Preclinical Profile of HBV Core Protein Inhibitor, ABI-H3733, a Potent Inhibitor of cccDNA Generation in HBV Infected Cells

Qi Huang, Simon Haydar, Yi Zhou, Dawei Cai, Xiang Xu, Ran Yan, Lida Guo, Esteban Carabajal, Xuman Tang, Michael A. Walker, Roopa Rai, Mark Bures, Leping Li and Richard Colonno

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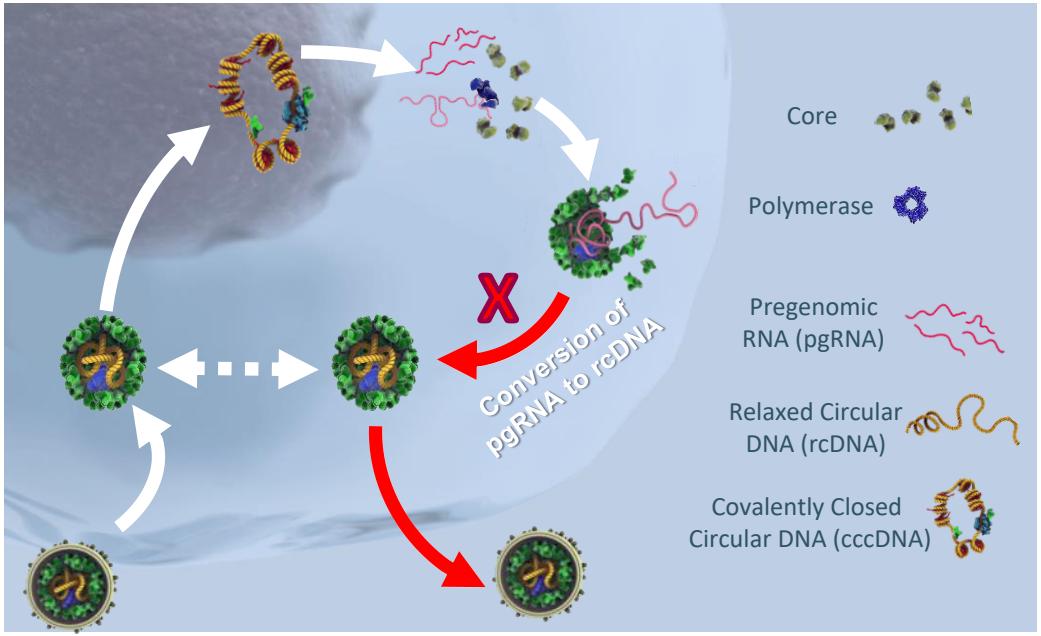
The information in this presentation contains forward-looking statements regarding future events, including statements about the clinical and therapeutic potential of Assembly Biosciences' HBV-cure program, the therapeutic potential of core protein inhibitors, the discovery and identification of new 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 "likely", "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. 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.

New Therapies are Needed to Increase Cure Rates in CHB



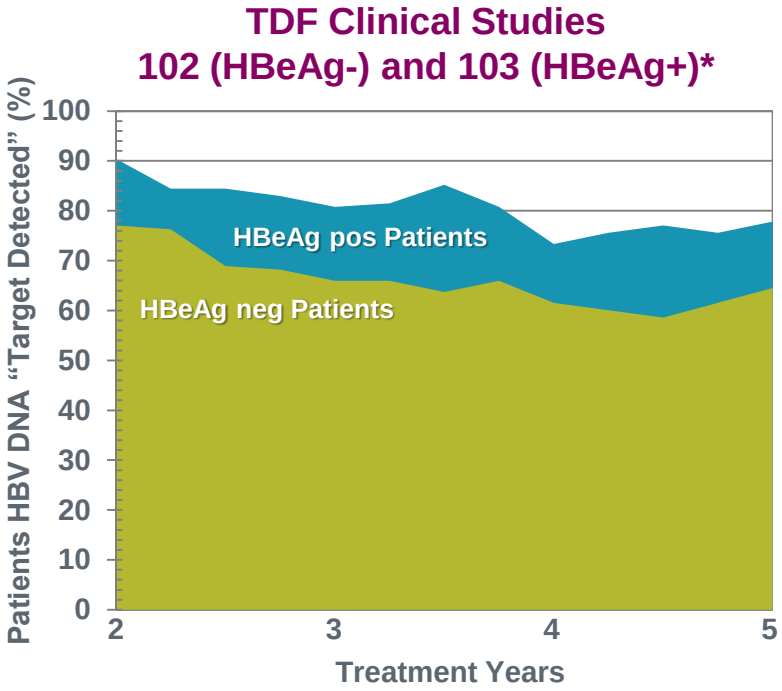
Nucleos(t)ide Pol Inhibitors (Nuc)

