylene, optionally substituted with one or more substituents Q.
5. The compound of claim 1, 3, or 4, wherein each X is independently 3-, 4-, 5-, 6-, or 7-membered heterocyclylene, each optionally substituted with one or more substituents Q.
6. The compound of any one of claims 1 and 3 to 5, wherein each X is independently 5-membered heterocyclylene, optionally substituted with one or more substituents Q.
7. The compound of claim 1 or 2, having the structure of Formula (II):
$$R^A - \left[S - L - R^1 \right]_m \quad (II)$$
or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof.
8. The compound of any one of claims 1 to 6, having the structure of Formula (III):



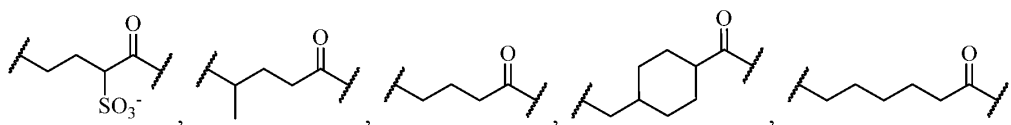
or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

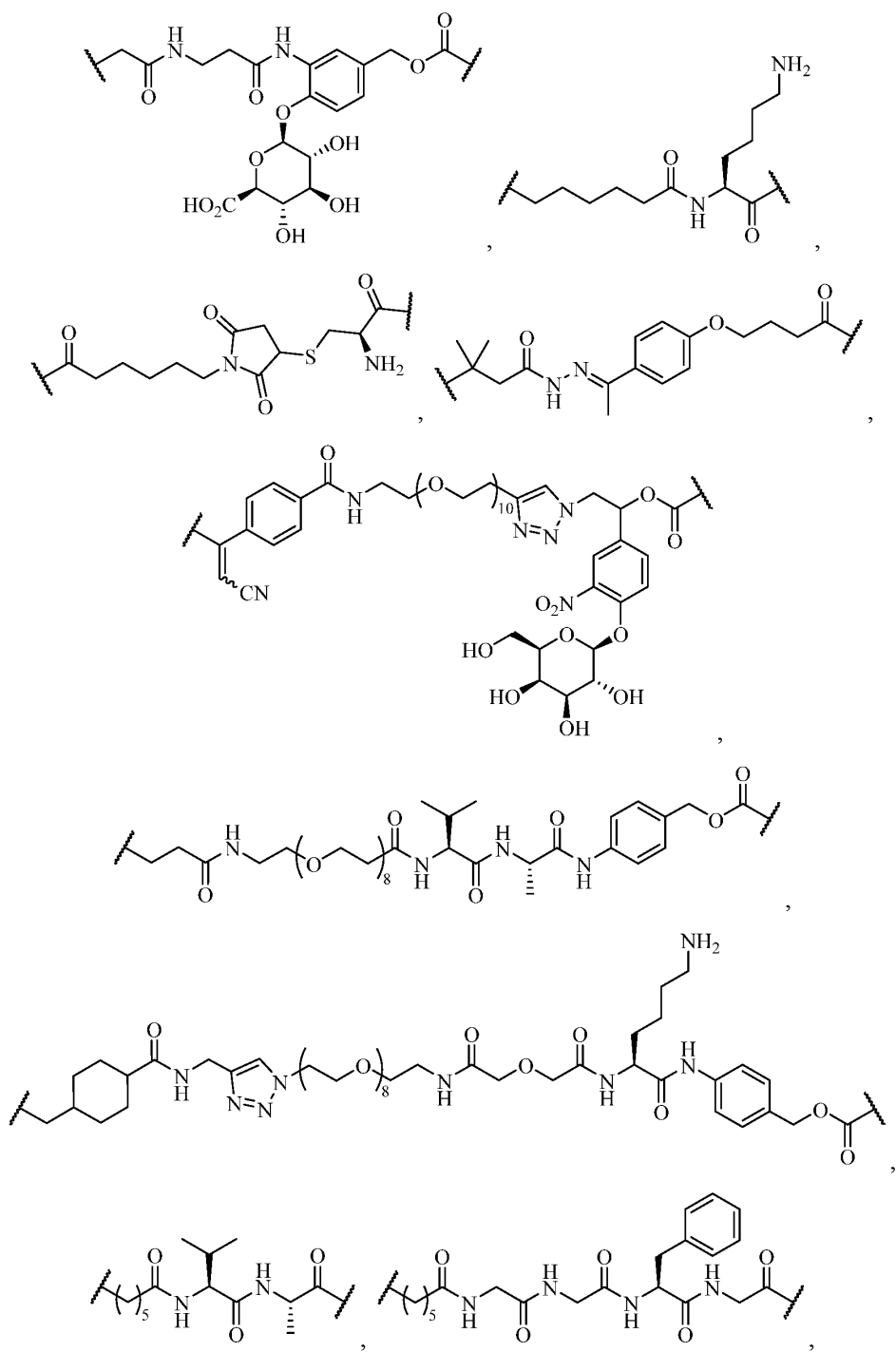
9. The compound of any one of claims 1 to 8, wherein each L is independently C₁₋₅₀ heteroalkylene, wherein one or more methylene groups are each independently and optionally replaced by a divalent group and each divalent group is independently C₆₋₁₄ arylene, heteroarylene, or heterocyclylene; and wherein each heteroalkylene, arylene, heteroarylene, and heterocyclylene is optionally substituted with one or more substituents Q.

