New Therapies to More Effectively Eliminate Viral Replication and Increase Cure Rates in CHB Patients

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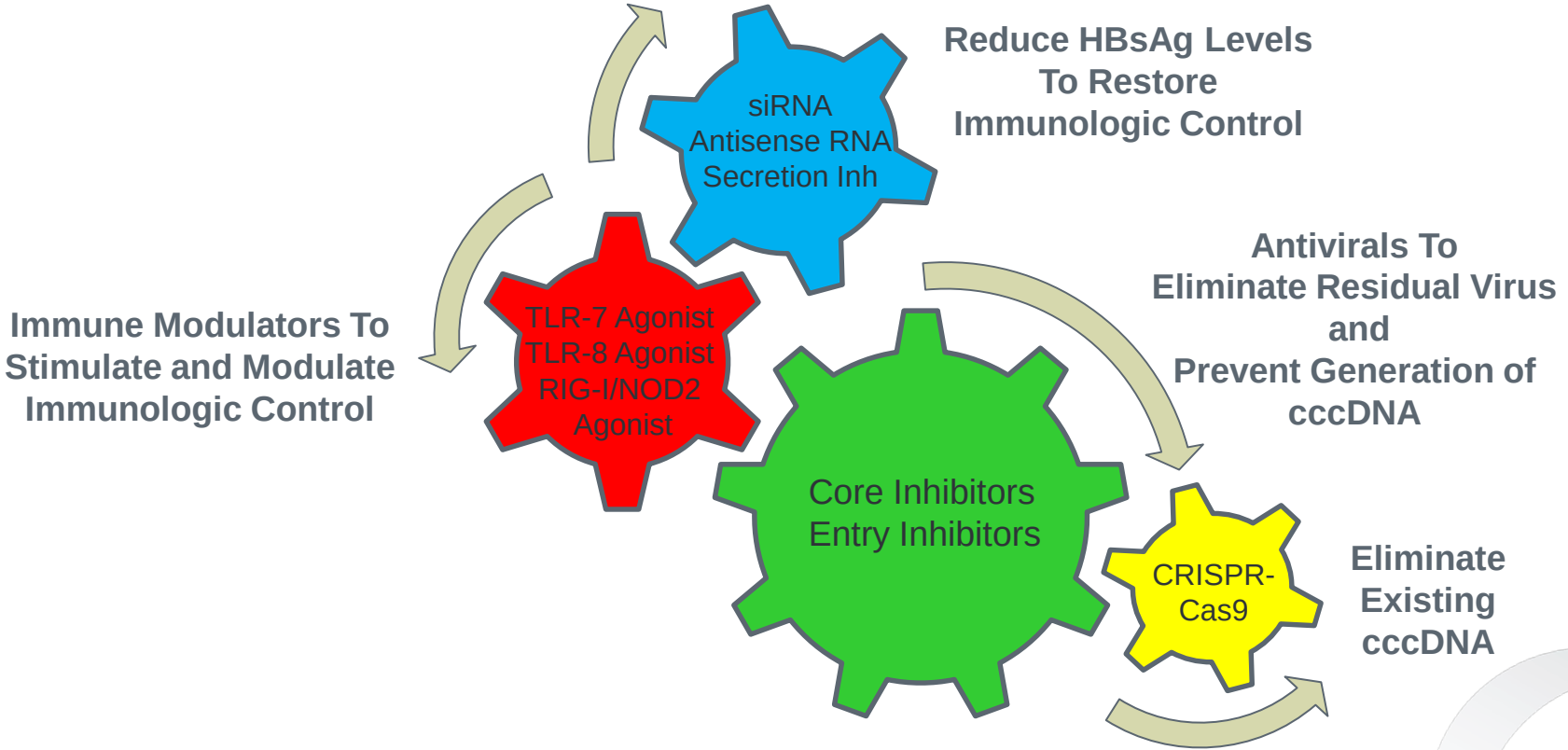
1st IASL - CFHPC Congress (Beijing June 2019)

Cautionary Note Regarding Forward-Looking Statements

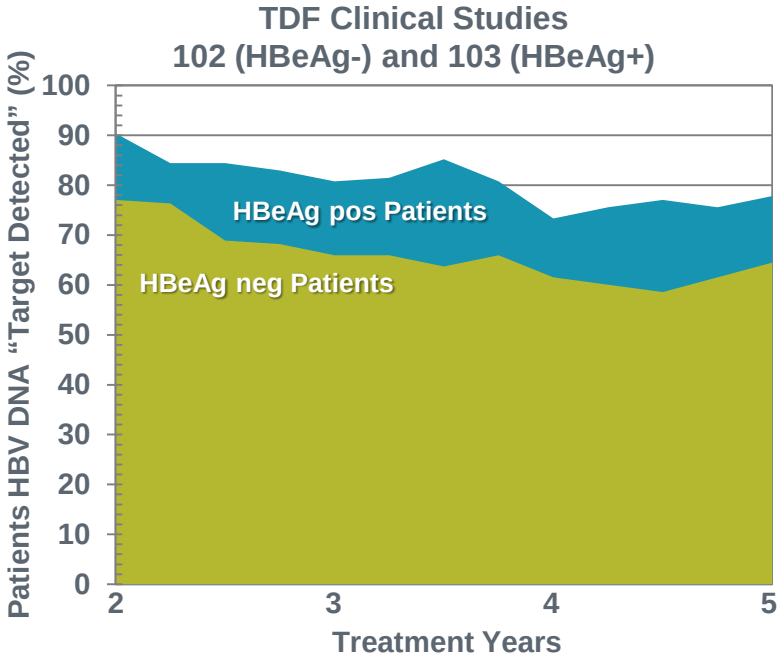
The information in this presentation contains forward-looking statements regarding future events, including statements about the clinical and therapeutic potential of Assembly Biosciences' HBV-cure program, the therapeutic potential of core protein inhibitors, the discovery and identification of new classes of core protein inhibitors, ongoing and planned preclinical studies and clinical studies in its HBV-cure program, and the plans, strategies and intentions related to its HBV-cure program. 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," "likely", "may," "potential," or "predictive," or "suggest." 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: the scientific theory for core inhibitors is unproven and novel; top-line or initial data may not accurately reflect the complete results of a particular study or trial; outcomes of clinical studies are uncertain and results of earlier preclinical and nonclinical studies may not be predictive of future clinical studies results. 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' Quarterly Report on Form 10-Q for the year ended March 31, 2019 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.

