
# Rapid, profound and durable antiviral effects in treatment-naïve or currently-not-treated subjects with chronic hepatitis B virus infection that received 300 mg pevifoscorvir sodium monotherapy for 96 weeks

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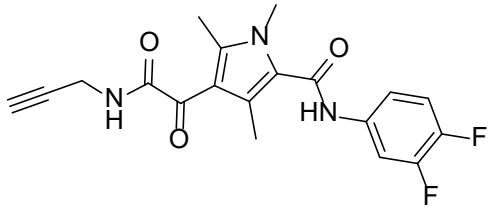
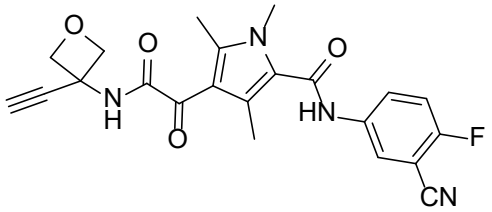
This presentation concerns drug candidates, some of which are undergoing nonclinical studies and others of which are under clinical investigation, and all of which have not yet been approved for marketing by the U.S. Food and Drug Administration. These drug candidates are currently limited by federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

# Pevifoscorvir Sodium (ALG-000184)

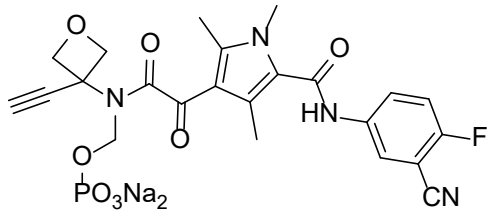


**GLP-26**
**Professor Raymond F. Schinazi**
**Emory University**

***Journal of Medicinal Chemistry***
(2024) 67, 23, 21126-21142



**ALG-001075**
**$EC_{50}$ (HepG2.117) = 0.63 nM**
**Solubility < 5 mg/mL**
**%F (rat, dog) = 34, 30**



**ALG-000184**
**Pevifoscorvir sodium**
**Prodrug of ALG-001075**
**Solubility > 100 mg/mL**
**%F (rat, dog) = 48, 84**

**Aligos / Emory collaboration led to the discovery of pevifoscorvir sodium, an investigational drug candidate being studied for the treatment of chronic hepatitis B**

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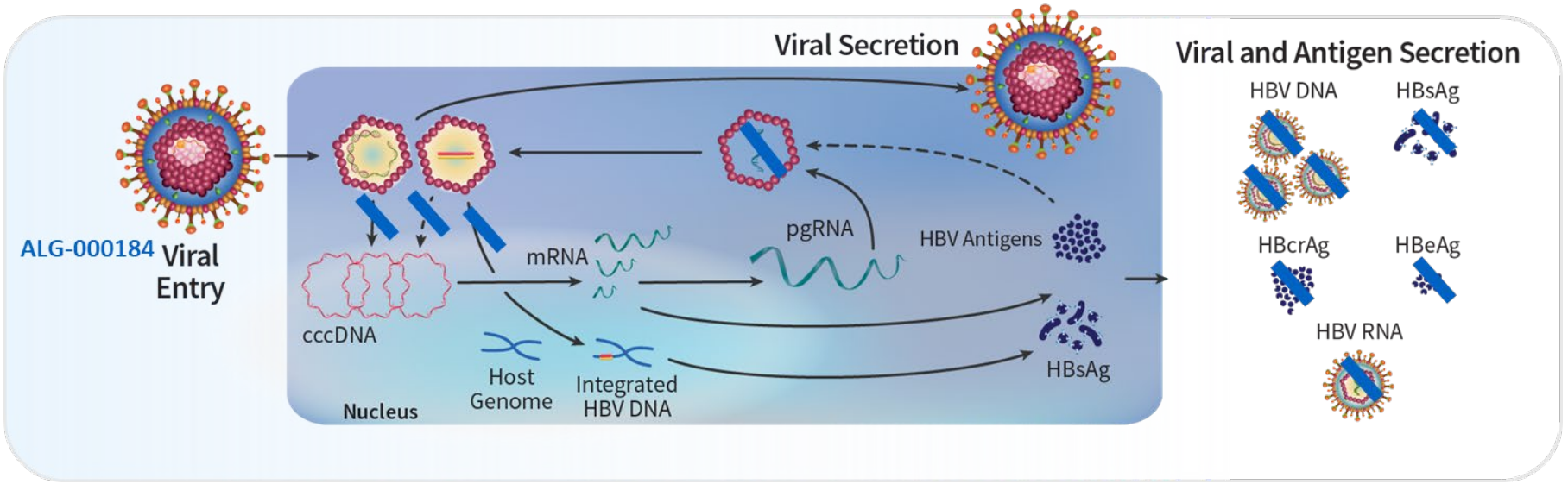
# Pevifoscorvir Sodium

## Potent Dual Mechanism of Action to Suppress the Entire HBV Lifecycle in Vitro




1st MOA causes the formation of empty capsids

- —Reduces viral secretion (HBV DNA/RNA)
- —In vitro $EC_{50}$ of ALG-001075: 0.53 – 0.64 nM[1]

2nd MOA prevents capsid disassembly at higher concentration of ALG-001075

- —Prevents establishment/replenishment of cccDNA[2], which produces HBcrAg/HBeAg/HBsAg
- —$EC_{90}$ of ALG-001075 in vitro on HBsAg inhibition was 266 nM[3]

[1]Sandrine Vendeville et. al, The Discovery and Preclinical Profile of ALG-000184, a Prodrug of the Potent Hepatitis B Virus Capsid Assembly Modulator ALG-001075; Journal of Medicinal Chemistry Vol. 67:23 21126-21142; [2]Jordi Verheyen et. al, AASLD Poster #1251; [3]Pevifoscorvir sodium data was generated by Aligos on the parent compound ALG-001075. Studies conducted in vitro.

