

ALG-000184 Late-Breaking Phase 1b Data from AASLD KOL Perspective on Emerging HBV Therapies

November 16, 2023

#### Disclosures

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Except where otherwise indicated, the information contained in this presentation speaks as of the date hereof or as of the date at which such information is expressed to be stated, as applicable, and such information may express preliminary estimated, unaudited results which shall be subject to audit or other year-end adjustments and such audited or adjusted results may materially differ from those contained in this presentation.

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.

# ALIGOS

# Mark Sulkowski Disclosures

- The terms of these arrangements are being managed by the Johns Hopkins University in accordance with its conflict of interest policies
  - Research (JHU): Abbvie, GSK, Janssen, Vir, Virion
  - Scientific advisory board: Abbvie, Aligos, Arbutus, Galapagos, Gilead, GSK, Precision, Vir, and Virion
  - DSMB: Gilead, Immunocore
  - Editorial board: Journal of Viral Hepatitis (Wiley)



Aligos overview and ALG-000184 profile for Chronic Hepatitis B (CHB)	Lawrence Blatt, Ph.D., MBA President and Chief Executive Officer Aligos Therapeutics	1:30 – 1:40 p.m.
ALG-000184 Phase 1 – Parts 1-3	Matthew McClure, M.D. Executive Vice President, Chief Medical Officer Aligos Therapeutics	1:40 – 1:50 p.m.
ALG-000184 Phase 1 – Part 4 Late-breaking data from AASLD	Mark Sulkowski, M.D. Professor of Medicine Johns Hopkins School of Medicine	1:50 – 2:05 p.m.
Moderated Q&A Session	<b>Corey Davis, Ph.D.</b> Managing Director, LifeSci Advisors, LLC	2:05 – 2:25 p.m.
Concluding Remarks	Lawrence Blatt, Ph.D., MBA President and Chief Executive Officer Aligos Therapeutics	2:25 – 2:30 p.m.



# Aligos Development Portfolio Multiple Milestones/Data Readouts Anticipated in 2023/2024

Candidate	Indication	MOA	2023/2024 Clinical Trial Timelines and Data Readouts					
			Q4 2023	Q1 2024		Q2 2024		Q3 2024
ALG-055009	NASH	THR-β Agonist	Ph2a filing Phase 2 Enabling Activities		(12 we	Phase 2a ek MRI-PDFF in	NASH)	
Oligonucleotide (including SMERCK)	ΝΑΟΠ	Undisclosed	Preclinical Activities					
ALG-097558	Covid-19*	Protease Inhibitor	Phase 1 (HV)					
ALG-000184	СПВ	CAM-E	AASLD (48 week data)	Up to 96 We	<b>T</b>	7	ASL	
ALG-125755	CHB	siRNA	Phase 1 (CHB)					

All timelines are approximate and subject to change based on enrollment and operational considerations. Presentations at conferences are subject to abstract approvals.

\*Our Covid protease inhibitor efforts are partly funded (>\$11M USD awarded) by the NIH and NIAID's AViDD Centers for Pathogens of Pandemic Concern program through the MAVDA consortium and our recently awarded NIAID Contract.

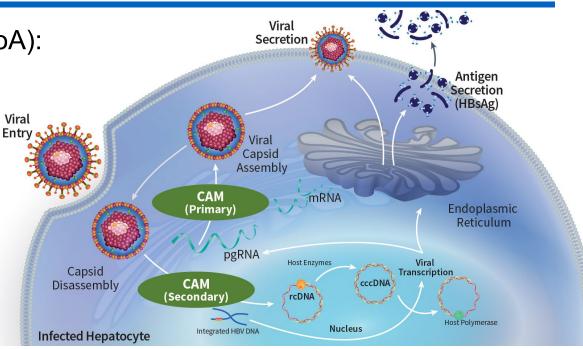
AASLD = American Association for the Study of Liver Diseases; APASL = Asian Pacific Association for the Study of the Liver; CAM-E = capsid assembly modulator (empty); CHB = chronic hepatitis B; Covid-19 = coronavirus disease of 2019 (SARS-CoV-2); EASL = European Association for the Study of the Liver;

