Targeting HBV Core Protein to Clear Infection and Achieve Higher Cure Rates

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5TH INTERNATIONAL WORKSHOP ON

HBV CURE

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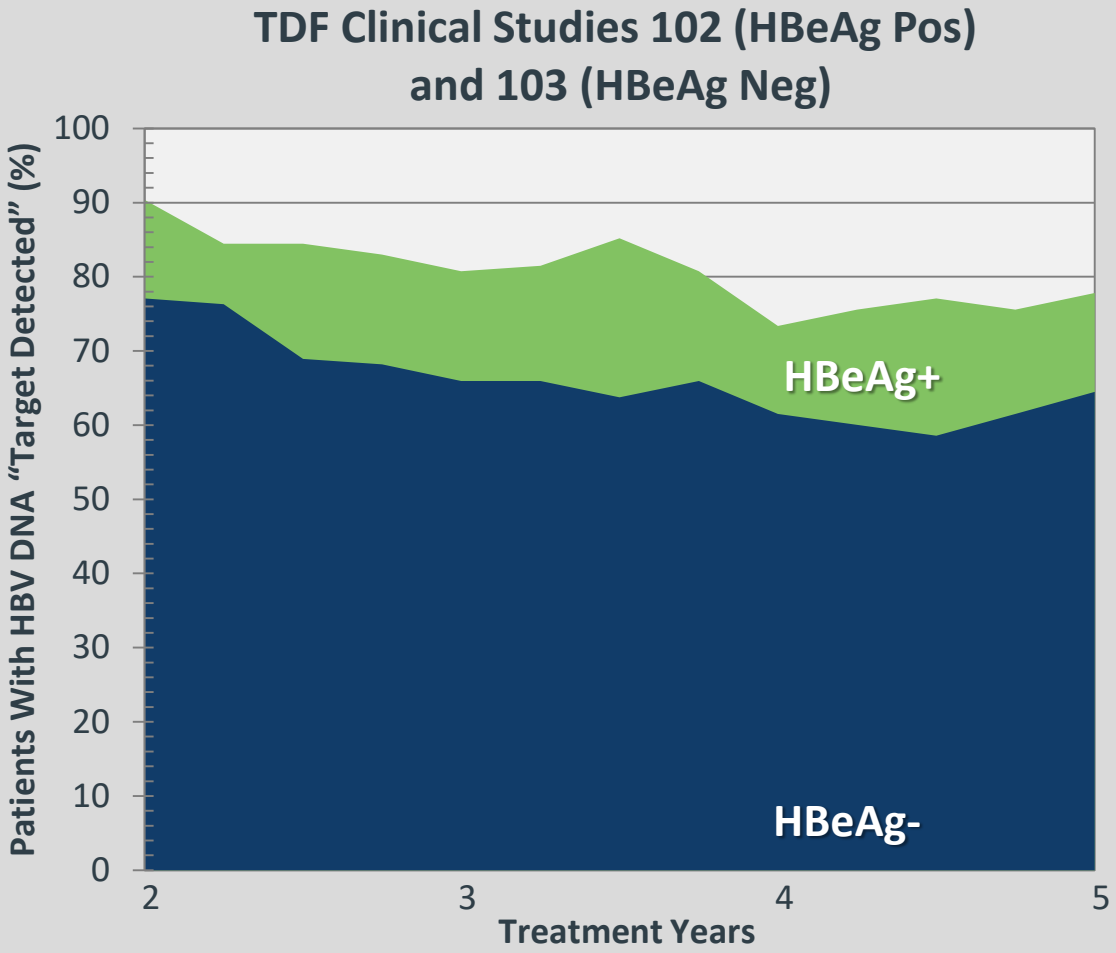
assembly biosciences

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

The information in this presentation contains estimates and other forward-looking statements regarding future events, including statements about the clinical and therapeutic potential of core inhibitors, including ABI-H0731, ABI-H2158 and ABI-H3733, Assembly's development programs, the initiation, progress and results of Assembly's ongoing and planned clinical and nonclinical studies and the timing of these events. Certain forward-looking statements may be identified by reference to a future period or periods or by use of forward-looking terminology such as "designed," "forecast," "believe," "planned," "initiate," "potential," "anticipated," or "expected." Such forward-looking statements, which we intend 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 nonclinical testing and clinical trials are uncertain; results of earlier nonclinical studies and clinical trials may not be predictive of future clinical trial results; the components, timing, patient enrollment and completion rates, cost and results of clinical trials and other development activities involving our product candidates; and our estimates regarding our capital requirements, and our need for future capital. 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 our Annual Report on Form 10-K for the year ended December 31, 2017 and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2018, each 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 we 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 we may make. 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.

