EASL 2019 Review

Conference call and Webcast

April 15, 2019

Cautionary Note Regarding Forward-Looking Statements

The information in this presentation contains forward-looking statements regarding future events, including statements about the clinical and therapeutic potential of Assembly Biosciences' core protein inhibitors, including ABI-H0731, ABI-H2158 and ABI-H3733, the initiation, timing, progress and results of nonclinical studies and clinical studies for our HBV-cure program, our regulatory strategies for our core inhibitors, and the strength of our capital position. Certain forward-looking statements may be identified by reference to a future period or periods or by use of forward-looking terminology such as "anticipated," "expected," "likely", "may," "potential," or "predictive." Such forward-looking statements, which are intended to be covered by the safe harbor provisions contained in Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, are just predictions and are subject to risks and uncertainties that could cause the actual events or results to differ materially. These risks and uncertainties include, among others: outcomes of clinical studies are uncertain; and results of earlier preclinical and nonclinical studies may not be predictive of future clinical studies results; the components, timing, patient enrollment and completion rates, cost and results of clinical trials and other development activities involving our product candidates; the duration and results of regulatory review of our product candidates by the FDA and foreign regulatory authorities; our estimates regarding our capital requirements, and our need for future capital; and the possible impairment of, or inability to obtain or protect, intellectual property rights and the costs of obtaining and protecting such rights. These and other potential risks and uncertainties that could cause actual results to differ from the results predicted are more fully detailed under the heading "Risk Factors" in Assembly Biosciences' Annual Report on Form 10-K for the year ended December 31, 2018 filed with the Securities and Exchange Commission (the "SEC") and any additional reports filed with the SEC following the date of this presentation. It is not possible for Assembly Biosciences management to predict all risks nor can it assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this presentation may not occur and actual results could differ materially and adversely from those anticipated. Any forward-looking statement speaks only as of the date on which it is made, and no obligation to update or revise any forward-looking statement is assumed, whether as a result of new information, future events or otherwise, except as required by law.

Developing a Potential Cure for Hepatitis B (HBV)

Cure is achievable

but currently at very low rates

Core Inhibitors

We believe backbone of **curative therapy**

Novel mechanism designed to **break the HBV life cycle**

Assembly Biosciences has a **deep pipeline of potent core inhibitors**

ASMB Presented Two Oral and Two Poster Presentations at EASL

- **ABI-H0731 Phase 2a Interim Results: Late Breaker Oral Presentation**, Dr. Jay Lalezari, Quest Clinical Research, San Francisco
  - *Interim Safety and Efficacy Results of the ABI-H0731 Phase 2a Program Exploring the Combination of ABI-H0731 with Nuc Therapy in Treatment-Naïve and Treatment-Suppressed Chronic Hepatitis B Patients*
  - *"Best of ILC"*
- **ABI-H2158 Phase 1a Results: Late Breaker Poster Presentation**
  - *Phase 1a Study of the Safety, Tolerability and Pharmacokinetics of ABI-H2158, a Novel Second-Generation HBV Core Inhibitor, In Healthy Volunteers*
- **ABI-H3733 Preclinical Profile: Oral Presentation**, Richard Colonno, SVP & CSO Virology Operations, ASMB
  - *Preclinical Profile of HBV Core Protein Inhibitor, ABI-H3733, a Potent Inhibitor of cccDNA Generation in HBV Infected Cells*
- **cccDNA Turnover Study: Poster Presentation**, Qi Huang, VP Virology Discovery, CSO Assembly China
  - *Rapid Turnover of HBV cccDNA in Nucleoside-Treated Chronic Hepatitis B Patients During Drug Resistance Emergence and Breakthrough*

ASMB HBV Core Inhibitor Program Portfolio

- Focused on identifying increasingly potent CIs while maintaining favorable drug-like properties
- Established pipeline of novel molecules with distinct chemical scaffolds

Drug Candidate	Discovery & Optimization	IND Enabling	Phase 1a	Phase 1b	Phase 2	Phase 3	NDA Filing	Worldwide Rights
ABI-H0731	Fast Track Designation, “Best of AASLD ‘18” “Best of ILC ‘19”					Phase 2a Studies EASL Oral LB-06		
ABI-H2158					Phase 1a Study EASL LB-12 Poster			
ABI-H3733			Preclinical Profile EASL Oral PS-073					
CI Discovery Program								

Program Designed to Assess Potential of CIs to Increase Cure Rates

Ongoing studies to define timelines for cccDNA loss, sustained suppression & potential cure

Proof of Concept for CI combination therapy is two-fold:

1. **POC Antiviral Superiority – Elimination of viremia via DNA and RNA declines**
2. **POC Cure – Declines in viral antigens and no relapse on therapy**

