

# Corporate Overview

January 2019



assembly  
biosciences

# CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

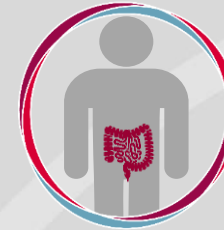
The information in this presentation contains estimates and other forward-looking statements regarding future events, including statements about the clinical and therapeutic potential of our HBV-cure program, the timing of the initiation of and availability of data from our ongoing and planned clinical trials in our HBV-cure and Microbiome program, and the plans, strategies, milestones, and intentions related to our HBV-cure and Microbiome programs. 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,” “believe,” “initiate,” “potential,” 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; the duration and results of regulatory review of those 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, intellectual property rights and the costs of obtaining such rights from third parties. 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. This presentation also contains estimates and other statistical data made by independent parties and by us relating to market potential. These estimates involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. 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 or estimate speaks only as of the date on which it is made, and we assume no obligation to update or revise any forward-looking statement or estimate, whether as a result of new information, future events or otherwise, except as required by law.

# ASSEMBLY BIOSCIENCES OVERVIEW

## HBV Cure



## Microbiome



Unmet Patient Need

No cure for almost all of the **>250 million patients** with chronic HBV

The gut microbiome is **essential** to human health, yet there are **no approved** microbiome therapies










Innovation

Core inhibitors designed to **break the life cycle** of HBV

**Targeted delivery of oral, synthetic, live bio-therapeutics** designed to address the diseases associated with the gut microbiome

# DEVELOPMENT PROGRAMS FOCUSED ON LARGE PATIENT POPULATIONS WITH HIGH UNMET NEED

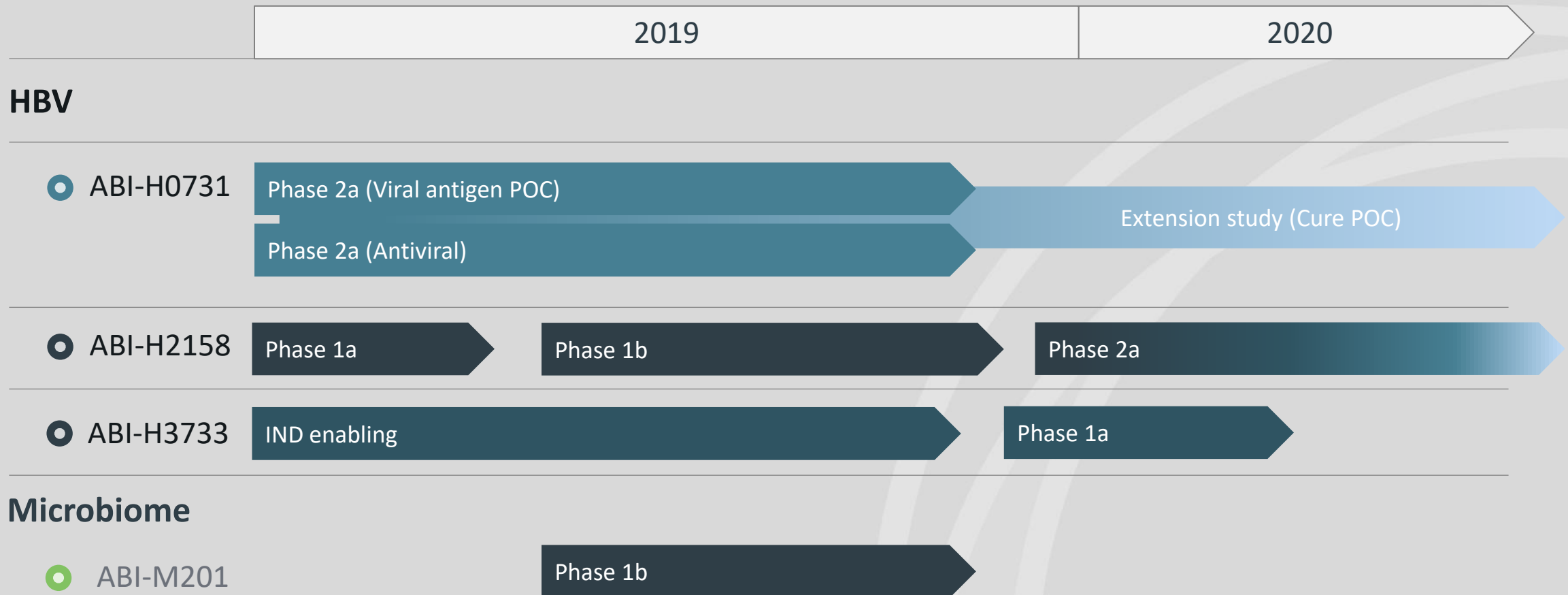
Drug Candidate (Mechanism/Indication)	Discovery & Lead Op/Selection	IND Enabling	Phase 1a	Phase 1b	Phase 2	Phase 3	NDA/BLA	Worldwide Rights
HBV Cure								
ABI-H0731 (Core Inhibitor)	<div></div>							
ABI-H2158 (Core Inhibitor)	<div></div>							
ABI-H3733 (Core Inhibitor)	<div></div>							
Core Inhibitor Discovery Program	<div></div>							
Microbiome								
ABI-M201 (Ulcerative Colitis)	<div></div>							
ABI-M301 (Crohn’s Disease)	<div></div>							
Irritable Bowel Syndrome	<div></div>							
NASH	<div></div>							
Immuno-oncology	<div></div>							

# ASMB: SIGNIFICANT PROGRESS IN 2018

- **Initiated two global Phase 2a clinical trials for ABI-H0731**
  - Fast Track Designation, “Best of AASLD 2019” selection
  - Enrollment completed
- **Expansion of HBV Portfolio:**
  - ABI-H2158: Ongoing Phase 1a study in healthy volunteers; Phase 1a and 1b expected to initiate in 2019
  - ABI-H3733: Selected as third core inhibitor candidate; IND Expected in 2019
- **FDA recently issued new draft guidance for chronic HBV<sup>1</sup>: Clarifies approval pathways**
- **Core inhibitor composition of matter patent allowed by USPTO**
  - 14 patent applications pending in the US and over 100 filings in other major geographies with anticipated patent terms through 2034-2039
- **Advanced first microbiome program toward clinical development & expanding pipeline**
- **Strengthened balance sheet: >\$230M in cash**

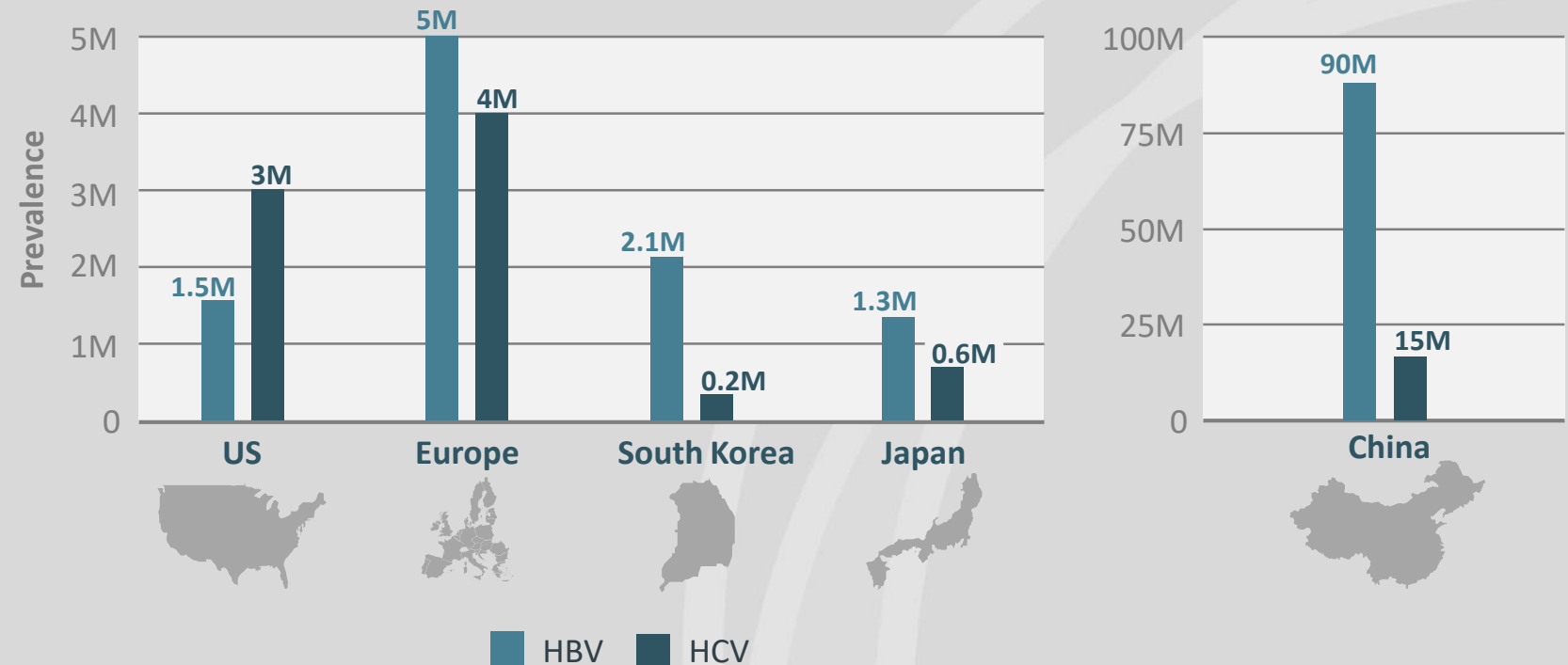
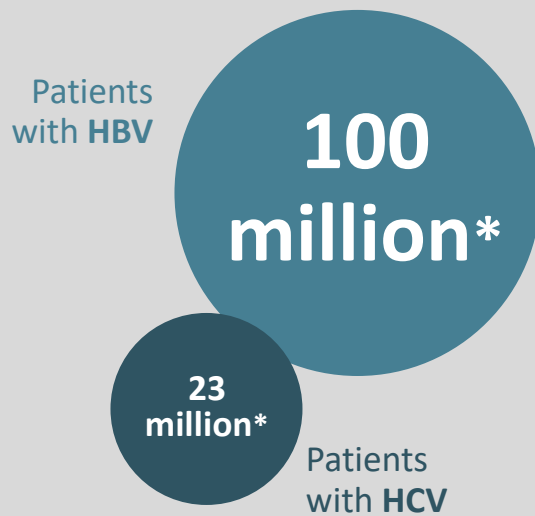
1. <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM624695.pdf>

# UPCOMING MILESTONES



# MORE HBV PATIENTS THAN HCV PATIENTS IN THE MAJOR GEOGRAPHIES

More total Hepatitis B patients in top 4 major geographies than Hepatitis C patients; this is not including China, which has an even higher incidence of HBV



# ASSEMBLY CHINA ESTABLISHED TO DEVELOP PROGRAMS IN CHINA

HBV is a **public health epidemic in China** – the government has made HBV one of their highest public health priorities