NUCS FAIL TO FULLY SUPPRESS VIRAL REPLICATION



- Reductions in HBsAg alone are insufficient, as the immune system fails to eliminate low-level persistent infection
- Numerous long-term Nuc-treated patients with low HBsAg levels continue to have detectable HBV DNA and fail to seroconvert

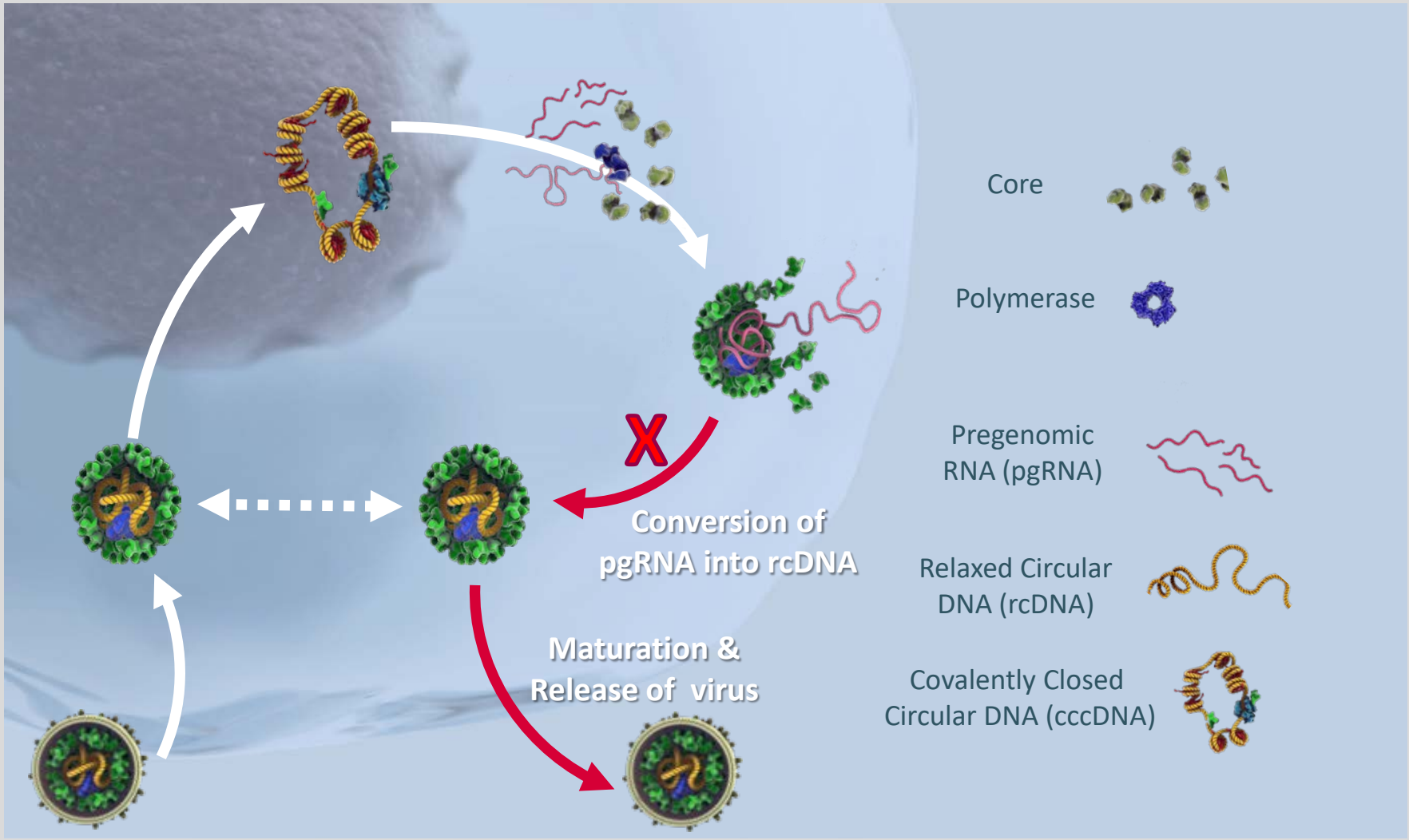
HBeAg Pos. Patient	Treatment	Treatment Years	HBsAg IU/mL	HBV DNA (copy/mL)
003	ADV/LVD	5	**6.6**	**1,530**
016	LVD/ADV/IFN	13	**3.8**	**1,040**
019	LVD/ADV/ETV/TDF	6.5	**4.7**	**1,840**
024	IFN	1	**0.6**	**188**

- **Cure is not possible if viral infection persists**

ADV = adefovir dipivoxil; IFN = interferon; LVD = lamivudine; TDF = tenofovir disoproxil fumarate.