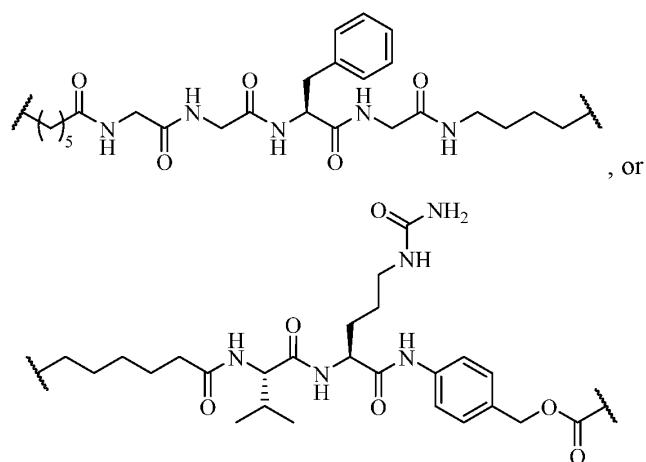
10. The compound of any one of claims 1 to 9, wherein each L is independently C₁₋₃₀ heteroalkylene, wherein one or more methylene groups are each independently and optionally replaced by a divalent group and each divalent group is independently each divalent group is independently cyclohexanediyl, phendiyl, triazoldiyl, 2,5-dioxopyrrolidindiyl, or piperazindiyl.

11. The compound of any one of claims 1 to 10, wherein each L is independently C₁₋₃₀ heteroalkylene, wherein one or more methylene groups are each independently and optionally replaced by a divalent group and each divalent group is independently each divalent group is independently cyclohexane-1,4-diyl, phen-1,3-diyl, phen-1,4-diyl, 1,2,3-triazol-1,4-diyl, 2,5-dioxopyrrolidin-1,3-diyl, or piperazin-1,4-diyl.

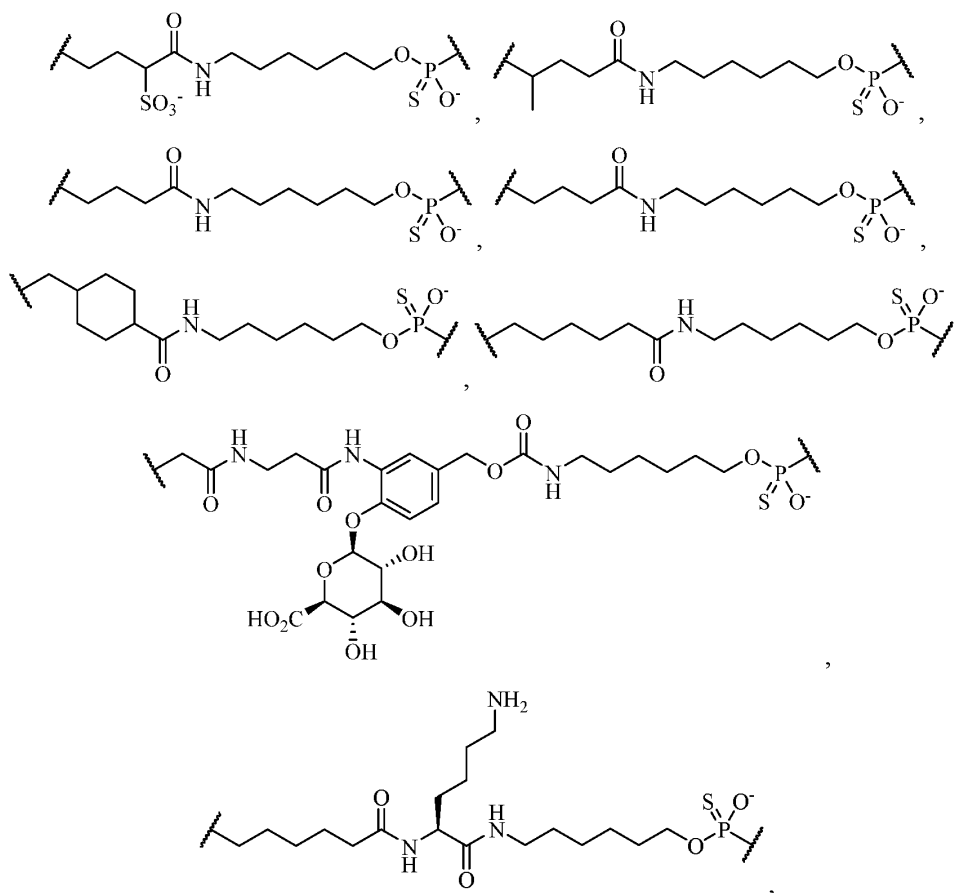
12. The compound of any one of claims 1 to 11, wherein each L is independently:





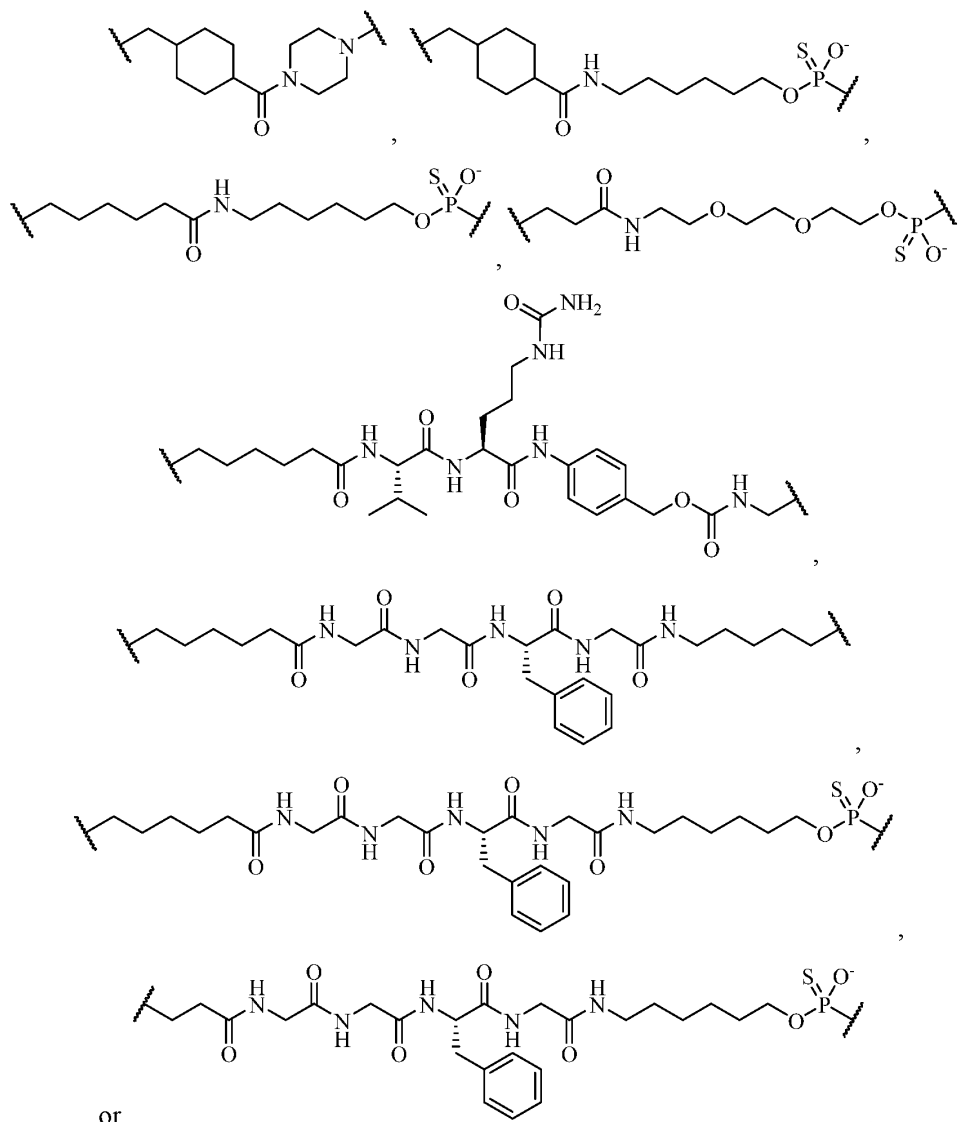


13. The compound of any one of claims 1 to 11, wherein each L is independently:

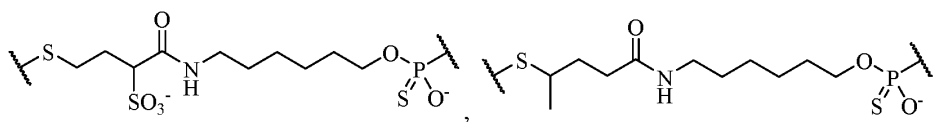