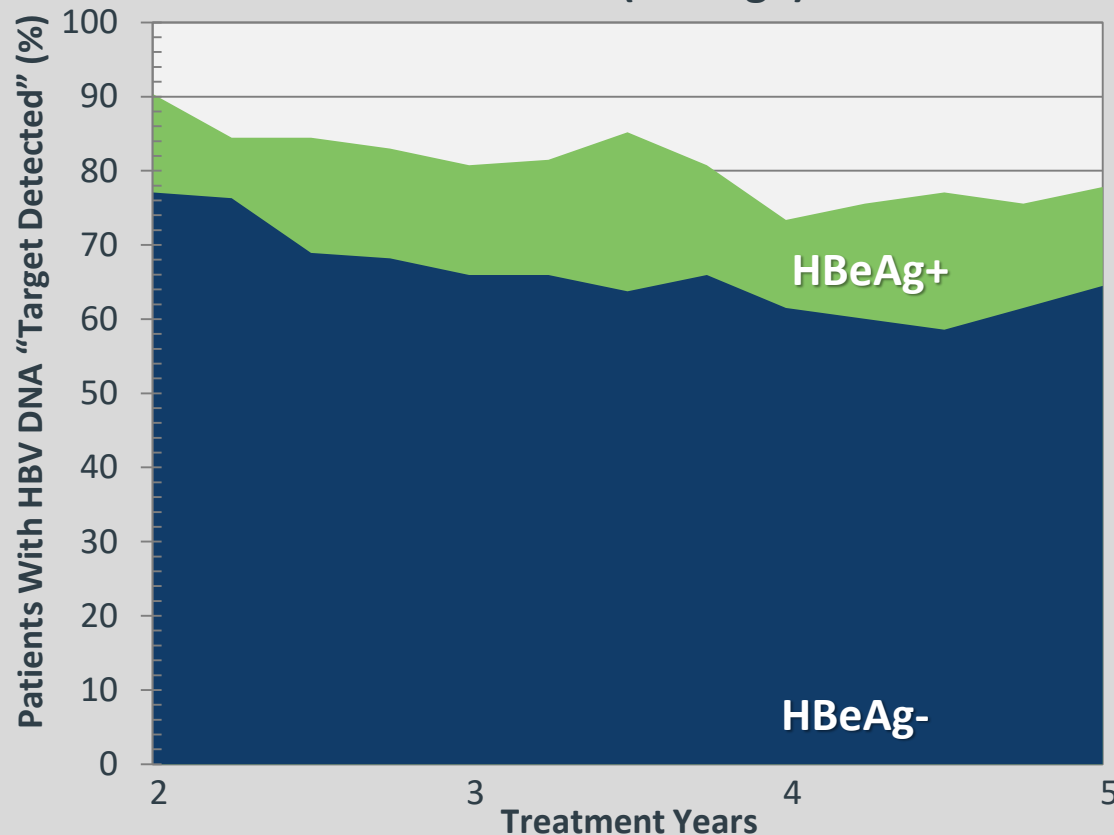
- China has made significant advances in regulatory, IP and business policies over the last few years
- Assembly China efforts began in 2015
  - ASMB China headquarters in Shanghai (Zhangjiang Hi-Tech Park)
  - Established a regulatory office in Beijing
- Currently establishing a dedicated team to develop our programs as a domestic Chinese entity



# VIRUS NOT FULLY SUPPRESSED IN PATIENTS ON NUCs

# NUCs FAIL TO FULLY SUPPRESS VIRAL REPLICATION

TDF Clinical Studies 102 (HBeAg-) and 103 (HBeAg+)



- Reductions in HBsAg alone is 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**

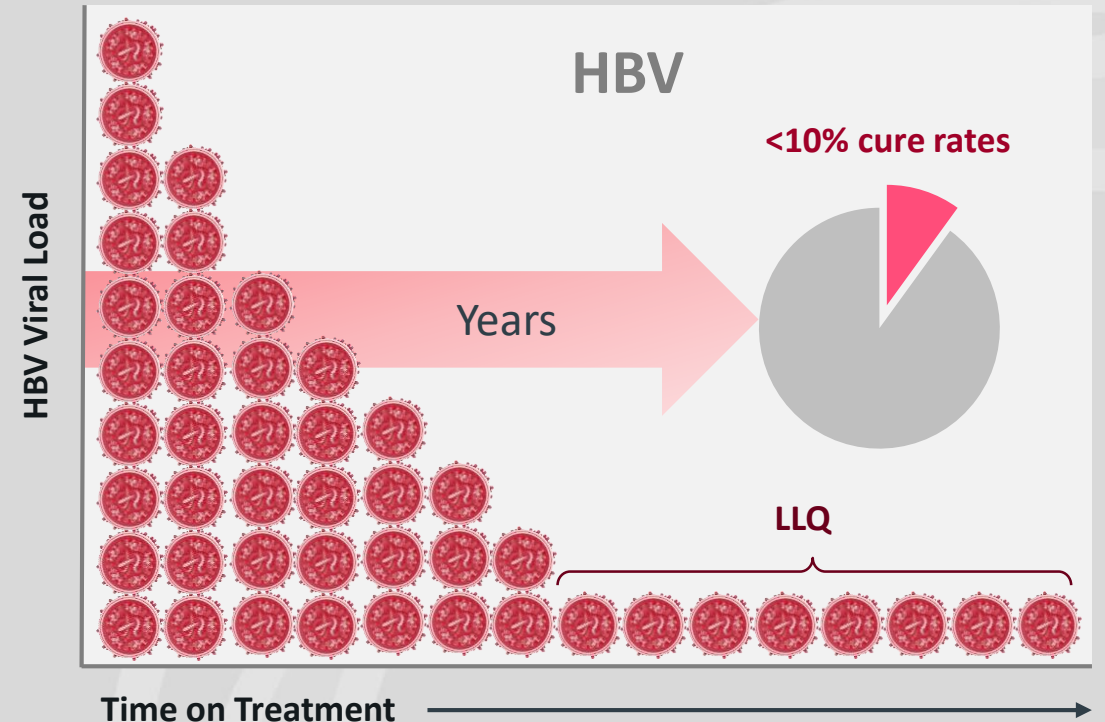
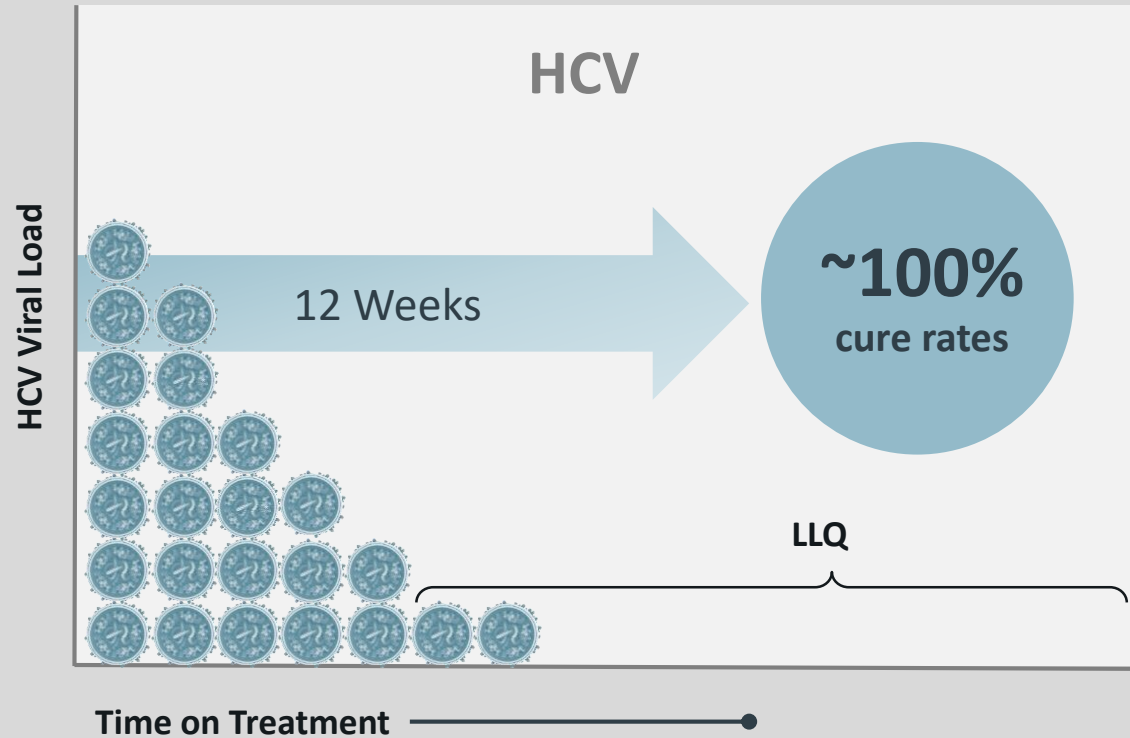
HBeAg Pos. Patient	Treatment	Treatment Years	HBsAg IU/mL	HBV DNA (copy/mL)
003	ADV/LVD	5	6.6	1,530
016	LVD/ADV/IFN	13	3.8	1,040
019	LVD/ADV/ETV/TDF	6.5	4.7	1,840
024	IFN	1	0.6	188

- **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.