- Current “Standard of Care” for HBV
- Inhibit conversion of pgRNA to dsDNA
- Safe and well tolerated
- High barrier to resistance

But Fail to ……

- Inhibit formation of cccDNA
- Have a sustained response off therapy

Prolonged Nuc Therapy Fails to Eliminate Viral Replication



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

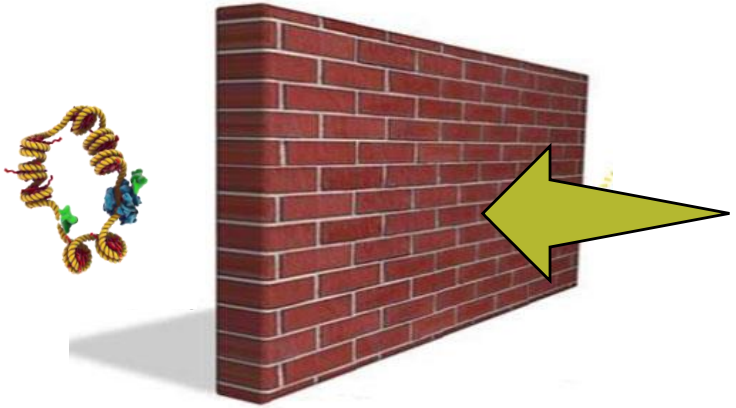
*Marcellin, et al, AASLD 2014, Poster 1861