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HV = healthy volunteers; MOA = mechanism of action; MRI-PDFF = Magnetic Resonance Imaging Proton Density Fat Fraction; NASH = nonalcoholic steatohepatitis; siRNA = small interfering ribonucleic acid (RNAi); THR-β = thyroid hormone receptor beta. 4

# Hepatitis B Virus (HBV) Treatment The Dual Role of Capsid Assembly Modulators (CAMs)

- In preclinical studies, 2 mechanisms of action (MoA):
  - Primary mechanism
    - Promotes the premature assembly of core protein, leading to the formation of empty capsids
    - Responsible for the deep reductions of HBV DNA and RNA observed clinically
  - Secondary mechanism
    - > Requires >10-fold higher drug concentrations
    - Prevents the establishment / replenishment of cccDNA, which produces HBcrAg, HBeAg, and (some of) HBsAg
- 1<sup>st</sup> generation CAMs in development since 2014
  - Consistently demonstrated DNA, RNA reductions (1<sup>st</sup> MoA)
  - To date, no clear evidence of effects on 2<sup>nd</sup> MoA



Observing both mechanisms clinically likely requires potent compounds with excellent PK properties



# ALG-000184 Superior Potency vs. Competitor CAM-Es

Compound	Current Status	HBV DNA reduction (EC <sub>50</sub> nM)	Cell Type	
	Dhana 4	0.63	HepG2.117	
Aligos ALG-000184	Phase 1	0.53	HepG2.2.15	_2 <sup>nd</sup>
Assembly ABI-4334	Phase 1	1.2	AD38	Gen
Assembly ABI-H3733	Partnered, BeiGene	5	AD38	
Enanta EDP-514	Phase 1	17	HepG2.115	
Vebicorvir	Discontinued	172	AD38	1st
Janssen JNJ-6379	Discontinued	54	HepG2.117	Gen
Arbutus AB-836	Discontinued	10	HepDE19	

ALG-000184 generally 10-300-fold more potent vs. other known CAM-Es Exposures also enhanced via PK optimization strategies



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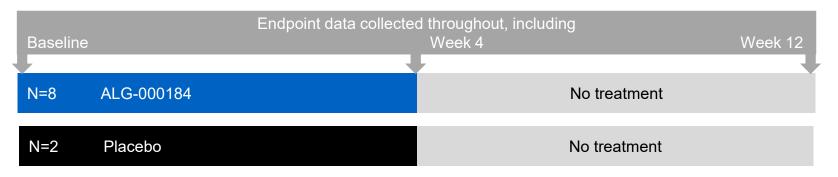


# ALG-000184-201 Phase 1 Study in HV (Parts 1& 2) and CHB Subjects (Parts 3-5)

Parts 1-3: Complete

- Part 1 (SAD): single oral doses (40, 100, 250 and 500 mg) in HV
- Part 2 (MAD): 7 QD oral doses (150 and 250 mg) in HV
- Part 3: QD oral doses (10-300 mg) x 28 days in treatment naïve (TN)/currently not treated (CNT) CHB

Multiple Doses in Currently Not Treated/Treatment Naïve CHB Subjects HBV DNA > 2000 IU/mL, HBeAg Negative or Positive Up to 6 cohorts (n=10 per Cohort, n=8 ALG-000184, n=2 Placebo) 28 daily oral doses Endpoints: PK, safety, antiviral activity (e.g., DNA, RNA)



Part 1 & 2: Single oral dose ≤500 mg and multiple oral daily doses ≤250 mg x 7 days well tolerated with linear PK in HV Part 3: multiple daily doses ≤300 mg well tolerated with linear PK and excellent antiviral activity (next slides)