**Pevifoscorvir sodium demonstrated a ~2-300-fold improvement in vitro potency (HBV DNA inhibition) compared to other known CAM-Es.**

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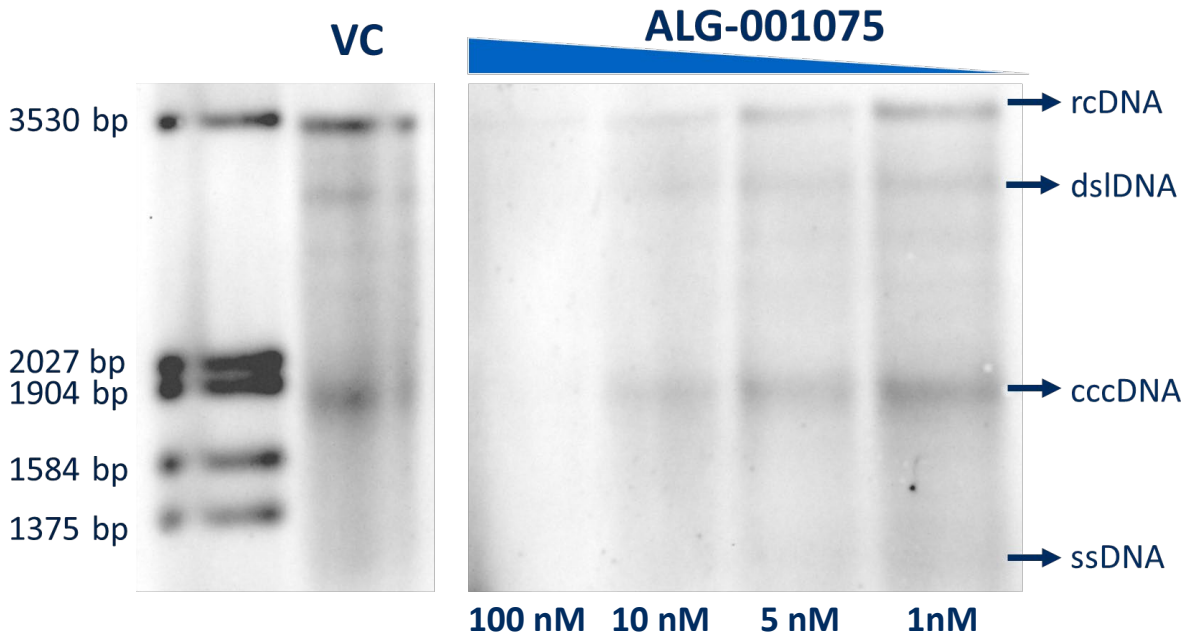
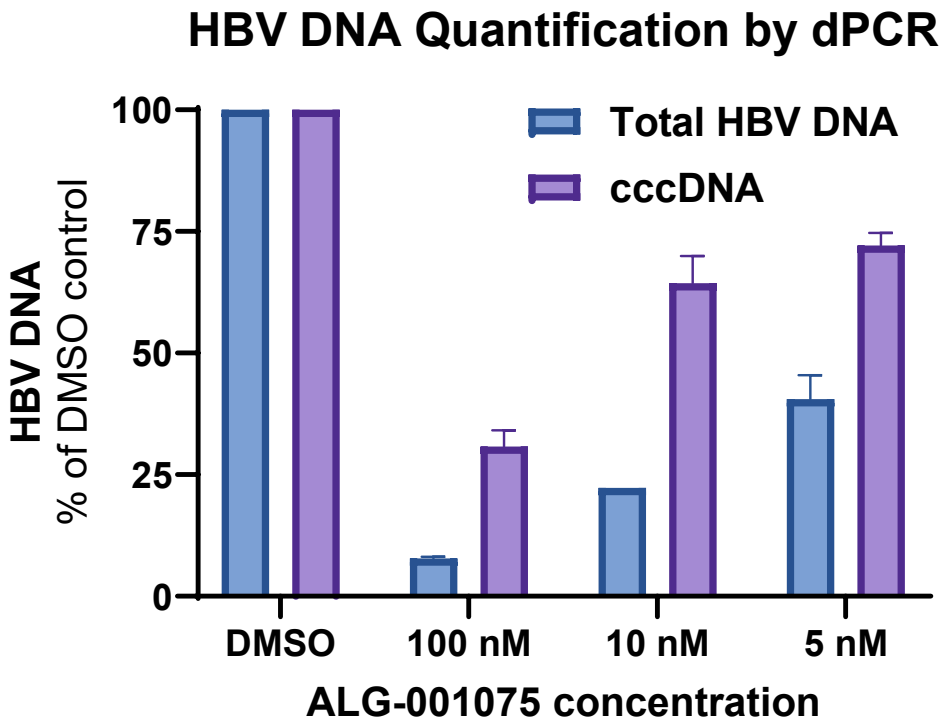
# Pevifoscorvir Sodium

## Prevention of HBV cccDNA Formation In Vitro




- **HBV-infected HepG2-NTCP cells**
- **ALG-001075 reduces rcDNA, dslDNA and cccDNA**

Jordi Verheyen et. al, AASLD 2025 Poster #1251.

**ALG-001075 blocks cccDNA establishment in vitro**

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# Study ALG-000184-201, a Multi-Part Phase 1 Study of Pevifoscorvir Sodium

## Completed Evaluation in Healthy Volunteers and Subjects with Untreated Chronic HBV Infection

Parts 1 to 3 highlights[1,2]: (SAD/MAD and once daily 10-300 mg pevifoscorvir sodium oral doses x 28 days in TN/CTN subjects, NCT04536337)

- **PK:** Dose proportional increase in exposure with low to moderate variability
- **Safety:** All doses were well tolerated without any dose adjustment or early discontinuation
- **Efficacy**:
  - Rapid and profound reduction in HBV DNA and HBV RNA with the lowest dose (10 mg) achieving maximum HBV DNA reductions
  - Dose-related reduction in HBsAg noted at 100 mg and 300 mg pevifoscorvir sodium
    - Indicating engagement of CAM's secondary MOA
    - The only CAM to date that has demonstrated meaningful HBsAg reduction within 28 days
  - Comparable safety and efficacy between Asians (HBV genotype B, C) and non-Asians (HBV genotype A, D)

SAD-single dose escalation; MAD-multiple dose escalation; TN-treatment naïve; CTN-currently not treated; PK-pharmacokinetics.

