polymerase, are provided by the host cell, and the HDV envelope is provided by HBV. When introduced into permissive cells, the HDV RNA genome replicates and associates with multiple copies of the HDV-encoded proteins to assemble a ribonucleoprotein (RNP) complex. The RNP is exported from the cell by the HBV envelope proteins, which are able to assemble lipoprotein vesicles that bud into the lumen of a pre-Golgi compartment before being secreted. Moreover, the HBV envelope proteins also provide a mechanism for the targeting of HDV to an uninfected cell, thereby ensuring the spread of HDV.

Complications caused by HDV include a greater likelihood of experiencing liver failure in acute infections and a rapid progression to liver cirrhosis, with an increased chance of developing liver cancer in chronic infections. In combination with hepatitis B virus, hepatitis D has the highest fatality rate of all the hepatitis infections, at 20% (Fattovich G, Giustina G, Christensen E, Pantalena M, Zagni I, Realdi G, Schalm SW. Influence of hepatitis delta virus infection on morbidity and mortality in compensated cirrhosis type B. Gut. 2000 Mar;46(3):420-6). The only approved therapy for chronic HDV infection is interferon-alpha. However, treatment of HDV with interferon-alpha is relatively inefficient and is not well-tolerated. Treatment with interferon-alpha results in sustained virological response six months post-treatment in one-fourth of the patients. Also, nucleos(t)ide analogs (NAs) have been widely tested in hepatitis delta, but they appear to be ineffective. Combination treatment using NAs with interferon also proved to be disappointing (Zaigham Abbas, Minaam Abbas Management of hepatitis delta: Need for novel therapeutic Options. World J Gastroenterol 2015 August 28; 21(32): 9461-9465).

Accordingly, new therapeutic options, such as new therapies with neutralizing activity against Hepatitis B and/or D infection are needed.

SUMMARY

In one aspect, the present disclosure relates to an antibody, or an antigen-binding fragment thereof, comprisinga heavy chain variable region (VH) comprising a CDRH1 amino acid sequence, a CDRH2 amino acid sequence, and a CDRH3 amino acid sequence; and a light chain variable region (VL) comprising a CDRL1 amino acid

sequence, a CDRL2 amino acid sequence, and a CDRL3 amino acid sequence, wherein the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences are according to SEQ ID NOs.:(i) 34, 35, 37, 41, 49, and 55, respectively; (ii)34, 35, 37, 41, 46, and 55, respectively; (iii) 34, 35, 37, 41, 47, and 55, respectively; (iv) 34, 35, 37, 41, 48, and 55, respectively; (v) 34, 35, 37, 41, 45, and 55, respectively; (vi) 34, 35, 37, 41, 50, and 55, respectively; (vii) 34, 35, 37, 41, 51, and 55, respectively;(viii) 34, 35, 37, 41, 52, and 55, respectively; (ix) 34, 35, 37, 41, 53, and 55, respectively; or (x) 34, 35, 37, 41, 44, and 55, respectively; wherein CDRs are defined according to the CCG numbering system, wherein, optionally, the VL comprises a R60N substitution mutation, a R60A substitution mutation, a R60K substitution mutation, a S64A substitution mutation, a I74A substitution mutation, or any combination thereof, relative to SEQ ID NO.:58 and wherein the amino acid numbering of the substitution mutation(s) is according to SEQ ID NO.:58, and still further optionally wherein the VL does not comprise any further mutation(s) relative to SEQ ID NO.:58, and wherein the antibody or antigen-binding fragment thereof is capable of binding to the antigenic loop region of HBsAg and, optionally, neutralizing infection by a hepatitis B virus (HBV) of genotype D, A, B, C, E, F, G, H, I, or J, or any combination thereof.

In another aspect, the present disclosure relates to an antibody or antigen-binding fragment, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and the VL comprise or consist of the amino acid sequences set forth in SEQ ID NOs.: (i) 38 and 62, respectively; (ii) 38 and 66, respectively; (iii) 38 and 67, respectively; (iv) 38 and 68, respectively; or (v) 38 and 72, respectively, wherein the antibody or antigen-binding fragment thereof is capable of binding to the antigenic loop region of HBsAg and neutralizing infection by a hepatitis B virus (HBV) of genotype D, A, B, C, E, F, G, H, I, or J, or any combination thereof.

In another aspect, the present disclosure relates to an antibody comprising: a heavy chain (HC) comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:75, optionally with the C-terminal lysine removed; and a light chain (LC), wherein the LC comprises or consists of (i) the VL amino acid sequence set forth in any one of SEQ ID NOs.:62, 58-61, and 63-72 and (ii) the CL amino acid sequence set forth in SEQ ID NO.:79.

In another aspect, the present disclosure relates to an antibody comprising: a heavy chain (HC) comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:76, optionally with the C-terminal lysine removed, and a light chain (LC), wherein the LC comprises or consists of (i) the VL amino acid sequence set forth in any one of SEQ ID NOs.:62, 58-61, and 63-72 and (ii) the CL amino acid sequence set forth in SEQ ID NO.:79.

In another aspect, the present disclosure relates to an antibody comprising: a heavy chain (HC) comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:77, optionally with the C-terminal lysine removed, and a light chain (LC), wherein the LC comprises or consists of (i) the VL amino acid sequence set forth in any one of SEQ ID NOs.:62, 58-61, and 63-72 and (ii) the CL amino acid sequence set forth in SEQ ID NO.:79.

In another aspect, the present disclosure relates to an antibody comprising: a heavy chain (HC) comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:78, optionally with the C-terminal lysine removed, and a light chain (LC), wherein the LC comprises or consists of (i) the VL amino acid sequence set forth in any one of SEQ ID NOs.:62, 58-61, and 63-72 and (ii) the CL amino acid sequence set forth in SEQ ID NO.:79.

In another aspect, the present disclosure relates to a polynucleotide comprising a nucleotide sequence that encodes the antibody, or the antigen-binding fragment as disclosed herein.

In another aspect, the present disclosure relates to a polynucleotide encoding a light chain variable region (VL) and, optionally, a light chain constant domain (CL) of the antibody, or the antigen-binding fragment, as disclosed herein.

In another aspect, the present disclosure relates to a vector comprising the polynucleotide as disclosed herein.

In another aspect, the present disclosure relates to a host cell comprising the polynucleotide and/or the vector as disclosed herein.

In another aspect, the present disclosure relates to a pharmaceutical composition comprising: (i) the antibody or antigen binding fragment as disclosed herein; (ii) the polynucleotide as disclosed herein; (iii) the vector according as disclosed herein; (iv) the

host cell as disclosed herein; or (v) any combination of (i)-(iv), and a pharmaceutically acceptable excipient, diluent or carrier.

In another aspect, the present disclosure relates to a kit comprising: (a) a component selected from:(i) the antibody or antigen-binding fragment as disclosed herein; (ii) the polynucleotide as disclosed herein; (iii) the vector as disclosed herein; (iv) the host cell as disclosed herein; (v) the pharmaceutical composition as disclosed herein; or (vi) any combination of (i)-(vi); and (b) (1) instructions for using the component to prevent, treat, attenuate, and/or diagnose a hepatitis B virus infection and/or a hepatitis D virus infection and/or (2) a means for administering the component to the subject.

In another aspect, the present disclosure relates to a method of producing the antibody or antigen binding fragment as disclosed herein, comprising culturing the host cell as disclosed herein under conditions and for a time sufficient to produce the antibody or antigen-binding fragment.

In yet another aspect, the present disclosure relates to use of: (i) the antibody or antigen-binding fragment as disclosed herein; (ii) the polynucleotide asd disclosed herein; (iii) the vector as disclosed herein; (iv) the host cell as disclosed herein; and/or (v) the pharmaceutical composition as disclosed herein in the manufacture of a medicament to prevent, treat, attenuate, and/or diagnose a hepatitis B virus infection and/or a hepatitis D virus infection in a subject.

In yet another aspect, the present disclosure relates to an antibody or antigen-binding fragment as disclosed herein, the polynucleotide as disclosed herein, the vector as disclosed herein, the host cell as disclosed herein, and/or the pharmaceutical composition as disclosed herein for use as a medicament.

In yet another aspect, the present disclosure relates to a pharmaceutical composition comprising the antibody or antigen-binding fragment as disclosed herein at a concentration ranging from 100 mg/mL to 200 mg/mL, and a pharmaceutically acceptable carrier, excipient, or diluent.

In yet another aspect, the present disclosure relates to a method for *in vitro* diagnosis of a hepatitis B virus infection, the method comprising: (i) contacting a sample from a subject with an antibody or antigen-binding fragment as disclosed herein; and (ii) detecting a complex comprising an antigen and the antibody, or comprising an antigen and the antigen-binding fragment.

In yet another aspect, the present disclosure relates to a method for detecting the presence or absence of an epitope in a correct conformation in an anti-hepatitis-B and/or an anti-hepatitis-D vaccine, the method comprising: (i) contacting the vaccine with an antibody or antigen-binding fragment as disclosed herein; and (ii) determining whether a complex comprising an antigen and the antibody, or comprising an antigen and the antigen binding fragment, has been formed.

In yet another aspect, the present disclosure relates to use of an anti-HBV antibody as disclosed herein in the manufacture of a medicament for treating chronic HBV infection in a subject in need thereof, wherein the anti-HBV antibody is to be administered to the subject with an agent that reduces HBV antigenic load; and/or an inhibitor of HBV gene expression; wherein the agent that reduces HBV antigenic load and/or the inhibitor of HBV gene expression is an RNAi agent that inhibits expression of an HBV transcript.

In yet another aspect, the present disclosure relates to an antibody or antigen-binding fragment comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and the VL comprise or consist of the amino acid sequences set forth in SEQ ID NOs.: 38 and 62, respectively; wherein the antibody or antigen-binding fragment thereof is capable of binding to the antigenic loop region of HBsAg and neutralizing infection by a hepatitis B virus (HBV) of genotype D, A, B, C, E, F, G, H, I, or J, or any combination thereof and/or capable of neutralizing infection by a hepatitis D virus (HDV).

In yet another aspect, the present disclosure relates to an antibody or antigen-binding fragment, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and the VL comprise or consist of the amino acid sequences set forth in SEQ ID NOs.: 38 and 66, respectively; wherein the antibody or antigen-binding fragment thereof is capable of binding to the antigenic loop region of HBsAg and neutralizing infection by a hepatitis B virus (HBV) of genotype D, A, B, C, E, F, G, H, I, or J, or any combination thereof and/or capable of neutralizing infection by a hepatitis D virus (HDV).

In yet another aspect, the present disclosure relates to use of an anti-HBV antibody as disclosed herein in the manufacture of a medicament for treating chronic HBV infection and/or HDV infection in a subject in need thereof.

