Monotherapy with the Capsid Assembly Modulator ALG-000184 Results in Rapid Viral Load Reduction and High Viral Suppression Rates in Untreated HBeAg-Negative Subjects with Chronic Hepatitis B Virus Infection

Edward Gane[1], Kosh Agarwal[2], Alina Jucov[3], Alexei Haceatrean[3], Min Wu[4], Kha Le[4], Thanh Van[4], Jen Rito[4], Lawrence M. Blatt[4], Sushmita Chanda[4], Tse-I Lin[4], Hardean E. Achneck[4], Man-Fung Yuen[5]

1. Faculty of Medicine, University of Auckland, Auckland, New Zealand; 2. King's College Hospital, Institute of Liver Studies, London, United Kingdom; 3. ARENSIA Exploratory Medicine, Republican Clinical Hospital and Nicolae Testemitanu State University of Medicine and Pharmacy, Chișinău, Moldova; 4. Aligos Therapeutics, Inc., South San Francisco, United States; 5. Department of Medicine, School of Clinical Medicine, The University of Hong Kong, Hong Kong, China

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Disclosure of Conflict of Interest

- Member of Scientific Advisory Board for Aligos, Assembly, AusperBio, Epigenetics Therapeutics, Gilead, GSK, Janssen, Roche, Surrozen, VIR, Virion, Precision Biosciences, Tune Therapeutics.
- Speaker for AbbVie, Roche Diagnostics.

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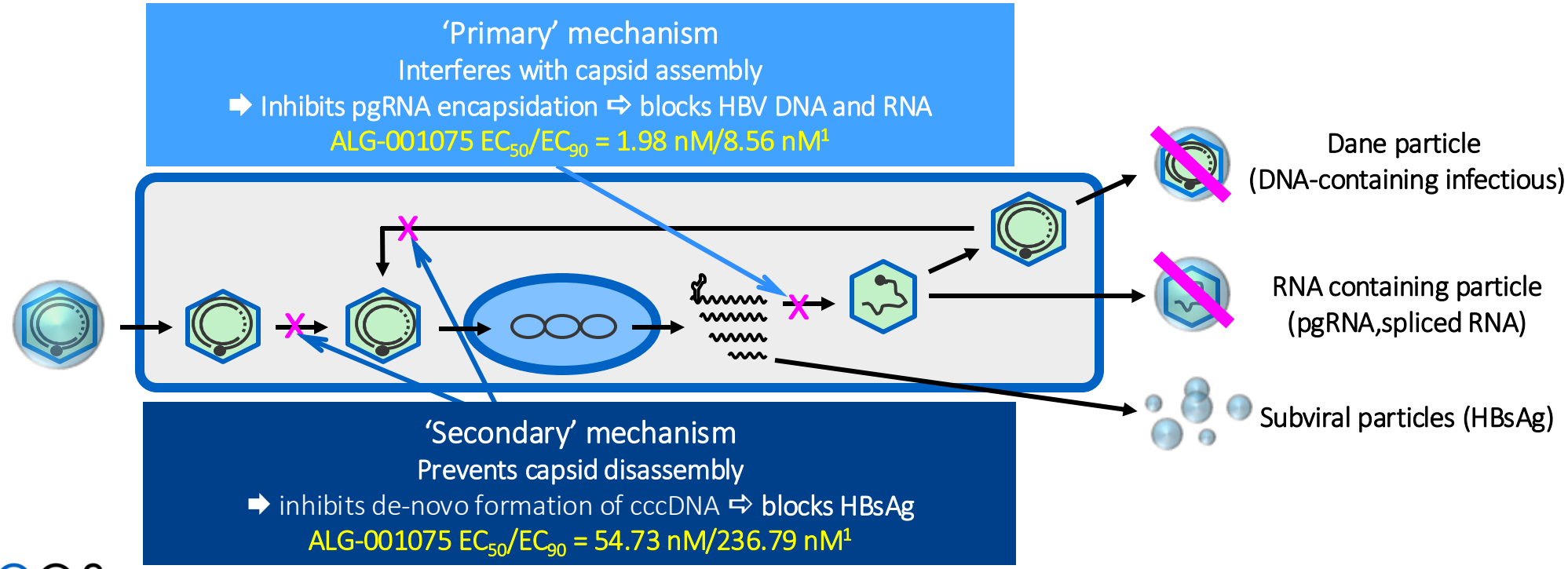
Background

