

CLAIMS

1. A therapeutic combination for use in treating a hepatitis B virus (HBV) infection in a subject in need thereof, comprising:
 - i) at least one of:
 - a) a truncated HBV core antigen consisting of an amino acid sequence that is at least 95% identical to SEQ ID NO: 2, and
 - b) a first non-naturally occurring nucleic acid molecule comprising a first polynucleotide sequence encoding the truncated HBV core antigen.
 - c) an HBV polymerase antigen having an amino acid sequence that is at least 90% identical to SEQ ID NO: 7, wherein the HBV polymerase antigen does not have reverse transcriptase activity and RNase H activity, and
 - d) a second non-naturally occurring nucleic acid molecule comprising a second polynucleotide sequence encoding the HBV polymerase antigen; and
 - ii) an anti-PD-1 or anti-PD-L1 antibody or antigen-binding fragment thereof, preferably selected from the group consisting of:
 - a) 17D8, 2D3, 4H1, 5C4, 4A11, 7D3, 5F4, H409A11, hPD-1.08A, hPD-1.09A, 109A-H, K09A-L-11, K09A-L-16, K09A-L-17, 409A-H, H1M7789N, H1M7799N, H1M7800N, H2M7780N, H2M7788N, H2M7790N, H2M7791N, H2M7794N, H2M7795N, H2M7796N, H2M7798N, H4H9019P, H4xH9034P2, H4xH9035P2, H4xH9037P2, H4xH9045P2, H4xH9048P2, H4H9057P2, H4H9068P2, H4xH9119P2, H4xH9120P2, H4xH9128P2, H4xH9135P2, H4xH9145P2, H4xH8992P, H4xH8999P, H4xH9008P, H4H7798N, H4H7795N2, H4H9008P, H4H9048P2, PD1-0103, PD1-0098, PD1-0050, PD1-0069, PD1-0073, PD1-0078, PD1-0102, PD1-0103_01, PD1-0103_02, PD1-0103_03, PD1-0103_04, PD1-0103-0312, PD1-0103-0313, PD1-0103-0314, PD1-0103-0315, 1.7.3 hAb, 1.49.9 hAb, 1.103.11 hAb, 1.103.11-v2 hAb, 1.139.15 hAb, 1.153.7 hAb, and variants thereof;
 - b) an antibody binding to an epitope having a sequence of SEHSI (SEQ ID NO: 25), DPFEL (SEQ ID NO: 26), KLNG (SEQ ID NO: 27), QTSWK (SEQ ID NO: 28),

- LHFEP (SEQ ID NO: 29), NDNGSY (SEQ ID NO: 30), TTLYVT (SEQ ID NO: 31), or LAAFPEDRSQPGQDCR (SEQ ID NO: 32); and
- c) Nivolumab (MDX-1 106, Opdivo; Bristol-Myers Squibb), Pembrolizumab (MK-3475, Keytruda, lambrolizumab, BMS-936558; Merck), TSR-042 (Tesaro, Inc.), REGN2810 (Regeneron Pharmaceuticals), EH12.2H7 (BioLegend, catalog no. 329902), Avelumab (Bavencio; EMD Serono, Pfizer), Durvalumab (Imfinzi, AstraZeneca), Cemiplimab (REGN-2810, Libtayo; Regeneron), BMS-936559, Atezolizumab (Tecentriq, Genentech), or an equivalent thereto.
2. The therapeutic combination of claim 1, comprising at least one of the HBV polymerase antigen and the truncated HBV core antigen.
 3. The therapeutic combination of claim 2, comprising the HBV polymerase antigen and the truncated HBV core antigen.
 4. The therapeutic combination of claim 1, comprising at least one of the first non-naturally occurring nucleic acid molecule comprising the first polynucleotide sequence encoding the truncated HBV core antigen and the second non-naturally occurring nucleic acid molecule comprising the second polynucleotide sequence encoding the HBV polymerase antigen.
 5. A therapeutic combination for use in treating a hepatitis B virus (HBV) infection in a subject in need thereof, comprising
 - i) a first non-naturally occurring nucleic acid molecule comprising a first polynucleotide sequence encoding a truncated HBV core antigen consisting of an amino acid sequence that is at least 95% identical to SEQ ID NO: 2; and
 - ii) a second non-naturally occurring nucleic acid molecule comprising a second polynucleotide sequence encoding an HBV polymerase antigen having an amino acid sequence that is at least 90% identical to SEQ ID NO: 7, wherein the HBV polymerase antigen does not have reverse transcriptase activity and RNase H activity; and
 - iii) an anti-PD-1 or anti-PD-L1 antibody or antigen-binding fragment thereof, preferably selected from the group consisting of:

- a) 17D8, 2D3, 4H1, 5C4, 4A11, 7D3, 5F4, H409A11, hPD-1.08A, hPD-1.09A, 109A-H, K09A-L-11, K09A-L-16, K09A-L-17, 409A-H, H1M7789N, H1M7799N, H1M7800N, H2M7780N, H2M7788N, H2M7790N, H2M7791N, H2M7794N, H2M7795N, H2M7796N, H2M7798N, H4H9019P, H4xH9034P2, H4xH9035P2, H4xH9037P2, H4xH9045P2, H4xH9048P2, H4H9057P2, H4H9068P2, H4xH9119P2, H4xH9120P2, H4xH9128P2, H4xH9135P2, H4xH9145P2, H4xH8992P, H4xH8999P, H4xH9008P, H4H7798N, H4H7795N2, H4H9008P, H4H9048P2, PD1-0103, PD1-0098, PD1-0050, PD1-0069, PD1-0073, PD1-0078, PD1-0102, PD1-0103_01, PD1-0103_02, PD1-0103_03, PD1-0103_04, PD1-0103-0312, PD1-0103-0313, PD1-0103-0314, PD1-0103-0315, 1.7.3 hAb, 1.49.9 hAb, 1.103.11 hAb, 1.103.11-v2 hAb, 1.139.15 hAb, 1.153.7 hAb, and variants thereof;
 - b) an antibody binding to an epitope having a sequence of SEHSI (SEQ ID NO: 25), DPFEL (SEQ ID NO: 26), KLNG (SEQ ID NO: 27), QTSWK (SEQ ID NO: 28), LHFEP (SEQ ID NO: 29), NDNGSY (SEQ ID NO: 30), TTTYVT (SEQ ID NO: 31), or LAAPEDRSQPGQDCR (SEQ ID NO: 32); and
 - c) Nivolumab (MDX-1 106, Opdivo; Bristol-Myers Squibb), Pembrolizumab (MK-3475, Keytruda, lambrolizumab, BMS-936558; Merck), TSR-042 (Tesar, Inc.), REGN2810 (Regeneron Pharmaceuticals), EH12.2H7 (BioLegend, catalog no. 329902), Avelumab (Bavencio; EMD Serono, Pfizer), Durvalumab (Imfinzi, AstraZeneca), Cemiplimab (REGN-2810, Libtayo; Regeneron), BMS-936559, Atezolizumab (Tecentriq, Genentech), or an equivalent thereto.
6. The therapeutic combination of claim 4 or 5, wherein the first non-naturally occurring nucleic acid molecule further comprises a polynucleotide sequence encoding a signal sequence operably linked to the N-terminus of the truncated HBV core antigen, and the second non-naturally occurring nucleic acid molecule further comprises a polynucleotide sequence encoding a signal sequence operably linked to the N-terminus of the HBV polymerase antigen, preferably, the signal sequence independently comprises the amino

acid sequence of SEQ ID NO: 9 or SEQ ID NO: 15, preferably the signal sequence is independently encoded by the polynucleotide sequence of SEQ ID NO: 8 or SEQ ID NO: 14.

7. The therapeutic combination of any one of claims 1-6, wherein
 - a) the truncated HBV core antigen consists of the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 4; and
 - b) the HBV polymerase antigen comprises the amino acid sequence of SEQ ID NO: 7.
8. The therapeutic combination of any one of claims 1-7, wherein each of the first, and second non-naturally occurring nucleic acid molecules is a DNA molecule, preferably the DNA molecule is present on a plasmid or a viral vector.
9. The therapeutic combination of any one of claims 4 to 8, comprising the first non-naturally occurring nucleic acid molecule and the second non-naturally occurring nucleic acid molecule in the same non-naturally nucleic acid molecule.
10. The therapeutic combination of any one of claims 4 to 8, comprising the first non-naturally occurring nucleic acid molecule and the second non-naturally occurring nucleic acid molecule in two different non-naturally occurring nucleic acid molecules.
11. The therapeutic combination of any one of claims 4 to 10, wherein the first polynucleotide sequence comprises a polynucleotide sequence having at least 90% sequence identity to SEQ ID NO: 1 or SEQ ID NO: 3.
12. The therapeutic combination of claim 11, wherein the first polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 1 or SEQ ID NO: 3.
13. The therapeutic combination of any one of claims 4 to 12, wherein the second polynucleotide sequence comprises a polynucleotide sequence having at least 90% sequence identity to SEQ ID NO: 5 or SEQ ID NO: 6.
14. The therapeutic combination of claim 13, wherein the second polynucleotide sequence comprises the polynucleotide sequence of SEQ ID NO: 5 or SEQ ID NO: 6.
15. The therapeutic combination of any one of claims 1-14, wherein the anti-PD-1 or anti-PD-L1 antibody or antigen-binding fragment thereof is Nivolumab (MDX-1 106, Opdivo; Bristol-Myers Squibb), Pembrolizumab (MK-3475, Keytruda, lambrolizumab, BMS-

936558; Merck), TSR-042 (Tesaro, Inc.), REGN2810 (Regeneron Pharmaceuticals), EH12.2H7 (BioLegend, catalog no. 329902), Avelumab (Bavencio; EMD Serono, Pfizer), Durvalumab (Imfinzi, AstraZeneca), Cemiplimab (REGN-2810, Libtayo; Regeneron), BMS-936559, or Atezolizumab (Tecentriq, Genentech), or an equivalent thereto.

16. A kit comprising the therapeutic combination of any one of claims 1-15, and instructions for using the therapeutic combination in treating a hepatitis B virus (HBV) infection in a subject in need thereof.
- The therapeutic combination of any one of claims 1 to 15 for use in treating a hepatitis B virus (HBV) infection in a subject in need thereof.