Subjects with Chronic Hepatitis B

HBV core protein (Cp) plays a critical role in multiple steps of the HBV life cycle, including the formation and secretion of virus particles. The presence of Cp in the virion is necessary for virus replication, and its functional integrity is a prerequisite for successful virus infection.

Currently approved treatments for chronic HBV include nucleos(t)ide analogs (Nuc), such as entecavir (ETV) and tenofovir, and interferons (IFN and PEG-IFN)1. While Nuc therapy is highly effective in achieving viral suppression, the emergence of drug resistance is a major challenge. Interferon therapy, although effective in reducing viral load, is associated with significant side effects.

Protein Allosteric Modifiers (CpAMs), has been discovered and developed to target HBV Cp and has shown promising preclinical activity in both cell culture and animal models. CpAMs have the potential to overcome resistance to Nuc therapy and to be used in combination with other therapies to achieve durable viral suppression.

**Clinical Study Objectives**

**Primary Objectives**

- Assess the dose-related safety and tolerability of ABI-H0731 after multiple oral doses in healthy human volunteers (Study ABI-H0731-102) and in CHB Patients (Study ABI-H0731-101(B))
- Assess the antiviral efficacy of multiple dose levels of orally administered ABI-H0731 in healthy volunteers and non-cirrhotic patients with chronic hepatitis B.

**Secondary Objectives**

- Assess serum, urine, and faecal metabolites following multiple doses of ABI-H0731
- Assess Cmax-related adverse effects of ABI-H0731 during short-term (28 days) treatment, as well as any changes in HBV core-related antigen (HBcAg) and HBsAg
- Assess for any potential changes in liver function tests

**Key Study Objectives**

1. Safety and tolerability of ABI-H0731 in healthy volunteers, as measured by adverse events (AEs), laboratory abnormalities, and vital signs
2. Safety and tolerability of ABI-H0731 in CHB patients, as measured by AEs, laboratory abnormalities, and vital signs
3. PK parameters of ABI-H0731 in healthy volunteers and CHB patients
4. Antiviral efficacy of ABI-H0731 in healthy volunteers and CHB patients

**PK Parameters**

- **Cmax** (maximum plasma concentration) measured at 0.5, 1, 2, and 3 hours post-dose
- **AUC (area under the curve)** calculated from time 0 to 24 hours
- **Tmax** (time to Cmax) measured at 0.5, 1, 2, and 3 hours post-dose

**Clinical Safety and Tolerability**

- Generally well tolerated, with no SAEs reported
- No clinically significant changes in vital signs, laboratory abnormalities, or ECGs
- No drug-related adverse events were observed
- No laboratory abnormalities noted among 30 volunteers treated with ABI-H0731, none were deemed related to study drug

**Antiviral Efficacy**

- Overall HBV viral DNA reductions increased with increasing dose
- HBsAg reductions were observed in both healthy volunteers and CHB patients
- Ongoing resistance monitoring has not identified any other patients with evidence of pre-existing or emerging CpAM-resistant mutations

**Conclusions**

- ABI-H0731 is a novel CpAM with selective and potent activity against all major HBV genotypes
- Four dose levels (100 mg, 200 mg, 300 mg and 400 mg) of ABI-H0731 were or are being evaluated in volunteers and/or CHB patients
- Overall HBV viral DNA reductions increased with increasing dose
- HBsAg reductions were observed in both healthy volunteers and CHB patients
- Ongoing resistance monitoring has not identified any other patients with evidence of pre-existing or emerging CpAM-resistant mutations

**Acknowledgments and Disclosures**

- The authors gratefully acknowledge the contributions of the study volunteers and the study staff.
- The study was supported by Gilead Sciences, Inc., Foster City, CA, USA.

**References**

3. Gilead, AbbVie, Alnylam, BMS, Intercept, Merck, Janssen, and Vir. EJG is an advisor for or speaker for Gilead, Sysmex Corporation. KA is a consultant for, speaker for, or received research grants from Roche, Abbott, and Echosens.