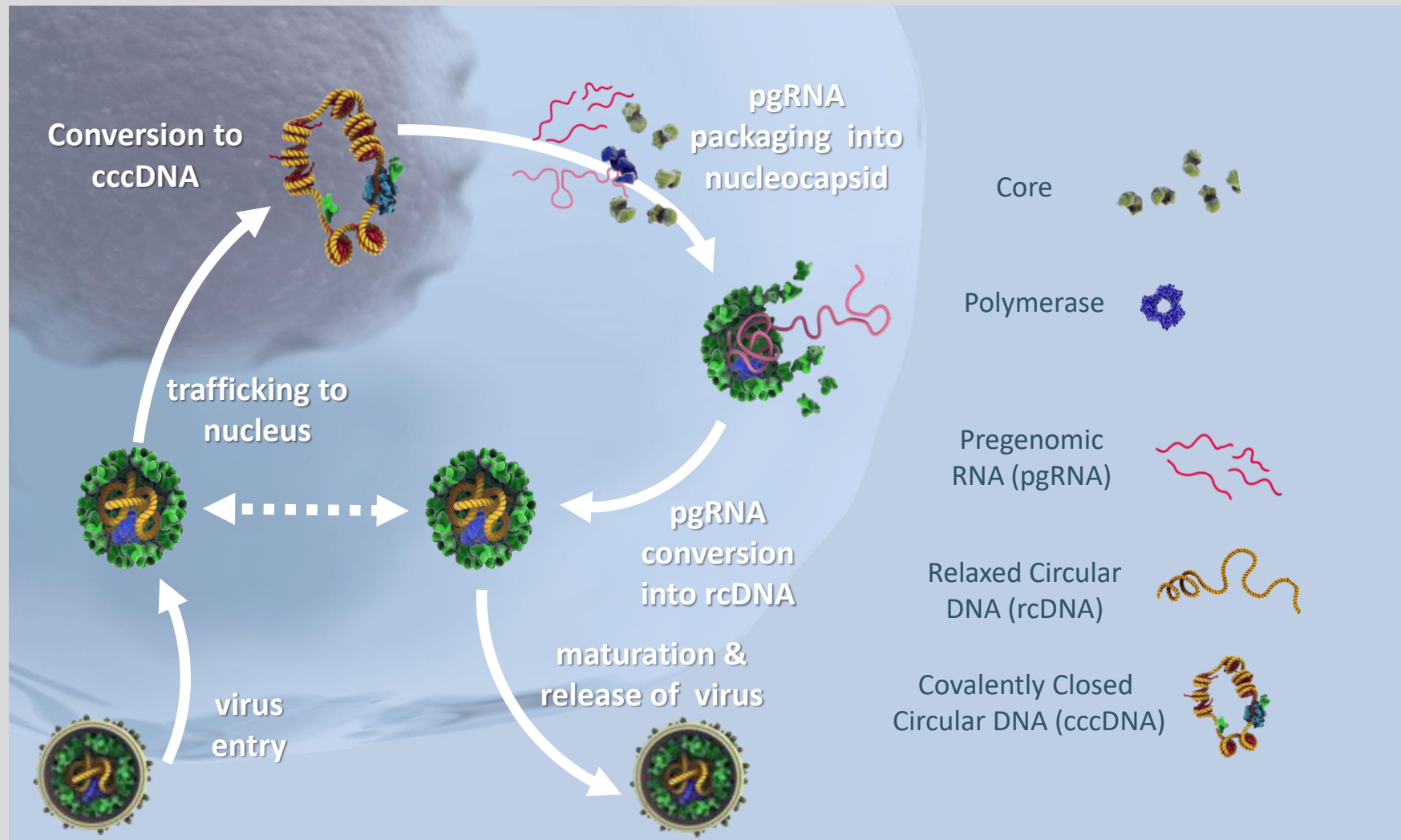
# LACK OF FULL VIRAL SUPPRESSION MAY BE REASON FOR LOW HBV CURE RATES



To improve cure rates...must eliminate residual virus

# HOW CAN THERAPY BE IMPROVED?

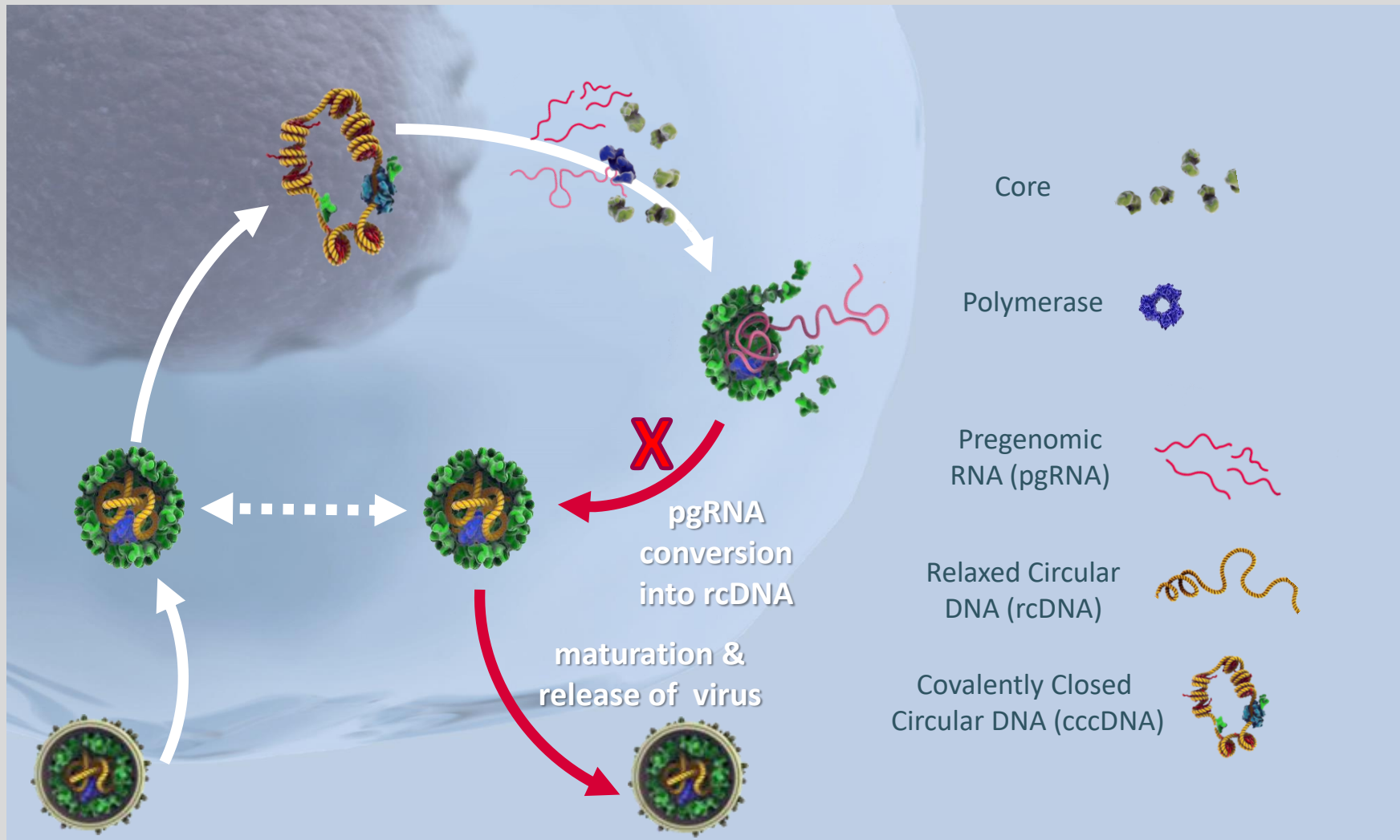
# CRITICAL ELEMENTS OF HBV LIFE CYCLE



## Core and polymerase proteins play critical roles in HBV life cycle

- Trafficking of nucleocapsid to nucleus
- Establishment of cccDNA
- Packaging of pgRNA into nucleocapsids
- Conversion of pgRNA into rcDNA

# NUCS REDUCE VIRUS LEVELS BUT FAIL TO PREVENT cccDNA ESTABLISHMENT

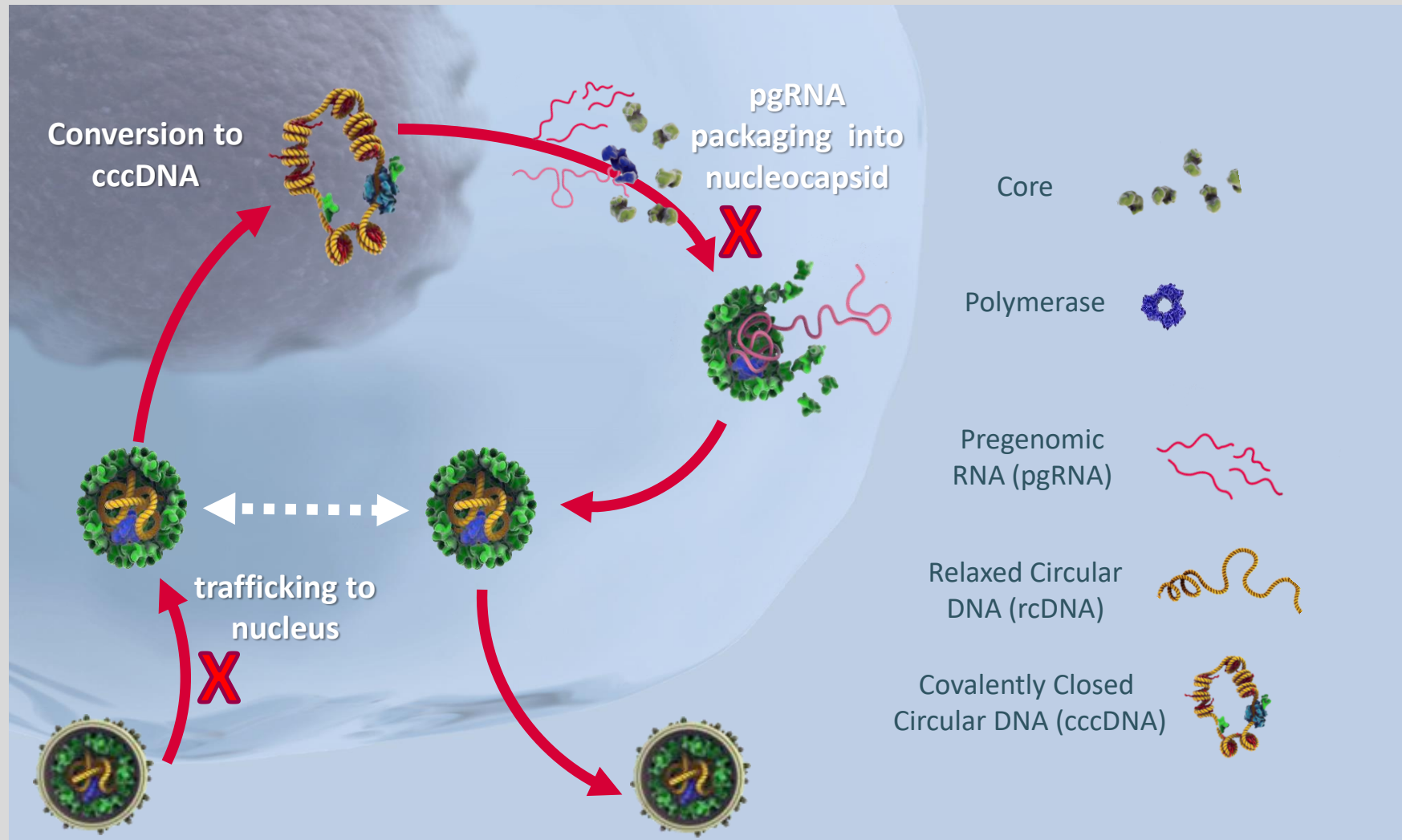


## Polymerase inhibition

- Prevents conversion of pgRNA to rcDNA
- Does not eliminate 100% of virus
- Has no effect on incoming virus
- Has a minimal effect on cccDNA pool