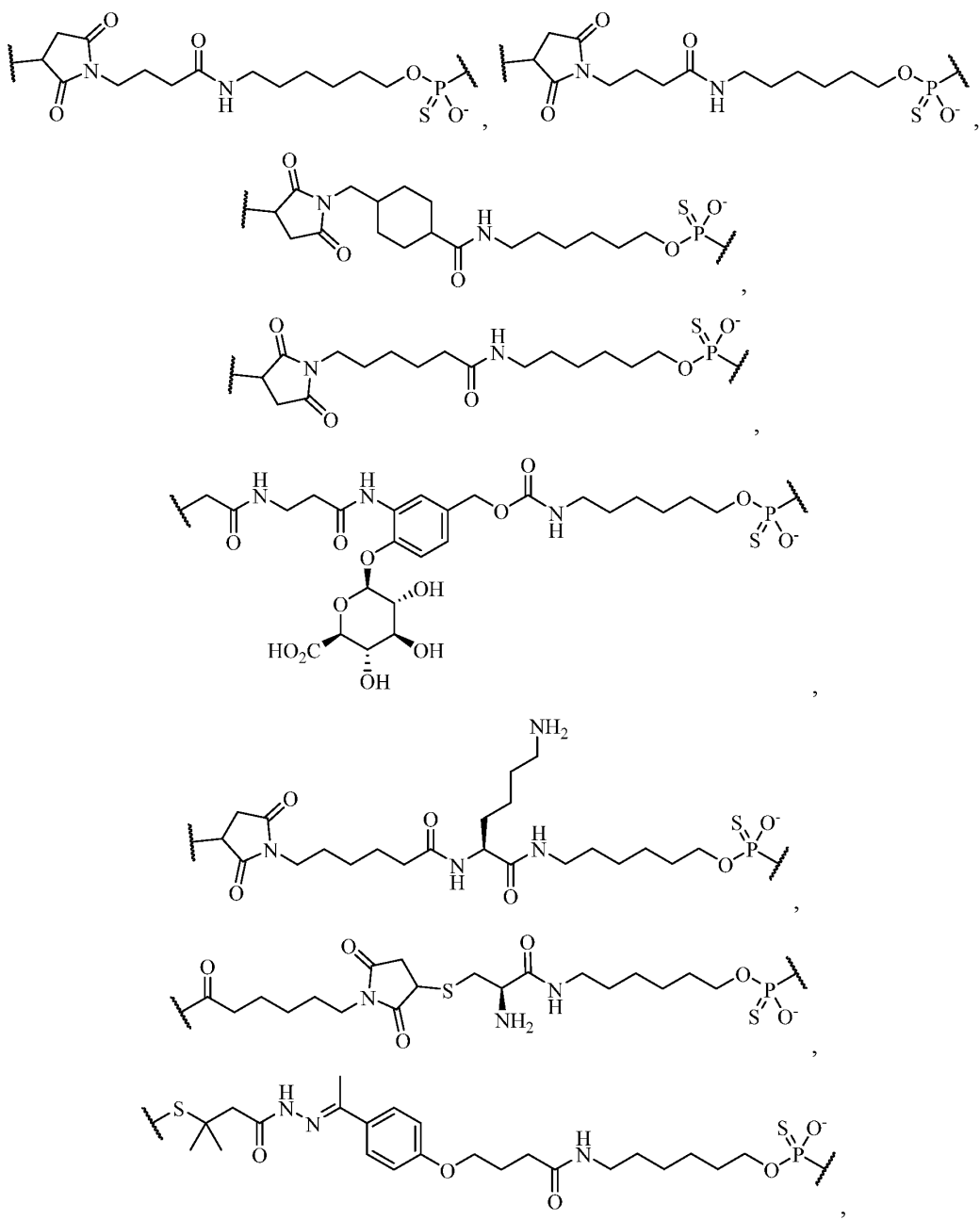


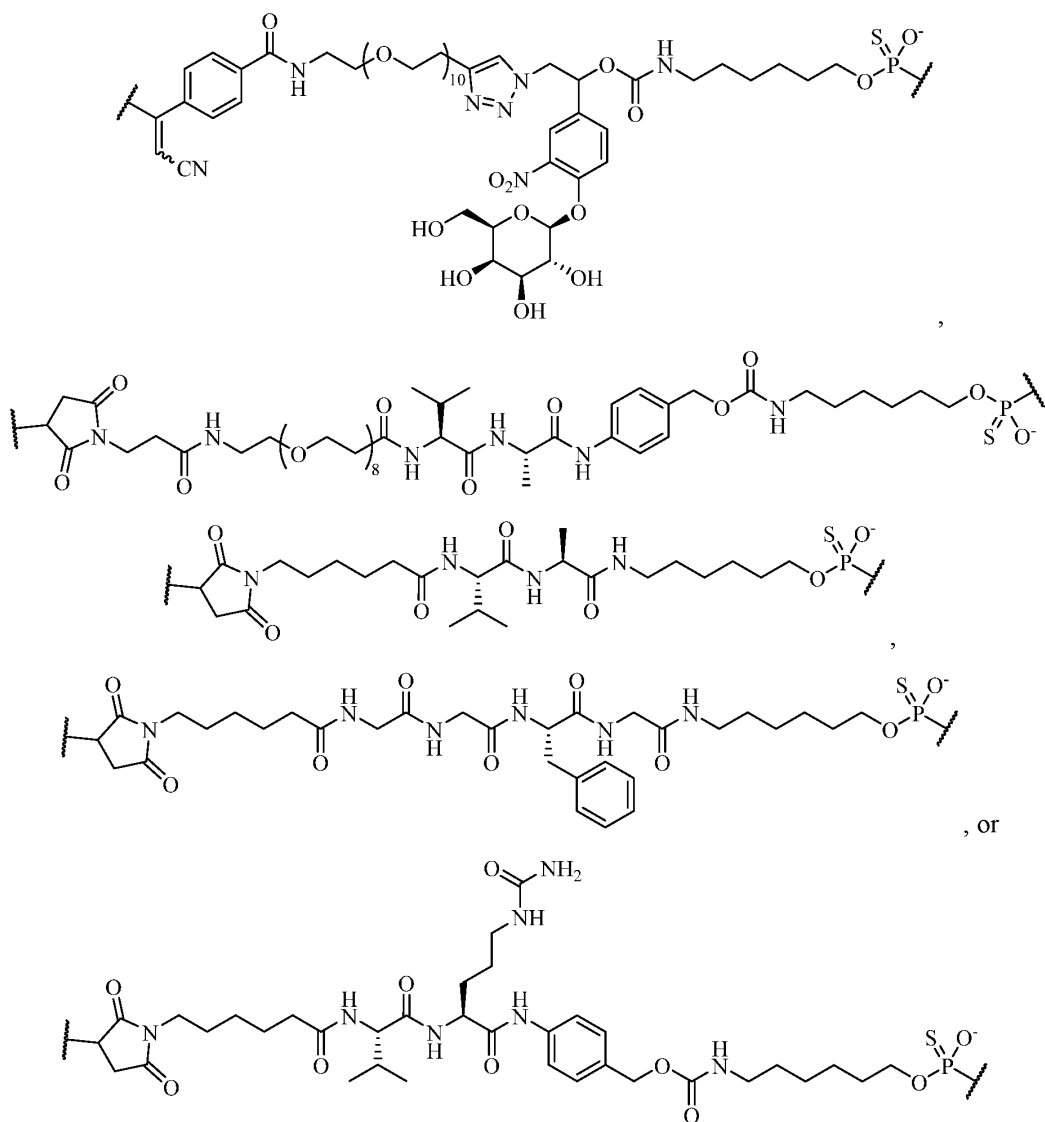
14. The compound of any one of claims 1 to 11, wherein each L moiety is independently:



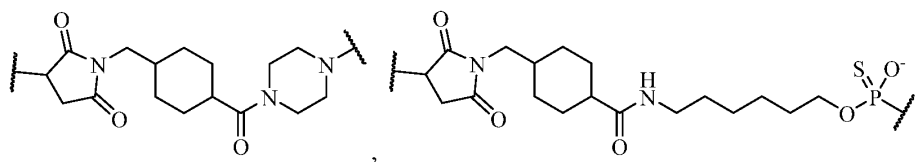
15. The compound of any one of claims 1 to 11, wherein each X-L moiety is independently:

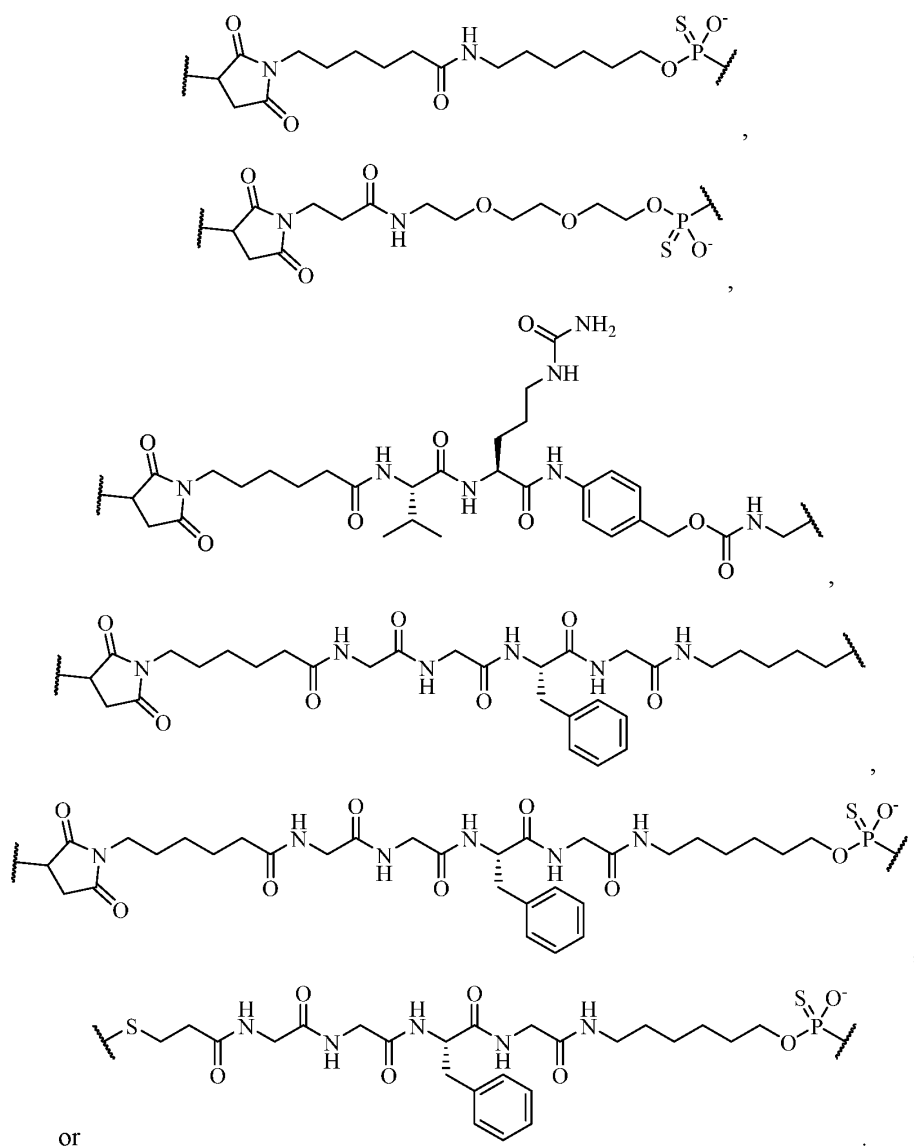




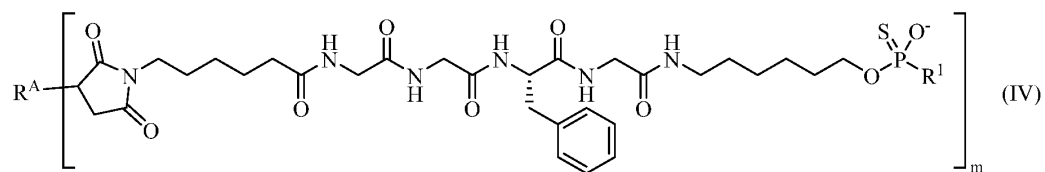


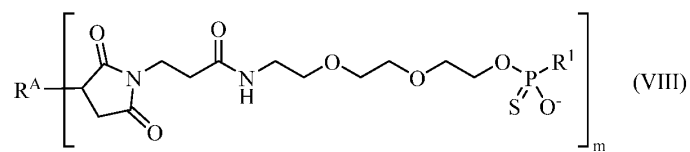
16. The compound of any one of claims 1 and 9 to 11, wherein each X-L moiety is independently:





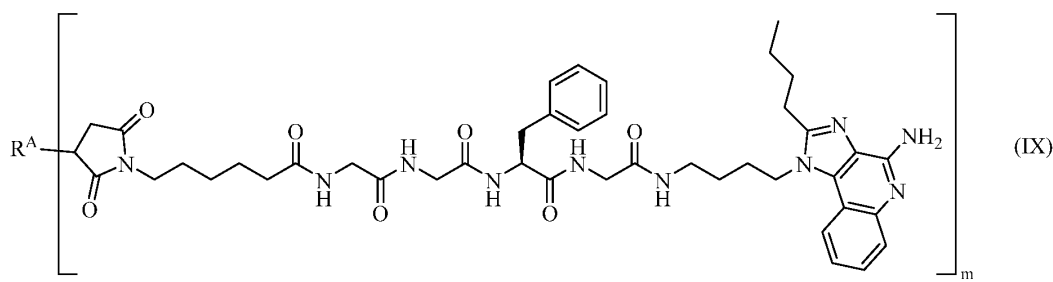
17. The compound of any one of claims 1 to 6, 8 to 11, 14, and 16, having the structure of Formula (IV):





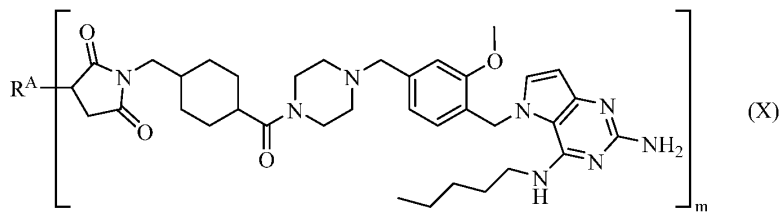
or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

22. The compound of any one of claims 1 to 6, 8 to 11, 14, and 16, having the structure of Formula (IX):



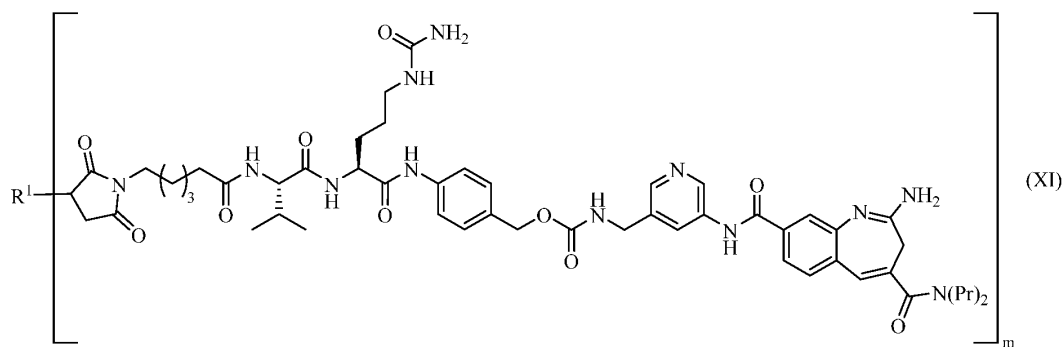
or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

23. The compound of any one of claims 1 to 6, 8 to 11, 14, and 16, having the structure of Formula (X):



or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

24. The compound of any one of claims 1 to 6, 8 to 11, 14, and 16, having the structure of Formula (XI):



or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

25. The compound of any one of claims 1 to 24, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a CDRL1 having the amino acid sequence of SEQ ID NO: 1; a CDRL2 having the amino acid sequence of AAS; a CDRL3 having the amino acid sequence of SEQ ID NO: 2; a CDRH1 having the amino acid sequence of SEQ ID NO: 3; a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and a CDRH3 having the amino acid sequence of SEQ ID NO: 5.

26. The compound of any one of claims 1 to 25, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a light chain variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 6; and a heavy chain variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 7.

27. The compound of any one of claims 1 to 26, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a light chain variable region having the amino acid sequence of SEQ ID NO: 6 and a heavy chain variable region having the amino acid sequence of SEQ ID NO: 7.

28. The compound of any one of claims 1 to 27, wherein R^A is an antibody comprising a light chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a heavy chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 11.

29. The compound of any one of claims 1 to 28, wherein R^A is an antibody

comprising a light chain having the amino acid sequence of SEQ ID NO: 10 and a heavy chain having the amino acid sequence of SEQ ID NO: 11.

30. The compound of any one of claims 1 to 24, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a CDRL1 having the amino acid sequence of SEQ ID NO: 12; a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; a CDRL3 having the amino acid sequence of SEQ ID NO: 14; a CDRH1 having the amino acid sequence of SEQ ID NO: 15; a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and a CDRH3 having the amino acid sequence of SEQ ID NO: 18.