Strategic Approaches Being Pursued To Improve Cure Rates



Our Focus is on Finding More Effective Antivirals – WHY?

Prolonged Nuc Therapy Fails to Eliminate Viral Replication



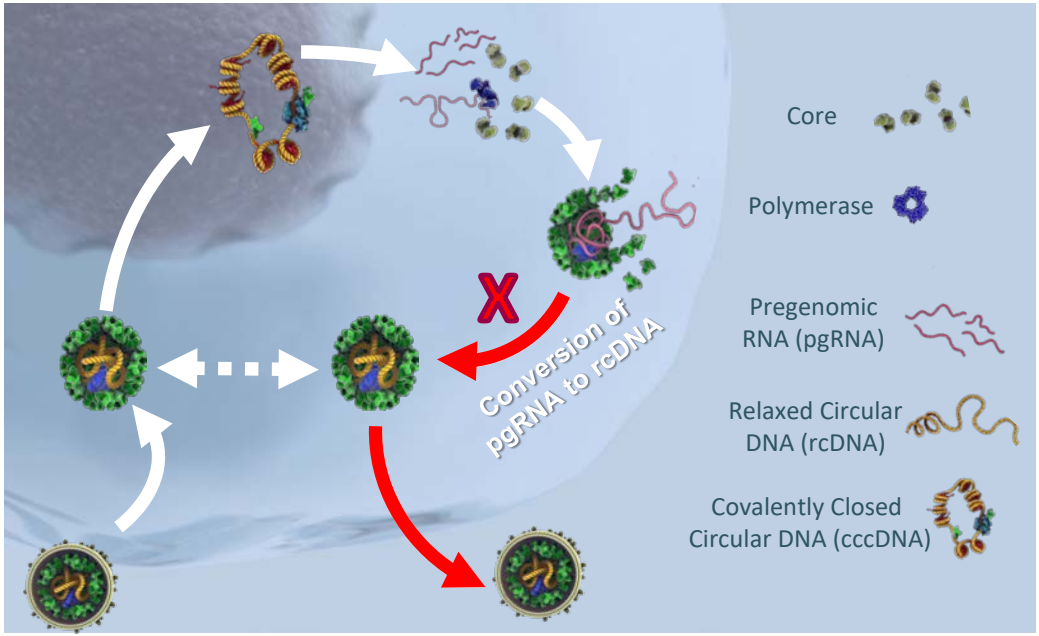
PCR-detectable HBV DNA persists in 70-80% of patients despite TDF treatment for 5 years[1]

Learnings from EASL 2019

- Detected DNA represents ***infectious virus***[2]
  - Residual viremia refractory to Nuc therapy
  - **Likely accounts for poor cure rates**
- **Over 80% of circulating HBsAg derived from integrated DNA[3]**
  - HBsAg may not be an appropriate biomarker of cccDNA loss
  - HBsAg does NOT lead to reinfection and is NOT a marker of ongoing infection
- Appropriate biomarkers of cure is an open question in the field
  - If DNA and RNA are undetectable, there is likely no remaining infectious virus
  - cccDNA ONLY source of pgRNA and virus

[1]Marcellin, et al., Poster 1861 AASLD 2014; [2]Burdette et al., PS-150 EASL 2019; [3]Podlaha et al., SAT-91 EASL 2019

New Therapies are Needed to Increase Cure Rates in CHB



Nucleos(t)ide Pol Inhibitors (Nuc)