- **Importance of HBV DNA Suppression:** Achieving undetectable levels of HBV DNA using most sensitive assays crucial for effective viral control, reducing risk of liver disease progression. [WHO 2015, AASLD 2018, EASL 2017].
- **ALG-000184:** a prodrug of a novel CAM, ALG-001075, with potent in vitro anti-HBV activity through a dual mechanism-of-action (MOA):



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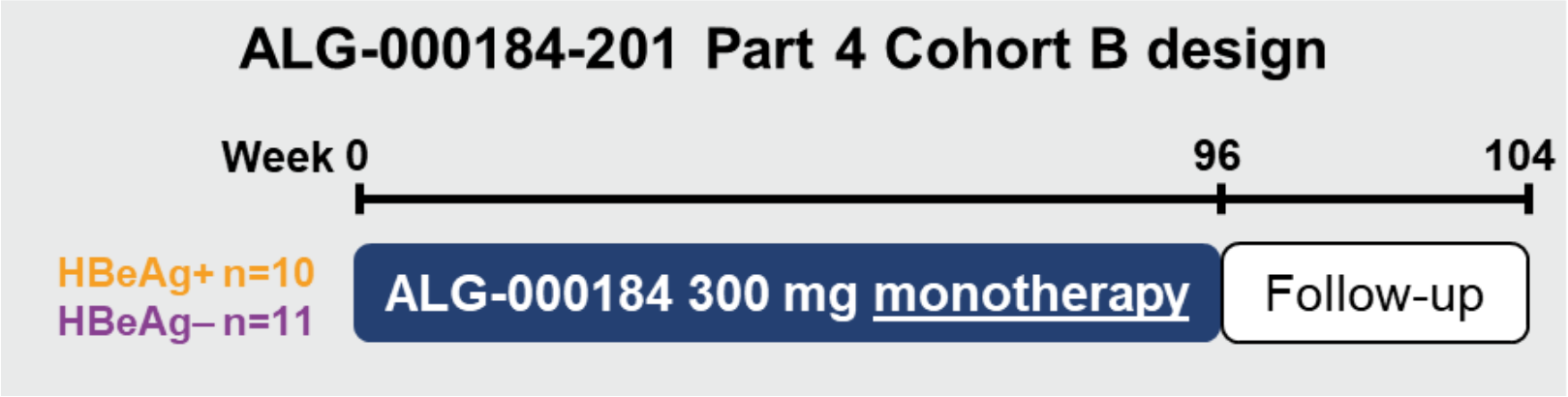
1 Sandrine Vendeville et. al, Journal of Medicinal Chemistry 67:23

Background

- **ALG-000184-201 Study:** An ongoing Phase 1 study has shown favorable safety and potent antiviral activity in treatment naive or current not treated chronic HBV infection subjects receiving 300 mg ALG-000184 monotherapy ≤ 92 weeks [AASLD 2024 poster]:
  - **Significant Reductions:** Multiple log declines in HBV DNA, RNA and all HBV antigen levels were detected;
  - **No Breakthrough:** No virologic breakthrough was observed in any subjects.
- **Emerging Data:** Efficacy and safety data in HBeAg-negative subjects receiving 300 mg ALG-000184 monotherapy for ≤ 96 weeks.



