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Limphong et al.(10) **Pub. No.: US 2017/0137821 A1**(43) **Pub. Date: May 18, 2017**(54) **MOLECULES AND AGENTS FOR TREATING
HEPATITIS B VIRUS****Publication Classification**(71) Applicant: **Arcturus Therapeutics, Inc.**, San
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Chivukula**, San Diego, CA (US)(52) **U.S. Cl.****CPC C12N 15/1131** (2013.01); **A61K 47/48815**
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2310/323 (2013.01); **C12N 2310/14** (2013.01);
C12N 2310/3515 (2013.01); **C12N 2320/32**
(2013.01); **C12N 2310/315** (2013.01); **C12N**
2310/322 (2013.01); **C12N 2310/321** (2013.01)(21) Appl. No.: **15/410,984**(22) Filed: **Jan. 20, 2017**

(57)

ABSTRACT**Related U.S. Application Data**(63) Continuation-in-part of application No. 15/212,279,
filed on Jul. 17, 2016.(60) Provisional application No. 62/193,997, filed on Jul.
17, 2015.

This invention encompasses compounds and compositions useful in methods for medical therapy, in general, for inhibiting Hepatitis B virus in a subject. The compounds have a first strand and a second strand, each of the strands being 19-29 monomers in length, the monomers comprising UNA monomers and nucleic acid monomers, and the compounds are targeted to a sequence of an HBV genome.