In yet another aspect, the present disclosure relates to use of an anti-HBV antibody as disclosed herein in the manufacture of a medicament for treating chronic HBV infection and/or HDV infection in a subject in need thereof, wherein the anti-HBV antibody is to be administered to the subject with an siRNA, wherein the siRNA has a sense strand comprising 5'- gsusguGfcAfCfUfucgcuucacaL96 -3' (SEQ ID NO:124) and an antisense strand comprising 5'- usGfsuga(Agn)gCfGfaaguGfcAfcacsusu -3' (SEQ ID NO:125); wherein a, c, g, and u are 2'-O-methyladenosine-3'-phosphate, 2'-O-methylcytidine-3'-phosphate, 2'-O-methylguanosine-3'-phosphate, and 2'-O-methyluridine-3'-phosphate, respectively; Af, Cf, Gf, and Uf are 2'-fluoroadenosine-3'-phosphate, 2'-fluorocytidine-3'-phosphate, 2'-fluoroguanosine-3'-phosphate, and 2'-fluorouridine-3'-phosphate, respectively; s is a phosphorothioate linkage; and L96 is N-[tris(GalNAc-alkyl)-amidodecanoyl)]-4-hydroxyprolinol.

BRIEF DESCRIPTION OF THE DRAWINGS

The figures provided herein are intended to illustrate subject matter included in the present disclosure in more detail. The figures are not intended to limit the disclosure in any way.

CLAIMS

1. An antibody, or an antigen-binding fragment thereof, comprising~~:~~

~~(i)~~ a heavy chain variable region (VH) comprising a CDRH1 amino acid sequence, a CDRH2 amino acid sequence, and a CDRH3 amino acid sequence; and~~that comprises therein the amino acid sequence of SEQ ID NO.:34, the amino acid sequence of SEQ ID NO.:35 or SEQ ID NO.:36, and the amino acid sequence of SEQ ID NO.:37; and~~

~~(ii)~~ a light chain variable region (VL) comprising a CDRL1 amino acid sequence, a CDRL2 amino acid sequence, and a CDRL3 amino acid sequence, wherein the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences are according to SEQ ID NOs.: ~~that comprises therein the amino acid sequence any one of SEQ ID NOs.:41, 40, 42, and 43, the amino acid sequence according to any one of SEQ ID NOs:49, 44-48, and 50-53, and the amino sequence according to SEQ ID NO.:55 or 56,~~

(i) 34, 35, 37, 41, 49, and 55, respectively;

(ii) 34, 35, 37, 41, 46, and 55, respectively;

(iii) 34, 35, 37, 41, 47, and 55, respectively;

(iv) 34, 35, 37, 41, 48, and 55, respectively;

(v) 34, 35, 37, 41, 45, and 55, respectively;

(vi) 34, 35, 37, 41, 50, and 55, respectively;

(vii) 34, 35, 37, 41, 51, and 55, respectively;

(viii) 34, 35, 37, 41, 52, and 55, respectively;

(ix) 34, 35, 37, 41, 53, and 55, respectively; or

(x) 34, 35, 37, 41, 44, and 55, respectively;

wherein CDRs are defined according to the CCG numbering system,

wherein, optionally, the VL comprises a R60N substitution mutation, a R60A substitution mutation, a R60K substitution mutation, a S64A substitution mutation, a I74A substitution mutation, or any combination thereof, relative to SEQ ID NO.:58 and wherein the amino acid numbering of the substitution mutation(s) is according to SEQ

ID NO.:58, and still further optionally wherein the VL does not comprise any further mutation(s) relative to SEQ ID NO.:58,

and wherein the antibody or antigen-binding fragment thereof is capable of binding to the antigenic loop region of HBsAg and, optionally, neutralizing infection by a hepatitis B virus (HBV) of genotype D, A, B, C, E, F, G, H, I, or J, or any combination thereof.

~~2. The antibody or antigen-binding fragment of claim 1, comprising:~~

~~(i) in the VH, the amino acid sequences according to SEQ ID NOs.:34, 35, and 37, respectively, and in the VL, the amino acid sequences according to SEQ ID NOs.:41, 49, and 55, respectively;~~

~~(ii) in the VH, the amino acid sequences according to SEQ ID NOs.:34, 35, and 37, and in the VL, the amino acid sequences according to SEQ ID NOs.: 41, 46, and 55, respectively;~~

~~(iii) in the VH, the amino acid sequences according to SEQ ID NOs.:34, 35, and 37, respectively, and in the VL, the amino acid sequences according to SEQ ID NOs.: 41, 47, and 55, respectively;~~

~~(iv) in the VH, the amino acid sequences according to SEQ ID NOs.:34, 35, and 37, respectively, and in the VL, the amino acid sequences according to SEQ ID NOs.:41, 48, and 55, respectively;~~

~~(v) in the VH, the amino acid sequences according to SEQ ID NOs.:34, 35, and 37, respectively, and in the VL, the amino acid sequences according to SEQ ID NOs.:41, 45, and 55, respectively;~~

~~(vi) in the VH, the amino acid sequences according to SEQ ID NOs.:34, 35, and 37, respectively, and in the VL, the amino acid sequences according to SEQ ID NOs.:41, 50, and 55, respectively;~~

~~(vii) in the VH, the amino acid sequences according to SEQ ID NOs.:34, 35, and 37, respectively, and in the VL, the amino acid sequences according to SEQ ID NOs.:41, 51, and 55, respectively;~~

(viii) in the VH, the amino acid sequences according to SEQ ID NOs.:34, 35, and 37, respectively, and in the VL, the amino acid sequences according to SEQ ID NOs.:41, 52, and 55, respectively; or

(ix) in the VH, the amino acid sequences according to SEQ ID NOs.:34, 35, and 37, respectively, and in the VL, the amino acid sequences according to SEQ ID NOs.:41, 53, and 55, respectively.

3. An antibody, or an antigen-binding fragment thereof, comprising:

(i) a heavy chain variable region (VH) comprising a CDRH1 amino acid sequence according to SEQ ID NO.:34, a CDRH2 amino acid sequence according to SEQ ID NO.:35 or 36, and a CDRH3 amino acid sequence according to SEQ ID NO.:37; and

(ii) a light chain variable region (VL) comprising a CDRL1 amino acid sequence according to any one of SEQ ID NOs.:40-43, a CDRL2 amino acid sequence according to any one of SEQ ID NOs:49, 44-48, and 50-53, and a CDRL3 amino acid sequence according to SEQ ID NO.:55 or 56,

wherein CDRs are defined according to the CCG numbering system, and

wherein the antibody or antigen-binding fragment thereof is capable of binding to the antigenic loop region of HBsAg and, optionally, neutralizing infection by a hepatitis B virus (HBV) of genotype D, A, B, C, E, F, G, H, I, or J, or any combination thereof, provided that the antibody or antigen-binding fragment does not comprise CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to SEQ ID NOs.:34, 35, 37, 41, 44, and 45, respectively.

4. The antibody or antigen-binding fragment of claim 3, wherein the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences are according to SEQ ID NOs.:

(i) 34, 35, 37, 41, 49, and 55, respectively;

(ii) 34, 35, 37, 41, 46, and 55, respectively;

(iii) 34, 35, 37, 41, 47, and 55, respectively;

(iv) 34, 35, 37, 41, 48, and 55, respectively;

(v) 34, 35, 37, 41, 45, and 55, respectively;

(vi) 34, 35, 37, 41, 50, and 55, respectively;

(vii) 34, 35, 37, 41, 51, and 55, respectively;

(viii) 34, 35, 37, 41, 52, and 55, respectively;

(ix) 34, 35, 37, 41, 53, and 55, respectively; or

(x) 34, 35, 37, 41, 44, and 55, respectively.

5. An antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and the VL comprise CDRH1, CDRH2, CDRH3 and CDRL1, CDRL2, CDRL3, respectively, according to: HBC34-v40; HBC34-v36; HBC34-v37; HBC34-v38; HBC34-v39; HBC34-v41; HBC34-v42; HBC34-v43; HBC34-v44; HBC34-v45; HBC34-v46; HBC34-v47; HBC34-v48; HBC34-v49; or HBC34-v50,

wherein the CDRs are defined according to IMGT numbering, optionally wherein the VL further comprises a R60N substitution mutation, a R60A substitution mutation, a R60K substitution mutation, a S64A substitution mutation, a I74A substitution mutation, or any combination thereof, relative to SEQ ID NO.:58 and wherein the amino acid numbering of the substitution mutation(s) is according to SEQ ID NO.:58, and further optionally wherein the VL does not comprise any further mutation(s) relative to SEQ ID NO.:58.

6. An antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and the VL comprise CDRH1, CDRH2, CDRH3 and CDRL1, CDRL2, CDRL3, respectively, according to: HBC34-v40; HBC34-v36; HBC34-v37; HBC34-v38; HBC34-v39; HBC34-v41; HBC34-v42; HBC34-v43; HBC34-v44; HBC34-v45; HBC34-v46; HBC34-v47; HBC34-v48; HBC34-v49; or HBC34-v50,

wherein the CDRs are defined according to CCG numbering, optionally wherein the VL further comprises a R60N substitution mutation, a R60A substitution mutation,

~~a R60K substitution mutation, a S64A substitution mutation, a I74A substitution mutation, or any combination thereof, relative to SEQ ID NO.:58 and wherein the amino acid numbering of the substitution mutation(s) is according to SEQ ID NO.:58, and further optionally wherein the VL does not comprise any other mutation(s) relative to SEQ ID NO.:58.~~

~~7. The antibody or antigen-binding fragment of any one of claims 1-6, wherein:~~

~~(i) the VH comprises or consists of an amino acid sequence having at least 90% identity to the amino acid sequence set forth in SEQ ID NO.: 38 or 39; and/or~~

~~(ii) the VL comprises or consists of an amino acid sequence having at least 90% identity to the amino acid sequence set forth in any one of SEQ ID NOs.: 62, 58-61, 63-66, 69, 71, and 72.~~

~~8. The antibody or antigen-binding fragment of any one of claims 1-7, wherein:~~

~~(i) the VH comprises or consists of an amino acid sequence having at least 90% (*i.e.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%, or any non-integer value therebetween) identity to the amino acid sequence set forth in SEQ ID NO.: 38 or 39; and/or~~

~~(ii) the VL comprises or consists of an amino acid sequence having at least 90% (*i.e.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%, or any non-integer value therebetween) identity to the amino acid sequence set forth in any one of SEQ ID NOs.: 62, 58-61, 63-66, 69, 71, and 72.~~

~~9~~2. The antibody or antigen-binding fragment of ~~any one of claims 1-8~~claim 1, wherein the VH and the VL comprise or consist of amino acid sequences having at least ~~90% (*i.e.*, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%~~RNN~~, or any non-integer value therebetween)~~ identity to the amino acid sequences set forth in SEQ ID NOs.: (i) 38 and 62, respectively; (ii) 38 and 59, respectively; (iii) 38 and 60,

respectively; (iv) 38 and 61, respectively; (v) 38 and 58, respectively; (vi) 38 and 63, respectively; (vii) 38 and 64, respectively; (viii) 38 and 65, respectively; (ix) 38 and 66, respectively; (x) 38 and 71, respectively; or (xi) 38 and 72, respectively.