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Baseline Characteristics in TN/CNT HBeAg-Negative Subjects 300 mg ALG-000184 monotherapy for ≤ 96 weeks

Baseline Characteristics	TN/CNT HBeAg-negative subjects (N=11)
Age, years, mean (SD)	48.5 (3.1)
Male, N (%)	6 (55)
Asian, N (%)	3 (27)
BMI, kg/m^2, mean (SD)	26.0 (1.1)
HBV Genotype B/C, N (%)	B:2(18), C:1(9), D:7(64), A:1(9)
HBV DNA, log_{10} IU/mL, median (SD)	4.3 (0.2)
HBV RNA, log_{10} copies/mL, median (SD)	2.0 (0.3)
HBsAg, log_{10} IU/mL, median (SD)	3.5 (0.2)
HBcrAg, log_{10} U/mL, mean (SD)	3.1 (0.3)
ALT, U/L, mean (SD)	35 (14.5)

Treatment Naïve (TN) subjects are defined as participants who have never received treatment with HBV antiviral medicines (NA, interferon [IFN]), or investigational anti-HBV agents including a CAM;
Current-not-treated (CNT) subjects are defined as participants who have not been on treatment with approved (NA, IFN) or investigational HBV antiviral medicines within 6 months prior to randomization

Majority were non-Asian (8/11)
Low-level viremia of HBV prior to dosing with ALG-000184