1. Marcellin P, et al. AASLD Poster 1861 (2014). 2. Huang, Q, et al. collaborative study in progress.(2018).

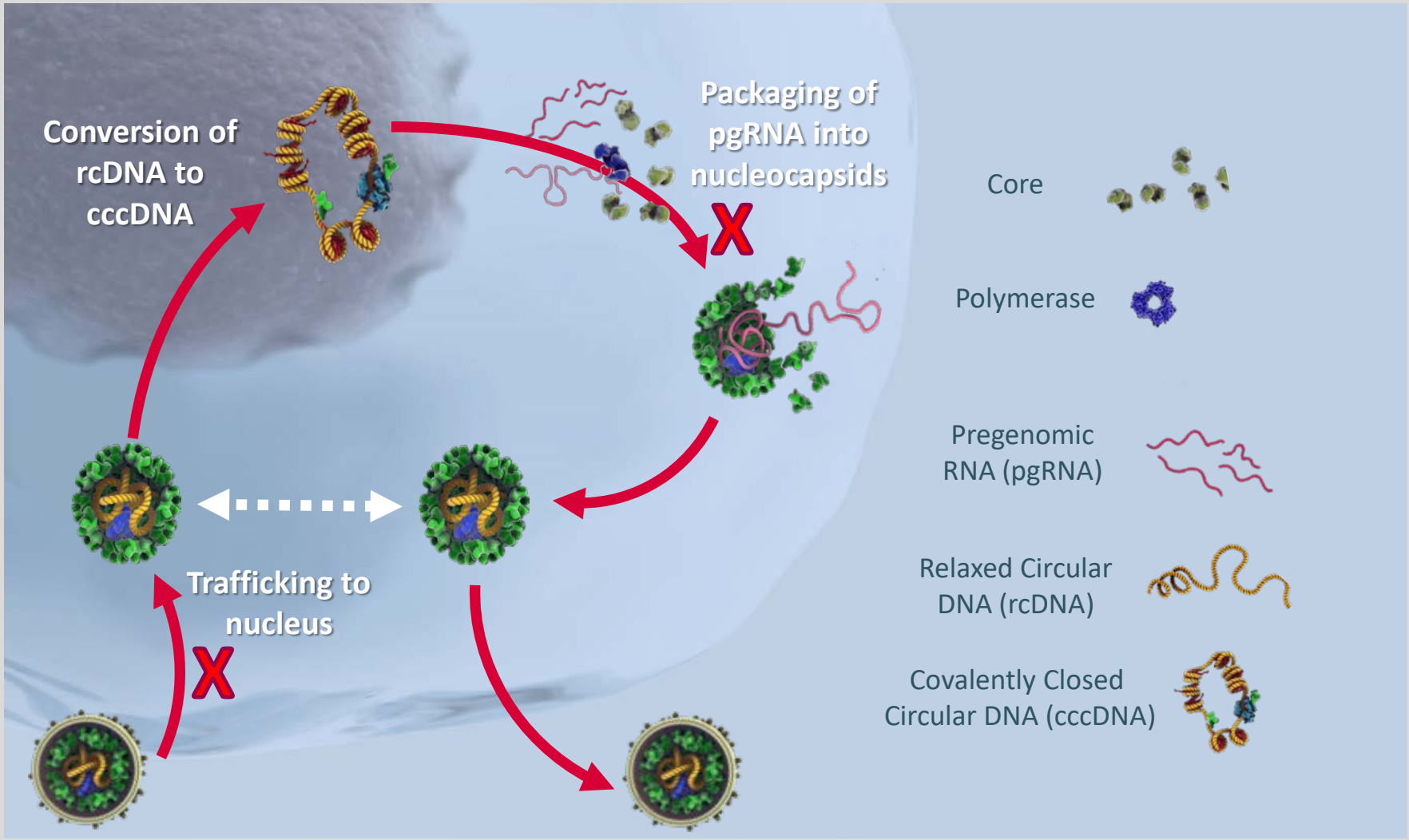
NUCS REDUCE VIRUS LEVELS BUT FAIL TO PREVENT cccDNA ESTABLISHMENT



Polymerase Inhibitors

- Prevent conversion of pgRNA to rcDNA
- Fail to eliminate 100% of virus
- No effect on incoming virus or generation of cccDNA
- Minimal effect on cccDNA pools

