

# Clinical Overview of AB-729, a potent siRNA in development for the treatment of chronic hepatitis B infection

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NASDAQ: ABUS | [www.arbutusbio.com](http://www.arbutusbio.com)

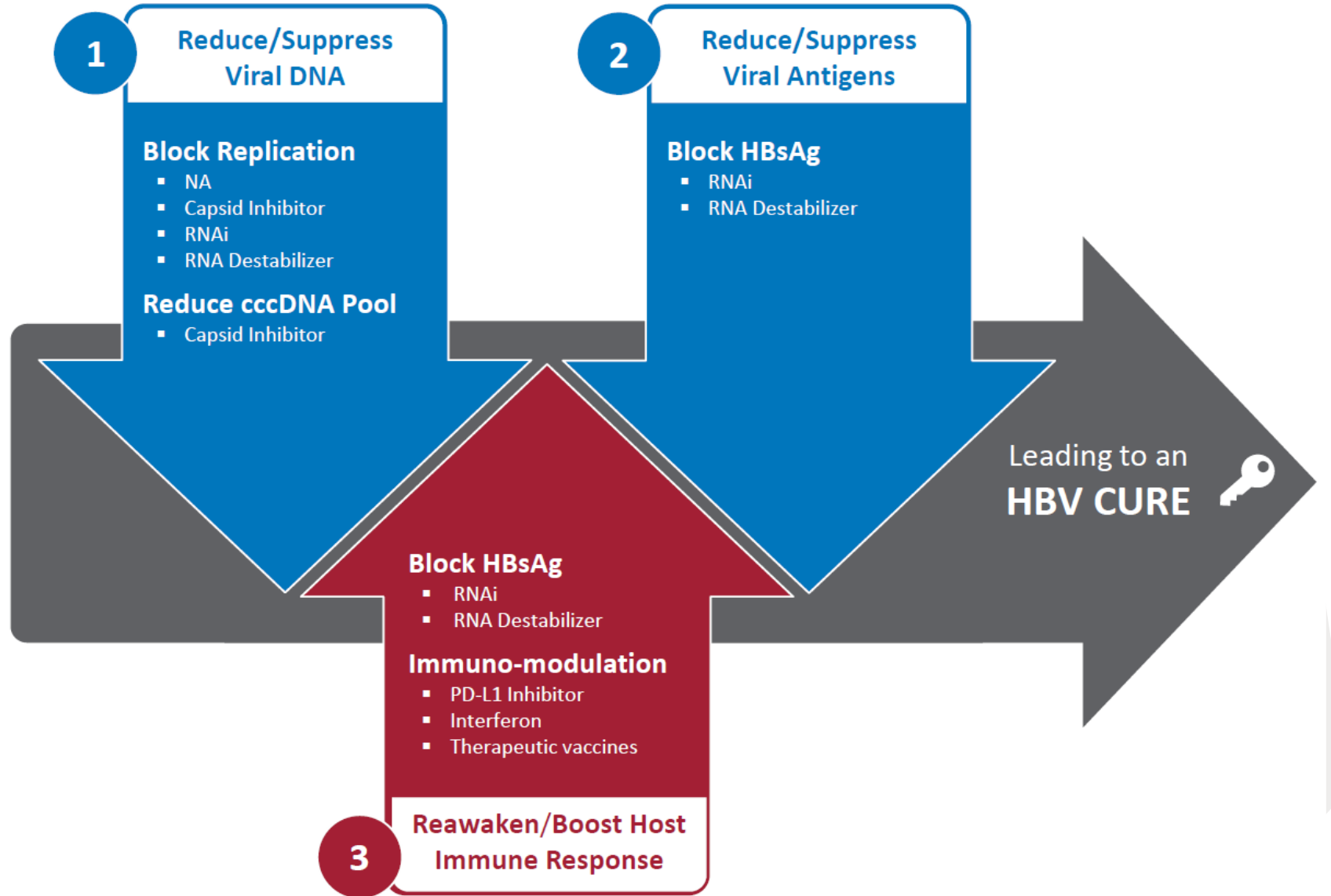


# Keys to Therapeutic Success

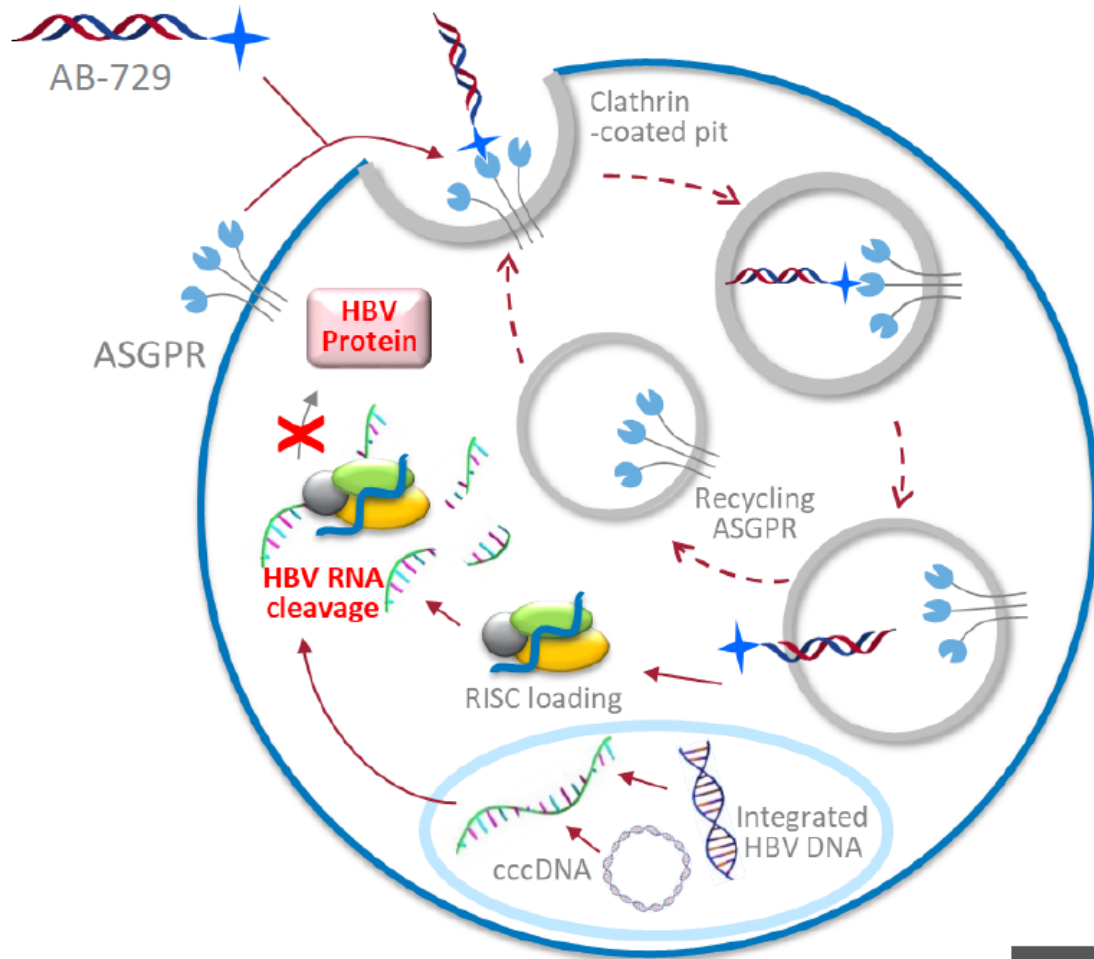
Suppress HBV DNA and viral antigens

Reawaken host immune response

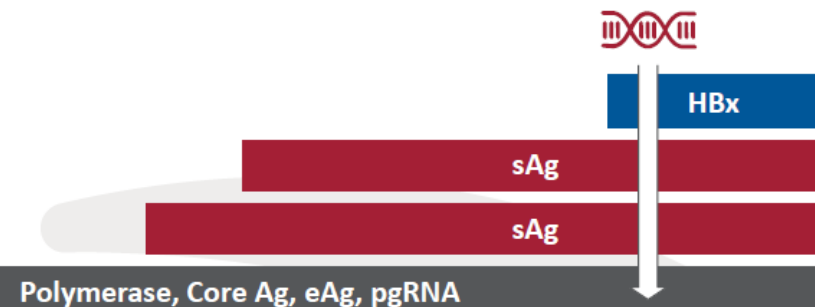
Therapeutic success will require a combination of agents with complementary MOAs



# AB-729 GalNAc-siRNA Therapeutic

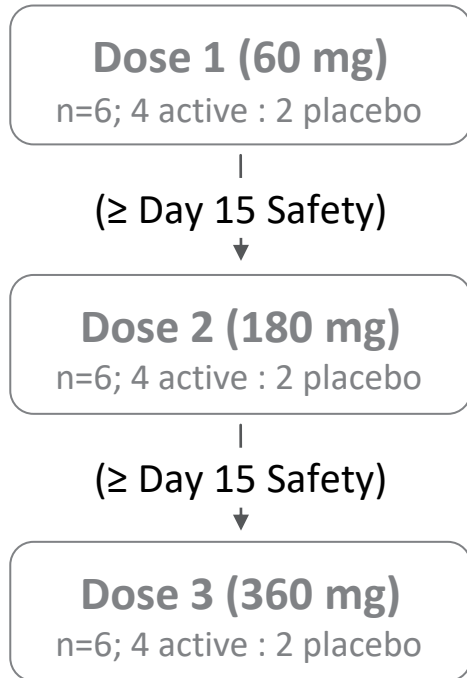