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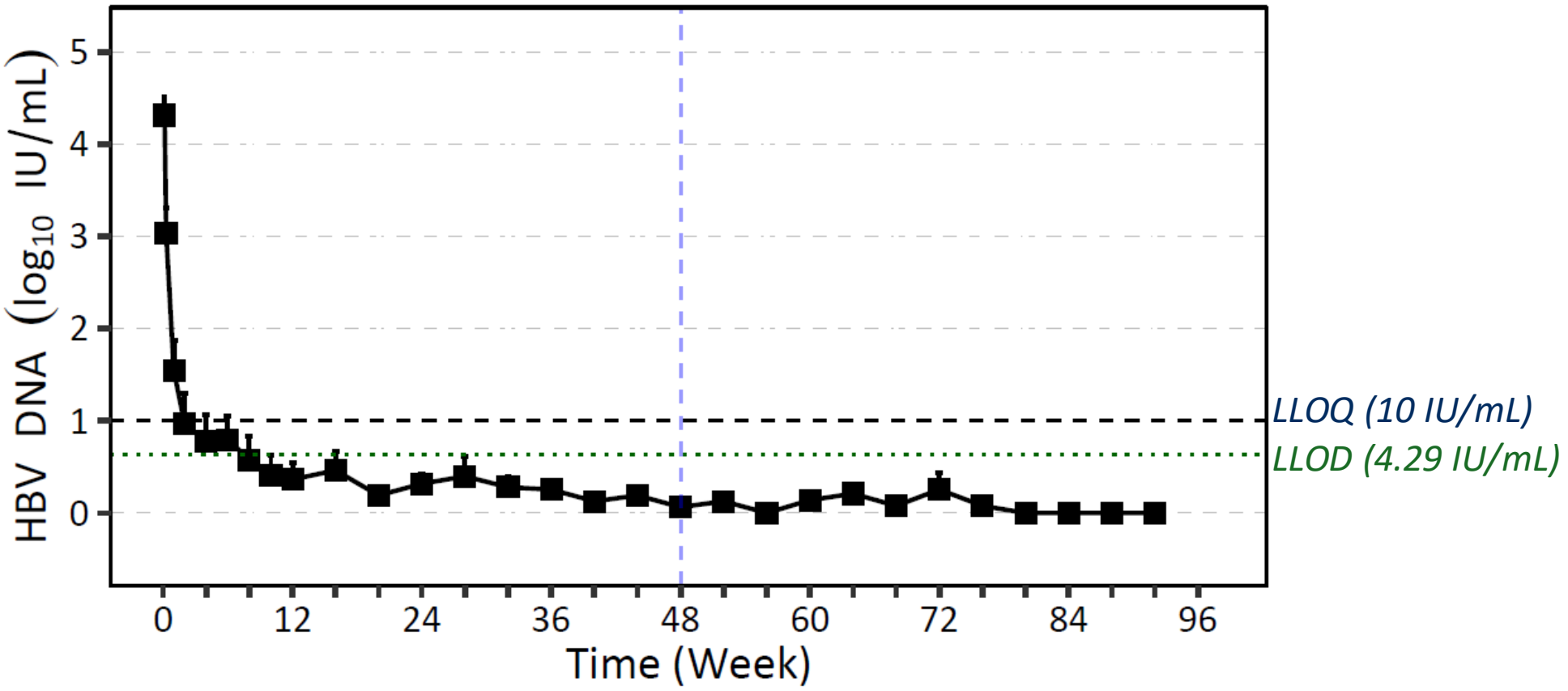
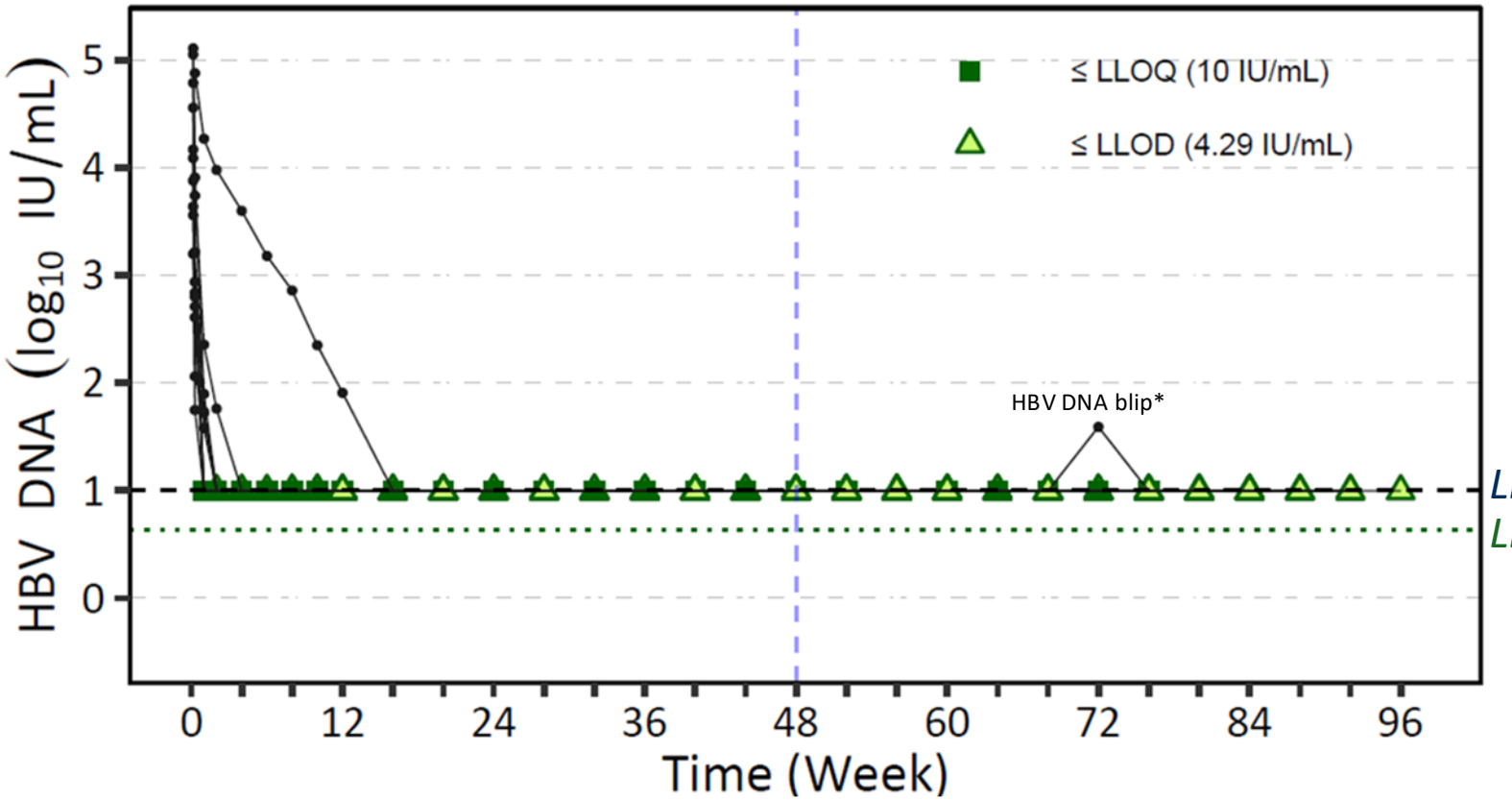
Mean HBV DNA Level
300 mg ALG-000184 monotherapy for ≤ 96 weeks