31. The compound of any one of claims 1 to 24 and 30, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a light chain variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 19; and a heavy chain variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 20.

32. The compound of any one of claims 1 to 24, 30, and 31, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a light chain variable region having the amino acid sequence of SEQ ID NO: 19 and a heavy chain variable region having the amino acid sequence of SEQ ID NO: 20.

33. The compound of any one of claims 1 to 24 and 30 to 32, wherein R^A is an antibody comprising a light chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 21; and a heavy chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 22.

34. The compound of any one of claims 1 to 24 and 30 to 33, wherein R^A is an antibody comprising a light chain having the amino acid sequence of SEQ ID NO: 21 and a heavy chain having the amino acid sequence of SEQ ID NO: 22.

35. The compound of any one of claims 1 to 24, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a CDRL1 having the amino acid sequence of SEQ ID NO: 23; a CDRL2 having the amino acid sequence of SEQ ID NO: 24; a CDRL3 having the amino acid sequence of SEQ ID NO: 25; a CDRH1 having the amino acid sequence of SEQ ID

NO: 26; a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and a CDRH3 having the amino acid sequence of SEQ ID NO: 28.

36. The compound of any one of claims 1 to 24 and 35, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a light chain variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 29; and a heavy chain variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 30.

37. The compound of any one of claims 1 to 24, 35, and 36, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a light chain variable region having the amino acid sequence of SEQ ID NO: 29 and a heavy chain variable region having the amino acid sequence of SEQ ID NO: 30.

38. The compound of any one of claims 1 to 24 and 35 to 37, wherein R^A is an antibody comprising a light chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 33; and a heavy chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 34.

39. The compound of any one of claims 1 to 24 and 35 to 38, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a light chain having the amino acid sequence of SEQ ID NO: 33 and a heavy chain having the amino acid sequence of SEQ ID NO: 34.

40. The compound of any one of claims 1 to 24, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a CDRL1 having the amino acid sequence of SEQ ID NO: 35; a CDRL2 having the amino acid sequence of AAS; a CDRL3 having the amino acid sequence of SEQ ID NO: 36; a CDRH1 having the amino acid sequence of SEQ ID NO: 37; a CDRH2 having the amino acid sequence of SEQ ID NO: 38; and a CDRH3 having the amino acid sequence of SEQ ID NO: 39.

41. The compound of any one of claims 1 to 24 and 40, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a light chain variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 40; and a heavy chain

variable region having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 41.

42. The compound of any one of claims 1 to 24, 40, and 41, wherein R^A is an antibody or an antigen-binding fragment thereof, comprising a light chain variable region having the amino acid sequence of SEQ ID NO: 40 and a heavy chain variable region having the amino acid sequence of SEQ ID NO: 41.

43. The compound of any one of claims 1 to 24 and 40 to 42, wherein R^A is an antibody comprising a light chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 42; and a heavy chain having at least about 80% sequence identity to the amino acid sequence of SEQ ID NO: 43.

44. The compound of any one of claims 1 to 24 and 40 to 43, wherein R^A is an antibody comprising a light chain having the amino acid sequence of SEQ ID NO: 42 and a heavy chain having the amino acid sequence of SEQ ID NO: 43.

45. The compound of any one of claims 1 to 44, wherein R^A is a human, humanized, or chimeric antibody, or an antigen-binding fragment thereof.

46. The compound of any one of claims 1 to 45, wherein R^A is an IgG1, IgG2, IgG3, or IgG4 antibody, or an antigen-binding fragment thereof.

47. The compound of any one of claims 1 to 46, wherein R^A is a monoclonal antibody or an antigen-binding fragment thereof.

48. The compound of any one of claims 1 to 21 and 25 to 47, wherein R^1 is a toll-like receptor 9 (TLR9) agonist.

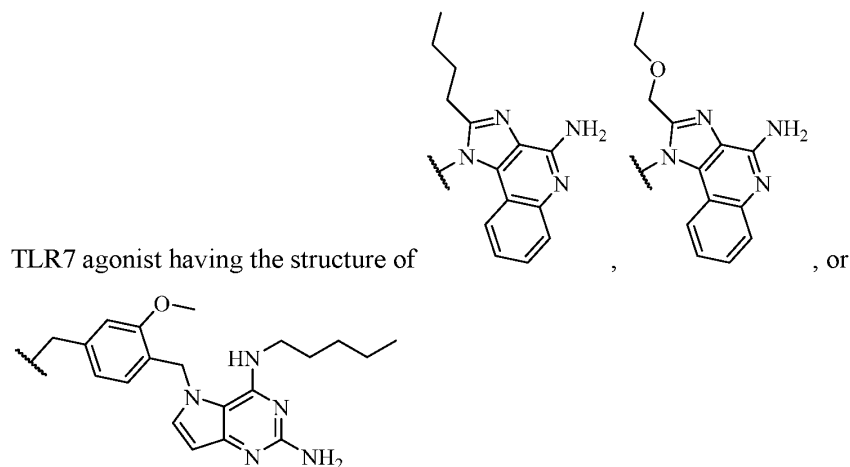
49. The compound of any one of claims 1 to 21 and 25 to 48, wherein R^1 is a single-stranded oligonucleotide.