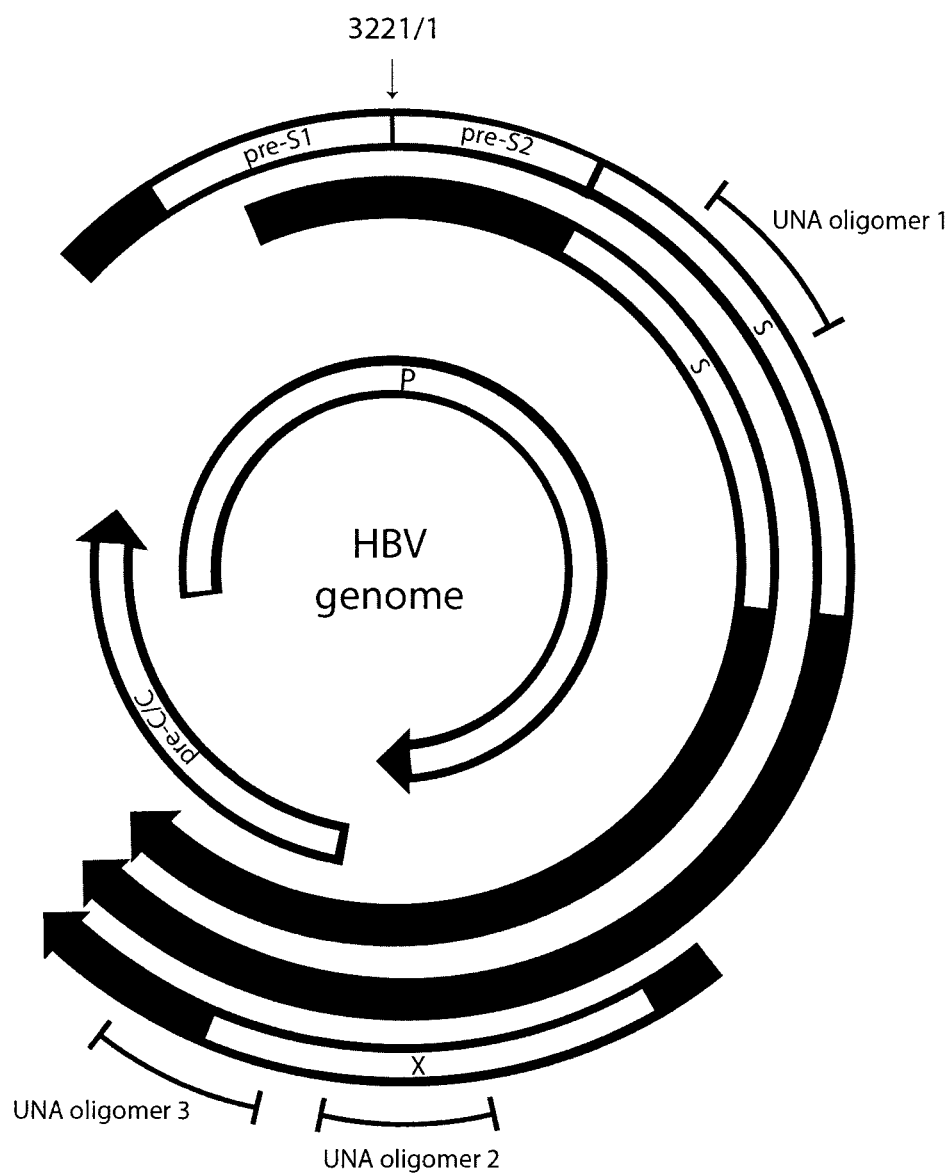


FIG. 1

FIG. 2

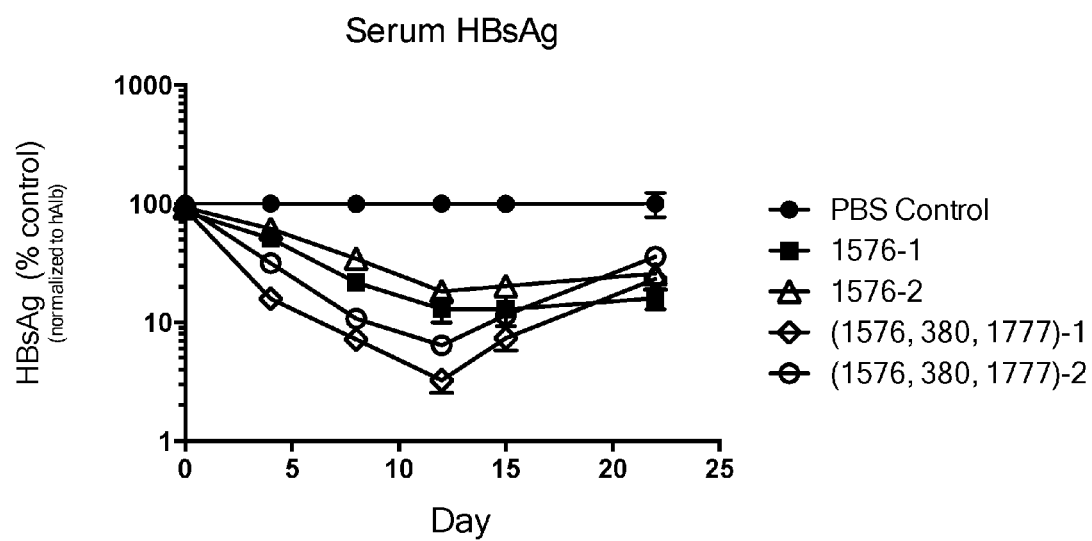


FIG. 3

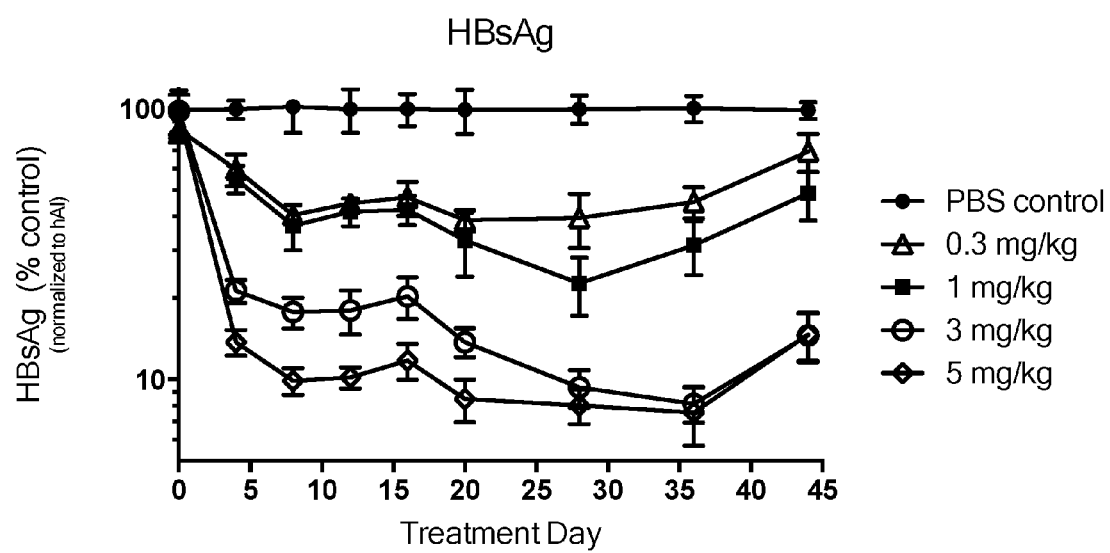


FIG. 4

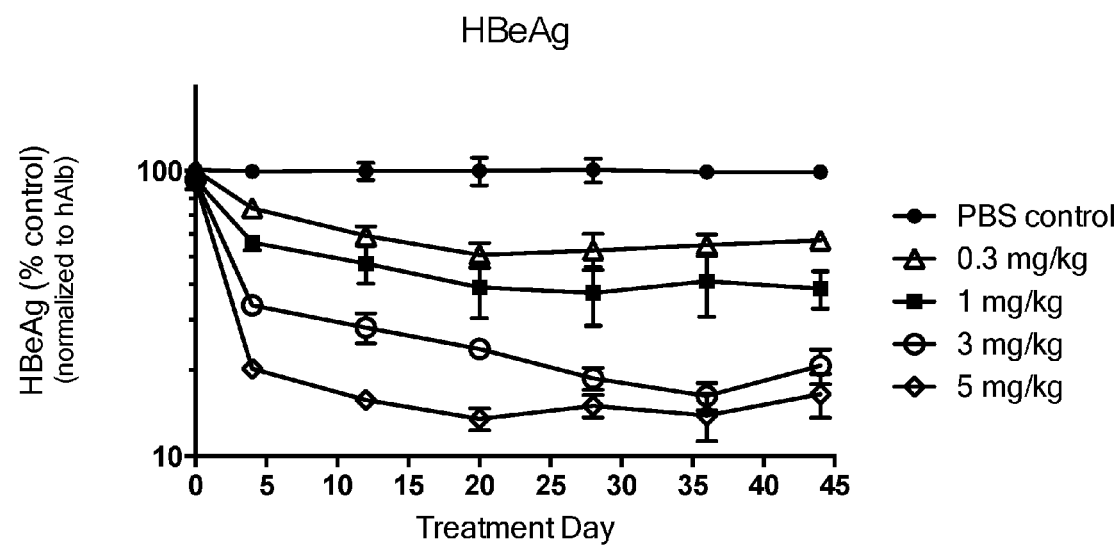


FIG. 5

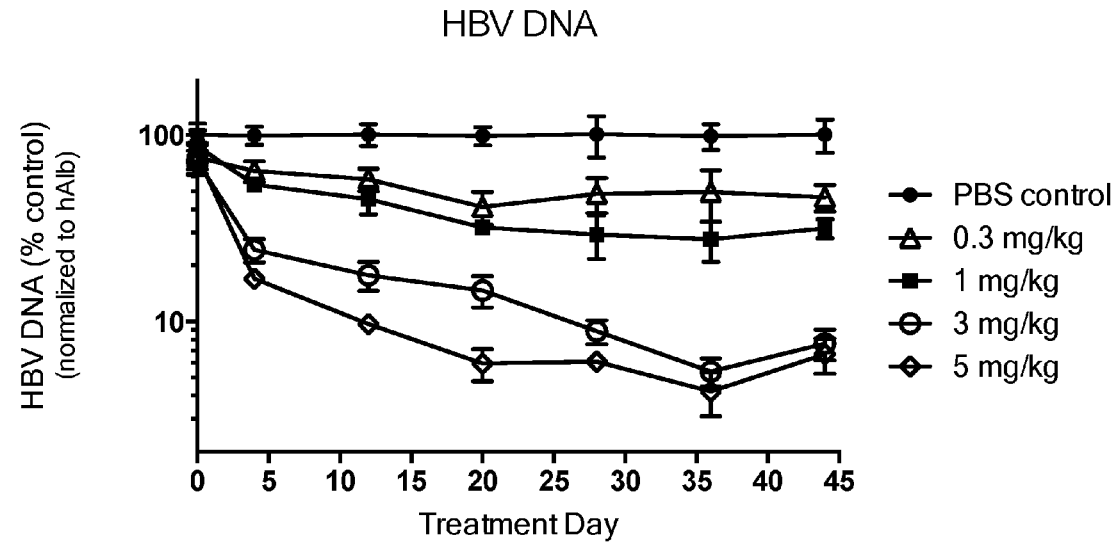


FIG. 6

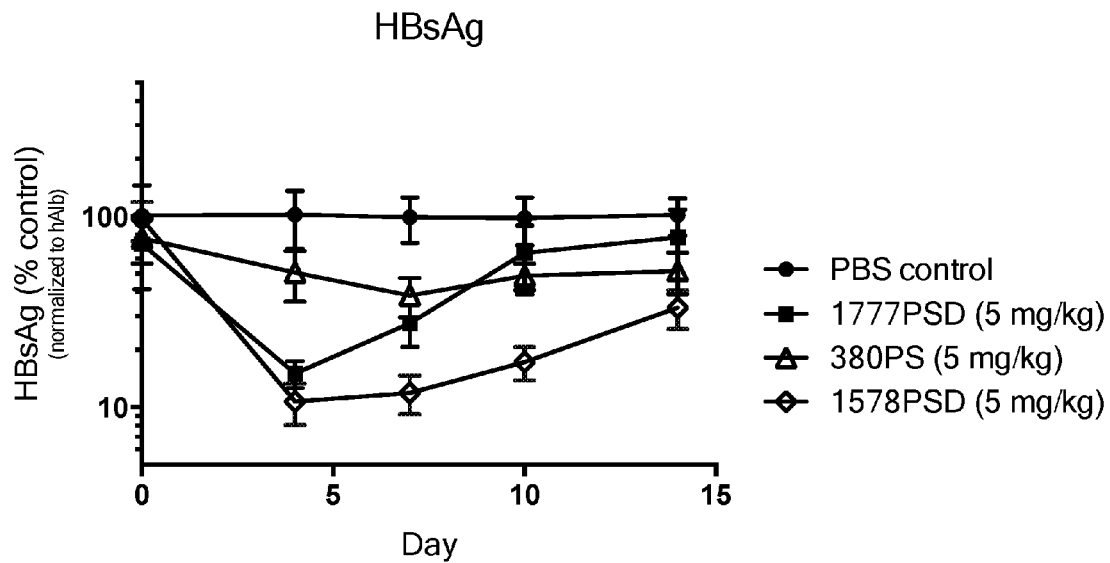


FIG. 7

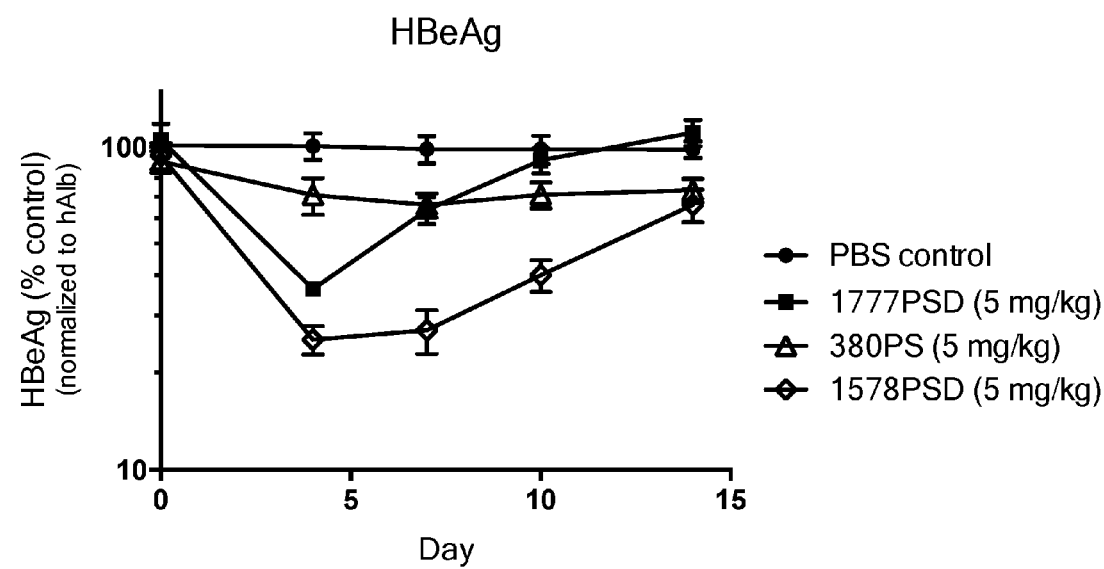


FIG. 8

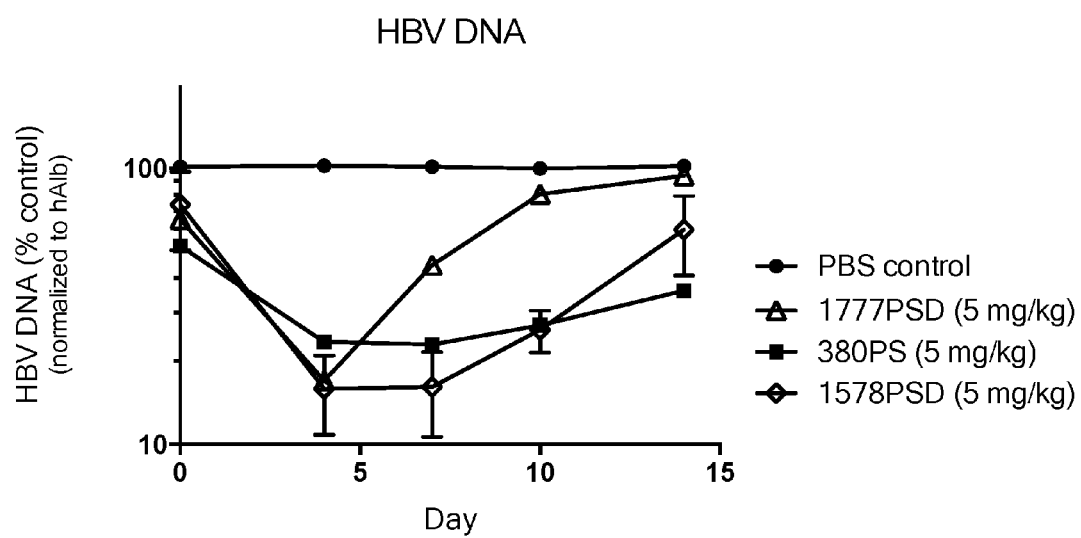


FIG. 9

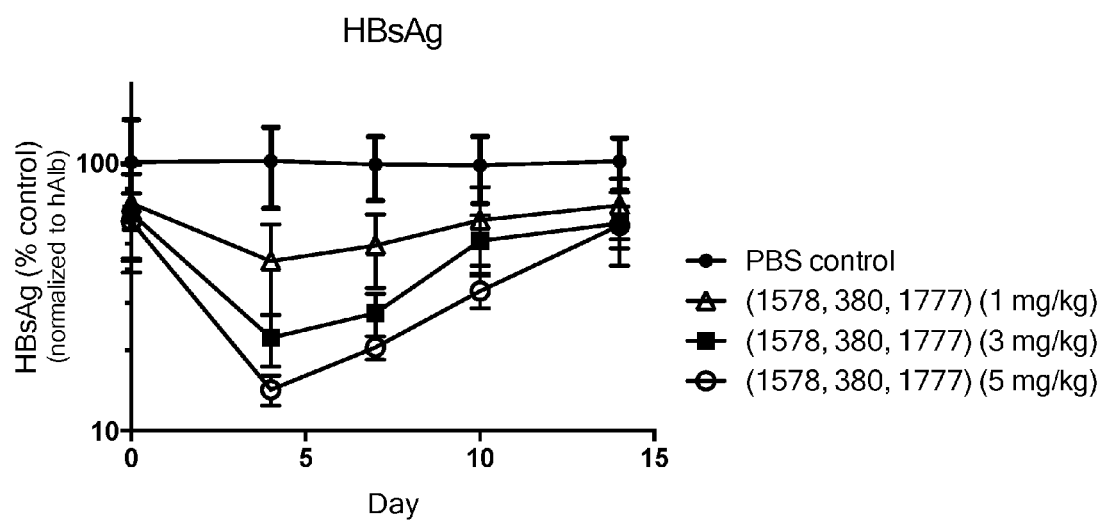


FIG. 10

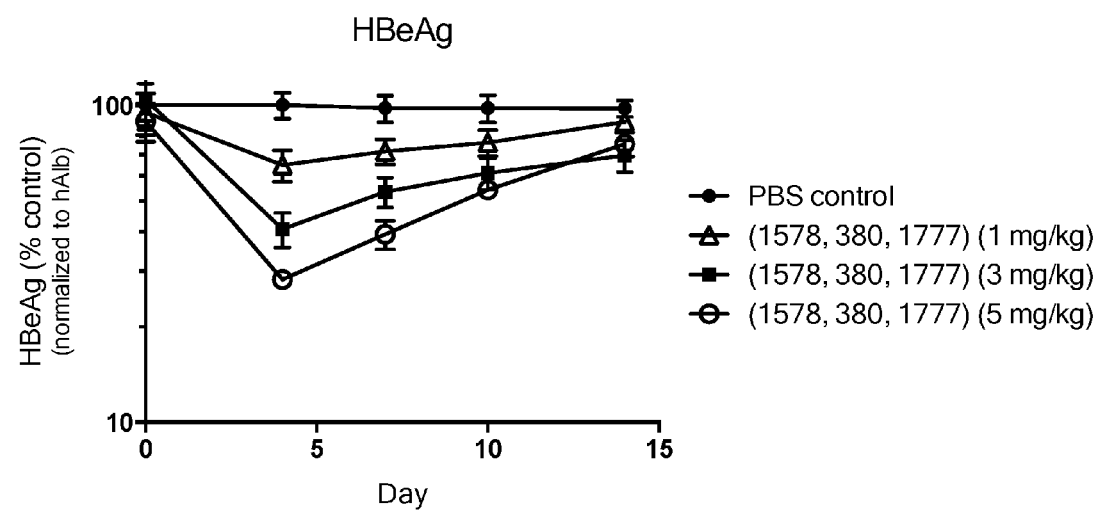


FIG. 11

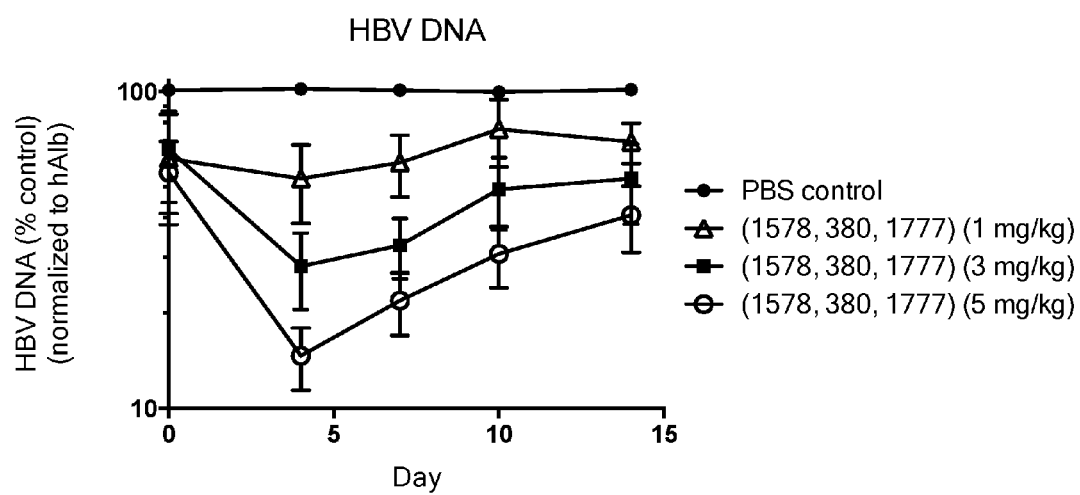


FIG. 12

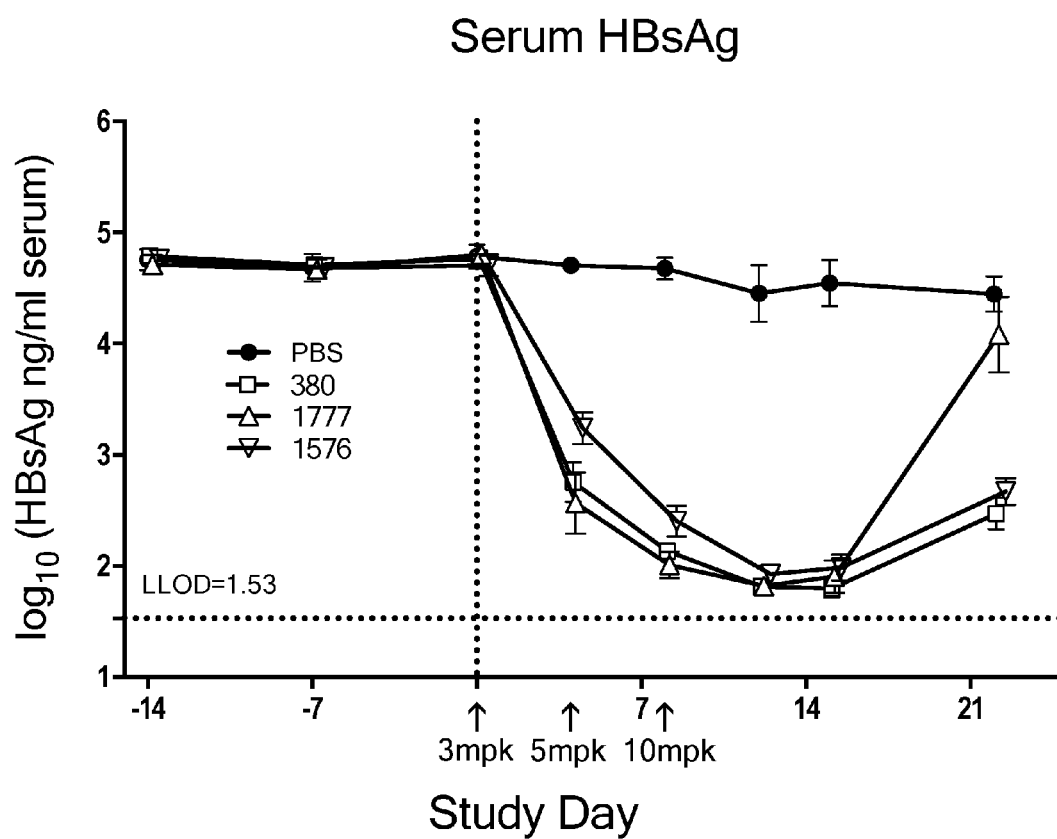


FIG. 13

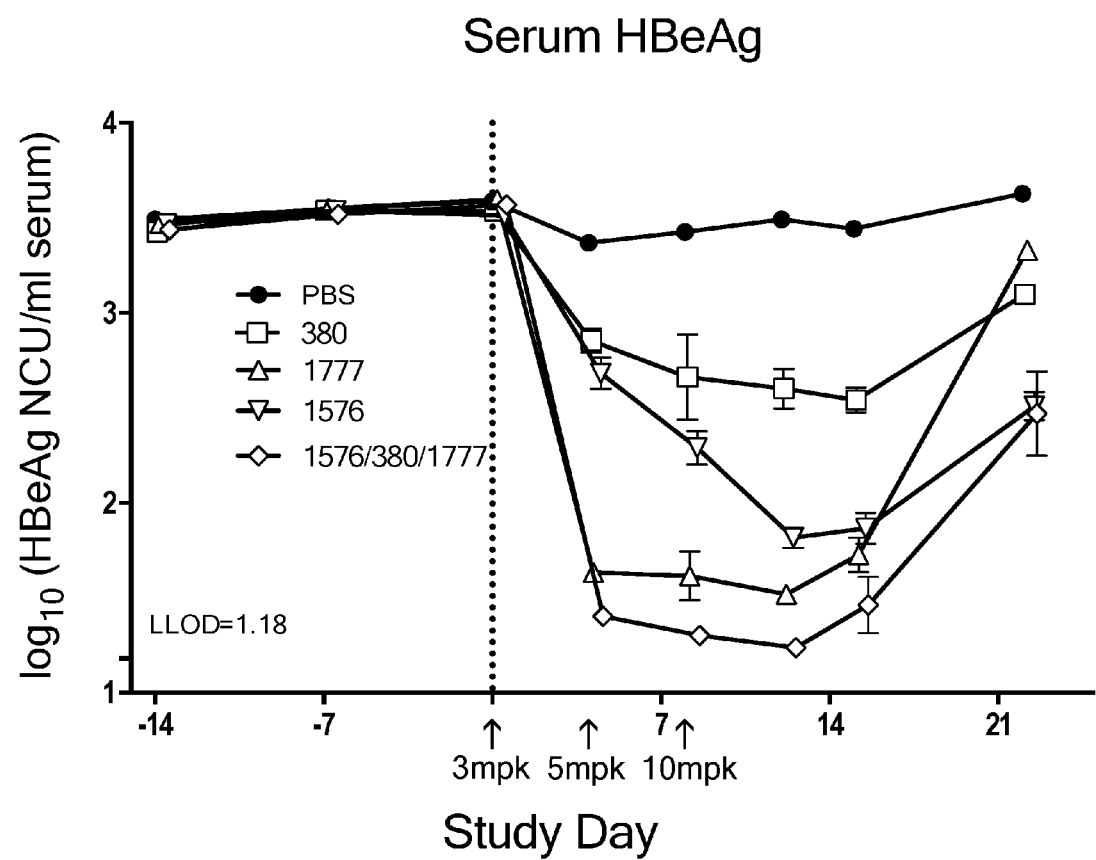


FIG. 14

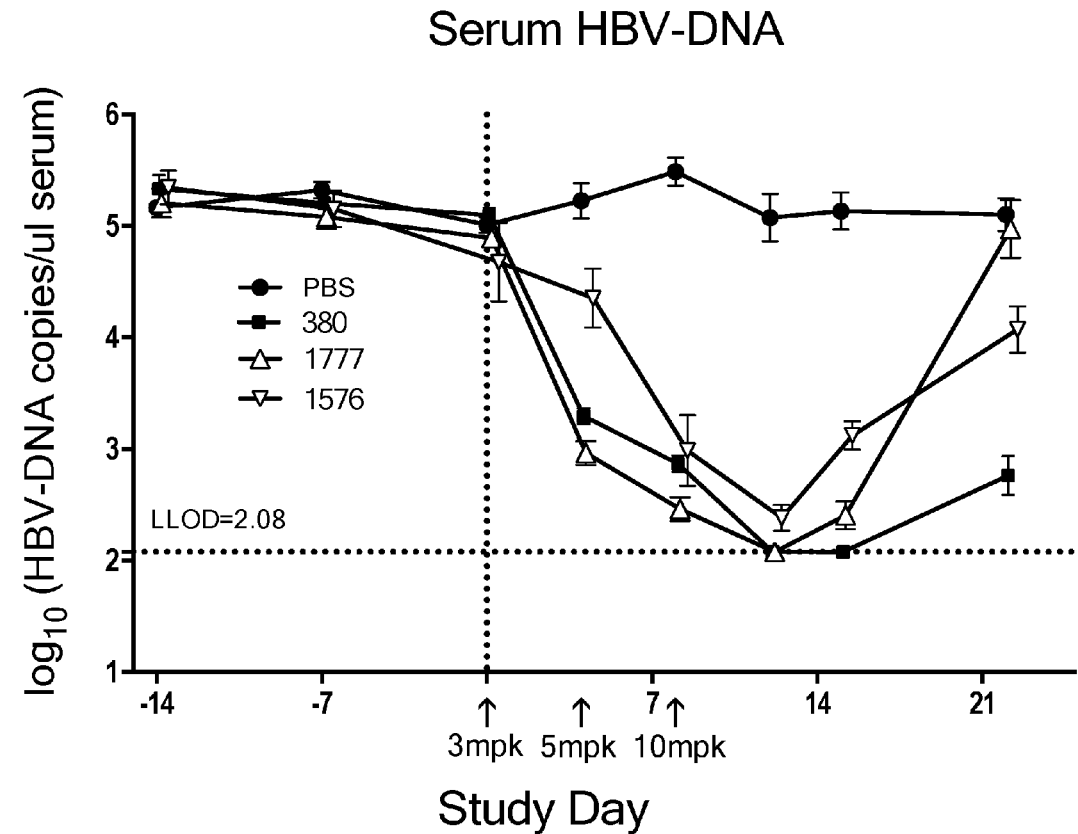


FIG. 15

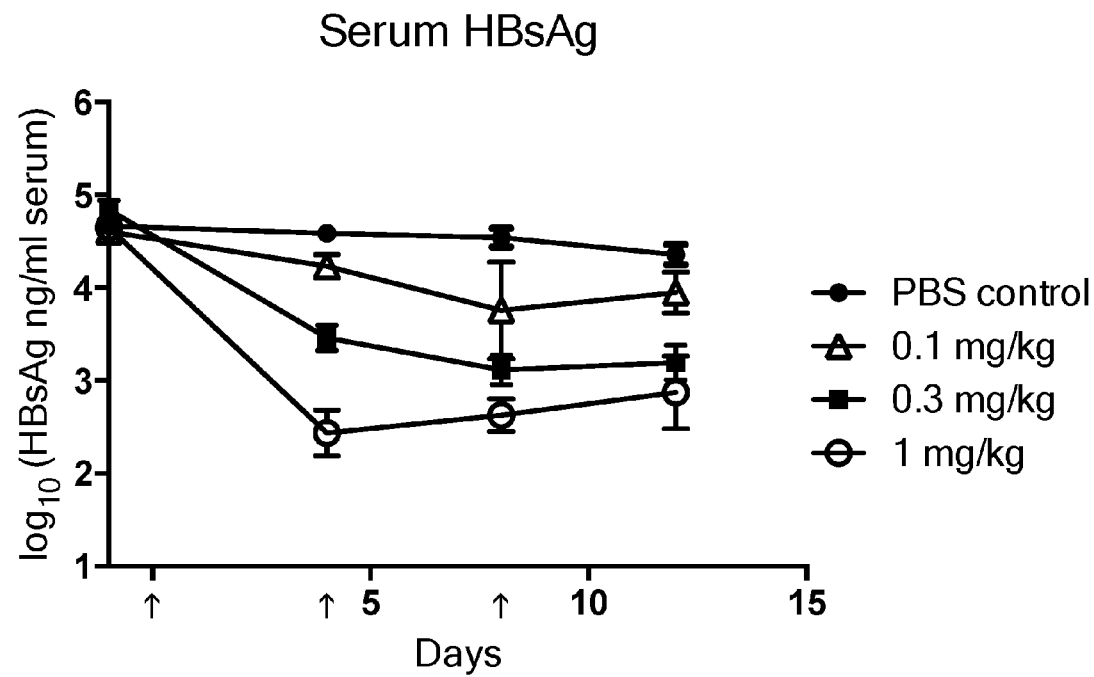


FIG. 16

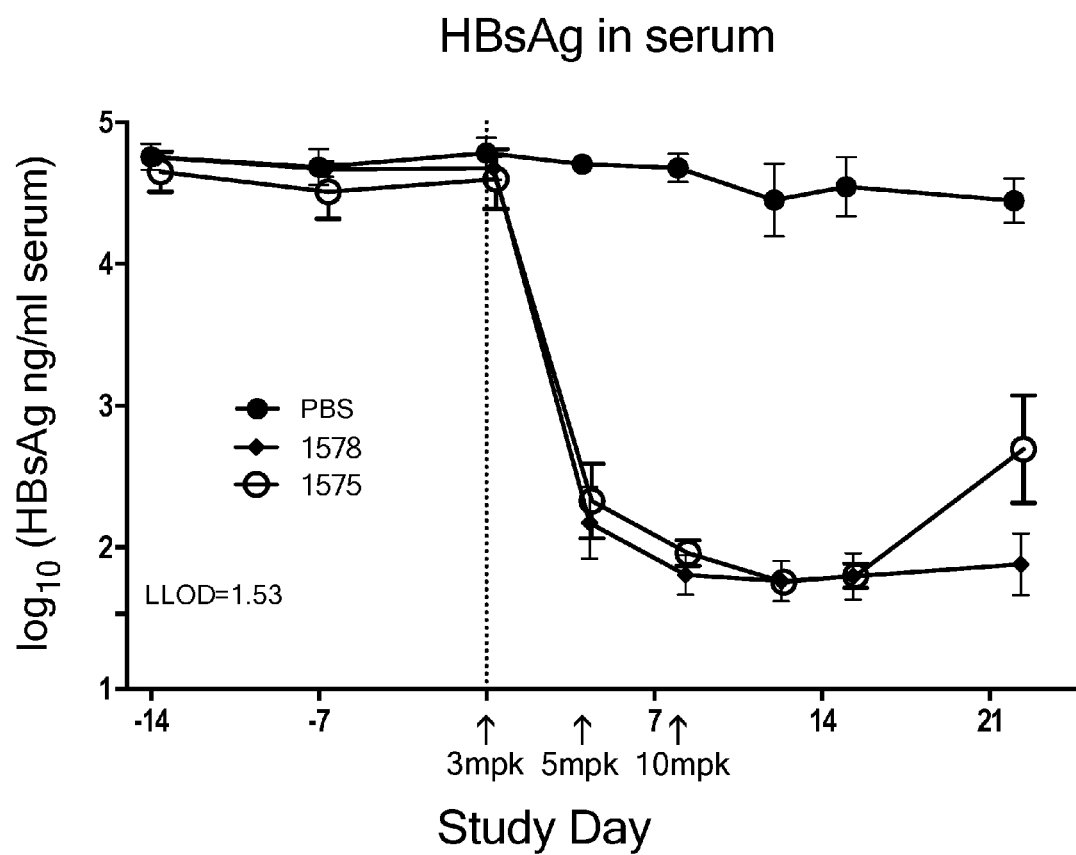


FIG. 17

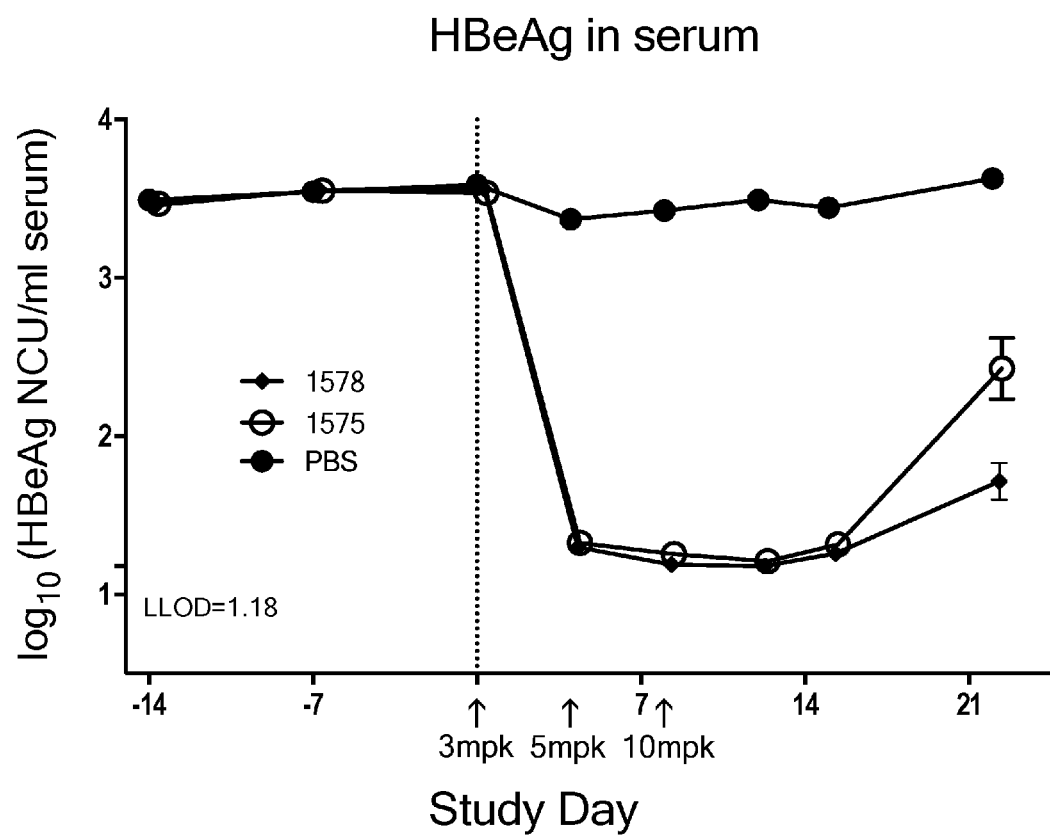
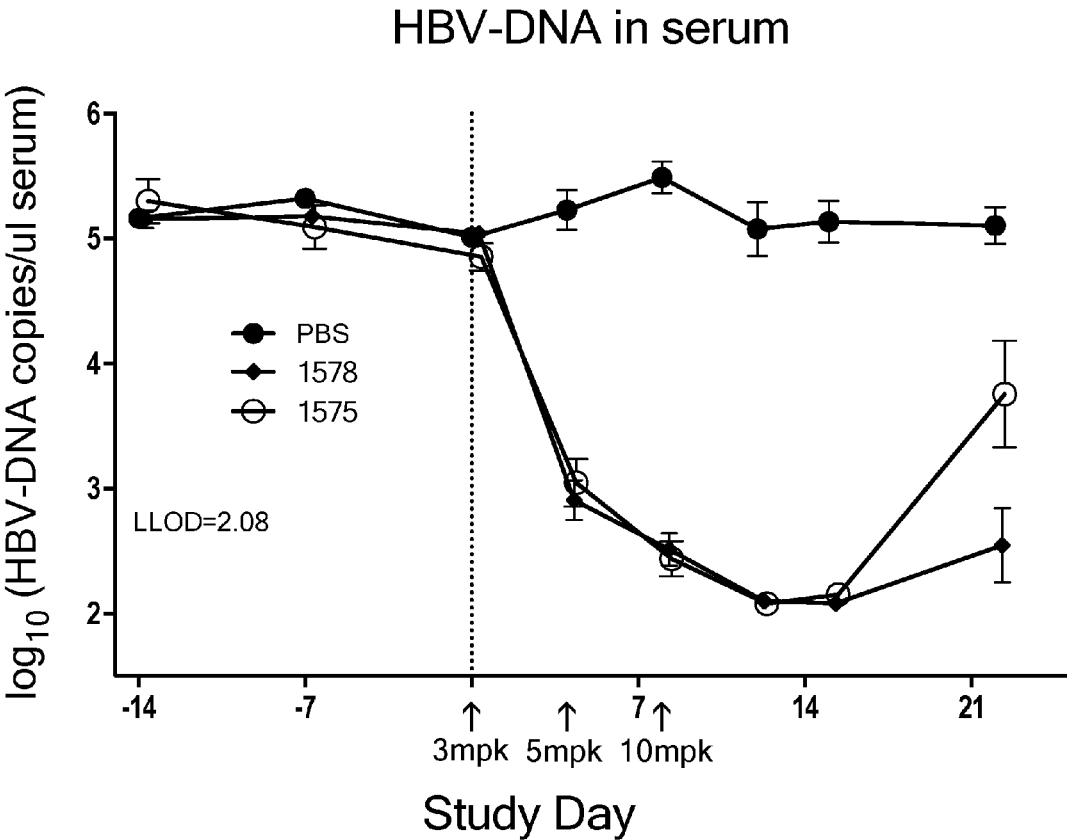


FIG. 18



MOLECULES AND AGENTS FOR TREATING HEPATITIS B VIRUS

SEQUENCE LISTING

[0001] This application includes a Sequence Listing submitted electronically as an ASCII file named ARC1444US_SL.txt.

BACKGROUND OF THE INVENTION

[0002] Hepatitis B is a liver disease that results from infection with the Hepatitis B virus (HBV). Its severity can be from a mild illness lasting a few weeks, to a serious, lifelong illness. Hepatitis B can be either acute or chronic. Acute Hepatitis B virus infection is a short-term illness that may lead to chronic infection. Chronic Hepatitis B virus infection is a long-term illness that can result in long-term health problems, such as cirrhosis of the liver, liver cancer, and death.

[0003] Hepatitis B is usually spread through transfer of a body fluid by sexual contact with an infected person, or through sharing needles for drug-injection. It can also be passed from an infected mother to her baby at birth. In endemic areas, Hepatitis B is most often spread from mother to child at birth, or by exposure to infected blood, especially from an infected child to an uninfected child during the first 5 years of life.

[0004] According to the latest WHO estimates, as many as 240 million people are chronically infected with Hepatitis B, defined as Hepatitis B surface antigen positive for at least 6 months. Approximately 780,000 persons die each year from Hepatitis B infection.

[0005] There is no specific treatment for acute hepatitis B. Chronic hepatitis B infection can be treated with drugs, including oral antiviral agents. WHO recommends the use of oral treatments such as tenofovir or entecavir. In most people, the treatment suppresses replication of the virus, but does not cure hepatitis B infection. Liver cancer progresses rapidly, and treatment options are limited. Surgery and chemotherapy, or liver transplantation can prolong life for up to a few years.

[0006] Laboratory diagnosis of hepatitis B infection can be done by detecting the hepatitis B surface antigen HBsAg. Acute hepatitis B virus infection is characterized by the presence of HBsAg and immunoglobulin M (IgM) antibody to the core antigen, HBcAg. During the initial phase of infection, patients are also seropositive for hepatitis B e-antigen (HBeAg). HBeAg is usually a marker of high levels of replication of the virus. The presence of HBeAg indicates that the blood and body fluids of the infected individual are highly contagious. Chronic infection is characterized by the persistence of HBsAg for at least 6 months, with or without concurrent HBeAg. Persistence of HBsAg is the principal marker of risk for developing chronic liver disease and liver cancer later in life.

[0007] HBV is a member of the hepadnavirus family. The virus particles, which can infect liver cells, are 30-42 nm in diameter and have an outer envelope and an icosahedral nucleocapsid core. The nucleocapsid encloses the viral DNA, and a DNA polymerase that can have reverse transcriptase activity. The outer envelope contains proteins that can be involved in viral binding and entry into cells.

[0008] In general, HBV has four identified genes, C, P, S, and X. Gene C codes for a core protein, HBcAg. An

extracellular protein HBeAg is processed from a pre-core protein. A DNA polymerase is encoded by gene P. Gene S codes for the small surface antigen HBsAg, which is one of three polypeptide surface proteins: large, middle, and small. Gene X may be associated with development of liver cancer.

[0009] HBV is a pararetrovirus, which is a non-retrovirus that uses reverse transcription in the replication process. The virus can enter the cell and multiply using RNA made by a host process. The viral genomic DNA can be transferred to the cell nucleus, acted upon by viral polymerase, and provide transcription of four viral mRNAs by host RNA polymerase. A large viral mRNA is used to make the new copies of the genome by reverse transcription, and to make the core protein and the viral DNA polymerase. The viral mRNAs are further processed to form new virus particles.

[0010] HBV can be described by four major serotypes based on epitopes presented by envelope proteins: adr, adw, ayr, ayw. HBV has been identified with eight genotypes, A-H, as well as subgenotypes. The genotypes can have distinct geographical distribution, and are used in tracking evolution and transmission of the virus.

[0011] What is needed are compositions and methods for treatment of Hepatitis B.

[0012] There is an urgent need for new methods and compositions for ameliorating or treating Hepatitis B infection.

BRIEF SUMMARY

[0013] This invention relates to the fields of biopharmaceuticals and therapeutics composed of oligomers for gene silencing. More particularly, this invention relates to structures, compositions and methods for therapeutic oligomers directed against Hepatitis B virus.

[0014] This invention provides novel molecules to be used as therapeutic agents against Hepatitis B infection. The molecules of this invention can be used as active pharmaceutical ingredients in compositions for ameliorating, preventing or treating Hepatitis B infection.

[0015] Molecules of this invention for treating Hepatitis B infection may act against any of the replication, maturation, growth, or transmission modalities of the Hepatitis B virus. By preventing the Hepatitis B virus from carrying out any one or more of its processes, the molecules of this invention can be used for ameliorating or treating Hepatitis B infection.

[0016] Embodiments of this invention can provide molecules having one or more properties that advantageously provide enhanced effectiveness against HBV, as well as compositions or formulations for therapeutic agents against Hepatitis B infection, which can provide clinical agents. The properties of the molecules of this invention arise according to their structure, and the molecular structure in its entirety, as a whole, can provide significant benefits and properties.

[0017] The active agents of this invention include oligomeric molecules that can inhibit expression of an HBV genome. Oligomers of this invention can provide potent action against HBV infection in a subject by silencing expression of an HBV genome.

[0018] In some embodiments, a wide range of novel molecules are provided, which can incorporate one or more linker groups. The linker groups can be attached in a chain in the molecule. Each linker group can also be attached to a nucleobase.

[0019] In some aspects, a linker group can be a monomer. Monomers can be attached to form a chain molecule. In a chain molecule of this invention, a linker group monomer can be attached at any point in the chain.

[0020] In certain aspects, linker group monomers can be attached in a chain molecule of this invention so that the linker group monomers reside near the ends of the chain. The ends of the chain molecule can be formed by linker group monomers.

[0021] In further aspects, the linker groups of a chain molecule can each be attached to a nucleobase. The presence of nucleobases in the chain molecule can provide a sequence of nucleobases.

[0022] In certain embodiments, this invention provides oligomer molecules having chain structures that incorporate novel combinations of the linker group monomers, along with certain natural nucleotides, or non-natural nucleotides, or modified nucleotides, or chemically-modified nucleotides.

[0023] The oligomer molecules of this invention can display a sequence of nucleobases that is targeted to a component of the HBV genome.

[0024] In additional aspects, this invention provides therapeutics for preventing, ameliorating, or treating a disease caused by Hepatitis B infection. An active compound or molecule of this invention may be used in the prevention or treatment of a viral infection caused by Hepatitis B virus.

[0025] This invention provides structures, methods and compositions for oligomeric agents that incorporate the linker group monomers. The oligomeric molecules of this invention can be used as active agents in formulations for gene silencing therapeutics targeted to HBV.

[0026] Embodiments of this invention include the following:

[0027] A compound comprising a first strand and a second strand, each of the strands being 19-29 monomers in length, the monomers comprising UNA monomers and nucleic acid monomers, wherein the compound has a duplex region of from 14 to 29 contiguous monomers in length, wherein the first strand is a passenger strand for RNA interference and the second strand is a guide strand for RNA interference, and wherein the compound comprises a sequence of bases targeted to inhibit expression of an HBV genome. The compound may contain from one to seven UNA monomers.

[0028] In some embodiments, the compound may contain a UNA monomer at the 1-end (5' end for non-UNA) of the first strand, a UNA monomer at the 3-end (3' end for non-UNA) of the first strand, and a UNA monomer at the second position from the 5' end of the second strand. A compound can contain a UNA monomer at any one or more of positions 2 to 8 from the 5' end of the second strand.

[0029] In certain embodiments, a compound may have a 3' overhang with one or more UNA monomers, natural nucleotides, non-natural nucleotides, modified nucleotides, or chemically-modified nucleotides, or combinations thereof. The 3' overhang can have one or more deoxythymidine nucleotides, 2'-O-methyl nucleotides, inverted abasic monomers, inverted thymidine monomers, L-thymidine monomers, or glyceryl nucleotides.

[0030] In some aspects, a compound may have one or more nucleic acid monomers that is a non-natural nucleotide, a modified nucleotide, or a chemically-modified nucleotide. A compound may have one or more monomers

connected by a phosphorothioate, a chiral phosphorothioate, or a phosphorodithioate linkage.

[0031] In further aspects, a compound may be conjugated to a delivery moiety, such as, for example, a moiety that binds to a glycoprotein receptor, a galactose, a galactosamine, a N-acetylgalactosamine, a GalNAc group, or a cholesterol delivery moiety. A compound may be conjugated to a delivery moiety and have increased uptake in the liver as compared to an unconjugated compound.

[0032] This invention includes lipid nanoparticle-oligomer compounds, in which one or more compounds are attached to a lipid nanoparticle.

[0033] A composition of this disclosure can include one or more compounds and a pharmaceutically acceptable carrier. The carrier may be lipid nanoparticles or liposomes.

[0034] A composition of this disclosure may contain a first compound targeted to a conserved region of HBV transcripts for genes X, C, P and S, a second compound targeted to inhibit HBsAg, a third compound targeted to a conserved region of HBV transcripts for genes X, C and S, and a pharmaceutically acceptable carrier.

[0035] Embodiments of this invention include compositions containing one or more compounds having reference positions from any of positions 1525 to 1582, 374 to 414, 1776 to 1782, 244 to 256, and 1818 to 1866. In certain embodiments, a composition may include a compound having a reference position from 1525 to 1582, a compound having a reference position from 374 to 414, and a compound having a reference position from 1776 to 1782.

[0036] Embodiments of this invention further contemplate methods for preventing, ameliorating or treating a disease or condition associated with HBV infection in a subject in need, by administering to the subject an effective amount of a composition above. The administration of the composition can reduce HBV viral titer in the subject. A subject may have been diagnosed with a disease associated with Hepatitis B virus infection, for example, a liver disease.

[0037] This invention includes methods for inhibiting the replication, maturation, growth, or transmission of a Hepatitis B virus in a subject in need, by administering to the subject an effective amount of a composition above. The composition may reduce serum concentration of HBsAg in the subject. In some embodiments, the administration of the composition may reduce serum concentration of HBsAg in the subject by 2-log₁₀-fold, or by 2-log₁₀-fold for at least 7 days. In certain embodiments, the administration of the composition can reduce HBeAg in the subject, or HBV DNA in the subject.

[0038] This invention also contemplates methods for inhibiting expression of a Hepatitis B virus polynucleotide in a subject in need, by administering to the subject a composition above, as well as the use of a composition above for preventing, ameliorating or treating a disease or condition associated with Hepatitis B infection in a subject in need.

[0039] In some aspects, this disclosure includes compositions for use in medical therapy, or for use in the treatment of the human or animal body. In certain aspects, this invention includes the use of a composition for preparing or manufacturing a medicament for preventing, ameliorating or treating a disease or condition associated with Hepatitis B infection in a subject in need.

BRIEF DESCRIPTION OF THE DRAWINGS

[0040] FIG. 1: FIG. 1 shows a map of HBV protein coding regions and selected transcripts for a reference genome. Nucleotide position 1/3221 is designated at the top. Further designations are as follows: pre-S1, large HBsAg; pre-S2, medium HBsAg; S, HBsAg; P, polymerase; X, HBx protein; pre-C, pre-core/HBeAg; C, HB core Ag. The 2.4 kb, 2.1 kb, and 0.7 kb transcripts coding for the pre-S1/pre-S2/S, as well as the transcript coding the X protein are shown. The pre-Core/HBeAg protein is generated from a long, 3.5 kb transcript (not shown) originating at position ~1700, while the core and polymerase proteins and the pre-genomic RNA used as a template for viral replication are generated from a ~200 nt shorter transcript. The ranges of reference positions for certain UNA oligomers, designated UNA oligomer 1, UNA oligomer 2, and UNA oligomer 3, are shown.

[0041] FIG. 2: FIG. 2 shows HBV inhibitory effect in vivo for UNA oligomers, observed in a humanized PXB Mouse model of HBV infection. The UNA oligomers of this invention exhibited profound reduction of HBV serum infection parameters in vivo. In this study, the UNA oligomers were contained in lipid nanoparticle formulations, -1 and -2, and an ascending dose was used. The UNA oligomers were formulated in lipid nanoparticles and injected intravenously into HBV-infected Phoenix Bio (PXB) mice containing human hepatocytes (70%). Treatment with both UNA oligomer 1576 and a UNA oligomer triad composition (1576, 380, 177) caused a rapid and sustained reduction in viral endpoint serum HBsAg.

[0042] FIG. 3: FIG. 3 shows HBV inhibitory effect in vivo for UNA oligomers, observed in a humanized PXB Mouse model of HBV infection. Treatment with UNA oligomer triad (1576, 380, 1777) caused a rapid and sustained reduction in viral endpoint serum HBsAg. The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition. The study used an ascending dose in which mice were administered every 4 days, up to day 40, and viral endpoints were monitored every 4 days through day 44.

[0043] FIG. 4: FIG. 4 shows HBV inhibitory effect in vivo for UNA oligomers, observed in a humanized PXB Mouse model of HBV infection. Treatment with UNA oligomer triad (1576, 380, 1777) caused a rapid and sustained reduction in viral endpoint serum HBeAg. The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition. The study used an ascending dose in which mice were administered every 4 days, up to day 40, and viral endpoints were monitored every 4 days through day 44.

[0044] FIG. 5: FIG. 5 shows HBV inhibitory effect in vivo for UNA oligomers, observed in a humanized PXB Mouse model of HBV infection. Treatment with UNA oligomer triad (1576, 380, 1777) caused a rapid and sustained reduction in viral endpoint serum HBV DNA. The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition. The study used an ascending dose in which mice were administered every 4 days, up to day 40, and viral endpoints were monitored every 4 days through day 44.

[0045] FIG. 6: FIG. 6 shows HBV inhibitory effect in vivo for UNA oligomers, observed in a humanized PXB Mouse model of HBV infection. Treatment with UNA oligomers 1777, 380 and 1578 caused a rapid and sustained reduction in viral endpoint serum HBsAg.

[0046] FIG. 7: FIG. 7 shows HBV inhibitory effect in vivo for UNA oligomers, observed in a humanized PXB Mouse model of HBV infection. Treatment with UNA oligomers 1777, 380 and 1578 caused a rapid and sustained reduction in viral endpoint serum HBeAg.

[0047] FIG. 8: FIG. 8 shows HBV inhibitory effect in vivo for UNA oligomers, observed in a humanized PXB Mouse model of HBV infection. Treatment with UNA oligomers 1777, 380 and 1578 caused a rapid and sustained reduction in viral endpoint serum HBV DNA.

[0048] FIG. 9: FIG. 9 shows HBV inhibitory effect in vivo for UNA oligomers, observed in a humanized PXB Mouse model of HBV infection. Treatment with a UNA oligomer triad composition (1578, 380, 1777) caused a rapid and sustained reduction in viral endpoint serum HBsAg. The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition.

[0049] FIG. 10: FIG. 10 shows HBV inhibitory effect in vivo for UNA oligomers, observed in a humanized PXB Mouse model of HBV infection. Treatment with a UNA oligomer triad composition (1578, 380, 1777) caused a rapid and sustained reduction in viral endpoint serum HBeAg. The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition.

[0050] FIG. 11: FIG. 11 shows HBV inhibitory effect in vivo for UNA oligomers, observed in a humanized PXB Mouse model of HBV infection. Treatment with a UNA oligomer triad composition (1578, 380, 1777) caused a rapid and sustained reduction in viral endpoint serum HBV DNA. The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition.

[0051] FIG. 12: FIG. 12 shows HBV inhibitory effect in vivo for UNA oligomers, observed in an AAV-HBV mouse model of HBV infection. The UNA oligomers of this invention exhibited profound reduction of HBV serum infection parameters in vivo. In general, the AAV-HBV mouse model is a robust model for investigating HBV infection. The UNA oligomers were formulated in lipid nanoparticles and injected intravenously into C57Bl/6 mice with active HBV replication after AAV-mediated delivery of a recombinant HBV genome to the liver. The study used an ascending dose, and serum viral endpoints were monitored 15 days before, and at least 22 days after treatment. Treatment with each of UNA oligomers 380, 1777, and 1576 caused a rapid and sustained reduction in viral endpoint serum HBsAg.

[0052] FIG. 13: FIG. 13 shows HBV inhibitory effect in vivo for UNA oligomers, observed in an AAV-HBV mouse model of HBV infection. The UNA oligomers were formulated in lipid nanoparticles and injected intravenously into C57Bl/6 mice with active HBV replication after AAV-mediated delivery of a recombinant HBV genome to the liver. Treatment with each of UNA oligomers 380, 1777, and 1576, as well as the UNA oligomer triad composition of the same compounds (1576, 380, 1777) caused a rapid and sustained reduction in viral endpoint serum HBeAg. This head-to-head comparison shows that the triad composition provided surprisingly increased potency throughout the duration of the effect, relative to the individual oligomers.

[0053] FIG. 14: FIG. 14 shows HBV inhibitory effect in vivo for UNA oligomers, observed in an AAV-HBV mouse model of HBV infection. The UNA oligomers were formulated in lipid nanoparticles and injected intravenously into C57Bl/6 mice with active HBV replication after AAV-mediated delivery of a recombinant HBV genome to the

liver. Treatment with each of UNA oligomers 380, 1777, and 1576 caused a rapid and sustained reduction in viral endpoint serum HBV DNA.

[0054] FIG. 15: FIG. 15 shows HBV inhibitory effect in vivo for UNA oligomers, observed in an AAV-HBV mouse model of HBV infection. The UNA oligomers were formulated in lipid nanoparticles and injected intravenously into C57Bl/6 mice with active HBV replication after AAV-mediated delivery of a recombinant HBV genome to the liver. The study was an ascending dose design in which mice were treated with 3 mg/kg on day 0, then 5 mg/kg on day 4, then 10 mg/kg on day 8, and serum viral endpoints were monitored up to day 12 after treatment. Treatment with the UNA oligomer triad composition (1777, 380, 1578) caused a rapid and sustained reduction in viral endpoint serum HBsAg. The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition.

[0055] FIG. 16: FIG. 16 shows HBV inhibitory effect in vivo for UNA oligomers, observed in an AAV-HBV mouse model of HBV infection. The UNA oligomers were formulated in lipid nanoparticles and injected intravenously into C57Bl/6 mice with active HBV replication after AAV-mediated delivery of a recombinant HBV genome to the liver. Treatment with each of UNA oligomers 1578 and 1575 caused a rapid and sustained reduction in viral endpoint serum HBsAg.

[0056] FIG. 17: FIG. 17 shows HBV inhibitory effect in vivo for UNA oligomers, observed in an AAV-HBV mouse model of HBV infection. The UNA oligomers were formulated in lipid nanoparticles and injected intravenously into C57Bl/6 mice with active HBV replication after AAV-mediated delivery of a recombinant HBV genome to the liver. Treatment with each of UNA oligomers 1578 and 1575 caused a rapid and sustained reduction in viral endpoint serum HBeAg.

[0057] FIG. 18: FIG. 18 shows HBV inhibitory effect in vivo for UNA oligomers, observed in an AAV-HBV mouse model of HBV infection. The UNA oligomers were formulated in lipid nanoparticles and injected intravenously into C57Bl/6 mice with active HBV replication after AAV-mediated delivery of a recombinant HBV genome to the liver. Treatment with each of UNA oligomers 1578 and 1575 caused a rapid and sustained reduction in viral endpoint serum HBV DNA.

DETAILED DESCRIPTION OF THE INVENTION

[0058] This invention provides a range of novel agents and compositions to be used as therapeutics against Hepatitis B infection. Molecules of this invention can be used as active pharmaceutical ingredients in compositions for ameliorating, preventing or treating Hepatitis B infection.

[0059] The galenic molecules of this invention can prevent Hepatitis B virus from carrying out one or more of its processes. Molecules of this invention can be used for ameliorating or treating Hepatitis B infection, and may act against any of the replication, maturation, growth, or transmission modes of the Hepatitis B virus.

[0060] Novel agents of this invention include oligomeric molecules that inhibit expression of an HBV genome.

[0061] Embodiments of this invention can provide extraordinary and surprisingly enhanced efficacy against HBV infection in a subject by attacking all portions of the HBV genome. More particularly, agents and compositions

of this invention can simultaneously inhibit all identified genes of HBV: C, P, S, and X. Thus, the compounds and compositions of this disclosure can inhibit the small surface antigen HBsAg, as well as the extracellular protein HBeAg, in addition to X protein and viral polymerase.

[0062] The properties of the compounds of this invention arise according to their molecular structure, and the structure of the molecule in its entirety, as a whole, can provide significant benefits based on those properties. Embodiments of this invention can provide molecules having one or more properties that advantageously provide enhanced effectiveness against HBV, as well as compositions or formulations for therapeutic agents against Hepatitis B infection, which can provide clinical agents.

[0063] A wide range of novel molecules are provided, each of which can incorporate specialized linker groups. The linker groups can be attached in a chain in the molecule. Each linker group can also be attached to a nucleobase.

[0064] In some aspects, a linker group can be a monomer. Monomers can be attached to form a chain molecule. In a chain molecule of this invention, a linker group monomer can be attached at any point in the chain.

[0065] In certain aspects, linker group monomers can be attached in a chain molecule of this invention so that the linker group monomers reside near the ends of the chain. The ends of the chain molecule can be formed by linker group monomers.

[0066] As used herein, a chain molecule can also be referred to as an oligomer.

[0067] In further aspects, the linker groups of a chain molecule can each be attached to a nucleobase. The presence of nucleobases in the chain molecule can provide a sequence of nucleobases.

[0068] In certain embodiments, this invention provides oligomer molecules having chain structures that incorporate novel combinations of the linker group monomers, along with certain natural nucleotides, or non-natural nucleotides, or modified nucleotides, or chemically-modified nucleotides.

[0069] The oligomer molecules of this invention can display a sequence of nucleobases that is targeted to a component of an HBV genome. In some embodiments, an oligomer can be targeted to a portion of the HBV genome that is conserved, or highly conserved, among a number of known HBV genomic sequences.

[0070] In some aspects, this invention provides active oligomer molecules that correspond to, or are complementary to at least a fragment of an HBV nucleic acid molecule, and that decrease expression of at least such a fragment present in a cell. In some embodiments, the active oligomer molecule can be double-stranded.

[0071] Without wishing to be bound by any one particular theory, it is believed that a cellular pathway may use active oligomers of this invention to be sequence-specific regulators in an RNA interference pathway. The active oligomers may bind to the RNA-induced silencing complex (RISC complex), where a sense strand, also referred to as the passenger strand, and an antisense strand, also referred to as the guide strand, can be unwound, and the antisense strand complexed in the RISC complex. The guide strand can bind to a complementary sequence to which it was targeted, for example, a target sequence in an mRNA, which can be subsequently cleaved, resulting in inactivation of the nucleic

acid molecule containing the target sequence. As a result, the expression of mRNA containing the target sequence can be reduced.

[0072] In some embodiments, an oligomeric molecule may be attached to a delivery moiety. Examples of delivery moieties include glycoprotein receptors, galactoses, galactosamines, N-acetylgalactosamines, GalNAc groups, cholesterol, sterols, phytosterols, steroids, zoosterols, lanosterols, stigmastanols, dihydrolanosterols, zymosterols, zymostenols, desmosterols, and 7-dehydrocholesterol s.

[0073] In additional aspects, this invention provides therapeutics for preventing, ameliorating, or treating a disease caused by Hepatitis B infection. An active compound or molecule of this invention may be used in the prevention or treatment of a viral infection caused by Hepatitis B virus.

[0074] This invention provides structures, methods and compositions for oligomeric agents that incorporate the linker group monomers. The oligomeric molecules of this invention can be used as active agents in formulations for gene silencing therapeutics targeted to HBV.

[0075] This invention provides a range of molecules that are useful for providing therapeutic effects because of their activity in regulating expression of a gene. The molecules of this invention are structured to provide gene regulating or silencing activity in vitro and in vivo.

[0076] Embodiments of this invention can provide molecules for use as therapeutic agents against Hepatitis B infection. The molecules can be used as active pharmaceutical ingredients in compositions for ameliorating, preventing or treating Hepatitis B infection.

[0077] In certain embodiments, an active molecule can be structured as an oligomer composed of monomers. The oligomeric structures of this invention may contain one or more linker group monomers, along with certain nucleotides.

[0078] Modalities of Action

[0079] Molecules of this invention for treating Hepatitis B infection may act against any of the replication, maturation, growth, or transmission modalities of the Hepatitis B virus. By preventing the Hepatitis B virus from carrying out any one or more of its normal processes, the molecules of this invention can be used for ameliorating or treating Hepatitis B infection.

[0080] This invention can provide unexpectedly advantageous efficacy against HBV infection in a subject by simultaneously modulating all portions of the HBV genome.

[0081] In some embodiments, inventive UNA oligomeric agents and compositions of this disclosure can inhibit expression of each of the HBV genes C, P, S, and X.

[0082] In some aspects, inventive UNA oligomeric agents and compositions of this disclosure can simultaneously inhibit expression of all genes of HBV, including genes C, P, S, and X.

[0083] In particular aspects, inventive UNA oligomeric compositions of this disclosure can simultaneously inhibit expression of multiple genes of HBV, such as genes P and C, or P and S, or P and X.

[0084] In further aspects, inventive UNA oligomeric compositions of this disclosure can simultaneously inhibit expression of multiple genes of HBV, such as genes P, S and C, or P, X and S, or P, C and X.

[0085] In certain aspects, the compounds of this invention can inhibit the small surface antigen HBsAg in vivo, regardless of the genomic source of HBsAg in the subject.

[0086] In further aspects, compounds and compositions of this invention can inhibit the HBV extracellular protein HBeAg, the X protein, and HBV viral polymerase.

[0087] In some aspects, a therapeutic molecule of this invention can be active in preventing or inhibiting a step of the replication cycle of hepatitis B virus.

[0088] Viral components of HBV can include a nucleocapsid, fully or partially double stranded DNA (relaxed circular, rcDNA), a polymerase, surface antigens, core proteins, a regulatory X-protein, and secreted proteins.

[0089] In some embodiments, a therapeutic molecule of this invention can be active in preventing or inhibiting attachment of viral components to cell-associated proteoglycans.

[0090] Certain embodiments of this invention provide a therapeutic molecule that can be active in preventing or inhibiting binding of a viral component to a hepatocyte receptor.

[0091] In further embodiments, a therapeutic molecule of this invention can be active in preventing or inhibiting entry of a viral component into a cell by endocytosis, or fusion of a viral component to a cell membrane.

[0092] A therapeutic molecule of this invention may be active in preventing or inhibiting release of a viral component into the cytoplasm of a cell.

[0093] In additional embodiments, a therapeutic molecule of this invention can be active in preventing or inhibiting internal cell transport of an HBV nucleocapsid.

[0094] Aspects of this disclosure can provide a therapeutic molecule, which can be active in preventing or inhibiting release of HBV rcDNA in a cell.

[0095] In some embodiments, a therapeutic molecule of this invention can be active in preventing or inhibiting operation of the viral polymerase.

[0096] Certain embodiments may provide a therapeutic molecule that can be active in preventing or inhibiting development of an HBV genomic DNA in a cell.

[0097] In further embodiments, a therapeutic molecule of this invention can be active in preventing or inhibiting production of a viral RNA in a cell.

[0098] A therapeutic molecule of this invention may be active in preventing or inhibiting viral replication in a cell.

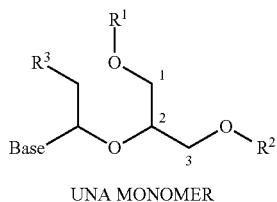
[0099] In additional embodiments, a therapeutic molecule may be active in preventing or inhibiting an HBV regulatory X-protein in a cell.

[0100] Further aspects of this disclosure can provide a therapeutic molecule that be active in preventing or inhibiting translation or reverse transcription of a viral RNA in a cell.

[0101] In some embodiments, a therapeutic molecule of this invention can be active in preventing or inhibiting maturation of a viral nucleocapsid in a cell.

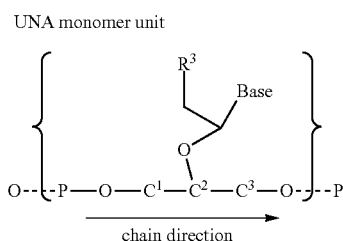
[0102] UNA Monomers

[0103] In some embodiments, linker group monomers can be unlocked nucleomonomers (UNA monomers), which are small organic molecules based on a propane-1,2,3-tri-yl-trisoxo structure as shown below:



where R^1 and R^2 are H, and R^1 and R^2 can be phosphodiester linkages, Base can be a nucleobase, and R^3 is a functional group described below.

[0104] In another view, the UNA monomer main atoms can be drawn in IUPAC notation as follows:

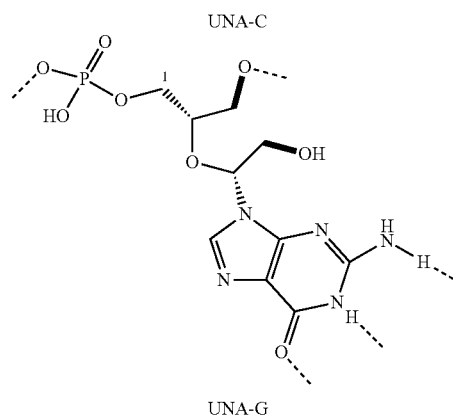
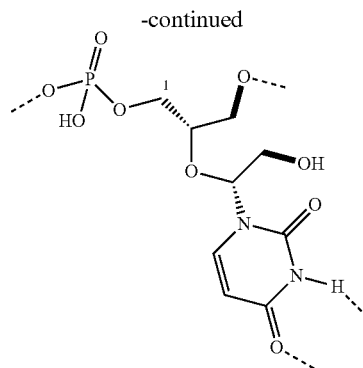
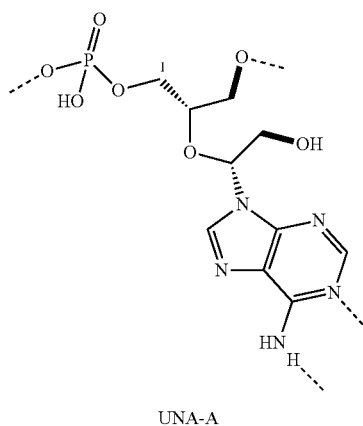


where the direction of progress of the oligomer chain is from the 1-end to the 3-end of the propane residue.