Number of subjects	11	11	11	11	11	10	9	6
Mean change from baseline	0	-4	-4	-4.1	-4.3	-4.2	-4	-4.2
Median change from baseline	0	-3.9	-4.1	-4.1	-4.2	-4.4	-4.2	-4.1
SEM	0	0.21	0.19	0.21	0.19	0.24	0.28	0.18

Individual HBV DNA Levels
300 mg ALG-000184 monotherapy for ≤ 96 weeks



LLOQ (10 IU/mL)
LLOD (4.29 IU/mL)

Number of subjects	11	11	11	11	11	10	9	6	1
n ≤ LLOQ (10 IU/mL)	0	10	11	11	11	10	8	6	1
n ≤ LLOD (4.29 IU/mL)	0	7	6	7	10	8	7	6	1

*One 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) and maintained this level during 300 mg ALG-000184 monotherapy.

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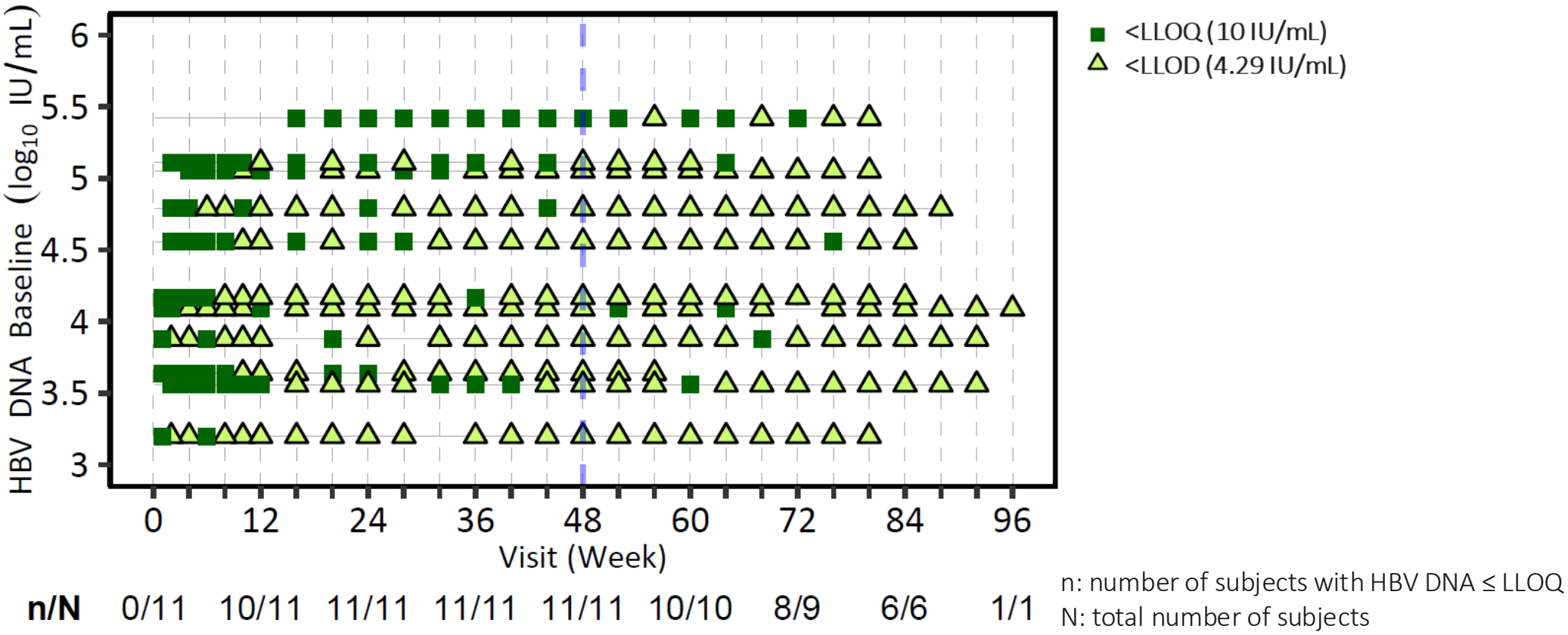
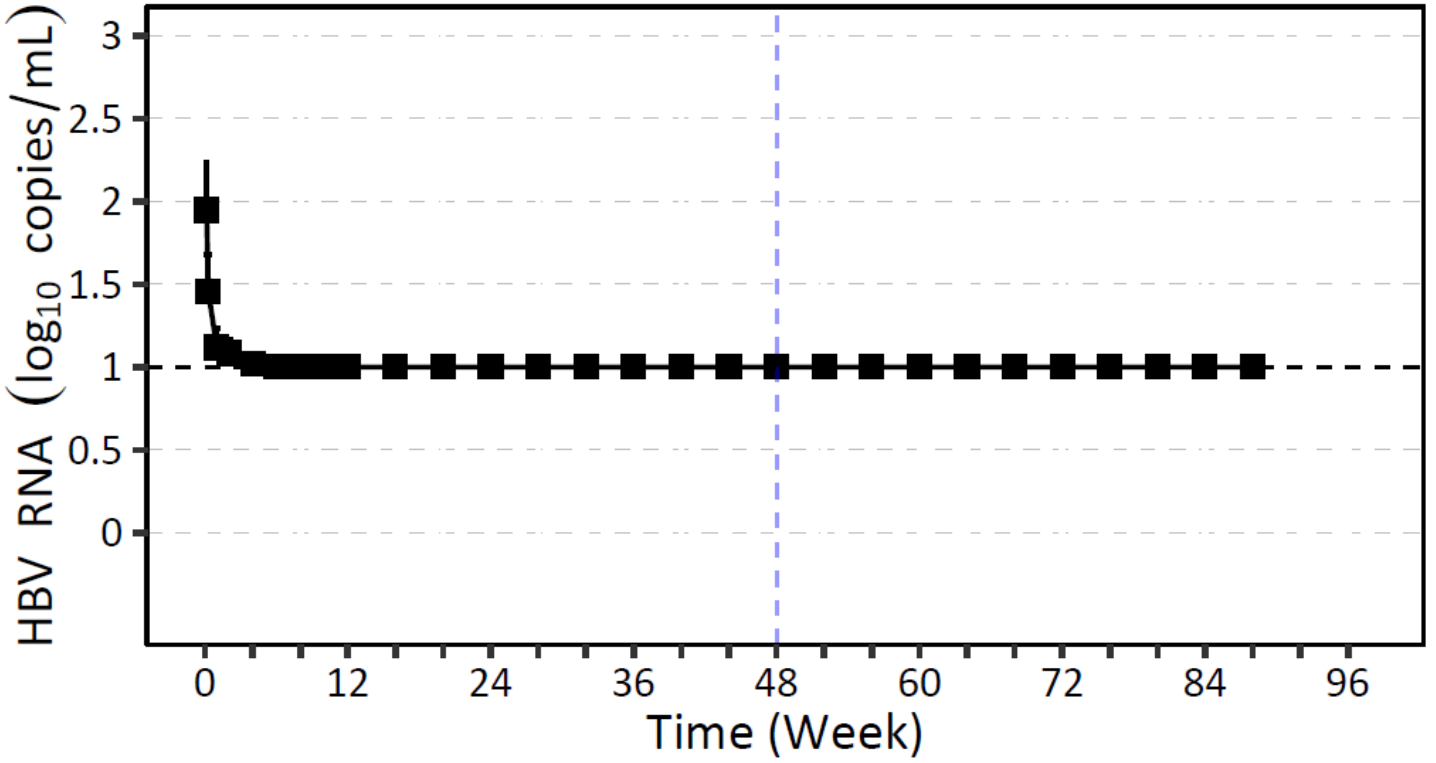
Individual Time to Reach HBV DNA < LLOQ or < LLOD
300 mg ALG-000184 monotherapy for ≤ 96 weeks



