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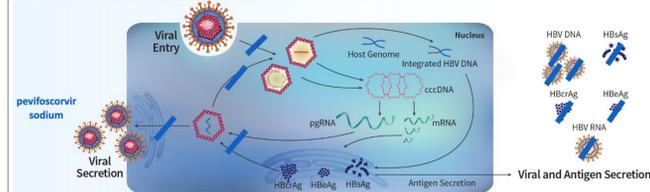
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## BACKGROUND

Pevifoscorvir sodium (PEVY, ALG-000184) is a prodrug of the Capsid Assembly Modulator (CAM), ALG-001075, which has demonstrated potent, pan-genotypic antiviral activity in vitro through the dual mechanism of action (MOA)<sup>1</sup> (Figure 1):

- inhibition of pg-RNA encapsidation (1st MOA)
- blocking cccDNA establishment/replenishment at higher concentrations (2nd MOA).

Figure 1: Mechanism of Action of Pevifoscorvir Sodium



The multipart Phase 1 study ALG-000184-201 (NCT04536337) demonstrated that PEVY 300 mg oral once daily (QD) ± entecavir (ETV) for ≤ 96 weeks was well tolerated and demonstrated potent antiviral activity, achieving profound suppression of HBV DNA and RNA, along with additional declines in HBV antigens in treatment-naïve/currently-not-treated (TN/CNT) subjects with chronic hepatitis B virus (HBV) infection<sup>2,3</sup>.

## METHODS

- A total of 21 TN/CNT subjects were enrolled and received open-label, once-daily, oral 300 mg PEVY monotherapy for 96 weeks (Figure 2).

Figure 2: Cohort Design for Once Daily 300 mg PEVY Monotherapy



- Throughout the study, safety assessments (adverse events [AEs], vital signs, electrocardiogram [ECG] and laboratories), PK, and viral biomarkers were collected at regular intervals. The Study Review Committee (SRC) and ALT Flare Committee (AFC) provided oversight of safety by reviewing safety and PK data on a regular basis.
- HBV biomarkers were analyzed at Sonic Laboratory. The Lower Limit of Quantification (LLOQ) and Detection (LOD) of HBV DNA are 10 IU/mL and ≤ 4.92 IU/mL, respectively. LLOQs of HBV RNA and HBsAg are 10 copies/mL and 0.05 IU/mL. LLOQs of HBcrAg are 3 log<sub>10</sub> U/mL for HBeAg+ subjects and 1.8 log<sub>10</sub> U/mL (iTACT-HBcrAg) for HBeAg- subjects, respectively.

Pevifoscorvir sodium monotherapy demonstrated rapid and profound HBV DNA suppression in treatment-naïve or currently-not-treated participants with chronic HBV infection. Moreover, substantial HBV RNA and HBV antigens reductions were observed during treatment and follow up, suggesting that PEVY monotherapy may reduce HBV cccDNA pool.

TABLE 1: BASELINE CHARACTERISTICS

Part 4 Cohort B	300 mg PEVY Monotherapy	
	HBeAg+	HBeAg-
<b>N</b>	10	11*
<b>Age, years, mean (SD)</b>	34.8 (9.1)	48.5 (10.2)
<b>Female, N (%)</b>	3 (30.0)	5 (45.5)
<b>Asian, N (%)</b>	9 (90.0)	3 (27.3)
<b>BMI, kg/m<sup>2</sup>, mean (SD)</b>	22.4 (2.4)	26.0 (3.5)
<b>HBV Genotype B/C, N (%)</b>	B: 5 (50), C: 4(40), D: 1 (10)	B:2(18), C:1(9), D:7(64), A:1(9)
<b>HBV DNA, log<sub>10</sub> IU/mL, mean (SD)</b>	8.0 (0.8)	4.3 (0.7)
<b>HBV RNA, log<sub>10</sub> copies/mL, mean (SD)</b>	5.3 (1.3)	2.0 (1.0)
<b>HBsAg, log<sub>10</sub> IU/mL, mean (SD)</b>	4.3 (0.5)	3.5 (0.5)
<b>HBeAg, log<sub>10</sub> PEI U/mL, mean (SD)</b>	2.6 (0.8)	NA
<b>HBcrAg, log<sub>10</sub> U/mL, mean (SD)</b>	8.3 (0.6)	3.3 (0.6)
<b>ALT, U/L, mean (SD)</b>	60.7 (36.9)	35.0 (14.5)