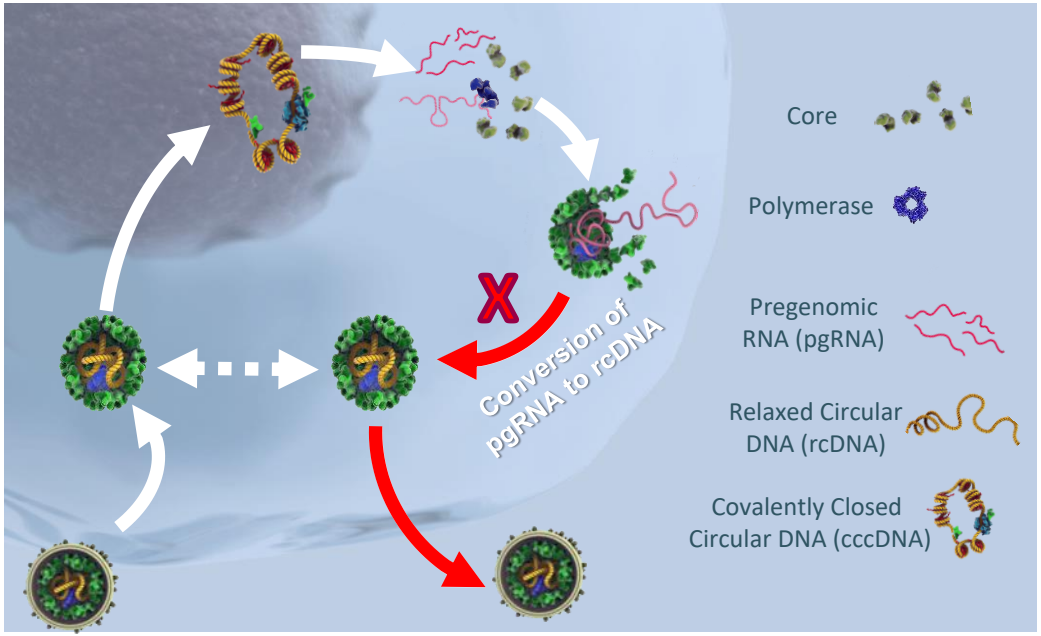
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM624695.pdf

TND:Target not detected by ASMB semi-quantitative PCR.

EASL Overview

Richard Colonno, PhD – EVP & CSO Virology Operations

New Therapies are Needed to Increase Cure Rates in CHB



Nucleos(t)ide Pol Inhibitors (Nuc)

- Current “Standard of Care” for HBV
- Safe, well tolerated, with minimal resistance
- Reduce HBV DNA

But Fail to ……

- Eliminate virus
- Prevent new cccDNA formation
- Indefinite treatment

Cure is not possible without elimination of residual virus

Prolonged Nuc Therapy Fails to Eliminate Viral Replication

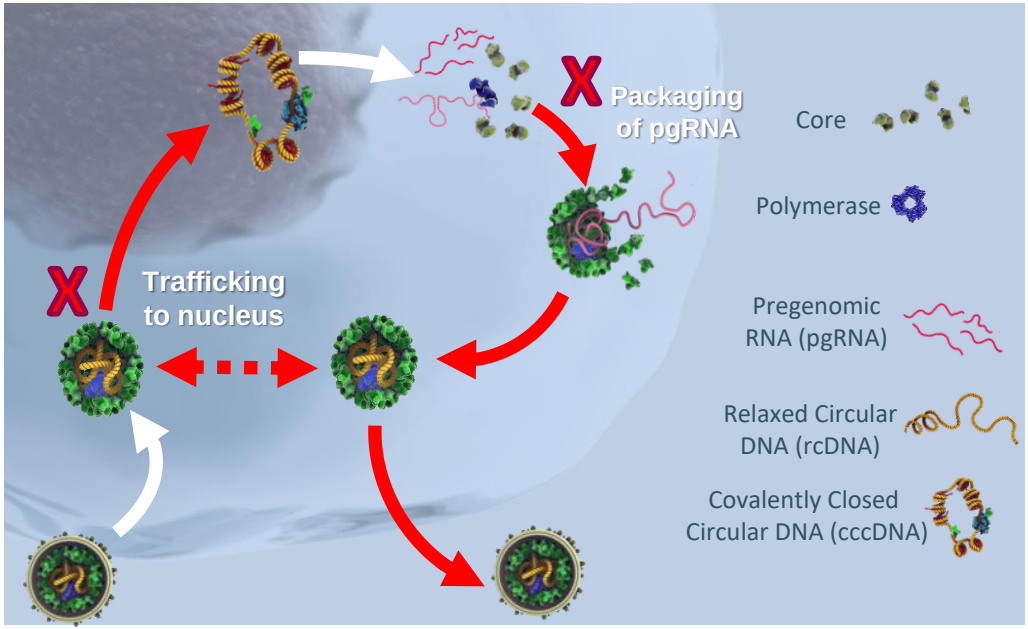
- PCR-detectable HBV DNA persists in 70-80% of patients despite TDF treatment for 5 years[1]
- Detected DNA represents ***infectious virus***!

  EASL 2019 (PS-150) – "Evidence for the presence of infectious virus in the serum from chronic hepatitis B patients suppressed on nucleos(t)ide therapy with detectable but not quantifiable HBV DNA" Burdette et al.