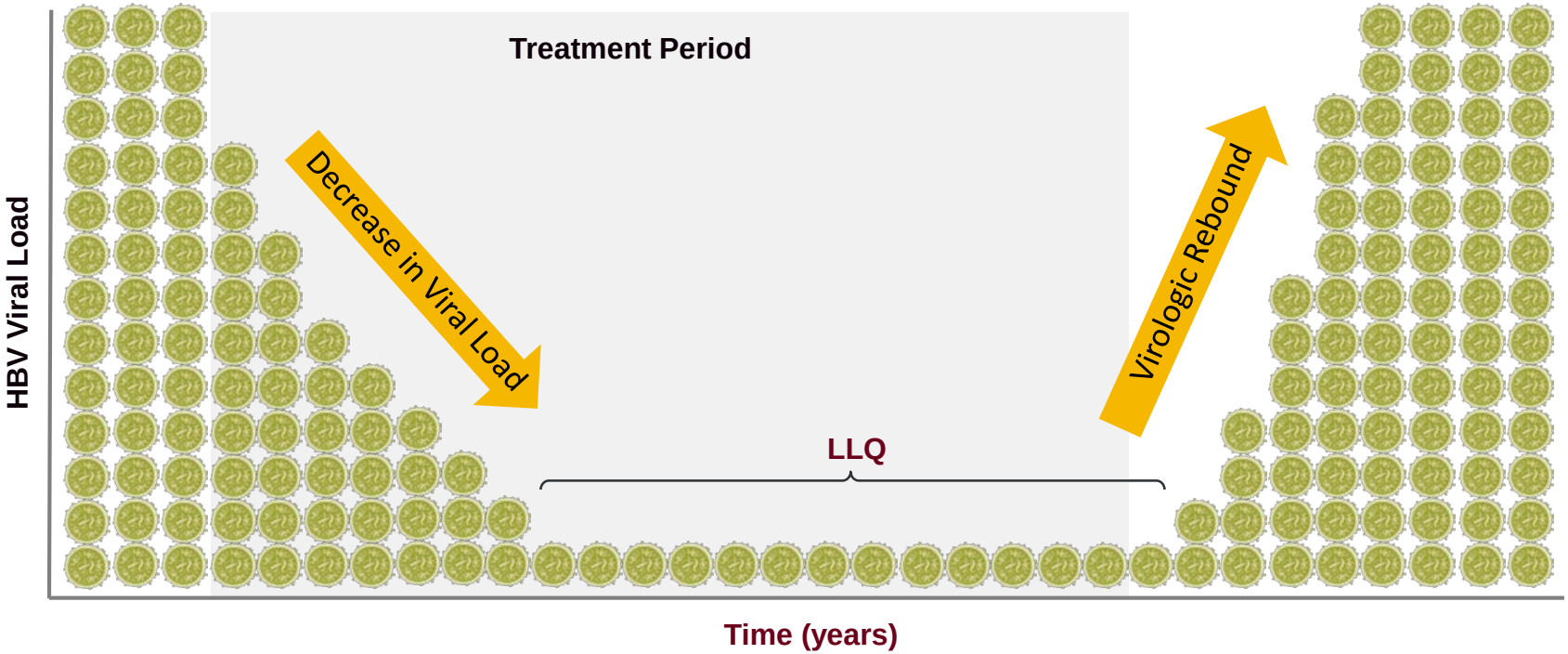
- Current “Standard of Care” for HBV
- Safe, well tolerated, with minimal resistance
- Reduce HBV DNA

But Fail to ……

- Fully eliminate virus
- Prevent new cccDNA formation
- Provide finite treatment duration

Cure is not possible without elimination of residual virus

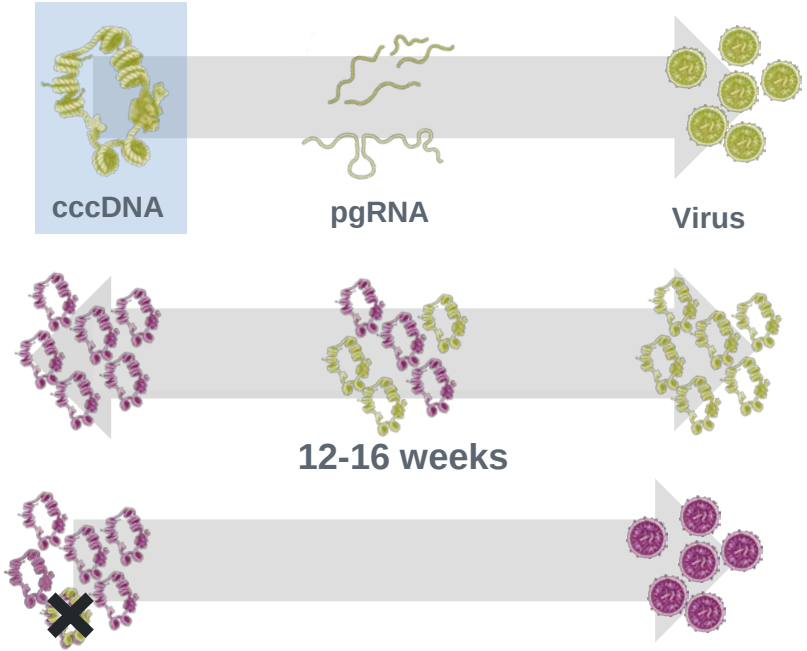
Remaining Virus Able to Re-infect Liver When Nuc Therapy Stops



To improve cure rates…must eliminate residual virus to prevent reinfection

LLQ = lower limit of quantification.

Key Findings of cccDNA Biosynthesis Studies



- 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

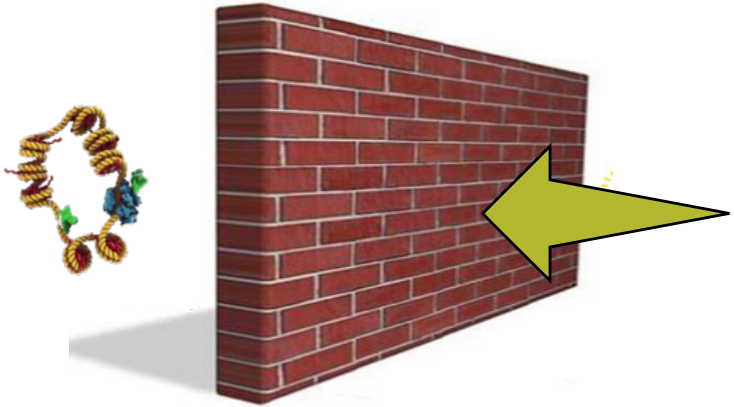
Huang et al. Poster Thr-216 EASL Apr 2019