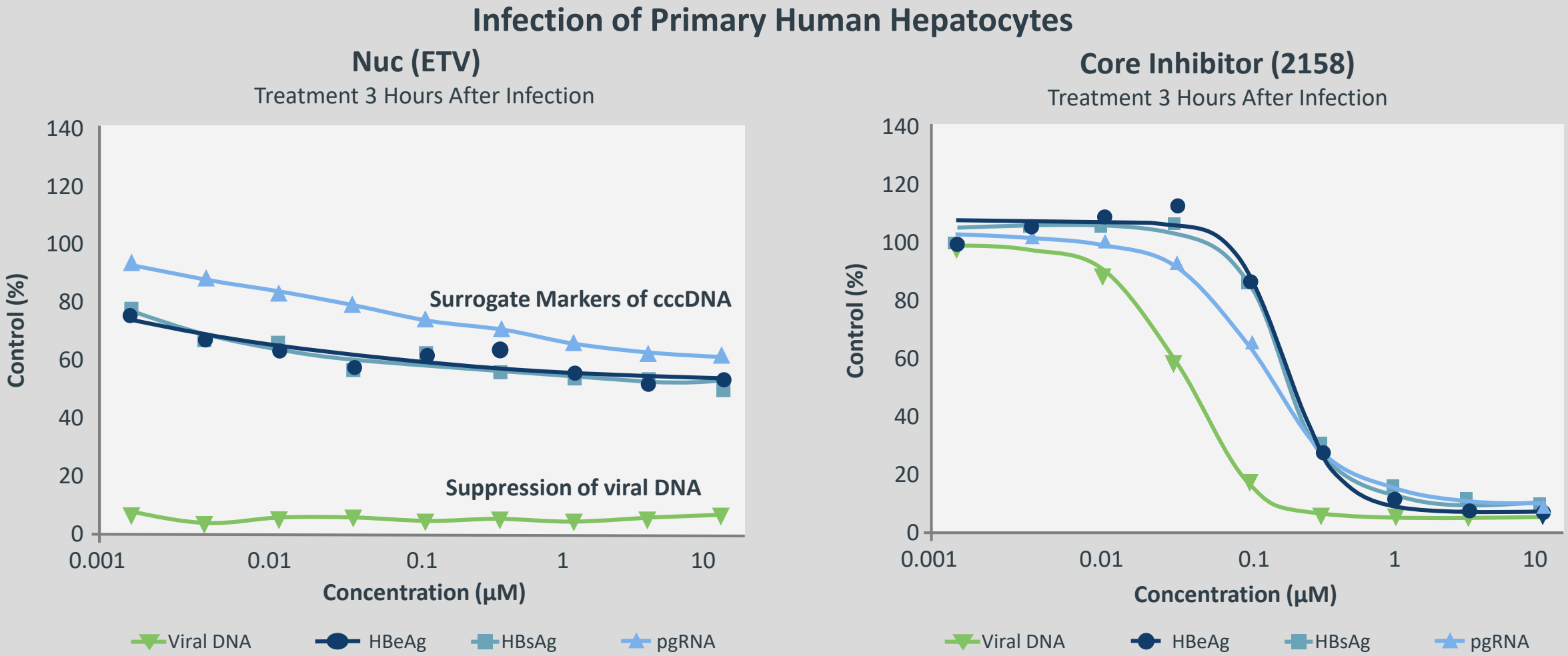
CORE INHIBITORS BLOCK VIRAL REPLICATION AND cccDNA ESTABLISHMENT



Core Inhibitors

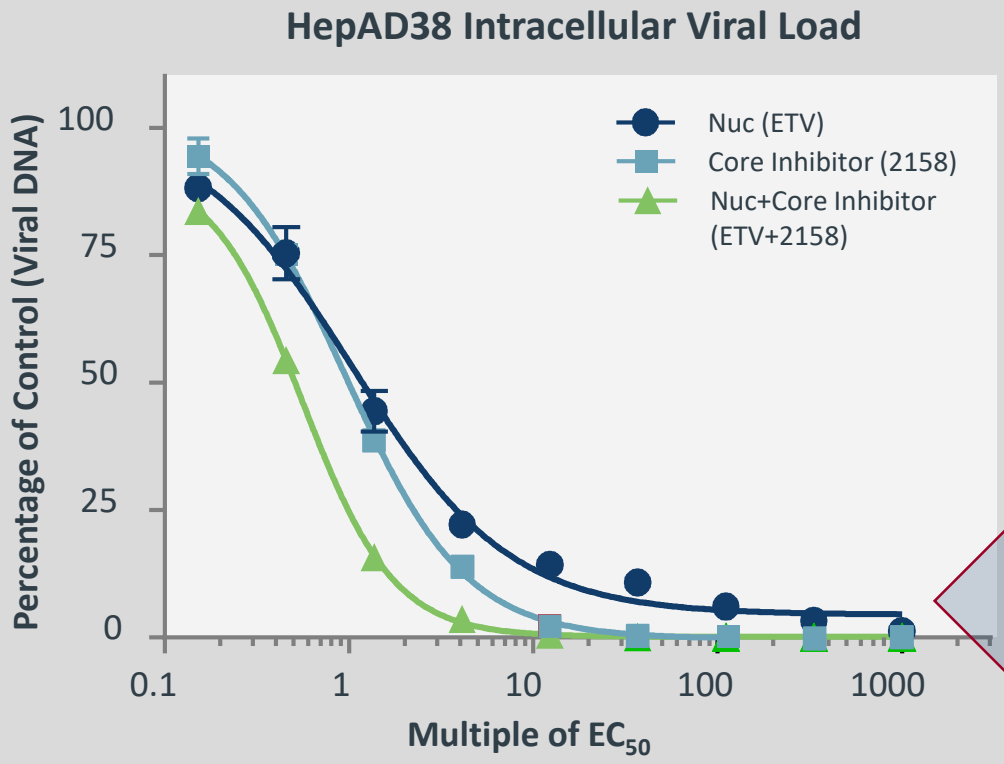
- Inhibit both production of new virus and trafficking of incoming nucleocapsid to nucleus
- Unlike Nucs, block establishment of cccDNA
- Potential to be synergistic with Nuc polymerase inhibition

