siRNAs were synthesized on a MerMade synthesizer. In vitro human PD-L1 knockdown was evaluated in the SNU-387 cell line by RT-qPCR. ALG-072585 and its parental siRNA, ALG-072571, were dosed SC mice. In double qPCR. GalNAc PD-L1 siRNA pharmacodynamics (PD) were studied. ALG-072519. Serial serum collections were tested for HBsAg, HBeAg, HBV DNA and ALT. Terminal serum samples were assayed for HBcAg infiltration in the liver and induced anti-HBsAg antibodies in the blood.

**RESULTS**

hPD-L1 was elevated in HBV preclinical models

**DISCUSSION**

1. hPD-L1 was elevated in HBV-infected 3-D liver chips and the livers of AAV-HBV infected hPD-1/PD-L1 double KI mice.

2. Parental hPD-L1 siRNA ALG-072571 reduced hPD-L1 in the livers of poly(I:C) treated hPD-1/PD-L1 double KI mice.

3. In AAV-HBV double KI mice, ALG-072571 reduced serum HBsAg, HBeAg and HBV DNA 3.3 log$_{10}$ IU/mL, 1.73 log$_{10}$ PEIU/mL and 4.5 log$_{10}$ IU/mL respectively as a single agent; 4.3 log$_{10}$ IU/mL, 2.0 log$_{10}$ PEIU/mL, and 6.9 log$_{10}$ IU/mL respectively when combined with an HBV siRNA.

4. Lead optimization of ALG-072571 by chemical destabilization yielded ALG-072585 which retained in vivo potency of its parent in reducing infected hepatocytes and serum HBsAg but did not induce ALT in uninfected double KI mice.

5. In AAV-HBV infected double KI mice, ALG-072585 increased T cell infiltration in the liver and induced anti-HBsAg antibodies in the blood.

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**FINANCIAL DISCLOSURE:** All authors are current or former employees of Aligos Therapeutics, Inc.