Critical Inhibitory Elements of New Treatment Paradigms

Eliminate Residual Virus Replication

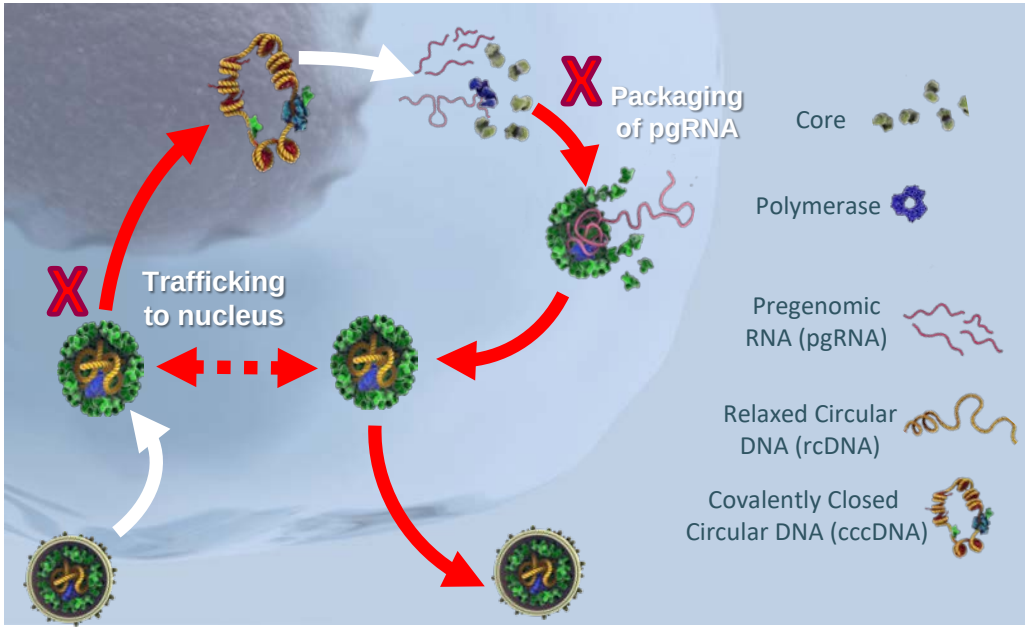
….To Stop New Infection of Hepatocytes

Block Generation of New cccDNA



….To Allow Decay of Existing cccDNA

CIs Block Viral Replication and cccDNA Establishment



Core Protein Inhibitors (CIs)

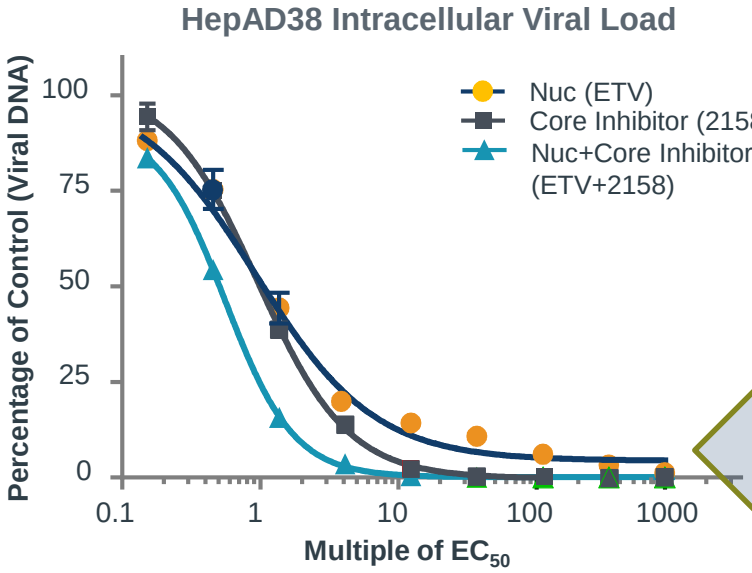
- Inhibit multiple steps in viral replication cycle
- Achieve deeper levels of viral inhibition than Nucs alone

AND…..

