Enrollment Criteria

Patient ID __ __ - __ **ID** __ - __ __ __

Date of Determination: **ERLDATE**

SECTION I: INCLUSION CRITERIA Check if rescreen: ☐ **RSC**

1. Enrolled in the HBRN Cohort Study or completed the necessary components of the Cohort baseline evaluation by the end of the baseline visit for this trial **INCOHORT**	☐ Yes	☐ No
2. Patient is at least 18 years of age at the time of randomization **INAGEIA**	☐ Yes	☐ No
3. Chronic HBV infection as evidenced by ***at least one*** of the following: **INCHB** a) HBsAg in serum within 8 weeks prior to randomization and another time at least 24 weeks prior to randomization, with no HBsAg negative result in between b) HBsAg positive plus absence of detectable anti-HBc IgM in serum within 8 weeks prior to randomization c) HBsAg positive within 8 weeks prior to randomization and HBV DNA ≥1,000 IU/mL on 2 occasions at least 24 weeks apart (can include result from screening visit within 8 weeks of randomization). d) HBsAg positive within 8 weeks prior to randomization plus evidence of chronic hepatitis B infection as indicated by a liver biopsy within 144 weeks of randomization.	☐ Yes	☐ No
4. HBeAg positive or negative **INHBPN**	☐ Yes	☐ No
5. Serum HBV DNA ≥1000 IU/mL on 2 occasions at least 4 weeks apart within 32 weeks prior to randomization (can include result from screening visit within 8 weeks of randomization). **INDNA** Level (IU/mL) / Date *(mm/dd/yy)* / Lower limit of detection First qualifying result: **__BDNA1___** / **BDNA1M/D/Y** / **_BDNALL1_** Second (or within 8 weeks): **__BDNA2___** / **BDNA2M/D/Y** / **_BDNALL2_**	☐ Yes	☐ No
6. At least two elevated serum ALT levels (> 45 IU/L for males and > 30 IU/L for females) at least 4 weeks apart, but no more than 32 weeks apart, with the second being within 8 weeks prior to randomization. **INALT** First qualifying result: **ALT1** IU/L **ALT1M/D/Y** *(mm/dd/yy)* ALT result within 8 weeks: **ALT8** IU/L **ALT8M/D/Y** *(mm/dd/yy)*	☐ Yes	☐ No
7. No recent treatment or limited treatment in the past: **INTRTLIM** a) No interferon or nucleos(t)ide analogues for hep B within 48 weeks of randomization b) Therapy with nucleos(t)ide analogues for hepatitis B at any time in the past must not exceed 48 weeks	☐ Yes	☐ No
8. Compensated liver disease, with total bilirubin ≤ 2 mg/dL (except if Gilbert's syndrome), direct bilirubin ≤ 0.5 mg/dL, INR ≤ 1.5, and serum albumin ≥ 3.5 g/dL **COMPL**	☐ Yes	☐ No
9. No evidence of HCC based upon AFP≤ 20ng/mL within 8 weeks prior to randomization: **NOHCC** a) Participants who meet AASLD criteria for HCC surveillance must have negative liver imaging as shown by US, CT or MRI within 28 weeks of randomization as part of standard of care. Imaging within 28 weeks **IMAGM/D/Y** *(mm/dd/yy)* b) Participants with AFP > 20 ng/mL must be evaluated clinically with additional imaging and shown not to have HCC on CT or MRI	☐ Yes	☐ No
10. Liver biopsy that shows findings consistent with chronic hepatitis B with histology activity index (Modified Ishak HAI) ≥ 3 (necroinflammatory component only) **or** Ishak fibrosis score ≥ 1 **or** both, as assessed by the local consortium study pathologist on a liver biopsy done within 144 weeks of randomization. Slides must be available for review by the consortium study pathologist and meet adequacy requirements. If the participant had received previous treatment for hepatitis B, the biopsy must have been done after discontinuation of treatment. **INBIOP** Biopsy: Modified Ishak HAI _ **HAI** _ Ishak score **ISHAK** **BIOPM/D/Y** *(mm/dd/yy)*	☐ Yes	☐ No
11. Females of child bearing potential must agree to use an adequate method of contraception throughout the study and must have a negative pregnancy test immediately prior to the start of treatment. **INBC** ☐ check if patient not of child bearing potential **NOCHILD**	☐ Yes or N/A	☐ No
12. Patient provided informed consent and agrees to adhere to the requirements of the study. **IACONS**	☐ Yes	☐ No