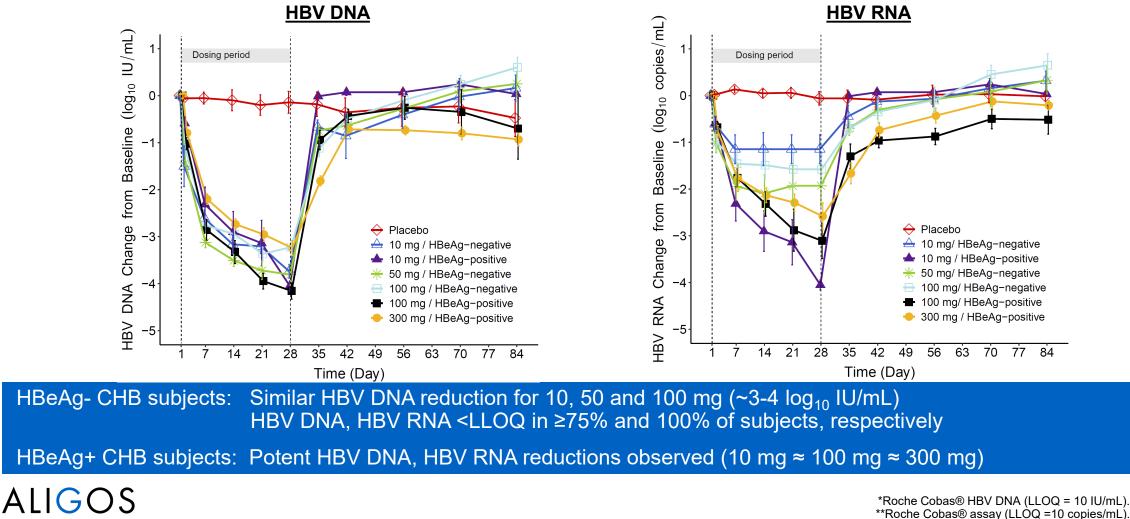


Gane Ed, APASL 2021; Gane Ed, HBV TAG 2021; Cohorts 1 & 2: Gane et al., AASLD 2021; Cohort 4: Yuen MF. et al., APASL 2022; Cohort 3: Yuen MF. et al., EASL 2022; Clinicaltrials.gov: NCT04485663.

# ALG-000184-201 - Part 3 Antiviral Activity Data in CHB Subjects

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Mean (SEM) Serum HBV DNA\* and HBV RNA\*\* Levels Change from Baseline Through the End of Study



# **ALG-000184** Antiviral Activity vs. Competitor CAMs (HBeAg Negative\*)\*\*

			HBV DNA		
Drug Name	Current Status	Dose	Mean Decline from BL to EOT (Log <sub>10</sub> IU/mL)	% < LLOQ at Day 28	
ALG-000184	Phase 1	10 mg	3.7	100	
ABI-H0731 <sup>1,2</sup>	Phase 2a	300 mg	2.5	25	
JNJ-6379 <sup>3,4</sup>	Phase 2	250 mg	2.7	56	
EDP-514⁵	Dhaca th	200 mg	2.9	N/A	
EDP-514°	Phase 1b	800 mg	3.4	N/A	
AB-836 <sup>6</sup>	Phase 1	100 mg	3.1	N/A	