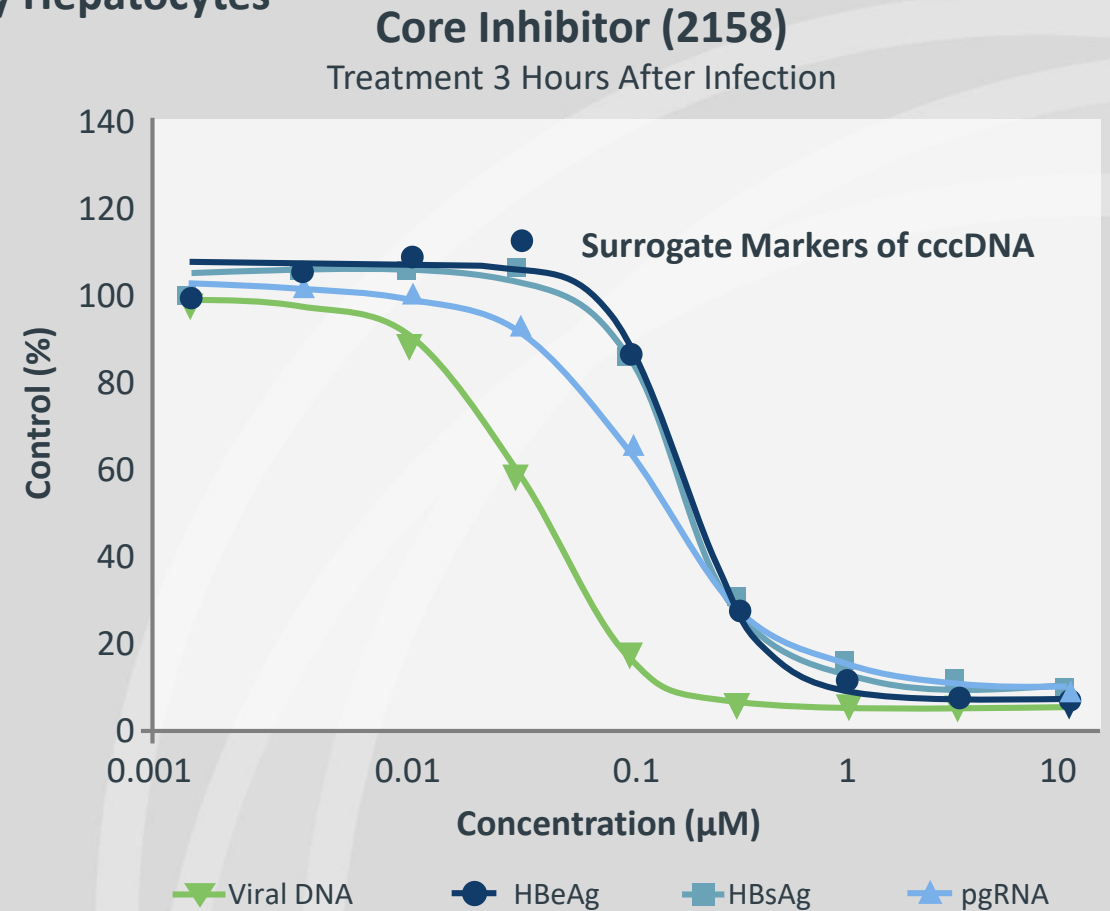
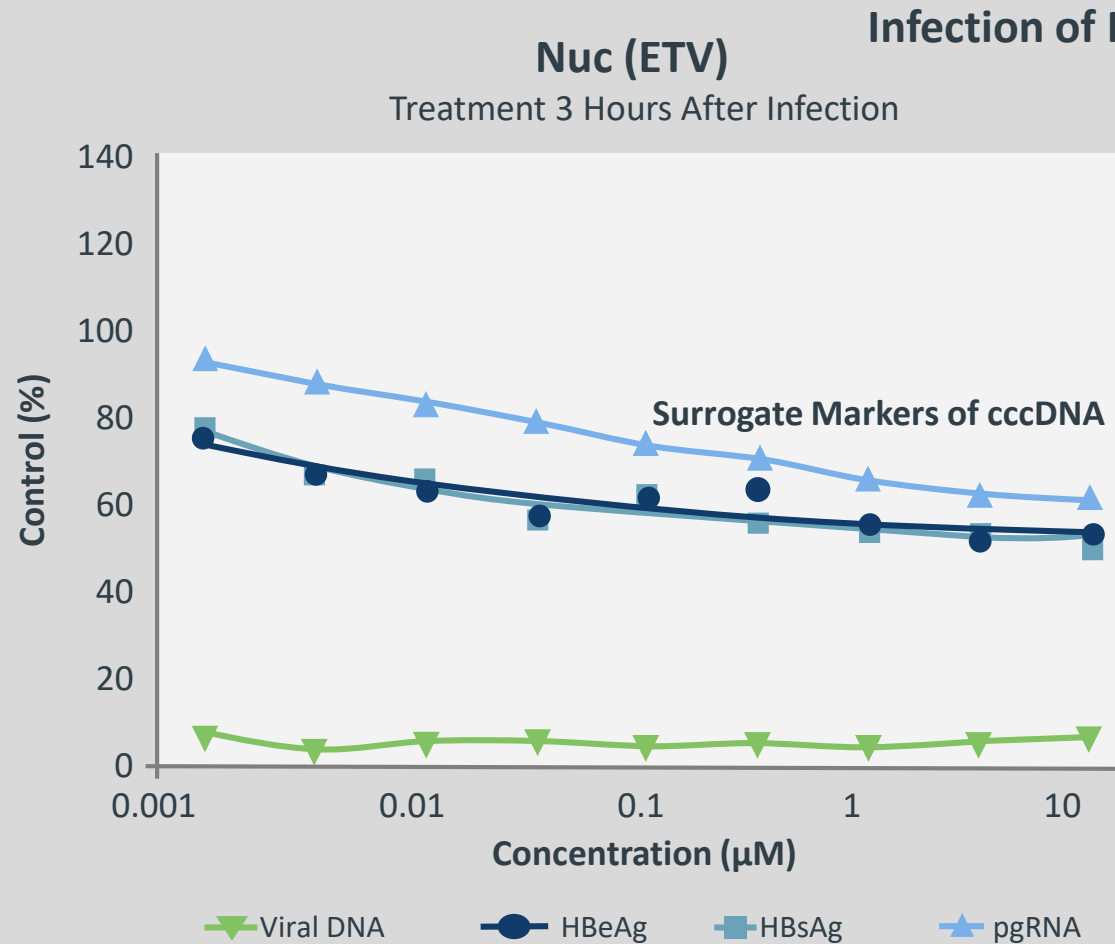
# CORE INHIBITORS ARE DESIGNED TO BLOCK VIRAL REPLICATION AND cccDNA ESTABLISHMENT



## Core inhibition

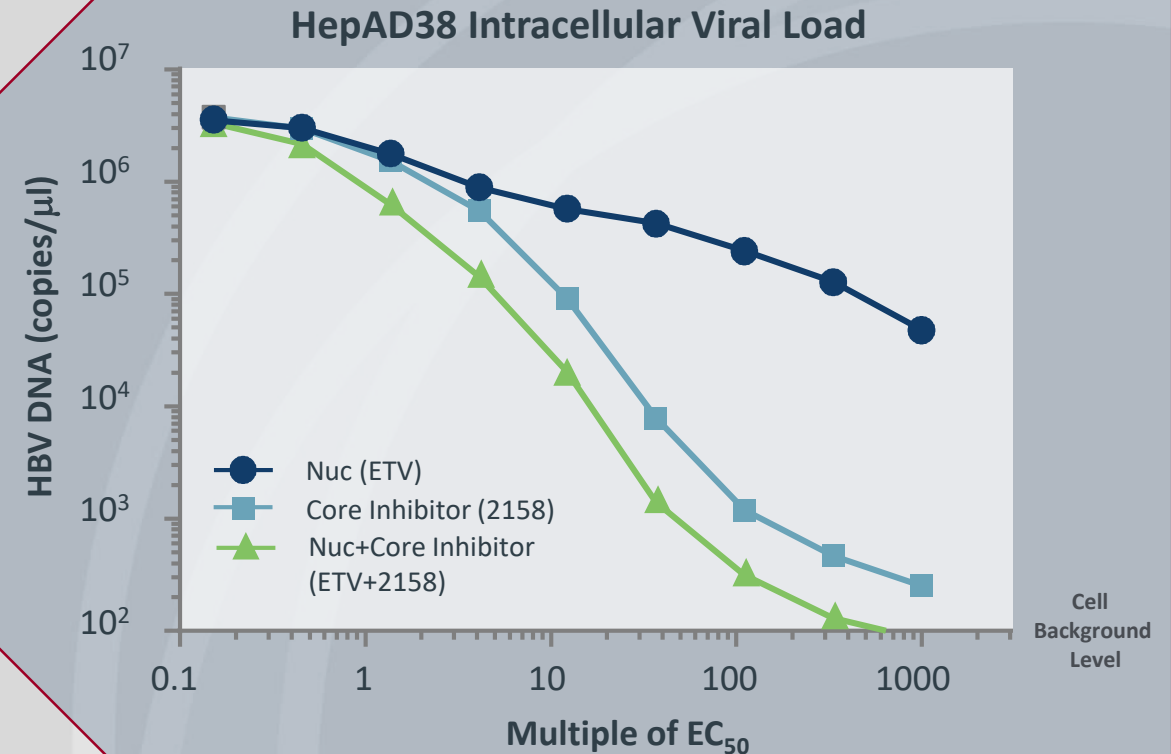
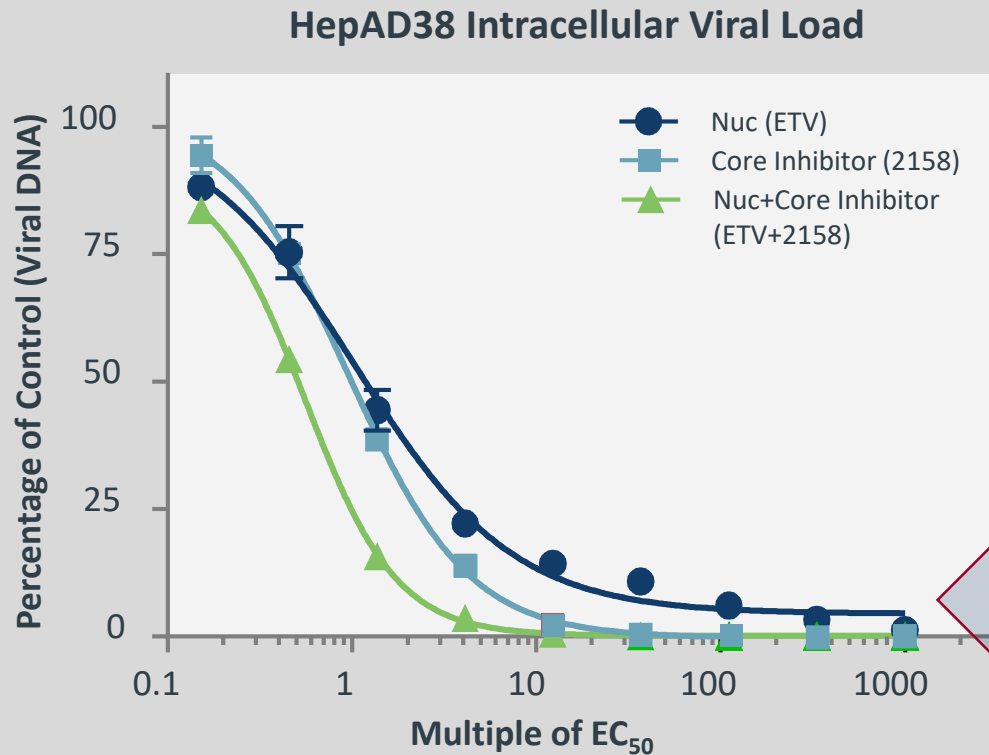
- Designed to inhibit both production of new virus and trafficking of incoming nucleocapsid to nucleus
- Unlike nucs, designed to block establishment of cccDNA
- Has potential to be additive or synergistic with polymerase inhibition

# CORE INHIBITORS REDUCED KEY SURROGATE MARKERS FOR cccDNA IN PRECLINICAL STUDIES





# BOTTOM LINE...CORE INHIBITORS ARE POTENTIALLY MORE EFFECTIVE ANTIVIRALS



HOW QUICKLY DO cccDNA  
AND INFECTED CELLS TURN OVER?