- Single trigger RNA interference agent administered subcutaneously
- Proprietary liver targeting technology based on GalNAc ligand interaction with ASGPR
- Inhibits HBV replication, reduces all HBV transcripts, and lowers all HBV antigens
- Pan-genotypic activity across HBV genotypes

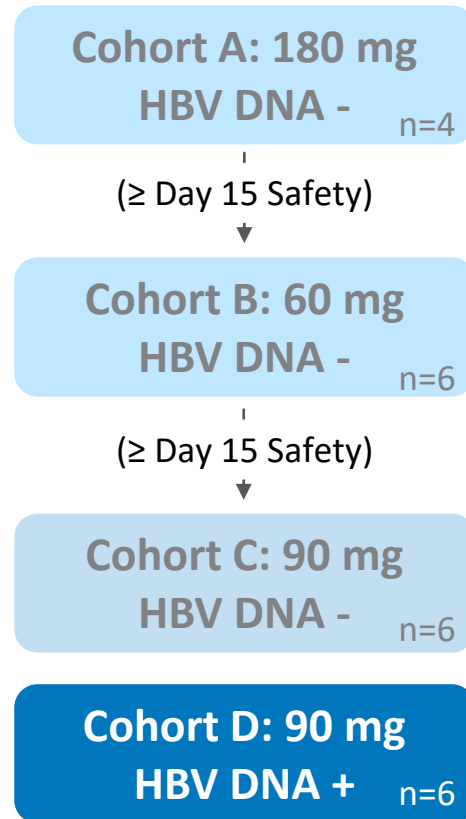


# AB-729-001 Study Overview

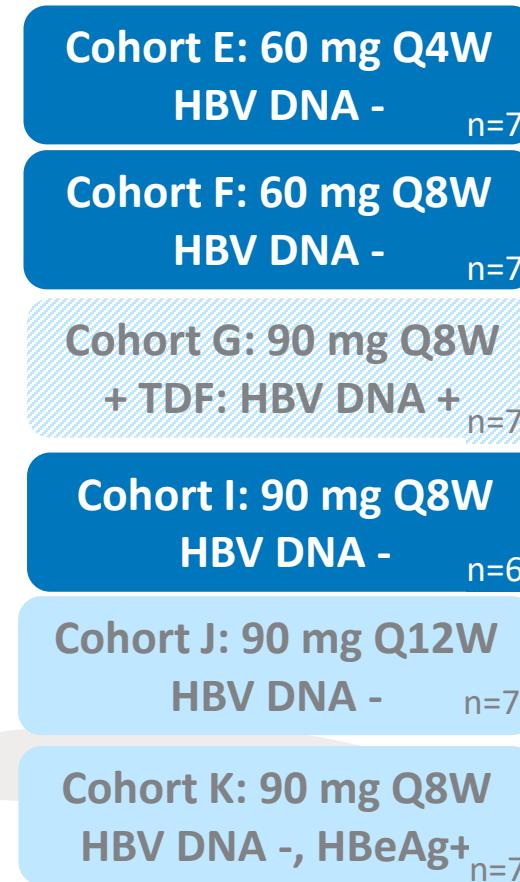
## Part 1: Single Ascending Dose in Healthy Subjects



## Part 2: Single Doses in Chronic Hepatitis B Subjects (open-label)



## Part 3: Repeat Doses in Chronic Hepatitis B Subjects (open-label)



Initially, AB-729 was dosed for 6 months.