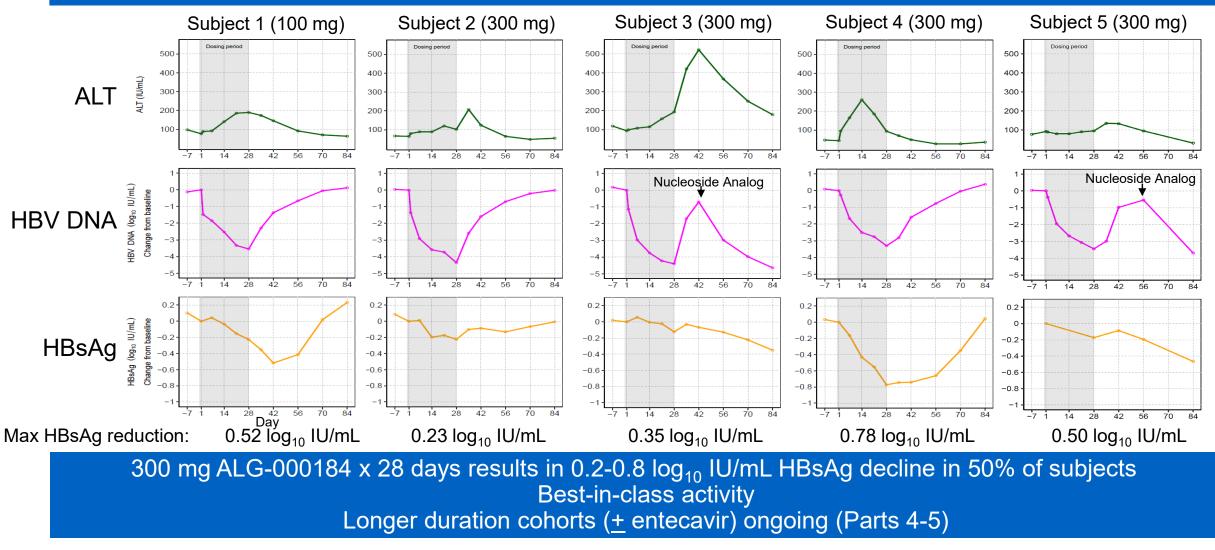
#### 10 mg dose of ALG-000184 has more antiviral activity than competitor CAMs dosed at 100-800 mg

\*89% of subjects were HBeAg negative in 250 mg JNJ-6379 arm. An unknown percentage of subjects dosed with 800 mg EDP-514 were HBeAg negative.

\*\*The comparisons shown in the table above are not based on data resulting from head-to-head trials and are not direct comparisons. Different protocol designs, trial designs, patient selection and populations, number of patients, trial endpoints, trial objectives and other parameters that are not the same between the relevant trials T H E R A P E U T I C S may lead to bias in the results causing comparisons of results from different trials to be unreliable.

N/A – not available; LLOQ (DNA) was ≤20 IU/mL for ABI and JNJ and 10 IU/mL for Aligos. 1. MF Yuen et al. Lancet Gastroenterol Hepatol 2019. 2. MF Yuen AASLD 2018. 3. Zoulim F., et al AASLD 2018. 4. Zoulim F., et al. Gastroenterology 2020. 3. Zoulim F., et al AASLD 2010. -. Zoulin F., et al AASLD 2021 (Poster 823). 6. HepDart 2021 (preliminary data). 5. MF Yuen, et al AASLD 2021 (Poster 823). 6. HepDart 2021 (preliminary data). 10