Critical Inhibitory Elements of New Treatment Paradigms

Eliminate Residual Virus Replication

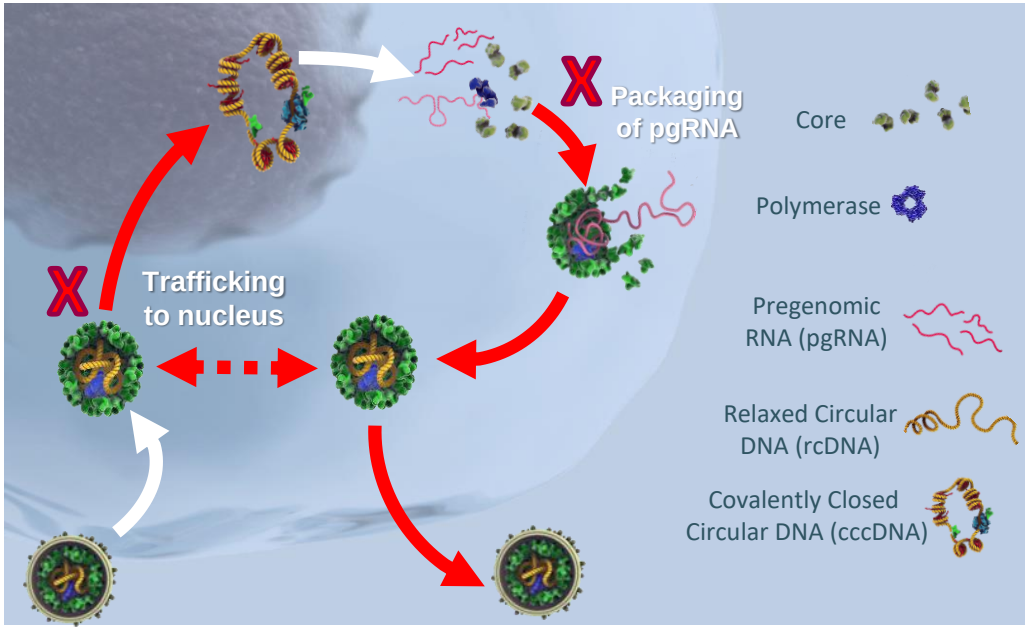
….To Stop New Infection of Hepatocytes

Block Generation of New cccDNA



….To Allow Decay of Existing cccDNA

CIs Block Viral Replication and cccDNA Establishment

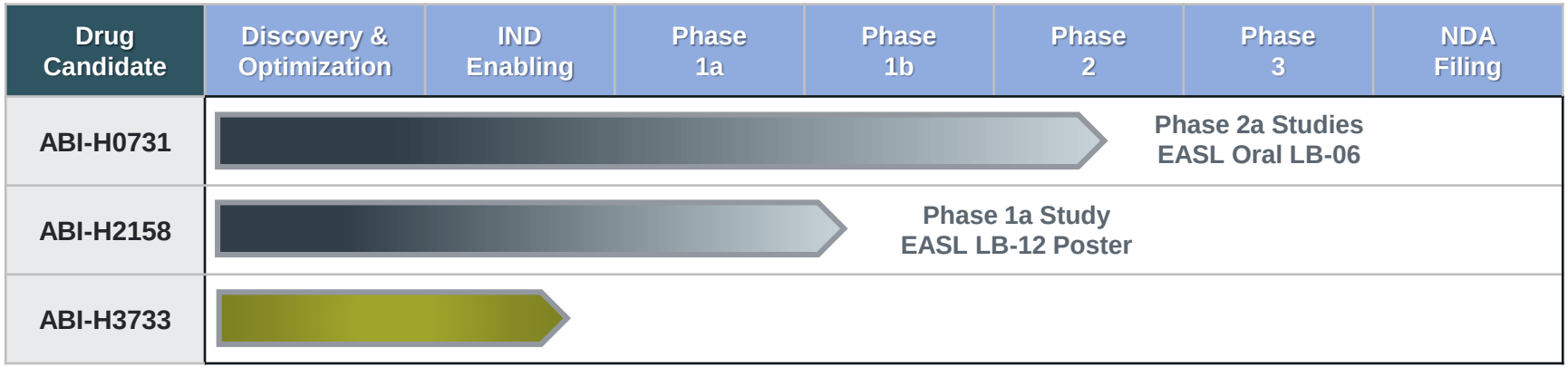


Core Protein Inhibitors (CIs)

- Bind to dimer-dimer interface of Core protein
- Trigger formation of aberrant capsids, preventing packaging of pgRNA and production of virus
- Disrupt trafficking of nucleocapsids to nucleus, blocking the generation of cccDNA

ASMB HBV Core Inhibitor Program Portfolio

- Established pipeline of novel CIs derived from distinct chemical scaffolds
- Focus on identifying increasingly potent CIs, while maintaining favorable drug-like properties

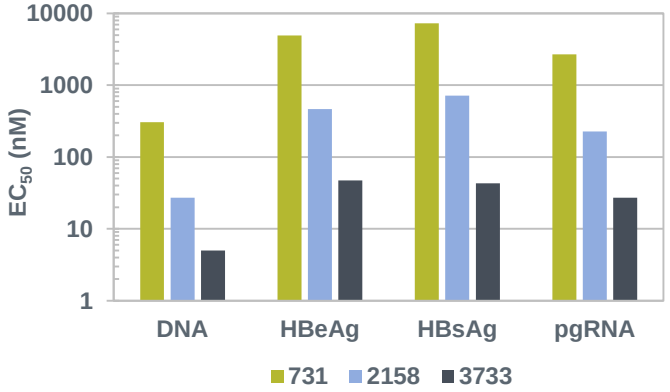


- Discovery efforts continue to advance additional new classes of CIs with distinct phenotypes