An optional 6 month treatment extension was amended to the protocol, with 48 weeks of follow-up.

# Key Inclusion Criteria

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## ▪ Cohorts E, F and I

- Age 18 – 65 years old
- At least 6 months of stable nucleos(t)ide analogue (NA) therapy (ETV, TDF, TAF) prior to Screening
- HBeAg positive or negative
- HBV-DNA < LLOQ and HBsAg  $\geq$  250 IU/mL at Screening
- Non-cirrhotic, Fibroscan<sup>®</sup> result of  $\leq$ 10 kPa
- ALT/AST  $\leq$ 2x ULN at Screening

## Baseline Characteristics

Baseline Measure	Cohort E AB-729 60 mg Q4W* (N=7)	Cohort F AB-729 60 mg Q8W (N=7)	Cohort I AB-729 90 mg Q8W (N=6)
Age in years, mean (range)	45.1 (33 – 63)	44.0 (31 – 59)	45.7 (38 – 54)
Male gender, n (%)	4 (57%)	4 (57%)	4 (67%)
BMI, mean (SD)	27.7 (5.01)	23.7 (2.17)	25.5 (3.11)
Race, n (%)			
Asian	1 (14%)	5 (71%)	5 (83%)
Black	0	1 (14%)	0
White	6 (86%)	1 (14%)	1 (14%)
ALT (U/L), mean (SD)	22.4 (10.52)	23.4 (15.22)	26.0 (10.20)
HBV eAg negative, n (%)	7 (100%)	6 (71%)**	5 (83%)
HBsAg (IU/mL), mean (range)	5,372 (584 – 11,761)	5,354 (667 – 18,605)	4,691 (338 – 19,017)

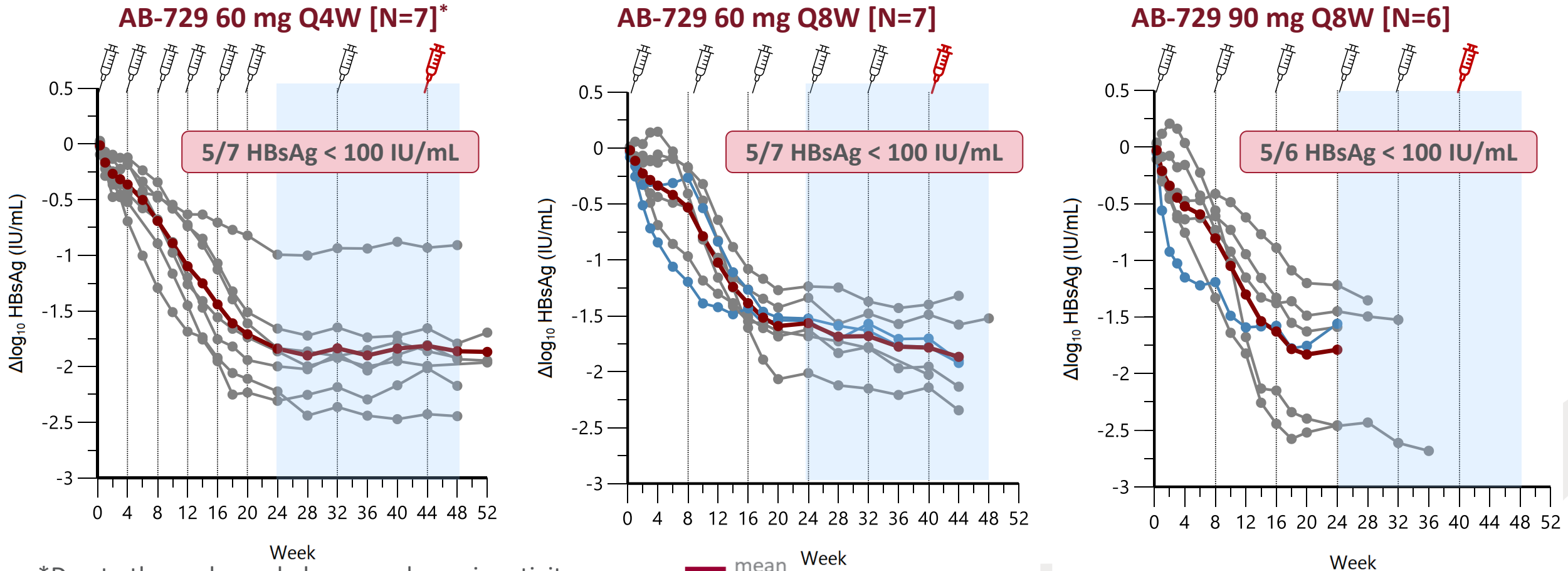
\*subjects switched to AB-729 60 mg Q12W after the Week 20 dose

\*\* 1 subject counted as HBeAg negative was identified as “HBeAg borderline” (baseline HBeAg = 0.18 IU/mL, LLOQ = 0.11 IU/mL)

- All subjects were virologically suppressed on an NA (ETV, TDF or TAF) with HBV DNA < LLOQ (20 IU/mL)
- HBV genotype was not determined

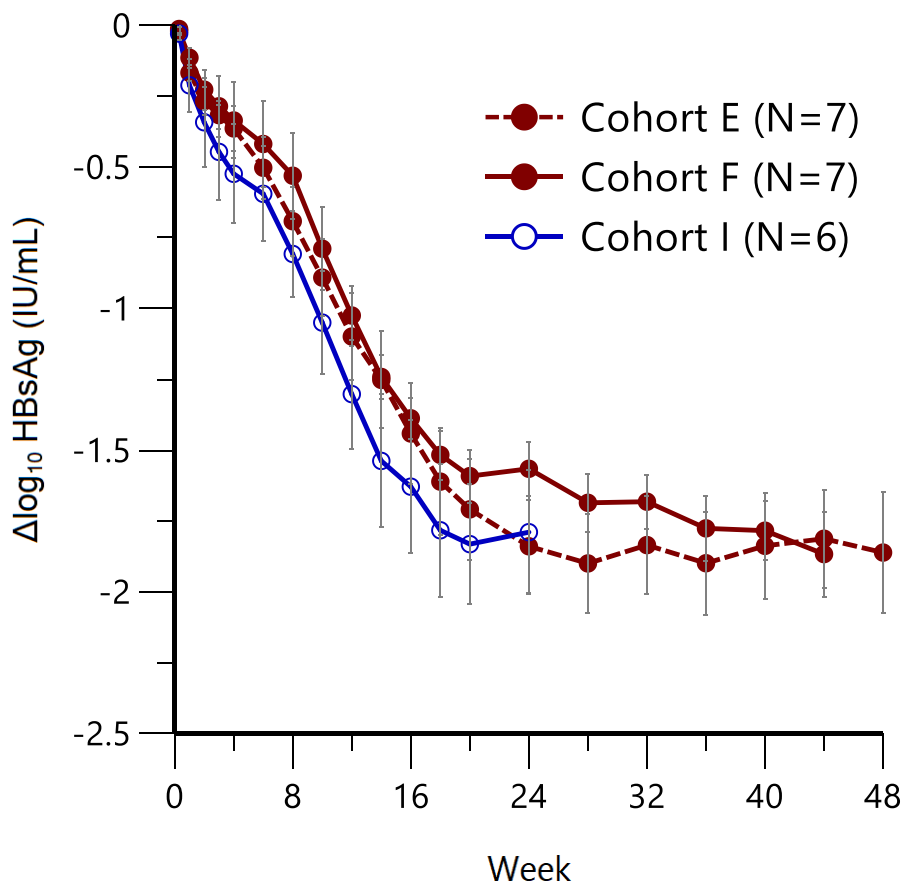
# Repeat dosing of AB-729 60 mg and 90 mg results in comparable HBsAg decline profiles with 75 percent of subjects reaching <100 IU/mL