- **Residual viremia refractory to elimination by Nuc therapy**
- **Likely accounts for poor cure rates**

[1]Marcellin, et al, AASLD 2014, Poster 1861

CIs Block Viral Replication and cccDNA Establishment



Core Protein Inhibitors (CIs)

- Inhibit multiple steps in viral replication cycle
- Achieve deeper levels of viral inhibition than Nucs alone

AND

- Can block the formation of cccDNA

Goal is to use combination therapy to increase cure rates with finite treatment duration

ABI-H0731: Interim Results from Ongoing Phase 2a Studies

HBV Core Inhibitor ABI-H0731

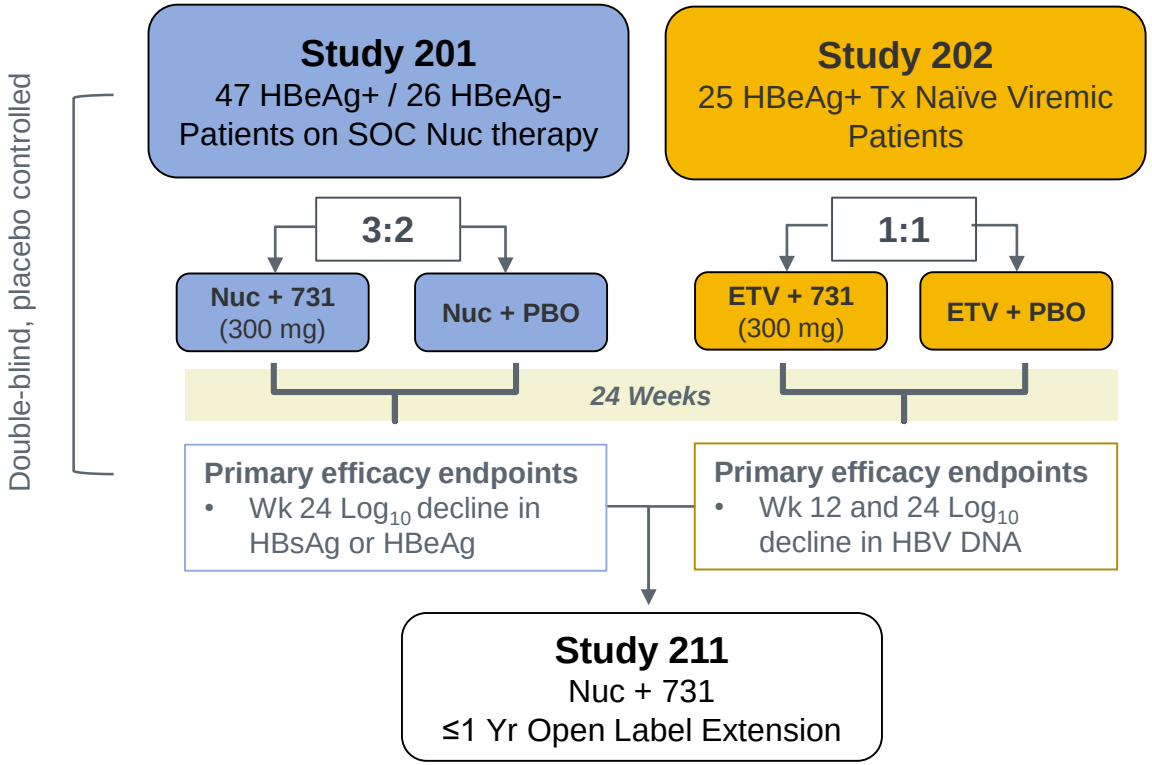
- Discovered and developed at ASMB
- Novel proprietary chemical class - DBAA (dibenzothiazepinecarboxamides)
- Well tolerated in Phase 1 studies
- Efficacious in a Phase 1b 28-day monotherapy study[1]
  - HBeAg pos patients (300 mg QD) exhibited
    - Mean DNA reduction = 2.9 $\log_{10}$ IU/mL
    - Mean RNA reduction = 2.0 $\log_{10}$ copies/mL

Phase 2 program explores critical steps needed to achieve higher cure rates

1. Faster and deeper elimination of viremia
2. Prevention of new cccDNA generation
3. Decay of existing cccDNA and infected cells
4. Demonstrate viral suppression sustained off therapy

[1]Yuen et al, AASLD 2018

Interim Review of ABI-H0731 Phase 2a Studies



# Subjects	D1	Wk 12	Wk 24
Study 201	73	65	11
Study 202	25	24	12

ETV: Entecavir; PBO: Placebo

Blinded, Pooled Safety Summary: Well Tolerated with Favorable Safety Profile

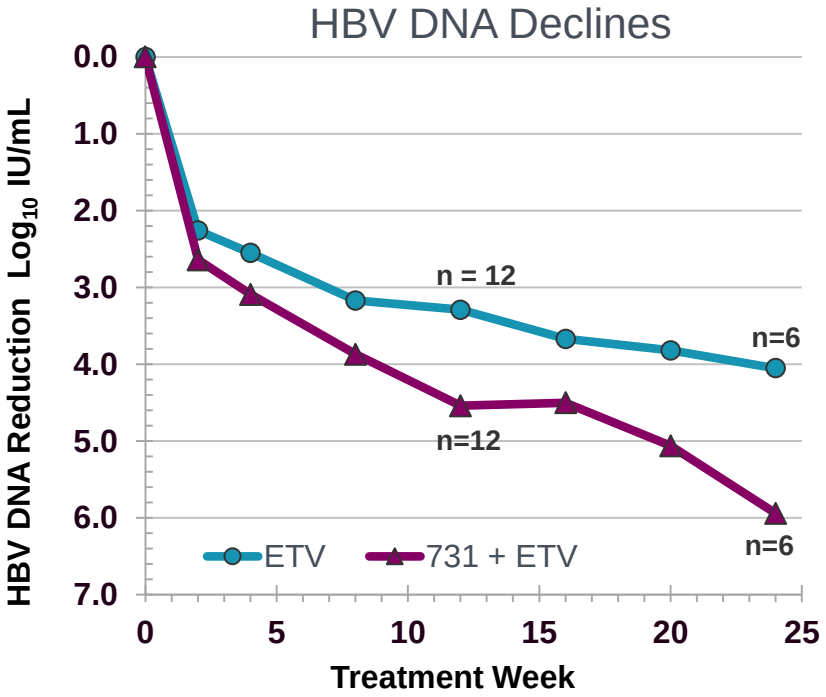
Summary of TEAEs (Studies 201 and 202)