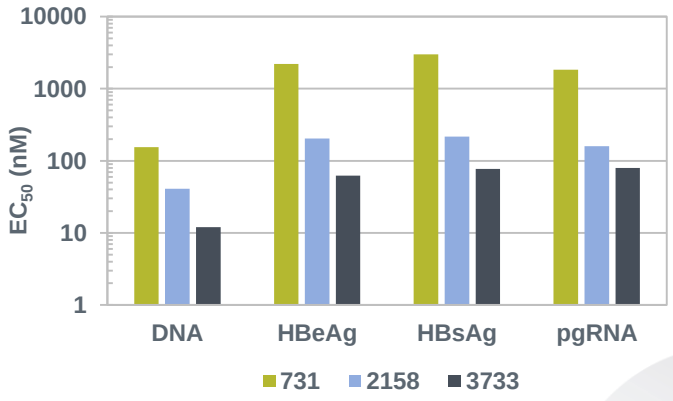
IND = Investigational New Drug Application; NDA = New Drug Application.

ABI-H3733 – Antiviral Profile

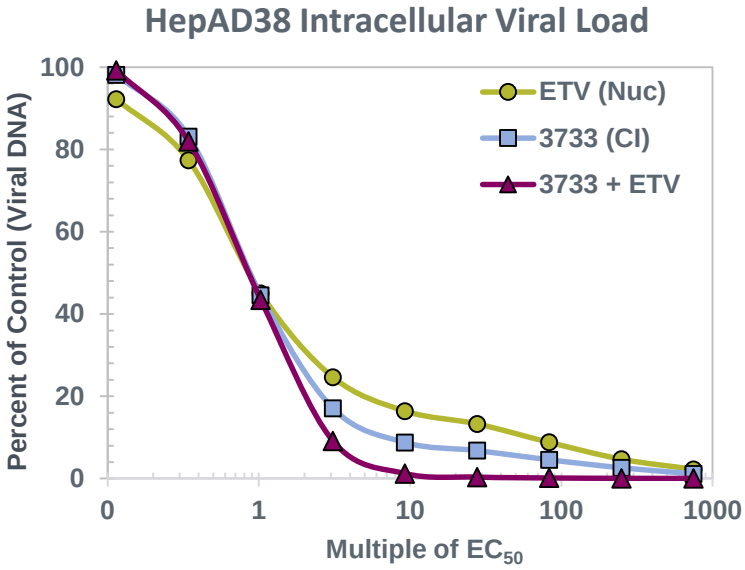
HBV Infection of Human Hepatocytes (HepG2-NTCP)		
Marker	EC_{50} (nM)	EC_{90} (nM)
HBV DNA	5	28
HBeAg	47	205
HBsAg	43	186
pgRNA	27	174



