

## **SUMMARY**

In one aspect, the present disclosure provides a use of a composition comprising an antibody, wherein the antibody comprises the heavy chain amino acid sequence of SEQ ID NO.:91 and the light chain amino acid sequence of SEQ ID NO.:93 in the manufacture of a pharmaceutical for treating a Hepatitis B virus (HBV) infection in a subject, wherein the use comprises that a single dose of the pharmaceutical is to be administered to the subject.

In another aspect, the present disclosure provides a pharmaceutical composition comprising an antibody, wherein the antibody comprises the heavy chain amino acid sequence of SEQ ID NO.:91 and the light chain amino acid sequence of SEQ ID NO.:93, wherein the pharmaceutical composition comprises the antibody 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.

## **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. Throughout the disclosure, exemplary antibody HBC34v35 (with or without Fc mutations such as MLNS and GAALIE) is also referred-to as HBC34-v35 and HBC34-V35. Accordingly, it will be understood that HBC34v35, HBC34-v35, and HBC34-V35 have the same meaning. Similarly, exemplary antibody HBC34v34 is also referred-to as HBC34-v34 and HBC34-V34, and exemplary antibody HBC34v7 is also referred-to as HBC34-v7 and HBC34-V7. Further, it will be understood “MLNS-GAALIE” has the same meaning as “MLNS\_GAALIE” (*i.e.*, M428L + N434S + G236A + A330L + I332E mutations (EU numbering) in a Fc moiety).

Figures 1A-1B show binding of HBC34-v7 and two engineered antibodies of the present disclosure („HBC34-v34“; „HBC34-v35“) at the indicated concentrations to HBsAg adw (1A) and HbsAg adr (1B), as determined in direct antigen-based ELISA assays. All antibodies were produced as IgG1 (g1m17, 1 allotype).

Figures 2A-2K show binding of HBC34-v7, HBC34-v34, and HBC34-v35 to all known HbsAg genotypes ((A)-(J), respectively) and to mock control (K).

Genotype-representative sequences representing the HbsAg antigenic outer loop, as shown in Example 5 of PCT Publication No. WO 2017/060504, were used. Staining was performed by FACS. Antibody concentrations were as indicated on the y-axis of the graphs.

Figures 3A and 3B show binding of HBC34-v7 and HBC34-v35 with wild type or variant Fc regions to HbsAg adw in a direct antigen-based ELISA assay (2 experiments; data from „Experiment 1“ is shown in Figure 3A, and data from „Experiment 2“ is shown in Figure 3B). Antigen-binding curves are shown in the top panel of each Figure. EC50 values (determined by fitting the curves using Graphpad prism) are shown in the middle panel of each Figure. Binding to uncoated plates (control) is shown in the bottom panel of each Figure. Fc regions: „HBC34v7“ and „HBC34-v35“ = wild-type; „HBC34-v35-MLNS" = M428L/N434S. "HBC34-v35-MLNS-GAALIE" =

## CLAIMS

1. Use of a composition comprising an antibody, wherein the antibody comprises the heavy chain amino acid sequence of SEQ ID NO.:91 and the light chain amino acid sequence of SEQ ID NO.:93 in the manufacture of a pharmaceutical for~~A method of~~ treating a Hepatitis B virus (HBV) infection in a subject, ~~the method comprising administering to the subject wherein the use comprises that~~ a single dose of the pharmaceutical is to be administered to the subject~~a pharmaceutical composition comprising an antibody, wherein the antibody comprises the heavy chain amino acid sequence of SEQ ID NO.:91 and the light chain amino acid sequence of SEQ ID NO.:93.~~
2. The ~~method-use~~ of claim 1, wherein the single dose of the pharmaceutical ~~composition~~ comprises the antibody in a range from 2 to 18 mg/kg (subject body weight).
3. The ~~method-use~~ of claim 1 or 2, wherein the single dose of 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.
4. The ~~method-use~~ of any one of claims 1-3, wherein the single dose of 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.
5. The ~~method-use~~ of any one of claims 1-4, wherein the single dose of the pharmaceutical ~~composition~~ comprises about 75 mg of the antibody.
6. The ~~method-use~~ of any one of claims 1-4, wherein the single dose of the pharmaceutical ~~composition~~ comprises about 90 mg of the antibody.
7. The ~~method-use~~ of any one of claims 1-4, wherein the single dose of the pharmaceutical ~~composition~~ comprises up to 300 mg of the antibody.
8. The ~~method-use~~ of any one of claims 1-4, wherein the single dose of the pharmaceutical ~~composition~~ comprises up to 900 mg of the antibody.