SD: standard deviation, NA: not applicable, PEVY: pevifoscorvir sodium  
 \* 2 HBeAg- subjects discontinued at Week 56 and 64, due to non-safety related personal decisions.

TABLE 2: SAFETY SUMMARY

	HBeAg+	HBeAg-
<b>Numbers of subjects with</b>	N=10	N=11
<b>at least one TEAE, n (%)</b>	9 (90)	9 (81.8)
<b>SAE</b>	0	0
<b>TEAE leading to study drug discontinuation</b>	0	0
<b>TEAE Grade ≥ 3</b>	3*	2*.#

\* Grade ≥3 TEAEs of ALT/AST elevation were observed in 3 HBeAg+ and 1 HBeAg- subjects with preserved synthetic and excretory liver functions. All events resolved in the setting of continued PEVY dosing and were not considered clinically concerning by the ALT Flare Committee.

# Grade 3 cholesterol/triglycerides increase in HBeAg- subject resolved in the setting of continued PEVY dosing.

## ANTIVIRAL ACTIVITY

TABLE 3: MEAN (SEM) CHANGES FROM BASELINE IN HBV MARKERS DURING 96 WEEKS OF 300 MG PEVY MONOTHERAPY

	HBeAg+	HBeAg-
<b>HBV DNA log<sub>10</sub> IU/mL (SEM), n</b>		
Week 48	-6.9 (0.2), 10	-3.3 (0.2), 11
Week 96	-7.0 (0.2), 10	-3.3 (0.2), 9
<b>HBV RNA log<sub>10</sub> copies/mL (SEM), n</b>		
Week 48	-4.3 (0.4), 10	-1.0 (0.3), 11
Week 96	-4.3 (0.4), 10	-1.0 (0.3), 9
<b>HBsAg log<sub>10</sub> IU/mL (SEM), n</b>		
Week 48	-0.7 (0.2), 10	0.1 (0.04), 11
Week 96	-0.9 (0.2), 10	-0.04 (0.04), 9
<b>HBeAg log<sub>10</sub> PEI U/mL (SEM), n</b>		
Week 48	-1.6 (0.2), 10	Not applicable
Week 96	-2.0 (0.2), 10	Not applicable
<b>HBcrAg log<sub>10</sub> U/mL (SEM), n</b>		
Week 48	-1.5 (0.2), 10	-0.3 (0.05), 11
Week 96	-2.1 (0.2), 10	-0.4 (0.09), 9

HBeAg+: HBeAg-positive, HBeAg-: HBeAg-negative, NA: nucleos(t)ide analogue

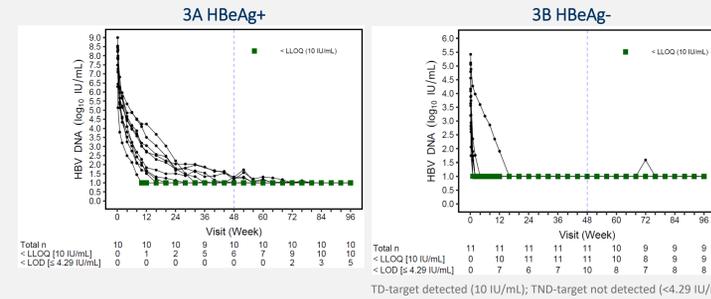


Figure 3: Reduction in Individual HBV DNA Level Over Time During 300 mg PEVY Monotherapy