# cccDNA BIOSYNTHESIS STUDY

## Strategy/Approach



Resistance emerges rapidly in lamivudine- and telbivudine-treated HBV patients



Obtain longitudinal clinical samples (paired plasma and biopsy)



Establish and validate isolation methodologies



Follow resistance signature mutations as genetic markers of cccDNA turnover, confirm pgRNA sequences reflect cccDNA sequences

## Objectives



Confirm that genetic source of resistance is cccDNA

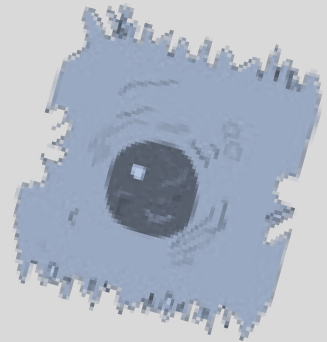


Determine the timeframe required to turn over existing cccDNA populations in patients

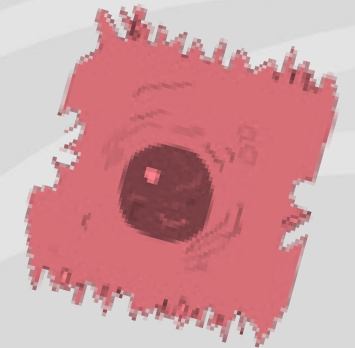
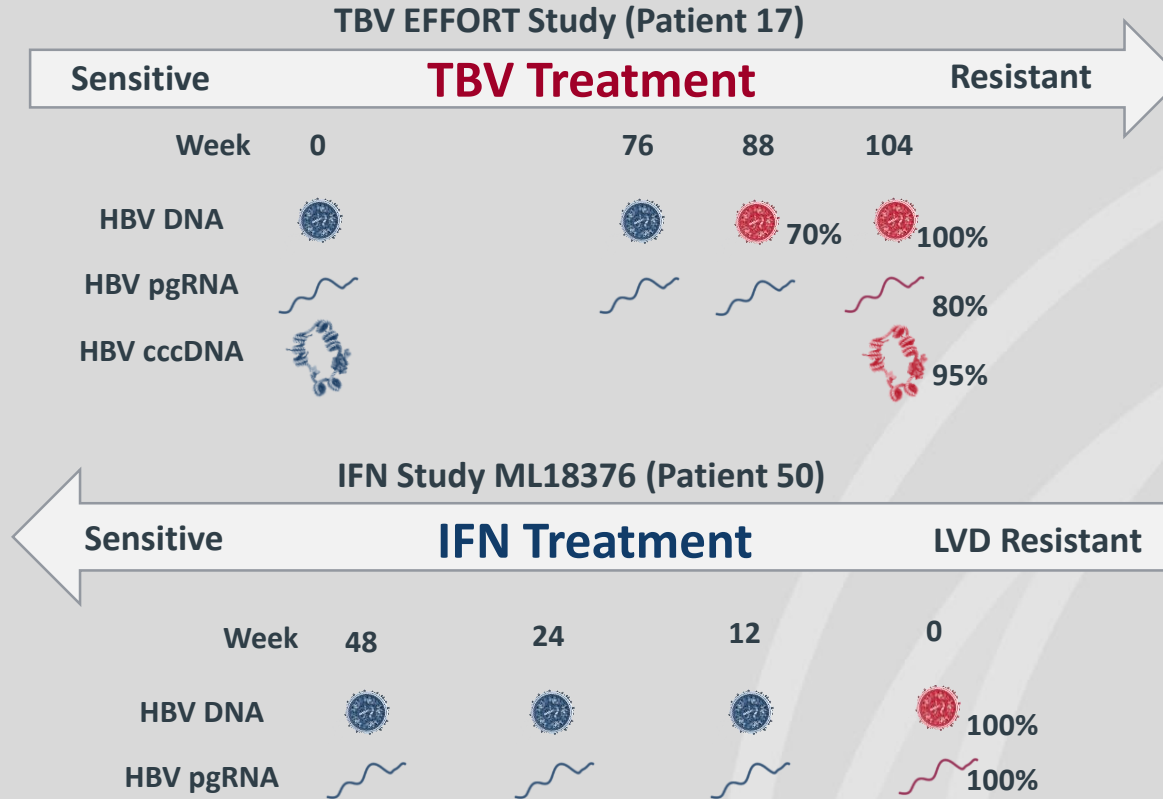


Determine if there are inactive subpopulations of cccDNA

# RAPID TURNOVER OF cccDNA IN AS LITTLE AS 12-16 WEEKS



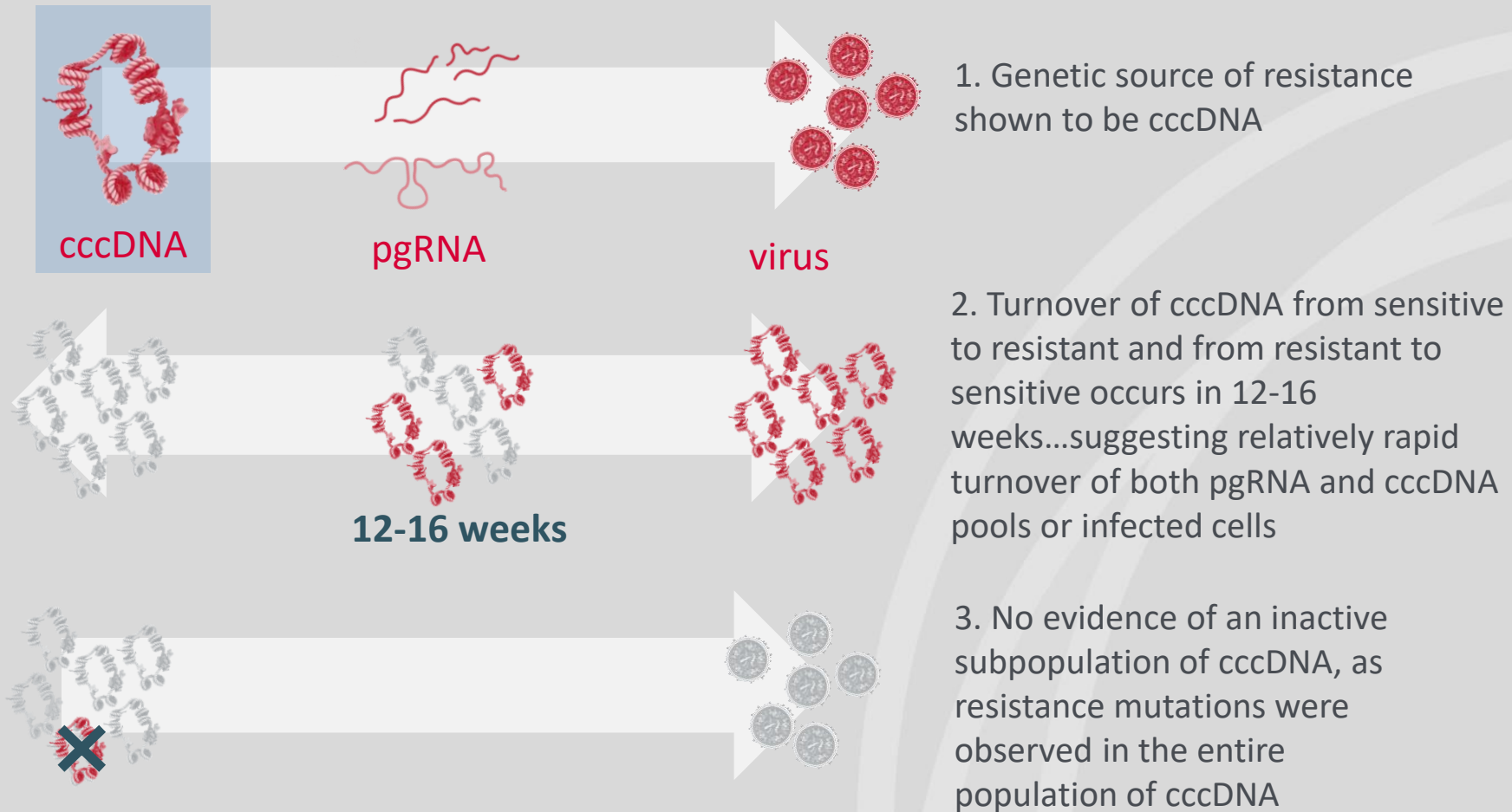
HBV-Infected  
Hepatocyte



HBV<sup>R</sup>-Infected  
Hepatocyte

Virus, pgRNA and cccDNA populations can be completely replaced in as little as 12 weeks









# SUMMARY RESULTS FROM ONGOING cccDNA BIOSYNTHESIS STUDY



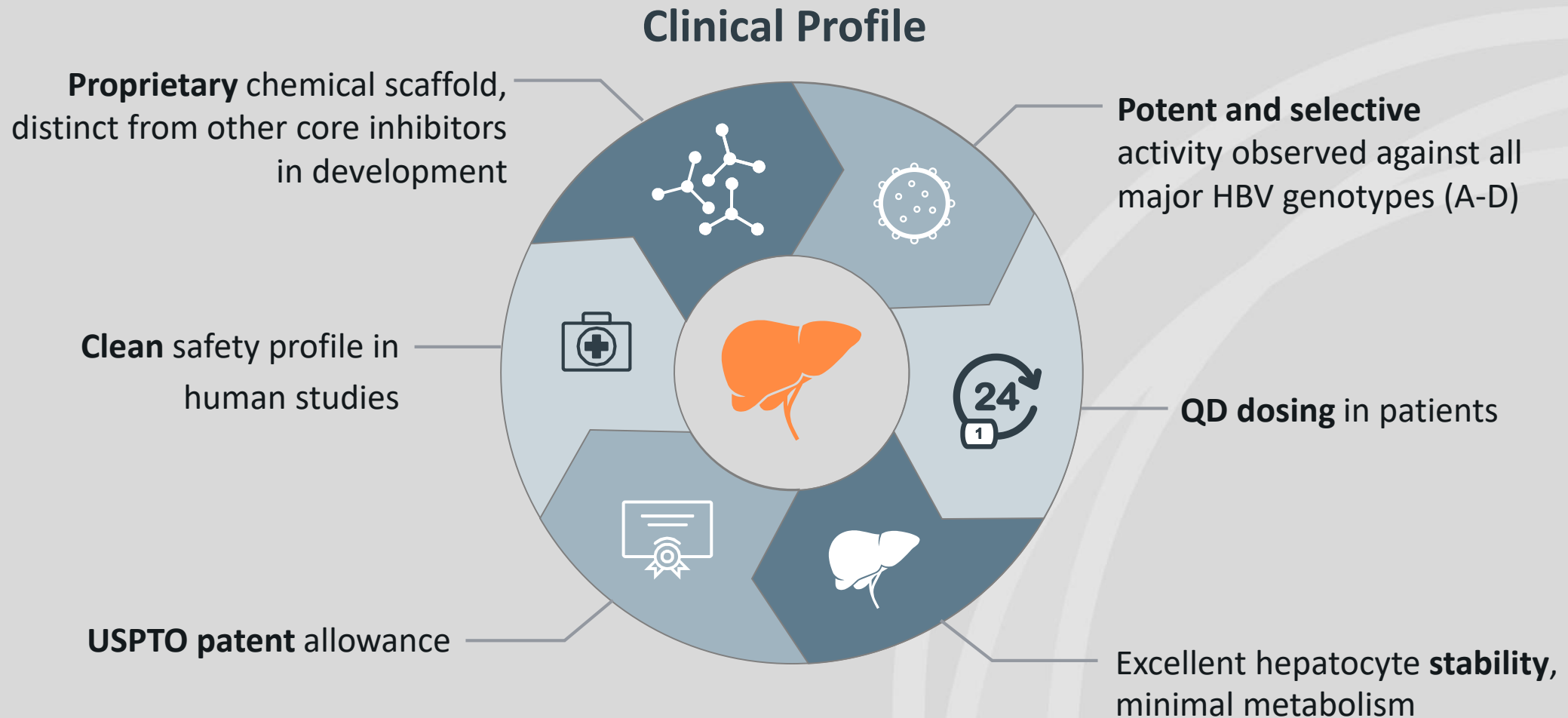
# PIPELINE OF POTENT CORE INHIBITORS

# ASMB HBV CORE INHIBITOR PROGRAM PORTFOLIO

Novel Molecules With Distinct Chemical Scaffolds Discovered at Assembly Biosciences

