



# Singularly Focused on HBV

August 2019

NASDAQ: ABUS

[www.arbutusbio.com](http://www.arbutusbio.com)

# Forward-Looking **Statements**

This presentation contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and Canadian securities laws. All statements that are not historical facts are hereby identified as forward-looking statements for this purpose and include, among others, statements relating to: the potential for HBV to have a larger market opportunity than HCV; our ability to meet a significant unmet medical need; our path to combination clinical trials with AB-506 and AB-729 in the second half of 2020; the sufficiency of our cash and cash equivalents to extend into the second half of 2020; our ability to develop a curative regimen for HBV and unlock significant market growth opportunities; our expectations to dose additional cohorts for the AB-506 Phase 1a/1b clinical trial and our expectation to have final results available in the first half of 2020; our expectation to make a decision regarding AB-452 clinical development in early 2020; our expectation for AB-729 for preliminary safety and efficacy data from both healthy subjects and several single dose cohorts of subjects with CHB to be available in the first quarter of 2020; and the timeline to a combination cure for HBV.

With respect to the forward-looking statements contained in this presentation, Arbutus has made numerous assumptions regarding, among other things: the timely receipt of expected payments; the effectiveness and timeliness of preclinical studies and clinical trials, and the usefulness of the data; the timeliness of regulatory approvals; the continued demand for Arbutus' assets; and the stability of economic and market conditions. While Arbutus considers these assumptions to be reasonable, these assumptions are inherently subject to significant business, economic, competitive, market and social uncertainties and contingencies. Forward-looking statements herein involve known and unknown risks, uncertainties and other factors that may cause the actual results, events or developments to be materially different from any future results, events or developments expressed or implied by such forward-looking statements. Such factors include, among others: anticipated pre-clinical and clinical trials may be more costly or take longer to complete than anticipated, and may never be initiated or completed, or may not generate results that warrant future development of the tested drug candidate; Arbutus may not receive the necessary regulatory approvals for the clinical development of Arbutus' products; economic and market conditions may worsen; and market shifts may require a change in strategic focus. A more complete discussion of the risks and uncertainties facing Arbutus appears in Arbutus' Annual Report on Form 10-K and Arbutus' periodic disclosure filings which are available at [www.sec.gov](http://www.sec.gov) and at [www.sedar.com](http://www.sedar.com).

The forward-looking statements made in connection with this presentation represent our views only as of the date of this presentation (or any earlier date indicated in such statement). While we may update certain forward-looking statements from time to time, we specifically disclaim any obligation to do so, even if new information becomes available in the future.

# Investment Highlights

Singular therapeutic focus - curing chronic Hepatitis B Virus (HBV)

Significant  
unmet medical  
need in **HBV**

Global HBV  
prevalence  
double that  
of HCV,  
potential for  
larger market  
opportunity

Team with  
antiviral  
**expertise &  
proven track  
record**

Applying  
knowledge gained  
from HIV and HCV  
success to find  
**HBV cure through  
proprietary drug  
combinations**

Robust  
HBV  
**Portfolio**

**HBV assets**  
generating  
clinical data

**Combination  
Proof-of-  
Concept  
Clinical Trial**

AB-506  
+ AB-729  
w/ NA in HBV pts  
**Expected  
2H 2020**

Strong  
**Financial**  
Position

\$95M cash at 6/30/19  
plus \$20M gross  
proceeds received  
from Onpattro  
royalty monetization  
completed in  
July 2019  
**Extends runway  
into 2H 2020**

# Proven Leadership Team

Successful track records in both the discovery, development, and commercialization of multiple antivirals: sofosbuvir, etravirine, rilpivirine, telaprevir and simeprevir