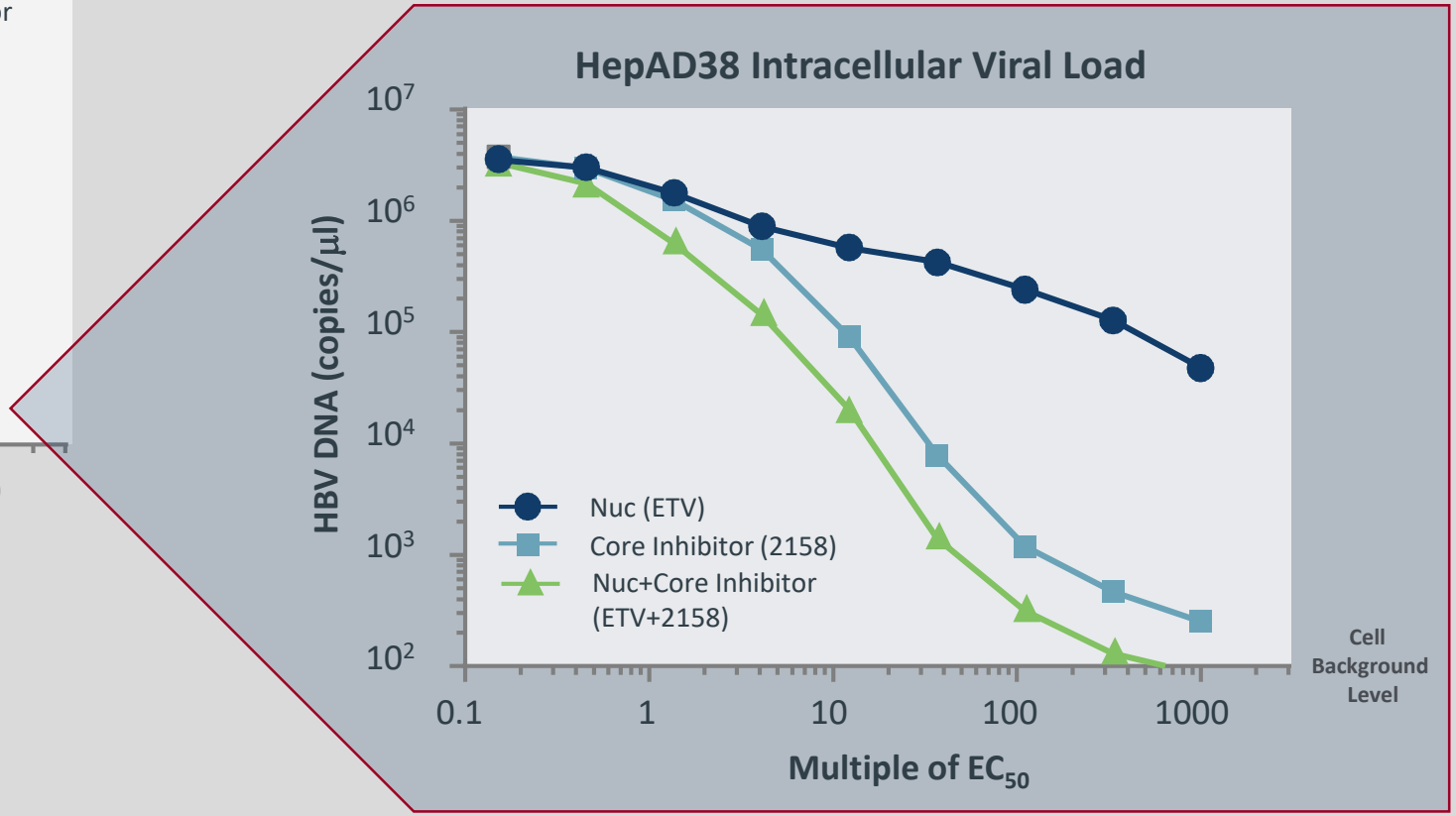
CORE INHIBITORS REDUCE KEY SURROGATE MARKERS FOR cccDNA