Drug Candidate	Discovery	Lead Op/ Selection	IND Enabling	Phase 1a	Phase 1b	Phase 2	Phase 3	NDA	Worldwide Rights
ABI-H0731									
ABI-H2158									
ABI-H3733									
Core Inhibitor Discovery Program									

# ABI-H0731- LEAD CANDIDATE NOVEL CORE INHIBITOR IN PHASE 2a



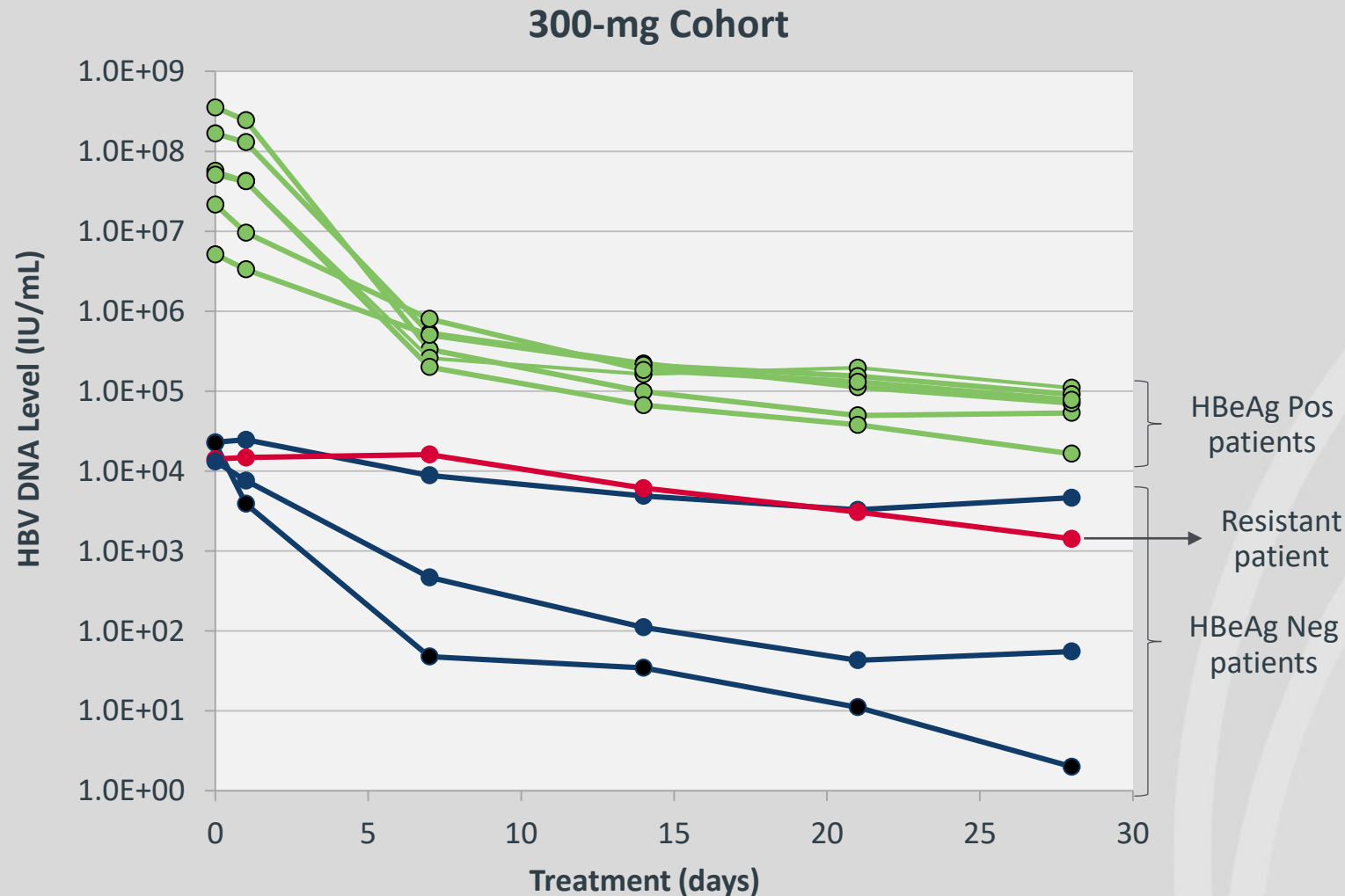


# ABI-H0731: PHASE 1 – CLINICAL SAFETY SUMMARY

Dose (n)	100 mg (20)	200 mg (20)	300 mg (20)	400 mg (2)	Placebo (12)
Grade 1 AEs	24	15	12	4	9
Grade 2 AEs	0	0	0	0	0
Grade 3 AEs	0	0	0	1	0

- Generally well tolerated, with **no SAEs reported** and **no dose-limiting toxicities**
- **AEs not dose dependent**
- **All TEAEs were grade 1** (mild), except for a single HBeAg (-) subject dosed at 400 mg with a grade 3 rash
  - Deemed probably related to study drug
  - Rash resolved rapidly following treatment discontinuation without additional medical intervention

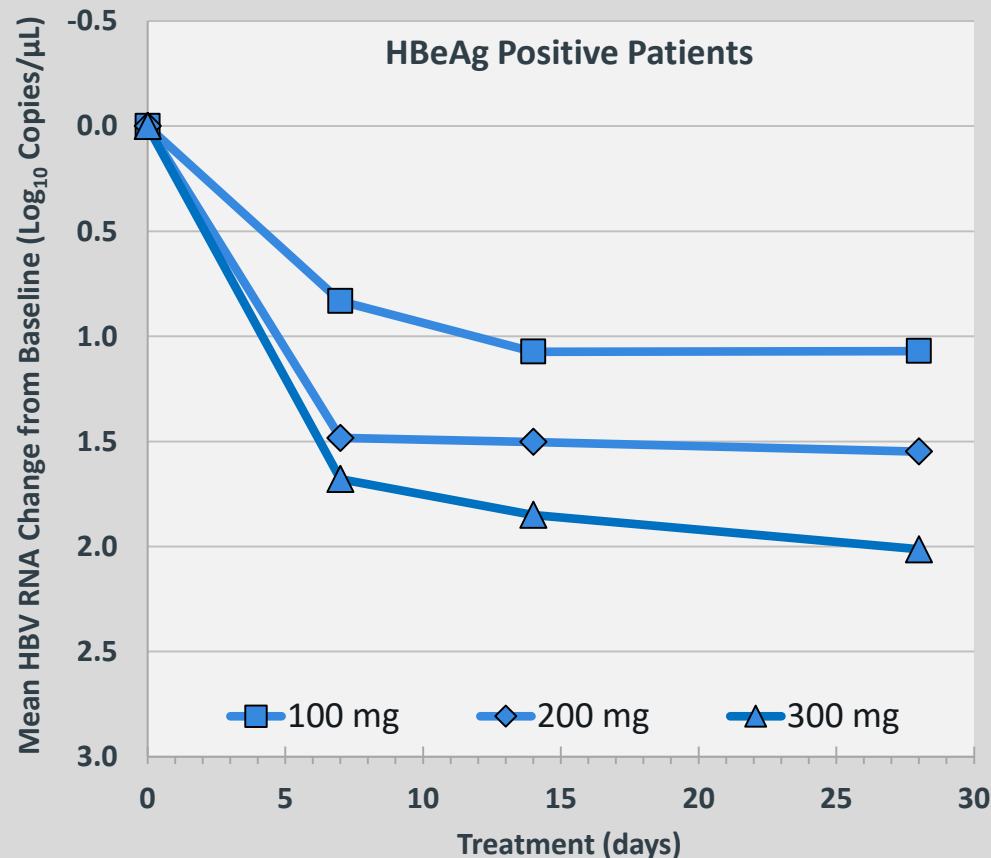
# PHASE 1b: POTENT REDUCTIONS IN HBV DNA



- Steady state exposures achieved in  $\leq 5$  days,  $\sim 2$ -fold accumulation observed over 28 days
- Observed to be efficacious at all dose levels evaluated
- Mean maximal HBV DNA reduction of 2.8 logs observed in 300-mg cohort
- Individual patients achieved maximal declines of up to 4.1 logs
- One patient harbored T109M resistance mutation at baseline but still experienced a 1 log decline
- **The 300-mg dose selected for evaluation in Phase 2a studies**

# PHASE 1b: PARALLEL REDUCTIONS IN HBV RNA

- HBV RNA reductions (1-2 logs) seen at all dose levels and correlated with HBV DNA reductions ( $p < 0.001$ )
- Mechanism-based reduction in viral RNA levels is a differentiating feature of core inhibitors



	Changes from Baseline	
Patients	HBsAg Pos	
Dose (mg)	N	Mean Copies/ $\mu\text{L}$ (Range)*
100 mg	6	1.2 (0.7 - 1.6)
200 mg	5	1.7 (1.1 - 2.2)
300 mg	6	2.3 (1.7 - 2.6)
400 mg	0	NA

\*Internal HBV RNA RT-qPCR assay, for HBsAg positive: LOQ = 10 copies/ $\mu\text{L}$

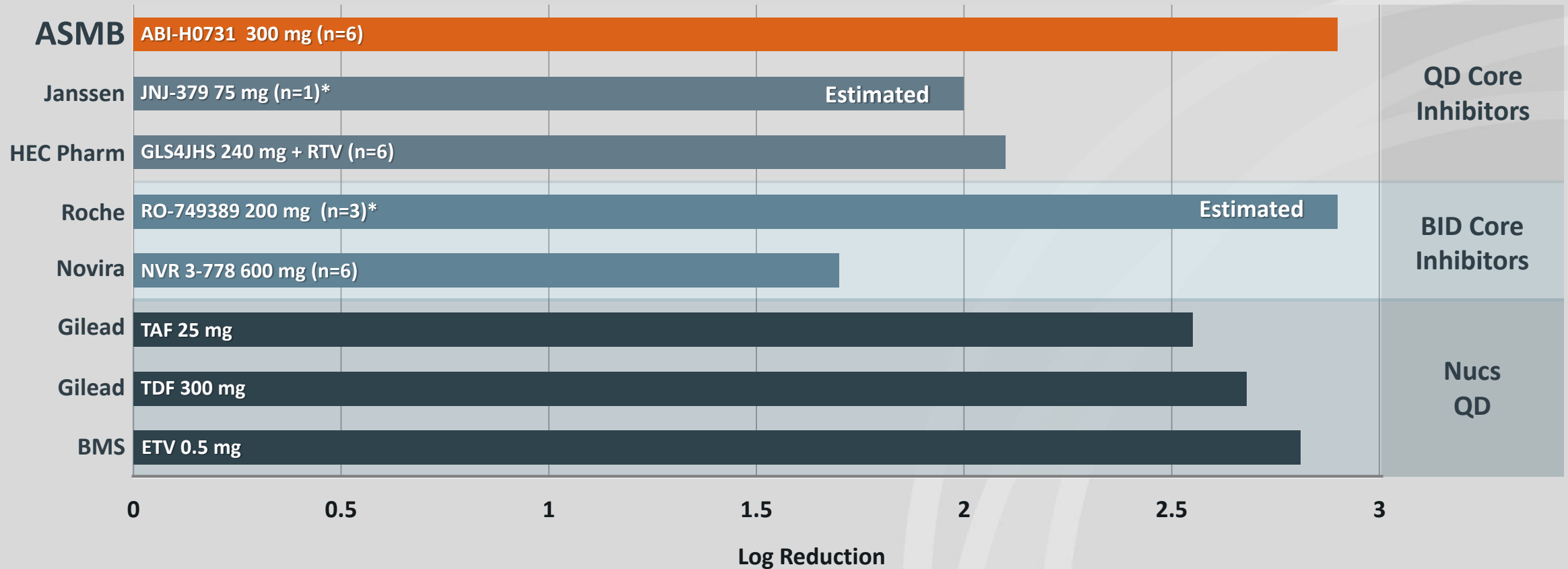
\*\*Both subjects declined on treatment

## HBsAg Neg subjects

- RNA levels were lower at baseline and more difficult to quantitate
- All subjects with detectable RNA at baseline had RNA declines on treatment

# ABI-H0731 IS POTENTIALLY AS POTENT AS ANY THERAPY FOR HBV

Phase 1b 28-Day Monotherapy Studies in HBV-Infected, HBeAg Positive Patients



\*Estimated.