[0105] Examples of a nucleobase include uracil, thymine, cytosine, 5-methylcytosine, adenine, guanine, inosine, and natural and non-natural nucleobase analogues.

[0106] In general, because the UNA monomers are not nucleotides, they can exhibit at least four forms in an oligomer. First, a UNA monomer can be an internal monomer in an oligomer, where the UNA monomer is flanked by other monomers on both sides. In this form, the UNA monomer can participate in base pairing when the oligomer is a duplex, for example, and there are other monomers with nucleobases in the duplex.

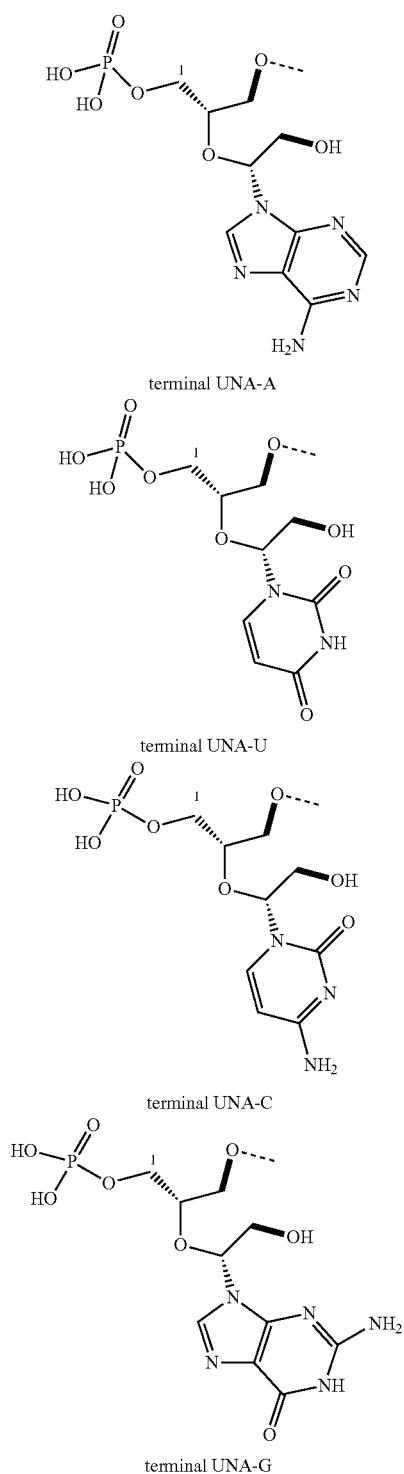
[0107] Examples of UNA monomer as internal monomers flanked at both the propane-1-yl position and the propane-3-yl position, where R^3 is $-\text{OH}$, are shown below.



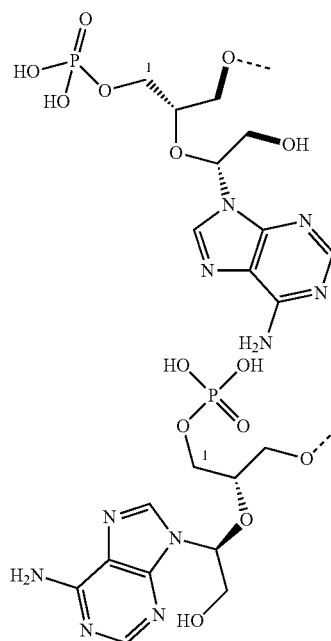
[0108] Second, a UNA monomer can be a monomer in an overhang of an oligomer duplex, where the UNA monomer is flanked by other monomers on both sides. In this form, the UNA monomer does not participate in base pairing. Because the UNA monomers are flexible organic structures, unlike nucleotides, the overhang containing a UNA monomer will be a flexible terminator for the oligomer.

[0109] A UNA monomer can be a terminal monomer in an overhang of an oligomer, where the UNA monomer is attached to only one monomer at either the propane-1-yl position or the propane-3-yl position. In this form, the UNA monomer does not participate in base pairing. Because the UNA monomers are flexible organic structures, unlike nucleotides, the overhang containing a UNA monomer can be a flexible terminator for the oligomer.

[0110] Examples of a UNA monomer as a terminal monomer attached at the propane-3-yl position are shown below.



[0111] Because a UNA monomer can be a flexible molecule, a UNA monomer as a terminal monomer can assume widely differing conformations. An example of an energy minimized UNA monomer conformation as a terminal monomer attached at the propane-3-yl position is shown below.



[0112] UNA-A terminal forms: the dashed bond shows the propane-3-yl attachment. Thus, UNA oligomers having a terminal UNA monomer are significantly different in structure from conventional nucleic acid agents, such as siRNAs. For example, siRNAs may require that terminal monomers or overhangs in a duplex be stabilized. In contrast, the conformability of a terminal UNA monomer can provide UNA oligomers with different properties.

[0113] Among other things, the structure of the UNA monomer allows it to be attached to naturally-occurring nucleotides. A UNA oligomer can be a chain composed of UNA monomers, as well as various nucleotides that may be based on naturally-occurring nucleosides.

[0114] In some embodiments, the functional group R^3 of a UNA monomer can be $-OR^4$, $-SR^4$, $-NR^4_2$, $-NH(C=O)R^4$, morpholino, morpholin-1-yl, piperazin-1-yl, or 4-alkanoyl-piperazin-1-yl, where R^4 is the same or different for each occurrence, and can be H, alkyl, a cholesterol, a lipid molecule, a polyamine, an amino acid, or a polypeptide.

[0115] The UNA monomers are organic molecules. UNA monomers are not nucleic acid monomers or nucleotides, nor are they naturally-occurring nucleosides or modified naturally-occurring nucleosides.

[0116] A UNA oligomer of this invention is a synthetic chain molecule. A UNA oligomer of this invention is not a nucleic acid, nor an oligonucleotide.

[0117] In some embodiments, as shown above, a UNA monomer can be UNA-A (designated $\tilde{A}$), UNA-U (designated $\tilde{U}$), UNA-C (designated $\tilde{C}$), and UNA-G (designated $\tilde{G}$).

[0118] Designations that may be used herein include mA, mG, mC, and mU, which refer to the 2'-O-Methyl modified ribonucleotides.

[0119] Designations that may be used herein include lower case c and u, which refer to the 2'-O-methyl modified ribonucleotides.

[0120] Designations that may be used herein include dT, which refers to a 2'-deoxy T nucleotide.

[0121] Additional Monomers for Oligomeric Agents

[0122] As used herein, in the context of oligomer sequences, the symbol X represents a UNA monomer.

[0123] As used herein, in the context of oligomer sequences, the symbol N represents any natural nucleotide monomer, or a modified nucleotide monomer.

[0124] As used herein, in the context of oligomer sequences, the symbol Q represents a non-natural, modified, or chemically-modified nucleotide monomer. When a Q monomer appears in one strand of the oligomer, and is unpaired with the other strand, the monomer can have any base attached. When a Q monomer appears in one strand of the oligomer, and is paired with a monomer in the other strand, the Q monomer can have any base attached that would be complementary to the monomer in the corresponding paired position in the other strand.

[0125] Examples of nucleic acid monomers include non-natural, modified, and chemically-modified nucleotides, including any such nucleotides known in the art.

[0126] Examples of non-natural, modified, and chemically-modified nucleotide monomers include any such nucleotides known in the art, for example, 2'-O-methyl ribonucleotides, 2'-O-methyl purine nucleotides, 2'-deoxy-2'-fluoro ribonucleotides, 2'-deoxy-2'-fluoro pyrimidine nucleotides, 2'-deoxy ribonucleotides, 2'-deoxy purine nucleotides, universal base nucleotides, 5-C-methyl-nucleotides, and inverted deoxybasic monomer residues.

[0127] Examples of non-natural, modified, and chemically-modified nucleotide monomers include 3'-end stabilized nucleotides, 3'-glyceryl nucleotides, 3'-inverted abasic nucleotides, 3'-inverted thymidine, and L-thymidine.

[0128] Examples of non-natural, modified, and chemically-modified nucleotide monomers include locked nucleic acid nucleotides, 2'-O,4'-C-methylene-(D-ribofuranosyl) nucleotides, 2'-methoxyethoxy (MOE) nucleotides, 2'-methyl-thio-ethyl, 2'-deoxy-2'-fluoro nucleotides, and 2'-O-methyl nucleotides.

[0129] Examples of non-natural, modified, and chemically-modified nucleotide monomers include 2'-amino nucleotides, 2'-O-amino nucleotides, 2'-C-allyl nucleotides, and 2'-O-allyl nucleotides.

[0130] Examples of non-natural, modified, and chemically-modified nucleotide monomers include N⁶-methyladenosine nucleotides.

[0131] Examples of non-natural, modified, and chemically-modified nucleotide monomers include nucleotide monomers with modified bases 5-(3-amino)propyluridine, 5-(2-mercapto)ethyluridine, 5-bromouridine, 8-bromoguanosine, or 7-deazaadenosine.

[0132] Examples of non-natural, modified, and chemically-modified nucleotide monomers include 2'-O-amino-propyl substituted nucleotides.

[0133] Examples of non-natural, modified, and chemically-modified nucleotide monomers include 2'-O-guanidinopropyl substituted nucleotides.

[0134] Examples of non-natural, modified, and chemically-modified nucleotide monomers include Pseudouridines.

[0135] Examples of non-natural, modified, and chemically-modified nucleotide monomers include replacing the 2'-OH group of a nucleotide with a 2'-R, a 2'-OR, a 2'-halo-

gen, a 2'-SR, or a 2'-amino, 2'-azido, where R can be H, alkyl, fluorine-substituted alkyl, alkenyl, or alkynyl.

[0136] Examples of non-natural, modified, and chemically-modified nucleotide monomers include replacing the 2'-OH group of a nucleotide with a 2'-R or 2'-OR, where R can be CN, CF₃, alkylamino, or aralkyl.

[0137] Examples of non-natural, modified, and chemically-modified nucleotide monomers include nucleotides with a modified sugar such as an F-HNA, an HNA, a CeNA, a bicyclic sugar, or an LNA.

[0138] Examples of non-natural, modified, and chemically-modified nucleotide monomers include 2'-oxa-3'-aza-4'a-carbanucleoside monomers, 3-hydroxymethyl-5-(1H-1,2,3-triazol)-isoxazolidine monomers, and 5'-triazolyl-2'-oxa-3'-aza-4'a-carbanucleoside monomers.

[0139] Some examples of modified nucleotides are given in Saenger, Principles of Nucleic Acid Structure, Springer-Verlag, 1984.

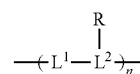
[0140] Oligomeric Compounds Containing UNA Monomers

[0141] Aspects of this invention can provide structures and compositions for UNA-containing oligomeric compounds. The oligomeric agents may incorporate one or more UNA monomers. Oligomeric molecules of this invention can be used as active agents in formulations for gene regulating or gene silencing therapeutics.

[0142] In some embodiments, this invention provides oligomeric compounds having a structure that incorporates novel combinations of UNA monomers with certain natural nucleotides, non-natural nucleotides, modified nucleotides, or chemically-modified nucleotides.

[0143] In further aspects, the oligomeric compounds can be pharmacologically active molecules. UNA oligomers of this invention can be used as active pharmaceutical ingredients for regulating gene expression, and in RNA interference methods, as well as antisense, RNA blocking, and micro-RNA strategies.

[0144] A UNA oligomer of this invention can have the structure of Formula I



Formula I

wherein L¹ is a linkage, n is from 19 to 29, and for each occurrence L² is a UNA linker group having the formula —C¹—C²—C³—, where R is attached to C² and has the formula —OCH(CH₂R³)R⁵, where R³ is —OR⁴, —SR⁴, —NR⁴₂, —NH(C=O)R⁴, morpholino, morpholin-1-yl, piperazin-1-yl, or 4-alkanoyl-piperazin-1-yl, where R⁴ is the same or different for each occurrence and is H, alkyl, a cholesterol, a lipid molecule, a polyamine, an amino acid, or a polypeptide, and where R⁵ is a nucleobase, or L²(R) is a sugar such as a ribose and R is a nucleobase, or L² is a modified sugar such as a modified ribose and R is a nucleobase. In certain embodiments, a nucleobase can be a modified nucleobase. L¹ can be a phosphodiester linkage.

[0145] A UNA oligomer of this invention can be a short chain molecule. A UNA oligomer can be a duplex pair. Thus, a UNA oligomer can have a first strand of the duplex and a second strand of the duplex, which is complementary to the

first strand with respect to the nucleobases, although up to three mismatches can occur. A UNA oligomer duplex can have overhangs.

[0146] Some UNA oligomers are discussed in U.S. Pat. No. 8,314,227, as well as US Patent Publication No. 20110313020 A1.

[0147] The target of a UNA oligomer can be a target nucleic acid. In some embodiments, the target can be any mRNA of a subject. A UNA oligomer can be active for gene silencing in RNA interference.

[0148] A UNA oligomer may comprise two strands that together provide a duplex. The duplex may be composed of a first strand, which may also be referred to as a passenger strand or sense strand, and a second strand, which may also be referred to as a guide strand or antisense strand.

[0149] In some aspects, a UNA oligomer of this invention can have any number of phosphorothioate intermonomer linkages in any position in any strand, or in both strands of a duplex structure.

[10150] In some embodiments, any one or more of the intermonomer linkages of a UNA oligomer can be a phosphodiester, a phosphorothioate including dithioates, a chiral phosphorothioate, and other chemically modified forms.

[0151] Examples of UNA oligomers of this invention include duplex pairs, which are in general complementary. Thus, for example, SEQ ID NO:1 can represent a first strand of a duplex and SEQ ID NO:2 can represent a second strand of the duplex, which is complementary to the first strand.

[0152] For example, the symbol “N” in the first strand can represent any nucleotide that is complementary to the monomer in the corresponding position in the second strand. Example UNA oligomers of this disclosure are shown with 2-monomer length overhangs, although overhangs of from 1 to 8 monomers, or longer, can be used.

[10153] The symbol “X” in a strand or oligomer represents a UNA monomer. When a UNA monomer appears in one strand of the oligomer, and is unpaired with the other strand, the monomer can have any base attached. When a UNA monomer appears in one strand of the oligomer, and is paired with a monomer in the other strand, the UNA monomer can have any base attached that would be complementary to the monomer in the corresponding paired position in the other strand.

[0154] Further, when the oligomer terminates in a UNA monomer, the terminal position has a 1-end, according to the positional numbering shown above, instead of a 5'-end as for a nucleotide, or the terminal position has a 3-end, according to the positional numbering shown above, instead of a 3'-end as for a nucleotide. For example, the UNA oligomer

[0156] In some embodiments, a UNA oligomer of this invention can have one or more UNA monomers at the 1-end of the first strand, and one or more UNA monomers at the 3-end of the first strand.

[0157] In further embodiments, a UNA oligomer of this invention can have one or more UNA monomers at the 3-end of the second strand.

[0158] In certain embodiments, a duplex UNA oligomer of this invention can have one or more UNA monomers at the 1-end of the first strand, one or more UNA monomers at the 3-end of the first strand, and one or more UNA monomers at the 3-end of the second strand.

[0159] A UNA oligomer of this invention the oligomer may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length.

[0160] In certain embodiments, a UNA oligomer of this invention may have a first strand that is 19-23 monomers in length.

[0161] In certain embodiments, a UNA oligomer of this invention may have a duplex region that is 19-21 monomers in length.

[0162] In further embodiments, a UNA oligomer of this invention may have a second strand that is 19-23 monomers in length.

[0163] In certain embodiments, a UNA oligomer of this invention may have a first strand that is 19 monomers in length, and a second strand that is 21 monomers in length.

[0164] In certain embodiments, a UNA oligomer of this invention may have a first strand that is 20 monomers in length, and a second strand that is 21 monomers in length.

[0165] In certain embodiments, a UNA oligomer of this invention may have a first strand that is 21 monomers in length, and a second strand that is 21 monomers in length.

[0166] In certain embodiments, a UNA oligomer of this invention may have a first strand that is 22 monomers in length, and a second strand that is 21 monomers in length.

[0167] A UNA oligomer of this invention for inhibiting gene expression can have a first strand and a second strand, each of the strands being 19-29 monomers in length. The

monomers can be UNA monomers and nucleic acid nucleoside monomers. The oligomer can have a duplex structure of from 14 to 29 monomers in length. The UNA oligomer can

be targeted to a target gene and can exhibit reduced off-target effects as compared to a conventional siRNA. In some embodiments, a UNA oligomer of this invention can have a first strand and a second strand, each of the strands being 19-23 monomers in length.

[0168] In another aspect, the UNA oligomer may have a blunt end, or may have one or more overhangs. In some embodiments, the first and second strands may be connected with a connecting oligomer in between the strands, and form a duplex region with a connecting loop at one end.

[0169] In certain embodiments, an overhang can be one or two monomers in length.

[0170] Examples of an overhang can contain one or more UNA monomers, natural nucleotides, non-natural nucleotides, modified nucleotides, or chemically-modified nucleotides, and combinations thereof.

[0171] Examples of an overhang can contain one or more deoxythymidine nucleotides, 2'-O-methyl nucleotides, inverted abasic monomers, inverted thymidine monomers, L-thymidine monomers, or glyceryl nucleotides.

[0172] A UNA oligomer can mediate cleavage of a target nucleic acid in a cell. In some processes, the second strand

SEQ ID NO: 1

1-X N N N N N N N N N N N N N N N N N X X-3

SEQ ID NO: 2
3-X.X.N.N.N.N.N.N.N.N.N.N.N.N.N.N.X.X.X.X.X.X.X.N-5'

has a UNA monomer 1-end on the first strand, a UNA monomer 3-end on the first strand, a UNA monomer 3-end on the second strand, and a nucleotide 5'-end on the second strand.

[0155] Complementarity of strands can involve mismatches. In certain embodiments, complementarity of strands can include one to three, or more, mismatches.

of the UNA oligomer, at least a portion of which can be complementary to the target nucleic acid, can act as a guide strand that can hybridize to the target nucleic acid.

[0173] The second strand can be incorporated into an RNA Induced Silencing Complex (RISC).

[0174] A UNA oligomer of this disclosure may comprise naturally-occurring nucleic acid nucleotides, and modifications thereof that are compatible with gene silencing activity.

[0175] In some aspects, a UNA oligomer is a double stranded construct molecule that is able to inhibit gene expression.

[0176] As used herein, the term strand refers to a single, contiguous chain of monomers, the chain having any number of internal monomers and two end monomers, where each end monomer is attached to one internal monomer on one side, and is not attached to a monomer on the other side, so that it ends the chain.

[0177] The monomers of a UNA oligomer may be attached via phosphodiester linkages, phosphorothioate linkages, gapped linkages, and other variations.

[0178] In some embodiments, a UNA oligomer can include mismatches in complementarity between the first and second strands. In other embodiments, a UNA oligomer may have 1, or 2, or 3 mismatches. The mismatches may occur at any position in the duplex region.

[0179] The target of a UNA oligomer can be a target nucleic acid of a target gene.

[0180] A UNA oligomer may have one or two overhangs outside the duplex region. The overhangs can be an unpaired portion at the end of the first strand or second strand. The lengths of the overhang portions of the first and second strands can be the same or different.

[0181] A UNA oligomer may have at least one blunt end. A blunt end does not have an overhang portion, and the duplex region at a blunt end terminates at the same position for both the first and second strands.

[0182] A UNA oligomer can be RISC length, which means that it has a duplex length of less than 25 base pairs.

[0183] In certain embodiments, a UNA oligomer can be a single strand that folds upon itself and hybridizes to itself to form a double stranded region having a connecting loop at the end of the double stranded region.

[0184] Examples of UNA oligomers containing five UNA monomers, and which contain one or more Q monomers are shown in Table 1.

TABLE 1

Oligomeric compounds containing five UNA monomers and additional Q monomers	
SEQ ID NO: OLIGOMER	
3	X Q.N.N.Q.N.Q.N.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
4	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.Q
5	X.Q.N.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
6	X.X.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q
7	X.Q.N.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.X.X
8	X.X.Q.N.Q.N.Q.N.Q.N.N.N.N.Q.N.Q.N.Q.N.Q.N.Q
9	X.Q.N.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.X.X
10	X.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q

TABLE 1-continued

Oligomeric compounds containing five UNA monomers and additional Q monomers	
SEQ ID NO: OLIGOMER	
11	X.Q.N.N.Q.N.Q.N.N.N.N.N.N.N.Q.N.Q.N.Q.N.X.X
12	X.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.Q.N.Q.N.Q
13	X.Q.N.N.Q.N.Q.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.X
14	X.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q
15	X.Q.N.N.Q.N.Q.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.X
16	X.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
17	X.Q.N.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.X
18	X.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
19	X.Q.N.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.X
20	X.X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
21	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.X
22	X.X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
23	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.X.X
24	X.X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
25	X-Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.X.X
26	X.X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
27	X-Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.X.X
28	X.X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q
29	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.X.X
30	X.X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q

[0185] Examples of UNA oligomers containing four UNA monomers and additional Q monomers are shown in Table 2.

TABLE 2

Oligomeric compounds containing four UNA monomers and additional Q monomers	
SEQ ID NO: OLIGOMER	
31	X Q.N.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
32	X.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.Q
33	X Q.N.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
34	X.X.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q
35	X.Q.N.N.Q.N.Q.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.X.Q
36	X.X.Q.N.Q.N.Q.N.Q.N.Q.N.N.N.N.Q.N.Q.N.Q.N.Q.N.Q
37	X.Q.N.N.Q.N.Q.N.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.X.Q
38	X.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q
39	X Q.N.N.Q.N.Q.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q.N.X.Q
40	X.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q
41	X.Q.N.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.Q
42	X.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q
43	X Q.N.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.Q
44	X.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
45	X Q.N.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.Q
46	X.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q

TABLE 2-continued

Oligomeric compounds containing four UNA monomers and additional Q monomers	
SEQ ID	NO: OLIGOMER
47	X Q.N.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.Q
48	X.X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
49	X Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.Q
50	X.X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
51	X Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.X.Q
52	X.X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
53	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.X.Q
54	X.X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
55	X Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.X.Q
56	X.X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
57	X Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.X.Q
58	X.X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q

[0186] Examples of UNA oligomers containing four UNA Monomers and additional Q monomers are shown in Table 3.

TABLE 3

Oligomeric compounds containing four UNA monomers and additional Q monomers	
SEQ ID	NO: OLIGOMER
59	X.Q.N.Q.N.Q.N.Q.N.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
60	Q.X.Q.N.Q.N.Q.N.Q.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q
61	X.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
62	Q.X.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q
63	X.Q.N.Q.N.Q.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.X.X
64	Q.X.Q.N.Q.N.Q.N.Q.N.N.N.N.Q.N.Q.N.Q.N.Q.N.Q
65	X.Q.N.Q.N.Q.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.X.X
66	Q.X.Q.N.Q.N.Q.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.Q
67	X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q.N.X.X
68	Q.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q
69	X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.X
70	Q.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q
71	X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.X
72	Q.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q
73	X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.X
74	Q.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
75	X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.X
76	Q.X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
77	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.X
78	Q.X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
79	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.X.X
80	Q.X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
81	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.X.X
82	Q.X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
83	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.X.X
84	Q.X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q

TABLE 3-continued

Oligomeric compounds containing four UNA monomers and additional Q monomers	
SEQ ID	NO: OLIGOMER
85	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.X.X
86	Q.X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q

[0187] Examples of UNA oligomers containing three UNA monomers and additional Q monomers are shown in Table 4.

TABLE 4

Oligomeric compounds containing three UNA monomers and additional Q monomers	
SEQ ID	NO: OLIGOMER
87	X.Q.N.Q.N.Q.N.Q.N.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
88	Q.X.Q.N.Q.N.Q.N.Q.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.Q
89	X.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
90	Q.X.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q
91	X.Q.N.Q.N.Q.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
92	Q.X.Q.N.Q.N.Q.N.Q.N.N.N.N.Q.N.Q.N.Q.N.Q.N.Q.N.Q
93	X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.X.Q
94	Q.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q
95	X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q.N.X.Q
96	Q.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q.N.Q
97	X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.Q
98	Q.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.Q
99	X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.Q
100	Q.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
101	X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.Q
102	Q.X.Q.N.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
103	X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.Q
104	Q.X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
105	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q.N.X.Q
106	Q.X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
107	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.X.Q
108	Q.X.Q.N.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
109	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.X.Q
110	Q.X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.Q
111	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q.N.X.Q
112	Q.X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q
113	X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.X.Q
114	Q.X.Q.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.N.Q

[0188] Examples of UNA oligomers containing six UNA Monomers and additional Q monomers are shown in Table 5.

TABLE 5

Oligomeric compounds containing six UNA monomers and additional Q monomers	
SEQ ID NO:	OLIGOMER
115	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
116	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.Q.X.Q
117	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
118	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.X.N.Q
119	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
120	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.X.Q.N.Q
121	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
122	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.X.N.Q.N.Q
123	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
124	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.Q.N.Q.N.Q
125	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
126	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.X.N.Q.N.Q.N.Q
127	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
128	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.X.Q.N.Q.N.Q.N.Q

[0189] Examples of UNA oligomers containing seven UNA monomers and additional Q monomers are shown in Table 6.

TABLE 6

Oligomeric compounds containing seven UNA monomers and additional Q monomers	
SEQ ID NO:	OLIGOMER
129	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
130	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.X.X.Q
131	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
132	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.X.Q.X.Q
133	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
134	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.X.N.Q.X.Q
135	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
136	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.Q.N.X.N.Q
137	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
138	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.X.X.Q.N.Q
139	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
140	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.X.N.Q.X.Q.N.Q
141	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
142	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.X.N.Q.N.Q

[0190] Examples of UNA oligomers containing five UNA monomers and additional Q monomers are shown in Table 7.

TABLE 7

Oligomeric compounds containing five UNA monomers and additional Q monomers	
SEQ ID NO:	OLIGOMER
143	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
144	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.Q.X.Q

TABLE 7-continued

Oligomeric compounds containing five UNA monomers and additional Q monomers	
SEQ ID NO:	OLIGOMER
145	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
146	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.X.N.Q
147	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
148	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.X.Q.N.Q
149	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
150	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.X.N.Q.N.Q
151	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
152	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.Q.N.Q.N.Q
153	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
154	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.X.N.Q.N.Q.N.Q
155	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
156	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.X.Q.N.Q.N.Q.N.Q

[0191] Examples of UNA oligomers containing six UNA monomers and additional Q monomers are shown in Table 8.

TABLE 8

Oligomeric compounds containing six UNA monomers and additional Q monomers	
SEQ ID NO:	OLIGOMER
157	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
158	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.X.X.Q
159	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
160	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.X.Q.X.Q
161	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
162	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.X.N.Q.X.Q
163	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
164	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.Q.N.X.N.Q
165	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
166	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.X.X.Q.N.Q
167	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
168	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.X.N.Q.X.Q.N.Q
169	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
170	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.X.N.Q.N.Q

[0192] Examples of UNA oligomers containing five UNA monomers and additional Q monomers are shown in Table 9.

TABLE 9

Oligomeric compounds containing five UNA monomers and additional Q monomers	
SEQ ID NO:	OLIGOMER
171	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
172	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.Q.X.Q

TABLE 9-continued

Oligomeric compounds containing five UNA monomers and additional Q monomers	
SEQ ID NO:	OLIGOMER
173	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
174	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.X.N.Q
175	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
176	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.X.Q.N.Q
177	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
178	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.X.N.Q.N.Q
179	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
180	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.Q.N.Q.N.Q
181	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
182	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.X.N.Q.N.Q.N.Q
183	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
184	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.X.Q.N.Q.N.Q.N.Q

[0193] Examples of UNA oligomers containing six UNA monomers and additional Q monomers are shown in Table 10.

TABLE 10

Oligomeric compounds containing six UNA monomers and additional Q monomers	
SEQ ID NO:	OLIGOMER
185	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
186	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.X.X.Q
187	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
188	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.X.Q.X.Q
189	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
190	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.X.N.Q.X.Q
191	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
192	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.Q.N.X.N.Q
193	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
194	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.X.X.Q.N.Q
195	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
196	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.X.N.Q.X.Q.N.Q
197	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
198	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.X.N.Q.N.Q

[0194] Examples of UNA oligomers containing four UNA monomers and additional Q monomers are shown in Table 11.

TABLE 11

Oligomeric compounds containing four UNA monomers and additional Q monomers	
SEQ ID NO:	OLIGOMER
199	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
200	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.Q.X.Q

TABLE 11-continued

Oligomeric compounds containing four UNA monomers and additional Q monomers	
SEQ ID NO:	OLIGOMER
201	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
202	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.X.N.Q
203	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
204	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.X.Q.N.Q
205	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
206	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.X.N.Q.N.Q
207	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
208	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.Q.N.Q.N.Q
209	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
210	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.X.N.Q.N.Q.N.Q
211	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
212	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.X.Q.N.Q.N.Q.N.Q

[0195] Examples of UNA oligomers containing five UNA monomers and additional Q monomers are shown in Table 12.

TABLE 12

Oligomeric compounds containing five UNA monomers and additional Q monomers	
SEQ ID NO:	OLIGOMER
213	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
214	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.N.X.X.Q
215	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
216	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.X.Q.X.Q
217	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
218	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.X.N.Q.X.Q
219	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
220	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.Q.N.X.N.Q
221	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
222	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.X.X.Q.N.Q
223	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
224	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.X.N.Q.X.Q.N.Q
225	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
226	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.X.N.Q.N.Q

[0196] Examples of UNA oligomers containing seven or more UNA monomers and additional Q monomers are shown in Table 13.

TABLE 13

Oligomeric compounds containing seven or more UNA monomers and additional Q monomers	
SEQ ID NO:	OLIGOMER
227	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
228	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.X.Q.X.Q.X.Q

TABLE 13-continued

Oligomeric compounds containing seven or more UNA monomers and additional Q monomers	
SEQ ID	
NO:	OLIGOMER
229	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
230	X.X.Q.N.Q.N.Q.N.N.N.N.N.Q.N.Q.N.Q.X.X.X.Q
231	X.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
232	Q.X.Q.N.Q.N.Q.N.N.N.N.N.Q.Q.N.X.X.X.N.Q.N.Q
233	X.Q.N.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.Q
234	Q.X.Q.N.Q.N.Q.N.Q.N.N.N.N.N.Q.Q.N.X.X.X.X.X.Q
235	X.Q.N.Q.N.Q.N.Q.N.Q.Q.Q.N.Q.N.Q.N.Q.N.Q.N.X.X
236	X.X.Q.N.Q.N.Q.N.Q.N.N.N.N.N.Q.N.X.X.X.X.X.X.Q

[0197] An oligomeric compound of this invention may have any one of the structures shown in Tables 1 to 13.

[0198] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a Q monomer.

[0199] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a Q monomer, and where the number of Q monomers is less than twenty.

[0200] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a Q monomer, and where the number of Q monomers is less than twelve.

[0201] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a Q monomer, and where the number of Q monomers is less than ten.

[0202] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a Q monomer, and where the number of Q monomers is less than eight.

[0203] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a Q monomer, and where the number of Q monomers is from 1 to 20.

[0204] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a Q monomer, and where the number of Q monomers is from 1 to 15.

[0205] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in

length, where any monomer that is not a UNA monomer can be a Q monomer, and where the number of Q monomers is from 1 to 9.

[0206] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a 2'-O-Methyl modified ribonucleotide.

[0207] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a 2'-O-Methyl modified ribonucleotide, and where the number of 2'-O-Methyl modified ribonucleotides is less than twenty.

[0208] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a 2'-O-Methyl modified ribonucleotide, and where the number of 2'-O-Methyl modified ribonucleotides is less than twelve.

[0209] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a 2'-O-Methyl modified ribonucleotide, and where the number of 2'-O-Methyl modified ribonucleotides is less than ten.

[0210] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a 2'-O-Methyl modified ribonucleotide, and where the number of 2'-O-Methyl modified ribonucleotides is less than eight.

[0211] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a 2'-O-Methyl modified ribonucleotide, and where the number of 2'-O-Methyl modified ribonucleotides is from 1 to 20.

[0212] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a 2'-O-Methyl modified ribonucleotide, and where the number of 2'-O-Methyl modified ribonucleotides is from 1 to 15.

[01213] In some embodiments, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a 2'-O-Methyl modified ribonucleotide, and where the number of 2'-O-Methyl modified ribonucleotides is from 1 to 9.

[0214] In further aspects, an oligomeric compound of this invention may have a first strand and a second strand, each of the strands independently being 19-23 monomers in length, where any monomer that is not a UNA monomer can be a Q monomer, and where the oligomeric compound does not contain fluorine.

[0215] Embodiments of this invention advantageously provide oligomeric compounds, which are active agents against HBV and do not contain fluorine.

[0216] Methods of this invention include the treatment and/or prevention of HBV disease in a subject. A subject can be a mammalian subject, including a human subject.

[0217] HBV Component Target Sequences

[0218] As used herein, "Ref Pos" refers to reference position, which is the numerical position of a reference nucleotide in an HBV genome. The reference position is the position that corresponds target-wise to the 5' end of the sense strand of the oligomeric compound of this invention. The reference positions are numerical nucleotide positions based on a reference genome, which as used herein is HBV Genotype A2, Accession No. HE974376. Thus, a reference position number by itself refers to one sequence from the reference genome, and each sequence can be used in an oligomeric compound of this invention. Table 14 shows genomic positions for the HBV reference genome.

TABLE 14

HBV genomic positions		
Start	End	Gene
1	835	S
1	1623	Pol
1374	1838	X
1901	2458	C
2307	3221	Pol
2854	3221	S

[0219] In FIG. 1 is shown a map of HBV protein coding regions and selected transcripts for the reference genome HE974376. Nucleotide position 1/3221 is designated at the top. Further designations are as follows: pre-S1, large HBsAg; pre-S2, medium HBsAg; S, HBsAg; P, polymerase; X, HBx protein; pre-C, pre-core/HBeAg; C, HB core Ag. The 2.4 kb, 2.1 kb, and 0.7 kb transcripts coding for the pre-S1/pre-S2/S, as well as the transcript coding the X protein are shown. The pre-Core/HBeAg protein is generated from a long, 3.5 kb transcript (not shown) originating at position ~1700, while the core and polymerase proteins and the pre-genomic RNA used as a template for viral replication are generated from a ~200 nt shorter transcript.

[0220] The ranges of reference positions for certain UNA oligomers, designated UNA oligomer 1, UNA oligomer 2, and UNA oligomer 3, are shown in FIG. 1.

[0221] In some aspects, the inventive oligomers of this disclosure may target the long transcript coding for HBV core and polymerase proteins.

[0222] UNA Oligomers Targeting HBV

[0223] Examples of base sequences of this invention targeted to an HBV component are shown in Table 15.

[0224] An oligomeric compound of this invention can be formed having a first strand and a second strand each being 21 monomers in length. The first strand can have 19 contiguous monomers with a sequence of attached bases shown in Table 15 (sense), and two additional overhang monomers on the 3' end. The second strand can have 19 contiguous monomers with a sequence of attached bases shown in Table 15 (antisense), and two additional overhang monomers on the 3' end. The overhang monomers can be any of NN, QQ,

XX, NX, NQ, XN, XQ, QN, and QX. For example, XQ can be UNA-U/mU, or UNA-U/*dT.

[0225] An oligomeric compound of this invention can be composed of monomers. The monomers can have attached bases. An oligomeric compound of this invention can have a sequence of attached bases. The sequences of bases shown in Table 15 do not indicate to which monomer each of the bases in the sequence is attached. Thus, each sequence shown in Table 15 refers to a large number of small molecules, each of which is composed of UNA monomers, as well as nucleic acid monomers.

[0226] In some aspects, an oligomeric compound of this invention can be described by a sequence of attached bases, for example as shown in Table 15, and being substituted forms thereof. As used herein, substituted forms include differently substituted UNA monomers, as well as differently substituted or modified nucleic acid monomers, as are further described herein.

[0227] In some embodiments, one or more of three monomers at each end of each strand can be connected by a phosphorothioate, a chiral phosphorothioate, or a phosphorodithioate linkage.