9. The ~~method~~use of any one of claims 1-4, wherein the single dose of the pharmaceutical ~~composition~~ comprises up to 3,000 mg of the antibody.
10. The ~~method~~use of any one of claims 1-9, wherein the ~~method~~use comprises ~~administering that~~ the single dose of the pharmaceutical is to be administered by subcutaneous injection.
11. The ~~method~~use of any one of claims 1-9, wherein the ~~method~~use comprises ~~administering that~~ the single dose of the pharmaceutical is to be administered by intravenous injection.
12. The ~~method~~use of any one of claims 1-11, wherein the pharmaceutical ~~composition~~ further comprises water, optionally USP water.
13. The ~~method~~use of any one of claims 1-12, 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~~.
14. The ~~method~~use of any one of claims 1-13, wherein the pharmaceutical ~~composition~~ further comprises a disaccharide, such as sucrose, optionally at 5%, 6%, 7%, 8%, or 9%, preferably about 7% (w/v).
15. The ~~method~~use of any one of claims 1-14, 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).
16. The ~~method~~use of any one of claims 1-15, 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.
17. The ~~method~~use of claim 16, 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.

18. The ~~method~~use of any one of claims 1-17, wherein the subject is an adult.

19. The ~~method~~use of claim 18, wherein the subject is in a range from 18 years of age to 65 years of age.

20. The ~~method~~use of any one of claims 1-19, wherein the subject weighs from 40 kg to 125 kg.

21. The ~~method~~use of any one of claims 1-20, 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.

22. The ~~method~~use of any one of claims 1-21, wherein the subject does not have cirrhosis.

23. The ~~method~~use of claim 22, 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.

24. The ~~method~~use of any one of claims 1-23, 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.

25. The ~~method~~use of claim 24, wherein the NRTI comprises one or more of: tenofovir; tenofovir disoproxil (*e.g.*, tenofovir disoproxil fumarate); tenofovir alafenamide; Entecavir; Lamivudine; Adefovir; and adefovir dipivoxil.

26. The ~~method~~use of any one of claims 1-25, 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.

27. The ~~method~~use of any one of claims 1-26, wherein the subject has a serum HBsAg concentration of less than 1,000 IU/mL prior to the single dose being administered.
28. The ~~method~~use of any one of claims 1-26, wherein the subject has a serum HBsAg concentration of greater than or equal to 1,000 IU/mL no more than 28 days prior to the single dose being administered.
29. The ~~method~~use of any one of claims 1-28, wherein the subject was HB e-antigen (HBeAg)-negative no more than 28 days prior to the single dose being administered.
30. The ~~method~~use of any one of claims 1-29, wherein the subject was negative for anti-HB antibodies no more than 28 days prior to the single dose being administered.
31. The ~~method~~use of any one of claims 1-30, 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).
32. The ~~method~~use of any one of claims 1-31, 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.
33. The ~~method~~use of any one of claims 1-32, 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.
34. The ~~method~~use of any one of claims 1-33, wherein the subject is male.
35. The ~~method~~use of any one of claims 1-33, wherein the subject is female.
36. A pharmaceutical composition comprising an antibody, wherein the antibody comprises the heavy chain amino acid sequence of SEQ ID NO.:91 and the light chain amino acid sequence

of SEQ ID NO.:93, wherein the pharmaceutical composition comprises the antibody 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.

37. The pharmaceutical composition of claim 36, 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.

38. The pharmaceutical composition of claim 36 or 37, wherein the pharmaceutical composition comprises about 75 mg of the antibody.

39. The pharmaceutical composition of claim 36 or 37, wherein the pharmaceutical composition comprises about 90 mg of the antibody.

40. The pharmaceutical composition of claim 36 or 37, wherein the pharmaceutical composition comprises about 300 mg of the antibody.

41. The pharmaceutical composition of claim 36 or 37, wherein the pharmaceutical composition comprises about 900 mg of the antibody.

42. The pharmaceutical composition of claim 36 or 37, wherein the pharmaceutical composition comprises about 3,000 mg of the antibody.

43. The pharmaceutical composition of any one of claims 36-42, wherein the pharmaceutical composition further comprises water, optionally USP water.

44. The pharmaceutical composition of any one of claims 36-43, wherein the pharmaceutical composition further comprises histidine, optionally at a concentration from 10 mM to 40 mM, such as 20 mM, in the pharmaceutical composition.

45. The pharmaceutical composition of any one of claims 36-44, wherein the pharmaceutical composition further comprises a disaccharide, such as sucrose, optionally at 5%, 6%, 7%, 8%, or 9%, preferably about 7% (w/v).

46. The pharmaceutical composition of any one of claims 36-45, wherein the pharmaceutical composition further 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).

47. The pharmaceutical composition of any one of claims 36-46, 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.

48. The pharmaceutical composition of any one of claims 36-47, 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.