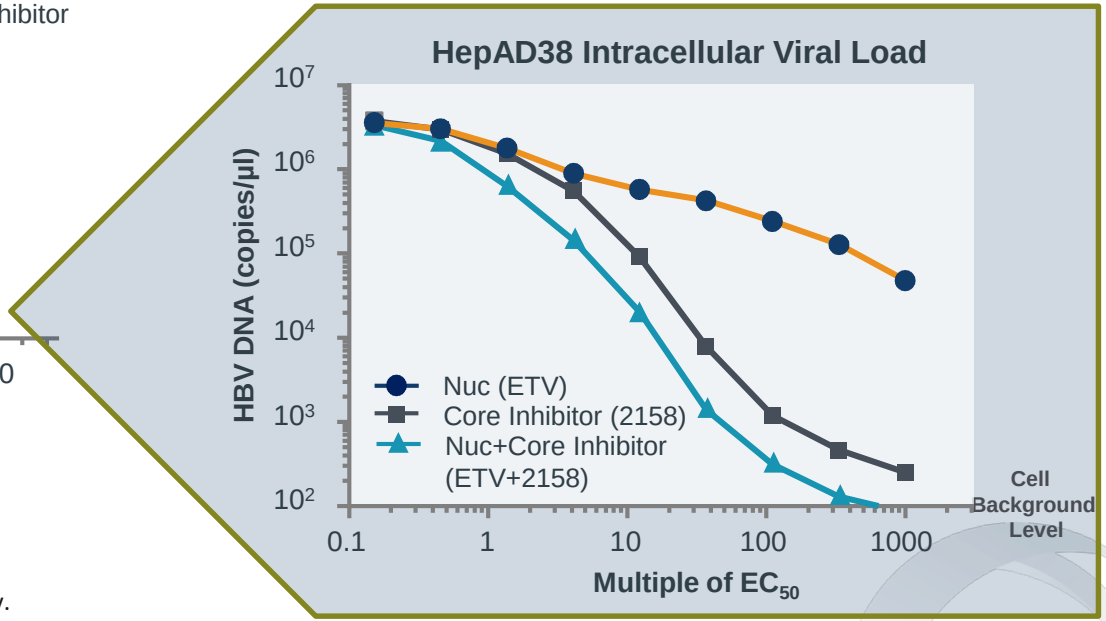
- Can block the formation of cccDNA

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

Superior Antiviral Effectiveness vs. ETV in Culture Assays



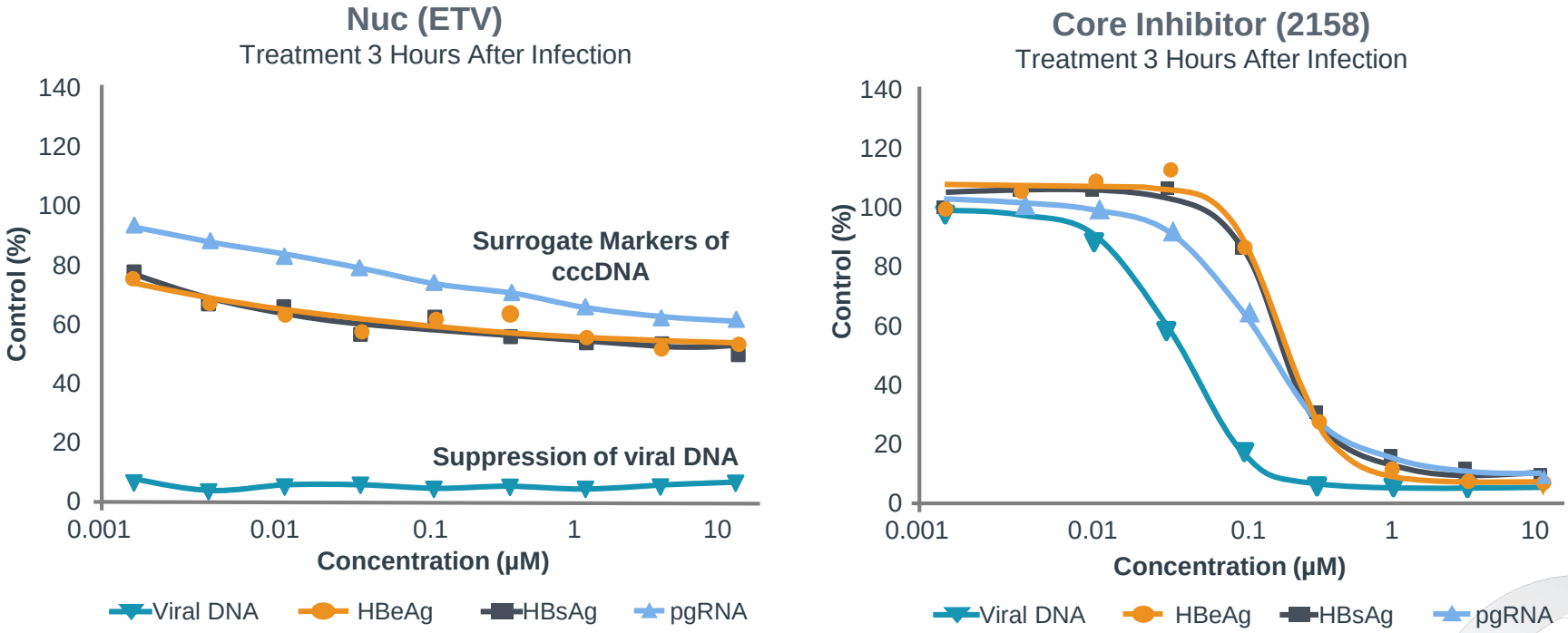
Core Inhibitors reduce virus levels deeper than Nucs



EC_{50} = Effective Concentration yielding a 50% reduction in activity.