[0228] For example, a compound may have one phosphorothioate linkage between two monomers at the 5' end of the first strand, one phosphorothioate linkage between two monomers at the 3' end of the first strand, one phosphorothioate linkage between monomers at the second and third positions from the 3' end of the first strand, and one phosphorothioate linkage between two monomers at the 3' end of the second strand.

[0229] In certain embodiments, a compound may have two or three phosphorothioate linkages at the 5' end of the first strand, two or three phosphorothioate linkages at the 3' end of the first strand, and one phosphorothioate linkage at the 3' end of the second strand.

[0230] In additional embodiments, a compound may have one to three phosphorothioate linkages at the 5' end of the first strand, two or three phosphorothioate linkages at the 3' end of the first strand, two phosphorothioate linkages at the 5' end of the second strand, and two phosphorothioate linkages at the 3' end of the second strand.

[0231] In some examples, a compound may have a deoxythymidine nucleotide at the 3' end of the first strand, at the 3' end of the second strand, or at both the 3' end of the first strand and the 3' end of the second strand.

[0232] In some aspects, a compound may contain one to five UNA monomers.

[0233] In certain aspects, a compound may contain three UNA monomers.

[0234] In some embodiments, a compound may contain a UNA monomer at the 1-end of the first strand (5' end), a UNA monomer at the 3-end of the first strand (3' end), and a UNA monomer at the second position from the 3' end of the second strand.

[0235] In certain embodiments, a compound may contain a UNA monomer at any one or more of positions 2 to 8 from the 5' end of the second strand (seed region).

TABLE 15

HBV sense and antisense sequences					
REF	SEQ	ID Sense (5'-3')	SEQ	Antisense (5'-3')	
POS	NO	SEQ ID NOS: 237 to 548	ID NO	SEQ ID NOS: 549 to 860	
1525	237	CGCACCUCUCUUUACGCGG	549	CCGCGUAAAGAGAGGUGCG	
251	238	GACUCGUGGUGGACUUCUC	550	GAGAAGUCCACCACGAGUC	
254	239	UCGUGGUGGACUUCUCUCA	551	UGAGAGAAGUCCACCACGA	
374	240	UGGAUGUGUCUGCGGCGUU	552	AACGCCCGCAGACACAUCCA	
1575	241	CCGUGUGCACUUCGCUUCA	553	UGAAGCGAAGUGCACACGG	
1577	242	GUGUGCACUUCGCUUCACC	554	GGUGAAGCGAAGUGCACAC	
1578	243	UGUGCACUUCGCUUCACCU	555	AGGUGAAGCGAAGUGCACA	
1579	244	GUGCACUUCGCUUCACCUC	556	GAGGUGAAGCGAAGUGCAC	
1581	245	GCACUUCGCUUCACCUCUG	557	CAGAGGUGAAGCGAAGUGC	
1863	246	UUCAAGCCUCCAAGCUGUG	558	CACAGCUUGGAGGCUUGAA	
1864	247	UCAAGCCUCCAAGCUGUGC	559	GCACAGCUUGGAGGCUUGA	
1865	248	CAAGCCUCCAAGCUGUGCC	560	GGCACAGCUUGGAGGCUUG	
1866	249	AAGCCUCCAAGCUGUGCCU	561	AGGCACAGCUUGGAGGCUU	
247	250	UCUAGACUCGUGGUGGACU	562	AGUCCACCACGAGUCUAGA	
248	251	CUAGACUCGUGGUGGACUU	563	AAGUCCACCACGAGUCUAG	
249	252	UAGACUCGUGGUGGACUUC	564	GAAGUCCACCACGAGUCUA	
250	253	AGACUCGUGGUGGACUUCU	565	AGAAGUCCACCACGAGUCU	
376	254	GAUGUGUCUGCGGCGUUUU	566	AAAACGCCCGCAGACACAUC	
378	255	UGUGUCUGCGGCGUUUUAU	567	AUAAAACGCCCGCAGACACA	
380	256	UGUCUGCGGCGUUUUAUCA	568	UGAUAAAACGCCCGCAGACA	
1776	257	GGAGGCUGUAGGCAUAAAU	569	AUUUAUGCCUACAGCCUCC	
1777	258	GAGGCUGUAGGCAUAAAUU	570	AAUUUAUGCCUACAGCCUC	
1779	259	GGCUGUAGGCAUAAAUUGG	571	CCAAUUUAUGCCUACAGCC	
1780	260	GCUGUAGGCAUAAAUUGGU	572	ACCAAUUUAUGCCUACAGC	
1818	261	AACUUUUUACCCUCUGCCU	573	AGGCAGAGGUGAAAAAGUU	
244	262	GAGUCUAGACUCGUGGUGG	574	CCACCACGAGUCUAGACUC	
245	263	AGUCUAGACUCGUGGUGGA	575	UCCACCACGAGUCUAGACU	
246	264	GUCUAGACUCGUGGUGGAC	576	GUCCACCACGAGUCUAGAC	
409	265	CAUCCUGCUGCUAUGCCUC	577	GAGGCAUAGCAGCAGGAUG	
411	266	UCCUGCUGCUAUGCCUCAU	578	AUGAGGCAUAGCAGCAGGA	
412	267	CCUGCUGCUAUGCCUCAUC	579	GAUGAGGCAUAGCAGCAGG	
413	268	CUGCUGCUAUGCCUCAUCU	580	AGAUGAGGCAUAGCAGCAG	
414	269	UGCUGCUAUGCCUCAUCUU	581	AAGAUGAGGCAUAGCAGCA	
1781	270	CUGUAGGCAUAAAUUGGUC	582	GACCAAUUUAUGCCUACAG	
1782	271	UGUAGGCAUAAAUUGGUCU	583	AGACCAAUUUAUGCCUACA	
252	272	ACUCGUGGUGGACUUCUCU	584	AGAGAAGUCCACCACGAGU	

TABLE 15-continued

HBV sense and antisense sequences										
REF	SEQ	ID	Sense (5'-3')				SEQ	Antisense (5'-3')		
POS	NO	SEQ	ID	NOS: 237 to 548			ID	NO	SEQ	ID NOS: 549 to 860
253	273	CUCGUGGUGGACUUCUCUC					585	GAGAGAAGUCCACCACGAG		
1576	274	CGUGUGCACUUCGCUUCAC					586	GUGAAGCGAAGUGCACACG		
1580	275	UGCACUUCGCUUCACCUCU					587	AGAGGUGAAGCGAAGUGCA		
1582	276	CACUUCGCUUCACCUCUGC					588	GCAGAGGUGAAGCGAAGUG		
1583	277	ACUUCGCUUCACCUCUGCA					589	UGCAGAGGUGAAGCGAAGU		
1867	278	AGCCUCCAAGCUGUGCCUU					590	AAGGCACAGCUUGGAGGCU		
1868	279	GCCUCCAAGCUGUGCCUUG					591	CAAGGCACAGCUUGGAGGC		
2382	280	GAACUCCCUCGCCUCGCAG					592	CUGCGAGGCGAGGGAGUUC		
2383	281	AACUCCCUCGCCUCGCAGA					593	UCUGCGAGGCGAGGGAGUU		
2384	282	ACUCCCUCGCCUCGCAGAC					594	GUCUGCGAGGCGAGGGAGU		
2385	283	CUCCCUCGCCUCGCAGACG					595	CGUCUGCGAGGCGAGGGAG		
56	284	CCUGCUGGUGGCUCCAGUU					596	AACUGGAGCCACCAGCAGG		
57	285	CUGCUGGUGGCUCCAGUUC					597	GAACUGGAGCCACCAGCAG		
375	286	GGAUGUGUCUGCGGCGUUU					598	AAACGCCGCAGACACAUCC		
377	287	AUGUGUCUGCGGCGUUUUA					599	UAAAACGCCGCAGACACAU		
379	288	GUGUCUGCGGCGUUUUAUC					600	GAUAAAACGCCGCAGACAC		
381	289	GUCUGCGGCGUUUUAUCAU					601	AUGAUAAAACGCCGCAGAC		
637	290	CCUAUGGGAGUGGGCCUCA					602	UGAGGCCCAUCCCAUAGG		
638	291	CUAUGGGAGUGGGCCUCAG					603	CUGAGGCCCAUCCCAUAG		
1584	292	CUUCGCUUCACCUCUGCAC					604	GUGCAGAGGUGAAGCGAAG		
1585	293	UUCGCUUCACCUCUGCACG					605	CGUGCAGAGGUGAAGCGAA		
1586	294	UCGCUUCACCUCUGCACGU					606	ACGUGCAGAGGUGAAGCGA		
1778	295	AGGCUUGAGGCAUAAAUG					607	CAAUUUAUGCCUACAGCCU		
1819	296	ACUUUUUCACCUCUGCCUA					608	UAGGCAGAGGUGAAAAGU		
410	297	AUCCUGCUGCUAUGCCUCA					609	UGAGGCAUAGCAGCAGGAU		
415	298	GCUGCUAUGCCUCAUCUUC					610	GAAGAUGAGGCAUAGCAGC		
416	299	CUGCUAUGCCUCAUCUUCU					611	AGAAGAUGAGGCAUAGCAG		
417	300	UGCUAUGCCUCAUCUUCUU					612	AAGAAGAUGAGGCAUAGCA		
1783	301	GUAGGCAUAAAUGGUCUG					613	CAGACCAAUUUAUGCCUAC		
1869	302	CCUCCAAGCUGUGCCUUGG					614	CCAAGGCACAGCUUGGAGG		
255	303	CGUGGUGGACUUCUCUCAA					615	UUGAGAGAAGUCCACCACG		
256	304	GUGGUGGACUUCUCUCAAU					616	AUUGAGAGAAGUCCACCAC		
257	305	UGGUGGACUUCUCUCAAUU					617	AAUUGAGAGAAGUCCACCA		
258	306	GGUGGACUUCUCUCAAUUU					618	AAAUUGAGAGAAGUCCACC		
259	307	GUGGACUUCUCUCAAUUUU					619	AAAAUUGAGAGAAGUCCAC		
260	308	UGGACUUCUCUCAAUUUUC					620	GAAAAUUGAGAGAAGUCCA		

TABLE 15-continued

HBV sense and antisense sequences					
REF POS	SEQ NO	ID Sense (5'-3') SEQ ID NOS: 237 to 548	SEQ ID NO	Antisense (5'-3') SEQ ID NOS: 549 to 860	
262	309	GACUUCUCUCAAUUUUCUA	621	UAGAAAAUUGAGAGAAGUC	
263	310	ACUUCUCUCAAUUUUCUAG	622	CUAGAAAAUUGAGAGAAGU	
264	311	CUUCUCUCAAUUUUCUAGG	623	CCUAGAAAAUUGAGAGAAG	
265	312	UUCUCUCAAUUUUCUAGGG	624	CCCUAGAAAAUUGAGAGAA	
266	313	UCUCUCAAUUUUCUAGGGG	625	CCCCUAGAAAAUUGAGAGA	
1264	314	AUCCAUAUCUGCGGAACUCC	626	GGAGUUCGCGAGUAUGGAU	
1265	315	UCCAUAUCUGCGGAACUCCU	627	AGGAGUUCGCGAGUAUGGA	
2376	316	GAAGAAGAACUCCUCGCC	628	GGCGAGGGAGUUCUUCUUC	
2377	317	AAGAAGAACUCCUCGCCU	629	AGGCGAGGGAGUUCUUCU	
2378	318	AGAAGAACUCCUCGCCUC	630	GAGGCGAGGGAGUUCUUCU	
2379	319	GAAGAACUCCUCGCCUCG	631	CGAGGCGAGGGAGUUCUUC	
2380	320	AAGAACUCCUCGCCUCGC	632	GCGAGGCGAGGGAGUUCU	
2381	321	AGAACUCCUCGCCUCGCA	633	UGCGAGGCGAGGGAGUUCU	
243	322	AGAGUCUAGACUCGUGGUG	634	CACCACGAGUCUAGACUCU	
261	323	GGACUUCUCUCAAUUUUCU	635	AGAAAAUUGAGAGAAGUCC	
1263	324	GAUCCAUAUCUGCGGAACUC	636	GAGUUCGCGAGUAUGGAUC	
1815	325	UGCAACUUUUUACCCUCUG	637	CAGAGGUGAAAAAGUUGCA	
1816	326	GCAACUUUUUACCCUCUGC	638	GCAGAGGUGAAAAAGUUGC	
1817	327	CAACUUUUUACCCUCUGCC	639	GGCAGAGGUGAAAAAGUUG	
301	328	UGGCCAAAAUUCGAGUCC	640	GGACUGCGAAUUUUGGCCA	
302	329	GGCCAAAAUUCGAGUCCC	641	GGGACUGCGAAUUUUGGCC	
1261	330	CCGAUCCAUAUCUGCGGAAC	642	GUUCCGCGAGUAUGGAUCGG	
1262	331	CGAUCCAUAUCUGCGGAACU	643	AGUUCGCGAGUAUGGAUCG	
1820	332	CUUUUUCACCCUCUGCCUAA	644	UUAGGCAGAGGUGAAAAAG	
1821	333	UUUUUACCCUCUGCCUAAU	645	AUUAGGCAGAGGUGAAAAA	
1822	334	UUUUCACCCUCUGCCUAAUC	646	GAUUAGGCAGAGGUGAAAA	
1823	335	UUUCACCCUCUGCCUAAUCA	647	UGAUUAGGCAGAGGUGAAA	
1874	336	AAGCUGUGCCUUGGGUGGC	648	GCCACCCAGGCACAGCUU	
1875	337	AGCUGUGCCUUGGGUGGCU	649	AGCCACCCAGGCACAGCU	
1876	338	GCUGUGCCUUGGGUGGCUU	650	AAGCCACCCAGGCACAGC	
1877	339	CUGUGCCUUGGGUGGCUUU	651	AAAGCCACCCAGGCACAG	
2267	340	GGAGUGUGGAUUCGCACUC	652	GAGUGCGAAUCCACACUCC	
2268	341	GAGUGUGGAUUCGCACUCC	653	GGAGUGCGAAUCCACACUC	
242	342	CAGAGUCUAGACUCGUGGU	654	ACCACGAGUCUAGACUCUG	
1654	343	AUAAGAGGACUCUUGGACU	655	AGUCCAAGAGUCCUCUUAU	
1774	344	UAGGAGGCUGUAGGCAUAA	656	UUAUGCCUACAGCCUCCUA	

TABLE 15-continued

HBV sense and antisense sequences					
REF POS	SEQ NO	ID Sense (5'-3') SEQ ID NOS: 237 to 548	SEQ ID NO	Antisense (5'-3') SEQ ID NOS: 549 to 860	
1775	345	AGGAGGCUGUAGGCAUAAA	657	UUUAUGCCUACAGCCUCCU	
1813	346	CAUGCAACUUUUUACCUC	658	GAGGUGAAAAAGUUGCAUG	
1814	347	AUGCAACUUUUUACCUCU	659	AGAGGUGAAAAAGUUGCAU	
1824	348	UUCACCUCUGCCUAAUCAU	660	AUGAUUAGGCAGAGGUGAA	
1825	349	UCACCUCUGCCUAAUCAUC	661	GAUGAUUAGGCAGAGGUGA	
1826	350	CACCUCUGCCUAAUCAUCU	662	AGAUGAUUAGGCAGAGGUG	
1870	351	CUCCAAGCUGUGCCUUGGG	663	CCCAAGGCACAGCUUGGAG	
1871	352	UCCAAGCUGUGCCUUGGGU	664	ACCCAAGGCACAGCUUGGA	
1872	353	CCAAGCUGUGCCUUGGGUG	665	CACCCAAGGCACAGCUUGG	
1873	354	CAAGCUGUGCCUUGGGUGG	666	CCACCCAAGGCACAGCUUG	
2373	355	CUAGAAGAAGAACUCCUC	667	GAGGGAGUUCUUCUUCUAG	
2374	356	UAGAAGAAGAACUCCUCG	668	CGAGGGAGUUCUUCUUCUA	
2375	357	AGAAGAAGAACUCCUCGC	669	GCGAGGGAGUUCUUCUUCU	
1862	358	GUUCAAGCCUCCAAGCUGU	670	ACAGCUUGGAGGCUUGAAC	
2297	359	AGACCACCAAUUGCCCCUA	671	UAGGGGCAUUUGGUGGUCU	
2298	360	GACCACCAAUUGCCCCUAU	672	AUAGGGGCAUUUGGUGGUC	
2299	361	ACCACCAAUUGCCCCUAUC	673	GAUAGGGGCAUUUGGUGGU	
599	362	UGUAUUCCCAUCCCAUCAU	674	AUGAUGGGGAAUGGAAUACA	
600	363	GUUAUCCCAUCCCAUCAUC	675	GAUGAUGGGGAAUGGAAUAC	
703	364	CGUAGGGCUUUCCCCACU	676	AGUGGGGGAAAGCCCUACG	
704	365	GUAGGGCUUUCCCCACUG	677	CAGUGGGGGAAAGCCCUAC	
705	366	UAGGGCUUUCCCCACUGU	678	ACAGUGGGGGAAAGCCCUA	
1259	367	UGCCGAUCCAACUGCGGA	679	UCCGCAUUAUGGAUCGGCA	
1260	368	GCCGAUCCAACUGCGGAA	680	UUCGCAUUAUGGAUCGGC	
1518	369	CACGGGGCGCACCCUCUUU	681	AAGAGAGGUGCGCCCCGUG	
1519	370	ACGGGGCGCACCCUCUUU	682	AAAGAGAGGUGCGCCCCGU	
1520	371	CGGGGCGCACCCUCUUUA	683	UAAAGAGAGGUGCGCCCCG	
1521	372	GGGGCGCACCCUCUUUAC	684	GUAAAGAGAGGUGCGCCCC	
1522	373	GGGCGCACCCUCUUUACG	685	CGUAAAGAGAGGUGCGCCC	
1523	374	GGCGCACCCUCUUUACGC	686	GCGUAAAGAGAGGUGCGCC	
1524	375	GCGCACCCUCUUUACGCG	687	CGCGUAAAGAGAGGUGCGC	
1859	376	ACUGUUCAAGCCUCCAAGC	688	GCUUGGAGGCUUGAACAGU	
1860	377	CUGUUCAAGCCUCCAAGCU	689	AGCUUGGAGGCUUGAACAG	
1861	378	UGUUCAAGCCUCCAAGCUG	690	CAGCUUGGAGGCUUGAACA	
459	379	GUAUGUUGCCCGUUUGUCC	691	GGACAAACGGGCAACAUAC	
460	380	UAUGUUGCCCGUUUGUCCU	692	AGGACAAACGGGCAACAUUA	

TABLE 15-continued

HBV sense and antisense sequences										
REF	SEQ	ID	Sense (5'-3')			SEQ	Antisense (5'-3')			
POS	NO	SEQ	ID	NOS: 237 to 548		ID	NO	SEQ	ID	NOS: 549 to 860
462	381	UGUUGCCCCGUUUGUCCUCU				693		AGAGGACAAACGGGCAACA		
1136	382	UGAACCUUUAACCCGUUGC				694		GCAACGGGGUAAAGGUUCA		
1266	383	CCAUACUGCGGAACUCCUA				695		UAGGAGUUCGCGAGUAUGG		
1267	384	CAUACUGCGGAACUCCUAG				696		CUAGGAGUUCGCGAGUAUG		
1268	385	AUACUGCGGAACUCCUAGC				697		GCUAGGAGUUCGCGAGUAU		
1517	386	CCACGGGGCGCACCUCUCU				698		AGAGAGGUGCGCCCCGUGG		
2371	387	CCCUAGAAGAAGAACUCCC				699		GGGAGUUCUUCUUCUAGGG		
2372	388	CCUAGAAGAAGAACUCCCU				700		AGGGAGUUCUUCUUCUAGG		
2380	389	UCCCUCCGCCUCGCGAGCGA				701		UCGUCUGCGAGGCGAGGGGA		
401	390	UUCUCUCUUAUCCUGCUGC				702		GCAGCAGGAUGAAGAGGAA		
402	391	UCCUCUUAUCCUGCUGCU				703		AGCAGCAGGAUGAAGAGGA		
403	392	CCUCUUAUCCUGCUGCUA				704		UAGCAGCAGGAUGAAGAGG		
404	393	CUCUUAUCCUGCUGCUAU				705		AUAGCAGCAGGAUGAAGAG		
405	394	UCUUAUCCUGCUGCUAUG				706		CAUAGCAGCAGGAUGAAGA		
406	395	CUUCAUCCUGCUGCUAUGC				707		GCAUAGCAGCAGGAUGAAG		
407	396	UUCAUCCUGCUGCUAUGCC				708		GGCAUAGCAGCAGGAUGAA		
408	397	UCAUCCUGCUGCUAUGCCU				709		AGGCAUAGCAGCAGGAUGA		
458	398	GGUAUGUUGCCCGUUUGUC				710		GACAAACGGGCAACAUAAC		
461	399	AUGUUGCCCGUUUGUCCUC				711		GAGGACAAACGGGCAACAU		
1426	400	UACGUCCCCGUCGGCGCUGA				712		UCAGCGCCGACGGGACGUA		
1427	401	ACGUCCCCGUCGGCGCUGAA				713		UUCAGCGCCGACGGGACGU		
1428	402	CGUCCCCGUCGGCGCUGAAU				714		AUUCAGCGCCGACGGGACG		
1429	403	GUCCCCGUCGGCGCUGAAUC				715		GAUUCAGCGCCGACGGGAC		
1430	404	UCCCGUCGGCGCUGAAUCC				716		GGAUUCAGCGCCGACGGGA		
2269	405	AGUGUGGAUUCGCACUCCU				717		AGGAGUGCGAAUCCACACU		
2370	406	CCCCUAGAAGAAGAACUCC				718		GGAGUUCUUCUUCUAGGGG		
455	407	CAAGGUUUGUUGCCCGUUU				719		AAACGGGCAACAUAACCUUG		
456	408	AAGGUUUGUUGCCCGUUUG				720		CAAACGGGCAACAUAACCUU		
457	409	AGGUUUGUUGCCCGUUUGU				721		ACAAACGGGCAACAUAACCU		
1513	410	CCGACCACGGGCGCACCU				722		AGGUGCGCCCCGUGGUCGG		
1514	411	CGACCACGGGCGCACCUUC				723		GAGGUGCGCCCCGUGGUCG		
1515	412	GACCACGGGCGCACCUUCU				724		AGAGGUGCGCCCCGUGGUC		
1516	413	ACCACGGGCGCACCUUCUC				725		GAGAGGUGCGCCCCGUGGU		
1545	414	CUCCCCGUCUGUGCCUUCU				726		AGAAGGCACAGACGGGGAG		
1546	415	UCCCCGUCUGUGCCUUCUC				727		GAGAAGGCACAGACGGGGA		
2417	416	CCGCGUCGCGAGAAGAUUC				728		GAGAUUCUUCGCGACGCGG		

TABLE 15-continued

HBV sense and antisense sequences					
REF	SEQ ID	Sense (5'-3')	SEQ	Antisense (5'-3')	
POS	NO	SEQ ID NOS: 237 to 548	ID NO	SEQ ID NOS: 549 to 860	
2418	417	CGCGUCGCGAGAAGAUUCUA	729	UGAGAUCUUCUGCGACGCG	
2419	418	GCGUCGCGAGAAGAUUCAA	730	UUGAGAUCUUCUGCGACGC	
2420	419	CGUCGCGAGAAGAUUCAAU	731	AUUGAGAUCUUCUGCGACG	
2421	420	GUCGCGAGAAGAUUCAAUC	732	GAUUGAGAUCUUCUGCGAC	
2422	421	UCGCGAGAAGAUUCAAUCU	733	AGAUGAGAUCUUCUGCGA	
181	422	AGGACCCCGUCGUCGUGUUA	734	UAACACGAGCAGGGGUCCU	
182	423	GGACCCCGUCGUCGUGUAC	735	GUAACACGAGCAGGGGUCC	
183	424	GACCCCGUCGUCGUGUACA	736	UGUAACACGAGCAGGGGUC	
184	425	ACCCCGUCGUCGUGUACAG	737	CUGUAACACGAGCAGGGGU	
185	426	CCCCGUCGUCGUGUACAGG	738	CCUGUAACACGAGCAGGGG	
368	427	UAUCGCGUGGAUGUGUCUGC	739	GCAGACACAUCAGCGAUA	
369	428	AUCGCGUGGAUGUGUCUGCG	740	CGCAGACACAUCAGCGAU	
370	429	UCGCGUGGAUGUGUCUGCGG	741	CCGCAGACACAUCAGCGA	
371	430	CGCUGGAUGUGUCUGCGGC	742	GCCGCAGACACAUCAGCG	
372	431	GCUGGAUGUGUCUGCGGCG	743	CGCCGCAGACACAUCAGC	
373	432	CUGGAUGUGUCUGCGGCGU	744	ACGCCGCAGACACAUCAG	
463	433	GUUGCCCGUUUGUCCUCUA	745	UAGAGGACAAACGGGCAAC	
686	434	CCAUUUGUUCAGUGGUUCG	746	CGAACCACUGAACAAUUG	
800	435	UUACCAUUUUUUUUUGUC	747	GACAAAAGAAAUUGGUAA	
1102	436	CCAACUUACAAGGCCUUUC	748	GAAAGGCCUUGUAAGUUG	
1103	437	CAACUUACAAGGCCUUUCU	749	AGAAAGGCCUUGUAAGUUG	
1183	438	UUUGCUGACGCAACCCCCA	750	UGGGGGUUGCGUCAGCAA	
1184	439	UUGCUGACGCAACCCCCAC	751	GUGGGGGUUGCGUCAGCAA	
1185	440	UGCUGACGCAACCCCCACU	752	AGUGGGGGUUGCGUCAGCA	
1186	441	GCUGACGCAACCCCCACUG	753	CAGUGGGGGUUGCGUCAGC	
1187	442	CUGACGCAACCCCCACUGG	754	CCAGUGGGGGUUGCGUCAG	
1553	443	CUGUGCCUUCUCAUCUGCC	755	GGCAGAUGAGAAGGCACAG	
1554	444	UGUGCCUUCUCAUCUGCCG	756	CGGCAGAUGAGAAGGCACA	
1555	445	GUGCCUUCUCAUCUGCCGG	757	CCGGCAGAUGAGAAGGCAC	
1805	446	ACCAGCACCAUGCAACUUU	758	AAAGUUGCAUGGUGCUGGU	
1806	447	CCAGCACCAUGCAACUUUU	759	AAAAGUUGCAUGGUGCUGG	
1807	448	CAGCACCAUGCAACUUUUU	760	AAAAAGUUGCAUGGUGCUG	
1808	449	AGCACCAUGCAACUUUUUC	761	GAAAAAGUUGCAUGGUGCU	
1809	450	GCACCAUGCAACUUUUUCA	762	UGAAAAAGUUGCAUGGUGC	
1810	451	CACCAUGCAACUUUUUCAC	763	GUGAAAAAGUUGCAUGGUG	
1811	452	ACCAUGCAACUUUUUACC	764	GGUGAAAAAGUUGCAUGGU	

TABLE 15-continued

HBV sense and antisense sequences										
REF	SEQ	ID	Sense (5'-3')				SEQ	Antisense (5'-3')		
POS	NO	SEQ	ID	NOS: 237 to 548			ID	NO	SEQ	ID NOS: 549 to 860
1812	453	CCAUGCAACUUUUUACCU					765	AGGUGAAAAAGUUGCAUGG		
2423	454	CGCAGAAGAUCUCAAUUC					766	GAGAUUGAGAUCUUCUGCG		
177	455	UCCUAGGACCCCUGCUCGU					767	ACGAGCAGGGGUCCUAGGA		
178	456	CCUAGGACCCCUGCUCGUG					768	CACGAGCAGGGGUCCUAGG		
179	457	CUAGGACCCCUGCUCGUGU					769	ACACGAGCAGGGGUCCUAG		
180	458	UAGGACCCCUGCUCGUGUU					770	AACACGAGCAGGGGUCCUA		
186	459	CCCUGCUCGUGUUAACAGGC					771	GCCUGUAACACGAGCAGGG		
187	460	CCUGCUCGUGUUAACAGGCG					772	CGCCUGUAACACGAGCAGG		
188	461	CUGCUCGUGUUAACAGGCGG					773	CCGCCUGUAACACGAGCAG		
685	462	GCCAUUUGUUCAGUGGUUC					774	GAACCACUGAACAAUUGGC		
1099	463	UCGCCAACUUACAAGGCCU					775	AGGCCUUGUAAGUUGCGA		
1100	464	CGCCAACUUACAAGGCCUU					776	AAGGCCUUGUAAGUUGGCG		
1101	465	GCCAACUUACAAGGCCUUU					777	AAAGGCCUUGUAAGUUGGC		
1230	466	GCGCAUGCGUGGAACUUU					778	AAAGGUUCCACGCAUGCGC		
1258	467	CUGCCGAUCCAUAUCGCGG					779	CCGCAGUAUGGAUCGCGAG		
1606	468	GCAUGGAGACCACCGUGAA					780	UUCACGGUGGUCUCCAUGC		
1607	469	CAUGGAGACCACCGUGAAC					781	GUUCACGGUGGUCUCCAUG		
1608	470	AUGGAGACCACCGUGAACG					782	CGUUCACGGUGGUCUCCA		
1609	471	UGGAGACCACCGUGAACGC					783	GCGUUCACGGUGGUCUCCA		
1610	472	GGAGACCACCGUGAACGCC					784	GGCGUUCACGGUGGUCUCC		
1611	473	GAGACCACCGUGAACGCC					785	GGGCGUUCACGGUGGUCUC		
1804	474	CACCAGCACCAUGCAACUU					786	AAGUUGCAUGGUGCUGGUG		
2381	475	CCCUCGCCUCGCAGACGAA					787	UUCGUCUGCGAGGCGAGGG		
3077	476	UGGGGUGGAGCCUCAGGC					788	GCCUGAGGGCUCCACCCCA		
303	477	GCCAAAAUUCGCAGUCCCC					789	GGGGACUCGCGAAUUUUGGC		
304	478	CCAAAAUUCGCAGUCCCCA					790	UGGGGACUCGCGAAUUUUGG		
305	479	CAAAAUUCGCAGUCCCCAA					791	UUGGGGACUCGCGAAUUUUG		
801	480	UACCAAUUUUCUUUUGUCU					792	AGACAAAAGAAAUUGGUA		
1174	481	UGCCAAGUGUUUGCUGACG					793	CGUCAGCAAACACUUGGCA		
1175	482	GCCAAGUGUUUGCUGACGC					794	GCGUCAGCAAACACUUGGC		
1176	483	CCAAGUGUUUGCUGACGCA					795	UGCGUCAGCAAACACUUGG		
2382	484	CCUCGCCUCGCAGACGAAG					796	CUUCGUCUGCGAGGCGAGG		
2408	485	UCUCAAUUCGCCGCGUCGCA					797	UGCGACGCGGCGAUUGAGA		
2409	486	CUCAAUUCGCCGCGUCGAG					798	CUGCGACGCGGCGAUUGAG		
2410	487	UCAAUUCGCCGCGUCGAGA					799	UCUGCGACGCGGCGAUUGA		
2463	488	CCUUGGACUCAUAAGGUGG					800	CCACCUUAUGAGUCCAAGG		

TABLE 15-continued

HBV sense and antisense sequences					
REF	SEQ	ID	Sense (5'-3')	SEQ	Antisense (5'-3')
POS	NO	SEQ	ID NOS: 237 to 548	ID NO	SEQ ID NOS: 549 to 860
2464	489	CUUGGACUCAUAAGGUGGG		801	CCCACCUUAUGAGUCCAAG
	55	490	UCCUGCUGGUGGCUCCAGU	802	ACUGGAGCCACCAGCAGGA
	668	491	UGGCUCAGUUUACUAGUGC	803	GCACUAGUAAACUGAGCCA
	701	492	UUCGUAGGGCUUCCCCCA	804	UGGGGGAAGCCCUACGAA
1177	493	CAAGUGUUUGCUGACGCAA		805	UUGCGUCAGCAAACACUUG
1178	494	AAGUGUUUGCUGACGCAAC		806	GUUGCGUCAGCAAACACUU
1179	495	AGUGUUUGCUGACGCAACC		807	GGUUGCGUCAGCAAACACU
1180	496	GUGUUUGCUGACGCAACCC		808	GGGUUGCGUCAGCAAACAC
1181	497	UGUUUGCUGACGCAACCCC		809	GGGGUUGCGUCAGCAAACA
1182	498	GUUUGCUGACGCAACCCCC		810	GGGGUUGCGUCAGCAAAC
1680	499	AUGUCAACGACCGACCUUG		811	CAAGGUCGGUCGUUGACAU
1681	500	UGUCAACGACCGACCUUGA		812	UCAAGGUCGGUCGUUGACA
1682	501	GUCAACGACCGACCUUGAG		813	CUCAAGGUCGGUCGUUGAC
1683	502	UCAACGACCGACCUUGAGG		814	CCUCAAGGUCGGUCGUUGA
1684	503	CAACGACCGACCUUGAGGC		815	GCCUCAAGGUCGGUCGUUG
2411	504	CAAUCGCCGCGUCGCAGAA		816	UUCUGCGACGCGGCGAUUG
2412	505	AAUCGCCGCGUCGCAGAAG		817	CUUCUGCGACGCGGCGAUU
2413	506	AUCGCCGCGUCGCAGAAGA		818	UCUUCUGCGACGCGGCGAU
2414	507	UCGCCGCGUCGCAGAAGAU		819	AUCUUCUGCGACGCGGCGA
2415	508	CGCCGCGUCGCAGAAGAUC		820	GAUCUUCUGCGACGCGGCG
2416	509	GCCGCGUCGCAGAAGAUCU		821	AGAUCUUCUGCGACGCGGC
	54	510	UUCUGCUGGUGGCUCCAG	822	CUGGAGCCACCAGCAGGAA
	700	511	GUUCGUAGGGCUUCCCCC	823	GGGGGAAGCCCUACGAAC
	702	512	UCGUAGGGCUUCCCCCAC	824	GUGGGGAAGCCCUACGA
1253	513	CUCCUCUGCCGAUCCAUAAC		825	GUAUGGAUCGGCAGAGGAG
1254	514	UCCUCUGCCGAUCCAUAUCU		826	AGUAUGGAUCGGCAGAGGA
1255	515	CCUCUGCCGAUCCAUAUCG		827	CAGUAUGGAUCGGCAGAGG
1439	516	CGCUGAAUCCCGCGGACGA		828	UCGUCCGCGGGAUUCAGCG
1547	517	CCCCGUCUGGCUUCUCA		829	UGAGAAGGCACAGACGGG
1548	518	CCCGUCUGGCUUCUCAU		830	AUGAGAAGGCACAGACGGG
1549	519	CCGUCUGGCUUCUCAUC		831	GAUGAGAAGGCACAGACGG
1550	520	CGUCUGGCUUCUCAUCU		832	AGAUGAGAAGGCACAGACG
1653	521	CAUAAGAGGACUCUUGGAC		833	GUCCAAGAGUCCCUUAUG
1910	522	GACCCUUAUAAAGAAUUUG		834	CAAAUUCUUUAUAGGGUC
2270	523	GUGUGGAUUCGCACUCCUC		835	GAGGAGUGCGAAUCCACAC
2361	524	GAGGCAGGUCCCCUAGAAG		836	CUUCUAGGGGACCUGCCUC

TABLE 15-continued

HBV sense and antisense sequences							
REF POS	SEQ NO	ID Sense (5'-3') SEQ ID NOS: 237 to 548	SEQ ID NO	Antisense (5'-3') SEQ ID NOS: 549 to 860			
2362	525	AGGCAGGUCCCCUAGAAGA	837	UCUUCUAGGGGACCUGCCU			
316	526	GUCCCCAACCUCCAAUAC	838	GUGAUUGGAGGUUGGGGAC			
317	527	UCCCCAACCUCCAAUACU	839	AGUGAUUGGAGGUUGGGGA			
452	528	UAUCAAGGUUAUGUUGCCCG	840	CGGGCAACAUAACCUUGAUA			
453	529	AUCAAGGUUAUGUUGCCCGU	841	ACGGGCAACAUAACCUUGAU			
687	530	CAUUUGUUCAGUGGUUCGU	842	ACGAACCACUGAACAAUG			
689	531	UUUGUUCAGUGGUUCGUAG	843	CUACGAACCACUGAACAAA			
690	532	UUGUUCAGUGGUUCGUAGG	844	CCUACGAACCACUGAACAA			
691	533	UGUUCAGUGGUUCGUAGGG	845	CCCUACGAACCACUGAACAA			
692	534	GUUCAGUGGUUCGUAGGGC	846	GCCCUACGAACCACUGAAC			
693	535	UUCAGUGGUUCGUAGGGCU	847	AGCCCUACGAACCACUGAA			
694	536	UCAGUGGUUCGUAGGGCUU	848	AAGCCCUACGAACCACUGA			
695	537	CAGUGGUUCGUAGGGCUUU	849	AAAGCCCUACGAACCACUG			
696	538	AGUGGUUCGUAGGGCUUUC	850	GAAAGCCCUACGAACCACU			
697	539	GUGGUUCGUAGGGCUUUC	851	GGAAAGCCCUACGAACCAC			
698	540	UGGUUCGUAGGGCUUUCCC	852	GGGAAAGCCCUACGAACCA			
699	541	GGUUCGUAGGGCUUUCCCC	853	GGGGAAGCCCUACGAACC			
1228	542	CAGCGCAUGCGUGGAACCU	854	AGGUUCCACGCAUGCGCUG			
1229	543	AGCGCAUGCGUGGAACCUU	855	AAGGUUCCACGCAUGCGCU			
1231	544	CGCAUGCGUGGAACCUUUG	856	CAAAGGUUCCACGCAUGCG			
1256	545	CUCUGCCGAUCCAUAUCUGC	857	GCAGUAUGGAUCGGCAGAG			
1257	546	UCUGCCGAUCCAUAUCUGCG	858	CGCAGUAUGGAUCGGCAGA			
1438	547	GCGCUGAAUCCCGCGGACG	859	CGUCCGCGGGAUUCAGCGC			
1827	548	ACCUCUGCCUAAUCAUCUC	860	GAGAUGAUUAGGCAGAGGU			

[0236] UNA Oligomers Targeting HBV

[0237] Examples of base sequences of this invention targeted to an HBV component are shown in Table 16.