# ALG-000184 - Part 3 HBsAg Reductions Observed in 28-Day Monotherapy (HBeAg+)





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# Dr. Mark Sulkowski



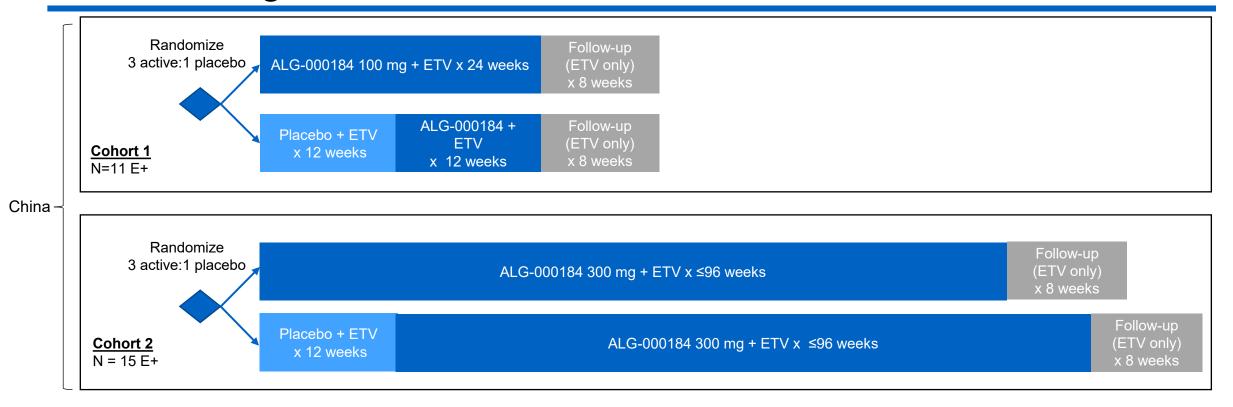
- Professor of Medicine at the Johns Hopkins University School of Medicine
- Director of the Division of Infectious Diseases at Johns Hopkins Bayview Medical Center
- Medical Director of the Viral Hepatitis Center in the Divisions of Infectious Diseases and Gastroenterology/Hepatology in the Department of Medicine
- Senior Associate Dean for Clinical Trials
- Principal investigator for more than 120 clinical trials related to the management of viral hepatitis B and C in persons with and without HIV co-infection
- Past-chair of the Hepatitis Transformative Sciences Group of the National Institute of Health-funded adult AIDS Clinical Trials Group (ACTG)
- Elected member of the American Society for Clinical Investigation (2011) and the American Association of Physicians (2017)
- More than 300 peer-reviewed articles, including works in Annals of Internal Medicine, New England Journal of Medicine, JAMA, Clinical Infectious Diseases
- MD, Temple University School of Medicine, Philadelphia, PA
- Internal Medicine, Duke University School of Medicine, Durham, NC
- Fellowship in Infectious Diseases, Johns Hopkins University School of Medicine

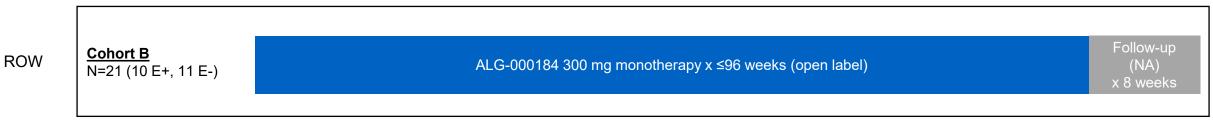


### ALG-000184-201 - Part 4 Cohort Designs

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All cohorts fully enrolled.

Yuen et al, AASLD 2023

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# ALG-000184-201 - Part 4 Cohort 2 & B Baseline Characteristics

Characteristic	P4C2 (n=15*)	P4CB (n=10)
Age, years, mean (SEM)	31.4 (3.3)	36.8 (2.9)
Male, n(%)	8 (53)	7 (70)
Asian, n(%)	3 (100)	9 (90)
BMI, kg/m², mean (SEM)	22.2 (0.8)	22.4 (0.8)
HBV Genotype, n(%)	B: 5 (33); C: 10 (67)	B: 5 (50); C: 4 (40); D: 1 (10)
HBV DNA, log <sub>10</sub> IU/mL, mean (SEM)	8.1 (0.2)	8.0 (0.2)
HBV RNA, log <sub>10</sub> copies/mL, mean (SEM)	6.7 (0.3)	5.3 (0.4)
HBsAg, log <sub>10</sub> IU/mL, mean (SEM)	4.4 (0.2)	4.3 (0.1)
HBeAg, log <sub>10</sub> PEI U/mL, mean (SEM)	2.4 (0.1)	2.6 (0.3)
HBcrAg, log <sub>10</sub> U/mL, mean (SEM)	8.3 (0.3)	8.3 (0.2)
ALT, U/L, mean (SEM)	38.7 (5.2)	60.7 (11.7)