Core Inhibitors Inhibit Establishment of cccDNA in Infected Cells

Infection of Primary Human Hepatocytes

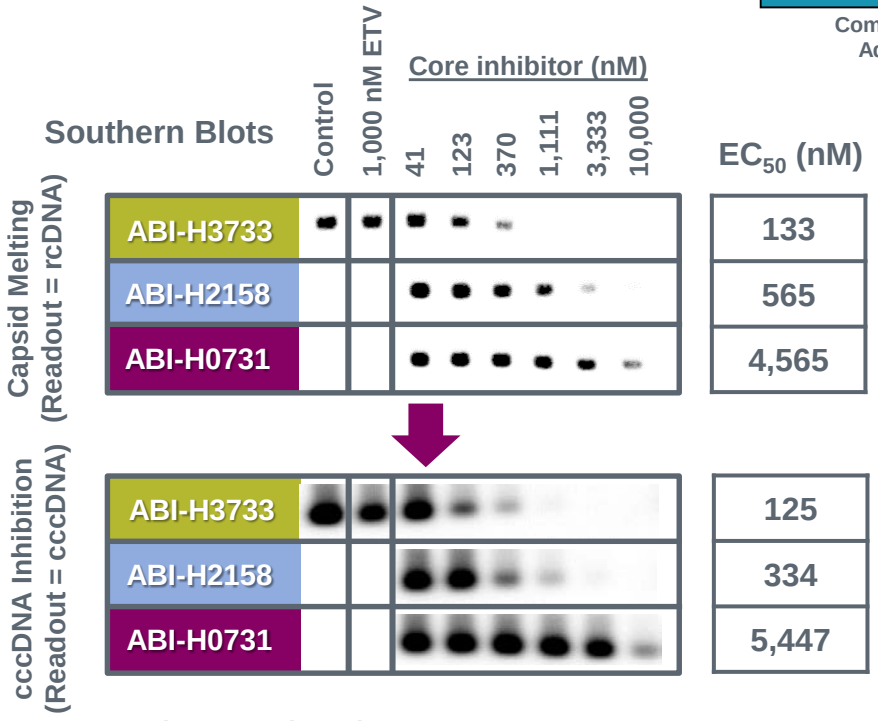


Huang Q, et al. Poster 922 AASLD Nov 2017

Relative Potency in Blocking cccDNA Generation

HBV Infection of HepG2-NTCP Cells

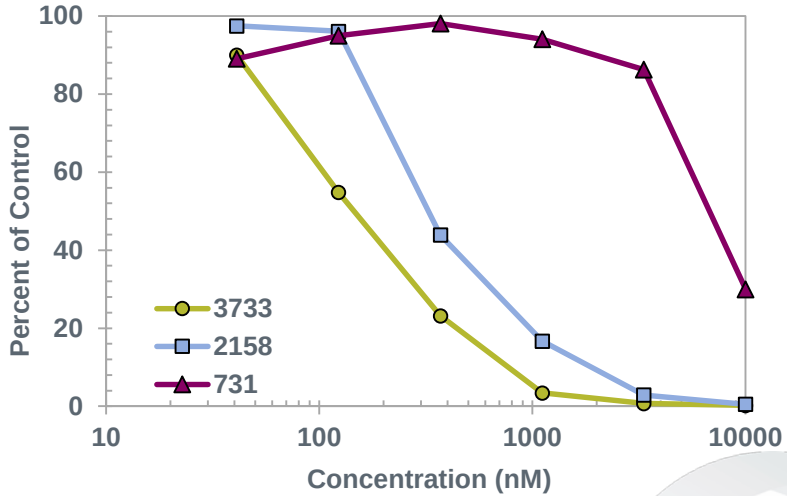
Southern Blots



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

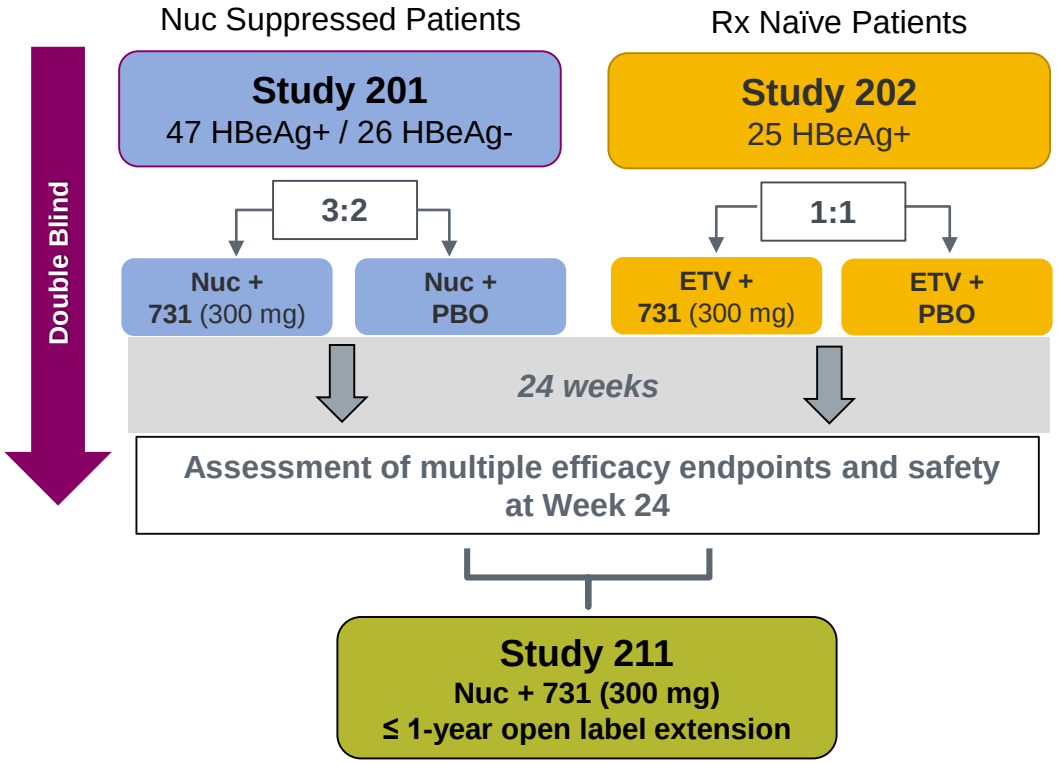
	EC_{50} (nM)
ABI-H3733	125
ABI-H2158	334
ABI-H0731	5,447

Inhibition of cccDNA Establishment



Colonno et al. Oral EASL Apr 2019

Interim Review of ABI-H0731 Phase 2a Studies (EASL - Apr 2019)



Study	201		202
Demographics	HBeAg + (n = 47)	HBeAg – (n = 26)	HBeAg + (n =25)
Asian (%)	87	81	96
Genotype B,C (%)	83	46	88
Mean Baseline Values			
ALT (U/L)	27	25	57
HBV DNA (log_{10} IU/mL)	BLQ	BLQ	7.8
HBV RNA (log_{10} copy/mL)	5.9[a]	≤ 2.3[b]	8.0
HBsAg (IU/mL)	5,569	2,970	57,179
HBeAg (PEU/mL)	29	N/A	791

[a] 37/47 patients with baseline RNA > 200; [b] 4/26 patients with RNA > 200 copies)

Metrics at Time of Interim Analysis

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

Lalezari et al. Oral LB-07 EASL Apr 2019

Blinded, Pooled Safety – Well Tolerated with Favorable Safety Profile

Blinded Summary of TEAEs (Studies 201 and 202) at interim data cut

- 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
- 1 patient in each study with 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)