1.Gane E, *et al.* Antiviral Therapy 2025 (in press) 2. Yuen MF, *et al.* Lancet Gastroenterology Hepatol 2025 (in press).

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# Long-Term Dosing in TN/CNT Subjects with Chronic HBV Infection

## Study ALG-000184-201 Part 4 Cohort Designs

### China

Randomize
4 active:1 placebo

**Cohort 2**
HBeAg$^+$
N = 15

- Pevifoscorvir sodium 300 mg + ETV x ≤96 weeks → Follow-up (ETV only) x 8 weeks
- Placebo + ETV x 12 weeks → Pevifoscorvir sodium 300 mg + ETV x ≤96 weeks → Follow-up (ETV only) x 8 weeks

### ROW

**Cohort B**
N=21
HBeAg$^+$ n=10
HBeAg$^-$ n=11

Pevifoscorvir sodium 300 mg monotherapy x ≤96 weeks (open label) → Follow-up (NA) x 8 weeks

Hou, JL. et al., EASL 2025. Yuen, M-F. et al., EASL 2025.
All cohorts fully enrolled. NCT04536337; ROW: rest of the world.
Note: TN-treatment naïve; CNT-currently not treated.
ETV-entecavir. HBeAg$^+$: HBeAg-positive; HBeAg$^-$: HBeAg-negative.

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# Study ALG-000184-201

## Part 4 Baseline Characteristics

| | HBeAg+ | | | HBeAg- |
|---|---|---|---|---|
| | Part 4 Cohort 2 | | Part 4 Cohort B | Part 4 Cohort B |
| | ETV ×12 Weeks followed by 300 mg pevifoscorvir sodium +ETV | 300 mg pevifoscorvir sodium +ETV | 300 mg pevifoscorvir sodium monotherapy | 300 mg pevifoscorvir sodium monotherapy |
| **N** | 3 | 12 | 10 | 11 |
| **Age, years, mean (SD)** | 28 (4.6) | 32.3 (10.2) | 34.8 (9.1) | 48.5 (12.0) |
| **Female, N (%)** | 2 (66.7) | 6 (50) | 3 (30.0) | 5 (45.5) |
| **Asian, N (%)** | 3 (100) | 12 (100) | 9 (90.0) | 3 (27.3) |
| **BMI, kg/m$^2$, mean (SD)** | 22.3 (2.8) | 22.2 (3.1) | 22.4 (2.4) | 26.0 (3.5) |
| **HBV Genotype, N (%)** | B: 1 (33)<br>C: 2 (67) | B: 4 (33)<br>C: 8 (67) | B: 5 (50), C: 4(40),<br>D: 1 (10) | B:2(18), C:1(9),<br>D:7(64), A:1(9) |
| **HBV DNA, $\log_{10}$ IU/mL, mean (SD)** | 7.8 (1.1) | 8.1 (0.8) | 8.0 (0.8) | 4.3 (0.7) |
| **HBV RNA, $\log_{10}$ copies/mL, mean (SD)** | 6.5 (0.9) | 6.7 (1.1) | 5.3 (1.3) | 2.0 (1.0) |
| **HBsAg, $\log_{10}$ IU/mL, mean (SD)** | 4.1 (0.4) | 4.5 (0.7) | 4.3 (0.5) | 3.5 (0.5) |
| **HBeAg, $\log_{10}$ PEI U/mL, mean (SD)** | 2.0 (0.3) | 2.5 (0.3) | 2.6 (0.8) | - |
| **HBcrAg, $\log_{10}$ U/mL, mean (SD)** | 8.0 (1.2) | 8.3 (0.5) | 8.3 (0.6) | 3.3 (0.6) |
| **ALT, U/L, mean (SD)** | 38.7 (9.1) | 41.5 (22.7) | 60.7 (36.9) | 35.0 (14.5) |

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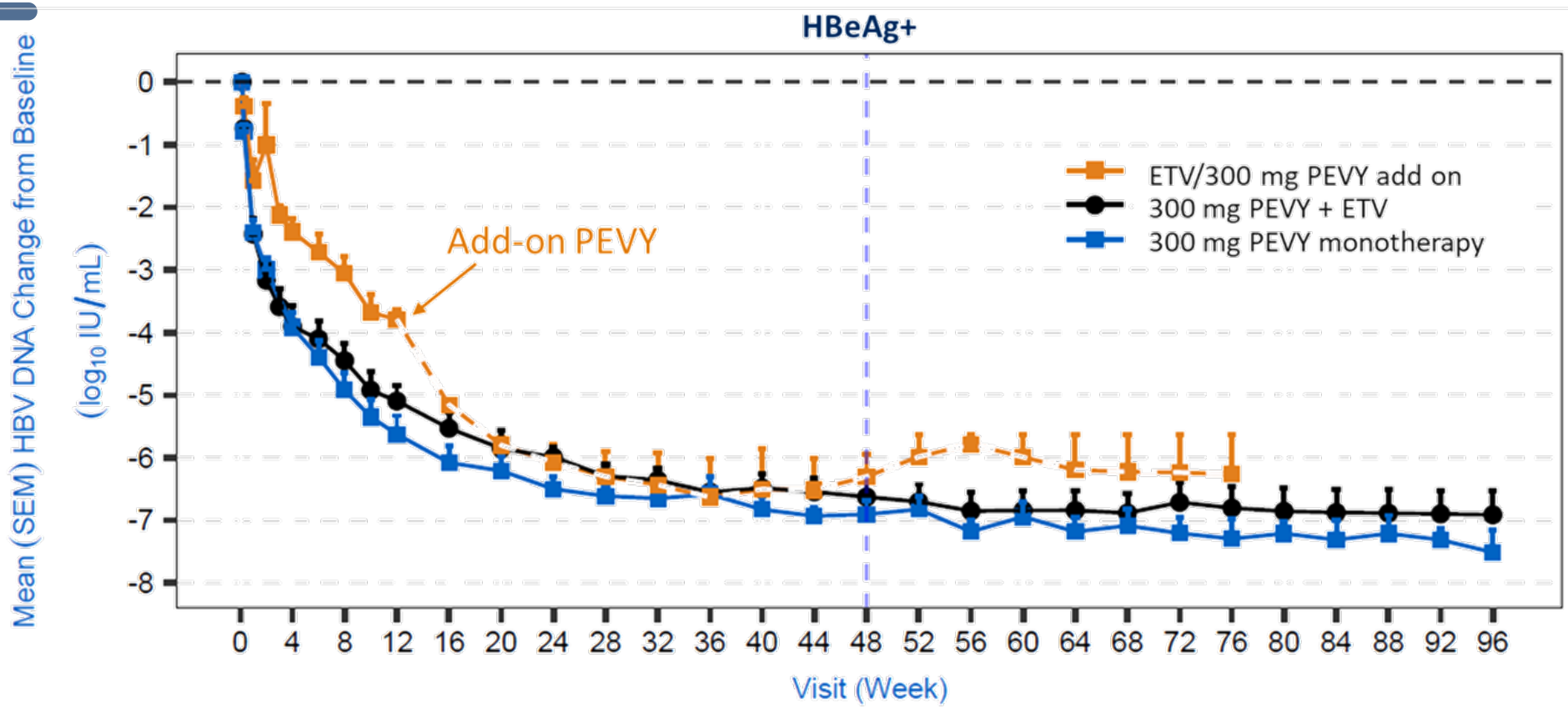
Yuen, M-F. et al; AASLD 2025.