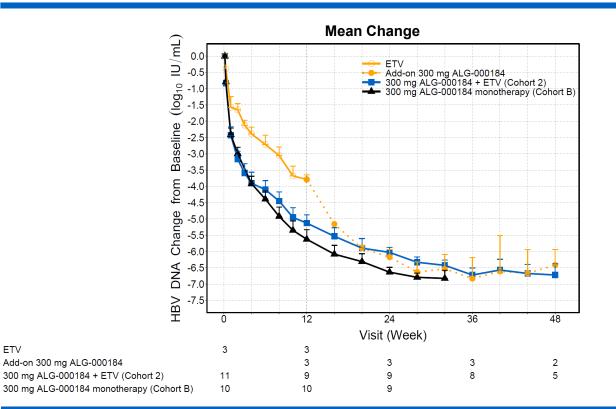
SEM: standard error of mean. \*Three subjects prematurely discontinued due to non-safety related personal reasons (n=2) and non-compliance of dosing (n=1)

Baseline characteristics were comparable and typical for a HBeAg+ population 53% of subjects with normal baseline ALT levels in P4C2 compared to only 10% in P4CB

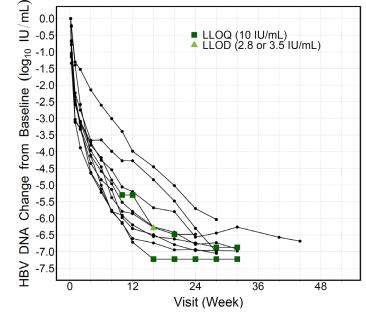


BMI = body mass index; SEM= standard error of the mean.

# Antiviral Effect - Part 4 Cohort 2 & B **HBV DNA Change from Baseline**



Individual changes of ALG-000184 monotherapy



#### 300 mg ALG-000184±ETV

- Showed greater HBV DNA reduction than ETV monotherapy

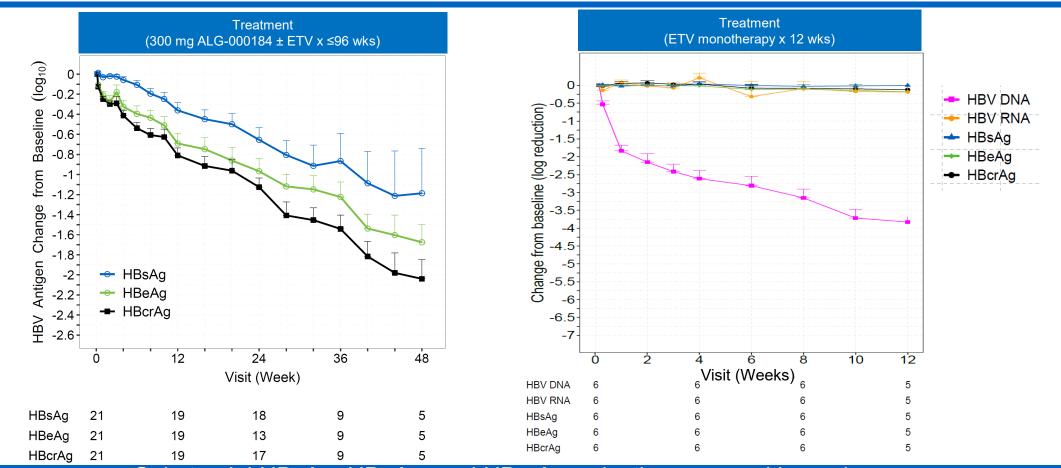
- Achieved similar DNA reductions

No viral breakthrough was observed in ALG-000184 monotherapy  $x \le 44$  weeks



ETV

# Antiviral Effect - Part 4 Cohort 2 & B HBV Antigen Change from Baseline



Substantial HBsAg, HBeAg, and HBcrAg reductions seen with combo Max declines: 2.0, 2.1 and 2.5 log<sub>10</sub>, respectively ETV alone only impacted HBV DNA; no impact on HBV RNA or antigens