- No SAEs or treatment related discontinuations or interruptions
- Adverse events were mostly mild, infrequent, and considered unrelated to study drug
- No Flares on treatment
- No clinical AE > grade 2
- 3 patients with rash considered “possibly related” (2x grade 1, 1x grade 2); none associated with systemic findings
- Only 1 patient in each study has had a grade 2 AE considered possibly related to study drug
  - Macular/maculopapular rash–resolved on antihistamine (Study 201)
  - ALT increase–resolved with continued treatment (Study 202)

Study 202
Interim Antiviral Efficacy

Highly Viremic Subjects

Study 202: Superior DNA Reductions with 731 Combination

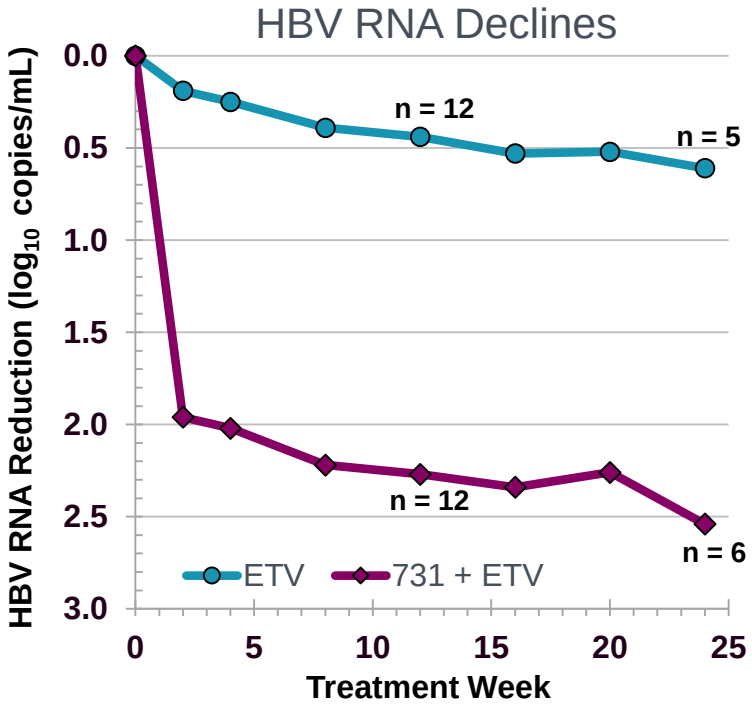


Mean Log_{10} HBV DNA Decline			
Week	**ETV**	**ETV + 731**	**P Value**
12	**3.29**	**4.54**	**<.011**
24	**3.99**	**5.94**	**<.005**

HBV DNA assessed by Roche Cobas qPCR; LOQ = 20 IU

- Significantly **faster** and **deeper** reductions in HBV DNA levels, as early as Week 2 (P=.03)
- Among subjects with abnormal ALT at entry, more rapid ALT normalization seen in combination arm
  - 5/7 vs. 0/5 by Week 4 (P <.05)
  - 7/7 vs. 2/5 by Week 12 (P <.05)

Study 202: Superior RNA Reductions with 731 Combination



Mean Log_{10} HBV RNA Decline			
Week	**ETV**	**731 + ETV**	**P Value**
12	0.44	2.27	<.005
24	0.61	2.54	<.005

HBV RNA assessed by RT qPCR; LOQ = 200 copies/mL

- **All patients on combination achieved a rapid decline in RNA levels**

Study 201
Interim Antiviral Efficacy

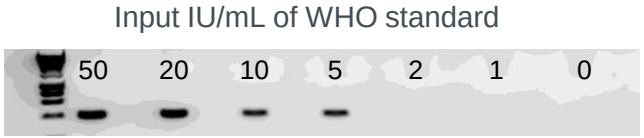
HBV DNA “Nuc Suppressed” Subjects

Elimination of Residual Viremia is an Important Unmet Medical Need

- **Nucs do not eliminate HBV viremia even after years on treatment**[1]
- **Detected DNA represents "infectious virus"**
  - ILC2019, PS-150: "Evidence for the presence of infectious virus in the serum from chronic hepatitis B patients suppressed on nucleos(t)ide therapy with detectable but not quantifiable HBV DNA"

- **A highly sensitive semi-quantitative PCR assay was developed at ASMB to detect viral DNA levels to 2-5 IU/mL to monitor loss of residual virus**