~~10. An antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region (VH) that comprises or consists of the amino acid sequence of SEQ ID NO.:38 or 39, and a light chain variable region (VL) that comprises a variant of any one of SEQ ID NOs.:62, 57-61, and 63-72, wherein the variant comprises any one or more of the following mutations: R60A; R60N; R60K; S64A; and I74A, and wherein, optionally, the VL variant does not comprise any further mutations as compared to SEQ ID NO.:62, 57-61, and 63-72, respectively.~~

~~11. An antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region (VH) that comprises or consists of the amino acid sequence of SEQ ID NO.:38 or 39, and a light chain variable region (VL) that comprises a variant of any one of SEQ ID NOs.:62, 57-61, and 63-72, wherein the variant comprises a substitution mutation (such as, for example, a conservative amino acid substitution, or a mutation to a germline-encoded amino acid) at Q78, D81, or both, and wherein, optionally, the VL variant does not comprise any further mutations as compared to SEQ ID NO.:62, 57-61, and 63-72, respectively.~~

~~12. The antibody or antigen-binding fragment of any one of claims 1-9, wherein: the VH comprises or consists of the amino acid sequence set forth in SEQ ID NO.: 38 or 39; and/or the VL comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.: 62, 58-61, 63-66, 69, 71, or 72.~~

~~13~~3. The antibody or antigen-binding fragment of any one of claims 1 or 2~~-9 and 12~~, wherein the VH and the VL comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:

(i) 38 and 62, respectively;

(ii) 38 and 59, respectively;

(iii) 38 and 60, respectively;

(iv) 38 and 61, respectively;

(v) 38 and 58, respectively;

(vi) 38 and 63, respectively;

(vii) 38 and 64, respectively;

(viii) 38 and 65, respectively;

(ix) 38 and 66, respectively;

(x) 38 and 71, respectively; or

(xi) 38 and 72, respectively.

~~14~~4. An antibody or antigen-binding fragment, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and the VL comprise or consist of the amino acid sequences set forth in SEQ ID NOs.:

(i) 38 and 62, respectively;

(ii) 38 and 66, respectively;

(iii) 38 and 67, respectively;

(iv) 38 and 68, respectively; or

(v) 38 and 72, respectively,

wherein the antibody or antigen-binding fragment thereof is capable of binding to the antigenic loop region of HBsAg and neutralizing infection by a hepatitis B virus (HBV) of genotype D, A, B, C, E, F, G, H, I, or J, or any combination thereof.

~~15~~5. The antibody or antigen-binding fragment of any one of claims 1-~~1~~4, which is capable of neutralizing infection by a hepatitis D virus (HDV).

~~16~~6. The antibody or antigen-binding fragment of any one of claims 1-~~1~~5, wherein, in a sample comprising a plurality of the antibody or antigen-binding fragment, less than 12%, 11% or less, 10% or less, 9% or less, 8% or less, 7% or less, 6% or less, 5% or less, 4% or less, 3% or less, or 2% or less of the plurality is

comprised in a dimer when the sample has been incubated for ~~about~~ 120 to ~~about~~ 168 hours at about 40ºC, wherein~~, optionally,~~ the presence of dimer is determined by absolute size-exclusion chromatography; and/or~~.~~

~~17. The antibody or antigen-binding fragment of any one of claims 1-16,~~ wherein incubation of a plurality of the antibody or antigen-binding fragment results in reduced formation of a dimer as compared to incubation of a plurality of a reference antibody or antigen-binding fragment,

wherein the reference antibody or antigen-binding fragment ~~comprises CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to the amino acid sequences set forth in SEQ ID NOs.:34, 35, 37, 41, 44, and 55, respectively, and optionally~~ comprises the VH amino acid sequence set forth in SEQ ID NO.:38 and the VL amino acid sequence set forth in SEQ ID NO.:57,

and wherein~~, optionally,~~ the presence of antibody dimer is determined by absolute size-exclusion chromatography.

~~18~~7. The antibody or antigen-binding fragment of any one of claims 1-~~617~~, which forms a lower amount of dimer, and/or forms dimers at a reduced frequency and/or as a lower percentage of total antibody or antigen-binding fragment molecules in a sample or composition as compared to a reference antibody:

(i) in a 5-day, a 15-day, and/or a 32-day incubation at 4◦C;

(ii) in a 5-day, a 15-day, and/or a 32-day incubation at 25◦C; and/or

(iii) in a 5-day, a 15-day, and/or a 32-day incubation at 40◦C,

wherein the reference antibody or antigen-binding fragment ~~comprises CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to the amino acid sequences set forth in SEQ ID NOs.:34, 35, 37, 41, 44, and 55, respectively, and optionally~~ comprises the VH amino acid sequence set forth in SEQ ID NO.:38 and the VL amino acid sequence set forth in SEQ ID NO.:57.

~~19. The antibody or antigen-binding fragment of any one of claims 1-18, wherein a percentage of antibody or antigen-binding fragment molecules in a~~

composition that are comprised in a dimer is less than 4/5, less than 3/4, less than 1/2, less than 1/3, less than 1/4, less than 1/5, less than 1/6, less than 1/7, less than 1/8, less than 1/9, or less than 1/10 the percentage of reference antibody molecules in a composition that are present in a dimer, respectively.

20. The antibody or antigen-binding fragment of any one of claims 1-19, wherein a host cell transfected with a polynucleotide encoding the antibody or antigen-binding fragment provides 1.5x or more, 2x or more, 3x or more, or 4x or more the amount of antibody or antigen-binding fragment, respectively, than a reference host cell transfected with a polynucleotide encoding a reference antibody or antigen-binding fragment, wherein the reference antibody or antigen-binding fragment comprises CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to the amino acid sequences set forth in SEQ ID NOs.:34, 35, 37, 41, 44, and 55, respectively, and optionally comprises the VH amino acid sequence set forth in SEQ ID NO.:38 and the VL amino acid sequence set forth in SEQ ID NO.:57.

21. The antibody or antigen-binding fragment of any one of claims 1-20, wherein the antibody or antigen-binding fragment thereof is produced in transfected cells at a higher titer as compared to a reference antibody or antigen-binding fragment is produced in reference transfected cells, wherein the reference antibody or antigen-binding fragment comprises CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to the amino acid sequences set forth in SEQ ID NOs.:34, 35, 37, 41, 44, and 55, respectively, and optionally comprises the VH amino acid sequence set forth in SEQ ID NO.:38 and the VL amino acid sequence set forth in SEQ ID NO.:57.

22. The antibody or antigen-binding fragment of any one of claims 1-21, wherein the antibody or antigen-binding fragment thereof is produced in transfected cells at titers of at least 1.5-fold, at least 2-fold, at least 3-fold, or at least 4-fold, higher than the titer at which a reference antibody or antigen-binding fragment is produced,

~~wherein the reference antibody or antigen-binding fragment comprises CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to the amino acid sequences set forth in SEQ ID NOs.:34, 35, 37, 41, 44, and 55, respectively, and optionally comprises the VH amino acid sequence set forth in SEQ ID NO.:38 and the VL amino acid sequence set forth in SEQ ID NO.:57.~~

~~23~~8. The antibody or antigen-binding fragment of any one of claims 1-~~72~~2, wherein the antibody or antigen-binding fragment is capable of binding to a HBsAg (adw) with an EC50 (ng/ml) of about 3.2 or less, less than 3.0, less than 2.5, less than 2.0, less than 1.5, or less than 1.0.

~~24. The antibody or antigen-binding fragment of any one of claims 1-23, wherein the antibody or antigen-binding fragment is capable of binding to a HBsAg (*e.g.*, of subtype adw) with an EC50 (ng/ml) of less than 3.5, less than 3.4, less than 3.3, less than 3.2, less than 3.1, less than 3.0, less than 2.9, less than 2.8, less than 2.7, less than 2.6, less than 2.5, less than 2.4, less than 2.3, less than 2.1, less than 2.0, less than 1.9, less than 1.8, less than 1.7, less than 1.6, less than 1.5, less than 1.4, less than 1.3, less than 1.2, less than 1.1, or less than 1.0.~~

~~25. The antibody or antigen-binding fragment of any one of claims 1-24, wherein the antibody or antigen-binding fragment is capable of binding to a HBsAg (*e.g.*, of subtype adw) with an EC50 (ng/ml) of between 0.9 and 2.0, or of between 0.9 and 1.9, or of between 0.9 and 1.8, or of between 0.9 and 1.7, or of between 0.9 and 1.6, or of between 0.9 and 1.5, or of between 0.9 and 1.4, or of between 0.9 and 1.3, or of between 0.9 and 1.2, or of between 0.9 and 1.1, or of between 0.9 and 1.0, or of between 1.0 and 2.0.~~

~~26. The antibody or antigen-binding fragment of any one of claims 1-25, wherein the antibody or antigen-binding fragment is capable of binding to a HBsAg (adw) with an EC50 (ng/ml) of 2.0 or less.~~

~~27. The antibody or antigen-binding fragment of any one of claims 1-26, which has a hepatitis B virus neutralization of infection EC50 of less than 20 ng/ml, preferably 15 ng/ml or less, more preferably 10 ng/mL or less.~~

~~28. The antibody or antigen-binding fragment of any one of claims 1-27, wherein the antibody or antigen-binding fragment thereof is capable of neutralizing hepatitis B virus infection with a neutralization of infection EC50 of 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, or 7 ng/mL.~~

~~29. The antibody or antigen-binding fragment of any one of claims 1-28, wherein the antibody or antigen-binding fragment thereof is capable of neutralizing hepatitis B virus infection with a neutralization of infection EC50 that is lower than the neutralization of infection EC50 of a reference antibody or antigen-binding fragment that comprises CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences according to the amino acid sequences set forth in SEQ ID NOs.:34, 35, 37, 41, 44, and 55, respectively, and optionally comprises the VH amino acid sequence set forth in SEQ ID NO.:38 and the VL amino acid sequence set forth in SEQ ID NO.:57.~~

~~30~~9. The antibody or antigen-binding fragment of any one of claims 1-~~8~~29, wherein the antibody, or the antigen-binding fragment thereof, comprises a human antibody, a monoclonal antibody, a purified antibody, a single chain antibody, a Fab, a Fab', a F(ab')2, a Fv, or a scFv.

~~31~~10. The antibody or antigen-binding fragment of any one of claims 1-~~9~~30, wherein the antibody or antigen-binding fragment is a multi-specific ~~antibody or antigen-binding fragment.~~

~~32. The antibody or antigen-binding fragment of any one of claims 1-31, wherein the antibody or antigen-binding fragment is~~ or a bispecific antibody or antigen-binding fragment.

~~33~~11. The antibody of any one of claims 1-10~~32~~, or an antigen-binding fragment thereof, wherein the antibody or the antigen-binding fragment comprises a Fc moiety.