BID = twice a day; POC = proof of concept; QD = once a day; RTV = ritonavir.

1. Yuen, et al. AASLD Poster LB-10 2015. 2. Ding, et al. AASLD Poster 920 2017. 3. Zoulim, et al. AASLD Poster LB-15. 2017. 4. Gane, et al. EASL Presentation 2018. 5. Yuen, et al. EASL Poster LBP-012 2018. 6. De Man, et al. *Hepatology*. Vol 34 2001. 7. Agarwal J. *Hepatology*. 2015;vol 62.

# ABI-H0731 PHASE 2a STRATEGY AND DESIGNS

Elimination of  
Viral Load

Decay of cccDNA/  
Infected Cells

Treatment  
Consolidation

No Relapse  
Off Therapy

## Viral Load Study

Patient population: nuc-naive, HBeAg+

300 mg 731 + 0.5 mg ETV

Placebo + 0.5 mg ETV

Goal: Demonstrate significant  
improvement in viral DNA declines

## Viral Antigen POC Study

Patient population: nuc-suppressed, HBeAg+ and HBeAg-

300 mg 731 + Continued nuc

Placebo + Continued nuc

Goal: Demonstrate significant decreases  
in cccDNA surrogate markers

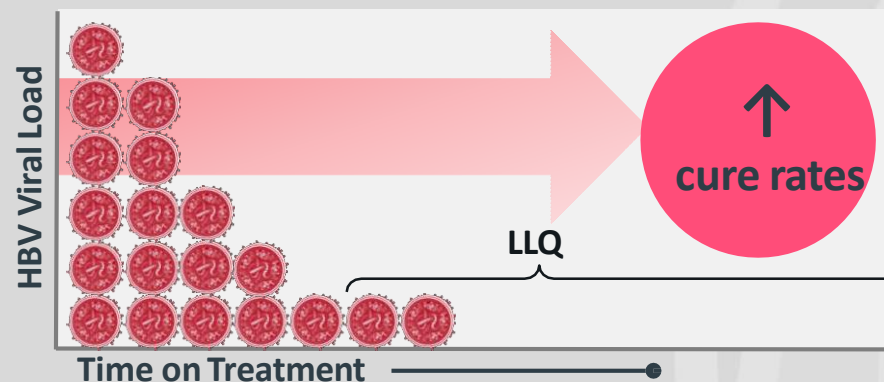
Initial data  
expected Q2 2019

0 Time (months) 6

# ABI-H0731 OPEN-LABEL EXTENSION STUDY DESIGNED TO DEMONSTRATE SVR AFTER 6 MONTHS POST-TREATMENT

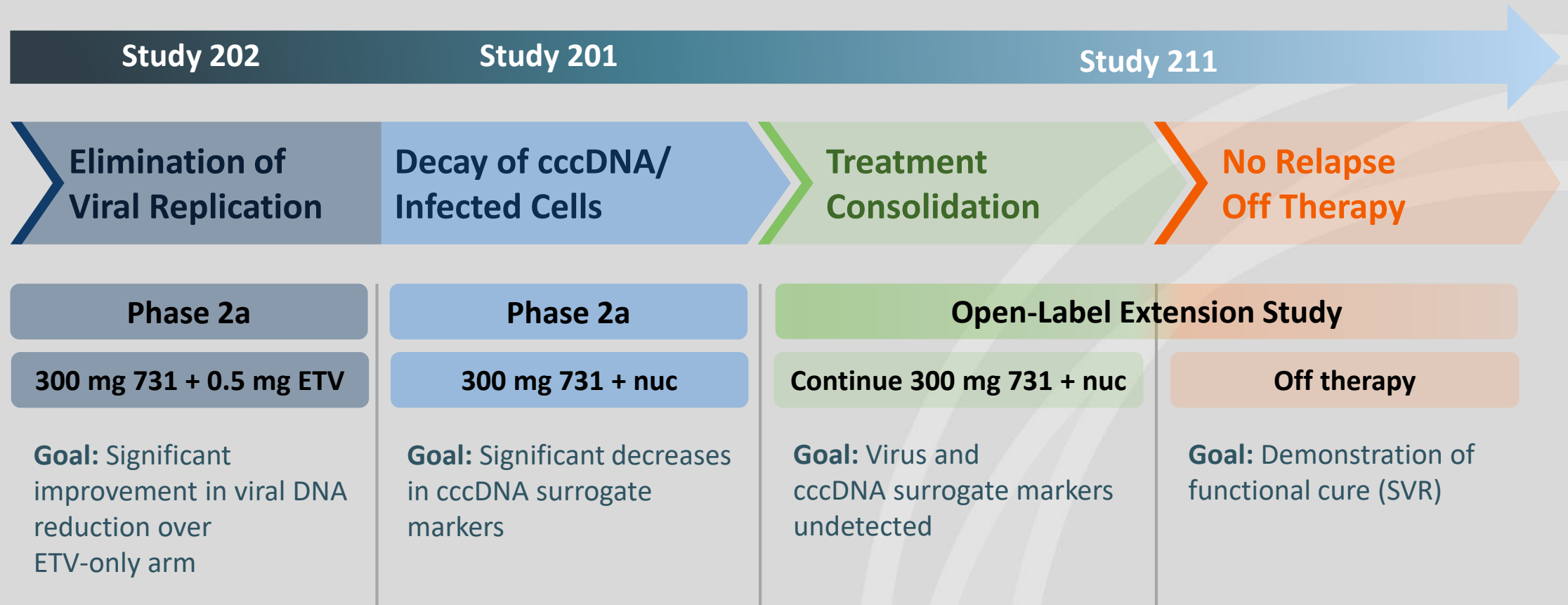


## Study 211



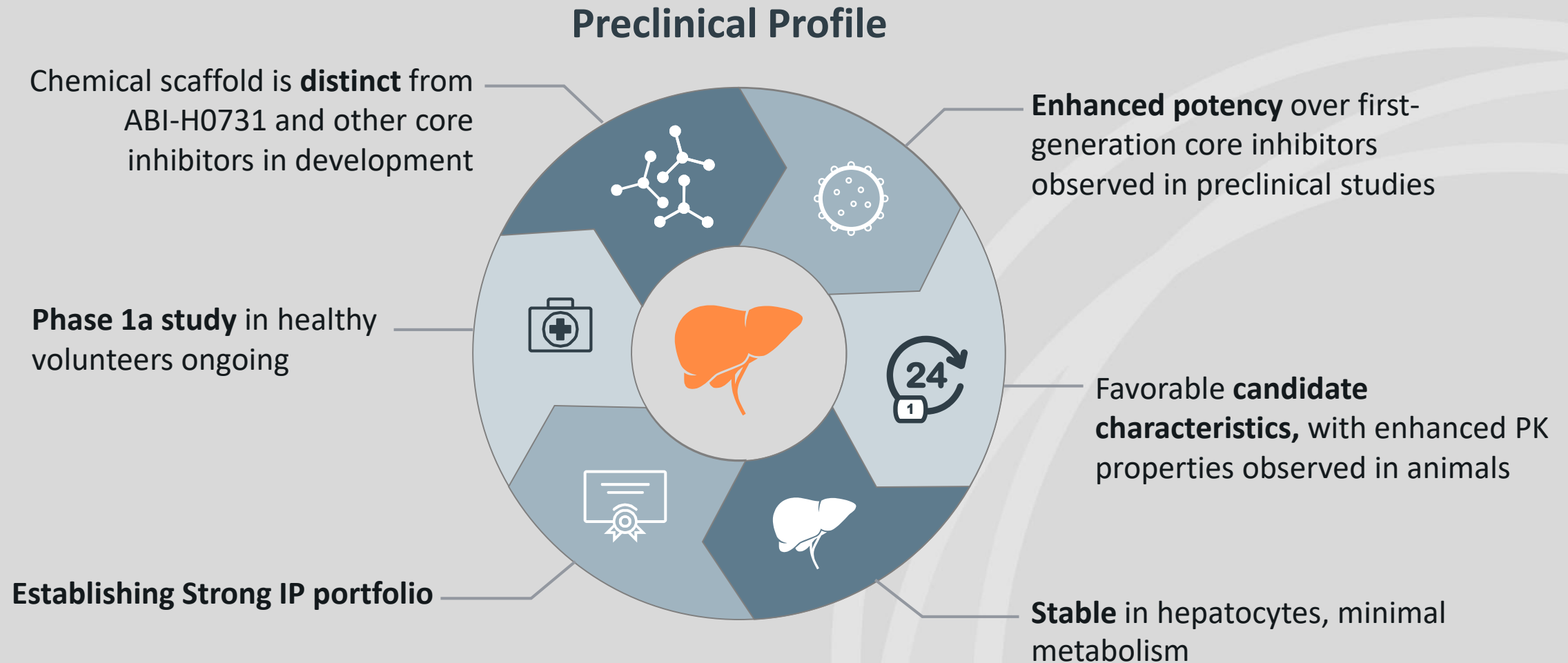
Goal: SVR off therapy

# PHASE 2 STUDIES WILL DEFINE TIMELINES TO SUSTAINED SUPPRESSION AND CURE



INITIAL DATA EXPECTED Q2 2019

# ABI-H2158 – SECOND-GENERATION CORE INHIBITOR IN PHASE 1a STUDY





# ENHANCED OBSERVED PROPERTIES OF ABI-H2158

HBV Infection of Primary Human Hepatocytes

Viral Marker	EC <sub>50</sub> (nM)		Fold Improvement
	ABI-H0731	ABI-H2158	
Viral DNA	154	41	<b>4</b>
HBeAg	2,210	204	<b>11</b>
HBsAg	3,000	216	<b>14</b>
pgRNA	1,840	160	<b>12</b>