Assay Standardization and Validation

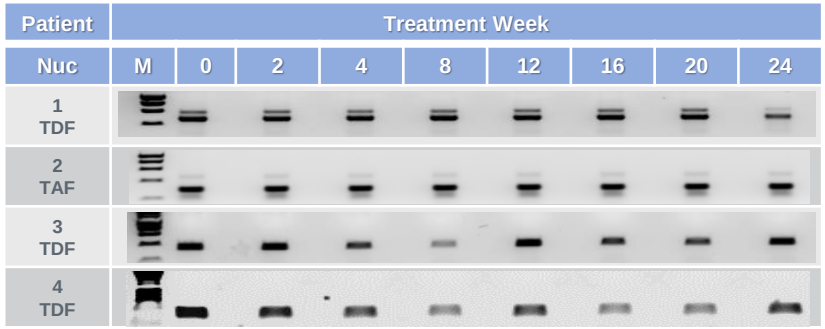


[1] Marcellin, et al, AASLD 2014, P1861

Study 201: Elimination of Detectable Virus Only on Combination

At Week 24, longitudinal serum samples were assayed for detectable virus

Nuc Monotherapy

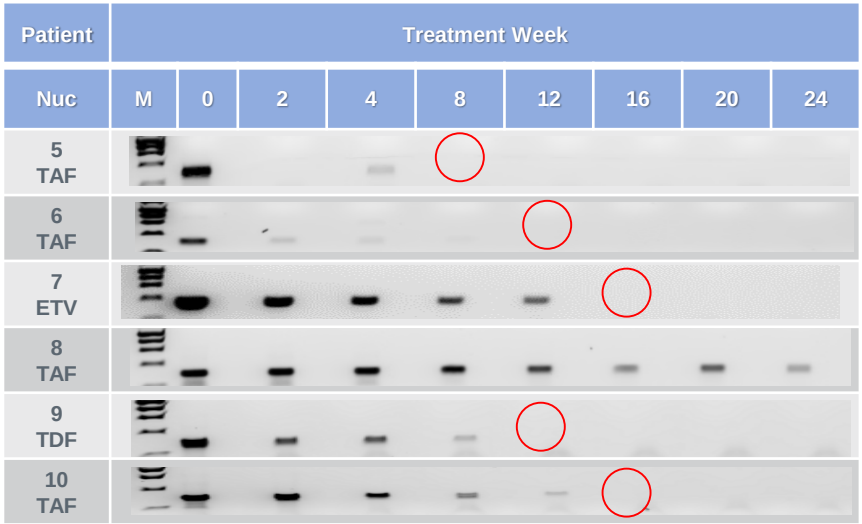


HBV DNA PCR Assay To Quantitate Low Level Viremia

- DNA purified from longitudinal serum samples (0 – 24 Wk)
- PCR amplification (40-45 cycles) using individually optimized primers

Residual viremia is not eliminated by Nuc therapy

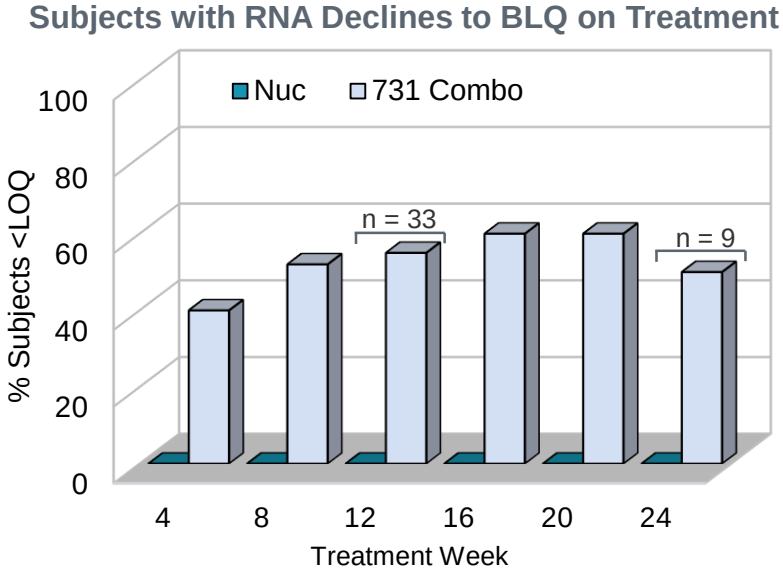
731 Combo Therapy



Elimination of detectable virus ONLY observed on combination

Study 201: RNA Reductions to BLQ Only on Combination

HBeAg Positive Patients with RNA >LOQ at Baseline (N = 37)



Mean Log_{10} HBV RNA Decline			
Week	**Nuc**	**731 + Nuc**	**P Value**
12	**0.05**	**2.34**	**<.001**
24	**0.15**	**2.20**	**.012**

- All subjects on combination arm achieved rapid RNA declines
- **Of subjects with detectable baseline RNA, 60% of 731 combo subjects achieved RNA <LOQ (200 copies/mL) by Week 16 vs. 0% on Nuc arm**

Study 201: Antigen Declines at Interim Analysis

Patients Treated 24 Weeks*		
Treatment	**Nuc**	**731 + Nuc**
DNA (TND[1])	**0/4 (0%)**	**5/6 (83%)**
RNA (<200 Copies/mL)	**0/3 (0%)[2]**	**3/6 (50%)**
HBeAg ≥ 0.5 Log_{10} Decline	**0/3 (0%)**	**1/6 (17%)**
HBsAg ≥ 0.5 Log_{10} Decline	**0/4 (0%)**	**0/6 (0%)**