n: number of subjects with HBV DNA ≤ LLOQ
N: total number of subjects

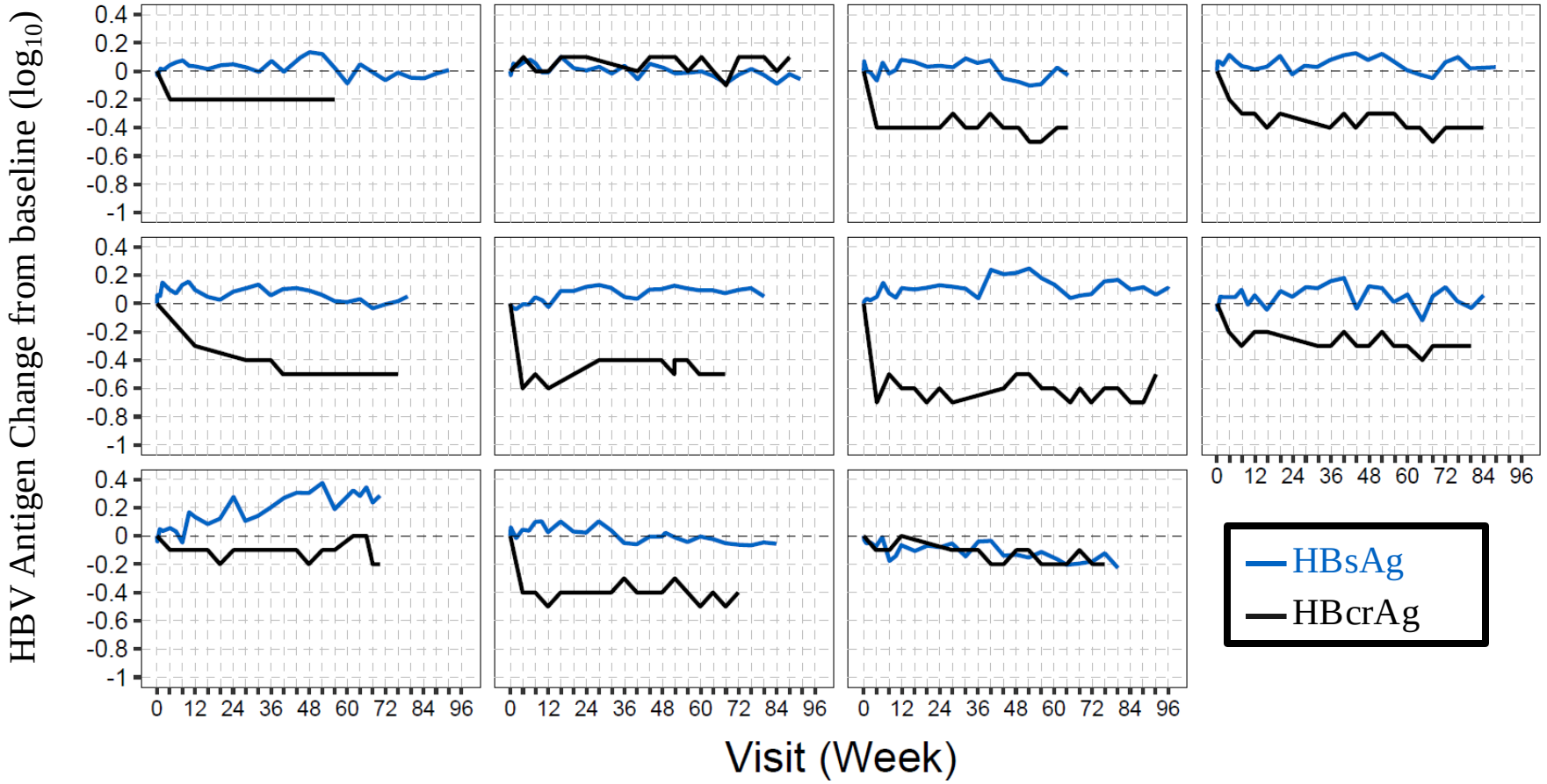
Time to HBV DNA suppression is dependent on baseline HBV DNA level
100% subjects achieved HBV DNA < LLOQ (10 IU/mL) at Week 20
100% subjects achieved < LLOD (4.29 IU/mL) by Week 80
No virologic breakthrough on ALG-000184 monotherapy