# 300 mg Pevifoscorvir Sodium ± ETV in HBeAg Positive Subjects

## Mean HBV DNA Change from Baseline




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| ETV/300 mg PEVY add on | 3 | 3 | 3 | 3 | 3 | 2 | 2 | | |
| 300 mg PEVY + ETV | 11* | 9 | 9 | 9 | 8 | 8 | 7 | 7 | 7 |
| 300 mg PEVY monotherapy | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

Yuen, M-F. et al; AASLD 2025. *One subject excluded due to dosing non-compliance; PEVY – pevifoscorvir sodium.

**300 mg pevifoscorvir sodium demonstrates greater HBV DNA reduction than ETV monotherapy**

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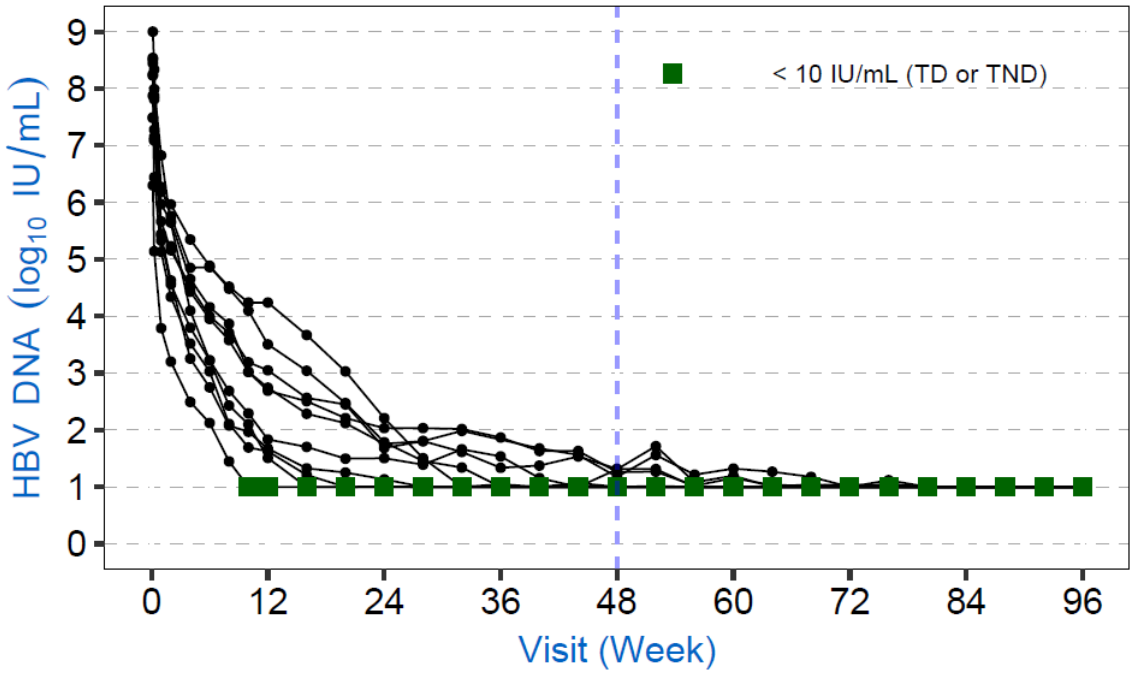
# 300 mg Pevifoscorvir Sodium Monotherapy