[0238] An oligomeric compound of this invention can be formed having a first strand and a second strand each being 21 monomers in length. The first strand can have 19 contiguous monomers with a sequence of attached bases shown

in Table 16 (sense), and two additional overhang monomers on the 3' end. The second strand can have 19 contiguous monomers with a sequence of attached bases shown in Table 16 (antisense), and two additional overhang monomers on the 3' end. The overhang monomers can be any of NN, QQ, XX, NX, NQ, XN, XQ, QN, and QX. For example, XQ can be UNA-U/mU, or UNA-U/*dT.

TABLE 16

HBV sense and antisense sequences							
REF POS	SEQ NO	ID Sense (5'-3') SEQ ID NOS: 861 to 901	SEQ ID NO	Antisense (5'-3') SEQ ID NOS: 902 to 942			
1525	861	CGCACCUCUCUUUACGCGG	902	CCGCGUAAAGAGAGGUGCG			
251	862	GACUCGUGGUGGACUUCUC	903	GAGAAGUCCACCACGAGUC			
254	863	UCGUGGUGGACUUCUCUCA	904	UGAGAGAAGUCCACCACGA			

TABLE 16-continued

HBV sense and antisense sequences									
REF	SEQ	ID	Sense (5'-3')		SEQ	Antisense (5'-3')			
POS	NO	SEQ	ID NOS: 861 to 901	ID	NO	SEQ	ID NOS: 902 to 942		
	374	864	UGGAUGUGUCUGCGCGUU		905	AACGCCGCAGACACAUCCA			
1575	865		CCGUGUGCACUUCGCUUCA		906	UGAAGCGAAGUGCACACGG			
1577	866		GUGUGCACUUCGCUUCACC		907	GGUGAAGCGAAGUGCACAC			
1578	867		UGUGCACUUCGCUUCACCU		908	AGGUGAAGCGAAGUGCACA			
1579	868		GUGCACUUCGCUUCACCUC		909	GAGGUGAAGCGAAGUGCAC			
1581	869		GCACUUCGCUUCACCUCUG		910	CAGAGGUGAAGCGAAGUGC			
247	870		UCUAGACUCGUGGUGGACU		911	AGUCCACCACGAGUCUAGA			
248	871		CUAGACUCGUGGUGGACUU		912	AAGUCCACCACGAGUCUAG			
249	872		UAGACUCGUGGUGGACUUC		913	GAAGUCCACCACGAGUCUA			
250	873		AGACUCGUGGUGGACUUCU		914	AGAAGUCCACCACGAGUCU			
1776	874		GGAGGCUGUAGGCAUAAAU		915	AUUUAUGCCUACAGCCUCC			
1777	875		GAGGCUGUAGGCAUAAAU		916	AAUUUAUGCCUACAGCCUC			
1779	876		GGCUGUAGGCAUAAAUUGG		917	CCAAUUUAUGCCUACAGCC			
1780	877		GCUGUAGGCAUAAAUUGGU		918	ACCAAUUUAUGCCUACAGC			
1781	878		CUGUAGGCAUAAAUUGGUC		919	GACCAAUUUAUGCCUACAG			
1782	879		UGUAGGCAUAAAUUGGUCU		920	AGACCAAUUUAUGCCUACA			
256	880		GUGGUGGACUUCUCUCAAU		921	AUUGAGAGAAGUCCACCAC			
1863	881		UUCAAGCCUCCAAGCUGUG		922	CACAGCUUGGAGGCUUGAA			
1864	882		UCAAGCCUCCAAGCUGUGC		923	GCACAGCUUGGAGGCUUGA			
1865	883		CAAGCCUCCAAGCUGUGCC		924	GGCACAGCUUGGAGGCUUG			
1866	884		AAGCCUCCAAGCUGUGCCU		925	AGGCACAGCUUGGAGGCUU			
376	885		GAUGUGUCUGCGCGUUUU		926	AAAACGCCCGCAGACAUUC			
378	886		UGUGUCUGCGCGUUUUAU		927	AUAAAACGCCCGCAGACACA			
380	887		UGUCUGCGCGUUUUUAUCA		928	UGAUAAAACGCCCGCAGACA			
1818	888		AACUUUUUACCCUCUGCCU		929	AGGCAGAGGUGAAAAAGUU			
244	889		GAGUCUAGACUCGUGGUGG		930	CCACCACGAGUCUAGACUC			
245	890		AGUCUAGACUCGUGGUGGA		931	UCCACCACGAGUCUAGACU			
246	891		GUCUAGACUCGUGGUGGAC		932	GUCCACCACGAGUCUAGAC			
409	892		CAUCCUGCUGCUAUGCCUC		933	GAGGCAUAGCAGCAGGAUG			
411	893		UCCUGCUGCUAUGCCUCAU		934	AUGAGGCAUAGCAGCAGGA			
412	894		CCUGCUGCUAUGCCUCAUC		935	GAUGAGGCAUAGCAGCAGG			
413	895		CUGCUGCUAUGCCUCAUCU		936	AGAUGAGGCAUAGCAGCAG			
414	896		UGCUGCUAUGCCUCAUCUU		937	AAGAUGAGGCAUAGCAGCA			
252	897		ACUCGUGGUGGACUUCUCU		938	AGAGAAGUCCACCACGAGU			
253	898		CUCGUGGUGGACUUCUCUC		939	GAGAGAAGUCCACCACGAG			
1576	899		CGUGUGCACUUCGCUUCAC		940	GUGAAGCGAAGUGCACACG			

TABLE 16-continued

HBV sense and antisense sequences										
REF	SEQ	ID	Sense (5'-3')			SEQ	Antisense (5'-3')			
POS	NO	SEQ	ID	NOS: 861 to 901			ID	NO	SEQ	ID NOS: 902 to 942
1580	900	UGCACUUCGCUUACCCUCU					941		AGAGGUGAAGCGAAGUGCA	
1582	901	CACUUCGCUUACCCUCUGC					942		GCAGAGGUGAAGCGAAGUG	

[0239] UNA Oligomers Targeting HBV

[0240] Embodiments of this invention can provide oligomeric molecules that are active agents targeted to HBV.

[0241] Examples of UNA oligomers of this invention that are targeted to an HBV component are shown in Table 17. Table 17 shows “sense” and “antisense” pairs.

TABLE 17

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF	SEQ	HBV (Sense (S)-Antisense (AS))		
POS	ID NO S/AS	(5'-3')		
244	943 S	UNA-G/mAGmUCmUAmGACUmCGmUGmGUmGG/UNA-U/mU		
244	944 AS	mCCmACmCmAmCGmAGmUmCmUAmGAmCmU/UNA-U/mU		
245	945 S	UNA-A/mGUmCmUAmGmACUmGUmGmUGmGA/UNA-U/mU		
245	946 AS	mUCmCmAmCCmACmGAmGmUmCmUAmGAmCmU/UNA-U/mU		
246	947 S	UNA-G/mUCmUAmGAmCmUGmUGmGmGmAC/UNA-U/mU		
246	948 AS	mGUmCCmACmCmAmCGmAmGmUmCmUAmGAmC/UNA-U/mU		
247	949 S	UNA-U/mCmUAmGmACmUCGUmGmUGmGAmCmU/UNA-U/mU		
247	950 AS	mAGmUCmCmAmCCmACmGmAmGUmCmUAmGmA/UNA-U/mU		
248	951 S	UNA-C/mUAmGAmCmUmCGUmGmUGmGmACmUU/UNA-U/mU		
248	952 AS	mAAmGUmCCmACmCmAmCmGmAGmUCmUAmG/UNA-U/mU		
249	953 S	UNA-U/mAGmACmUCmGUGmUGmGAmCmUmC/UNA-U/mU		
249	954 AS	mGAmAGmUCmCmAmCCmAmCmGAmGUmCmUA/UNA-U/mU		
250	955 S	UNA-A/mGAmCmUmCGmUGGUmGmGmACmUmCmU/UNA-U/mU		
250	956 AS	mAGmAAmGUmCCmACmCmAmCGmAGmUCmU/UNA-U/mU		
251	957 S	UNA-G/mACmUCmGUmGGUmGAmCmUmCmUC/UNA-U/mU		
251	958 AS	mGAmGAmAGmUCmCmAmCmACmGAmGUmC/UNA-U/mU		
252	959 S	UNA-A/mCmCGmUGmGUGmACmUmCmUmCmU/UNA-U/mU		
252	960 AS	mAGmAGmAAmGUmCCmAmCmCmAmCGmAGmU/UNA-U/mU		
253	961 S	UNA-C/mUCmGUmGGmUGGAmCmUmCmUmCmUC/UNA-U/mU		
253	962 AS	mGAmGAmGAmAGmUCmCmAmCCmACmGAmG/UNA-U/mU		
254	963 S	UNA-U/mCGmUGmGUmGGACmUmCmUmCmUA/UNA-U/mU		
254	964 AS	mUGmAGmAGmAAmGUmCmCmACmCmAmCGmA/UNA-U/mU		
256	965 S	UNA-G/mUGmGUmGGmACUmCmUmCmAmAU/UNA-U/mU		
256	966 AS	mAUmUGmAGmAGmAAmGmUmCCmACmCmAmC/UNA-U/mU		
374	967 S	UNA-U/mGGmAUmGUmGUCUmGmGmGmCmUU/UNA-U/mU		
374	968 AS	mAAmCGmCCmGCmAGmAmCmACmAUmCCmA/UNA-U/mU		

TABLE 17-continued

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))			
REF POS	SEQ ID NO S/AS	HBV (Sense (S)-Antisense (AS)) (5' -3')	
376	969 S	UNA-G/mAUmGUmGUmCUGCmGGmCGmUUmUU/UNA-U/mU	
376	970 AS	mAAmAAmCGmCCmGCmAmGmACmACmAUmC/UNA-U/mU	
378	971 S	UNA-U/mGUmGUmCUmGCGGmCGmUUmUUmAU/UNA-U/mU	
378	972 AS	mAUmAAmAAmCGmCCmGmCmAGmACmACmA/UNA-U/mU	
380	973 S	UNA-U/mGUmCUmGmCGCGmUUmUUmAUmCA/UNA-U/mU	
380	974 AS	mUGmAUmAAmAAmCGmCmCmGCmAGmACmA/UNA-U/mU	
409	975 S	UNA-C/mAUmCCmUGmCUGCmUAmUGmCCmUC/UNA-U/mU	
409	976 AS	mGAmGGmCAmUAmGCmAmGmCAmGGmAUmG/UNA-U/mU	
411	977 S	UNA-U/mCCmUGmCUmGCUAmUGmCCmUCmAU/UNA-U/mU	
411	978 AS	mAUmGAmGGmCAmUAmGmCmAGmCAmGGmA/UNA-U/mU	
412	979 S	UNA-C/mCUmGCmUGmCUAUmGCmCUmCAmUC/UNA-U/mU	
412	980 AS	mGAmUGmAGmGCmAUmAmGmCAmGCmAGmG/UNA-U/mU	
413	981 S	UNA-C/mUGmCUmGCmUAUGmCCmUCmAUmCU/UNA-U/mU	
413	982 AS	mAGmAUmGAmGGmCAmUmAmGmCAmCAmG/UNA-U/mU	
414	983 S	UNA-U/mGCmUGmCUmAUGCmCUmCAmUCmUU/UNA-U/mU	
414	984 AS	mAAmGAmUGmAGmGCmAmUmAGmCAmGCmA/UNA-U/mU	
1525	985 S	UNA-C/mGCmACmCUmCUCUmUUmACmGCmGG/UNA-U/mU	
1525	986 AS	mCCmGCmGUmAAmAGmAmGmAGmGUmGCmG/UNA-U/mU	
1575	987 S	UNA-C/mCGmUGmUGmCACUmUCmGCmUUmCA/UNA-U/mU	
1575	988 AS	mUGmAAmGmCAmAGmUmGmCAmCAmCGmG/UNA-U/mU	
1576	989 S	UNA-C/mGUmGUmGCmACUUmCGmCUmUCmAC/UNA-U/mU	
1576	990 AS	mGUmGAmAGmCGmAAmGmUmGCmACmCAmG/UNA-U/mU	
1577	991 S	UNA-G/mUGmUGmCAmCUUmGCmUUmCAmCC/UNA-U/mU	
1577	992 AS	mGGmUGmAAmGmCAmAmGmUGmCAmCAmC/UNA-U/mU	
1578	993 S	UNA-U/mGUmGCmCAmUUCGmCUmUCmACmCU/UNA-U/mU	
1578	994 AS	mAGmGUmGAmAGmCGmAmAmGUmGCmCAmA/UNA-U/mU	
1579	995 S	UNA-G/mUGmCAmCUmUCGmUUmCAmCCmUC/UNA-U/mU	
1579	996 AS	mGAmGGmUGmAAmGmCAmAGmUGmCAmC/UNA-U/mU	
1580	997 S	UNA-U/mGCmACmUUmCGCmUUmCAmCUmCU/UNA-U/mU	
1580	998 AS	mAGmAGmGUmGAmAGmCmGmAAGmUGmCA/UNA-U/mU	
1581	999 S	UNA-G/mCAmCUmUCmGCUUmCAmCCmUCmUG/UNA-U/mU	
1581	1000 AS	mCAmGAmGGmUGmAAmGmCmGAmAGmUGmC/UNA-U/mU	
1582	1001 S	UNA-C/mACmUUmCGmCUUmCAmCUmCmGC/UNA-U/mU	
1582	1002 AS	mGCmAGmAGmGUmGAmAmGmCGmAAGmUGmG/UNA-U/mU	
1776	1003 S	UNA-G/mGAmGGmCUmGUAGmGCmAUmAAmAU/UNA-U/mU	
1776	1004 AS	mAUmUUmAUmGCmCmAmCAmAGmCCmUCmC/UNA-U/mU	

TABLE 17-continued

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))			
REF POS	SEQ ID NO	S/AS	HBV (Sense (S)-Antisense (AS)) (5' -3')
1777	1005	S	UNA-G/mAGmGCmUGmUAGGmCmUAmAAmUU/UNA-U/mU
1777	1006	AS	mAAmUUmUAmUGmCCmUmAmCmGmCmC/UNA-U/mU
1779	1007	S	UNA-G/mGCmUGmUAmGGCmUAmAAmUUmGG/UNA-U/mU
1779	1008	AS	mCCmAAmUUmUAmUGmCmCmUAmCmGmC/UNA-U/mU
1780	1009	S	UNA-G/mCmUGmUAmGmGCAUmAmAUmUGmGU/UNA-U/mU
1780	1010	AS	mACmCAmAUmUUmAUmGmCmCmUAmCmAGmC/UNA-U/mU
1781	1011	S	UNA-C/mUGmUAmGGmCAUAmAAmUUmGGmUC/UNA-U/mU
1781	1012	AS	mGAmCCmAAmUUmUAmUGmCCmUAmCmAG/UNA-U/mU
1782	1013	S	UNA-U/mGUmAGmGCmAUAUmAUmUGmGUmCU/UNA-U/mU
1782	1014	AS	mAGmACmCAmAUmUUmAUmGmCmCmUAmCA/UNA-U/mU
1818	1015	S	UNA-A/mACmUUmUUmUCACmCmCmUGmCmC/UNA-U/mU
1818	1016	AS	mAGmGCmAGmAGmGUmGmAmAAmAAmGUmU/UNA-U/mU
1863	1017	S	UNA-U/mUCmAAmGCmCUCCmAAmGCmUGmUG/UNA-U/mU
1863	1018	AS	mCAmCAmGCmUUmGGmAmGmGCmUUmGAmA/UNA-U/mU
1864	1019	S	UNA-U/mCAmAGmCCmUCCAmAGmCmUGmUGC/UNA-U/mU
1864	1020	AS	mGCmACmAGmCmUUmGmAmGmGCmUUmGmA/UNA-U/mU
1865	1021	S	UNA-C/mAAmGCmCmCCAAmGCmUGmUGmCC/UNA-U/mU
1865	1022	AS	mGGmCAmCAmGCmUUmGmGmAGmGCmUUmG/UNA-U/mU
1866	1023	S	UNA-A/mAGmCCmUCmCAAGmCmUGmUGmCmC/UNA-U/mU
1866	1024	AS	mAGmGCmACmAGmCmUUmGmGAmGGmCmU/UNA-U/mU

[0242] UNA Oligomers Targeting HBV

[0243] Embodiments of this invention can provide oligomeric molecules that are active agents targeted to HBV.

[0244] Examples of UNA oligomers of this invention that are targeted to an HBV component are shown in Table 18. Table 18 shows “sense” and “antisense” pairs.

TABLE 18

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID NO	S/ AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
1576	1025	S	UNA-C/mGrUmGrUmGrCmArCrUrUmCrGmCrUmUrCmArC/UNA-U/mU	
1576	1026	AS	mGrUmGrAmArGmC/UNA-G/mArAmGmUmGrCmArCmArCmG/UNA-U/mU	
1576	1027	S	UNA-C*/mGrUmGrUmGrCmArCrUrUmCrGmCrUmUrCmArC*/UNA-U*/mU	
1576	1028	AS	mGrUmGrAmArGmC/UNA-G/mArAmGmUmGrCmArCmArCmG/UNA-U*/mU	
1576	1029	S	UNA-C*/mG*rU*mGrUmGrCmArCrUrUmCrGmCrUmUrCmArC*/UNA-U*/mU	
1576	1030	AS	mGrUmGrAmArGmC/UNA-G/mArAmGmUmGrCmArCmArCmG/UNA-U*/mU	
1576	1031	S	UNA-C*/mG*rU*mGrUmGrCmArCrUrUmCrGmCrUmUrCmArC*rC*/UNA-U*/mU	
1576	1032	AS	mGrUmGrAmArGmC/UNA-G/mArAmGmUmGrCmArCmArCmG/UNA-U*/mU	

TABLE 18-continued

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID NO	S/ AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
1576	1033	S	UNA-C*/mGrUmGrUmGrCmArCrUrUmCrGmCrUmUrCmArC*/UNA-U*/mU	
1576	1034	AS	mG*rU*mGrAmArGmC/UNA-G/mArAmGmUmGrCmArCmArCmG*/UNA-U*/mU	
1576	1035	S	UNA-C*/mG*rUmGrUmGrCmArCrUrUmCrGmCrUmUrCmArC*/UNA-U*/mU	
1576	1036	AS	mG*rU*mGrAmArGmC/UNA-G/mArAmGmUmGrCmArCmArCmG*/UNA-U*/mU	
1576	1037	S	UNA-C*/mG*rU*mGrUmGrCmArCrUrUmCrGmCrUmUrCmArC*/UNA-U*/mU	
1576	1038	AS	mG*rU*mGrAmArGmC/UNA-G/mArAmGmUmGrCmArCmArCmG*/UNA-U*/mU	
1576	1039	S	UNA-C*/mG*rU*mGrUmGrCmArCrUrUmCrGmCrUmUrCmA*rC*/UNA-U*/mU	
1576	1040	AS	mG*rU*mGrAmArGmC/UNA-G/mArAmGmUmGrCmArCmArCmG*/UNA-U*/mU	
1575	1041	S	UNA-C*/mC*rGmUrGmUrGmCrArCrUmUrCmGrCmUrUmCrA*/UNA-U*/mU	
1575	1042	AS	mUrGmAra/UNA-G/rCmGrAmArGmUmGmCrAmCrAmCrGmG/UNA-U*/mU	
1575	1043	S	UNA-C*/mC*rGmUrGmUrGmCrArCrUmUrCmGrCmUrUmCrA*/UNA-U*/mU	
1575	1044	AS	mUrGmAraAmGrC/UNA-G/rAmArGmUmGmCrAmCrAmCrGmG/UNA-U*/mU	
1575	1045	S	UNA-C*/mC*rGmUrGmUrGmCrArCrUmUrCmGrCmUrUmCrA*/UNA-U*/mU	
1575	1046	AS	mUrGmAraAmGrCmG/UNA-A/mArGmUmGmCrAmCrAmCrGmG/UNA-U*/mU	
1578	1047	S	UNA-U*/mG*rU*mGrCmArCmUrUrCrGmCrUmUrCmArCmC*rU*/UNA-U*/mU	
1578	1048	AS	mArGmGrU/UNA-G/rAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U*/mU	
1578	1049	S	UNA-U*/mG*rU*mGrCmArCmUrUrCrGmCrUmUrCmArCmC*rU*/UNA-U*/mU	
1578	1050	AS	mArGmGrUmG/UNA-A/mArGmCrGmAmAmGrUmGrCmArCmA/UNA-U*/mU	
1578	1051	S	UNA-U*/mG*rU*mGrCmArCmUrUrCrGmCrUmUrCmArCmC*rU*/UNA-U*/mU	
1578	1052	AS	mArGmGrUmGrAmA/UNA-G/mCrGmAmAmGrUmGrCmArCmA/UNA-U*/mU	
1818	1053	S	UNA-A/mArCmUrUmUrUmUrCrArCmCrUmCrUmGrCmCrU/UNA-U/mU	
1818	1054	AS	mArGmGrC/UNA-A/rGmAraGmGrUmGmAmArAmArAmGrUmU/UNA-U/mU	
1818	1055	S	UNA-A/mArCmUrUmUrUmUrCrArCmCrUmCrUmGrCmCrU/UNA-U/mU	
1818	1056	AS	mArGmGrCmA/UNA-G/mArGmGrUmGmAmArAmArAmGrUmU/UNA-U/mU	
1818	1057	S	UNA-A/mArCmUrUmUrUmUrCrArCmCrUmCrUmGrCmCrU/UNA-U/mU	
1818	1058	AS	mArGmGrCmAraG/UNA-A/rGmGrUmGmAmArAmArAmGrUmU/UNA-U/mU	
245	1059	S	UNA-A/mGrUmCrUmArGmArCrUrCmGrUmGrGmUrGmGrA/UNA-U/mU	
245	1060	AS	mUrCmCrAmCrC/-UNA-A/rCmGrAmGmUmCrUmArGmArCmU/UNA-U/mU	
1580	1061	S	UNA-U/mGrCmArCmUrUmCrGrCrUmUrCmArCmCrUmCrU/UNA-U/mU	
1580	1062	AS	mArGmAraG/UNA-G/rUmGrAmArGmCmGmArAmGrUmGrCmA/UNA-U/mU	
1580	1063	S	UNA-U/mGrCmArCmUrUmCrGrCrUmUrCmArCmCrUmCrU/UNA-U/mU	
1580	1064	AS	mArGmAraGmG/UNA-U/mGrAmArGmCmGmArAmGrUmGrCmA/UNA-U/mU	
1580	1065	S	UNA-U/mGrCmArCmUrUmCrGrCrUmUrCmArCmCrUmCrU/UNA-U/mU	
1580	1066	AS	mArGmAraGmGrU/UNA-G/rAmArGmCmGmArAmGrUmGrCmA/UNA-U/mU	
1580	1067	S	UNA-U/mGrCmArCmUrUmCrGrCrUmUrCmArCmCrUmCrU/UNA-U/mU	
1580	1068	AS	mArGmAraGmGrUmG/UNA-A/mArGmCmGmArAmGrUmGrCmA/UNA-U/mU	

[0245] UNA Oligomers Targeting HBV

[0246] Embodiments of this invention can provide oligomeric molecules that are active agents targeted to HBV.

[0247] Examples of UNA oligomers of this invention that are targeted to an HBV component are shown in Table 19. Table 19 shows “sense” and “antisense” pairs.

TABLE 19

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))					
REF POS	SEQ ID NO	S/ AS	HBV (Sense (S)-Antisense (AS)) (5'-3')		
1578	1069	S	UNA-U*/mGrUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU*/UNA-U*/mU		
1578	1070	AS	mArGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U*/mU		
1578	1071	S	UNA-U*/mG*rUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU*/UNA-U*/mU		
1578	1072	AS	mArGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U*/mU		
1578	1073	S	UNA-U*/mG*rU*mGrCmArCmUrUrCrGmCrUmUrCmArCmCrU*/UNA-U*/mU		
1578	1074	AS	mArGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U*/mU		
1578	1075	S	UNA-U*/mG*rU*mGrCmArCmUrUrCrGmCrUmUrCmArCmC*rU*/UNA-U*/mU		
1578	1076	AS	mArGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U*/mU		
1578	1077	S	UNA-U*/mGrUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU*/UNA-U*/mU		
1578	1078	AS	mA*rGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U*/mU		
1578	1079	S	UNA-U*/mG*rUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU*/UNA-U*/mU		
1578	1080	AS	mA*rGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U*/mU		
1578	1081	S	UNA-U*/mG*rU*mGrCmArCmUrUrCrGmCrUmUrCmArCmCrU*/UNA-U*/mU		
1578	1082	AS	mA*rGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U*/mU		
1578	1083	S	UNA-U*/mG*rU*mGrCmArCmUrUrCrGmCrUmUrCmArCmC*rU*/UNA-U*/mU		
1578	1084	AS	mA*rGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U*/mU		
1578	1085	S	UNA-U*/mGrUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU*/UNA-U*/mU		
1578	1086	AS	mA*rGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA*/UNA-U*/mU		
1578	1087	S	UNA-U*/mG*rUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU*/UNA-U*/mU		
1578	1088	AS	mA*rGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA*/UNA-U*/mU		
1578	1089	S	UNA-U*/mG*rU*mGrCmArCmUrUrCrGmCrUmUrCmArCmCrU*/UNA-U*/mU		
1578	1090	AS	mA*rGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA*/UNA-U*/mU		
1578	1091	S	UNA-U*/mG*rU*mGrCmArCmUrUrCrGmCrUmUrCmArCmC*rU*/UNA-U*/mU		
1578	1092	AS	mA*rGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA*/UNA-U*/mU		
1578	1093	S	UNA-U*/mGrUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU*/UNA-U*/mU		
1578	1094	AS	mA*rG*mGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA*/UNA-U*/mU		
1578	1095	S	UNA-U*/mG*rUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU*/UNA-U*/mU		
1578	1096	AS	mA*rG*mGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA*/UNA-U*/mU		
1578	1097	S	UNA-U*/mG*rU*mGrCmArCmUrUrCrGmCrUmUrCmArCmCrU*/UNA-U*/mU		
1578	1098	AS	mA*rG*mGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA*/UNA-U*/mU		
1578	1099	S	UNA-U*/mG*rU*mGrCmArCmUrUrCrGmCrUmUrCmArCmC*rU*/UNA-U*/mU		
1578	1100	AS	mA*rG*mGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA*/UNA-U*/mU		
1777	1101	S	UNA-G*/mArGmGrCmUrGmUrArGrGmCrAmUrAmArAmUrU*/UNA-U*/mU		
1777	1102	AS	mArAmUrUmUrAmUrGmCrCmUmAmCrAmGrCmCrUmC/UNA-U*/mU		

TABLE 19-continued

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID NO	S/ AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
1777	1103	S	UNA-G*/mA*rGmGrCmUrGmUrArGrGmCrAmArAmUrU*/UNA-U*/mU	
1777	1104	AS	mArAmUrUmUrAmUrGmCrCmUmAmCrAmGrCmCrUmC*/UNA-U*/mU	
1777	1105	S	UNA-G*/mA*rG*mGrCmUrGmUrArGrGmCrAmUrAmArAmUrU*/UNA-U*/mU	
1777	1106	AS	mArAmUrUmUrAmUrGmCrCmUmAmCrAmGrCmCrU*mC*/UNA-U*/mU	
380	1107	S	UNA-U*/mG*rUmCrUmGrCmGrGrCrGmUrUmUrUmArUmCrA*/UNA-U*/mU	
380	1108	AS	mUrGmArUmArAmArAmCrGmCmCmGrCmArGmArCmA/UNA-U*/mU	
380	1109	S	UNA-U*/mG*rUmCrUmGrCmGrGrCrGmUrUmUrUmArUmCrA*/UNA-U*/mU	
380	1110	AS	mUrGmArUmArAmArAmCrGmCmCmGrCmArGmArCmA/UNA-U*/mU	
380	1111	S	UNA-U*/mG*rUmCrUmGrCmGrGrCrGmUrUmUrUmArUmCrA*/UNA-U*/mU	
380	1112	AS	mU*rGmArUmArAmArAmCrGmCmCmGrCmArGmArCmA/UNA-U*/mU	
380	1113	S	UNA-U*/mG*rU*mCrUmGrCmGrGrCrGmUrUmUrUmArUmCrA*/UNA-U*/mU	
380	1114	AS	mU*rGmArUmArAmArAmCrGmCmCmGrCmArGmArCmA/UNA-U*/mU	
1576	1115	S	UNA-C*/mGrUmGrUmGrCmArCrUrUmCrGmCrUmUrCmA*/UNA-U*/mU	
1576	1116	AS	mGrUmGrAmArGmCrGmArAmGmUmGrCmArCmA/C/UNA-U*/mU	
1575	1117	S	UNA-C*/mC*rGmUrGmUrGmCrArCrUmUrCmGrCmUrUmCrA*/UNA-U*/mU	
1575	1118	AS	mUrGmArAmGrCmGrAmArGmUmGmCrAmCrAmCrGmG/UNA-U*/mU	
1580	1119	S	UNA-U*/mG*rC*mArCmUrUmCrGrCrUmUrCmArCmCrUmCrU*/UNA-U*/mU	
1580	1120	AS	mArGmArGmGrUmGrAmArGmCmGmArAmGrUmGrCmA*/UNA-U*/mU	

[0248] UNA Oligomers Targeting HBV**[0249]** Embodiments of this invention can provide oligomeric molecules that are active agents targeted to HBV.**[0250]** Examples of UNA oligomers of this invention that are targeted to an HBV component are shown in Table 20. Table 20 shows “sense” and “antisense” pairs.

TABLE 20

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID NO	S/ AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
1578	1121	S	UNA-U*/mGrUmGrCmArCmUrUrCrGmCrUmUrCmA/CrU*/UNA-U*/T	
1578	1122	AS	mArGmGrUmGrAmArGmCrGmAmGrUmGrCmA/C/UNA-U*/T	
1578	1123	S	UNA-U*/fGrUfGrCfArCfUrUrCrGfCfUfUrCfArCfCfU*/UNA-U*/dT	
1578	1124	AS	fArGfGrUfGrAfArGfCrGfAfAfGrUfGrCfArCfA/UNA-U*/dT	
1578	1125	S	UNA-U*/rGfUrGfCrAfCfUfUfCrGfCfUfUfCrAfCfCfU*/UNA-U*/dT	
1578	1126	AS	rArGrGfUrGrArArGfCrGrArArGfUrGfCrAfCfA/UNA-U*/dT	
1578	1127	S	UNA-U*/mGfUmGfCmAfCmUfUfCfGmCfUmUfCmAfCmCfU*/UNA-U*/T	
1578	1128	AS	mAfGmGfUmGfAmAfGmCfGmAmAmGfUmGfCmAfCmA/UNA-U*/T	
1777	1129	S	UNA-G*/mArGmGrCmUrGmUrArGrGmCrAmUrAmArAmUrU*/UNA-U*/T	
1777	1130	AS	UNA-G*/mArGmGrCmUrGmUrArGrGmCrAmUrAmArAmUrU*/UNA-U*/T	
1777	1131	S	UNA-G*/fArGfGrCfUrGfUrArGrGfCrAfUrAfArAfUrU*/UNA-U*/T	

TABLE 20-continued

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))					
REF	SEQ	S/	HBV (Sense (S)-Antisense (AS))		
POS	ID	NO	AS (5'-3')		
1777	1132	AS	fArAfUrUfUrAfUrGfCrCfUfAfCrAfGrCfCrUfC/UNA-U/* /T		
1777	1133	S	UNA-G/* /rArGrGfCfUrGfUrArGrGfCrAfUrArArAfUfU/* /UNA-U/* /T		
1777	1134	AS	rArAfUfUfUrAfUrGfCfCfUrAfCrArGfCfCfUfC/UNA-U/* /T		
1777	1135	S	UNA-G/* /mAfGmGfCmUfGmUfAfGfGmCfAmUfAmAfAmUfU/* /UNA-U/* /T		
1777	1136	AS	UNA-G/* /mAfGmGfCmUfGmUfAfGfGmCfAmUfAmAfAmUfU/* /UNA-U/* /T		
380	1137	S	UNA-G/* /mAfGmGfCmUfGmUfAfGfGmCfAmUfAmAfAmUfU/* /UNA-U/* /T		
380	1138	AS	mUrGmArUmArAmArAmCrGmCmCmGrCmArGmArCmA/UNA-U/* /mU		
380	1139	S	UNA-U/* /fGrUfCrUfGrCfGrGrCrGfUrUfUrUfArUfCrA/* /UNA-U/* /fU		
380	1140	AS	fUrGfArUfArAfArAfCrGfCfCfGrCfArGfArCfA/UNA-U/* /fU		
380	1141	S	UNA-U/* /rGfUfCfUrGfCrGrGfCrGfUfUfUfUrAfUfCrA/* /UNA-U/* /fU		
380	1142	AS	fUrGrAfUrArArArAfCrGfCfCrGfCrArGrAfCrA/UNA-U/* /fU		
380	1143	S	UNA-U/* /mGfUmCfUmGfCmGfGfCfGmUfUmUfUmAfUmCfA/* /UNA-U/* /mU		
380	1144	AS	UNA-U/* /mGfUmCfUmGfCmGfGfCfGmUfUmUfUmAfUmCfA/* /UNA-U/* /mU		

[0251] In Tables herein, rN refers to N, which is a ribonucleotide, mN refers to a chemically-modified 2'-OME ribonucleotide, an asterisk * between characters refers to a phosphorothioate linkage, dN refers to a deoxyribonucleotide, f refers to a 2'-deoxy-2'-fluoro ribonucleotide.

[0252] Additional compounds of this invention are shown in Table 21.