[1] Target not detected by ASMB semi-quantitative PCR
[2] a 4th subject on Nuc was BLQ at baseline

*Subjects with available data

- Antigen declines anticipated to follow elimination of residual viremia
- Study subjects continue to be treated and followed in open label Study 211
- Safety, viremia and viral antigens continue to be monitored over time

Summary of Interim Data for Phase 2a Studies on ABI-H0731

Favorable safety and tolerability profile

- AEs and lab abnormalities were generally considered unrelated, grade 1 and transient

Combination of 731+Nuc demonstrated superior antiviral activity vs. Nuc alone

- In treatment naïve patients, faster and deeper declines in HBV DNA observed starting at Week 2
- In Nuc “suppressed” patients, HBV DNA reductions to below limits of high-sensitivity PCR assay
- In both studies, significant HBV RNA declines

Elimination of residual viremia will likely be required to prevent new cccDNA formation and increase cure rates

- HBeAg and HBsAg decline are anticipated to follow elimination of viremia

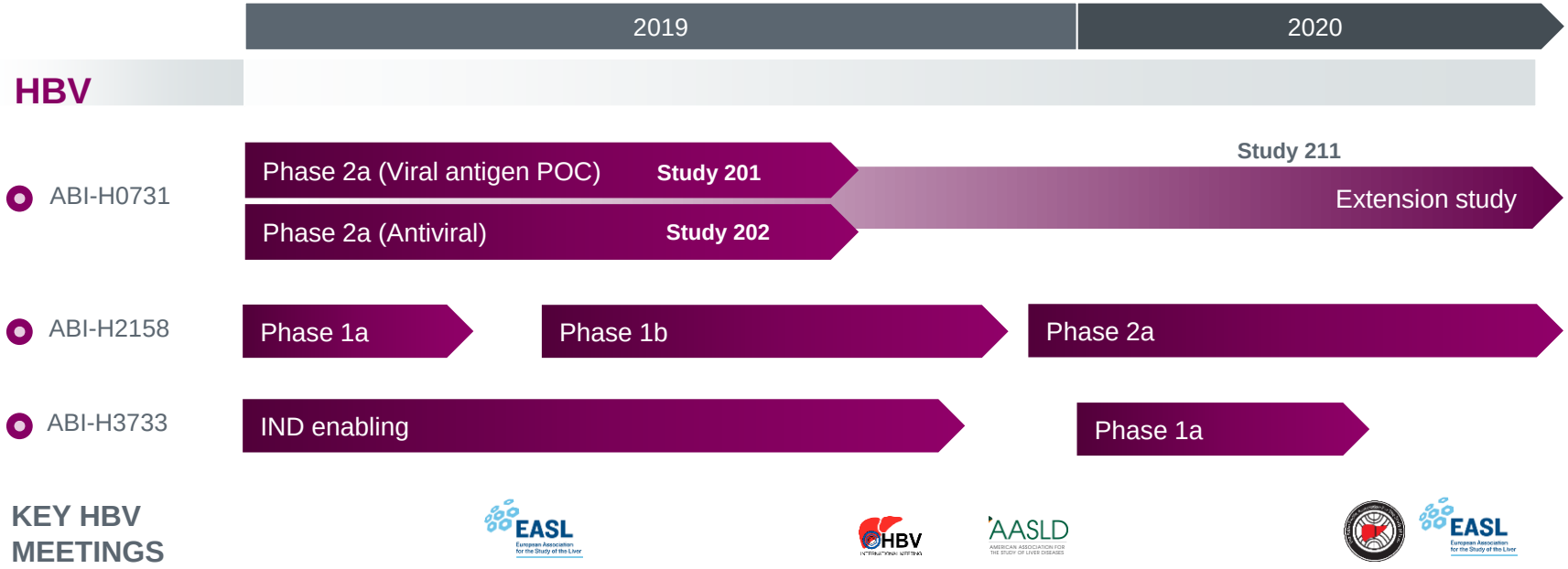
Ongoing Studies to Define Timelines to cccDNA Loss, Sustained Suppression & Potential Cure

Next Steps & Upcoming Milestones

EASL Highlights and Next Steps

- **Nucs are effective, but do not eliminate residual HBV DNA and HBV RNA**
- **Combination of 731+ Nuc demonstrated potential to eliminate residual HBV DNA**
- **Core Inhibitors have the potential to be the backbone of future HBV regimens**
  - We believe that elimination of residual viremia will likely be a critical milestone required to increase rates of cure
- **2158 currently in dose finding Phase 1b study and Phase 2a studies expected to follow immediately**
- **3733 expected to initiate Phase 1a study in early 2020**
- **Initiating discussions with global regulatory bodies regarding design of next studies and pathways to approval for 731 + Nuc combination**

Strong Trajectory in 2019: Upcoming Milestones



STRONG BALANCE SHEET: ~$218M in cash (as of 12/31/2018)