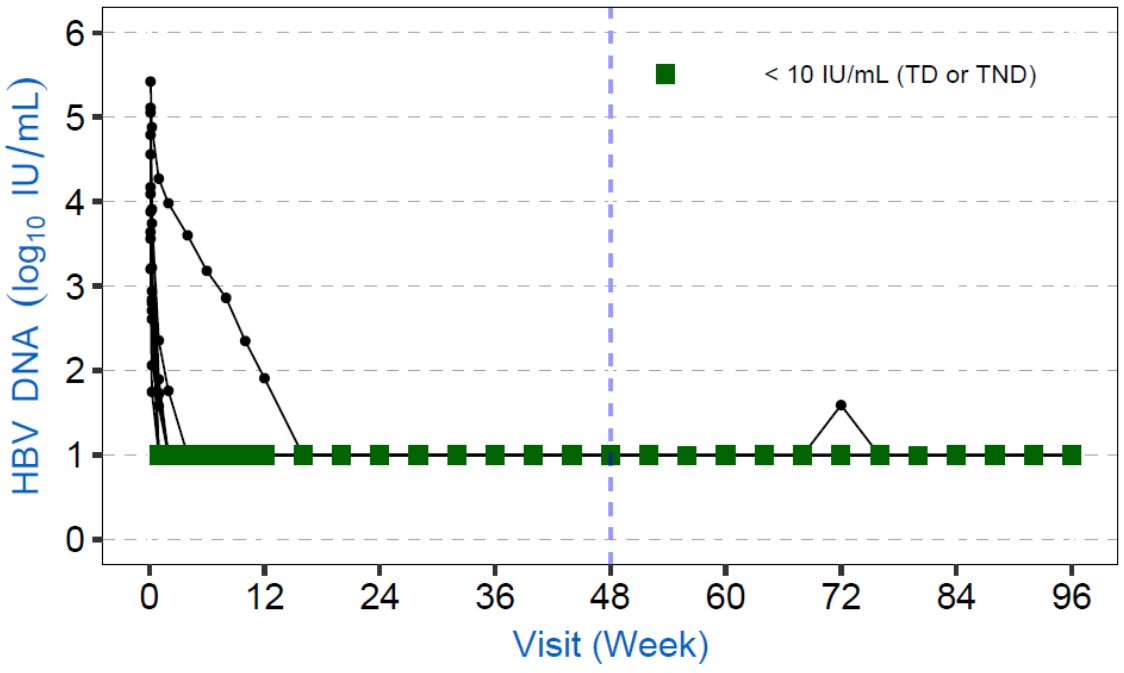
## Reduction in Individual HBV DNA Level Over Time

**HBeAg+**




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Total n | 10 | 10 | 10 | 9 | 10 | 10 | 10 | 10 | 10 |
| < 10 IU/mL (TD or TND) | 0 | 1 | 2 | 5 | 6 | 7 | 9 | 10 | 10 |
| < 10 IU/mL (TND) | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 3 | 5 |

**HBeAg-**




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 11 | 11 | 11 | 11 | 11 | 10 | 9 | 9 | 9 |
| | 0 | 10 | 11 | 11 | 11 | 10 | 8 | 9 | 9 |
| | 0 | 7 | 6 | 7 | 10 | 8 | 7 | 8 | 8 |

Yuen, M-F. et al; AASLD 2025. TD – target detected; TND – target not detected, LOD ≤ 4.29 IU/mL.

Note: one HBeAg- subject had transient HBV DNA increase from < LLOQ to 39 IU/mL at Week 72. At the subsequent visit (Week 76) HBV DNA was < LLOQ (10 IU/mL).

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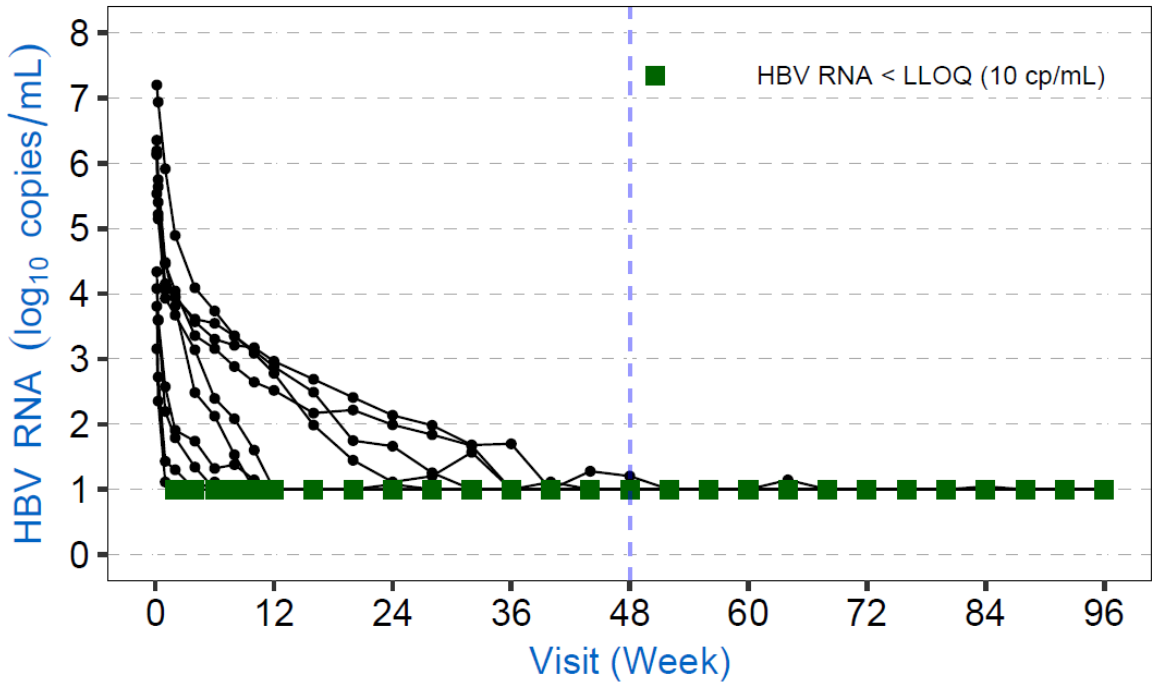
**300 mg pevifoscorvir sodium monotherapy demonstrates profound HBV DNA reduction in TN/CNT subjects with chronic HBV infection; no viral breakthrough observed**