Plateau in response observed around Week 20, regardless of dose or dosing interval



\*Due to the prolonged pharmacodynamic activity observed after a single dose of AB-729 (Yuen, AASLD 2020), subjects switched to AB-729 60 mg Q12W after Week 20

# There are no significant differences in mean HBsAg response between AB-729 doses and dosing intervals to date



## Mean (range) $\Delta$ HBsAg with repeat dosing of AB-729

Visit	Cohort E AB-729 60 mg Q4W <sup>†</sup>	Cohort F AB-729 60 mg Q8W	Cohort I AB-729 90 mg Q8W	<i>p</i> value between Cohorts
Week 16	-1.44 (-0.71 to -1.95)	-1.39 (-1.61 to -1.08)	-1.63 (-0.89 to -2.44)	<i>p</i> ≥ 0.4
Week 24	-1.84 (-0.99 to -2.31)	-1.57 (-1.24 to -2.01)	-1.79 (-1.22 to -2.46)	<i>p</i> ≥ 0.2
Week 32	-1.84 (-0.94 to -2.36)	-1.68 (-1.37 to -2.15)	---	<i>p</i> = 0.5
Week 40	-1.84 (-0.88 to -2.47)	-1.78* (-1.40 to -2.14)	---	<i>p</i> = 0.7
Week 44	-1.81* (-0.93 to -2.43)	-1.87* (-1.32 to -2.34) [N=6]	---	<i>p</i> = 0.8
Week 48	-1.89* (-0.91 to -2.44)	---	---	---

<sup>†</sup> subjects switched to AB-729 60 mg Q12W after Week 20 dose

\*Data updated since EASL 2021 ILC



# Repeat dosing of AB-729 was generally safe and well tolerated

- No SAEs or discontinuations due to AEs
- No Grade 3 or 4 TEAEs or laboratory abnormalities other than 1 transient Grade 3 CK elevation in a Cohort I subject
- All TEAEs were Grade 1 except 2 unrelated AEs of Grade 2 COVID-19 disease, one with fever
- Most common TEAEs were injection-site AEs
  - All were Grade 1 and none appear to be dose- or interval-dependent
- No ALT elevations were considered AEs by the Investigators, and no bilirubin or liver synthetic function changes were seen
  - ALT/AST elevations improved or stabilized with continued dosing
  - All Gr 2 elevations improved to Gr 1, 6 of 7 Gr 1 improved to Gr 0
- No clinically meaningful changes in ECGs or vital signs were seen

Subjects, n (%)	Cohort E (60 mg Q4W*) [N=7]	Cohort F (60 mg Q8W) [N=7]	Cohort I (90 mg Q8W) [N=6]	TOTAL [N=20]
Subjects with any TEAE	4 (57)	5 (71)	1 (17)	10 (50)
SAEs	0	0	0	0
Subjects with related TEAEs (all Grade 1)	2 (29)	4 (57)	1 (17)	7 (35)
Most common related TEAEs (in ≥ 2 subjects):				
Injection site pain	0	2 (29)	1 (17)	3 (2) <sup>#</sup>
Injection site erythema	2 (29)	1 (14)	0	4 (3) <sup>#</sup>
Injection site bruising	2 (29)	0	0	2 (2) <sup>#</sup>
Laboratory Abnormalities (in ≥ 2 subjects):				
ALT elevation <sup>‡</sup>				
Grade 1	2 (29)	3 (43)	2 (33)	7 (35)
Grade 2	2 (29)	1 (14) <sup>†</sup>	2 (33)	5 (25)
AST elevation <sup>‡</sup>				
Grade 1	1 (14)	3 (43)	2 (33)	6 (30)
Grade 2	1 (14)	0	0	1 (5)
Sodium (low)	1 (14)	1 (14)	1 (17)	3 (15)
Glucose (low)	0	2 (29)	2 (33)	4 (20)
Lipase	0	1 (14)	1 (17)	2 (10)
Phosphate	1 (14)	0	1 (17)	2 (10)

TEAE: treatment-emergent adverse event; Grading criteria based on Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, V2.1

\* subjects in Cohort E were switched to AB-729 60 mg Q12W after the Week 20 dose