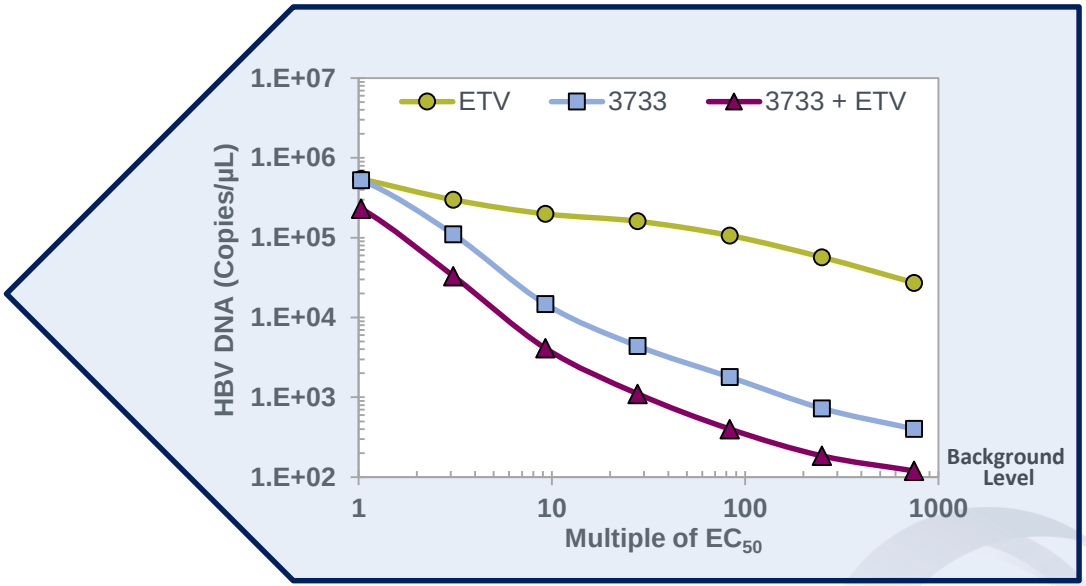
HBV Infection of Primary Human Hepatocytes (PHH)		
Marker	EC_{50} (nM)	EC_{90} (nM)
HBV DNA	12	35
HBeAg	62	157
HBsAg	77	181
pgRNA	80	176



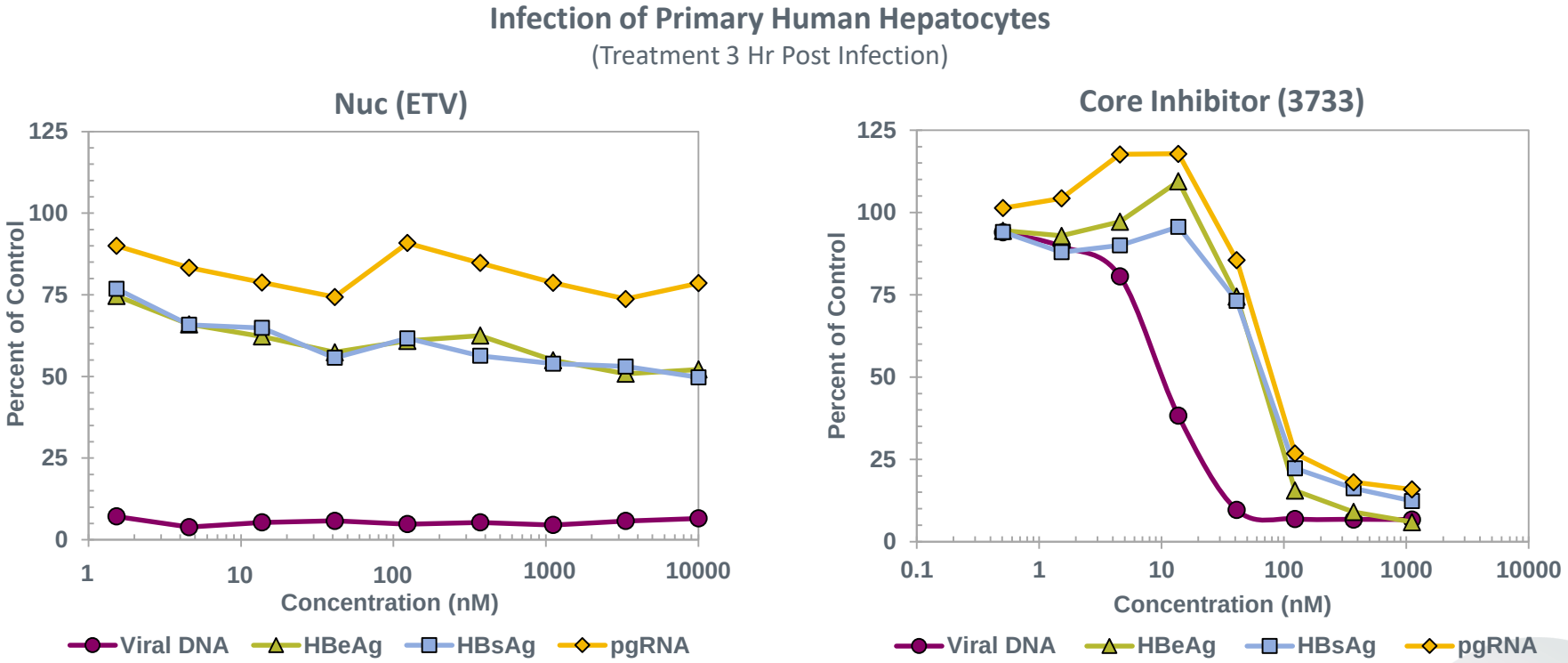
ABI-H3733 - Superior Antiviral Effectiveness vs. ETV