TABLE 21

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))					
REF	SEQ	S/	HBV (Sense (S)-Antisense (AS))		
POS	ID	NO	AS (5'-3')		
1575	1182	S	UNA-C*/mCrGmUrGmUrGmCrArCrUmUrCmGrCmUrUmCrA*/UNA-U*/dT		
1575	1183	AS	mUrGmArAmGrCmGrAmArGmUmGmCrAmCrAmCrGmG/UNA-U*/dT		
1576	1184	S	UNA-C*/mGrUmGrUmGrCmArCrUrUmCrGmCrUmUrCmArC*/UNA-U*/dT		
1576	1185	AS	mGrUmGrAmArGmCrGmArAmGmUmGrCmArCmArCmG/UNA-U*/dT		
1581	1186	S	UNA-G*/mCAmCUmUCmGCUUmCAmCCmUCmUG*/UNA-U*/dT		
1581	1187	AS	mCAmGAmGGmUGmAAmGmCmGAmAGmUGmC/UNA-U*/dT		
1580	1188	S	UNA-U*/mGrCmArCmUrUmCrGrCrUmUrCmArCmCrUmCrU*/UNA-U*/dT		
1580	1189	AS	mArGmArGmGrUmGrAmArGmCmGmArAmGrUmGrCmA/UNA-U*/dT		
376	1190	A	UNA-G*/mAUmGUmGUmCUGCmGGmCGmUUmUU*/UNA-U*/dT		
376	1191	AS	mAaMAAmCGmCCmGmAmGmACmACmAUmC/UNA-U*/dT		
378	1192	S	UNA-U*/mGUmGUmCmGCGGmCGmUUmUUAU*/UNA-U*/dT		
378	1193	AS	mAUmAAmAAmCGmCCmGmCmAGmACmACmA/UNA-U*/dT		
380	1194	S	UNA-U/* /mGrUmCrUmGrCmGrGrCrGmUrUmUrUmArUmCrA/* /UNA-U/* /dT		

TABLE 21-continued

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))					
REF	SEQ	S/	HBV (Sense (S)-Antisense (AS))		
POS	ID	NO	AS (5'-3')		
380	1195	AS	mUrGmArUmArAmArAmCrGmCmCmGrCmArGmArCmA/UNA-U/*dT		
413	1196	S	UNA-C/*mUGmCmUGmCmUAUGmCCmUCmAUmCU/*UNA-U/*dT		
413	1197	AS	mAGmAUmGAmGGmCAmUmAmGmCAmG/UNA-U/*dT		
411	1198	S	UNA-U/*mCCmUGmCmUGCUAmUGmCCmUCmAU/*UNA-U/*dT		
411	1199	AS	mAUmGAmGGmCAmUmAmGmCAmGGmA/UNA-U/*dT		
1777	1200	S	UNA-G/*mArGmGrCmUrGmUrArGrGmCrAmUrAmArAmUrU/*UNA-U/*dT		
1777	1201	AS	mArAmUrUmUrAmUrGmCrCmUmAmCrAmGrCmCrUmC/UNA-U/*dT		
1780	1202	S	UNA-G/*mCmUGmAmGCAUmAAmAUmUGmGU/*UNA-U/*dT		
1780	1203	AS	mACmCAmAUmUUmAmGmCmUmACmAGmC/UNA-U/*dT		
1781	1204	S	UNA-C/*mUGmUAmGGmCAUmAAmAUmUGmUC/*UNA-U/*dT		
1781	1205	AS	mGAmCCmAAmUUmAmUmGmCCmUAmCAmG/UNA-U/*dT		
1782	1206	S	UNA-U/*mGUmAmGmGCmAUAAmAUmUGmGUmCU/*UNA-U/*dT		
1782	1207	AS	mAGmACmCAmAUmUUmAmUmGmCmUmACmA/UNA-U/*dT		

[0253] Compositions for Use Against HBV

[0254] Embodiments of this invention can provide compositions of oligomeric molecules that are active agents targeted to HBV.

[0255] A composition for use against HBV viral infection can provide targeting for suppressing multiple viral gene products.

[0256] Without wishing to be bound by any one particular theory, certain open reading frames (ORF) encoding the P, S, C, and X genes of HBV can overlap.

[0257] In some embodiments, a composition of this invention may contain an oligomeric compound targeted to an HBV genomic transcript or ORF for HBsAg. For example, these embodiments can inhibit expression of HBsAg, regardless of the location of the HBV genomic DNA.

[0258] In additional embodiments, a composition may contain an oligomeric compound targeted to an HBV genomic transcript or ORF for HBeAg.

[0259] In further embodiments, a composition may contain an oligomeric compound targeted to an HBV genomic transcript or ORF for X protein.

[0260] In further embodiments, a composition may contain an oligomeric compound targeted to an HBV genomic transcript or ORF for DNA polymerase (P).

[0261] In certain embodiments, a composition may contain an oligomeric compound targeted to a conserved HBV genomic region of the transcripts or open reading frames from genes X, S, and C.

[0262] In certain embodiments, a composition may contain an oligomeric compound targeted to a conserved HBV genomic region of the transcripts or open reading frames from genes X, S, C and P.

[0263] In some aspects, a composition of this invention includes a dyad of oligomeric compounds as the active agents targeted to HBV.

[0264] Examples of dyad compositions include a composition containing a compound with a reference position in

the range 1403 to 1623, and a compound with a reference position in the range 155 to 550.

[0265] Examples of dyad compositions include a composition containing a compound with a reference position in the range 1575 to 1581, and a compound with a reference position in the range 245 to 414.

[0266] Examples of dyad compositions include a composition containing a compound with a reference position in the range 1525 to 1604, and a compound with a reference position in the range 374 to 414.

[0267] Examples of dyad compositions include a composition containing a compound with a reference position in the range 1525 to 1604, and a compound with a reference position in the range 1776 to 1818.

[0268] Examples of dyad compositions include a composition containing a compound with a reference position in the range 374 to 414, and a compound with a reference position in the range 1776 to 1782.

[0269] Examples of dyad compositions include a composition containing a compound with the reference position 1578 and a compound with the reference position 380. Examples of dyad compositions include a composition containing a compound with the reference position 1578 and a compound with the reference position 376 or 411.

[0270] Examples of dyad compositions include compositions containing compounds with the reference positions 1575 and 376, 1575 and 380, 1575 and 511, 1581 and 376, 1581 and 380, as well as 1581 and 411.

[0271] Examples of dyad compositions include compositions containing a compound with the reference position 1578 and a compound with the reference position 1777.

[0272] Examples of dyad compositions include compositions containing compounds with the reference positions 1578 and 1780, or 1578 and 1782, or 1575 and 1777, or 1575 and 1780, or 1575 and 1782, or 1581 and 1777, or 1581 and 1780, or 1581 and 1782, or 1576 and 1777, or 1576 and 1780, or 1576 and 1782.

[0273] For example, a dyad composition may contain the compounds 1578 and 380 shown in Table 22.

TABLE 22

Dyad composition of UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID	S/ NO AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
1578	1208	S	UNA-U/*mGrUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU/*UNA-U/*dT	
1578	1209	AS	mArGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U/*dT	
380	1210	S	UNA-U/*mGrUmCrUmGrCmGrGrCrGmUrUmUrUmArUmCrA/*UNA-U/*mU	
380	1211	AS	mUrGmArUmArAmArAmCrGmCmCmGrCmArGmArCmA/UNA-U/*mU	

[0274] UNA Oligomer Triad Compositions for HBV

[0275] In some aspects, a composition of this invention includes triads of oligomeric compounds as the active agents targeted to HBV.

[0276] Examples of triad compositions include a composition containing a compound with a reference position in the range 1403 to 1623, a compound with a reference position in the range 155 to 550, and a compound with a reference position in the range 1624 to 1930.

[0277] Examples of triad compositions include a composition containing a compound with a reference position in the range 1525 to 1582, a compound with a reference position in the range 245 to 414, and a compound with a reference position in the range 1777 to 1818.

[0278] Examples of triad compositions include a composition containing a compound with a reference position in the range 1525 to 1604, a compound with a reference position in the range 374 to 414, and a compound with a reference position in the range 1776 to 1782.

[0279] Examples of triad compositions include a composition containing a compound with a reference position in the range 1525 to 1582, a compound with a reference position in the range 374 to 414, and a compound with a reference position in the range 1776 to 1782.

[0280] Examples of triad compositions include a composition containing a compound with the reference position 1578, a compound with the reference position 380, and a compound with the reference position 1777.

[0281] Examples of triad compositions include a composition containing a compound with the reference position 1576, a compound with the reference position 380, and a compound with the reference position 1777.

[0282] Examples of triad compositions include a composition containing a compound with the reference position

1575, a compound with the reference position 380, and a compound with the reference position 1777.

[0283] Examples of triad compositions include a composition containing a compound with the reference position 1578, a compound with the reference position 1777, and a compound with the reference position 376 or 411.

[0284] Examples of triad compositions include a composition containing a compound with the reference position 1578, a compound with the reference position 1780 or 1782, and a compound with the reference position 376 or 411.

[0285] Examples of triad compositions include compositions containing compounds with the reference positions: 1578, 1777 and 376; 1578, 1777 and 380; 1578, 1777 and 411; 1578, 1780 and 376; 1578, 1780 and 380; 1578, 1780 and 411; 1578, 1782 and 376; 1578, 1782 and 380; 1578, 1782 and 411;

1575, 1777 and 376; 1575, 1777 and 380; 1575, 1777 and 411; 1575, 1780 and 376; 1575, 1780 and 380; 1575, 1780 and 411; 1575, 1782 and 376; 1575, 1782 and 380; 1575, 1782 and 411;

1581, 1777 and 376; 1581, 1777 and 380; 1581, 1777 and 411; 1581, 1780 and 376; 1581, 1780 and 380; 1581, 1780 and 411; 1581, 1782 and 376; 1581, 1782 and 380; 1581, 1782 and 411;

1576, 1777 and 376; 1576, 1777 and 380; 1576, 1777 and 411; 1576, 1780 and 376; 1576, 1780 and 380; 1576, 1780 and 411; 1576, 1782 and 376; 1576, 1782 and 380; 1576, 1782 and 411;

1578, 1818 and 376; 1578, 1818 and 380; 1578, 1818 and 411;

1575, 1818 and 376; 1575, 1818 and 380; 1575, 1818 and 411.

[0286] For example, a triad composition may contain the compounds 1578, 380 and 1777 shown in Table 23.

TABLE 23

Triad composition of UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID	S/ NO AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
1578	1175	S	UNA-U/*mGrUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU/*UNA-U/*dT	
1578	1176	AS	mArGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U/*dT	
380	1177	S	UNA-U/*mGrUmCrUmGrCmGrGrCrGmUrUmUrUmArUmCrA/*UNA-U/*dT	
380	1178	AS	mUrGmArUmArAmArAmCrGmCmCmGrCmArGmArCmA/UNA-U/*dT	

TABLE 23-continued

Triad composition of UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID NO	S/ AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
1777	1179	S	UNA-G/*mArGmGrCmUrGmUrArGrGmCrAmUrAmArAmUrU/*UNA-U/*dT	
1777	1180	AS	mArAmUrUmUrAmUrGmCrCmUmAmCrAmGrCmCrUmC/UNA-U/*dT	

[0287] In Tables herein, rN refers to N, which is a ribonucleotide, mN refers to a chemically-modified 2'-OMe ribonucleotide, an * between characters refers to a phosphorothioate linkage, and dN refers to a deoxyribonucleotide.

[0288] This invent includes a compounds containing a UNA monomer at the 1-end (5' end for non-UNA) of the first strand, a UNA monomer at the 3-end or second position from the 3-end (3' end for non-UNA) of the sense strand, and a UNA monomer at the 3-end or second position from the 3-end (3' end for non-UNA) of the antisense strand.

[0289] Embodiments of this invention include a compound wherein the sense strand comprises SEQ ID NO:271 and the antisense strand comprises SEQ ID NO:583.

[0290] Embodiments of this invention include a compound wherein the sense strand comprises SEQ ID NO:266 and the antisense strand comprises SEQ ID NO:578.

[0291] Embodiments of this invention include a compound wherein the sense strand comprises SEQ ID NO:275 and the antisense strand comprises SEQ ID NO:587.

[0292] Embodiments of this invention include compounds wherein the first and second strands are a sense-antisense pair selected from any of Tables 33 to 38.

[0293] This invention includes compositions comprising a triad of compounds, wherein the triad is selected from the following: the first compound comprises SEQ ID NO:867 and 908, the second compound comprises SEQ ID NO:887 and 928, and the third compound comprises SEQ ID NO:879 and 920; the first compound comprises SEQ ID NO: 867 and 908, the second compound comprises SEQ ID NO:893 and 934, and the third compound comprises SEQ ID NO:875 and 916; the first compound comprises SEQ ID NO:900 and 941, the second compound comprises SEQ ID NO:887 and 928, and the third compound comprises SEQ ID NO:875 and 916.

[0294] siRNA Structures

[0295] In further aspects, this invention describes siRNA molecules comprising nucleotides, wherein the siRNA is targeted to HBV. The siRNA molecules are not composed of any UNA monomers.

[0296] A siRNA may have a first strand and a second strand, each of the strands being 19-29 nucleotides in length, wherein the siRNA has a duplex region of from 14 to 29 contiguous monomers in length, wherein the first strand is a sense strand for RNA interference and the second strand is an antisense strand for RNA interference, and wherein the compound comprises a sequence of bases targeted to inhibit expression of an HBV genome. Each of the strands may be 19-21 nucleotides in length.

[0297] A siRNA molecule of this invention may comprise SEQ ID NOs:900 and 941, and substituted forms thereof.

[0298] A siRNA molecule of this invention may comprise SEQ ID NO:893 and 934, and substituted forms thereof.

[0299] A siRNA molecule of this invention may comprise SEQ ID NO:879 and 920, and substituted forms thereof.

[0300] This invent further contemplates methods for preventing, ameliorating or treating a disease or condition associated with HBV infection in a subject in need, the method comprising administering to the subject an effective amount of a composition of a siRNA above. The administration of the siRNA, or a c composition thereof, can reduce HBV viral titer in the subject. The subject may have been diagnosed with a disease associated with Hepatitis B virus infection, or a liver disease.

[0301] Methods of this invention include inhibiting the replication, maturation, growth, or transmission of a Hepatitis B virus in a subject in need, by administering to the subject an effective amount of a siRNA above, or a composition thereof. The administration can reduce serum concentration of HBsAg in the subject by 2-log₁₀-fold for at least 7 days. The administration can reduce HBeAg in the subject, or reduce HBV DNA in the subject.

[0302] In some embodiments, this invention includes methods for inhibiting expression of a Hepatitis B virus polynucleotide in a subject in need, by administering to the subject a siRNA above, or a composition thereof.

[0303] HBV Sequences

[0304] Some examples of known sequences for HBV are shown in Table 24.

TABLE 24

Sequences for HBV		
ACC #	Genotype	Description
HE974383.1	A	HBV genotype A2 complete genome, isolate Mart-B74
HE974381.1	A	HBV genotype A1 complete genome, isolate Mart-B64
HE974376.1	A	HBV genotype A2 complete genome, isolate Mart-B45
HE974375.1	A	HBV genotype A1 complete genome, isolate Mart-B43
HE974374.1	A	HBV genotype A2 complete genome, isolate Mart-B42
HE974371.1	A	HBV genotype A2 complete genome, isolate Mart-B34
HE974370.1	A	HBV genotype A1 complete genome, isolate Mart-B27
HE974367.1	A	HBV genotype A2 complete genome, isolate Mart-B22
HE974365.1	A	HBV genotype A1 complete genome, isolate Mart-B16
HE974364.1	A	HBV genotype A2 complete genome, isolate Mart-B15

TABLE 24-continued

Sequences for HBV		
ACC #	Genotype	Description
HE974363.1	A	HBV genotype A1 complete genome, isolate Mart-B06
HE974362.1	A	HBV genotype A1 complete genome, isolate Mart-B01
AB778116.1	A	HBV genotype A gene for polymerase, complete cds, strain: OCU01
AB299858.1	adr	Hepatitis B virus subtype adr DNA, complete genome, clone: HBVVFH0204
AB176642.1	adr	Hepatitis B virus subtype ADR DNA, complete genome, isolate: HBV-115
HW390268.1	adw	JP 2013537423-A/508: RNA Interference Mediated Inhibition of Hepatitis B Virus (HBV)
AM282986.1	adw	Hepatitis B virus (SUBTYPE ADW2), genotype A, complete genome
D00331.1	adw	HPBADW3 Hepatitis B virus subtype ADW genomic DNA, complete genome, clone: pIDW420
D00330.1	adw	HPBADW2 Hepatitis B virus subtype ADW genomic DNA, complete genome, clone: pODW282
D00329.1	adw	HPBADW1 Hepatitis B virus subtype ADW genomic DNA, complete genome, clone: pJDW233
AB540582.1	B	HBV genotype B DNA, complete genome, strain: B0901189(NT15)
AB554017.1	B	HBV genotype B DNA, complete genome, isolate: NMB09010
AB602818.1	B	HBV genotype B DNA, complete genome, isolate: AH-2
AB644287.1	C	HBV genotype C DNA, complete genome, isolate: NAB52
AB644286.1	C	HBV genotype C DNA, complete genome, isolate: NAB47
AB644284.1	C	HBV genotype C DNA, complete genome, isolate: NAB32
AB644283.1	C	HBV genotype C DNA, complete genome, isolate: NAB28
AB644281.1	C	HBV genotype C DNA, complete genome, isolate: NAB9
AB644280.1	C	HBV genotype C DNA, complete genome, isolate: NAB1
AB560662.1	C	HBV genotype C DNA, complete genome, isolate: 60PU
AB560661.1	C	HBV genotype C DNA, complete genome, isolate: 58PU
AB554025.1	C	HBV genotype C DNA, complete genome, isolate: MRK89073
AB554022.1	C	HBV genotype C DNA, complete genome, isolate: GRS08325
AB554021.1	C	HBV genotype C DNA, complete genome, isolate: GRS08298
AB554020.1	C	HBV genotype C DNA, complete genome, isolate: NMB09124
AB554019.1	C	HBV genotype C DNA, complete genome, isolate: NMB09122
AB554018.1	C	HBV genotype C DNA, complete genome, isolate: NMB09075
AB554015.1	C	HBV genotype C DNA, complete genome, isolate: TRF08111
AB554014.1	C	HBV genotype C DNA, complete genome, isolate: TRF08029
AB540585.1	C	HBV genotype C DNA, complete genome, strain: C0901192(NT18)
AB540584.1	C	HBV genotype C DNA, complete genome, strain: C0901190(NT16)
AB540583.1	C	HBV genotype C DNA, complete genome, strain: C0901177(NT3)
HE974382.1	D	HBV genotype D4 complete genome, isolate Mart-B70
HE974379.1	D	HBV genotype D3 complete genome, isolate Mart-B58
HE974378.1	D	HBV genotype D4 complete genome, isolate Mart-B50
HE974377.1	D	HBV genotype D3 complete genome, isolate Mart-B47
HE974373.1	D	HBV genotype D4 complete genome, isolate Mart-B37
HE974372.1	D	HBV genotype D4 complete genome, isolate Mart-B36
HE815465.1	D	HBV genotype D, serotype ayw3, complete genome
AB554024.1	D	HBV genotype D DNA, complete genome, isolate: GRS08538
AB554023.1	D	HBV genotype D DNA, complete genome, isolate: GRS08457
AB554016.1	D	HBV genotype D DNA, complete genome, isolate: TRF08226
AB267090.1	D	Hepatitis B virus ayw/Japan/Ehime 22-HS/2005 DNA, complete genome
HE974384.1	E	HBV genotype E complete genome, isolate Mart-B84
HE974380.1	E	HBV genotype E complete genome, isolate Mart-B63
AP007262.1	E	HBV genotype E DNA, complete genome, isolate: HB-JI411F
HE974369.1	F	HBV genotype F2 complete genome, isolate Mart-B26
HE974368.1	F	HBV genotype F4 complete genome, isolate Mart-B24
HE974366.1	F	HBV genotype F2 complete genome, isolate Mart-B18
AB625343.1	G	HBV genotype G DNA, complete genome, isolate: MEX921M
AB625342.1	G	HBV genotype G DNA, complete genome, isolate: MEX918M
AP007264.1	G	HBV genotype G DNA, complete genome, isolate: HB-JI444GF
AB846650.1	H	HBV genotype H DNA, complete genome, isolate: B-MHJ9014
AB516395.1	H	HBV genotype H DNA, complete genome, isolate: MEX914M
AB516394.1	H	HBV genotype H DNA, complete genome, isolate: MEX912M
AB516393.1	H	HBV genotype H DNA, complete genome, isolate: 904MEXM
AP007261.1	H	HBV genotype H DNA, complete genome, isolate: HB-JI260F
AB298362.1	H	HBV genotype H DNA, complete genome, isolate: HBV ST0404
AB246338.1	Ae	Hepatitis B virus DNA, complete genome, clone: Ae_JPN
AB246341.1	Bj	Hepatitis B virus DNA, complete genome, clone: Bj_JPN35
AB246345.1	C	Hepatitis B virus DNA, complete genome, clone: C_JPNAT
AB246347.1	D	Hepatitis B virus DNA, complete genome, clone: D_IND60

[0305] Methods for Treating HBV Disease

[0306] Methods of this invention include the treatment and prevention of various diseases in mammalian subjects. A subject can be a human or mammal.

[0307] In the methods of this invention, a subject in need of treatment or prevention can be administered an effective amount of an oligomeric compound of this invention.

[0308] An effective amount of an oligomeric compound of this invention can be a dose ranging from 0.001 mg/kg to 50.0 mg/kg.

[0309] In the methods of this invention, target mRNA expression can be reduced in a subject for at least 5 days. In certain embodiments, target mRNA expression can be reduced in a subject for at least 10 days, or 15 days.

[0310] In the methods of this disclosure, the administration of an oligomeric compound may not result in an inflammatory response.

[0311] In further embodiments, this invention includes methods for inhibiting expression of a target gene in a cell, by treating the cell with an oligomeric compound of this invention.

[0312] In additional embodiments, this invention includes methods for inhibiting expression of a target gene in a mammal, by administering to the mammal a composition containing an oligomeric compound of this invention.

[0313] Pharmaceutical Compositions

[0314] In some aspects, this invention provides pharmaceutical compositions containing an oligomeric compound and a pharmaceutically acceptable carrier.

[0315] A pharmaceutical composition can be capable of local or systemic administration. In some aspects, a pharmaceutical composition can be capable of any modality of administration. In certain aspects, the administration can be intravenous, subcutaneous, pulmonary, intramuscular, intraperitoneal, dermal, oral, or nasal administration.

[0316] Embodiments of this invention include pharmaceutical compositions containing an oligomeric compound in a lipid formulation.

[0317] In some embodiments, a pharmaceutical composition may comprise one or more lipids selected from cationic lipids, anionic lipids, sterols, pegylated lipids, and any combination of the foregoing.

[0318] In certain embodiments, a pharmaceutical composition can be substantially free of liposomes.

[0319] In further embodiments, a pharmaceutical composition can include liposomes or nanoparticles.

[0320] Some examples of lipids and lipid compositions for delivery of an active molecule of this invention are given in WO/2015/074085, which is hereby incorporated by reference in its entirety.

[0321] In additional embodiments, a pharmaceutical composition can contain an oligomeric compound within a viral or bacterial vector.

[0322] A pharmaceutical composition of this disclosure may include carriers, diluents or excipients as are known in the art. Examples of pharmaceutical compositions are described, for example, in *Remington's Pharmaceutical Sciences*, Mack Publishing Co. (A. R. Gennaro ed. 1985).

[0323] Examples of excipients for a pharmaceutical composition include antioxidants, suspending agents, dispersing agents, preservatives, buffering agents, tonicity agents, and surfactants.

EXAMPLES

Example 1: Luciferase Reporter Assay

[0324] Luciferase-based reporter plasmid was constructed based on psiCHECKTM2 vector (Promega, Madison, Wis.). Reporter p(1-20) was generated with oligonucleotides containing the sequence from position 1 through 2500 relative to Eco RI digestion site cloned into the multiple cloning region downstream of the stop codon of the SV40 promoted *Renilla* luciferase gene in psiCHECKTM2, which made the expression of *Renilla* luciferase gene under the regulation of the artificial 3'UTR sequence. *Renilla* luciferase activity was then used as an indicator of the effect of the artificial 3'UTR on transcript stability and translation efficiency. The psiCHECKTM-2 Vector also contained a constitutively expressed *Firefly* luciferase gene, which served as an internal control to normalize transfection efficiency.

[0325] A total of 5,000 HepB3 cells (American Type Culture Collection) were plated onto a well of 96-well plate one day before the transfection. The cells were incubated at 37° C. in 100 µl of DMEM (Life Technologies, Carlsbad, Calif.) supplemented with 0.1 mM nonessential amino acids and 10% FBS (Life Technologies, Carlsbad, Calif.). The culture medium was changed to 90 µl of fresh medium just before the transfection. The reporter plasmid and UNA Oligomer were co-transfected with transfection reagent, LipofectamineTM 3000 (Life Technologies, Carlsbad, Calif.) was used to transfect reporter plasmid (100 ng) and a various amount of UNA Oligomer together with P3000 into the cells according to manufacturer's instruction.

[0326] Dual-Luciferase Reporter Assay System (DLR assay system, Promega, Madison, Wis.) was used to perform dual-reporter assays on psiCHECK2 based reporter systems. Twenty-four hours after transfection, the cells were washed gently with phosphate buffered saline once. A 50 µl well of Passive Lysis Buffer (Promega, Madison, Wis.) was added to the cells and incubated with gentle rocking for 20 min at room temperature. Luciferase activities were measured using Cytation 3 imaging reader (BioTek, Winooski, Vt.) and the effect of the UNA Oligomer on reporter expression was calculated based on ratio of *Renilla*/*Firefly* to normalize cell number and transfection efficiency.

Example 2

[0327] The HBV inhibitory effect of UNA oligomers was observed with a psiCHECK2 assay. At 1 nM concentration for 6 days, the percent inhibition of target expression for each of the UNA oligomeric compounds in Table 19 designated as having Reference Position 1578 was determined to be from 77% to 97%. Thus, all of the UNA oligomeric compounds in Table 19 having Reference Position 1578 were operable for silencing target expression.

Example 3

[0328] The HBV inhibitory effect of UNA oligomers was observed with a psiCHECK2 assay. At 1 nM concentration for 6 days, the percent inhibition of target expression for each of the UNA oligomeric compounds in Table 19 designated as having Reference Position 1777 was determined to be from 77% to 92%. Thus, all of the UNA oligomeric compounds in Table 19 having Reference Position 1777 were operable for silencing target expression.

Example 4

[0329] The HBV inhibitory effect of UNA oligomers was observed with a psiCHECK2 assay. At 1 nM concentration for 6 days, the percent inhibition of target expression for each of the UNA oligomeric compounds in Table 19 designated as having Reference Position 380 was determined to be from 87% to 94%. Thus, all of the UNA oligomeric compounds in Table 19 having Reference Position 380 were operable for silencing target expression.

Example 5

[0330] The HBV inhibitory effect of UNA oligomers was observed with a psiCHECK2 assay. At 1 nM concentration for 6 days, the percent inhibition of target expression for the UNA oligomeric compound in Table 19 designated as having Reference Position 1576 was determined to be 93%. Thus, UNA oligomeric compounds having Reference Position 1576 were operable for modulating target expression.

Example 6

[0331] The HBV inhibitory effect of UNA oligomers was observed with a psiCHECK2 assay. At 1 nM concentration for 6 days, the percent inhibition of target expression for the UNA oligomeric compound in Table 19 designated as having Reference Position 1575 was determined to be 90%. Thus, UNA oligomeric compounds having Reference Position 1575 were operable for modulating target expression.

Example 7

[0332] The HBV inhibitory effect of UNA oligomers was observed with a psiCHECK2 assay. At 1 nM concentration for 6 days, the percent inhibition of target expression for the UNA oligomeric compound in Table 19 designated as having Reference Position 1580 was determined to be 95%. Thus, UNA oligomeric compounds having Reference Position 1580 were operable for modulating target expression.

Example 8

[0333] The HBV inhibitory effect of UNA oligomers was observed with a psiCHECK2 assay. UNA oligomers of this invention in Table 17 were found to exhibit IC50 for inhibiting target expression as shown in Table 25.

TABLE 25

IC50 of UNA oligomers targeted to HBV	
Reference Position	IC50 pM (6 days)
244	917
245	328
246	816
248	148
251	554
252	374
253	703
254	44
256	8
376	16
378	114
380	6.7
409	328
411	58
412	298
413	123

TABLE 25-continued

IC50 of UNA oligomers targeted to HBV	
Reference Position	IC50 pM (6 days)
414	363
1575	65
1576	137
1577	472
1578	63
1580	255
1581	22
1776	461
1777	26
1779	348
1780	151
1781	227
1782	177
1818	49

[0334] Thus, UNA oligomeric compounds of this invention were operable for modulating HBV target expression. The UNA oligomeric compounds of this invention exhibited picomolar activity in vitro for inhibiting target expression. In some embodiments, the UNA oligomeric compounds of this invention exhibited surprisingly high activity in vitro of about IC50<200 pM for inhibiting target expression.

Example 9

[0335] The HBV inhibitory effect in vivo for UNA oligomers was observed in a humanized PXB Mouse model of HBV infection. The UNA oligomers of this invention exhibited profound reduction of HBV serum infection parameters in vivo. In this study, the UNA oligomers were contained in lipid nanoparticle formulations, -1 and -2.

[0336] The UNA oligomers were formulated or co-formulated in lipid nanoparticles and injected intravenously into HBV-infected Phoenix Bio (PXB) mice. The mice were Genotype: cDNA-uPA^{wild/+}/SCID [cDNA-uPA^{wild/+}; B6;129SvEv-Plau, SCID: C.B-17/lcr-scld/scld Jcl] containing human hepatocytes with an estimated replacement index of 70% or more.

[0337] The study used an ascending dose in which mice were treated with 3 mg/kg on day 0, then 5 mg/kg on day 4, then 10 mg/kg on day 8.

[0338] As shown in FIG. 2, treatment with both UNA oligomer 1576 and UNA oligomer triad (1576, 380, 177) caused a rapid and sustained reduction in viral endpoint serum HBsAg compared to PBS control group. (Mean±SEM).

[0339] As shown in Table 26, treatment with both UNA oligomer 1576 and UNA oligomer triad (1576, 380, 177) caused a sustained reduction in viral endpoint serum HBeAg compared to PBS control group. (Mean±SEM).

TABLE 26

Serum HBeAg viral endpoint	
UNA oligomer formulation	HBeAg (% control) (normalized to hAlb) Day 12
PBS control	100
1576-1	48.2
1576-2	59.8

TABLE 26-continued

Serum HBeAg viral endpoint	
UNA oligomer formulation	HBeAg (% control) (normalized to hAlb) Day 12
(1576, 380, 177)-1	10.5
(1576, 380, 177)-2	15.0

[0340] As shown in Table 27, treatment with both UNA oligomer 1576 and UNA oligomer triad (1576, 380, 177) caused a sustained reduction in viral endpoint serum HBV DNA compared to PBS control group. (Mean±SEM).

TABLE 27

Serum HBV DNA viral endpoint	
UNA oligomer formulation	HBV DNA (% control) (normalized to hAlb) Day 12
PBS control	100
1576-1	31.2
1576-2	52.4
(1576, 380, 177)-1	4.1
(1576, 380, 177)-2	7.7

[0341] The compositions in FIG. 2 and Tables 26 and 27 were UNA oligomer triad composition (1777 (SEQ ID NO:1005 and 1006), 380 (SEQ ID NO:973 and 974), 1576 (SEQ ID NO:989 and 990)).

[0342] Thus, the UNA oligomers of this invention demonstrated significant and unexpectedly advantageous HBV inhibition efficacy in vivo. For all viral endpoints, HBsAg, HBeAg, and HBV DNA, the treatment with UNA oligomer triad composition (1576, 380, 177) was significantly superior to UNA oligomer 1576.

Example 10

[0343] The HBV inhibitory effect in vivo for UNA oligomers was observed in a PXB Mouse model of HBV infection. The UNA oligomers of this invention exhibited profound reduction of HBV serum infection parameters in vivo. In this study, the UNA oligomers were contained in lipid nanoparticle formulation.

[0344] The UNA oligomers were co-formulated in lipid nanoparticles and injected intravenously into HBV-infected Phoenix Bio (PXB) mice. The mice were Genotype: cDNA-uPA^{wild/+}/SCID [cDNA-uPA^{wild/+}; B6;129SvEv-Plau, SCID: C.B-17/lcr-scld/scld Jcl] containing human hepatocytes with an estimated replacement index of 70% or more.

[0345] The study used an ascending dose in which mice were administered every 4 days, up to day 40, and viral endpoints were monitored every 4 days through day 44.

[0346] As shown in FIG. 3, treatment with UNA oligomer triad (1576, 380, 1777) caused a rapid and sustained reduction in viral endpoint serum HBsAg compared to PBS control group. (Mean±SEM). The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition. The composition in FIG. 3 was UNA oligomer triad composition (1777 (SEQ ID NO:1005 and 1006), 380 (SEQ ID NO:973 and 974), 1576 (SEQ ID NO:989 and 990)).

[0347] As shown in FIG. 4, treatment with UNA oligomer triad (1576, 380, 1777) caused a rapid and sustained reduction in viral endpoint serum HBeAg compared to PBS control group. (Mean±SEM). The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition. The composition in FIG. 4 was UNA oligomer triad composition (1777 (SEQ ID NO:1005 and 1006), 380 (SEQ ID NO:973 and 974), 1576 (SEQ ID NO:989 and 990)).

[0348] As shown in FIG. 5, treatment with UNA oligomer triad (1576, 380, 1777) caused a rapid and sustained reduction in viral endpoint serum HBV DNA compared to PBS control group. (Mean±SEM). The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition. The composition in FIG. 5 was UNA oligomer triad composition (1777 (SEQ ID NO:1005 and 1006), 380 (SEQ ID NO:973 and 974), 1576 (SEQ ID NO:989 and 990)).

[0349] Thus, the UNA oligomers of this invention demonstrated significant and unexpectedly advantageous HBV inhibition efficacy in vivo.

Example 11

[0350] The HBV inhibitory effect in vivo for UNA oligomers was observed in a PXB Mouse model of HBV infection. The UNA oligomers of this invention exhibited profound reduction of HBV serum infection parameters in vivo. In this study, the UNA oligomers were contained in lipid nanoparticle formulation.

[0351] The UNA oligomers were formulated or co-formulated in lipid nanoparticles and injected intravenously into HBV-infected Phoenix Bio (PXB) mice. The mice were Genotype: cDNA-uPA^{wild/+}/SCID [cDNA-uPA^{wild/+}; B6;129SvEv-Plau, SCID: C.B-17/lcr-scld/scld Jcl] containing human hepatocytes with an estimated replacement index of 70% or more.

[0352] Serum viral endpoints were monitored up to 15 days after the single injection.

[0353] As shown in FIG. 6, treatment with each of UNA oligomers 1777 (SEQ ID NO:1179 and 1180), 380 (SEQ ID NO:1173 and 1174) and 1578 (SEQ ID NO:1175 and 1176) caused a rapid and sustained reduction in viral endpoint serum HBsAg compared to PBS control group. (Mean±SEM).

[0354] As shown in FIG. 7, treatment with each of UNA oligomers 1777 (SEQ ID NO:1179 and 1180), 380 (SEQ ID NO:1173 and 1174) and 1578 (SEQ ID NO:1175 and 1176) caused a rapid and sustained reduction in viral endpoint serum HBeAg compared to PBS control group. (Mean±SEM).

[0355] As shown in FIG. 8, treatment with each of UNA oligomers 1777 (SEQ ID NO:1179 and 1180), 380 (SEQ ID NO:1173 and 1174) and 1578 (SEQ ID NO:1175 and 1176) caused a rapid and sustained reduction in viral endpoint serum HBV DNA compared to PBS control group. (Mean±SEM).

[0356] As shown in FIG. 9, treatment with UNA oligomer triad composition (1777 (SEQ ID NO:1179 and 1180), 380 (SEQ ID NO:1173 and 1174), 1578 (SEQ ID NO:1175 and 1176)) caused a rapid and sustained reduction in viral endpoint serum HBsAg compared to PBS control group. (Mean±SEM). The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition.

[0357] As shown in FIG. 10, treatment with UNA oligomer triad composition (1777 (SEQ ID NO:1179 and 1180), 380 (SEQ ID NO:1173 and 1174), 1578 (SEQ ID NO:1175 and 1176)) caused a rapid and sustained reduction in viral endpoint serum HBeAg compared to PBS control group. (Mean±SEM). The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition.

[0358] As shown in FIG. 11, treatment with UNA oligomer triad composition (1777 (SEQ ID NO:1179 and 1180), 380 (SEQ ID NO:1173 and 1174), 1578 (SEQ ID NO:1175 and 1176)) caused a rapid and sustained reduction in viral endpoint serum HBV DNA compared to PBS control group. (Mean±SEM). The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition.

[0359] Thus, the UNA oligomers of this invention demonstrated significant and unexpectedly advantageous HBV inhibition efficacy in vivo.

Example 12

[0360] The HBV inhibitory effect in vivo for UNA oligomers was observed in an AAV-HBV mouse model of HBV infection. The UNA oligomers of this invention exhibited profound reduction of HBV serum infection parameters in vivo. In general, the AAV-HBV mouse model is a robust model for investigating HBV infection, and can provide direct clinical pertinence for drug efficacy and potency. In this study, the UNA oligomers were contained in lipid nanoparticle formulation.

[0361] The UNA oligomers were formulated or co-formulated in lipid nanoparticles and injected intravenously into C57Bl/6 mice with active HBV replication after AAV-mediated delivery of a recombinant HBV genome to the liver.

[0362] The study was an ascending dose design in which mice were treated with 3 mg/kg on day 0, then 5 mg/kg on day 4, then 10 mg/kg on day 8.

[0363] Serum viral endpoints were monitored 15 days before, and at least 22 days after treatment.