~~34~~12. The antibody or antigen-binding fragment of claim 11~~33~~, wherein the Fc moiety comprises a mutation that enhances binding to FcRn as compared to a reference Fc moiety that does not comprise the mutation.

~~35~~13. The antibody or antigen-binding fragment of claim 11~~33~~ or 12~~34~~, wherein the Fc moiety comprises a mutation that enhances binding to a FcγR~~, preferably a FcγRIIA and/or a FcγRIIIA,~~ as compared to a reference Fc moiety that does not comprise the mutation.

~~36~~14. The antibody or antigen-binding fragment of any one of claims 11-13~~33-35~~, wherein the Fc moiety is an IgG isotype, ~~such as IgG1,~~ or is derived from an IgG isotype~~, such as IgG1~~.

~~37~~15. The antibody or antigen-binding fragment of any one of claims 11-14~~33-36~~, which comprises or is derived from Ig G1m17, 1 (IgHG1*01).

~~38~~16. The antibody or antigen-binding fragment of any one of claims 12-15~~34-37~~, wherein the mutation that enhances binding to FcRn comprises:

(i) M428L/N434S;
(ii) M252Y/S254T/T256E;
(iii) T250Q/M428L;
(iv) P257I/Q311I;
(v) P257I/N434H;
(vi) D376V/N434H;
(vii) T307A/E380A/N434A; or
(viii) any combination of (i)-(vii),

wherein amino acid numbering of the Fc moiety is according to the EU numbering system.

~~39~~17. The antibody or antigen-binding fragment of claim 16~~38~~, wherein the mutation that enhances binding to FcRn comprises M428L/N434S.

~~40~~18. The antibody or antigen-binding fragment of any one of claims 13-17~~35-39~~, wherein the mutation that enhances binding to a FcγR comprises S239D; I332E; A330L; G236A; or any combination thereof, wherein amino acid numbering of the Fc moiety is according to the EU numbering system.

~~41~~19. The antibody or antigen-binding fragment of claim ~~40~~18, wherein the mutation that enhances binding to a FcγR comprises:

(i) S239D/I332E;

(ii) S239D/A330L/I332E;

(iii) G236A/S239D/I332E; or

(iv) G236A/A330L/I332E.

~~42~~20. The antibody or antigen-binding fragment of claim ~~40~~ 18 or ~~41~~19, wherein the mutation that enhances binding to a FcγR comprises or consists of G236A/A330L/I332E, and optionally wherein the antibody or antigen-binding fragment does not comprise S239D, and wherein the antibody or antigen-binding fragment further optionally comprises a native S at position 239.

~~43~~21. The antibody or antigen-binding fragment of any one of claims ~~33-42~~11-20, wherein the Fc moiety comprises the amino acid substitution mutations: M428L; N434S; G236A; A330L; and I332E, and optionally does not comprise S239D.

~~44~~22. The antibody or antigen-binding fragment of any one of claims 1-~~43~~21, comprising a light chain constant region (CL) that comprises or consists of an amino

acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the amino acid sequence of SEQ ID NO.:79.

~~45~~23. The antibody or antigen-binding fragment of any one of claims 1-~~44~~22, comprising a CH1-CH2-CH3 that comprises or consists of an amino acid sequence having 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the amino acid sequence of SEQ ID NO.:73, or a variant thereof that comprises one or more of the following amino acid substitutions (EU numbering): G236A; A330L; I332E; M428L; N434S.

~~46~~24. The antibody or antigen-binding fragment of claim ~~45~~23, wherein the CH1-CH2-CH3 has a C-terminal lysine removed.

~~47~~25. An antibody comprising: a heavy chain (HC) comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:75, optionally with the C-terminal lysine removed; and a light chain (LC), wherein the LC comprises or consists of (i) the VL amino acid sequence set forth in any one of SEQ ID NOs.:62, 58-61, and 63-72 and (ii) the CL amino acid sequence set forth in SEQ ID NO.:79.

~~48~~26. The antibody of claim ~~47~~25, wherein the LC comprises the VL amino acid sequence set forth in any one of SEQ ID NOs.:62, 66, 67, and 72.

~~49~~27. An antibody comprising: a heavy chain (HC) comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:76, optionally with the C-terminal lysine removed, and a light chain (LC), wherein the LC comprises or consists of (i) the VL amino acid sequence set forth in any one of SEQ ID NOs.:62, 58-61, and 63-72 and (ii) the CL amino acid sequence set forth in SEQ ID NO.:79.

~~50~~28. The antibody of claim ~~49~~27, wherein the LC comprises the VL amino acid sequence set forth in any one of SEQ ID NOs.:62, 66, 67, and 72.

~~51~~29. An antibody comprising: a heavy chain (HC) comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:77, optionally with the C-terminal lysine removed, and a light chain (LC), wherein the LC comprises or consists of (i) the VL amino acid sequence set forth in any one of SEQ ID NOs.:62, 58-61, and 63-72 and (ii) the CL amino acid sequence set forth in SEQ ID NO.:79.

~~52~~30. The antibody of claim ~~51~~29, wherein the LC comprises the VL amino acid sequence set forth in any one of SEQ ID NOs.:62, 66, 67, and 72.

~~53~~31. An antibody comprising: a heavy chain (HC) comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:78, optionally with the C-terminal lysine removed, and a light chain (LC), wherein the LC comprises or consists of (i) the VL amino acid sequence set forth in any one of SEQ ID NOs.:62, 58-61, and 63-72 and (ii) the CL amino acid sequence set forth in SEQ ID NO.:79.

~~54~~32. The antibody of claim ~~53~~31, wherein the LC comprises the VL amino acid sequence set forth in any one of SEQ ID NOs.:62, 66, 67, and 72.

~~55. The antibody or antigen-binding fragment of any one of claims 1-54, wherein the antibody or the antigen-binding fragment is capable of binding an HBsAg of a genotype selected from the HBsAg genotypes A, B, C, D, E, F, G, H, I, and J, or any combination thereof.~~

~~56. The antibody or antigen-binding fragment of any one of claims 1-55, wherein the antibody or antigen-binding fragment is capable of reducing a serum concentration of HBV DNA in a mammal having an HBV infection.~~

~~57. The antibody or antigen-binding fragment of any one of claims 1-56, wherein the antibody or antigen-binding fragment is capable of reducing a serum concentration of HBsAg in a mammal having an HBV infection.~~

~~58. The antibody or antigen binding fragment of any one of claims 1-57, wherein the antibody or antigen-binding fragment is capable of reducing a serum concentration of HBeAg in a mammal having an HBV infection.~~

~~59. The antibody or antigen binding fragment of any one of claims 1-58, wherein the antibody or antigen-binding fragment is capable of reducing a serum concentration of HBcrAg in a mammal having an HBV infection.~~

~~60~~33. A polynucleotide comprising a nucleotide sequence that encodes the antibody, or the antigen-binding fragment, of any one of claims 1-~~59~~32.

~~61~~34. A polynucleotide encoding a light chain variable region (VL) and, optionally, a light chain constant domain (CL) of the antibody, or the antigen-binding fragment, of any one of claims 1-~~59~~32.

~~62~~35. The polynucleotide of claim ~~60~~ 33 or ~~61~~34, wherein the nucleotide sequence that encodes the antibody or the antigen-binding fragment is codon optimized for expression in a host cell.

~~63~~36. The polynucleotide of claim ~~62~~35, comprising a nucleotide sequence having at least 50% identity to the nucleotide sequence according to any one of SEQ ID Nos.:89, 85-88, and 90-99.

~~64~~37. The polynucleotide of any one of claims ~~60-63~~33-36, comprising (i) the polynucleotide sequence set forth in SEQ ID NO.:81 or SEQ ID NO.:82, and (ii) the polynucleotide sequence set forth in any one or more of SEQ ID NOs.:89, 85-88, and 90-99.

~~65~~38. The polynucleotide of any one of claims ~~60-63~~33-36, comprising (i) the polynucleotide sequence set forth in SEQ ID NO.:83, and (ii) the polynucleotide sequence set forth in any one or more of SEQ ID NOs.:89, 85-88, and 90-99.

~~66~~39. The polynucleotide of any one of claims ~~60-63~~33-36, comprising (i) the polynucleotide sequence set forth in SEQ ID NO.:84, and (ii) the polynucleotide sequence set forth in any one or more of ~~of~~ SEQ ID NOs.:89, 85-88, and 90-99.

~~67~~40. A vector comprising the polynucleotide of any one of claims ~~60-66~~33-39.

~~68~~41. The vector of claim ~~67~~40, wherein the vector comprises a lentiviral vector or a retroviral vector.

~~69~~42. A host cell comprising the polynucleotide of any one of claims ~~60-66~~33-39 and/or the vector of claim ~~67-~~40 or ~~68~~41.

~~70~~43. A pharmaceutical composition comprising:

(i) the antibody or antigen binding fragment of any one of claims 1-~~59~~32;

(ii) the polynucleotide according to any one of claims ~~60-66~~33-39;

(iii) the vector according to claim ~~67-~~40 or ~~68~~41;

(iv) the host cell of claim ~~69~~42; or

(v) any combination of (i)-(iv),

and a pharmaceutically acceptable excipient, diluent or carrier.

~~71~~44. A kit comprising:

(a) a component selected from:

(i) the antibody or antigen-binding fragment of any one of claims 1-~~59~~32;

(ii) the polynucleotide according to any one of claims ~~60-66~~33-39;

(iii) the vector according to claim ~~67-~~40 or ~~68~~41;

(iv) the host cell of claim ~~69~~42;

(v) the pharmaceutical composition of claim ~~70~~43; or

(vi) any combination of (i)-(vi); and

(b) (1) instructions for using the component to prevent, treat, attenuate, and/or diagnose a hepatitis B virus infection and/or a hepatitis D virus infection and/or (2) a means for administering the component to the subject~~, such as a syringe~~.

~~72~~45. The composition of claim ~~70~~ 42 or the kit of claim ~~71~~44, further comprising:

(i) a polymerase inhibitor, wherein the polymerase inhibitor optionally comprises Lamivudine, Adefovir, Entecavir, Telbivudine, Tenofovir, or any combination thereof;

(ii) an interferon, wherein the interferon optionally comprises IFNbeta and/or IFNalpha;

(iii) a checkpoint inhibitor, wherein the checkpoint inhibitor optionally comprises an anti-PD-1 antibody or antigen binding fragment thereof, an anti-PD-L1 antibody or antigen binding fragment thereof, and/or an anti-CTLA4 antibody or antigen binding fragment thereof;

(iv) an agonist of a stimulatory immune checkpoint molecule; or

(v) any combination of (i)-(iv).

~~73. The composition or kit of claim 72, wherein the polymerase inhibitor comprises lamivudine.~~

~~74~~46. A method of producing the antibody or antigen binding fragment of any one of claims 1-~~59~~32, comprising culturing the host cell of claim ~~69~~ 42 under conditions and for a time sufficient to produce the antibody or antigen-binding fragment.