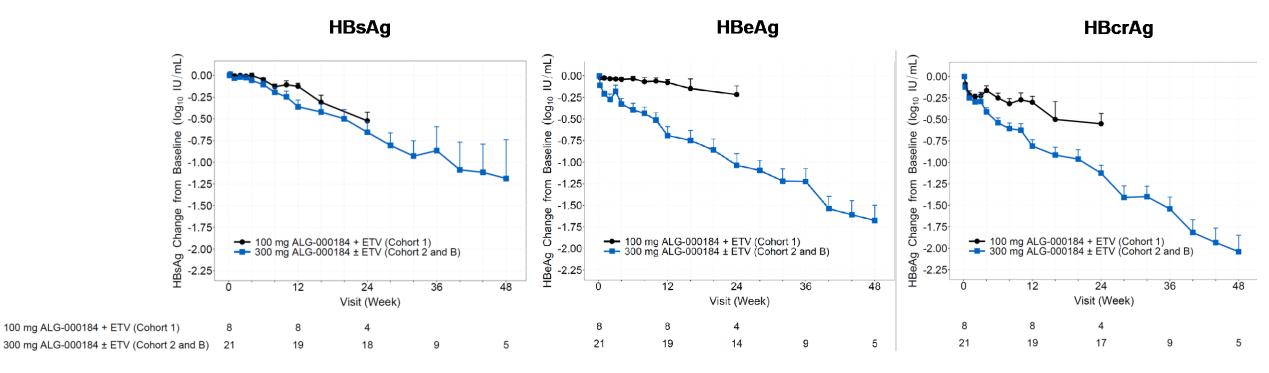


Graph plots subjects initially randomized to

ALG-000184 + ETV and were compliant (confirmed by PK)

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#### Antiviral Effect HBV Antigen Change from Baseline: P4C1 vs P4C2



Dose-dependent HBsAg, HBeAg and HBcrAg declines



#### Safety Overview – TEAEs

300 mg ALG-000184 +/- ETV	P4C2 (n=15)	P4CB (n=10)
Serious Adverse Events (SAEs)	None	
Treatment emergent AEs (TEAEs) leading to study drug discontinuation	None	
Subjects with Grade ≥3 TEAEs	$\begin{array}{c} 2 \\ ALT/AST\uparrow (n=2) \\ neutropenia\uparrow (n=1)^* \end{array} \qquad \begin{array}{c} 3 \\ ALT/AST\uparrow \end{array}$	
Concerning TEAE, laboratory, ECG, vital sign, or physical examination findings or trends	None	

• Neutropenia considered probably related to an acute upper respiratory infection and resolved following resolution of this infection in the setting of continued dosing with study drug

• Five Grade ≥3 TEAEs of liver transaminase elevations were transient, resolved on study drug, and associated with decline in antigens. None were considered clinically concerning by the AFC.

A favorable safety profile was observed in untreated HBeAg+ CHB subjects with long term ( $\leq$  48 weeks) treatment with 300 mg ALG-000184 ± ETV



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# **Executive Summary** ALG-000184

- AASLD data show that daily oral dosing with 300 mg ALG-000184±ETV x ≤48 weeks in untreated HBeAg+ CHB pts results in:
  - A favorable safety profile
  - Greater suppression of HBV DNA and RNA vs. ETV alone (1<sup>st</sup> MOA)
  - No viral breakthrough when ALG-000184 is given as monotherapy x ≤44 weeks
  - Multi-log reductions in HBsAg, HBeAg, & HBcrAg, which appear to be mediated by ALG-000184 (2<sup>nd</sup> MOA)
- ALG-000184 appears to lower cccDNA levels via 1<sup>st</sup> and 2<sup>nd</sup> MOA
- ALG-000184 may play an important role in enhancing rates of chronic suppression (superior/non-inferior to NAs) and functional cure
- Next steps
  - Continue ongoing ≤96 week cohorts
  - Phase 2 enabling activities underway



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# ALIGOS THERAPEUTICS