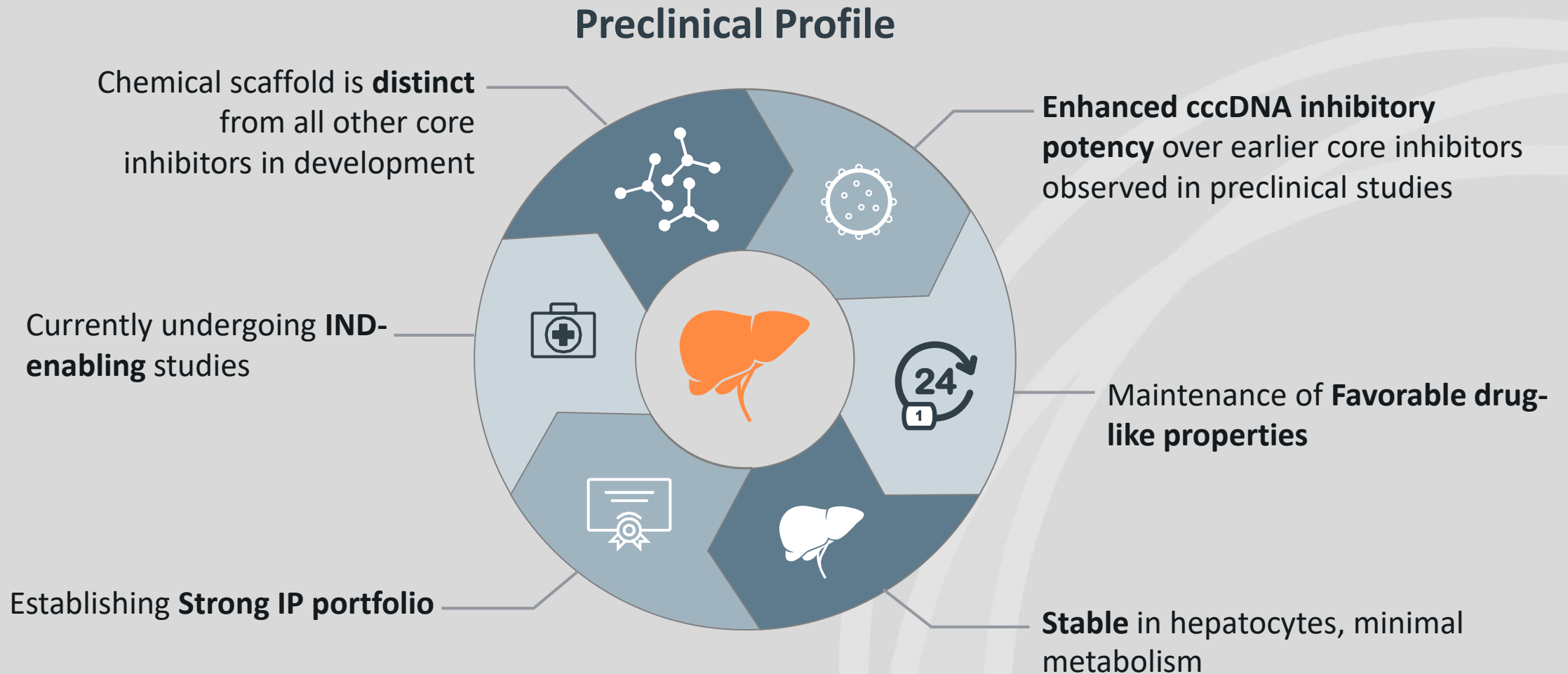
- Both compounds were observed to be highly stable and have shown positive results in human hepatocytes
- ABI-H2158 exhibited >11-fold enhanced potency in reducing surrogate markers of cccDNA**

PK Parameters at 30-mg/kg Dose

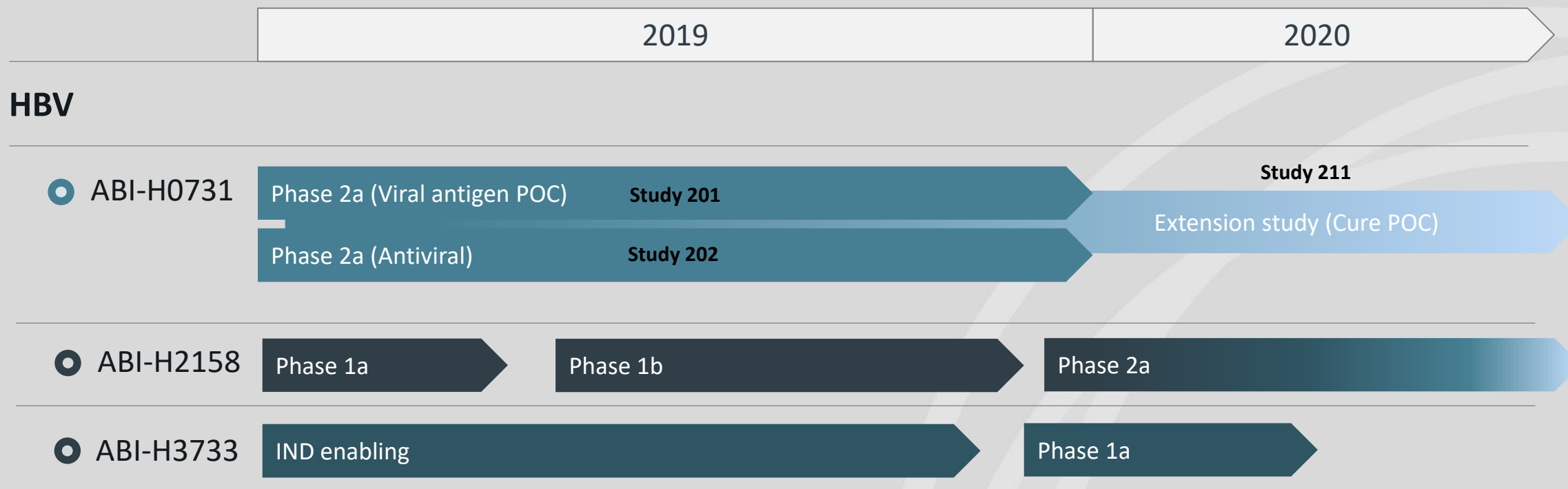
Animal Species	ABI-H0731	ABI-H2158	ABI-H0731	ABI-H2158
	C <sub>max</sub> (µg/mL)	C <sub>max</sub> (µg/mL)	AUC <sub>inf</sub> (µg*hr/mL)	AUC <sub>inf</sub> (µg*hr/mL)
Rat	6.4	24.8	62.1	445
Monkey	3.2	45.4	45.2	328
Dog	2.1	49.9	3.9	763

- Both compounds exhibited high bioavailability and terminal half-life supportive of QD human dosing
- ABI-H2158 exhibited 4- to 24-fold increase in C<sub>max</sub> and 7 to 195-fold increase in AUC<sub>inf</sub> when dosed at 30 mg/kg in animals**

# ABI-H3733 – NEXT-GENERATION CORE INHIBITOR IN IND-ENABLING STUDIES



# UPCOMING MILESTONES







Key HBV Meetings



# MICROBIOME PROGRAM

# ASMB MICROBIOME PROGRAM PORTFOLIO

Drug Candidate (Mechanism/Indication)	Discovery & Lead Op/Selection	IND Enabling	Phase 1b	Phase 2	Worldwide Rights*
Microbiome					
ABI-M201 (Ulcerative Colitis)	<div></div>				
ABI-M301 (Crohn’s Disease)	<div></div>				
Irritable Bowel Syndrome	<div></div>				
NASH	<div></div>				
Immuno-oncology	<div></div>				
Other Platform Development	<div></div>				

# ALLERGAN/ASMB MICROBIOME COLLABORATION VALUED UP TO \$2.8 BILLION

## Key Disclosed Terms

Rights for GI Development Programs	Financial Highlights	Milestones and Royalties	Development Funding
<ul style="list-style-type: none"><li>• Ulcerative colitis</li><li>• Crohn's disease</li><li>• IBS</li></ul>	<ul style="list-style-type: none"><li>• \$50M upfront payment</li></ul>	<ul style="list-style-type: none"><li>• Up to ~\$2.8B in development and commercial milestones</li><li>• Tiered royalties up to mid-teens on net sales</li></ul>	<ul style="list-style-type: none"><li>• \$75M R&amp;D funding through POC</li><li>• Allergan assumes all post-POC development costs</li></ul>

## Collaboration Summary

Expedites our efforts into multiple GI indications

Leverages our end-to-end microbiome technology platform

Advances our ability to move microbiome candidates rapidly into clinical development with strategic partners



**Allergan**

# ASMB PROPRIETARY MICROBIOME PLATFORM

Differentiated and Fully-Integrated Platform Designed to Deliver Synthetic Live Bio-Therapeutics

**Proprietary and scientifically rigorous rational strain selection methodologies, including:**

Human FMT studies

Sequencing and analysis protocols

Pathology-driven mechanisms

*In vitro* and *in vivo* models

**Gemicel® delivery technology**

- Designed for targeted delivery to specific regions of the colon
- Select strains of vegetative bacteria delivered
  - Spores
  - Non-spores



**Differentiated manufacturing approach**

- Isolation
- Development of appropriate culture media and cultivation conditions
- Scalability
- GMP cell banking of pure strains and bulk drug substance

# GEMICEL<sup>®</sup>

## Targeted Delivery Technology

The colon is an attractive site for drug delivery, particularly for microbiotic therapies if they can be delivered reliably



### Gemicel<sup>®</sup> capsule

- Manufacturing amenable to biologic products

API = active pharmaceutical ingredient.

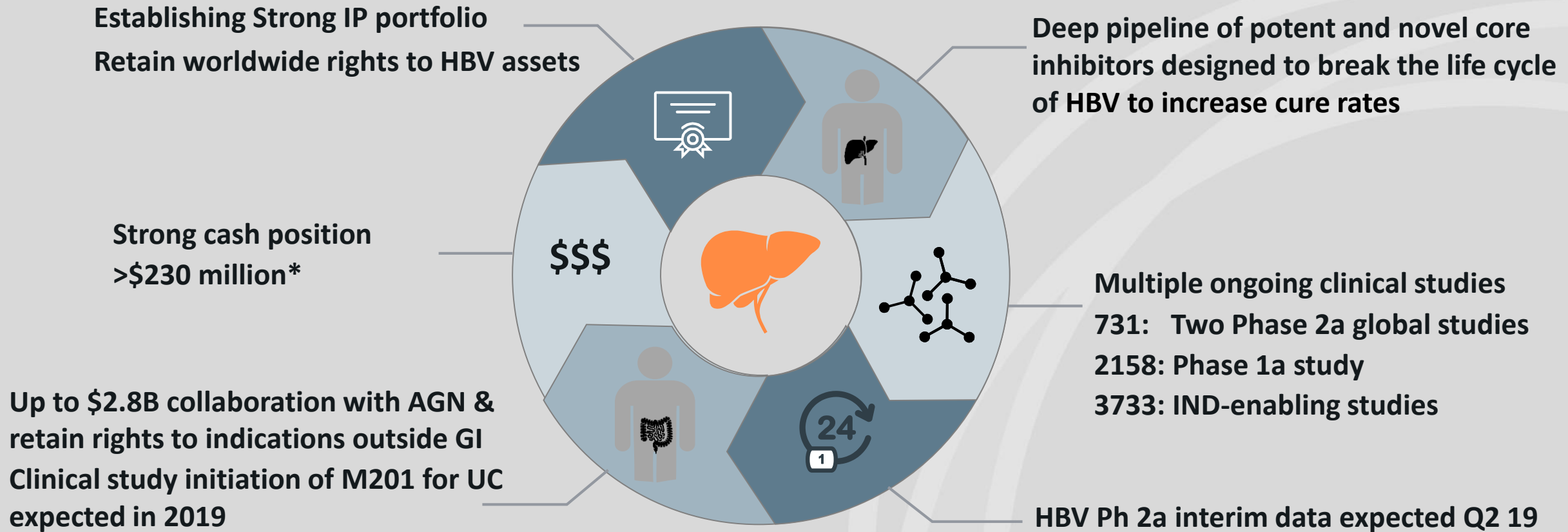
**Second (inner) capsule**  
for bolus release of API  
in right colon

**First (outer) capsule**  
for bolus release of API  
in ileum



# ASSEMBLY BIOSCIENCES SUMMARY

# ASSEMBLY BIOSCIENCES: KEY INVESTOR HIGHLIGHTS



\* As of 9/30/18  
IP = intellectual property.