~~75~~47. Use of: (i) the antibody or antigen-binding fragment of any one of claims 1-~~59~~32; (ii) the polynucleotide of any one of claims ~~60-66~~33-39; (iii) the vector of claim ~~67-~~40 or 41~~68~~; (iv) the host cell of claim ~~69~~42; and/or (v) the pharmaceutical composition of claim ~~70, 72,~~43 or ~~73~~45, in the manufacture of a medicament to prevent, treat, attenuate, and/or diagnose a hepatitis B virus infection and/or a hepatitis D virus infection in a subject.

48. An antibody or antigen-binding fragment of any one of claims 1-32, the polynucleotide of any one of claims 33-39, the vector of claim 40 or 41, the host cell of claim 42, and/or the pharmaceutical composition of any one of claims 43 or 44 for use as a medicament.

~~76. A method of treating, preventing, and/or attenuating a hepatitis B and/or hepatitis D infection in a subject, comprising administering to the subject an effective amount of: (i) the antibody or antigen-binding fragment of any one of claims 1-59; (ii) the polynucleotide of any one of claims 60-66; (iii) the vector of claim 67 or 68; (iv) the host cell of claim 69; and/or (v) the pharmaceutical composition of claim 70, 72, or 73.~~

~~77. The method of claim 76, further comprising administering to the subject one or more of: (vi) a polymerase inhibitor, wherein the polymerase inhibitor optionally comprises Lamivudine, Adefovir, Entecavir, Telbivudine, Tenofovir, or any combination thereof; (vii) an interferon, wherein the interferon optionally comprises IFNbeta and/or IFNalpha; (viii) a checkpoint inhibitor, wherein the checkpoint inhibitor optionally comprises an anti-PD-1 antibody or antigen binding fragment thereof, an anti-PD-L1 antibody or antigen binding fragment thereof, and/or an anti-CTLA4 antibody or antigen binding fragment thereof; (ix) an agonist of a stimulatory immune checkpoint molecule; or (x) any combination of (vi)-(ix).~~

~~78. The method of claim 76 or 77, wherein the hepatitis B infection is a chronic hepatitis B infection.~~

~~79. The method of any one of claims 76-78, wherein the subject has received a liver transplant.~~

~~80. The method of any one of claims 76-79, wherein the subject is non-immunized against hepatitis B.~~

~~81. The method of any one of claims 76-80, wherein the subject is a newborn.~~

~~82. The method of any one of claims 76-81, wherein the subject is undergoing or has undergone hemodialysis.~~

~~8349~~. The ~~method of any one of claims 76-82~~ use of claim 47, wherein the ~~method~~ use comprises that any one of the following is to be administered ~~administering~~ to the subject: a single dose of the medicament comprising the ~~a~~ pharmaceutical composition comprising the antibody or antigen-binding fragment; and/or~~.~~

~~84. The method of claim 83, wherein~~ the single dose of the medicament comprising the pharmaceutical composition comprises the antibody in a range from 2 to 18 mg/kg (subject body weight); and/or~~.~~

~~85. The method of claim 83 or 84, wherein~~ the single dose of the medicament comprising the pharmaceutical composition comprises up to 6 mg, up to 10 mg, up to 15 mg, up to 18 mg, up to 25 mg, up to 30 mg, up to 35 mg, up to 40 mg, up to 45 mg, up to 50 mg, up to 55 mg, up to 60 mg, up to 75 mg, up to 90 mg, up to 300 mg, up to 900 mg, or up to 3000 mg of the antibody,

or wherein the single dose of the medicament comprising the pharmaceutical composition comprises the antibody in an amount that is in a range from 1 mg to 3000 mg, or in a range from 5 mg to 3000 mg, or in a range from 10 mg to 3000 mg, or in a

range from 25 mg to 3000 mg, or in a range from 30 mg to 3000 mg, or in a range from 50 mg to 3000 mg, or in a range from 60 mg to 3000 mg, or in a range from 75 mg to 3000 mg, or in a range from 90 mg to 3000 mg, or in a range from 100 mg to 3000 mg, or in a range from 150 mg to 3000 mg, or in a range from 200 mg to 3000 mg, or in a range from 300 mg to 3000 mg, or in a range from 500 mg to 3000 mg, or in a range from 750 mg to 3000 mg, or in a range from 900 mg to 3000 mg, or in a range from 1500 mg to 3000 mg, or in a range from 2000 mg to 3000 mg,

or wherein the single dose of the medicament comprising the pharmaceutical composition comprises the antibody in an amount that is in a range from 1 mg to 900 mg, or in a range from 5 mg to 900 mg, or in a range from 10 mg to 900 mg, or in a range from 25 mg to 900 mg, or in a range from 30 mg to 900 mg, or in a range from 50 mg to 900 mg, or in a range from 60 mg to 900 mg, or in a range from 75 mg to 900 mg, or in a range from 90 mg to 900 mg, or in a range from 100 mg to 900 mg, or in a range from 150 mg to 900 mg, or in a range from 200 mg to 900 mg, or in a range from 300 mg to 900 mg, or in a range from 500 mg to 900 mg, or in a range from 750 mg to 900 mg,

or wherein the single dose of the medicament comprising the pharmaceutical composition comprises the antibody in an amount that is wherein the single dose of the pharmaceutical composition comprises the antibody in an amount that is in a range from 1 mg to 500 mg, or in a range from 5 mg to 500 mg, or in a range from 10 mg to 500 mg, or in a range from 25 mg to 500 mg, or in a range from 30 mg to 500 mg, or in a range from 50 mg to 500 mg, or in a range from 60 mg to 500 mg, or in a range from 75 mg to 500 mg, or in a range from 90 mg to 500 mg, or in a range from 100 mg to 500 mg, or in a range from 150 mg to 500 mg, or in a range from 200 mg to 500 mg, or in a range from 300 mg to 500 mg, or in a range from 400 mg to 500 mg,

or wherein the single dose of the medicament comprising the pharmaceutical composition comprises the antibody in an amount that is in a range from 1 mg to 300 mg, or in a range from 5 mg to 300 mg, or in a range from 10 mg to 300 mg, or in a range from 25 mg to 300 mg, or in a range from 30 mg to 300 mg, or in a range from 50 mg to 300 mg, or in a range from 60 mg to 300 mg, or in a range from 75 mg to 300

mg, or in a range from 90 mg to 300 mg, or in a range from 100 mg to 300 mg, or in a range from 150 mg to 300 mg, or in a range from 200 mg to 300 mg,

or wherein the single dose of the medicament comprising the pharmaceutical composition comprises the antibody in an amount that is in a range from 1 mg to 200 mg, or in a range from 5 mg to 200 mg, or in a range from 10 mg to 200 mg, or in a range from 25 mg to 200 mg, or in a range from 30 mg to 200 mg, or in a range from 50 mg to 200 mg, or in a range from 60 mg to 200 mg, or in a range from 75 mg to 200 mg, or in a range from 90 mg to 200 mg, or in a range from 100 mg to 200 mg, or in a range from 150 mg to 200 mg,

or wherein the single dose of the medicament comprising the pharmaceutical composition comprises the antibody in an amount that is in a range from 1 mg to 100 mg, or in a range from 5 mg to 100 mg, or in a range from 10 mg to 100 mg, or in a range from 25 mg to 100 mg, or in a range from 30 mg to 100 mg, or in a range from 50 mg to 100 mg, or in a range from 60 mg to 100 mg, or in a range from 75 mg to 100 mg, or in a range from 75 mg to 100 mg, or in a range from 90 mg to 100 mg,

or wherein the single dose of the medicament comprising the pharmaceutical composition comprises the antibody in an amount that is in a range from 1 mg to 25 mg, or in a range from 5 mg to 25 mg, or in a range from 10 mg to 25 mg, or in a range from 15 mg to 25 mg, or in a range from 20 mg to 25 mg,

or wherein the single dose of the medicament comprising the pharmaceutical composition comprises the antibody in an amount that is in a range from 1 mg to 50 mg, or in a range from 1 mg to 25 mg, or in a range from 5 mg to 50 mg, or in a range from 5 mg to 25 mg, or in a range from 10 to 50 mg, or in a range from 10 to 25 mg, or in a range from 1 to 15 mg, or in a range from 5 mg to 15 mg, or in a range from 10 mg to 15 mg,or wherein the single dose of the medicament comprising the pharmaceutical composition comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, 255, 260, 265, 270, 275, 280, 285, 290, 295, 300, 305, 310, 315, 320, 325, 330, 335, 340, 345, 350, 355, 360, 365, 370, 375, 380,

385, 390, 395, 400, 405, 410, 415, 420, 425, 430, 435, 440, 445, 450, 455, 460, 465, 470, 475, 480, 485, 490, 495, 500, 505, 510, 515, 520, 525, 530, 535, 540, 545, 550, 555, 560, 565, 570, 575, 580, 585, 590, 595, 600, 605, 610, 615, 620, 625, 630, 635, 640, 645, 650, 655, 660, 665, 670, 675, 680, 685, 690, 695, 700, 705, 710, 715, 720, 725, 730, 735, 740, 745, 750, 755, 760, 765, 770, 775, 780, 785, 790, 795, 800, 805, 810, 815, 820, 825, 830, 835, 840, 845, 850, 855, 860, 865, 870, 875, 880, 885, 890, 895, 900, 905, 910, 915, 920, 925, 930, 935, 940, 945, 950, 955, 960, 965, 970, 975, 980, 985, 990, 995, or 1000 mg, or more, of the antibody,

or wherein the single dose of the medicament comprising the pharmaceutical composition comprises the antibody in an amount that is less than 3000 mg, less than 2500 mg, less than 2000 mg, less than 1500 mg, less than 1000 mg, less than 900 mg, less than 500 mg, less than 300 mg, less than 200 mg, less than 100 mg, less than 90 mg, less than 75 mg, less than 50 mg, less than 25 mg, or less than 10 mg, but is more than 1 mg, more than 2 mg, more than 3 mg, more than 4 mg, or more than 5 mg; and/or.

~~86. The method of any one of claims 83-85, wherein~~ the single dose of the medicament comprising the pharmaceutical composition comprises the antibody at a concentration in a range from 100 mg/mL to 200 mg/mL~~, such as 100 mg/mL, 110 mg/mL, 120 mg/mL, 130 mg/mL, 140 mg/mL, 150 mg/mL, 160 mg/mL, 170 mg/mL, 180 mg/mL, 190 mg/mL, or 200 mg/mL, preferably 150 mg/mL~~.