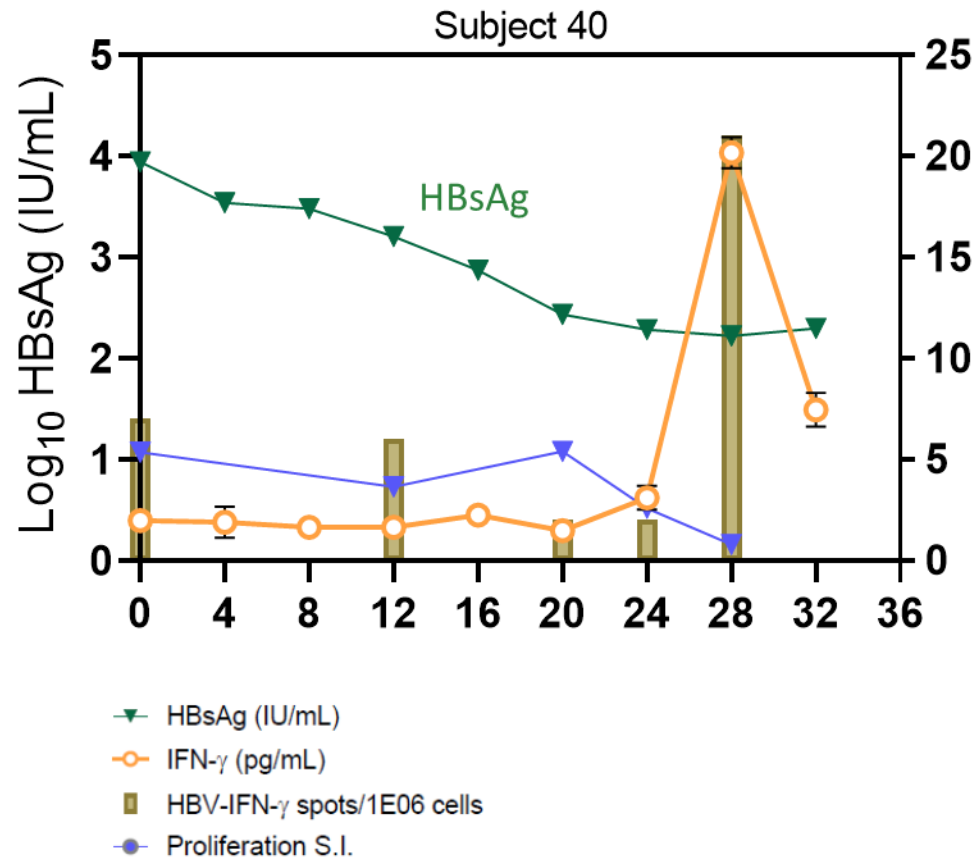
<sup>#</sup> n, % is number of events out of 122 total AB-729 doses administered

<sup>‡</sup> for each subject only the highest grade is shown

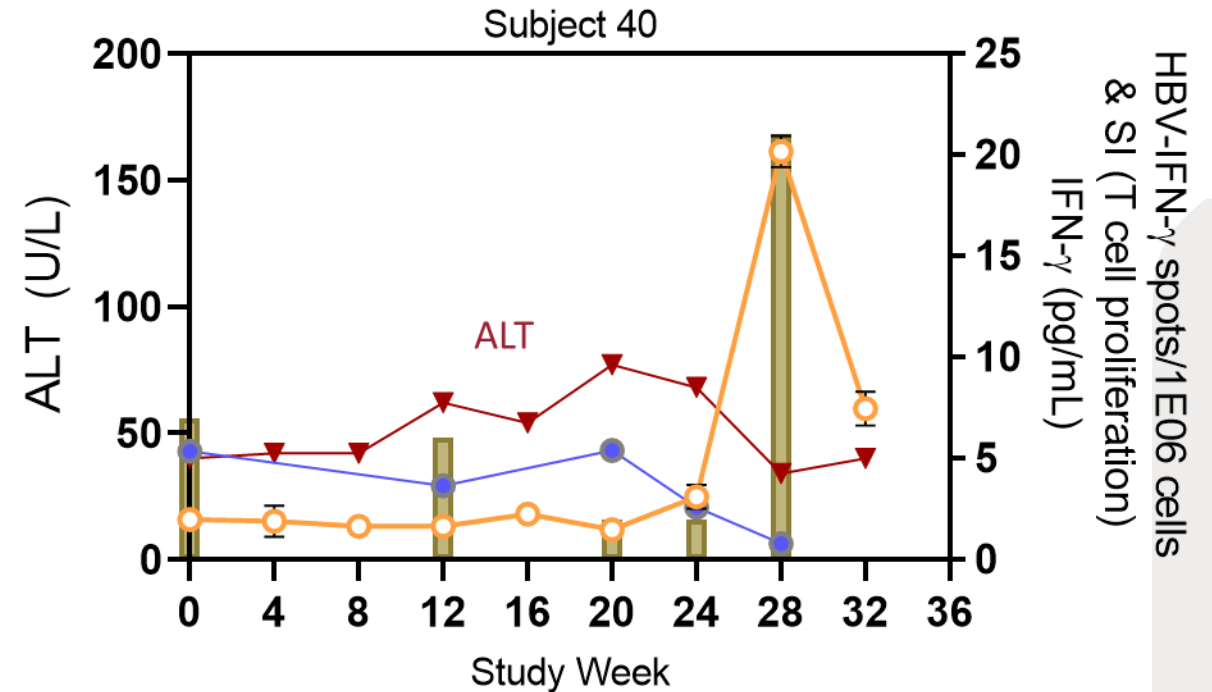
<sup>†</sup> subject had history of pre-study Grade 1 ALT abnormalities and concurrent CK elevations