# 300 mg Pevifoscorvir Sodium Monotherapy

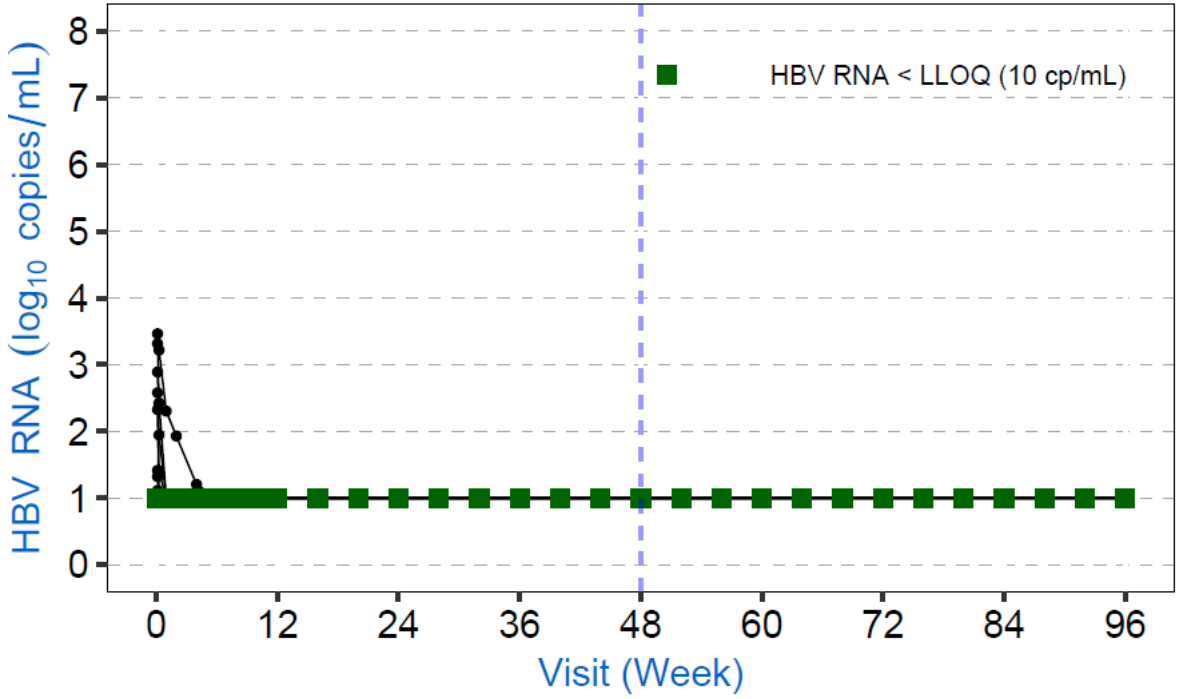
## Reduction in Individual HBV RNA Level Over Time

**HBeAg+**




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Total n | 10 | 10 | 10 | 9 | 10 | 10 | 10 | 10 | 10 |
| < 10 cp/mL | 0 | 6 | 5 | 8 | 9 | 10 | 10 | 9 | 10 |

**HBeAg-**




| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 11 | 11 | 11 | 11 | 11 | 10 | 9 | 9 | 9 |
| | 3 | 11 | 11 | 11 | 11 | 10 | 9 | 9 | 9 |

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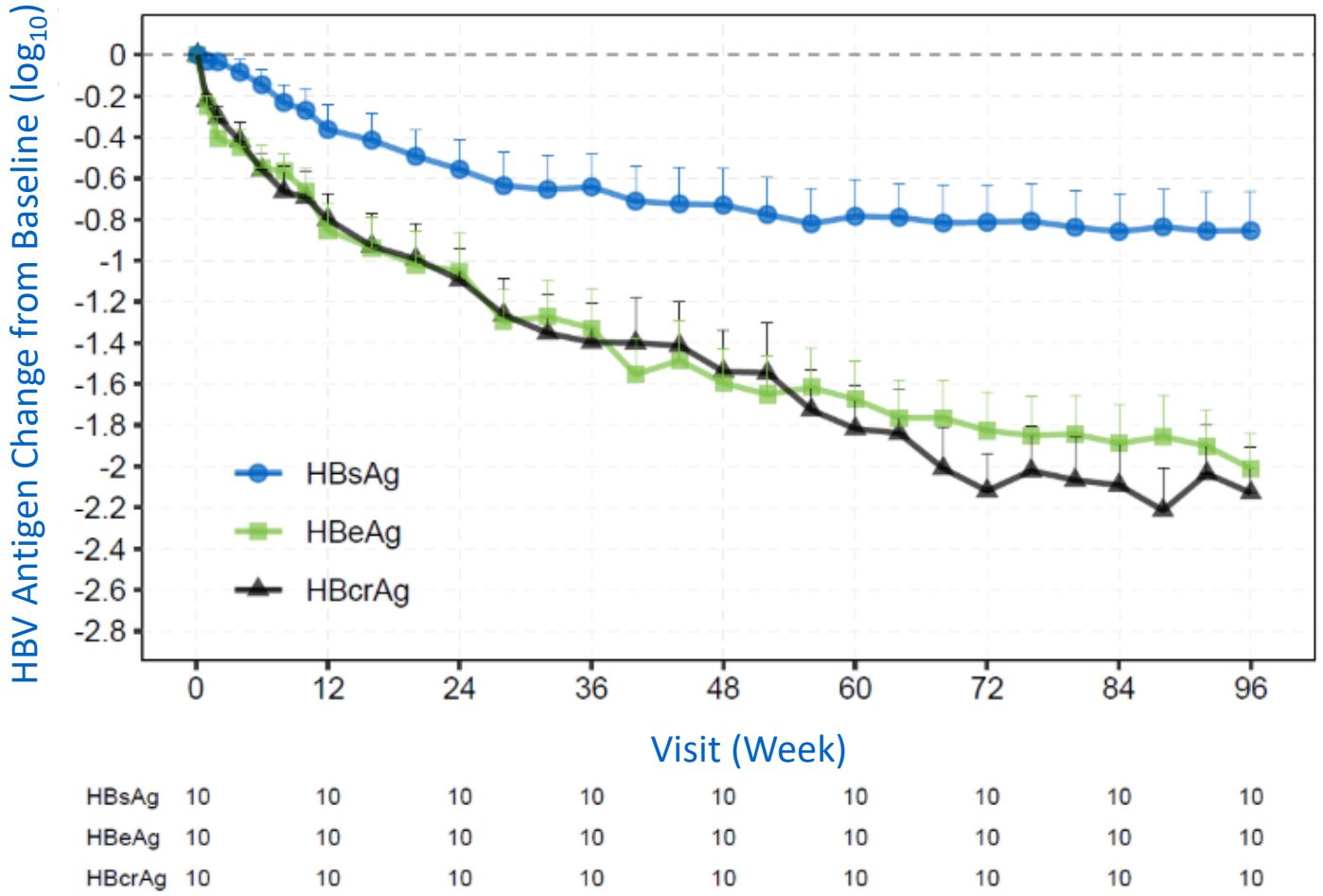
**300 mg pevifoscorvir sodium monotherapy demonstrates a rapid and profound HBV RNA reduction in TN/CNT subjects with chronic HBV infection**

# 300 mg Pevifoscorvir Sodium Monotherapy in HBeAg Positive Subjects

## Mean HBV Antigen Change From Baseline




Yuen, M-F. et al; AASLD 2025. Note: Data represents Mean (SEM) at each visit.