Mean HBV RNA Level
300 mg ALG-000184 monotherapy for ≤ 96 weeks



n/N	3/11	11/11	11/11	11/11	11/11	10/10	9/9	4/4
n: number of subjects with HBV RNA ≤ LLOQ N: total number of subjects								
Mean change from baseline	0	-0.95	-0.95	-0.95	-0.95	-1	-0.91	-0.36
Median change from baseline	0	-0.41	-0.41	-0.41	-0.41	-0.87	-0.41	-0.06
SEM	0	0.3	0.3	0.3	0.3	0.32	0.34	0.32

Individual HBcrAg & HBsAg Changes from Baseline 300 mg ALG-000184 Monotherapy for ≤ 96 weeks



Mean HBcrAg change from baseline -0.3 log_{10} U/mL; maximum decline 0.7 log_{10} U/mL; 6/11 (55%) TN/CNT HBeAg-negative subjects had HBcrAg reduction ≥ 0.5 log_{10} U/mL.

Safety
300 mg ALG-000184 monotherapy for ≤ 96 weeks

	TN/CNT HBeAg-negative subjects
Numbers of subjects with	N=11
at least one TEAE, n (%)	6 (55)
SAE	0
TEAE leading to study drug discontinuation	0
TEAE Grade ≥3	2 ALT/AST elevations (n=1) Cholesterol and triglycerides increase (n=1)

300 mg ALG-000184 monotherapy for ≤ 96 weeks has favorable safety profile
1 Grade ≥3 TEAE of cholesterol/triglycerides increase.
1 Grade ≥3 TEAE of ALT/AST elevation with preserved synthetic and excretory functions not considered clinical concerning by ALT Flare Committee.
Both ≥3 TEAEs resolved in setting of continuedALG-000184 dosing .

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Summary

300 mg ALG-000184 monotherapy in TN/CNT HBeAg-negative subjects for ≤ 96 weeks demonstrated:

- A favorable safety profile
- Rapid and profound suppression in HBV DNA and HBV RNA:
  - All subjects achieved HBV DNA < LLOQ (10 IU/mL) by Week 20 and achieved < LLOD (4.29 IU/mL) by Week 80.
  - Sustained HBV RNA < LLOQ (10 copies/mL) by Week 8 for all subjects.
  - Significant declines in HBcrAg levels
  - No virologic breakthrough was observed in any subject.
- No HBsAg reductions observed in HBeAg negative patients, suggesting that most HBsAg in derived from integrated HBs gene rather than cccDNA.

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Conclusions

- These results suggest that 300 mg ALG-000184 monotherapy achieves faster and more pronounced HBV DNA reduction than historically observed with nucleos(t)ide analogues, with no evidence of breakthrough
- ALG-000184 monotherapy could become a favorable option for chronic suppressive therapy in patients with chronic HBV infection.

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Acknowledgement

Sincere gratitude to all individuals and organizations that contributed to this HBV data presentation.

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- To the CRO Novotech for their invaluable insights and support.

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