~~87. The method of any one of claims 83-86, wherein the single dose of the pharmaceutical composition comprises about 75 mg of the antibody.~~

~~88. The method of any one of claims 83-87, wherein the single dose of the pharmaceutical composition comprises about 90 mg of the antibody.~~

~~89. The method of any one of claims 83-88, wherein the single dose of the pharmaceutical composition comprises up to 300 mg of the antibody.~~

~~90. The method of any one of claims 83-89, wherein the single dose of the pharmaceutical composition comprises up to 900 mg of the antibody.~~

~~91. The method of any one of claims 83-90, wherein the single dose of the pharmaceutical composition comprises up to 3,000 mg of the antibody.~~

~~92. The method of any one of claims 83-91, wherein the method comprises administering the single dose by subcutaneous injection, optionally wherein the single dose comprises or consists of 6 mg of the antibody or 18 mg of the antibody.~~

~~93. The method of any one of claims 83-92, wherein the method comprises administering the single dose by intravenous injection.~~

~~94. The method of any one of claims 83-93, wherein the pharmaceutical composition further comprises water, optionally USP water.~~

~~95. The method of any one of claims 83-94, wherein the pharmaceutical composition further comprises histidine, optionally at a concentration in a range from 10 mM to 40 mM, such as 20 mM, in the pharmaceutical composition.~~

~~96. The method of any one of claims 83-95, wherein the pharmaceutical composition further comprises a disaccharide, such as sucrose, optionally at 5%, 6%, 7%, 8%, or 9%, preferably about 7% (w/v).~~

~~97. The method of any one of claims 83-96, wherein the pharmaceutical composition further comprises a surfactant or a triblock copolymer, optionally a polysorbate or poloxamer-188, preferably polysorbate 80 (PS80), wherein, optionally, the polysorbate or poloxamer-188 is present in a range from 0.01% to 0.05% (w/v), preferably 0.02% (w/v).~~

98. The method of any one of claims 83-97, wherein the pharmaceutical composition has a pH in a range from 5.8 to 6.2, in a range from 5.9 to 6.1, or of 5.8, of 5.9, of 6.0, of 6.1, or of 6.2.

99. The method of claim 98, wherein the pharmaceutical composition comprises:

(i) the antibody at 150 mg/mL;

(ii) USP water;

(iii) 20 mM histidine;

(iv) 7% sucrose; and

(v) 0.02% PS80,

wherein the pharmaceutical composition comprises a pH of 6.

100. The method of any one of claims 83-99, wherein the subject is an adult.

101. The method of claim 100, wherein the subject is in a range from 18 years of age to 65 years of age.

102. The method of any one of claims 83-101, wherein the subject weighs from 40 kg to 125 kg and/or the subject has a body mass index (BMI) from 18 to 35 kg/m^2.

103. The method of any one of claims 83-102, wherein the subject has a chronic HBV infection; *e.g.*, defined by positive serum HBsAg, HBV DNA, and/or HBeAg on 2 occasions, wherein the 2 occasions are at least 6 months apart.

104. The method of any one of claims 83-103, wherein the subject does not have cirrhosis.

~~105. The method of claim 104, wherein absence of cirrhosis is determined by:~~

~~Fibroscan evaluation (*e.g.*, within 6 months prior to administering the single dose of the pharmaceutical composition); or~~

~~liver biopsy (*e.g.*, within 12 months prior to administering the single dose of the pharmaceutical composition),~~

~~wherein, preferably the absence of cirrhosis is determined by the absence of Metavir F3 fibrosis or the absence of F4 cirrhosis.~~

~~106. The method of any one of claims 83-105, wherein the subject has received a nucleos(t)ide reverse transcriptase inhibitor (NRTI), optionally within 120 days, further optionally within 60 days, prior to the single dose being administered.~~

~~107. The method of claim 106, wherein the NRTI comprises one or more of: tenofovir; tenofovir disoproxil (e.g., tenofovir disproxil fumarate); tenofovir alafenamide; Entecavir; Lamivudine; Adefovir; and adefovir dipivoxil.~~

~~108. The method of any one of claims 83-107, wherein the subject has a serum HBV DNA concentration of less than 100 IU/mL no more than 28 days prior to the single dose being administered.~~

~~109. The method of any one of claims 83-108, wherein the subject has a serum HBsAg concentration of less than 3,000 IU/mL prior to the single dose being administered, and optionally less than 1,000 IU/mL prior to the single dose being administered.~~

~~110. The method of any one of claims 83-109, wherein the subject has a serum HBsAg concentration of greater than or equal to 3,000 IU/mL no more than 28 days prior to the single dose being administered, and optionally greater than or equal to 1,000 IU/mL no more than 28 days prior to the single dose being administered.~~

~~111. The method of any one of claims 83-110, wherein the subject was HB e-antigen (HBeAg) negative no more than 28 days prior to the single dose being administered.~~

~~112. The method of any one of claims 83-111, wherein the subject was negative for anti-HB antibodies no more than 28 days prior to the single dose being administered.~~

~~113. The method of any one of claims 83-112, wherein the subject, prior to administration of the single dose:~~

~~(i) does not have fibrosis and/or does not have cirrhosis; and/or~~

~~(ii) has alanine aminotransferase (ALT) < 2 x Upper Limit of Normal (ULN).~~

~~114. The method of any one of claims 83-113, wherein at 56 days following administration of the single dose, the subject has a > 2-fold reduction in serum HBsAg (e.g., concentration of HBsAg in serum, e.g., as determined using an Abbott ARCHITECT assay) as compared to the subject's serum HBsAg at from 0 days to 28 days prior to administration of the single dose.~~

~~115. The method of any one of claims 83-114, wherein following administration of the single dose (e.g., at 56 days following administration of the single dose), the subject has:~~

~~(i) has reduced or less severe intrahepatic spread of HBV as compared to a reference subject; and/or~~

~~(ii) comprises an adaptive immune response against HBV.~~

~~116. The method of any one of claims 83-115, wherein the subject is male.~~

~~117. The method of any one of claims 83-115, wherein the subject is female.~~

~~118~~50. A pharmaceutical composition comprising the antibody or antigen-binding fragment of any one of claims 1-~~32~~59 at a concentration ranging from 100 mg/mL to 200 mg/mL, ~~such as 100 mg/mL, 110 mg/mL, 120 mg/mL, 130 mg/mL, 140 mg/mL, 150 mg/mL, 160 mg/mL, 170 mg/mL, 180 mg/mL, 190 mg/mL, or 200 mg/mL, preferably 150 mg/mL~~and a pharmaceutically acceptable carrier, excipient, or diluent.

~~119. The pharmaceutical composition of claim 118, wherein the pharmaceutical composition comprises up to 6 mg, up to 18 mg, up to 75 mg, up to 90 mg, up to 300 mg, up to 900 mg, or up to 3000 mg of the antibody.~~

~~120. The pharmaceutical composition of claim 118 or 119, wherein the pharmaceutical composition comprises about 75 mg of the antibody.~~

~~121. The pharmaceutical composition of claim 118 or 119, wherein the pharmaceutical composition comprises about 90 mg of the antibody.~~

~~122. The pharmaceutical composition of claim 118 or 119, wherein the pharmaceutical composition comprises about 300 mg of the antibody.~~

~~123. The pharmaceutical composition of claim 118 or 119, wherein the pharmaceutical composition comprises about 900 mg of the antibody.~~

~~124. The pharmaceutical composition of claim 118 or 119, wherein the pharmaceutical composition comprises about 3,000 mg of the antibody.~~

~~125~~51. The pharmaceutical composition of ~~any one of claims 118-124~~claim 50, wherein the pharmaceutical composition comprises water, optionally USP water; and/or.

~~126. The pharmaceutical composition of any one of claims 118-125, wherein~~ the pharmaceutical composition comprises histidine, optionally at a concentration from 10 mM to 40 mM~~, such as 20 mM,~~ in the pharmaceutical composition~~.~~;and/or

~~127. The pharmaceutical composition of any one of claims 118-126, wherein~~ the pharmaceutical composition comprises a disaccharide, ~~such as sucrose,~~ optionally at 5%, 6%, 7%, 8%, or 9%~~, preferably about 7% (w/v).~~; and/or

~~128. The pharmaceutical composition of any one of claims 118-127, wherein~~ the pharmaceutical composition comprises a surfactant, optionally a polysorbate, ~~preferably polysorbate 80 (PS80),~~ wherein, optionally, the polysorbate is present in a range from 0.01% to 0.05% (w/v)~~, preferably 0.02% (w/v).~~; and/or

~~129. The pharmaceutical composition of any one of claims 118-128, wherein~~ the pharmaceutical composition has a pH ranging from 5.8 to 6.2, ranging from 5.9 to 6.1, or of 5.8, of 5.9, of 6.0, of 6.1, or of 6.2.

~~130~~52. The pharmaceutical composition of any one of claims ~~118-129~~50 or 51, wherein the pharmaceutical composition comprises:

(i) the antibody at 150 mg/mL;

(ii) USP water;

(iii) 20 mM histidine;

(iv) 7% sucrose; and

(v) 0.02% PS80,

wherein the pharmaceutical composition comprises a pH of 6.

~~131. The method of any one of claims 83-117, wherein following administration of the single dose, serum HBsAg of the subject is reduced as compared to baseline by 1.0 $\log^{10}$ IU/mL, 1.5 $\log^{10}$ IU/mL, or more, wherein, optionally, the reduction persists for 1, 2, 3, 4, 5, 6, 7, 8, or more days following administration of the single dose.~~

~~132. The method of any one of claims 83-117 and 131, wherein following administration of the single dose, serum HBsAg of the subject is reduced as compared to baseline for at least 8, at least 15, at least 22, or at least 29 days.~~

~~133~~53. A method for *in vitro* diagnosis of a hepatitis B virus ~~and/or a hepatitis D~~ infection, the method comprising:

(i) contacting a sample from a subject with an antibody or antigen-binding fragment of any one of claims 1-~~59~~32; and

(ii) detecting a complex comprising an antigen and the antibody, or comprising an antigen and the antigen-binding fragment.

~~134. The method of claim 133, wherein the sample comprises blood isolated from the subject.~~

~~135~~54. A method for detecting the presence or absence of an epitope in a correct conformation in an anti-hepatitis-B and/or an anti-hepatitis-D vaccine, the method comprising:

(i) contacting the vaccine with an antibody or antigen-binding fragment of any one of claims 1-~~59~~32; and

(ii) determining whether a complex comprising an antigen and the antibody, or comprising an antigen and the antigen binding fragment, has been formed.