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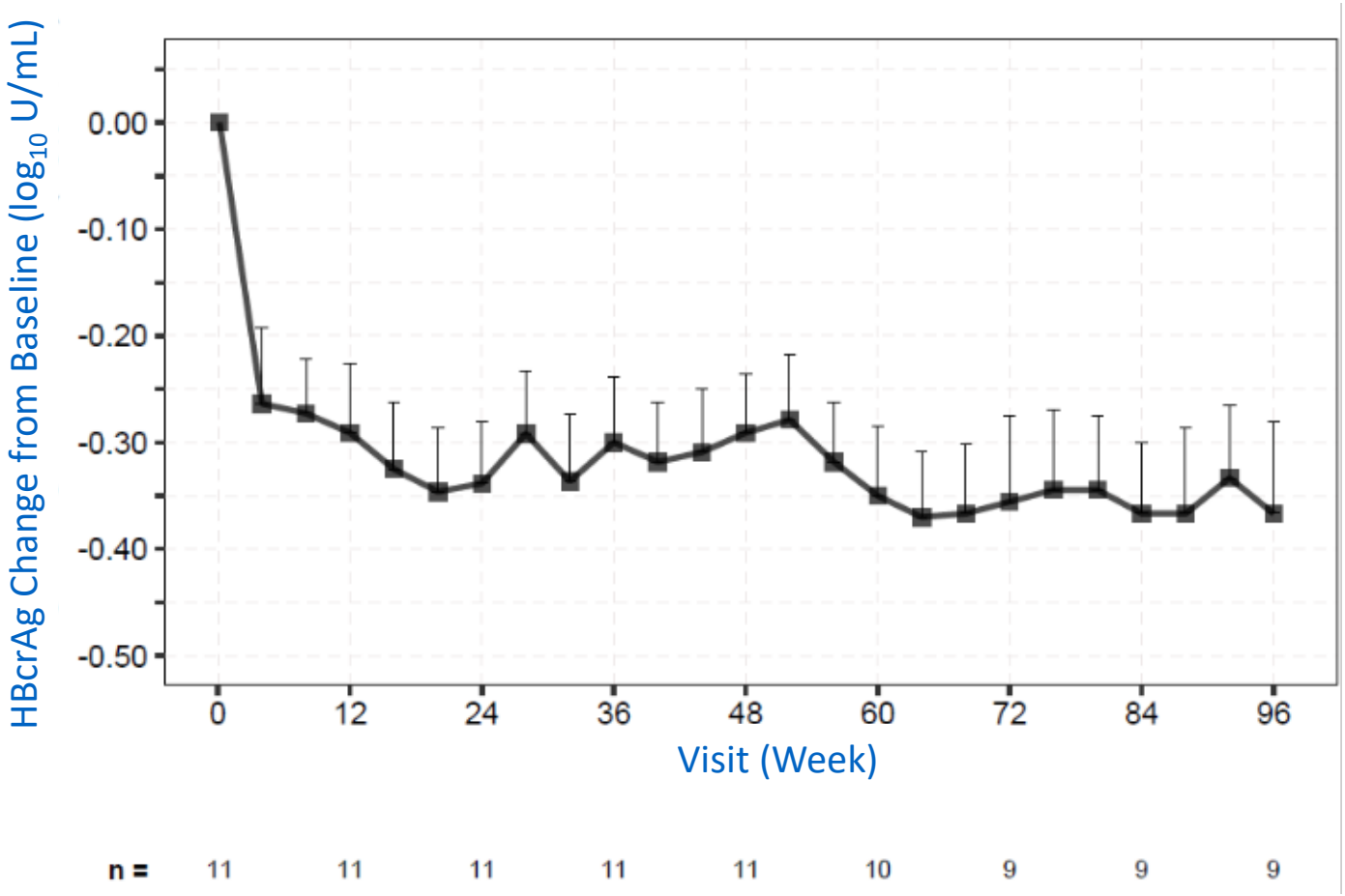
**Substantial HBsAg, HBeAg, and HBcrAg reductions noted in HBeAg+ subjects**

# 300 mg Pevifoscorvir Sodium Monotherapy in HBeAg Negative Subjects

## Mean HBcrAg Change From Baseline




Yuen, M-F. et al; AASLD 2025. Data represents Mean (SEM) at each visit.

**Meaningful HBcrAg reduction in HBeAg- subjects, no change in HBsAg**

# 96-Week 300 mg Pevifoscorvir Sodium Monotherapy Post Treatment Data

## 8-Week NA Follow Up

| HBeAg Status | Viral Marker | Data |
|---|---|---|
| E- | HBV DNA | 8/8 subjects had HBV DNA level < 10 IU/mL during NA only 8 Week follow-up |
| | HBV RNA | HBV RNA rebounds slightly after switching to NA but remains lower than baseline |
| | HBV Antigens | HBcrAg decline was maintained during the NA only 8 Week follow-up |
| E+ | HBV DNA | 6/8 subjects had HBV DNA level < 10 IU/mL during the NA only 8 Week follow-up |
| | HBV RNA | HBV RNA rebounds after switching to NA but remains lower than baseline |
| | HBV Antigens | No apparent HBV antigens increase observed during the NA only 8 Week follow-up |

Yuen, M-F. et al; AASLD 2025.