Core Inhibitors reduce virus levels deeper than Nucs



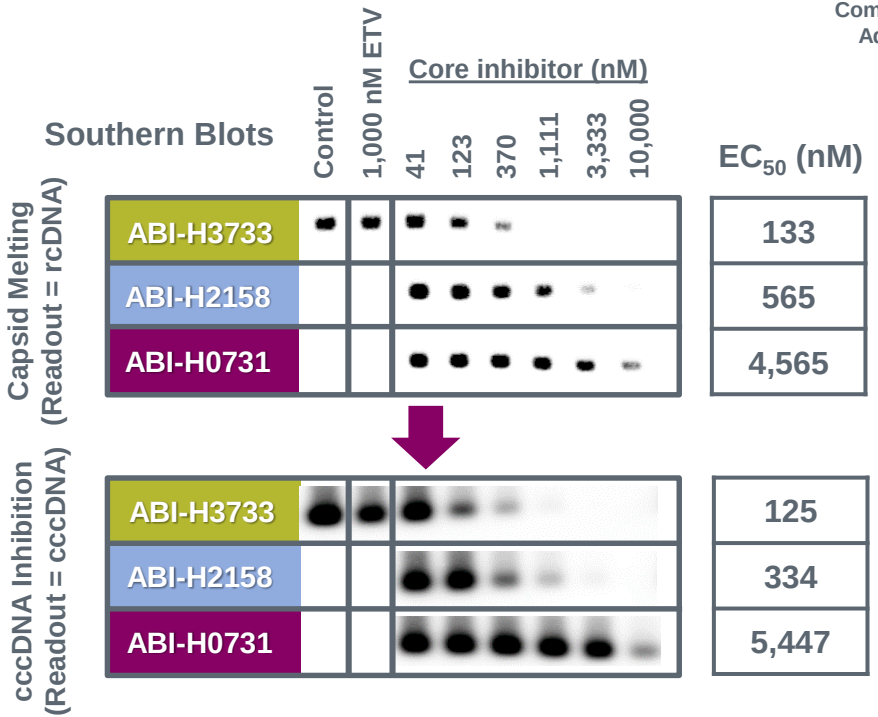
ABI-H3733 Inhibits Surrogate Markers of cccDNA