~~136. The antibody or antigen-binding fragment of any one of claims 1-59, wherein the antibody or antigen-binding fragment:~~

~~(i) has enhanced binding to a human FcγRIIA, a human FcγRIIIA, or both, as compared to a reference polypeptide that includes a Fc moiety that does not comprise G236A/A330L/I332E, wherein the human FcγRIIA is optionally H131 or R131, and/or the human FcγRIIIA is optionally F158 or V158;~~

~~(ii) has reduced binding to a human FcγRIIB, as compared to a reference polypeptide that includes a Fc moiety that does not comprise G236A/A330L/I332E;~~

~~(iii) does not bind to a human FcγRIIB;~~

~~(iv) has reduced binding to a human C1q, as compared to a reference polypeptide that includes a Fc moiety that does not comprise G236A/A330L/I332E;~~

~~(v) does not bind to a human C1q; (vi) activates a FcγRIIA, a human FcγRIIIA, or both, to a greater degree than does a reference polypeptide that includes a Fc moiety that does not comprise G236A/A330L/I332E, wherein the human FcγRIIA is optionally H131 or R131, and/or the human FcγRIIIA is optionally F158 or V158;~~

~~(vii) does not activate a human FcγRIIB;~~

~~(viii) activates a human natural killer (NK) cell in the presence of HBsAg to a greater degree than does a reference polypeptide that includes a Fc moiety that does not comprise G236A/A330L/I332E, wherein the reference polypeptide is optionally an antibody that binds to an HB Ag, optionally an HBsAg;~~

~~(ix) is capable of binding to an HBsAg variant comprising HBsAg-Y100C/P120T, HBsAg-P120T, HBsAg-P120S/S143L, HBsAg-C121S, HBsAg-R122D, HBsAg-R122I, HBsAg-T123N, HBsAg-Q129H, HBsAg-Q129L, HBsAg-M133H, HBsAg-M133L, HBsAg-M133T, HBsAg-K141E, HBsAg-P142S, HBsAg-S143K, HBsAg-D144A, HBsAg-G145R, HBsAg-N146A, or any combination thereof; and/or (x) has improved binding to an HBsAg variant comprising HBsAg-Y100C/P120T, HBsAg-P120T, HBsAg-P120S/S143L, HBsAg-C121S, HBsAg-R122D, HBsAg-R122I, HBsAg-T123N, HBsAg-Q129H, HBsAg-Q129L, HBsAg-M133H, HBsAg-M133L, HBsAg-M133T, HBsAg-K141E, HBsAg-P142S, HBsAg-S143K, HBsAg-D144A, HBsAg-G145R, HBsAg-N146A, or any combination thereof, as compared to a reference antibody or antigen binding fragment that binds to HBsAg and that includes a Fc moiety that does not comprise G236A/A330L/I332E.~~

~~137~~55. Use of an anti-HBV antibody from any one of claims 1-32 in the manufacture of a medicament for ~~A method of~~ treating chronic HBV infection in a subject in need thereof, wherein the anti-HBV antibody is to be administered to the subject with ~~comprising:~~

~~administering to the subject~~ an agent that reduces HBV antigenic load; and/or

~~administering to the subject an anti-HBV antibody from any one of claims 1-59.~~

~~138. A method of treating chronic HBV infection in a subject in need thereof, comprising:~~

~~administering to the subject~~ an inhibitor of HBV gene expression; ~~and~~

~~administering to the subject an anti-HBV antibody from any one of claims 1-59.~~wherein the agent that reduces HBV antigenic load and/or the inhibitor of HBV gene expression is an RNAi agent that inhibits expression of an HBV transcript.

~~139~~56. The ~~method~~use according to claim~~s 137 or 138~~55, wherein the RNAi agent comprises a sense strand and an antisense strand forming a double-stranded region, wherein the sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from nucleotides 1579-1597 of SEQ ID NO:116.

~~140. The method according to any one of claims 137-139, wherein the RNAi agent comprises a sense strand and an antisense strand, wherein the sense strand comprises nucleotides 1579-1597 of SEQ ID NO:116.~~

~~141. The method according to any one of claims 137-140, wherein at least one strand of the RNAi agent comprises a 3' overhang of at least 1 nucleotide.~~

~~142. The method according to any one of claims 137-140, wherein at least one strand of the RNAi agent comprises a 3' overhang of at least 2 nucleotides.~~

~~143~~57. The ~~method~~ use according to any one of claims ~~137-142~~55 or 56, wherein the double-stranded region of the RNAi agent is 15-30 nucleotide pairs in length, or wherein each strand of the RNAi agent has 15-30 nucleotides.

~~144. The method according to any one of claims 137-142, wherein the double-stranded region of the RNAi agent is 17-23 nucleotide pairs in length.~~

~~145. The method according to any one of claims 137-142, wherein the double-stranded region of the RNAi agent is 17-25 nucleotide pairs in length.~~

~~146. The method according to any one of claims 137-142, wherein the double-stranded region of the RNAi agent is 23-27 nucleotide pairs in length.~~

~~147. The method according to any one of claims 137-142, wherein the double-stranded region of the RNAi agent is 19-21 nucleotide pairs in length.~~

~~148. The method according to any one of claims 137-142, wherein the double-stranded region of the RNAi agent is 21-23 nucleotide pairs in length.~~

~~149. The method according to any one of claims 137-142, wherein each strand of the RNAi agent has 15-30 nucleotides.~~

~~150. The method according to any one of claims 137-142, wherein each strand of the RNAi agent has 19-30 nucleotides.~~

~~151~~58. The ~~method~~ use according to any one of the claims ~~137-150~~55-57, wherein the RNAi agent is an siRNA.

~~152~~59. The ~~method~~ use according to claim ~~151~~58, wherein (a)the siRNA inhibits expression of an HBV transcript that encodes an HBsAg protein, an HBcAg protein, and HBx protein, or an HBV DNA polymerase protein;~~.~~

~~153. The method according to claim 151 or claim 152, wherein~~ (b)the siRNA binds to at least 15 contiguous nucleotides of a target encoded by: P gene, nucleotides 2309-3182 and 1-1625 of NC_003977.2; S gene (encoding L, M, and S proteins), nucleotides 2850-3182 and 1-837 of NC_003977.2; HBx, nucleotides 1376-1840 of NC_003977.2; or C gene, nucleotides 1816-2454 of NC_003977.2;~~.~~

~~154. The method according to claim 151 or claim 152, wherein~~ (c) the siRNA that comprises an antisense strand, wherein the antisense strand of the siRNA comprises at least 15 contiguous nucleotides of the nucleotide sequence of 5'-UGUGAAGCGAAGUGCACACUU -3' (SEQ ID NO:119); and/or~~.~~

~~155. The method according to claim 151 or 152, wherein the antisense strand of the siRNA comprises at least 19 contiguous nucleotides of the nucleotide sequence of 5'- UGUGAAGCGAAGUGCACACUU -3' (SEQ ID NO:119).~~

~~156. The method according to claim 151 or 152, wherein the antisense strand of the siRNA comprises the nucleotide sequence of 5'- UGUGAAGCGAAGUGCACACUU -3' (SEQ ID NO:119).~~

~~157. The method according to claim 151 or 152, wherein the antisense strand of the siRNA consists of the nucleotide sequence of 5'- UGUGAAGCGAAGUGCACACUU -3' (SEQ ID NO:119).~~

~~158. The method according to any one of claims 154-157, wherein the sense strand of the siRNA comprises the nucleotide sequence of 5'- GUGUGCACUUCGCUUCACA -3' (SEQ ID NO:118).~~

~~159. The method according to any one of claims 154-157, wherein the sense strand of the siRNA consists of the nucleotide sequence of 5'- GUGUGCACUUCGCUUCACA -3' (SEQ ID NO:118).~~

~~160. The method according to claim 151 or 152,~~ (d) the siRNA that comprises an antisense strand, wherein the antisense strand of the siRNA comprises at least 15 contiguous nucleotides of the nucleotide sequence of 5'-UAAAAUUGAGAGAAGUCCACCAC -3' (SEQ ID NO:121).

~~161. The method according to claim 151 or 152, wherein the antisense strand of the siRNA comprises at least 19 contiguous nucleotides of the nucleotide sequence of 5'- UAAAAUUGAGAGAAGUCCACCAC -3' (SEQ ID NO:121).~~

~~162. The method according to claim 151 or 152, wherein the antisense strand of the siRNA comprises the nucleotide sequence of 5'-UAAAAUUGAGAGAAGUCCACCAC-3' (SEQ ID NO:121).~~

~~163. The method according to claim 151 or 152, wherein the antisense strand of the siRNA consists of the nucleotide sequence of 5'-UAAAAUUGAGAGAAGUCCACCAC-3' (SEQ ID NO:121).~~

~~164. The method according to any one of claims 154-157, wherein the sense strand of the siRNA comprises the nucleotide sequence of 5'-GGUGGACUUCUCUCAAUUUUA-3' (SEQ ID NO:120).~~

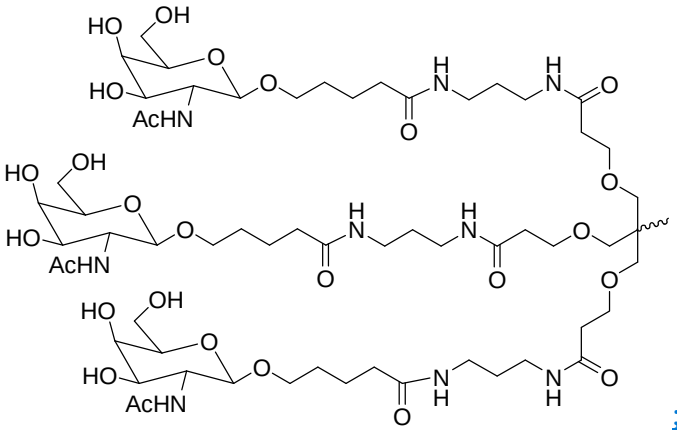
~~165. The method, composition for use, or use according to any one of claims 154-157, wherein the sense strand of the siRNA consists of the nucleotide sequence of 5'-GGUGGACUUCUCUCAAUUUUA-3' (SEQ ID NO:120).~~

~~166~~60. The ~~method~~ use according to any one of claims ~~151-165~~58-59, wherein substantially all of the nucleotides of said sense strand and substantially all of the nucleotides of said antisense strand are modified nucleotides, and

wherein said sense strand is conjugated to a ligand attached at the 3'-terminus.

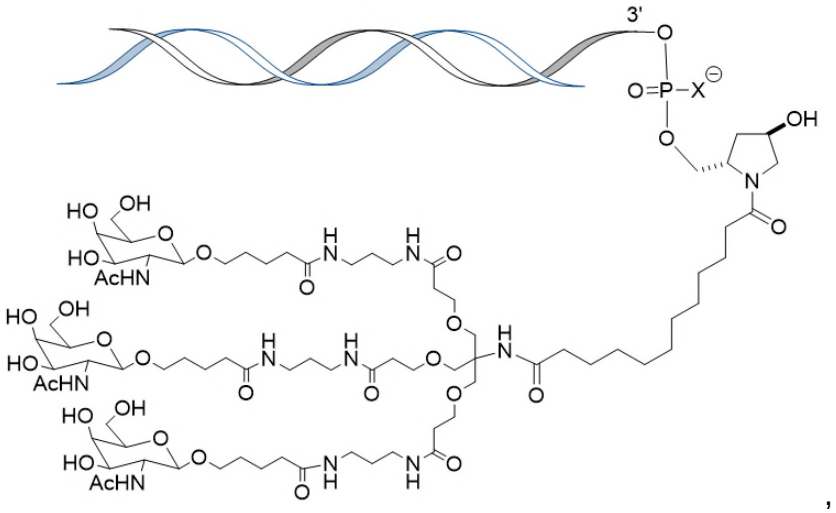
~~167~~61. The ~~method~~ use according to claim ~~166~~60, wherein (a) the ligand is one or more GalNAc derivatives attached through a monovalent linker, bivalent branched linker, or trivalent branched linker; or~~.~~

~~168. The method according to claim 166 or 167, wherein~~ (b) the ligand is



;or.