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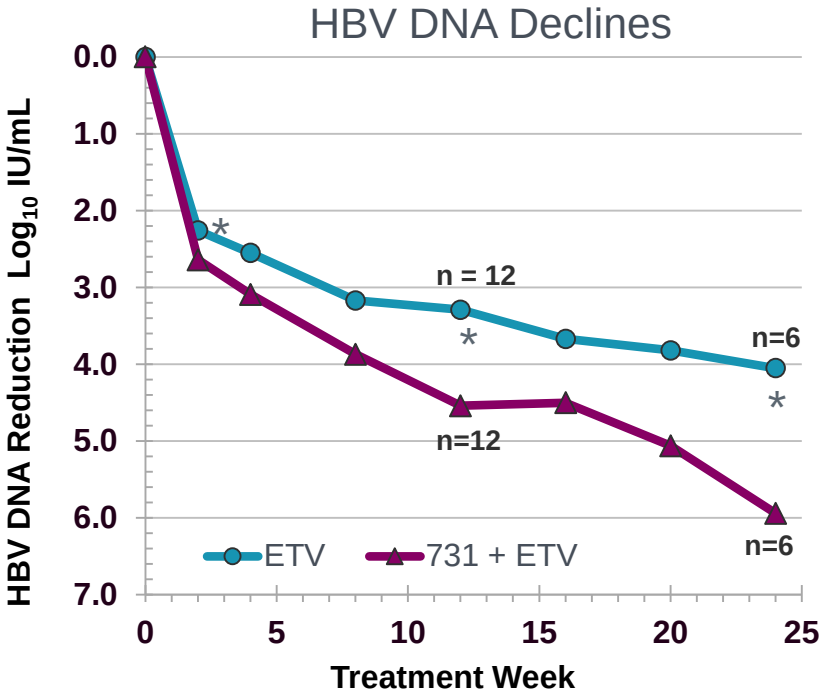
Study 202: Superior DNA Reductions with 731 Combination



*Statistically significant at (P < .05 or better)

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)

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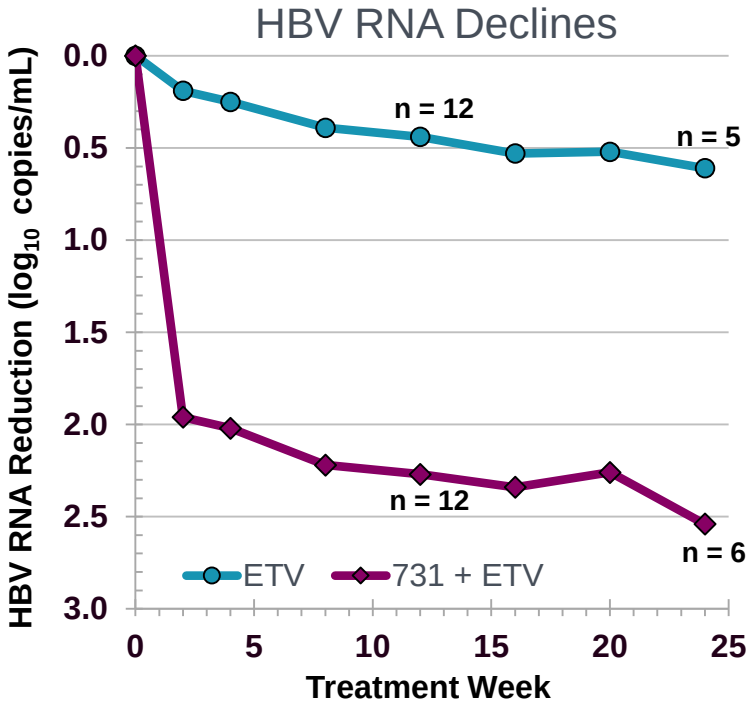
Study 202: Superior RNA Reductions with 731 Combination



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**

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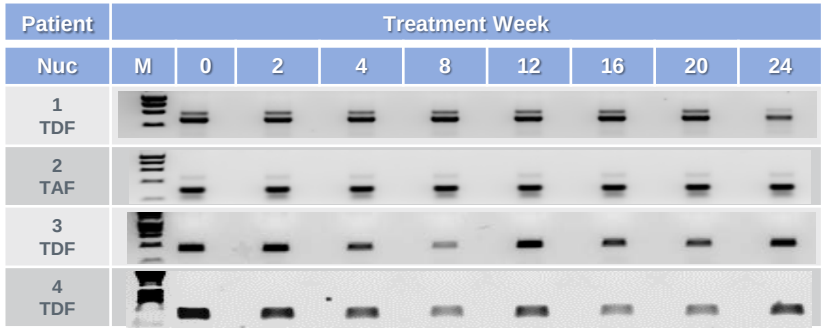
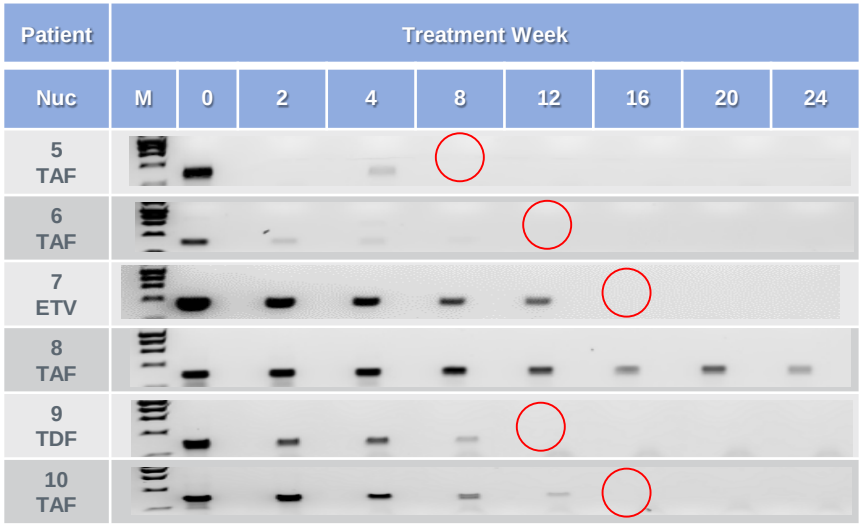
Study 201: Elimination of Detectable Virus Only on Combination