SECTION II: EXCLUSION CRITERIA

1. Serum ALT > 450 IU/L for males and > 300 IU/L for females (participants are eligible for rescreen if ALT levels fall to the range of eligibility) **EXALT**	☐ Yes	☐ No
2. Any history of hepatic decompensation, including but not limited to ascites, variceal bleeding, or hepatic encephalopathy **EXHDC**	☐ Yes	☐ No
3. Known allergy or intolerance to any of the study medications **EXALGY**	☐ Yes	☐ No
4. Female patient who is pregnant or breastfeeding **EXPREG**	☐ Yes	☐ No or N/A
5. Previous organ transplantation including engrafted bone marrow transplant **EXORG**	☐ Yes	☐ No
6. Any other concomitant liver disease, including hemochromatosis or hepatitis C or D. Non-alcoholic fatty liver disease (NAFLD) with steatosis and/or mild to moderate steatohepatitis is acceptable but NALFD with severe steatohepatitis is exclusionary. **OTHLVDX**	☐ Yes	☐ No
7. Positive anti-HIV (test to be completed within the 8 weeks prior to randomization) **EXHIV**	☐ Yes	☐ No
8. Renal insufficiency with calculated (by MDRD method) creatinine clearance < 60 mL/min within 8 weeks prior to randomization **EXRENAL**	☐ Yes	☐ No
9. Platelet count <90,000/mm^3, hemoglobin <13 g/dL (males) or <12 g/dL (females), ANC <1500/mm^3 (<1000/mm^3 for African Americans) within 8 weeks prior to randomization **EXLAB**	☐ Yes	☐ No
10. History of alcohol or drug abuse within 48 weeks of randomization **EXALC**	☐ Yes	☐ No
11. Pre-existing psychiatric condition(s), including but not limited to: **EXPSY** a. Current moderate or severe depression as determined by the study physician b. History of depression requiring hospitalization within the past 10 years c. History of suicidal or homicidal attempt within the past 10 years d. History of severe psychiatric disorders including, but not limited to, schizophrenia, psychosis, bipolar disorder as determined by a study physician	☐ Yes	☐ No
12. History of immune-mediated or cerebrovascular, chronic pulmonary or cardiac disease associated with functional limitation, retinopathy, uncontrolled thyroid disease, poorly controlled diabetes or uncontrolled seizure disorder, as determined by the study physician **OTHDX**	☐ Yes	☐ No
13. Any medical condition that would, in the opinion of the study physician, be predicted to be exacerbated by therapy or that would limit study participation **EXDXPI**	☐ Yes	☐ No
14. Any medical condition requiring or likely to require chronic systemic administration of corticosteroids or other immunosuppressive medications during the course of the study **IMMTX**	☐ Yes	☐ No
15. Evidence of active or suspected malignancy, or a history of malignancy within the last 144 weeks prior to randomization (except adequately treated carcinoma in situ or basal cell carcinoma of the skin) **EXCANC**	☐ Yes	☐ No
16. Expected need for ongoing use of any antivirals with activity against HBV during the course of the study **ANTIVTX**	☐ Yes	☐ No
17. Participation in any other clinical trial involving investigational drugs within 30 days of randomization or intention to participate in another clinical trial involving investigational drugs during participation in this study **INVRX2**	☐ Yes	☐ No
18. Any other condition or situation that, in the opinion of the study physician, would make the patient unsuitable for enrollment or could interfere with the patient participating in and completing the study? **PIOTH** If Yes, specify _____ **PIOTHS** _____	☐ Yes	☐ No

If the responses to all inclusion criteria are YES and all exclusion criteria are NO, the patient is eligible to participate in the Immune Active Trial.

Is the patient eligible to participate in the Immune Active trial? ☐ Yes ☐ No **ENROLLIA**

Investigator signature: _____

Data collector initials: **DCID**

Date data collection completed *(mm/dd/yy)*: **DCM/DCD/DCY**