[0364] As shown in FIG. 12, treatment with each of UNA oligomers 380 (SEQ ID NO:973 and 974), 1777 (SEQ ID NO:1005 and 1006), and 1576 (SEQ ID NO:1003 and 1004) caused a rapid and sustained reduction in viral endpoint serum HBsAg compared to PBS control group. (Mean±SEM).

[0365] As shown in FIG. 13, treatment with each of UNA oligomers 380 (SEQ ID NO:973 and 974), 1777 (SEQ ID NO:1005 and 1006), and 1576 (SEQ ID NO:1003 and 1004), as well as the UNA oligomer triad composition of the same compounds (1576, 380, 1777) caused a rapid and sustained reduction in viral endpoint serum HBeAg compared to PBS control group. (Mean±SEM). This head-to-head comparison shows that the triad composition provided surprisingly increased potency throughout the duration of the effect, relative to the individual oligomers.

[0366] As shown in FIG. 14, treatment with each of UNA oligomers 380 (SEQ ID NO:973 and 974), 1777 (SEQ ID NO:1005 and 1006), and 1576 (SEQ ID NO:1003 and 1004) caused a rapid and sustained reduction in viral endpoint serum HBV DNA compared to PBS control group. (Mean±SEM).

[0367] Thus, the UNA oligomers of this invention demonstrated significant and unexpectedly advantageous HBV inhibition efficacy in vivo.

Example 13

[0368] The HBV inhibitory effect in vivo for UNA oligomers was observed in an AAV-HBV mouse model of HBV infection. The UNA oligomers of this invention exhibited profound reduction of HBV serum infection parameters in vivo. In this study, the UNA oligomers were contained in lipid nanoparticle formulation.

[0369] The UNA oligomers were co-formulated in lipid nanoparticles and injected intravenously into C57Bl/6 mice with active HBV replication after AAV-mediated delivery of a recombinant HBV genome to the liver.

[0370] The study was an ascending dose design in which mice were treated with 3 mg/kg on day 0, then 5 mg/kg on day 4, then 10 mg/kg on day 8.

[0371] Serum viral endpoints were monitored up to day 12 after treatment.

[0372] As shown in FIG. 15, treatment with the UNA oligomer triad composition (1777 (SEQ ID NO:1179 and 1180), 380 (SEQ ID NO:1173 and 1174), 1578 (SEQ ID NO:1175 and 1176)) caused a rapid and sustained reduction in viral endpoint serum HBsAg compared to PBS control group. (Mean±SEM). The dose-dependent response in vivo shows a pharmacological effect of the UNA oligomer composition.

[0373] Thus, the UNA oligomers of this invention demonstrated significant and unexpectedly advantageous HBV inhibition efficacy in vivo.

Example 14

[0374] The HBV inhibitory effect in vivo for UNA oligomers was observed in an AAV-HBV mouse model of HBV infection. The UNA oligomers of this invention exhibited profound reduction of HBV serum infection parameters in vivo. In general, the AAV-HBV mouse model is a robust model for investigating HBV infection, and can provide direct clinical pertinence for drug efficacy and potency. In this study, the UNA oligomers were contained in lipid nanoparticle formulation.

[0375] The UNA oligomers were formulated or co-formulated in lipid nanoparticles and injected intravenously into C57Bl/6 mice with active HBV replication after AAV-mediated delivery of a recombinant HBV genome to the liver.

[0376] The study was an ascending dose design in which mice were treated with 3 mg/kg on day 0, then 5 mg/kg on day 4, then 10 mg/kg on day 8.

[0377] Serum viral endpoints were monitored 15 days before, and at least 22 days after treatment.

[0378] As shown in FIG. 16, treatment with each of UNA oligomers 1578 (SEQ ID NO:993 and 994) and 1575 (SEQ ID NO:988 and 989) caused a rapid and sustained reduction in viral endpoint serum HBsAg compared to PBS control group. (Mean±SEM).

[0379] As shown in FIG. 17, treatment with each of UNA oligomers 1578 (SEQ ID NO:993 and 994) and 1575 (SEQ ID NO:988 and 989) caused a rapid and sustained reduction in viral endpoint serum HBeAg compared to PBS control group. (Mean±SEM).

[0380] As shown in FIG. 18, treatment with each of UNA oligomers 1578 (SEQ ID NO:993 and 994) and 1575 (SEQ ID NO:988 and 989) caused a rapid and sustained reduction in viral endpoint serum HBV DNA compared to PBS control group. (Mean $\pm$ SEM).

[0381] Thus, the UNA oligomers of this invention demonstrated significant and unexpectedly advantageous HBV inhibition efficacy in vivo.

Example 15

[0382] The HBV inhibitory effect of UNA oligomers was observed with a psiCHECK2 assay. The percent inhibition of target expression for UNA oligomeric compounds containing one or more 2'-deoxy-2'-fluoro ribonucleotides was measured.

[0383] As shown in Table 28, UNA oligomeric compounds exhibited at least 87% inhibition of target expression at 10 nM.

TABLE 28

Activity of UNA oligomer	
UNA oligomer	Relative RLuc/FLuc at 0.1 nM, 1 nM, 10 nM
1578 (SEQ ID NO: 1127 and 1128)	0.65, 0.18, 0.08
1777 (SEQ ID NO: 1135 and 1136)	0.56, 0.14, 0.13
380 (SEQ ID NO: 1143 and 1144)	0.40, 0.14, 0.13

[0384] Thus, the UNA oligomers of this invention demonstrated advantageous HBV inhibition efficacy in vitro.

Example 16

[0385] The HBV inhibitory effect in vivo for UNA oligomers was observed in a PXB Mouse model of HBV infection. The UNA oligomers of this invention exhibited profound reduction of HBV serum infection parameters in vivo. In this study, the UNA oligomers were contained in lipid nanoparticle formulation.

[0386] The UNA oligomers were formulated or co-formulated in lipid nanoparticles and injected intravenously into HBV-infected Phoenix Bio (PXB) mice. The mice were Genotype: cDNA-uPA^{wild/+}/SCID [cDNA-uPA^{wild/+}; B6;129SvEv-Plau, SCID: C.B-17/Icr-scld/scld Jcl] containing human hepatocytes with an estimated replacement index of 70% or more.

[0387] As shown in Table 29, treatment with both UNA oligomers caused a rapid and sustained reduction in viral endpoint serum HBsAg compared to a PBS control group.

TABLE 29

HBsAg (% control) (normalized to hAlb)				
UNA oligomer Ref. Pos.	% Inhibition Day 5 3.3 nM	% Inhibition Day 10 3.3 nM	% Inhibition Day 15 3.3 nM	% Inhibition Day 20 3.3 nM
1580 (SEQ ID NO: 997 and 998)	72.0	71.0	59.0	49.0
1578 (SEQ ID NO: 993 and 994)	70.0	59.0	39.0	25.3
1575 (SEQ ID NO: 987 and 988)	75.0	58.0	39.0	22.2

TABLE 29-continued

HBsAg (% control) (normalized to hAlb)				
UNA oligomer Ref. Pos.	% Inhibition Day 5 3.3 nM	% Inhibition Day 10 3.3 nM	% Inhibition Day 15 3.3 nM	% Inhibition Day 20 3.3 nM
1818 (SEQ ID NO: 1015 and 1016)	55.0	56.0	56.0	17.7
380 (SEQ ID NO: 973 and 974)	62.0	55.0	33.0	30.5
1576 (SEQ ID NO: 989 and 990)	42.0	48.0	44.0	38.2
1777 (SEQ ID NO: 1005 and 1006)	65.0	43.0	21.0	12.7
1782 (SEQ ID NO: 1013 and 1014)	65.0	43.0	25.0	20.4
1581 (SEQ ID NO: 999 and 1000)	50.0	42.0	28.0	11.7

[0388] Thus, the UNA oligomers of this invention demonstrated significant and unexpectedly advantageous HBV inhibition efficacy in vivo.

Example 17

[0389] The HBV inhibitory effect in vivo for UNA oligomers was observed in a PXB Mouse model of HBV infection. The UNA oligomers of this invention exhibited profound reduction of HBV serum infection parameters in vivo. In this study, the UNA oligomers were contained in lipid nanoparticle formulation.

[0390] The UNA oligomers were formulated or co-formulated in lipid nanoparticles and injected intravenously into HBV-infected Phoenix Bio (PXB) mice. The mice were Genotype: cDNA-uPA^{wild/+}/SCID [cDNA-uPA^{wild/+}; B6;129SvEv-Plau, SCID: C.B-17/Icr-scld/scld Jcl] containing human hepatocytes with an estimated replacement index of 70% or more.

[0391] As shown in Table 30, treatment with a triad UNA oligomer composition caused a rapid and sustained reduction in viral endpoint serum HBsAg compared to a PBS control group.

TABLE 30

Serum HBsAg (% control) (normalized to hAlb)				
UNA oligomer composition Ref. Pos.	% Inhibition Day 5 3.3 nM	% Inhibition Day 10 3.3 nM	% Inhibition Day 15 3.3 nM	% Inhibition Day 20 3.3 nM
380/1777/1575	82.0	67.0	39.9	28.0
380/1777/1578	82.0	70.0	47.3	33.2
380/1777/1576	79.0	64.0	44.8	29.1

[0392] The compositions in Table 30 were:

UNA oligomer triad composition (1777 (SEQ ID NO:1005 and 1006), 380 (SEQ ID NO:973 and 974), 1575 (SEQ ID NO:987 and 988));

UNA oligomer triad composition (1777 (SEQ ID NO:1005 and 1006), 380 (SEQ ID NO:973 and 974), 1578 (SEQ ID NO:993 and 994)); and

UNA oligomer triad composition (1777 (SEQ ID NO:1005 and 1006), 380 (SEQ ID NO:973 and 974), 1576 (SEQ ID NO:989 and 990)).

[0393] Thus, the triad UNA oligomer compositions of this invention demonstrated significant and unexpectedly advantageous HBV inhibition efficacy in vivo.

Example 18

[0394] The HBV inhibitory effect in vivo for UNA oligomers was observed in a PXB Mouse model of HBV infection. The UNA oligomers of this invention exhibited profound reduction of HBV serum infection parameters in vivo. In this study, the UNA oligomers were contained in lipid nanoparticle formulation.

[0395] The UNA oligomers were formulated or co-formulated in lipid nanoparticles and injected intravenously into HBV-infected Phoenix Bio (PXB) mice. The mice were Genotype: cDNA-uPA^{wild/+}/SCID [cDNA-uPA^{wild/+}; B6;129SvEv-Plau, SCID: C.B-17/lcr-scld/scld Jcl] containing human hepatocytes with an estimated replacement index of 70% or more.

[0396] As shown in Table 31, treatment with a triad UNA oligomer composition caused a rapid and sustained reduction in viral endpoint serum HBsAg compared to a PBS control group, for Genotypes Ae, Bj, C, and D.

TABLE 31					
Serum HBsAg (% control) (normalized to hAlb)					
UNA oligomer composition (Ref. Pos.)	Genotype	% Inhibition Day 5 3 nM	% Inhibition Day 10 3 nM	% Inhibition Day 5 15 nM	% Inhibition Day 10 15 nM
380/1777/1578	Ae	79.2	71.0	87.5	79.0
380/1777/1578	Bj	75.4	62.2	85.0	79.0
380/1777/1578	C	—	68.8	—	82.8
380/1777/1578	D	80.7	68.9	88.5	81.4

[0397] The composition in Table 31 was UNA oligomer triad composition (1777 (SEQ ID NO:1005 and 1006), 380 (SEQ ID NO:973 and 974), 1578 (SEQ ID NO:993 and 994)).

[0398] Thus, the triad UNA oligomer compositions of this invention demonstrated significant and unexpectedly advantageous HBV inhibition efficacy in vivo over a range of genotypes.

Example 19

[0399] The HBV inhibitory effect in vivo for UNA oligomers was observed in a PXB Mouse model of HBV infection. The UNA oligomers of this invention exhibited profound reduction of HBV serum infection parameters in

vivo with phosphorothioate linkages present. In this study, the UNA oligomers were contained in lipid nanoparticle formulation.

[0400] The UNA oligomers were formulated or co-formulated in lipid nanoparticles and injected intravenously into HBV-infected Phoenix Bio (PXB) mice. The mice were Genotype: cDNA-uPA^{wild/+}/SCID [cDNA-uPA^{wild/+}; B6;129SvEv-Plau, SCID: C.B-17/lcr-scld/scld Jcl] containing human hepatocytes with an estimated replacement index of 70% or more.

[0401] As shown in Table 32, treatment with UNA oligomers caused a rapid and sustained reduction in viral endpoint serum HBsAg compared to a PBS control group.

TABLE 32				
HBsAg (% control) (normalized to hAlb)				
UNA oligomer Ref. Pos.	% Inhibition Day 5 3.3 nM	% Inhibition Day 10 3.3 nM	% Inhibition Day 15 3.3 nM	% Inhibition Day 20 3.3 nM
1575 (SEQ ID NO: 987 and 988)	76.2	60.4	25.0	3.0
1575PS (SEQ ID NO: 1117 and 1118)	79.0	77.5	58.5	35.7
1578 (SEQ ID NO: 993 and 994)	77.0	65.6	34.4	5.7
1578PS (SEQ ID NO: 1069 and 1070)	78.1	72.7	53.5	18.3
380 (SEQ ID NO: 973 and 974)	72.4	69.5	48.1	23.9
380PS (SEQ ID NO: 1107 and 1108)	68.1	69.9	52.4	35.2

[0402] Thus, the UNA oligomers of this invention with phosphorothioate linkages (PS) demonstrated significant and unexpectedly advantageous HBV inhibition efficacy in vivo with longer duration (Day 15 to Day 20). The phosphorothioate linkages were as follows: one phosphorothioate linkage between two monomers at the 5' end of the first strand, one phosphorothioate linkage between two monomers at the 3' end of the first strand, one phosphorothioate linkage between monomers at the second and third positions from the 3' end of the first strand, and one phosphorothioate linkage between two monomers at the 3' end of the second strand.

Example 20

[0403] HBV reference genome HB974376 (3221 bp).

SEQ ID NO: 1181

1 ttccactgcc ttccaccaag ctctgcagga tcccagagtc aggggtctgt attttcctgc

61 tgggtgctcc agttcaggaa cagtaaacc tgcctcgaat attgcctctc acatctcgtc

121 aatctccgcg aggactgggg accctgtgac gaacatggag aacatcacat caggattcct

181 aggacccctg ctctgtgttac aggcggggtt tttctgttg acaagaatcc tcacaatacc

241 gcagagtcta gactcgtggt ggacttctct caattttcta gggggatcac ccgtgtgtct

301 tggccaaaat tcgcagtcct caacctccaa tcactcacca acctcctgtc tccaatttg

361 tcctggttat cgctggatgt gtctgcggcg ttttatcata ttctctctca tctgtctgct

421 atgcctcact ttcttattgg ttcttctgga ttatcaaggt atgttgcccg tttgtcctct

481 aattccagga tcaacaacaa ccagtaggg accatgcaaa acctgcaaga ctctctctca

-continued

541 aggcaactct atgtttccct catgttgctg tacaaaacct acggatggaa attgcacctg
601 tattcccata ccatcgctct gggctttcgc aaaataccta tgggagtggg cctcagtcog
661 tttctcttgg ctcagtttac tagtgccatt tgttcagtgg ttcgtagggc tttccccac
721 tgtttggtct tcagctatat ggatgatgtg gtattggggg ccaagtctgt acagcatcgt
781 gagtcccttt ataccgctgt taccaatttt cttttgtctc tgggtataca tttaaacct
841 aacaaaacaa aaagatgggg ttattcccta aacttcattg gttacataat tggaagttgg
901 ggaactttgc cacaggatca tattgtacaa aagatcaaac actgttttag aaaacttct
961 gttaacaggc ctattgattg gaaagtatgt caaagaattg tgggtctttt gggctttgct
1021 gctccattta cacaatgttg atatcctgcc ttaatgcctt tgtatgcatg tatacaagct
1081 aaacaggctt tcactttctc gccaaacttac aaggcctttc taagtaaaca gtacatgaac
1141 ctttaccctg ttgctcggca acggcctggg ctgtgccaa tgtttgctga cgcaaccccc
1201 actggctggg gcttgggcat agggccatcag cgcattgcgt gaacctttgt ggctcctctg
1261 ccgatccata ctgcggaact cctagccgct tgttttgctc gcagccgggc tggagcaaag
1321 ctcatcgga ctgacaattc tgcgtctctc tcgcggaaat atacatcgtt tccatggctg
1381 ctaggctgta ctgccaaact gatccttcgc gggacgtcct ttgtttacgt cccgtcggcg
1441 ctgaatcccg cggacgacct ctctcggggc cgttgggac tctctcgtcc ccttctcgt
1501 ctgccgttcc agccgaccac ggggcgcacc tctctttacg cggctctccc gtctgtgcct
1561 tctcatctgc cggctcgtgt gcacttcgtc tcacctctgc acgttgcatg gagaccaccg
1621 tgaacgcca tcagatcctg cccaaggtct tacataagag gactcttgga ctcccagcaa
1681 tgtaacgac cgaccttgag gcctacttca aagactgtgt gtttaagac tgggaggagc
1741 tgggggagga gattaggtta aaggctttg tattaggagg ctgtaggcat aaattggtct
1801 gcgcaccagc accatgcaac tttttcacct ctgcctaact atctcttgta catgtcccac
1861 tgttcaagcc tccaagctgt gccttgggtg gctttggggc atggacattg acccttataa
1921 agaatttgga gctactgttg agttactctc gtttttgctt tctgacttct ttccttcgt
1981 cagagatctc ctacacccg cctcagctct gtatcgagaa gccttagaat ctctgagca
2041 ttgtcacct caccatactg cactcaggca agccattctc tgcgtggggg aattgatgac
2101 tctagctacc tgggtgggta ataatttgga agatccagca tccagggato tagtagtcaa
2161 ttatgttaat actaacatgg gtttaaagat caggcaacta ttgtggttct atatatcttg
2221 ccttactttt ggaagagaga ctgtacttga atatttggtc tctttcggag tgtggattcg
2281 cactcctcca gcctatagac caccaaatgc ccctatctta tcaacacttc cggaactac
2341 tgttggttaga cgacgggacc gaggcaggtc ccctagaaga agaactccct cgcctcgag
2401 acgcagatct caatcgccgc gtcgcagaag atctcaatct cgggaatctc aatgttagta
2461 ttccttgga ctaaatgtg ggaacttta cggggcttta ttcctctaca gtacatctc
2521 ttaactctga atggcaaaact ccttcctttc ctaagattca tttacaagag gacattatta
2581 atagggtgta acaatttggt ggcctctca ctgtaaatga aaagagaaga ttgaaattaa
2641 ttatgcctgc tagattctat cctactcaca ctaaatattt gcccttagac aaaggaatta
2701 aaccttatta tccagatcag gtagttaatc attacttcca aaccagacat tatttacata
2761 ctcttttgaa ggctggtatt ctatataaga gggaaccac acgtagcgca tcattttgtg
2821 ggtcaccata ttcttgggaa caagagctac agcatgggag gttggtcatc aaaacctcgc

-continued

2881 aaaggcatgg ggacgaatct ttctgttccc aacctcttgg gattctttcc cgatcatcag
 2941 ttggaccctg cattcgagc caactcaaac aatccagatt gggacttcaa ccccatcaag
 3001 gaccactggc cagcagccaa ccaggtagga gcgggagcat tcgggcccagg gctcaccct
 3061 ccacacggcg gtattctggg gtggagccct caggctcagg gcatattgac cacagtgtca
 3121 acaattcttc ctctgcctc caccaatcgg cagtcaggaa ggcagcctac tcccatctct
 3181 ccacctctaa gagacagtca tctcaggcc atgcagtgga a

Example 21

[0404] Additional compounds of this invention are shown in Table 33.

[0405] Additional compounds of this invention are shown in Table 33.

TABLE 33

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF	SEQ	S/	HBV (Sense (S)-Antisense (AS))	
POS	ID	NO	AS (5'-3')	
1577	1182	S	UNA-G/*mArGmGrCmUrGmUrArGrGmCrAmUrAmArAmUrU/*UNA-U/*dT	
1577	1183	AS	mArAmUrUmUrAmUrGmCrCmUmAmCrAmGrCmCrUmC/UNA-U/*dT	
1577	1184	S	UNA-G/*rArGrGmCmUrGmUrArGrGmCrAmUrArArAmUmU/*UNA-U/*dT	
1577	1185	AS	mArA/*mUrUmUrAmUrGmCrCmUmAmCrAmGrCmCrUmC/UNA-U/*dT	
1577	1186	S	UNA-G/*rArGrGmCmUrGmUrArGrGmCrAmUrArArAmUmU/*UNA-U/*dT	
1577	1187	AS	mArArUmUmUrArUrGmCrCmUrArCrAmGmCmCrUmC/UNA-U/*dT	
1577	1188	S	UNA-G/*rArGrGmCmUrGmUrArGrGmCrAmUrArArAmUmU/*UNA-U/*dT	
1577	1189	AS	mArAmUrUmU/*rAmU/*rGmCrCmU/*mAmC/*rAmGrCmCrUmC/UNA-U/*dT	
1577	1190	S	UNA-G/*rArGrGmCmUrGmUrArGrGmCrAmUrArArAmUmU/*UNA-U/*dT	
1577	1191	AS	mArAmUrUmUrAmUrGmCrCmUmAmCrAmGrCmCrUmA/UNA-U/*dT	
1577	1192	S	UNA-G/*rArGrGmCmUrGmUrArGrGmCrAmUrArArAmUmU/*UNA-U/*dT	
1577	1193	AS	mArAmUrUdUrAmUrGmCrCmUmAmCrAdGrCmCrUmC/UNA-U/*dT	
1577	1194	S	UNA-G/*rArGrGmCmUrGmUrArGrGmCrAmUrArArAmUmU/*UNA-U/*dT	
1577	1195	AS	rArAmUmUmUrAmUrGmCmUmAmCrArGmCmCmUmC/UNA-U/*dT	
1577	1196	S	UNA-G/*rArGrGfCfUrGfUrArGrGfCrAfUrArArAfUfU/*UNA-U/*dT	
1577	1197	AS	rArAfUrUfUrAfUrGfCfCfUrAfCrArGfCfCfUfC/UNA-U/*dT	
1577	1198	S	UNA-G/*fArGfGrCfUrGfUrArGrGfCrAfUrAfArAfUrU/*UNA-U/*dT	
1577	1199	AS	fArAfUrUfUrAfUrGfCfUfAfCrAfGrCfCrUfC/UNA-U/*dT	

[0406] Designations used in Table 33 include rN for RNA, mN for 2'-O-methyl, rN* for RNA-3'-phosphorothioate, dN for DNA, and fN for 2'-fluoro. Underline bold indicates mismatch.

Example 22

[0407] Additional compounds of this invention are shown in Table 34.

[0408] Additional compounds of this invention are shown in Table 34.

TABLE 34

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID NO	S/ AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
380	1200	S	UNA-U/*/ <u>mGrUmCrUmGrCmGrGrCrGmUrUmUrAmUmCrA</u> */UNA-U/*/ <u>dT</u>	
380	1201	AS	mUrGmArUmArAmArAmCrGmCmCmGrCmArGmArCmA/UNA-U/*/ <u>dT</u>	
380	1202	S	UNA-U/*/ <u>rGmUmCmUrGmCrGrGmCrGmUmUmUrAmUmCrA</u> */UNA-U/*/ <u>dT</u>	
380	1203	AS	mUrG/*/ <u>mArUmArAmArAmCrGmCmCmGrCmArGmArCmA</u> /UNA-U/*/ <u>dT</u>	
380	1204	S	UNA-U/*/ <u>rGmUmCmUrGmCrGrGmCrGmUmUmUrAmUmCrA</u> */UNA-U/*/ <u>dT</u>	
380	1205	AS	mUrGrAmUmArArArAmCrGmCrGrCmAmGmArCmA/UNA-U/*/ <u>dT</u>	
380	1206	S	UNA-U/*/ <u>rGmUmCmUrGmCrGrGmCrGmUmUmUrAmUmCrA</u> */UNA-U/*/ <u>dT</u>	
380	1207	AS	mU/*/ <u>rGmArU</u> */ <u>mArAmArAmCrGmCmCmGrC</u> */ <u>mArGmArC</u> */ <u>mA</u> /UNA-U/*/ <u>dT</u>	
380	1208	S	UNA-U/*/ <u>rGmUmCmUrGmCrGrGmCrGmUmUmUrAmUmCrA</u> */UNA-U/*/ <u>dT</u>	
380	1209	AS	mUrGmArUmArAmArAmCrGmCmCmGrCmArGmArCmC/UNA-U/*/ <u>dT</u>	
380	1210	S	UNA-U/*/ <u>rGmUmCmUrGmCrGrGmCrGmUmUmUrAmUmCrA</u> */UNA-U/*/ <u>dT</u>	
380	1211	AS	mUrGmArUdArAmArAmCrGmCmCmGrCdArGmArCmA/UNA-U/*/ <u>dT</u>	
380	1212	S	UNA-U/*/ <u>rGmUmCmUrGmCrGrGmCrGmUmUmUrAmUmCrA</u> */UNA-U/*/ <u>dT</u>	
380	1213	AS	mUrGrAmUrArArArAmCrGmCmCmCrArGrAmCrA/UNA-U/*/ <u>dT</u>	
380	1214	S	UNA-U/*/ <u>rGfUfCfUrGfCrGrGfCrGfUfUfUfUrAfUfCrA</u> */UNA-U/*/ <u>dT</u>	
380	1215	AS	fUrGrAfUrArArArAfCrGfCfCrGfCrArGrAfCrA/UNA-U/*/ <u>dT</u>	
380	1216	S	UNA-U/*/ <u>fGrUfCrUfGrCfGrGrGrGfUrUfUrUfArUfCrA</u> */UNA-U/*/ <u>dT</u>	
380	1217	AS	fUrGfArUfArAfArAfCrGfCfCfGrCfArGfArCfA/UNA-U/*/ <u>dT</u>	

[0409] Designations used in Table 34 include rN for RNA, mN for 2'-O-methyl, rN* for RNA-3'-phosphorothioate, dN for DNA, and fN for 2'-fluoro. Underline bold indicates mismatch.

Example 23

[0410] Additional compounds of this invention are shown in Table 35.

[0411] Additional compounds of this invention are shown in Table 35.

TABLE 35

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID NO	S/ AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
1575	1218	S	UNA-C/*/ <u>mCrGmUrGmUrGmCrArCrUmUrCmGrCmUrUmCrA</u> */UNA-U/*/ <u>dT</u>	
1575	1219	AS	mUrGmArAmGrCmGrAmArGmUmGmCrAmCrAmCrGmG/UNA-U/*/ <u>dT</u>	
1575	1220	S	UNA-C/*/ <u>mCrGmUrGmUrGmCrAmCmUrUrCmGmCmUmUmCrA</u> */UNA-U/*/ <u>dT</u>	

TABLE 35-continued

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID NO	S/ AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
1575	1221	AS	mUrG/* / mArAmGrCmGrAmArGmUmGmCrAmCrAmCrGmG/UNA-U/* /dT	
1575	1222	S	UNA-C/* / mCrGmUrGmUrGmCrAmCmUrUrCmGmCmUmUmCrA/* /UNA-U/* /dT	
1575	1223	AS	mUrGrAmAmGrCrGrAmArGmUrGrCrAmCmAmCrGmG/UNA-U/* /dT	
1575	1224	S	UNA-C/* / mCrGmUrGmUrGmCrAmCmUrUrCmGmCmUmUmCrA/* /UNA-U/* /dT	
1575	1225	AS	mU/* / rGmArAmGrCmGrAmArGmU/* / mGmC/* / rAmC/* / rAmCrGmG/UNA-U/* /dT	
1575	1226	S	UNA-C/* / mCrGmUrGmUrGmCrAmCmUrUrCmGmCmUmUmCrA/* /UNA-U/* /dT	
1575	1227	AS	mUrGmArAmGrCmGrAmArGmUmGmCrAmCrAmCrGmA/UNA-U/* /dT	
1575	1228	S	UNA-C/* / mCrGmUrGmUrGmCrAmCmUrUrCmGmCmUmUmCrA/* /UNA-U/* /dT	
1575	1229	AS	mUrGmArAdGrCmGrAmArGmUmGmCrAdCrAmCrGmG/UNA-U/* /dT	
1575	1230	S	UNA-C/* / mCrGmUrGmUrGmCrAmCmUrUrCmGmCmUmUmCrA/* /UNA-U/* /dT	
1575	1231	AS	mUrGrArArGmCrGrArArGmUrGmCrAmCrAmCrGrG/UNA-U/* /dT	
1575	1232	S	UNA-C/* / fCrGfUrGfUrGfCrAfCfUfUfCrGfCfUrUfCrA/* /UNA-U/* /dT	
1575	1233	AS	fUrGrArArGfCrGrArArGfUrGfCrAfCrAfCrGrG/UNA-U/* /dT	
1575	1234	S	UNA-C/* / fCrGfUrGfUrGfCrArCrUfUfCfGrCfUrUfCrA/* /UNA-U/* /dT	
1575	1235	AS	fUrGfArAfGrCfGrAfArGfUfGfCrAfCrAfCrGfG/UNA-U/* /dT	
1575	1236	S	UNA-U/* / mGrUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU/* /UNA-U/* /dT	
1575	1237	AS	mArGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U/* /dT	

[0412] Designations used in Table 35 include rN for RNA, mN for 2'-O-methyl, rN* for RNA-3'-phosphorothioate, dN for DNA, and fN for 2'-fluoro. Underline bold indicates mismatch.

Example 24

[0413] Additional compounds of this invention are shown in Table 36.
[0414] Additional compounds of this invention are shown in Table 36.

TABLE 36

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID NO	S/ AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
1578	1238	S	UNA-U/* / mGrUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU/* /UNA-U/* /dT	
1578	1239	AS	mArGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U/* /dT	
1578	1240	S	UNA-U/* / rGmUrGmCrAmCmUmUmCrGmCmUmUmCrAmCmCmU/* /UNA-U/* /dT	
1578	1241	AS	mArG/* / mGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U/* /dT	
1578	1242	S	UNA-U/* / rGmUrGmCrAmCmUmUmCrGmCmUmUmCrAmCmCmU/* /UNA-U/* /dT	
1578	1243	AS	mArGrGmUmGrArArGmCrGmArArGrUmGmArCmA/UNA-U/* /dT	
1578	1244	S	UNA-U/* / rGmUrGmCrAmCmUmUmCrGmCmUmUmCrAmCmCmU/* /UNA-U/* /dT	
1578	1245	AS	mArGmGrU/* / mGrAmArGmCrGmAmAmGrU/* / mGrC/* / mArC/* / mA/UNA-U/* /dT	
1578	1246	S	UNA-U/* / rGmUrGmCrAmCmUmUmCrGmCmUmUmCrAmCmCmU/* /UNA-U/* /dT	
1578	1247	AS	mArGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmC/UNA-U/* /dT	
1578	1248	S	UNA-U/* / rGmUrGmCrAmCmUmUmCrGmCmUmUmCrAmCmCmU/* /UNA-U/* /dT	

TABLE 36-continued

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID NO	S/ AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
1578	1249	AS	mArGmGrUdGrAmArGmCrGmAmAmGrUdGrCmArCmA/UNA-U/*dT	
1578	1250	S	UNA-U/*rGmUrGmCrAmCmUmUmCrGmCmUmUmCrAmCmCmU/*UNA-U/*dT	
1578	1251	AS	rArGrGmUrGrArArGmCrGrArArGmUrGmCrAmCrA/UNA-U/*dT	
1578	1252	S	UNA-U/*rGfUrGfCrAfCfUfUfCrGfCfUfUfCrAfCfCfU/*UNA-U/*dT	
1578	1253	AS	rArGrGfUrGrArArGfCrGrArArGfUrGfCrAfCrA/UNA-U/*dT	
1578	1254	S	UNA-U/*fGrUfGrCfArCfUrUrCrGfCrUfUrCfArCfCrU/*UNA-U/*dT	
1578	1255	AS	fArGfGrUfGrAfArGfCrGfAfAfGrUfGrCfArCfA/UNA-U/*dT	

[0415] Designations used in Table 36 include rN for RNA, mN for 2'-O-methyl, rN* for RNA-3'-phosphorothioate, dN for DNA, and fN for 2'-fluoro. Underline bold indicates mismatch.

Example 25

[0416] Additional compounds of this invention are shown in Table 37.

[0417] Additional compounds of this invention are shown in Table 37.

TABLE 37

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF POS	SEQ ID NO	S/ AS	HBV (Sense (S)-Antisense (AS)) (5'-3')	
1576	1256	S	UNA-C/*mGrUmGrUmGrCmArCrUrUmCrGmCrUmUrCmArC/*UNA-U/*dT	
1576	1257	AS	mGrUmGrAmArGmC/UNA-G/mArAmGmUmGrCmArCmArCmG/UNA-U/*dT	
1576	1258	S	UNA-C/*rGmUrGmUrGmCrAmCmUmUmCrGmCmUmUrCrAmC/*UNA-U/*dT	
1576	1259	AS	mGrU/*mGrAmArGmC/UNA-G/mArAmGmUmGrCmArCmArCmG/UNA-U/*dT	
1576	1260	S	UNA-C/*rGmUrGmUrGmCrAmCmUmUmCrGmCmUmUrCrAmC/*UNA-U/*dT	
1576	1261	AS	mGrU/*rGmAmArGrC/UNA-G/mArAmGrUrGrCmAmCmArCmG/UNA-U/*dT	
1576	1262	S	UNA-C/*rGmUrGmUrGmCrAmCmUmUmCrGmCmUmUrCrAmC/*UNA-U/*dT	
1576	1263	AS	mGrU/*mGrAmArGmC/UNA-G/mArAmGmU/*mGrC/*mArC/*mArCmG/UNA-U/*dT	
1576	1264	S	UNA-C/*rGmUrGmUrGmCrAmCmUmUmCrGmCmUmUrCrAmC/*UNA-U/*dT	
1576	1265	AS	mGrUmGrAmArGmC/UNA-G/mArAmGmUmGrCmArCmArCmA/UNA-U/*dT	
1576	1266	S	UNA-C/*rGmUrGmUrGmCrAmCmUmUmCrGmCmUmUrCrAmC/*UNA-U/*dT	
1576	1267	AS	mGrU/*rGmAdArGrC/UNA-G/mArAmGrUrGrCdAmCmArCmG/UNA-U/*dT	
1576	1268	S	UNA-C/*rGmUrGmUrGmCrAmCmUmUmCrGmCmUmUrCrAmC/*UNA-U/*dT	
1576	1269	AS	rGmUrGrArArGmC/UNA-G/rArArGmUrGmCrAmCrAmCrG/UNA-U/*dT	
1576	1270	S	UNA-C/*rGfUrGfUrGfCrAfCfUfUfCrGfCfUfUfCrAfC/*UNA-U/*dT	
1576	1271	AS	rGfUrGrArArGfC/UNA-G/rArArGfUrGfCrAfCrAfCrG/UNA-U/*dT	
1576	1272	S	UNA-C/*fGrUfGrUfGrCfArCrUrUfCrGfCrUfUrCfArC/*UNA-U/*dT	
1576	1273	AS	fGrUfGrAfArGfC/UNA-G/fArAfGfUfGrCfArCfArCfG/UNA-U/*dT	

[0418] Designations used in Table 37 include rN for RNA, mN for 2'-O-methyl, rN* for RNA-3'-phosphorothioate, dN for DNA, and fN for 2'-fluoro. Underline bold indicates mismatch.

Example 26

[0419] Additional compounds of this invention are shown in Table 38.

[0420] Additional compounds of this invention are shown in Table 38.

TABLE 38

UNA oligomers targeted to HBV (Sense (S)-Antisense (AS))				
REF	SEQ	S/	HBV (Sense (S)-Antisense (AS))	
POS	ID	NO	AS	(5'-3')
1578	1274	S	UNA-U/mGrUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU/UNA-U/mU	
1578	1275	AS	mArGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U/mU	
1578	1276	S	UNA-U/mGrUmGrCmArCmUrUrCrGmCrUmUrCmArCmCrU/UNA-U/mU	
1578	1277	AS	5Phos/mArGmGrUmGrAmArGmCrGmAmAmGrUmGrCmArCmA/UNA-U/mU	
1777	1278	S	UNA-G/mArGmGrCmUrGmUrArGrGmCrAmUrAmArAmUrU/UNA-U/mU	
1777	1279	AS	mArAmUrUmUrAmUrGmCrCmUmAmCrAmGrCmCrUmC/UNA-U/mU	
1777	1280	S	UNA-G/mArGmGrCmUrGmUrArGrGmCrAmUrAmArAmUrU/UNA-U/mU	
1777	1281	AS	5Phos/mArAmUrUmUrAmUrGmCrCmUmAmCrAmGrCmCrUmC/UNA-U/mU	
380	1282	S	UNA-U/mGrUmCrUmGrCmGrGrCmUrUmUrUmArUmCrA/UNA-U/mU	
380	1283	AS	mUrGmArUmArAmArAmCrGmCmCmGrCmArGmArCmA/UNA-U/mU	
380	1284	S	UNA-U/mGrUmCrUmGrCmGrGrCmUrUmUrUmArUmCrA/UNA-U/mU	
380	1285	AS	5Phos/mUrGmArUmArAmArAmCrGmCmCmGrCmArGmArCmA/UNA-U/mU	

[0421] Designations used in Table 38 include rN for RNA, mN for 2'-O-methyl, rN* for RNA-3'-phosphorothioate, and Phos for phosphoro.