At Week 24, longitudinal serum samples were assayed for detectable virus using sensitive PCR assay

Nuc Monotherapy



731 Combo Therapy



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 not eliminated by Nuc

Residual viremia decline below detection (2-5 IU/mL)

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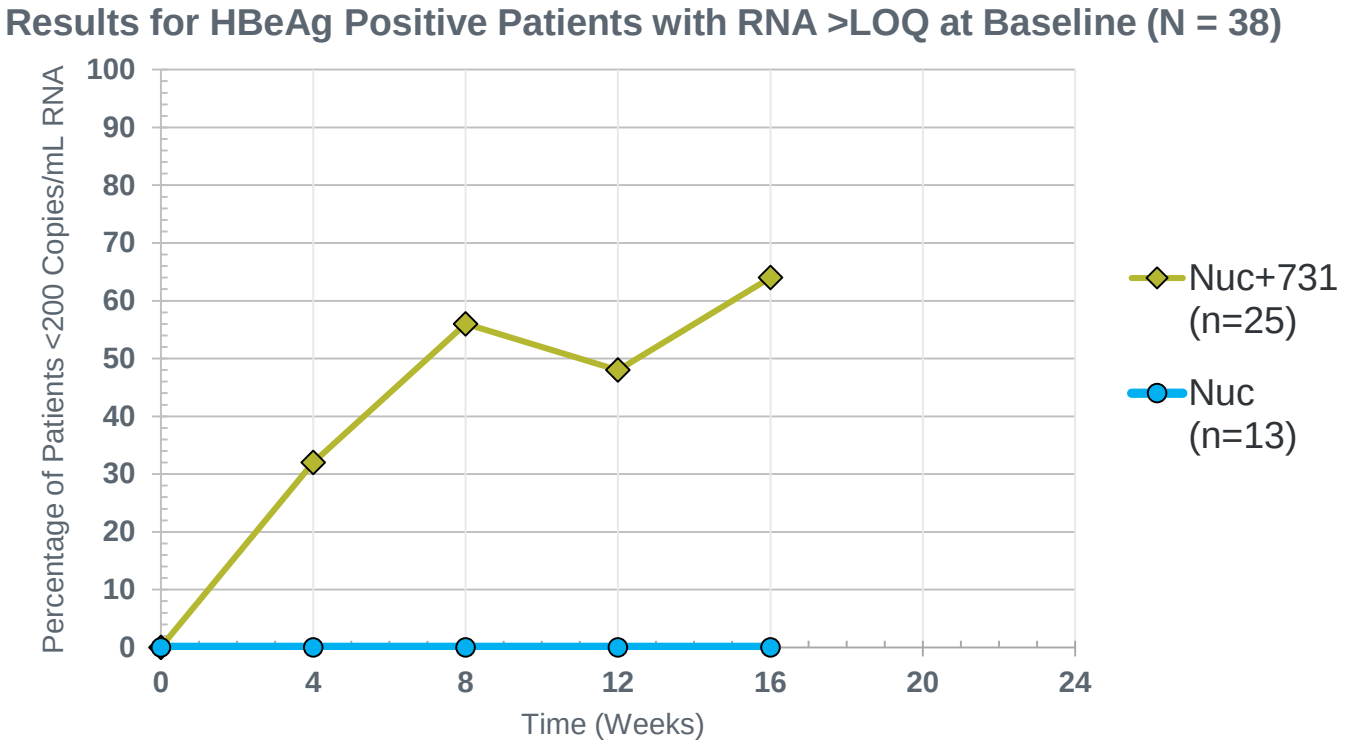
Study 201: RNA Reductions to BLQ Only on Combination



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Study 201: Summary of Results at Time of 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%)**

*Subjects with available data

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

- Antigen declines anticipated to follow elimination of residual viremia and RNA
- High level expression of HBsAg from integrated sequences limits ability of Core Inhibitors to decrease HBsAg levels from this source
- Study subjects continue to be treated and monitored in open label Study 211

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ASMB Core Inhibitor Program Summary

- **Core inhibitors have the potential to be the backbone of future HBV regimens**
  - Highly potent antivirals that disrupt viral replication at multiple steps
  - Potential to eliminate residual viremia (deficiency of Nuc therapy)
  - Inhibit the generation of new cccDNA
- **Summary of Interim Data for Phase 2a Studies on ABI-H0731**
  - Favorable safety profile (AEs and lab abnormalities generally considered unrelated, grade 1 and transient)
  - Combination of 731+Nuc demonstrated superior antiviral activity vs. Nuc alone
    - In Rx-naïve patients, faster and deeper declines in HBV DNA observed starting at Week 2
    - DNA reductions to below limits of high-sensitivity PCR assay observed in Nuc “suppressed” patients
    - Significant HBV RNA declines In both studies
  - Elimination of residual viremia will likely be required to prevent new cccDNA formation and increase cure rates

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- The Patients
- The (many) clinical study teams

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Thank You!