Huang Q, et al. AASLD Poster 922 2017.

BOTTOM LINE…CORE INHIBITORS ARE MORE EFFECTIVE ANTIVIRALS

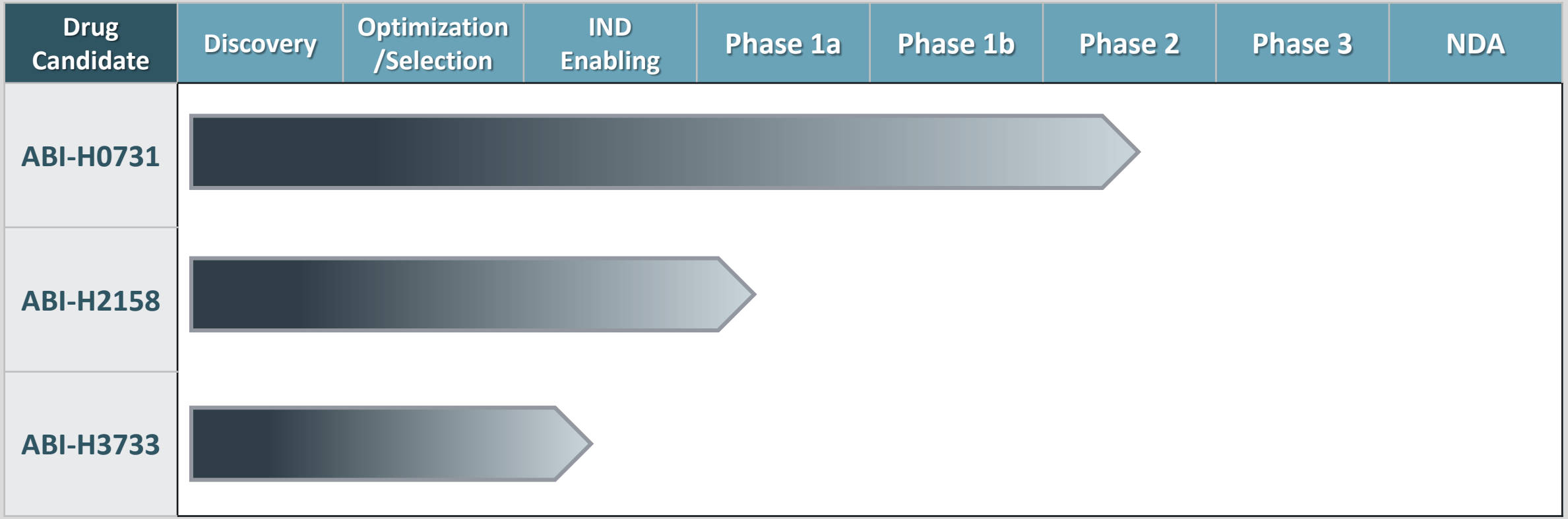




EC_{50} = Effective Concentration yielding a 50% reduction in activity.