# AB-729 mediated HBsAg reduction is associated with increased HBV-specific immune responses in 3/5\* evaluable subjects

Increase in HBV T-cell IFN-gamma following HBsAg reduction by AB-729

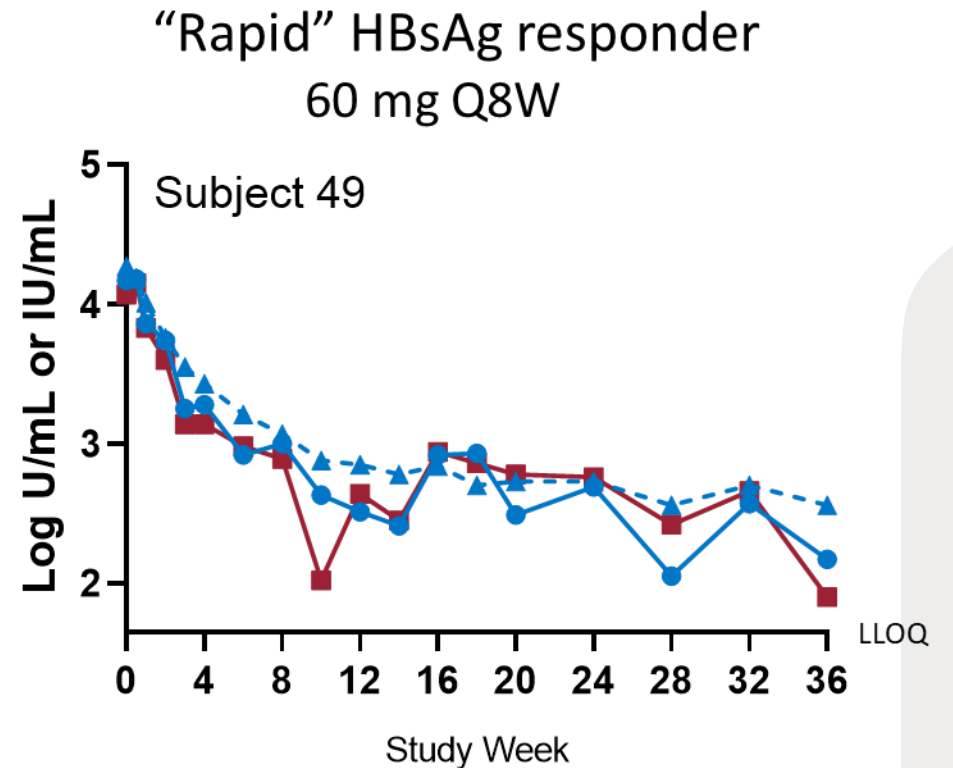
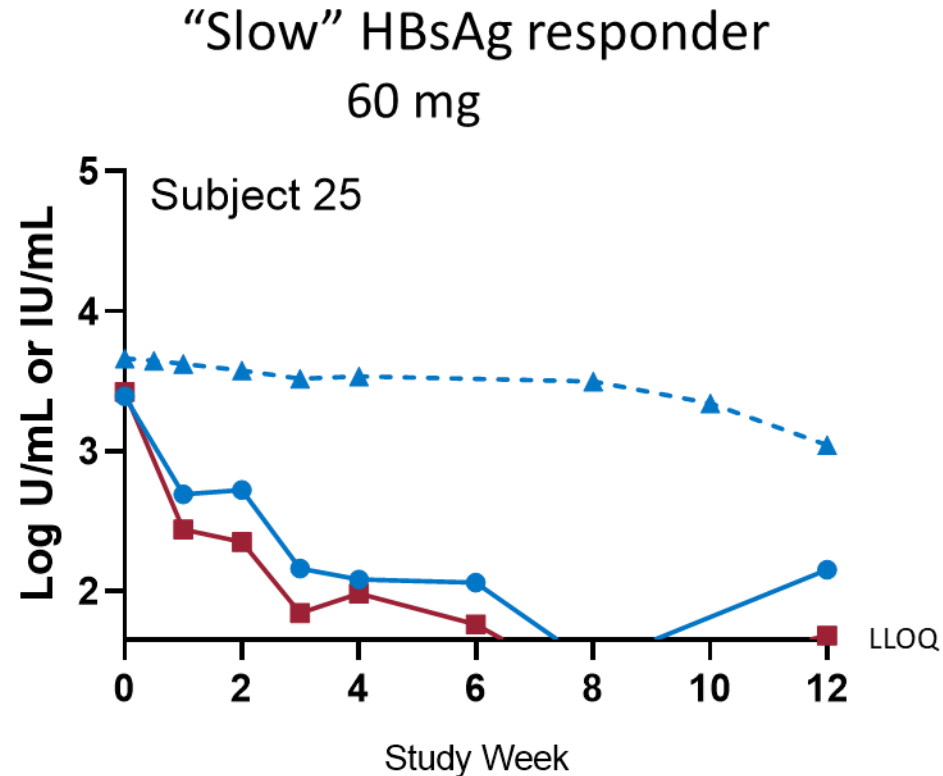


ALT elevation precedes IFN-gamma-producing HBV-specific T-cells



\*5/7 Cohort E subjects had available PBMCs for analyses

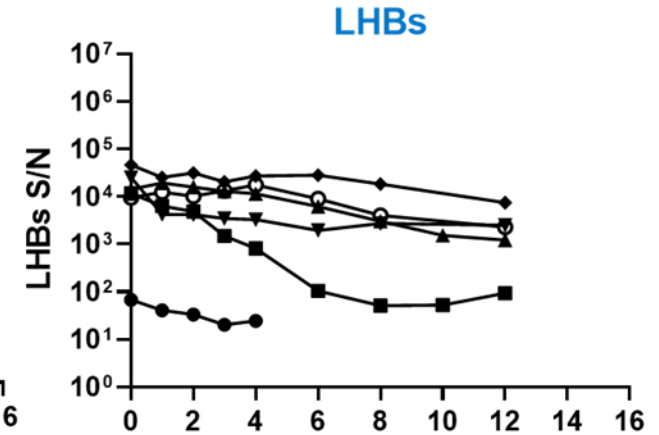
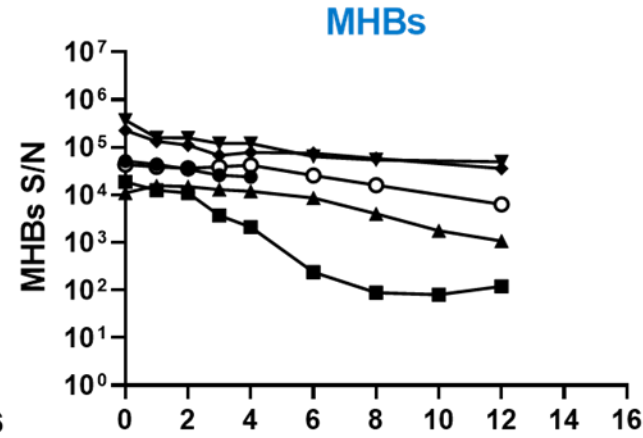
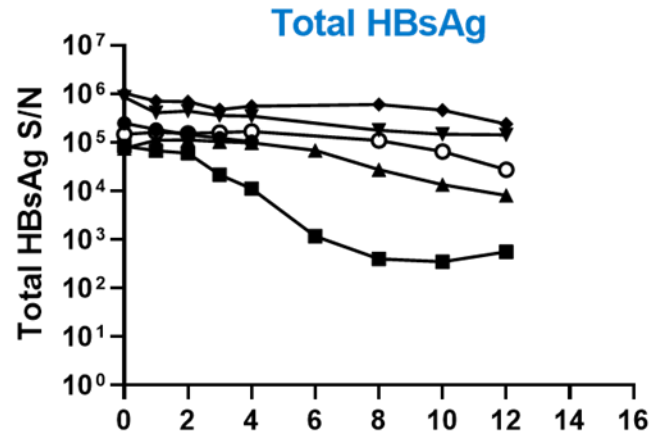
# AB-729 reduces HBV RNA in rapid and slow responders demonstrating broad target engagement