50. The compound of any one of claims 1 to 21 and 25 to 49, wherein R^1 is a single-stranded CpG oligodeoxynucleotide.

51. The compound of claim 50, wherein the single-stranded CpG oligodeoxy-nucleotide comprises from about 15 to about 30 deoxynucleotide.
52. The compound of claim 50 or 51, wherein the single-stranded CpG oligodeoxy-nucleotide comprises from about 1 to about 20 unmethylated CpG dideoxynucleotide motifs.
53. The compound of any one of claims 50 to 52, wherein the single-stranded CpG oligodeoxynucleotide has one or more phosphate linkage groups replaced with phosphorothioate or phosphorodithioate.
54. The compound of any one of claims 50 to 53, wherein the single-stranded CpG oligodeoxynucleotide has all phosphate linkage groups replaced with phosphorothioate.
55. The compound of any one of claims 1 to 21 and 25 to 54, wherein R¹ is a TLR9 agonist of Class A, B, C, or P.
56. The compound of any one of claims 1 to 21 and 25 to 55, wherein R¹ is a TLR9 agonist of Class B.
57. The compound of any one of claims 1 to 21 and 25 to 56, wherein R¹ is a TLR9 agonist comprising the nucleotide sequence of any one of SEQ ID NOs: 44 to 49 and 55.
58. The compound of any one of claims 1 to 21 and 25 to 57, wherein R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 44, 45, 46, or 55.
59. The compound of any one of claims 1 to 21 and 25 to 55, wherein R¹ is a TLR9 agonist of Class A.
60. The compound of any one of claims 1 to 21, 25 to 55, and 59, wherein R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 50 or 51.
61. The compound of any one of claims 1 to 21 and 25 to 55, wherein R¹ is a TLR9 agonist of Class C.
62. The compound of any one of claims 1 to 21, 25 to 55, and 61, wherein R¹ is a TLR9 agonist comprising the nucleotide sequence of SEQ ID NO: 52, 53 or 54.

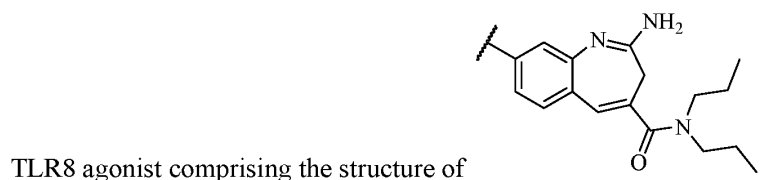
63. The compound of any one of claims 1 to 21 and 25 to 47, wherein R¹ is a TLR7 agonist.

64. The compound of any one of claims 1 to 21, 25 to 47, and 63, wherein R¹ is a



65. The compound of any one of claims 1 to 21 and 25 to 47, wherein R¹ is a TLR8 agonist.

66. The compound of any one of claims 1 to 21, 25 to 47, and 65, wherein R¹ is a



67. The compound of any one of claims 1 to 66, wherein m is an integer of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12.

68. The compound of any one of claims 1 to 67, wherein m is an integer of 4, 5, 6, 7, or 8.

69. The compound of any one of claims 17 to 21, wherein each R¹ is a single-stranded CpG oligonucleotide of SEQ ID NO: 44, 45, 46, 53, or 55 with its 3'- or 5'-terminus connected to R^A via the X-L moiety; and R^A is an antibody comprising:

- (i) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 1; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 2; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 3; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 4; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 5;
- (ii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 12; (b) a CDRL2 having the amino acid sequence of EVK or SEQ ID NO: 13; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 14; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 15; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 16 or 17; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 18;
- (iii) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 23; (b) a CDRL2 having the amino acid sequence of SEQ ID NO: 24; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 25; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 26; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 27; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 28; or
- (iv) (a) a CDRL1 having the amino acid sequence of SEQ ID NO: 35; (b) a CDRL2 having the amino acid sequence of AAS; (c) a CDRL3 having the amino acid sequence of SEQ ID NO: 36; (d) a CDRH1 having the amino acid sequence of SEQ ID NO: 37; (e) a CDRH2 having the amino acid sequence of SEQ ID NO: 38; and (f) a CDRH3 having the amino acid sequence of SEQ ID NO: 39.

70. The compound of claim 1, wherein the compound is one of antibody-immunostimulator conjugates **AOC-A1** to **AOC-A10**, **AOC-B1** to **AOC-B8**, **AOC-C1**, **AOC-C2**, **AOC-D1**, and **ISAC-A1** to **ISAC-A3**.

71. A pharmaceutical composition comprising the compound of any one of claims 1 to 70, or a diastereomer, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, solvate, or hydrate thereof; and a pharmaceutically acceptable excipient.

72. The pharmaceutical composition of claim 71, wherein the composition is in single dosage form.

73. The pharmaceutical composition of claim 71 or 72, wherein the composition is in a parenteral or intravenous dosage form.

74. The pharmaceutical composition of claim 73, wherein the composition is formulated in an intravenous dosage form.

75. A method of treating, preventing, or ameliorating one or more symptoms of an HBV infection in a subject, comprising administering to the subject in need thereof a therapeutically effective amount of a compound of any one of claims 1 to 70 or a pharmaceutical composition of any one of claims 71 to 74.

76. The method of claim 75, wherein the HBV infection is acute.

77. The method of claim 75, wherein the HBV infection is chronic.