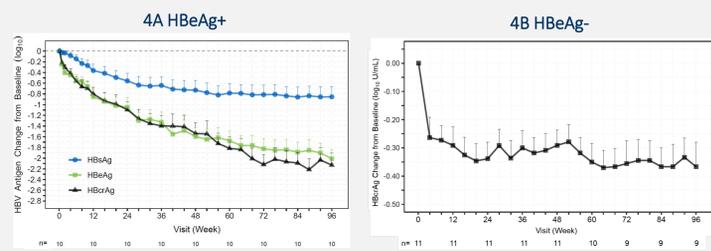


Figure 4: Mean HBV Antigen Changes from Baseline During 96 Weeks of 300 mg PEVY Monotherapy

## ANTIVIRAL ACTIVITY – HBV BIOMARKER CHANGES DURING THE NUCLEOSIDE (NA) ONLY 8-WEEK FOLLOW UP PERIOD

- Among the 16 subjects (8 HBeAg+ and 8 HBeAg-) that switched from PEVY to NA monotherapy at Week 96, HBV DNA level increased to detectable level (>10 IU/mL) in 2 HBeAg+ subjects.
- HBV RNA partially reversed after switching to NA but remained lower than baseline (Figure 5).
- No apparent HBV antigen increase was observed during 8-week follow-up period (Figure 5).

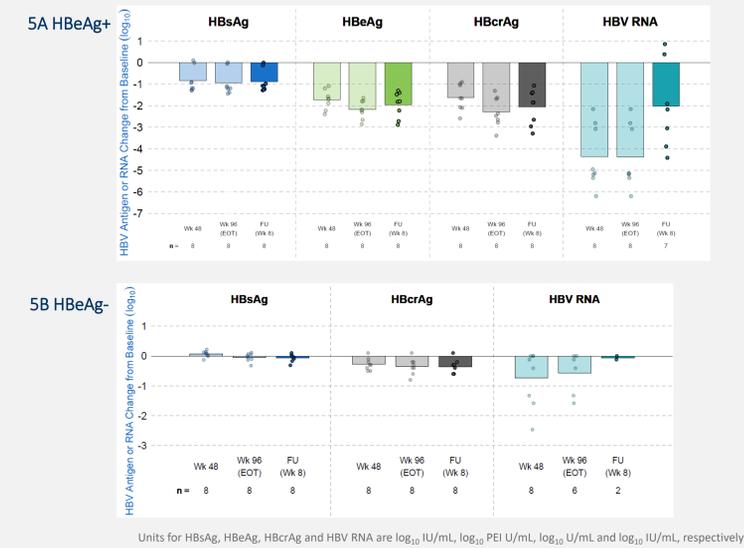


Figure 5: Mean HBV RNA and HBV Antigen Changes from Baseline Including NA Only 8-Week Follow-Up

## 300 mg PEVY monotherapy in TN/CNT HBeAg+ and HBeAg- subjects for 96 weeks demonstrated:

- Favorable safety profile
- Rapid, profound, and durable reduction in HBV DNA without viral breakthrough (Table 3, Figure 3)
  - In HBeAg+ subjects, 60% (6/10) subjects achieved HBV DNA LLOQ < 10 IU/mL (TD or TND) at Week 48, increased to 100% (10/10) at Week 96
  - In HBeAg- subjects, 100% (11/11) achieved HBV DNA LLOQ < 10 IU/mL (TD or TND) by Week 20, and 89% (8/9) achieved HBV DNA < 10 IU/mL TND (LOD ≤ 4.29 IU/mL) at Week 96

- Multiple log reduction in HBV antigens and RNA were achieved (Figure 4)
- HBV antigen and HBV RNA reductions were maintained during NA only 8-Week follow-up suggesting that PEVY potentially reduces cccDNA pool.

- The Phase 2, B-SUPREME study (NCT06963710) evaluating 300 mg PEVY monotherapy compared to NA monotherapy in TN/CNT subjects with chronic HBV infection, including a liver biopsy sub study, is currently ongoing