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**These data suggest that pevifoscorvir sodium may reduce the cccDNA pool through engagement of its secondary mechanism of action**

# 300 mg Pevifoscorvir Sodium Monotherapy

## Safety Following 96 Weeks of Treatment

| | HBeAg+ | HBeAg- |
|---|---|---|
| **Numbers of subjects with** | N=10 | N=11^ |
| • **At least one TEAE, n (%)** | 9 (90) | 9 (81.8) |
| • **SAE** | 0 | 0 |
| • **TEAE leading to study drug discontinuation** | 0 | 0 |
| • **TEAE Grade ≥3** | 3* | 2*,# |

^ Two HBeAg-negative subjects withdrew at Week 56 and 64 due to non-safety personal decisions.
* Grade ≥3 TEAEs of ALT/AST elevation were observed in 3 HBeAg-positive and 1 HBeAg-negative subjects with preserved synthetic and excretory functions. All events resolved in the setting of continued pevifoscorvir sodium dosing and were not considered clinically concerning by the ALT Flare Committee.
# Grade 3 cholesterol/triglycerides increase in HBeAg-negative subject resolved in the setting of continued pevifoscorvir sodium dosing.

Yuen, M-F. et al; AASLD 2025.

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**Favorable safety profile observed in TN/CNT HBeAg+ and HBeAg- subjects with chronic HBV infection who received 300 mg pevifoscorvir sodium monotherapy for 96 weeks**

# Chronic Suppression

## Well Defined, Validated Approval Pathway

- Regulatory pathway for chronic suppressive therapy endorsed by FDA, CHMP (EMA), and National Medical Products Administration in China
- Primary endpoint: Subjects with HBV DNA <LLOQ (10 IU/mL) at Week 48 following treatment with investigational agent versus standard of care (nucleos(t)ide analogs)

a. Chronic suppressive therapy

Sponsors developing drugs for chronic suppressive therapy of CHB should consider the following trial design options:

- A randomized controlled noninferiority (NI) (or superiority) trial comparing the investigational drug with an approved active control arm—The primary efficacy endpoint should be undetectable HBV DNA[13] after 48 weeks on-treatment in HBeAg-positive subjects, HBeAg-negative subjects, or both. The active comparator should be an antiviral drug that is recommended for treatment of CHB and reflects current practice at the time of trial initiation. The patient population may be treatment-naïve or previously treated subjects with detectable HBV DNA. Potential concerns related to the development of resistance when evaluating an investigational drug with a low barrier to resistance as a monotherapy should be addressed. For an NI design, determination of the NI margin should be discussed with the FDA.

HBV Guidance from: FDA 2022; EMA 2006; China 2023; LLOQ: lower limit of quantitation.

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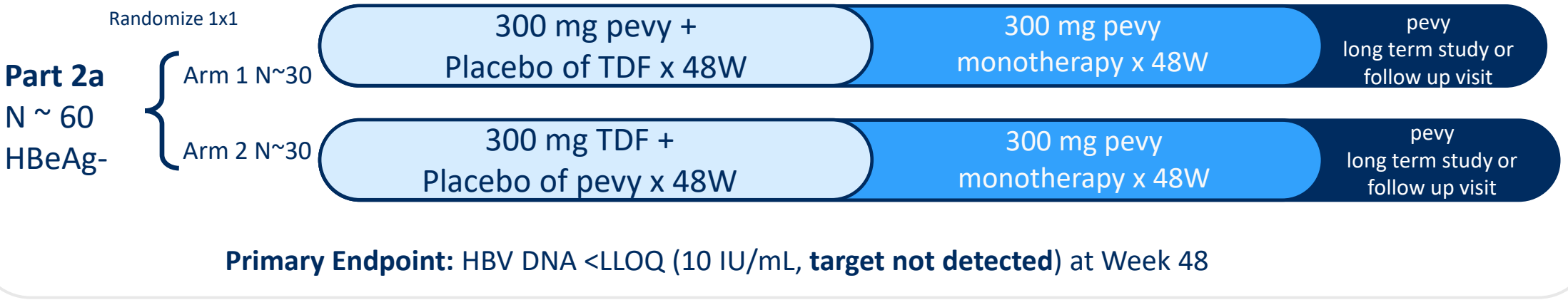
**Aligos has received FDA, CHMP (EMA), and National Medical Products Administration in China feedback supporting subsequent studies utilizing this pathway**

# B-SUPREME – Phase 2 Study Design

## Primary Analysis at 48 Weeks; Extension Period Analysis at 96 Weeks; Interim Readouts Planned


**Primary Endpoint:** HBV DNA <LLOQ (10 IU/mL, **target detected *or* target not detected**) at Week 48




**Primary Endpoint:** HBV DNA <LLOQ (10 IU/mL, **target not detected**) at Week 48

Part 1b will be a liver biopsy sub-study inclusive of n≈12. Part 2b will be a liver biopsy sub-study inclusive of n≈12. pevy = pevifoscorvir sodium.

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**The Phase 2 B-SUPREME study is currently enrolling and dosing subjects**

# Summary

## Pevifoscorvir Sodium 300 mg Monotherapy for 96 Weeks

- Pevifoscorvir sodium 300 mg monotherapy in TN/CNT HBeAg+ and HBeAg- subjects for 96 weeks in our Phase 1 study demonstrated:
  - Favorable safety profile
  - Rapid, profound and durable reduction in HBV DNA without viral breakthrough
    - In HBeAg-positive subjects, 60% subjects achieved HBV DNA level < 10 IU/mL at Week 48, and increased to 100% at Week 96
    - In HBeAg-negative subjects, 100% achieved HBV DNA < 10 IU/mL by Week 20 and 89% (8/9) achieved < LOD (≤ 4.29 IU/mL) at Week 96
  - Rapid and profound reduction in HBV RNA
  - Multiple log reduction in HBV antigens were achieved
- HBV antigen and HBV RNA reduction were maintained during NA only 8-Week follow up suggesting pevifoscorvir sodium potentially reduces cccDNA pool due to engagement of the CAM-E secondary MOA
- The Phase 2, B-SUPREME study (NCT06963710) evaluating 300 mg pevifoscorvir sodium monotherapy compared to NA monotherapy in TN/CNT subjects with chronic HBV infection, including liver biopsy sub-study, is currently ongoing

# Acknowledgements

FRONTIERS IN DRUG DEVELOPMENT FOR HEPATOLOGY

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