[0422] All publications, patents and literature specifically mentioned herein are incorporated by reference for all purposes.

[0423] It is understood that this invention is not limited to the particular methodology, protocols, materials, and reagents described, as these may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention, which will be encompassed by the appended claims.

[0424] It must be noted that as used herein and in the appended claims, the singular forms “a”, “an”, and “the”

include plural reference unless the context clearly dictates otherwise. As well, the terms “a” (or “an”), “one or more” and “at least one” can be used interchangeably herein. It is also to be noted that the terms “comprises,” “comprising,” “containing,” “including”, and “having” can be used interchangeably.

[0425] Without further elaboration, it is believed that one skilled in the art can, based on the above description, utilize the present invention to its fullest extent. The following specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

[0426] All of the features disclosed in this specification may be combined in any combination. Each feature disclosed in this specification may be replaced by an alternative feature serving the same, equivalent, or similar purpose.

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<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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<400> SEQUENCE: 18

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nnnnnnnnnn nnnnnnnnnn nn 22

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based on a propane-1,2,3-tri-yl-trisoxy structure

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<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 33

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 34
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 34

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 35
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(22)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 35

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 36
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 36

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 37
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(22)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 37

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 38
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 38

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 39
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(22)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 39

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 40
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 40

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 41
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(22)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 41

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 42
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 42

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 43
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(22)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 43

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 44
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 44

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 45
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(22)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 45

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 46
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 46

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 47
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(22)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 47

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 48
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 48

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 49
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(22)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 49

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 50
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 50

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 51
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(22)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 51

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 52
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 52

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 53
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(22)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 53

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 54
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 54

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 55
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(22)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 55

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 56
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 56

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 57
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(22)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 57

nnnnnnnnnn nnnnnnnnnn nn 22

<210> SEQ ID NO 58
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 58

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 59
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 59

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 60
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 60

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 61
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 61

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 62
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 62

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 63
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 63

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 64
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 64

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 65
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 65

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 66
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 66

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 67
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 67

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 68
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 68

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 69
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 69

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 70
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 70

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 71
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 71

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 72
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 72

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 73
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 73

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 74
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 74

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 75
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 75

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 76
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 76

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 77
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 77

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 78
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 78

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 79
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 79

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 80
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 80

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 81
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 81

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 82
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 82

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 83
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 83

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 84
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 84

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 85
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 85

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 86
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 86

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 87
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 87

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 88
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 88

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 89
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 89

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 90
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 90

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 91
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 91

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 92
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 92

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 93
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or chemically-
modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 93

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 94
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 94

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 95
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 95

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 96
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 96

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 97
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 97

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 98
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 98

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 99
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 99

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 100
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 100

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 101
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or chemically- modified nucleotide; may or may not be modified based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 101

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 102
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or chemically- modified nucleotide; may or may not be modified based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 102

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 103
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or chemically- modified nucleotide; may or may not be modified based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 103

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 104
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or chemically- modified nucleotide; may or may not be modified based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 104

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 105
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 105

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 106
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 106

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 107
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 107

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 108
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 108

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 109
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 109

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 110
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 110

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 111
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 111

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 112
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 112

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 113
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 113

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 114
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 114

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 115
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 115

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 116
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 116

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 117
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 117

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 118
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 118

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 119
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 119

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 120
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 120

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 121
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 121

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 122
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 122

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 123
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 123

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 124
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 124

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 125
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 125

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 126
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 126

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 127
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 127

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 128
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 128

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 129
<211> LENGTH: 21
<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 129

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 130
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 130

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 131
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 131

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 132
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 132

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 133
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 133

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 134
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 134

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 135
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 135

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 136
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 136

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 137
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 137

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 138
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 138

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 139
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 139

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 140
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 140

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 141
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 141

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 142
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 142

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 143
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 143

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 144
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 144

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 145
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 145

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 146
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 146

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 147
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 147

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 148
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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oligonucleotide
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<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 148

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 149
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 149

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 150
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 150

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 151
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 151

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 152
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 152

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 153
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 153

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 154
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 154

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 155
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 155

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 156
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 156

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 157
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 157

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 158
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 158

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 159
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 159

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 160
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 160

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 161
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 161

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 162
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 162

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 163
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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oligonucleotide
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<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 163

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 164
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 164

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 165
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 165

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 166
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 166

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 167
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 167

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 168
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 168

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 169
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 169

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 170
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 170

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 171
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 171

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 172
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 172

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 173
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 173

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 174
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 174

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 175
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 175

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 176
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 176

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 177
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 177

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 178
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 178

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 179
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 179

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 180
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 180

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 181
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 181

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 182
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 182

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 183
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 183

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 184
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 184

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 185
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 185

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 186
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 186

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 187
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 187

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 188
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 188

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 189
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 189

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 190
<211> LENGTH: 21
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 190

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 191
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 191

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 192
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 192

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 193
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 193

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 194
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 194

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 195
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 195

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 196
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 196

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 197
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 197

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 198
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 198

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 199
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 199

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 200
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxo structure

<400> SEQUENCE: 200

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 201
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 201

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 202
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 202

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 203
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 203

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 204
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 204

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 205
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 205

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 206
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 206

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 207
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 207

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 208
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 208

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 209
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 209

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 210
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 210

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 211
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 211

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 212
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 212

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 213
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 213

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 214
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 214

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 215
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 215

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 216
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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<400> SEQUENCE: 216

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 217
<211> LENGTH: 21
<212> TYPE: RNA
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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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<400> SEQUENCE: 217

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 218
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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<400> SEQUENCE: 218

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 219
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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<400> SEQUENCE: 219

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 220
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 220

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 221
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 221

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 222
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 222

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 223
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 223

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 224
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 224

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 225
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or chemically- modified nucleotide; may or may not be modified based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 225

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 226
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or chemically- modified nucleotide; may or may not be modified based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 226

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 227
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or chemically- modified nucleotide; may or may not be modified based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 227

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 228
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or chemically- modified nucleotide; may or may not be modified based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 228

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 229
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 229

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 230
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 230

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 231
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 231

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 232
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide
<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 232

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 233
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
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based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 233

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 234
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 234

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 235
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 235

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 236
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<220> FEATURE:
<221> NAME/KEY: modified_base
<222> LOCATION: (1)..(21)
<223> OTHER INFORMATION: Any natural, non-natural, modified, or
chemically- modified nucleotide; may or may not be modified
based on a propane-1,2,3-tri-yl-trisoxy structure

<400> SEQUENCE: 236

nnnnnnnnnn nnnnnnnnnn n 21

<210> SEQ ID NO 237
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 237

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cgcaccucuc uuuaacgcgg 19

<210> SEQ ID NO 238
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 238

gacucguggu ggacuucuc 19

<210> SEQ ID NO 239
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 239

ucguggugga cuucucuca 19

<210> SEQ ID NO 240
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 240

uggauguguc ugcggcguu 19

<210> SEQ ID NO 241
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 241

ccgugugcac uucgcuuca 19

<210> SEQ ID NO 242
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 242

gugugcacuu cgcuucacc 19

<210> SEQ ID NO 243
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 243

ugugcacuuc gcuuaccu 19

<210> SEQ ID NO 244
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 244

gugcacuucg cuucaccuc 19

<210> SEQ ID NO 245
<211> LENGTH: 19
<212> TYPE: RNA

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<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 245

gcacucgcu ucaccucg 19

<210> SEQ ID NO 246

<211> LENGTH: 19

<212> TYPE: RNA

<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 246

uucaagccuc caagcugug 19

<210> SEQ ID NO 247

<211> LENGTH: 19

<212> TYPE: RNA

<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 247

ucaagccucc aagcugugc 19

<210> SEQ ID NO 248

<211> LENGTH: 19

<212> TYPE: RNA

<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 248

caagccucca agcugugcc 19

<210> SEQ ID NO 249

<211> LENGTH: 19

<212> TYPE: RNA

<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 249

aagccuccaa gcugugccu 19

<210> SEQ ID NO 250

<211> LENGTH: 19

<212> TYPE: RNA

<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 250

ucuagacucg ugguggacu 19

<210> SEQ ID NO 251

<211> LENGTH: 19

<212> TYPE: RNA

<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 251

cuagacucgu gguggacuu 19

<210> SEQ ID NO 252

<211> LENGTH: 19

<212> TYPE: RNA

<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 252

uagacucgug guggacuuc 19

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<210> SEQ ID NO 253
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 253

agacucgugg uggacuucu 19

<210> SEQ ID NO 254
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 254

gaugugucug cggcguuuu 19

<210> SEQ ID NO 255
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 255

ugugucugcg gcguuuuau 19

<210> SEQ ID NO 256
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 256

ugucugcggc guuuuauca 19

<210> SEQ ID NO 257
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 257

ggaggcugua ggcauaaaau 19

<210> SEQ ID NO 258
<211> LENGTH: 19
<212> TYPE: RNA
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<400> SEQUENCE: 258

gaggcuguag gcauaaaau 19

<210> SEQ ID NO 259
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 259

ggcuguaggc auaaaauugg 19

<210> SEQ ID NO 260
<211> LENGTH: 19
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<213> ORGANISM: Hepatitis B virus

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<400> SEQUENCE: 260

gcuguaggca uaaauggu 19

<210> SEQ ID NO 261
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 261

aacuuuuuca ccucugccu 19

<210> SEQ ID NO 262
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 262

gagucuagac ucguggugg 19

<210> SEQ ID NO 263
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 263

agucuagacu cguggugga 19

<210> SEQ ID NO 264
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 264

gucuagacuc gugguggac 19

<210> SEQ ID NO 265
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 265

cauccugcug cuaugccuc 19

<210> SEQ ID NO 266
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 266

uccugcugcu augccucau 19

<210> SEQ ID NO 267
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 267

ccugcugcua ugccucauc 19

<210> SEQ ID NO 268

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<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 268

cugcugcuau gccucaucu 19

<210> SEQ ID NO 269
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 269

ugcugcuau g ccucaucu 19

<210> SEQ ID NO 270
<211> LENGTH: 19
<212> TYPE: RNA
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<400> SEQUENCE: 270

cuguaggcau aaauugguc 19

<210> SEQ ID NO 271
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 271

uguaggcaua aaauuggucu 19

<210> SEQ ID NO 272
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<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 272

acucguggug gacuucucu 19

<210> SEQ ID NO 273
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 273

cucguggugg acuucucuc 19

<210> SEQ ID NO 274
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 274

cgugugcacu ucgcucac 19

<210> SEQ ID NO 275
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 275

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ugcacuucgc uucaccucu 19

<210> SEQ ID NO 276
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 276

cacuucgcuu caccucugc 19

<210> SEQ ID NO 277
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 277

acuucgcuuc accucugca 19

<210> SEQ ID NO 278
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 278

agccuccaag cugugccuu 19

<210> SEQ ID NO 279
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 279

gccuccaagc ugugccuug 19

<210> SEQ ID NO 280
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 280

gaacucccuc gccucgcag 19

<210> SEQ ID NO 281
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 281

aacucccucg ccucgcaga 19

<210> SEQ ID NO 282
<211> LENGTH: 19
<212> TYPE: RNA
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<400> SEQUENCE: 282

acucccucgc cucgcagac 19

<210> SEQ ID NO 283
<211> LENGTH: 19
<212> TYPE: RNA

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<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 283

cucccucgcc ucgcagacg 19

<210> SEQ ID NO 284

<211> LENGTH: 19

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auaaaaacgcc gcagacaca 19

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ugauaaaacg ccgcagaca 19

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agagaagucc accacgagu 19

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gagagaaguc caccacgag 19

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caaggcacag cuuggaggc 19

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cugcgaggcg agggaguuc 19

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augauaaaac gccgcagac 19

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agaagaugag gcgauagcag 19

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aagaagauga ggcauagca 19

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aggaguuccg caguaugga 19

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ggcgaggag uucuucuuc 19

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gaggcgagg aguuucuuc 19

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agaggugaaa aaguugcau 19

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gaugauuagg cagagguga 19

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cuaggaguuc cgcaguaug 19

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auagcagcag gaugaagag 19

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cauagcagca ggaugaaga 19

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gagaucuucu gcgacgcgg 19

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gaaaggccuu guaaguugg 19

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agaaaggccu uguaaguug 19

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<213> ORGANISM: Hepatitis B virus

<400> SEQUENCE: 758

aaaguugcau ggugcuggu

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<210> SEQ ID NO 759

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<400> SEQUENCE: 759

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<213> ORGANISM: Hepatitis B virus

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<213> ORGANISM: Hepatitis B virus

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gaaaaaguug cauggugcu

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<400> SEQUENCE: 771

gccuguaaca cgagcaggg 19

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<400> SEQUENCE: 772

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<400> SEQUENCE: 774

gaaccacuga acaaauggc 19

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aaagguucca cgcaugcgc 19

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<211> LENGTH: 19

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<400> SEQUENCE: 780

uucacggugg ucuccaugc 19

<210> SEQ ID NO 781

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guucacggug guccuccaug 19

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<400> SEQUENCE: 782

cguucacggu ggucuccau 19

<210> SEQ ID NO 783

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gcuucacgg ugguccca 19

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<400> SEQUENCE: 784

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acuggagcca ccagcagga 19

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cuacgaacca cugaacaaa 19

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19

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<210> SEQ ID NO 859

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<210> SEQ ID NO 871

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<210> SEQ ID NO 874

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aacuuuuuca ccucugccu 19

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gagucuagac ucguggugg 19

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<400> SEQUENCE: 893

uccugcugcu augccucau 19

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ccugcugcua ugccucauc 19

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cugcugcuau gccucauc 19

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ugcugcuauug ccucaucuu 19

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cucguggugg acuucucuc 19

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<400> SEQUENCE: 904

ugagagaagu ccaccacga 19

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aacgccgcag acacaucca 19

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<213> ORGANISM: Hepatitis B virus

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19

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<212> TYPE: RNA

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aguccaccac gagucuaga

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aaguccacca cgagucuag

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gaaguccacc acgagucua

19

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<400> SEQUENCE: 914

agaaguccac cacgagucu 19

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<400> SEQUENCE: 915

auuuuagccu acagccucc 19

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aaauuagcc uacagccuc 19

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ccaaauuauug ccuacagcc 19

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accaauuuau gccuacagc 19

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gaccaauuua ugccuacag 19

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agaccaauuu augccuaca 19

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auugagagaa guccaccac 19

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<400> SEQUENCE: 922

cacagcuugg aggcugaa 19

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gcacagcuug gaggcuga 19

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ggcacagcuu ggaggcuug 19

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aggcacagcu uggaggcuu 19

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aaaacgccgc agacacauc 19

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auaaaaacgcc gcagacaca 19

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ugauaaaacg ccgcagaca 19

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<213> ORGANISM: Hepatitis B virus

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<211> LENGTH: 19

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<400> SEQUENCE: 930

ccaccacgag ucuagacuc 19

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<400> SEQUENCE: 931

uccaccacga gucuagacu 19

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<211> LENGTH: 19

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<400> SEQUENCE: 932

guccaccacg agucuagac 19

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gaggcrauagc agcaggau 19

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<400> SEQUENCE: 934

augaggcaua gcagcagga 19

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gaugaggcau agcagcagg 19

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<213> ORGANISM: Hepatitis B virus

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aagaugaggc auagcagca 19

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<400> SEQUENCE: 938

agagaaguucc accacgagu 19

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gagagaaguc caccacgag 19

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gugaagcgaa gugcacacg 19

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agaggugaag cgaagugca 19

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gcagagguga agcgaagug 19

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gagucuagac ucgugguggu u 21

<210> SEQ ID NO 944
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oligonucleotide

<400> SEQUENCE: 944

ccaccacgag ucuagacucu u 21

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oligonucleotide

<400> SEQUENCE: 946

uccaccacga gucuagacuu u 21

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<400> SEQUENCE: 947

gucuagacuc gugguggacu u 21

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oligonucleotide

<400> SEQUENCE: 948

guccaccacg agucuagacu u 21

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<400> SEQUENCE: 949

ucuagacucg ugguggacuu u 21

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oligonucleotide

<400> SEQUENCE: 950

aguccaccac gagucuagau u 21

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<400> SEQUENCE: 951

cuagacucgu gguggacuuu u 21

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<400> SEQUENCE: 952

aaguccacca cgagucuagu u 21

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oligonucleotide

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uagacucgug guggacuuc u 21

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<400> SEQUENCE: 954

gaaguccacc acgagucuau u 21

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<400> SEQUENCE: 955

agacucgugg uggacuucuu u 21

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<400> SEQUENCE: 956

agaaguccac cacgagucuu u 21

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oligonucleotide

<400> SEQUENCE: 957

gacucguggu ggacuucucu u 21

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oligonucleotide

<400> SEQUENCE: 958

gagaagucca ccacgagucu u 21

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oligonucleotide

<400> SEQUENCE: 959

acucguggug gacuucucu u 21

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oligonucleotide

<400> SEQUENCE: 960

agagaagucc accacgaguu u 21

<210> SEQ ID NO 961
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oligonucleotide

<400> SEQUENCE: 961

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cucguggugg acuucucucu u 21

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oligonucleotide

<400> SEQUENCE: 962

gagagaaguc caccacgagu u 21

<210> SEQ ID NO 963
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oligonucleotide

<400> SEQUENCE: 963

ucguggugga cuucucucau u 21

<210> SEQ ID NO 964
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<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 964

ugagagaagu ccaccacgau u 21

<210> SEQ ID NO 965
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oligonucleotide

<400> SEQUENCE: 965

gugguggacu ucucucauu u 21

<210> SEQ ID NO 966
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<212> TYPE: RNA
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<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 966

auugagagaa guccaccacu u 21

<210> SEQ ID NO 967
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<400> SEQUENCE: 967

uggauguguc ugcggcguuu u

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<210> SEQ ID NO 968

<211> LENGTH: 21

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 968

aacgccgcag acacauccau u

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<210> SEQ ID NO 969

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<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 969

gaugugucug cggcguuuuu u

21

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<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

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oligonucleotide

<400> SEQUENCE: 970

aaaacgccgc agacacauu u

21

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<211> LENGTH: 21

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 971

ugugucugcg gcguuuuuu u

21

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<211> LENGTH: 21

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 972

auaaaaacgcc gcagacacau u

21

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<211> LENGTH: 21

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 973

ugucugcggc guuuuaucau u 21

<210> SEQ ID NO 974
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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oligonucleotide

<400> SEQUENCE: 974

ugauaaaacg ccgcagacau u 21

<210> SEQ ID NO 975
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 975

cauccugcug cuaugccucu u 21

<210> SEQ ID NO 976
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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oligonucleotide

<400> SEQUENCE: 976

gaggcauagc agcaggaugu u 21

<210> SEQ ID NO 977
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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oligonucleotide

<400> SEQUENCE: 977

uccugcugcu augccucauu u 21

<210> SEQ ID NO 978
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<212> TYPE: RNA
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oligonucleotide

<400> SEQUENCE: 978

augaggcaua gcagcaggau u 21

<210> SEQ ID NO 979
<211> LENGTH: 21
<212> TYPE: RNA

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<213> ORGANISM: Artificial Sequence
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oligonucleotide

<400> SEQUENCE: 979

ccugcugcua ugccucaucu u 21

<210> SEQ ID NO 980
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 980

gaugaggcua agcagcaggu u 21

<210> SEQ ID NO 981
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oligonucleotide

<400> SEQUENCE: 981

cugcugcuau gccucaucuu u 21

<210> SEQ ID NO 982
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<212> TYPE: RNA
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oligonucleotide

<400> SEQUENCE: 982

agaugaggca uagcagcagu u 21

<210> SEQ ID NO 983
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<212> TYPE: RNA
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<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 983

ugcugcuauug ccucaucuuu u 21

<210> SEQ ID NO 984
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 984

aagaugaggc auagcagcau u 21

<210> SEQ ID NO 985

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<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 985

cgccaccucuc uuucacgcggu u 21

<210> SEQ ID NO 986
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 986

ccgcguuaag agaggugcgu u 21

<210> SEQ ID NO 987
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oligonucleotide

<400> SEQUENCE: 987

ccgugugcac uucgcucau u 21

<210> SEQ ID NO 988
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 988

ugaagcgaag ugcacacggu u 21

<210> SEQ ID NO 989
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 989

cgugugcacu ucgcuucacu u 21

<210> SEQ ID NO 990
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 990

gugaagcgaa gugcacacgu u 21

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<210> SEQ ID NO 991
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oligonucleotide

<400> SEQUENCE: 991

gugugcacuu cgcuuaccu u 21

<210> SEQ ID NO 992
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oligonucleotide

<400> SEQUENCE: 992

ggugaagcga agugcacacu u 21

<210> SEQ ID NO 993
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<220> FEATURE:
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oligonucleotide

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ugugcacuuc gcuuaccuu u 21

<210> SEQ ID NO 994
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<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 994

aggugaagcg aagugcacau u 21

<210> SEQ ID NO 995
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 995

gugcacuucg cuuaccucu u 21

<210> SEQ ID NO 996
<211> LENGTH: 21
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 996

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gaggugaagc gaagugcacu u 21

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 997

ugcacuucgc uaccucuu u 21

<210> SEQ ID NO 998
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<213> ORGANISM: Artificial Sequence
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oligonucleotide

<400> SEQUENCE: 998

agaggugaag cgaagugcau u 21

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<213> ORGANISM: Artificial Sequence
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oligonucleotide

<400> SEQUENCE: 999

gcacuucgcu uaccucugu u 21

<210> SEQ ID NO 1000
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<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 1000

cagaggugaa gcgaagugcu u 21

<210> SEQ ID NO 1001
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 1001

cacuucgcuu caccucugcu u 21

<210> SEQ ID NO 1002
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<400> SEQUENCE: 1002

gcagagguga agcgaagugu u 21

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ggaggcugua ggcauaaaau u 21

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auuuuagccu acagccuccu u 21

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aaauuugcc uacagccucu u 21

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ggcuguaggc auaaaauuggu u 21

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oligonucleotide

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ccaaauuaug ccuacagccu u 21

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accaauuuau gccuacagcu u 21

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uguaggcaua aauggucuu u 21

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agaccaauuu augccuacau u 21

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aacuuuuuca ccucugccuu u 21

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aggcagaggu gaaaaaguuu u 21

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uucaagccuc caagcugugu u 21

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cacagcuugg aggcugaau u 21

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ucaagccucc aagcugugcu u 21

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aggcacagcu uggaggcuuu u 21

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cgugugcacu ucgcucacu u 21

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gugaagcgaa ggcacacgu u 21

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<400> SEQUENCE: 1027

cgugugcacu ucgcucacu u 21

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oligonucleotide

<400> SEQUENCE: 1028

gugaagcgaa ggcacacgu u 21

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oligonucleotide

<400> SEQUENCE: 1029

cgugugcacu ucgcucacu u 21

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gugaagcgaa ggcacacgu u 21

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<400> SEQUENCE: 1031

cgugugcacu ucgcucacu u 21

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oligonucleotide

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gugaagcgaa gugcacacgu u 21

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cgugugcacu ucgcuucacu u 21

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oligonucleotide

<400> SEQUENCE: 1034

gugaagcgaa gugcacacgu u 21

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oligonucleotide

<400> SEQUENCE: 1035

cgugugcacu ucgcuucacu u 21

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oligonucleotide

<400> SEQUENCE: 1036

gugaagcgaa gugcacacgu u 21

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oligonucleotide

<400> SEQUENCE: 1037

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cgugugcacu ucgcuuacac u 21

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oligonucleotide

<400> SEQUENCE: 1038

gugaagcgaa gugcacacgu u 21

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oligonucleotide

<400> SEQUENCE: 1039

cgugugcacu ucgcuuacac u 21

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<400> SEQUENCE: 1040

gugaagcgaa gugcacacgu u 21

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oligonucleotide

<400> SEQUENCE: 1041

ccgugugcac uucgcuuac u 21

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oligonucleotide

<400> SEQUENCE: 1042

ugaagcggaag ugcacacggu u 21

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oligonucleotide

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<400> SEQUENCE: 1043

ccgugugcac uucgcuuau u

21

<210> SEQ ID NO 1044

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<220> FEATURE:

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ugaagcgaag ugcacacggu u

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<212> TYPE: RNA

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<400> SEQUENCE: 1045

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21

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<211> LENGTH: 21

<212> TYPE: RNA

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<220> FEATURE:

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oligonucleotide

<400> SEQUENCE: 1046

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21

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<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 1047

ugugcacuuc gcuucacuu u

21

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<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

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oligonucleotide

<400> SEQUENCE: 1048

aggugaagcg aagucacau u

21

<210> SEQ ID NO 1049

<211> LENGTH: 21

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 1049

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<213> ORGANISM: Artificial Sequence
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oligonucleotide

<400> SEQUENCE: 1050

aggugaagcg aagugcacau u 21

<210> SEQ ID NO 1051
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oligonucleotide

<400> SEQUENCE: 1051

ugugcacuuc gcuucacuu u 21

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oligonucleotide

<400> SEQUENCE: 1052

aggugaagcg aagugcacau u 21

<210> SEQ ID NO 1053
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<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 1053

aacuuuuuca ccucugccuu u 21

<210> SEQ ID NO 1054
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oligonucleotide

<400> SEQUENCE: 1054

aggcagaggu gaaaaaguuu u 21

<210> SEQ ID NO 1055
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<213> ORGANISM: Artificial Sequence
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oligonucleotide

<400> SEQUENCE: 1055

aacuuuuuca ccucugccuu u 21

<210> SEQ ID NO 1056
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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oligonucleotide

<400> SEQUENCE: 1056

aggcagaggu gaaaaaguuu u 21

<210> SEQ ID NO 1057
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oligonucleotide

<400> SEQUENCE: 1057

aacuuuuuca ccucugccuu u 21

<210> SEQ ID NO 1058
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<213> ORGANISM: Artificial Sequence
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oligonucleotide

<400> SEQUENCE: 1058

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<400> SEQUENCE: 1059

agucuagacu cgugguggau u 21

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<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 1060

uccaccacga gucuagacuu u 21

<210> SEQ ID NO 1061

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<211> LENGTH: 21
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oligonucleotide

<400> SEQUENCE: 1061

ugcacuucgc uuccaccucu u 21

<210> SEQ ID NO 1062
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oligonucleotide

<400> SEQUENCE: 1062

agaggugaag cgaagugcau u 21

<210> SEQ ID NO 1063
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oligonucleotide

<400> SEQUENCE: 1063

ugcacuucgc uuccaccucu u 21

<210> SEQ ID NO 1064
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<212> TYPE: RNA
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oligonucleotide

<400> SEQUENCE: 1064

agaggugaag cgaagugcau u 21

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oligonucleotide

<400> SEQUENCE: 1065

ugcacuucgc uuccaccucu u 21

<210> SEQ ID NO 1066
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oligonucleotide

<400> SEQUENCE: 1066

agaggugaag cgaagugcau u 21

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oligonucleotide

<400> SEQUENCE: 1067

ugcacuucgc uuccaccuu u 21

<210> SEQ ID NO 1068
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oligonucleotide

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agaggugaag cgaagugcau u 21

<210> SEQ ID NO 1069
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<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 1069

ugugcacuuc gcuuccaccuu u 21

<210> SEQ ID NO 1070
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<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 1070

aggugaagcg aagugcacau u 21

<210> SEQ ID NO 1071
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<212> TYPE: RNA
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<400> SEQUENCE: 1071

ugugcacuuc gcuuccaccuu u 21

<210> SEQ ID NO 1072
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<220> FEATURE:
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oligonucleotide

<400> SEQUENCE: 1072

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aggugaagcg aagugcacau u 21

<210> SEQ ID NO 1073
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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oligonucleotide

<400> SEQUENCE: 1073

ugugcacuuc gcuucaccuu u 21

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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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oligonucleotide

<400> SEQUENCE: 1074

aggugaagcg aagugcacau u 21

<210> SEQ ID NO 1075
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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 1075

ugugcacuuc gcuucaccuu u 21

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oligonucleotide

<400> SEQUENCE: 1076

aggugaagcg aagugcacau u 21

<210> SEQ ID NO 1077
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oligonucleotide

<400> SEQUENCE: 1077

ugugcacuuc gcuucaccuu u 21

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oligonucleotide

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<400> SEQUENCE: 1078

aggugaagcg aagugcacau u 21

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<212> TYPE: RNA

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oligonucleotide

<400> SEQUENCE: 1079

ugugcacuuc gcuucaccuu u 21

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<212> TYPE: RNA

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<400> SEQUENCE: 1080

aggugaagcg aagugcacau u 21

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<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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ugugcacuuc gcuucaccuu u 21

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<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 1082

aggugaagcg aagugcacau u 21

<210> SEQ ID NO 1083

<211> LENGTH: 21

<212> TYPE: RNA

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<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 1083

ugugcacuuc gcuucaccuu u 21

<210> SEQ ID NO 1084

<211> LENGTH: 21

<212> TYPE: RNA

<213> ORGANISM: Artificial Sequence

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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic

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oligonucleotide

<400> SEQUENCE: 1084

aggugaagcg aagugcacau u 21

<210> SEQ ID NO 1085
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

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<400> SEQUENCE: 1116

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<400> SEQUENCE: 1117

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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<400> SEQUENCE: 1120

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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<212> TYPE: DNA

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<223> OTHER INFORMATION: Description of Combined DNA/RNA Molecule:
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<223> OTHER INFORMATION: Description of Combined DNA/RNA Molecule:
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<212> TYPE: DNA

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<223> OTHER INFORMATION: Description of Combined DNA/RNA Molecule:

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<400> SEQUENCE: 1124

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<400> SEQUENCE: 1126

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<400> SEQUENCE: 1132

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<400> SEQUENCE: 1137

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<210> SEQ ID NO 1138
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<212> TYPE: RNA
<213> ORGANISM: Artificial Sequence
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<400> SEQUENCE: 1138

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<210> SEQ ID NO 1142
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<400> SEQUENCE: 1142
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<400> SEQUENCE: 1145

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<400> SEQUENCE: 1146

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<400> SEQUENCE: 1147

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<223> OTHER INFORMATION: Description of Combined DNA/RNA Molecule:
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<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<220> FEATURE:

<223> OTHER INFORMATION: Description of Combined DNA/RNA Molecule:
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<400> SEQUENCE: 1150

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21

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<212> TYPE: DNA

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<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<223> OTHER INFORMATION: Description of Combined DNA/RNA Molecule:
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<400> SEQUENCE: 1151

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21

<210> SEQ ID NO 1152

<211> LENGTH: 21

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<223> OTHER INFORMATION: Description of Combined DNA/RNA Molecule:
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<400> SEQUENCE: 1152

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<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
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<223> OTHER INFORMATION: Description of Combined DNA/RNA Molecule:
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<400> SEQUENCE: 1153

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21

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<212> TYPE: DNA

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<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic

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<210> SEQ ID NO 1159
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<400> SEQUENCE: 1166

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<400> SEQUENCE: 1167

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<400> SEQUENCE: 1171

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<400> SEQUENCE: 1176

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<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic oligonucleotide

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<400> SEQUENCE: 1179

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<400> SEQUENCE: 1180

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<210> SEQ ID NO 1181
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<213> ORGANISM: Hepatitis B virus

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What is claimed is:

1. A compound comprising a first strand and a second strand, each of the strands being 19-29 monomers in length, the monomers comprising UNA monomers and nucleic acid monomers, wherein the compound has a duplex region of from 14 to 29 contiguous monomers in length, wherein the first strand is a sense strand for RNA interference and the second strand is an antisense strand for RNA interference, and wherein the compound comprises a sequence of bases targeted to inhibit expression of an HBV genome.

2. The compound of claim 1, wherein the compound contains one to seven UNA monomers.

3. The compound of claim 1, wherein the compound contains a UNA monomer at the 1-end (5' end for non-UNA) of the first strand, a UNA monomer at the 3-end or second position from the 3-end (3' end for non-UNA) of the sense strand, and a UNA monomer at the 3-end or second position from the 3-end (3' end for non-UNA) of the antisense strand.

4. The compound of claim 1, wherein the sense strand comprises SEQ ID NO:900 and the antisense strand comprises SEQ ID NO:941.

5. The compound of claim 1, wherein the sense strand comprises SEQ ID NO:893 and the antisense strand comprises SEQ ID NO:934.

6. The compound of claim 1, wherein the sense strand comprises SEQ ID NO:879 and the antisense strand comprises SEQ ID NO:920.

7. The compound of claim 1, wherein the first and second strands are a sense-antisense pair selected from any of Tables 33 to 38.

8. The compound of claim 1, wherein the compound has a 3' overhang comprising one or more UNA monomers, natural nucleotides, non-natural nucleotides, modified nucleotides, or chemically-modified nucleotides, and combinations thereof.

9. The compound of claim 1, wherein the compound has a 3' overhang comprising one or more deoxythymidine nucleotides, 2'-O-methyl nucleotides, inverted abasic monomers, inverted thymidine monomers, L-thymidine monomers, or glyceryl nucleotides.

10. The compound of claim 1, wherein one or more of the nucleic acid monomers is a non-natural nucleotide, a modified nucleotide, or a chemically-modified nucleotide.

11. The compound of claim 1, wherein one or more of three monomers at each end of each strand is connected by a phosphorothioate, a chiral phosphorothioate, or a phosphorodithioate linkage.

12. The compound of claim 1, wherein the compound is conjugated to a delivery moiety.

13. The compound of claim 1, wherein the compound is conjugated to a delivery moiety that binds to a glycoprotein receptor, wherein the delivery moiety comprises a galactose, a galactosamine, or a N-acetylgalactosamine.

14. The compound of claim 1, wherein the compound is conjugated to a GalNAc delivery moiety or a cholesterol delivery moiety.

15. A lipid nanoparticle-oligomer compound comprising one or more compounds of claim 1 attached to the lipid nanoparticle.

16. A composition comprising one or more compounds of claim 1 and a pharmaceutically acceptable carrier.

17. The composition of claim 16, wherein the carrier comprises lipid nanoparticles or liposomes.

18. A composition comprising a triad of compounds, wherein the triad is selected from the following:

the first compound comprises SEQ ID NO:867 and 908, the second compound comprises SEQ ID NO:887 and 928, and the third compound comprises SEQ ID NO:879 and 920, and substituted forms thereof;

the first compound comprises SEQ ID NO: 867 and 908, the second compound comprises SEQ ID NO:893 and 934, and the third compound comprises SEQ ID NO:875 and 916, and substituted forms thereof; and

the first compound comprises SEQ ID NO:900 and 941, the second compound comprises SEQ ID NO:887 and 928, and the third compound comprises SEQ ID NO:875 and 916, and substituted forms thereof.

19. An siRNA comprising nucleotides, wherein the siRNA is targeted to HBV and comprises SEQ ID NO:900 and 941, and substituted forms thereof.

20. An siRNA comprising nucleotides, wherein the siRNA is targeted to HBV and comprises SEQ ID NO:893 and 934, and substituted forms thereof.

21. An siRNA comprising nucleotides, wherein the siRNA is targeted to HBV and comprises SEQ ID NO:879 and 920, and substituted forms thereof.

22. A method for preventing, ameliorating or treating a disease or condition associated with HBV infection in a subject in need, the method comprising administering to the subject an effective amount of a composition of claim 16.

23. The method of claim 22, wherein the administration of the composition reduces HBV viral titer in the subject.

24. The method of claim 22, wherein the subject has been diagnosed with a disease associated with Hepatitis B virus infection.

25. The method of claim 22, wherein the subject has been diagnosed with liver disease.

26. A method for inhibiting the replication, maturation, growth, or transmission of a Hepatitis B virus in a subject in need, the method comprising administering to the subject an effective amount of a composition of claim 16.

27. The method of claim 26, wherein the administration of the composition reduces serum concentration of HBsAg in the subject by 2-log₁₀-fold for at least 7 days.

28. The method of claim 26, wherein the administration of the composition reduces HBeAg in the subject.

29. The method of claim 26, wherein the administration of the composition reduces HBV DNA in the subject.

30. A method for inhibiting expression of a Hepatitis B virus polynucleotide in a subject in need, the method comprising administering to the subject a composition of claim 16.

* * * * *