ASMB HBV CORE INHIBITOR PROGRAM PORTFOLIO

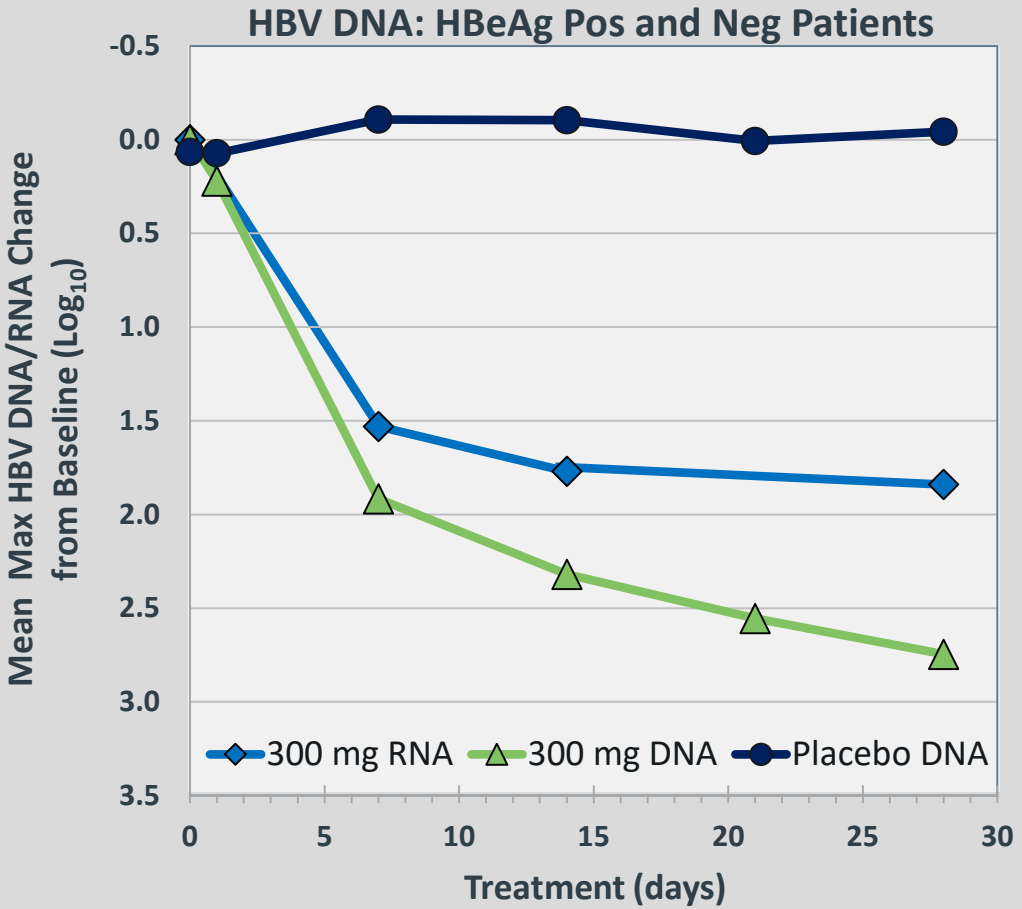
Novel Molecules With Distinct Chemical Scaffolds Discovered at Assembly Biosciences



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

ABI-H0731 REDUCTIONS IN HBV DNA & RNA LEVELS

- Dose response, and near-equivalent maximum reductions of up to 4 logs for top two doses tested (300 and 400 mg)
- The 300 mg dose in combination with Nuc therapy chosen for ongoing Phase 2 studies



300 mg QD	Change from Baseline			
Patients	HBeAg Pos		HBeAg Neg	
Marker	N	Mean (Range)	N	Mean (Range)
Log_{10} DNA (IU/mL)	6	2.9 (1.8 - 3.9)	4	2.5* (0.8 - 4.1)
Log_{10} RNA (copies/µL)	6	2.0 (1.7 – 2.6)	1	1.3

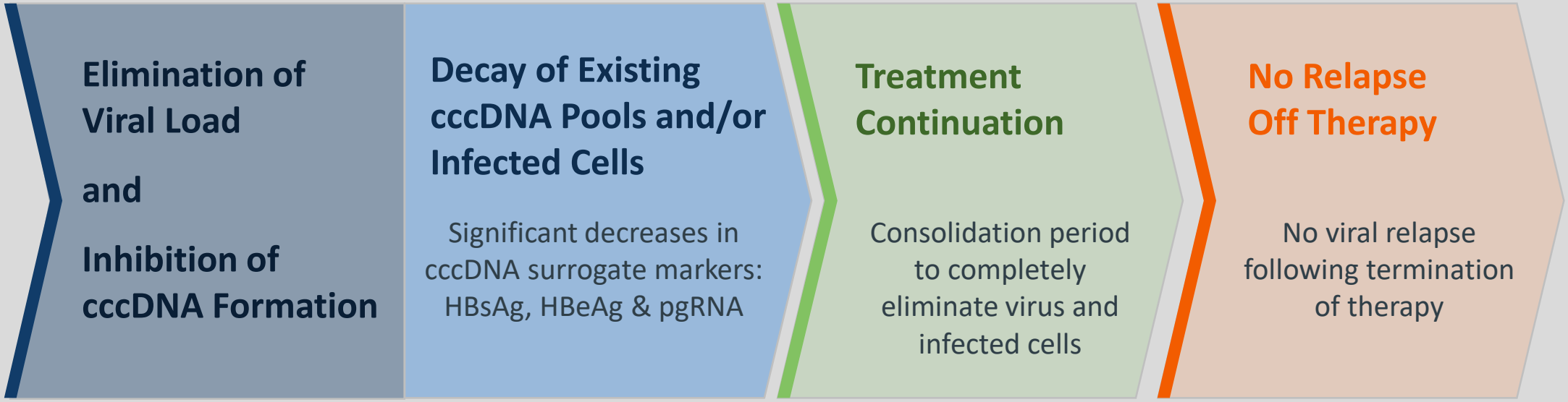
*Excludes HBeAg patient with Baseline resistance

- **Mechanism-based reduction in viral RNA levels by Core inhibitors is a differentiating feature vs. Nuc-based therapy**

Yuen, MF, et al. AASLD 2018.