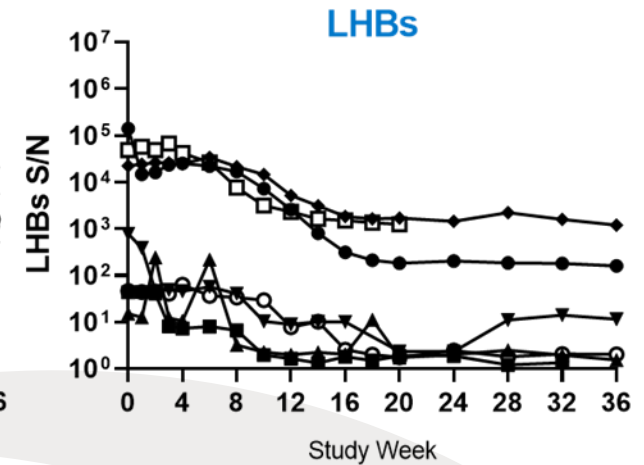
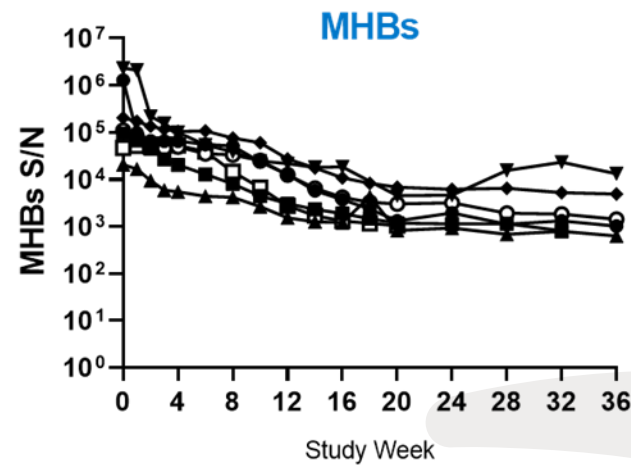
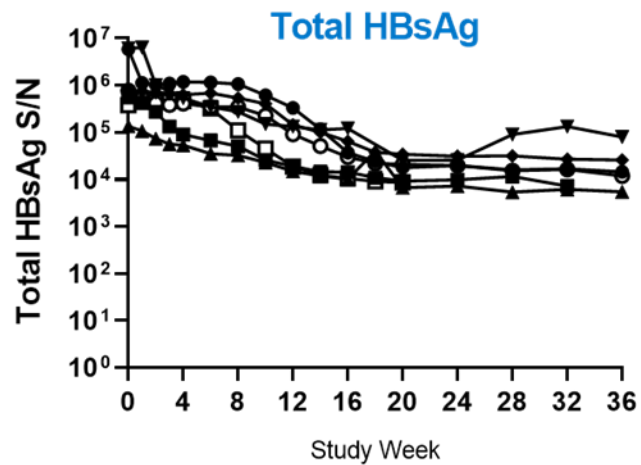
- ▲- HBsAg
- Total HBV RNA
- pgRNA

# AB-729 is active against all isoforms\* of HBsAg

60 mg Single Dose



60 mg Q8W Repeat Dose



\*As measured with the RUO Abbott isoform assay

MHB = medium HBsAg

LHB = large HBsAg

From Thi, et al. Poster #2822, EASL 2021

# AB-729 90 mg Single Dose Reduces HBsAg and HBV DNA in HBV DNA Positive CHB subjects

Figure 1. Individual and mean change from baseline HBsAg following a single dose of AB-729 90 mg in HBV DNA+ subjects

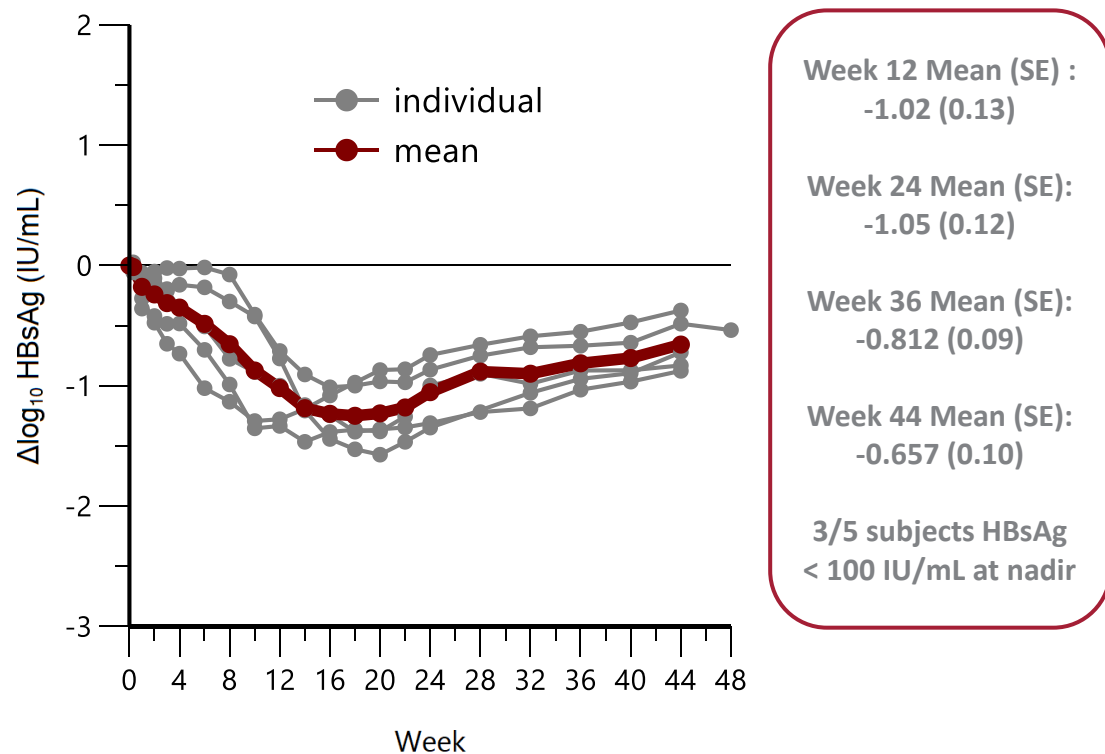
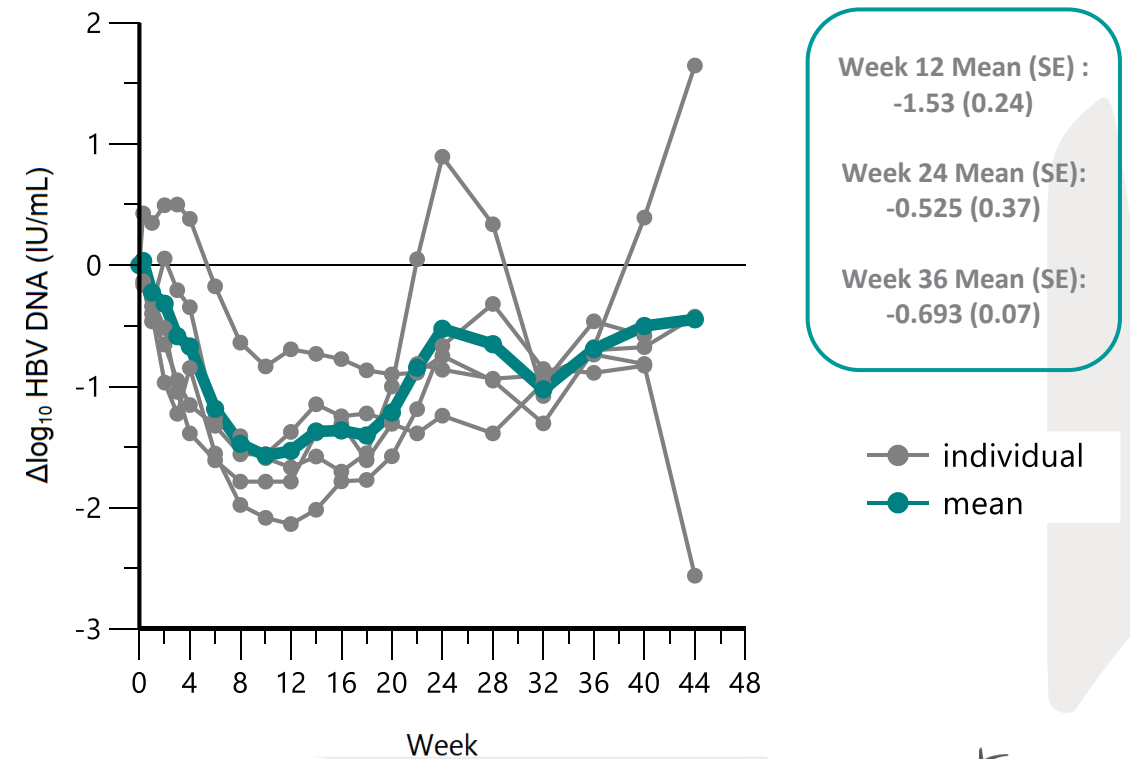