Q&A

EASL Highlights and Next Steps

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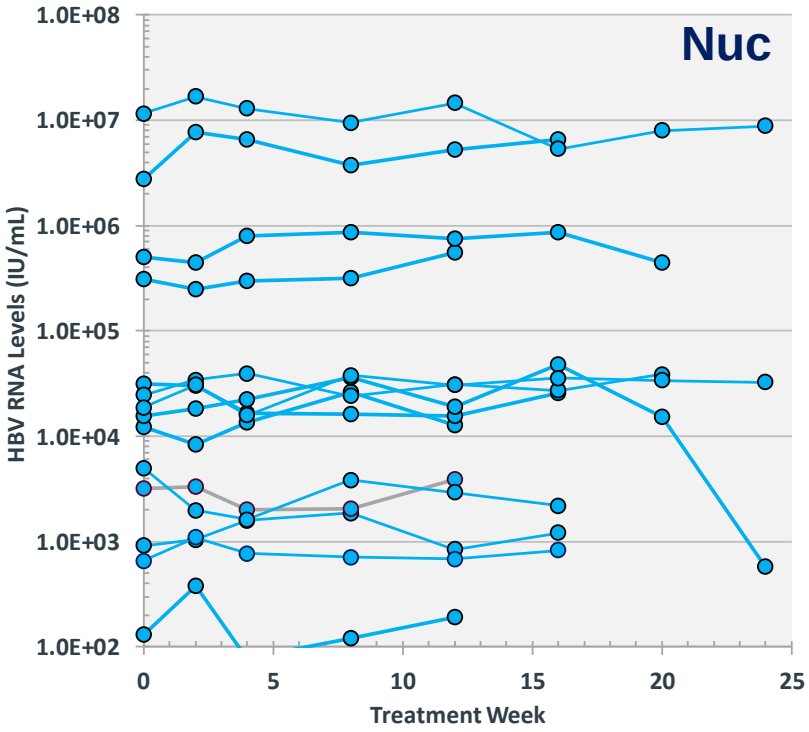
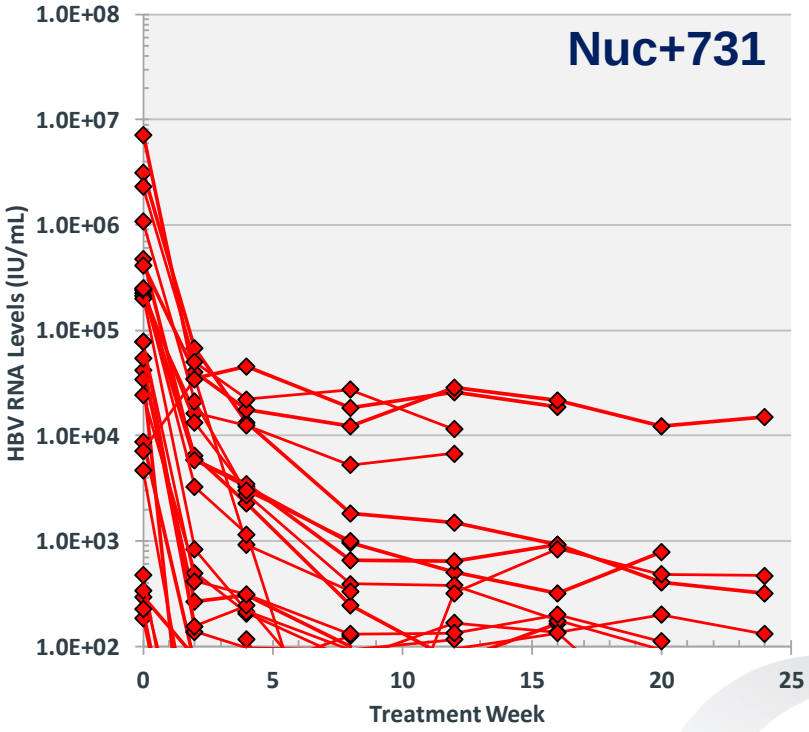
Thank You!

Appendix

ABI-H0731: Study 201 – Actual RNA Levels





ABI-H2158: Second Generation Core Protein Inhibitor

Phase 1a Safety, Tolerability and PK in 48 Healthy Volunteers

- No dose dependent TEAEs, pattern of clinical safety or laboratory abnormalities observed
- Exposures increased in a roughly dose-proportional fashion
- Steady-state concentrations achieved quickly in the MAD cohort, with accumulation of ≈1.5-fold at steady state
- No significant food effect observed

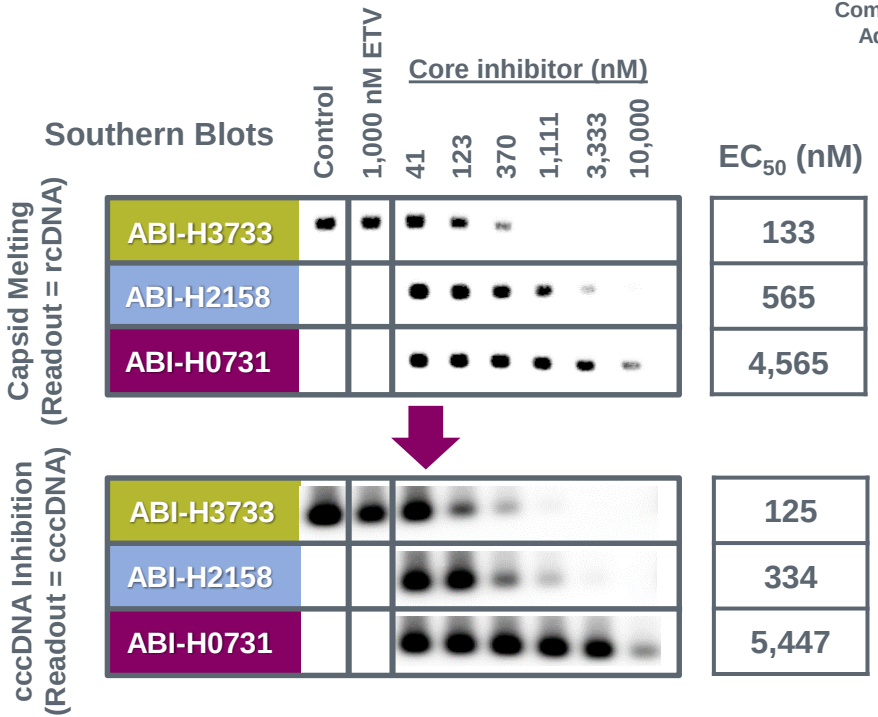
Trough liver concentrations are projected to exceed the *in vitro* EC_{90} (334 nM) for inhibition of cccDNA establishment with QD dosing of 100 mg and higher