HBV CURE: CLINICAL COMPONENTS

Expected Treatment Components to Achieve Cure



PHASE 2A STUDY STRATEGY AND DESIGNS

Elimination of Viral Load → **Decay of cccDNA/ Infected Cells** → Treatment Consolidation → No Relapse Off Therapy

Viral Load Study 202

Patient population: Nuc-naive, HBeAg pos

- 0.5 mg ETV + 300 mg ABI-H0731
- 0.5 mg ETV + Placebo

Goal: Demonstrate significant improvement in speed and depth of viral load reduction

Viral Antigen POC Study 201

Patient population: nuc-suppressed, HBeAg pos, HBeAg neg (under amendment)

- Continued Nuc + 300 mg ABI-H0731
- Continued Nuc + Placebo

Goal: Demonstrate significant decreases in cccDNA surrogate markers

0 — Time (months) — 6

Initial Data Expected

H1 2019

HBeAg = hepatitis B e antigen; POC = proof of concept.

COMBO THERAPY POTENTIALLY DRIVES SUSTAINED SUPPRESSION

Elimination of Viral Load → Decay of cccDNA/ Infected Cells → **Treatment Consolidation** → **No Relapse Off Therapy**

Goal: Demonstrate significant decreases in cccDNA surrogate markers (HBsAg and HBeAg)

Nuc-Suppressed
45 HBeAg Pos
25 HBeAg Neg

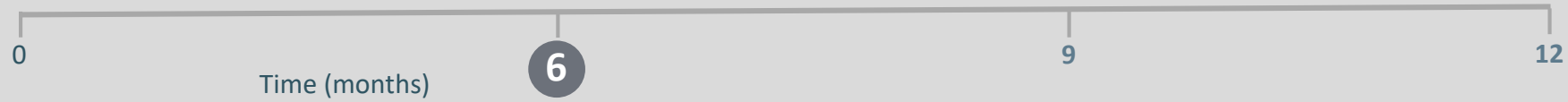
Nuc-Naive Patients
24 HBeAg Pos

SOC Nuc + Placebo vs. SOC Nuc + 300 mg 731

SOC ETV + Placebo vs. SOC ETV + 300 mg 731

Open-label Extension Study 211
SOC Nuc + 300 mg 731

"Proof of Concept"



SOC = standard of care.

PORTFOLIO OF POTENT CORE INHIBITORS

Parameters	ABI-H2158	ABI-H3733
AD38 VL EC_{50} (nM)	22	5
HC9AT HBeAg EC_{50} (nM)	400	43
PHH VL EC_{50} (nM)	23	12
PHH HBeAg EC_{50} (nM)	170	61

- ASMB Core Inhibitors ABI-H0731, ABI-H2158 and ABI-H3733 represent **distinct and proprietary chemical scaffolds**, exhibit balance of potency AND favorable drug-like properties

HepG2-NTCP cccDNA Generation (Southern Blot)

	ABI-H2158	ABI-H3733
EC_{50}	334	125

ASMB CORE INHIBITOR PROGRAM SUMMARY

To Cure (sustained suppression off therapy): Must eliminate residual virus and cccDNA

Core Inhibitors: Highly effective antivirals designed to disrupt viral replication at multiple steps AND inhibit the generation of new cccDNA

ABI-H0731
First Candidate

- Favorable safety and PK profile enabling QD dosing
- Potent antiviral efficacy in Phase 1b 28-Day efficacy study in HBV patients
- 300 mg dose selected for ongoing POC Phase 2a studies
- Results to be reported 1H19

ABI-H2158 & ABI-H3733
Second & Third Candidates

- Enhanced potency, while retaining favorable drug-like properties
- Potent inhibition of cccDNA generation in cell culture assays
- **ABI-H2158** Phase 1 study initiated
- **ABI-H3733** IND-enabling studies underway

Future combinations regimens of core inhibitors and Nucs may result in

More rapid and deeper reduction in viral levels (eradication)

Depletion of cccDNA levels

INCREASED CURE RATES

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Assembly Biosciences Virology Team

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