Figure 2. Individual and mean change from baseline HBV DNA following a single dose of AB-729 90 mg in HBV DNA+ subjects



# Takeaways

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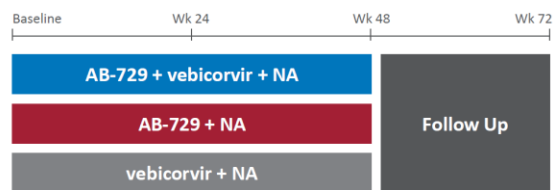
- AB-729 60 mg Q4W, 60 mg Q8W, and 90 mg Q8W result in similar mean HBsAg declines to date
  - 15/20 subjects (75%) achieve HBsAg < 100 IU/mL
- A plateau in HBsAg response appears to occur around Week 20 of repeat dosing, regardless of AB-729 dose or dosing interval
- The doses and dose intervals of AB-729 explored were generally safe and well tolerated
- Preliminary data suggest that long-term suppression of HBsAg with AB-729 results in increased HBV-specific immune response
- The available clinical data supports our view that AB-729 60 mg every 8 weeks is an appropriate and convenient dose to explore in Phase 2a combination trials

# Proof-of-concept Phase 2a combination trials using AB-729 as the cornerstone agent

## AB-729 Clinical Collaboration



Provides accelerated AB-729 combination proof-of-concept (POC) with Assembly's capsid inhibitor and a NA



Initiated Phase 2 Clinical Trial Feb 2021  
 ~60 virologically-suppressed subjects with chronic HBV infection  
 Equal sharing of expertise and costs for this POC open-label trial  
 No financial requirements or restrictions and no business requirements or restrictions

## AB-729 Clinical Collaboration



**POC Phase 2a clinical trial**  
 Evaluating AB-729 in combination with Vaccitech's immunotherapeutic, VTP-300, and a NA

Clinical trial will evaluate the safety, pharmacokinetics, immunogenicity and anti-viral activity of the triple combination of AB-729, VTP-300 and an NA compared to the double combinations of AB-729 with an NA and VTP-300 with an NA

Expected to file CTA in the second half of 2021 and initiate in early 2022

Full rights retained by the Companies of their respective product candidates and all costs will be split equally

Assuming positive results parties intend to undertake a larger Phase 2b clinical trial

## AB-729 Clinical Collaboration



**POC Phase 2a clinical trial**  
 AB-729 in combination with Antios' proprietary active site polymerase inhibitor nucleotide (ASPIN), ATI-2173, and a NA

Clinical trial will evaluate AB-729, ATI-2173 and a NA in a single cohort in the ongoing Antios Phase 2a ANTT201 clinical trial

Expected to initiate in the second half of 2021

Antios will be responsible for the costs and Arbutus will be responsible for supply of AB-729

Trial cohort will include 10 subjects with chronic HBV assigned 8:2 to active drug or matching placebos; in combination with an NA

## IND Authorized for a Phase 2a POC clinical trial



AB-729 in combination with ongoing NA therapy and short courses of Peg-IFN $\alpha$ -2a in CHB subjects

The trial is expected to enroll 40 stably NA-suppressed, HBeAg negative, non-cirrhotic CHB subjects\*

After a 24-week dosing period of AB-729 (60 mg every 8 weeks (Q8W)), subjects will be randomized into one of 4 groups:

- A1: AB-729 + NA + weekly Peg-IFN $\alpha$ -2a for 24 weeks (N = 12)
- A2: NA + weekly Peg-IFN $\alpha$ -2a for 24 weeks (N = 12)
- B1: AB-729 + NA + weekly Peg-IFN $\alpha$ -2a for 12 weeks (N = 8)
- B2: NA + weekly Peg-IFN $\alpha$ -2a for 12 weeks (N = 8)

After completion of the assigned Peg-IFN $\alpha$ -2a treatment period, all subjects will remain on NA therapy for the initial 24-week follow up period, and then will discontinue NA treatment if treatment stopping criteria are met

Expected to initiate in the third quarter of 2021

# Acknowledgments

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## AB-729 Investigators

M-F. Yuen  
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**Thank you**