Relative Potency in Blocking cccDNA Generation

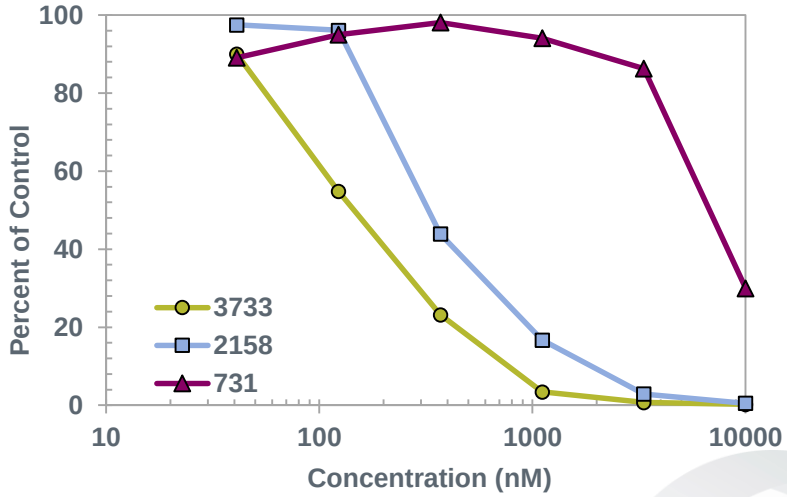
HBV Infection of HepG2-NTCP Cells

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

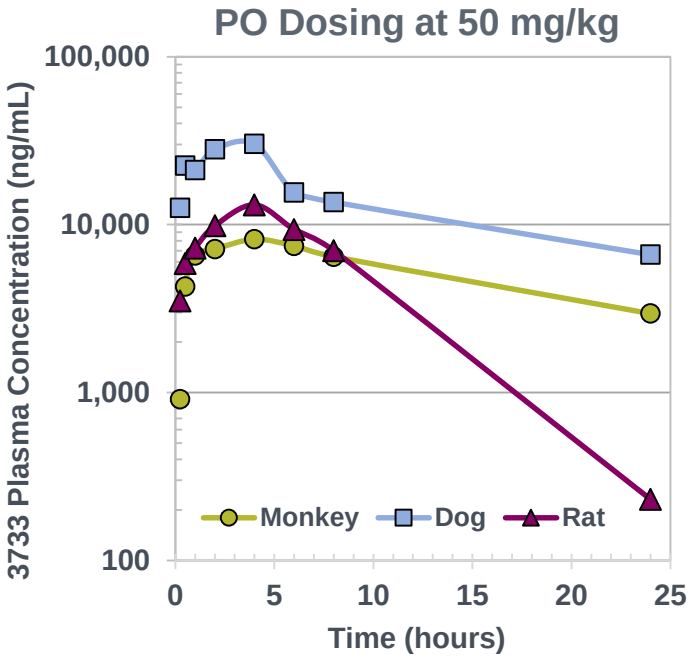


Favorable Drug-Like Properties and Preclinical Profile

- Kinetic solubility: 30 µM at pH 7.4, >100 µM at pH 1.6
- Protein binding: 95%, 3-4 fold potency shift in presence of 40% HPL
- Human liver microsome stability: 93%, no loss of potency in PHH assay
- Low DDI potential: CYP panel and P-gp inhibition (IC_{50} >10 µM)
- Safety Profile: Ames neg, hERG IC_{50} >30 µM
  - GLP toxicology studies to be initiated

HPL = Human Platelet Lysate; DDI = drug-drug interactions

ABI-H3733 Cross-Species Pharmacokinetics



PK Plasma Parameters

Species	Half-life (hr)	C_{max} (ng/mL)	$AUC_{0\text{-}inf}$ (ng*hr/mL)	Bioavailablity (%)
Rat	3.3	13,100	108,000	>100
Monkey	12	8,840	176,000	77
Dog	12	30,200	440,000	>100

- Good bioavailability and exposure levels across species
- Favorable liver levels (liver/plasma ratios ~7)
- Half-life predictive of QD dosing in humans

ASMB Core Inhibitor Program Summary

- Core inhibitors will likely be the backbone of future HBV regimens
  - Highly effective antivirals that disrupt viral replication at multiple steps
  - Potential to eliminate residual viremia (deficiency of Nuc therapy)
  - Inhibit the generation of new cccDNA
- Portfolio of CIs identified from distinct chemical series that possess increasing superior potency levels, especially for inhibition of new cccDNA generation
- All three ASMB inhibitors, including ABI-H3733, being developed to understand impact of greater potency and the potential to enhance clinical efficacy and shorten treatment timelines
- ABI-H3733 Phase 1a studies are anticipated to initiate early next year

Thank You!