~~169. The method according to claim 168, wherein~~ the siRNA is conjugated to the ligand as shown in the following structure:



,

wherein X is O or S.

~~170~~62. The ~~method~~ use according to any one of claims ~~151-169~~58-61, wherein at least one nucleotide of the siRNA is a modified nucleotide comprising a deoxy-nucleotide, a 3'-terminal deoxy-thymine (dT) nucleotide, a 2'-O-methyl modified nucleotide, a 2'-fluoro modified nucleotide, a 2'-deoxy-modified nucleotide, a locked nucleotide, an unlocked nucleotide, a conformationally restricted nucleotide, a constrained ethyl nucleotide, an abasic nucleotide, a 2'-amino-modified nucleotide, a 2'-O-allyl-modified nucleotide, 2'-C-alkyl-modified nucleotide, 2'-hydroxyl-modified nucleotide, a 2'-methoxyethyl modified nucleotide, a 2'-O-alkyl-modified nucleotide, a

morpholino nucleotide, a phosphoramidate, a non-natural base comprising nucleotide, a tetrahydropyran modified nucleotide, a 1,5-anhydrohexitol modified nucleotide, a cyclohexenyl modified nucleotide, a nucleotide comprising a phosphorothioate group, a nucleotide comprising a methylphosphonate group, a nucleotide comprising a 5'-phosphate, an adenosine-glycol nucleic acid, or a nucleotide comprising a 5'-phosphate mimic; and/or.

~~171. The method according to any one of claims 151-169, wherein~~ the siRNA comprises a phosphate backbone modification, a 2' ribose modification, 5' triphosphate modification, or a GalNAc conjugation modification; and/or.

~~172. The method according to claim 171, wherein~~ the phosphate backbone modification comprises a phosphorothioate bond; and/or.

~~173. The method according to claim 171 or claim 172, wherein~~ the 2' ribose modification comprises a fluoro or -O-methyl substitution.

~~174~~63. The ~~method~~ use according to any one of claims ~~151-159 and 166-173~~58-62, wherein

(a) the siRNA has a sense strand comprising 5'-gsusguGfcAfCfUfucgcuucacaL96 -3' (SEQ ID NO:122) and an antisense strand comprising 5'- usGfsugaAfgCfGfaaguGfcAfcacsusu -3' (SEQ ID NO:123),

~~wherein a, c, g, and u are 2'-O-methyladenosine-3'-phosphate, 2'-O-methylcytidine-3'-phosphate, 2'-O-methylguanosine-3'-phosphate, and 2'-O-methyluridine-3'-phosphate, respectively;~~

~~Af, Cf, Gf, and Uf are 2'-fluoroadenosine-3'-phosphate, 2'-fluorocytidine-3'-phosphate, 2'-fluoroguanosine-3'-phosphate, and 2'-fluorouridine-3'-phosphate, respectively;~~

~~s is a phosphorothioate linkage; and~~

~~L96 is N-[tris(GalNAc-alkyl)-amidodecanoyl)]-4-hydroxyprolinol.~~

~~175. The method according to any one of claims 151-159 and 166-173, wherein~~ (b) the siRNA has a sense strand comprising 5'-gsusguGfcAfCfUfucgcuucacaL96 -3' (SEQ ID NO:124) and an antisense strand comprising 5'- usGfsuga(Agn)gCfGfaaguGfcAfcacsusu -3' (SEQ ID NO:125), and/or

~~wherein a, c, g, and u are 2'-O-methyladenosine-3'-phosphate, 2'-O-methylcytidine-3'-phosphate, 2'-O-methylguanosine-3'-phosphate, and 2'-O-methyluridine-3'-phosphate, respectively;~~

~~Af, Cf, Gf, and Uf are 2'-fluoroadenosine-3'-phosphate, 2'-fluorocytidine-3'-phosphate, 2'-fluoroguanosine-3'-phosphate, and 2'-fluorouridine-3'-phosphate, respectively;~~

~~(Agn) is adenosine-glycol nucleic acid (GNA);~~

~~s is a phosphorothioate linkage; and~~

~~L96 is N-[tris(GalNAc-alkyl)-amidodecanoyl)]-4-hydroxyprolinol.~~

~~176. The method, compositions for use, or use according to any one of claims 151-153 and 160-173, wherein~~(c) the siRNA has a sense strand comprising 5'-gsgsuggaCfuUfCfUfcucaAfUfuuuaL96 -3' (SEQ ID NO:126) and an antisense strand comprising 5'- usAfsaaaUfuGfAfgagaAfgUfccaccsasc -3' (SEQ ID NO:127); and ~~,~~

wherein a, c, g, and u are 2'-O-methyladenosine-3'-phosphate, 2'-O-methylcytidine-3'-phosphate, 2'-O-methylguanosine-3'-phosphate, and 2'-O-methyluridine-3'-phosphate, respectively;

Af, Cf, Gf, and Uf are 2'-fluoroadenosine-3'-phosphate, 2'-fluorocytidine-3'-phosphate, 2'-fluoroguanosine-3'-phosphate, and 2'-fluorouridine-3'-phosphate, respectively;

s is a phosphorothioate linkage; and

L96 is N-[tris(GalNAc-alkyl)-amidodecanoyl)]-4-hydroxyprolinol.

64. An antibody or antigen-binding fragment comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and the VL comprise or consist of the amino acid sequences set forth in SEQ ID NOs.: 38 and 62, respectively;

wherein the antibody or antigen-binding fragment thereof is capable of binding to the antigenic loop region of HBsAg and neutralizing infection by a hepatitis B virus (HBV) of genotype D, A, B, C, E, F, G, H, I, or J, or any combination thereof and/or capable of neutralizing infection by a hepatitis D virus (HDV).

65. An antibody or antigen-binding fragment, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and the VL comprise or consist of the amino acid sequences set forth in SEQ ID NOs.: 38 and 66, respectively;

wherein the antibody or antigen-binding fragment thereof is capable of binding to the antigenic loop region of HBsAg and neutralizing infection by a hepatitis B virus (HBV) of genotype D, A, B, C, E, F, G, H, I, or J, or any combination thereof and/or capable of neutralizing infection by a hepatitis D virus (HDV).

66. The antibody of claim 64 or 65, wherein the antibody comprises:

a heavy chain (HC) comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:76, and

a light chain constant region (CL) that comprises or consists of an amino acid sequence set forth in SEQ ID NO.:79.

67. The antibody of claim 64 or 65, wherein the antibody comprises:

a heavy chain (HC) comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:77, and

a light chain constant region (CL) that comprises or consists of an amino acid sequence set forth in SEQ ID NO.:79.

68. The antibody of claim 64 or 65, wherein the antibody comprises:

a heavy chain (HC) comprising or consisting of the amino acid sequence set forth in SEQ ID NO.:78, and

a light chain constant region (CL) that comprises or consists of an amino acid sequence set forth in SEQ ID NO.:79.

69. Use of an anti-HBV antibody from any one of claims 64-68 in the manufacture of a medicament for treating chronic HBV infection and/or HDV infection in a subject in need thereof.

70. Use of an anti-HBV antibody from any one of claims 64-68 in the manufacture of a medicament for treating chronic HBV infection and/or HDV infection in a subject in need thereof, wherein the anti-HBV antibody is to be administered to the subject with an siRNA, wherein the siRNA has a sense strand comprising 5'-gsusguGfcAfCfUfucgcuucacaL96 -3' (SEQ ID NO:124) and an antisense strand comprising 5'- usGfsuga(Agn)gCfGfaaguGfcAfcacsusu -3' (SEQ ID NO:125);

wherein a, c, g, and u are 2'-O-methyladenosine-3'-phosphate, 2'-O-methylcytidine-3'-phosphate, 2'-O-methylguanosine-3'-phosphate, and 2'-O-methyluridine-3'-phosphate, respectively;

Af, Cf, Gf, and Uf are 2'-fluoroadenosine-3'-phosphate, 2'-fluorocytidine-3'-phosphate, 2'-fluoroguanosine-3'-phosphate, and 2'-fluorouridine-3'-phosphate, respectively;

s is a phosphorothioate linkage; and

L96 is N-[tris(GalNAc-alkyl)-amidodecanoyl)]-4-hydroxyprolinol.

~~177. The method according to any one of claims 137-176, wherein the subject is a human and a therapeutically effective amount of RNAi agent or siRNA is administered to the subject; and wherein the effective amount of the RNAi agent or siRNA is from about 1 mg/kg to about 8 mg/kg.~~

~~178. The method according to any one of claims 137-177, wherein the RNAi agent or siRNA is administered to the subject twice daily, once daily, every two days, every three days, twice per week, once per week, every other week, every four weeks, or once per month.~~

~~179. The method according to any one of claims 137-177, wherein the RNAi agent or siRNA is administered to the subject every four weeks.~~

~~180. The method according to any one of claims 151-179, wherein two siRNAs each directed to an HBV gene are administered, and the first siRNA has an~~

antisense strand comprising SEQ ID NO:119, SEQ ID NO:120, or SEQ ID NO:126; and the second siRNA comprises an siRNA having a sense strand that comprises at least 15 contiguous nucleotides of nucleotides 2850-3182 of SEQ ID NO:116.

181. The method according to any one of claims 151-179, wherein two siRNAs directed to an HBV gene are administered, wherein the two siRNAs comprise: an siRNA directed to an HBV X gene and an siRNA directed to an HBV S gene.

182. The method according to any one of claims 151-179, wherein two siRNAs each directed to an HBV gene are administered, and the first siRNA has an antisense strand comprising SEQ ID NO:119, SEQ ID NO:123, or SEQ ID NO:125; and the second siRNA has an antisense strand that comprises SEQ ID NO:121 or SEQ ID NO:127.

183. The method according to claim 181, wherein the first siRNA has a sense strand comprising SEQ ID NO:118, SEQ ID NO:122, or SEQ ID NO:124; and the second siRNA has a sense strand comprising SEQ ID NO:120 or SEQ ID NO:126.

184. The method according to any one of claims 179-183, wherein the two siRNAs are administered simultaneously.

185. The method according to any one of the claims 137-184, further comprising administering a nucleot(s)ide analog to the subject, or wherein the subject is also administered a nucleot(s)ide analog.

186. The method, composition for use, or use according to claim 185, wherein the nucleot(s)ide analog is tenofovir disoproxil fumarate (TDF), tenofovir alafenamide (TAF), lamivudine, adefovir dipivoxil, entecavir (ETV), telbivudine, AGX-1009, emtricitabine (FTC), clevudine, ritonavir, dipivoxil, lobucavir, famvir, N-Acetyl-

~~Cysteine (NAC), PC1323, theradigm-HBV, thymosin-alpha, and ganciclovir, besifovir (ANA-380/LB-80380), or tenofvir-exaliades (TLX/CMX157).~~