Phase 1b ongoing….

ABI-H3733: Relative Potency in Blocking cccDNA Generation

HBV Infection of HepG2-NTCP Cells

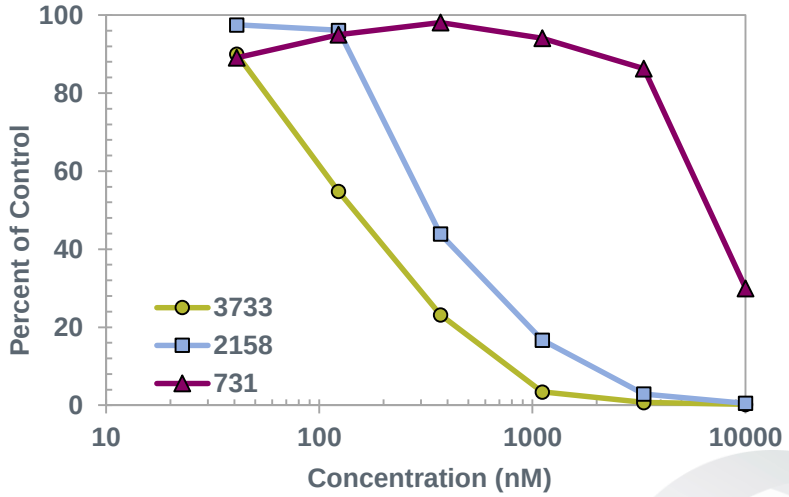
Southern Blots



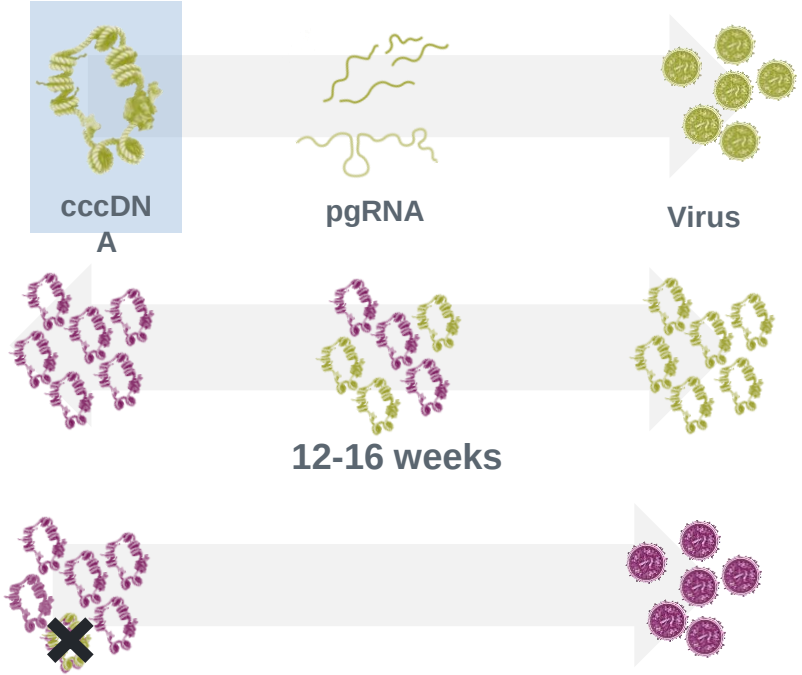
	EC_{50} (nM)
ABI-H3733	133
ABI-H2158	565
ABI-H0731	4,565

ABI-H3733	125
ABI-H2158	334
ABI-H0731	5,447

Inhibition of cccDNA Establishment



Summary Results From Expanded cccDNA Biosynthesis Study



- Genetic source of resistance shown to be cccDNA
- pgRNA closely reflects genetic composition of cccDNA pools

- Turnover of cccDNA from sensitive to resistant and from resistant to sensitive occurs in 12-16 weeks
- Suggests relatively rapid biologic turnover of both pgRNA and cccDNA pools and/or infected cells

- No evidence to support existence of inactive subpopulation of cccDNA, as genetic changes are observed in the entire population of cccDNA

Results indicate that existing cccDNA has a limited half-life, suggesting that therapies inhibiting establishment of new cccDNA may lead to higher cure rates for patients with HBV