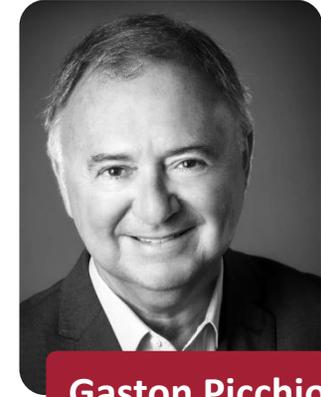
**William H. Collier**

President and CEO



**Michael J. Sofia, PhD**

Chief Scientific Officer



**Gaston Picchio, PhD**

Chief Development Officer



**David C. Hastings**

Chief Financial Officer



**Elizabeth Howard, PhD, JD**

EVP, General Counsel and Chief Compliance Officer



**Michael McElhaugh**

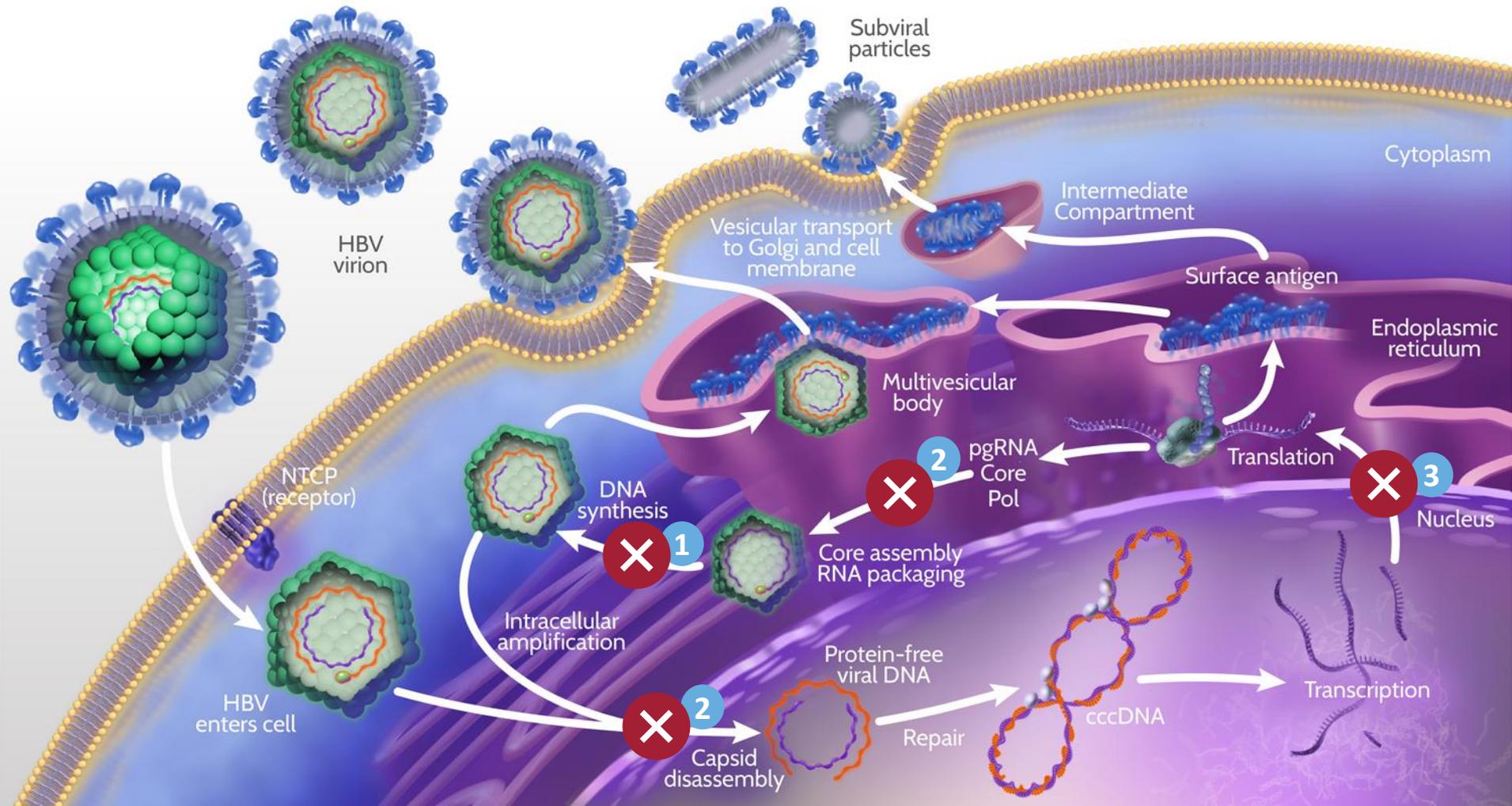
Chief Business Officer



# HBV Lifecycle Illustrates Key Points for Intervention

A combination of agents with complementary MOA is needed to cure HBV

- 1 – NA
- 2 – AB-506
- 3 – AB-729
- 3 – RNA destabilizer

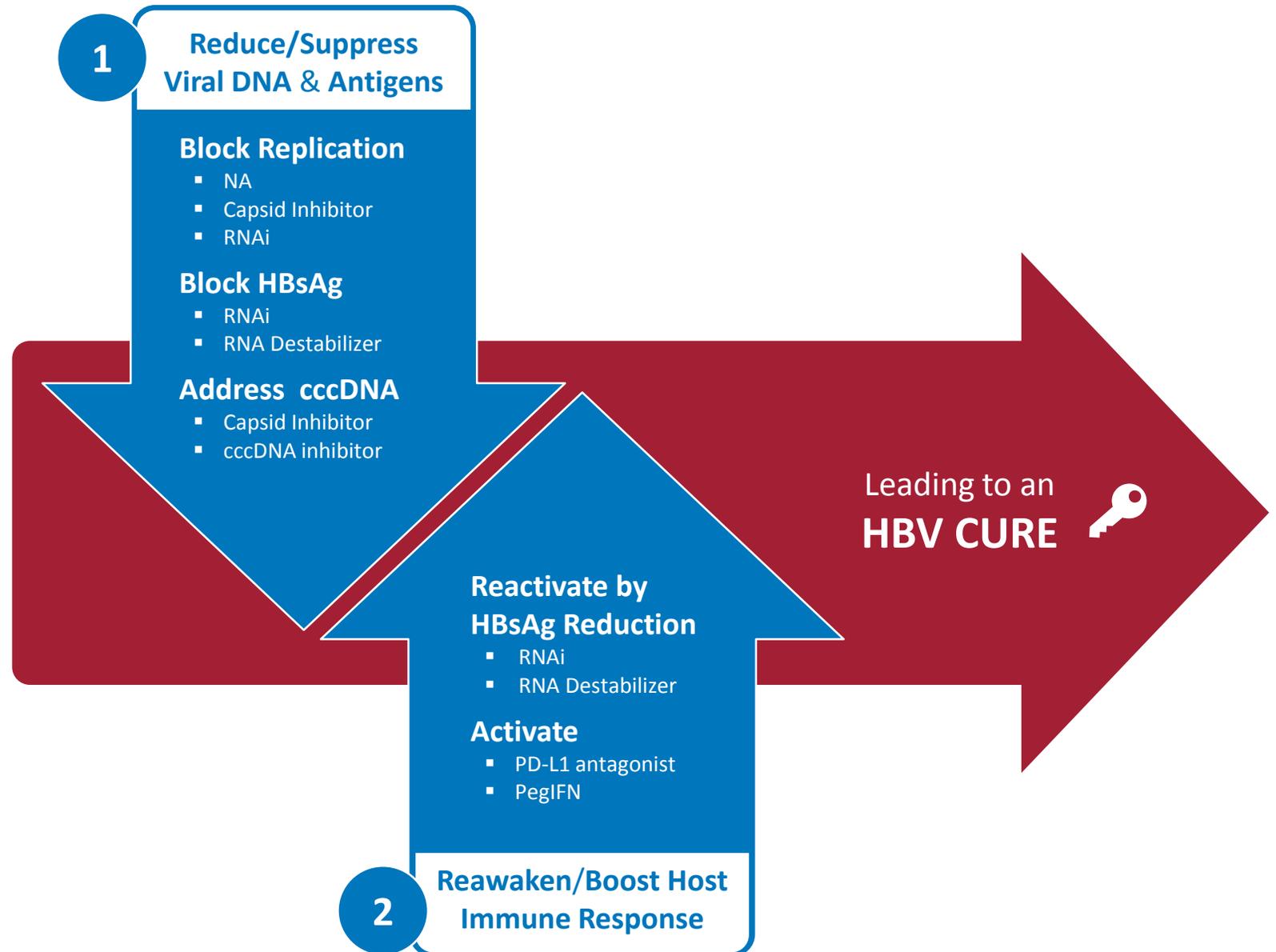


# Keys to Therapeutic Success

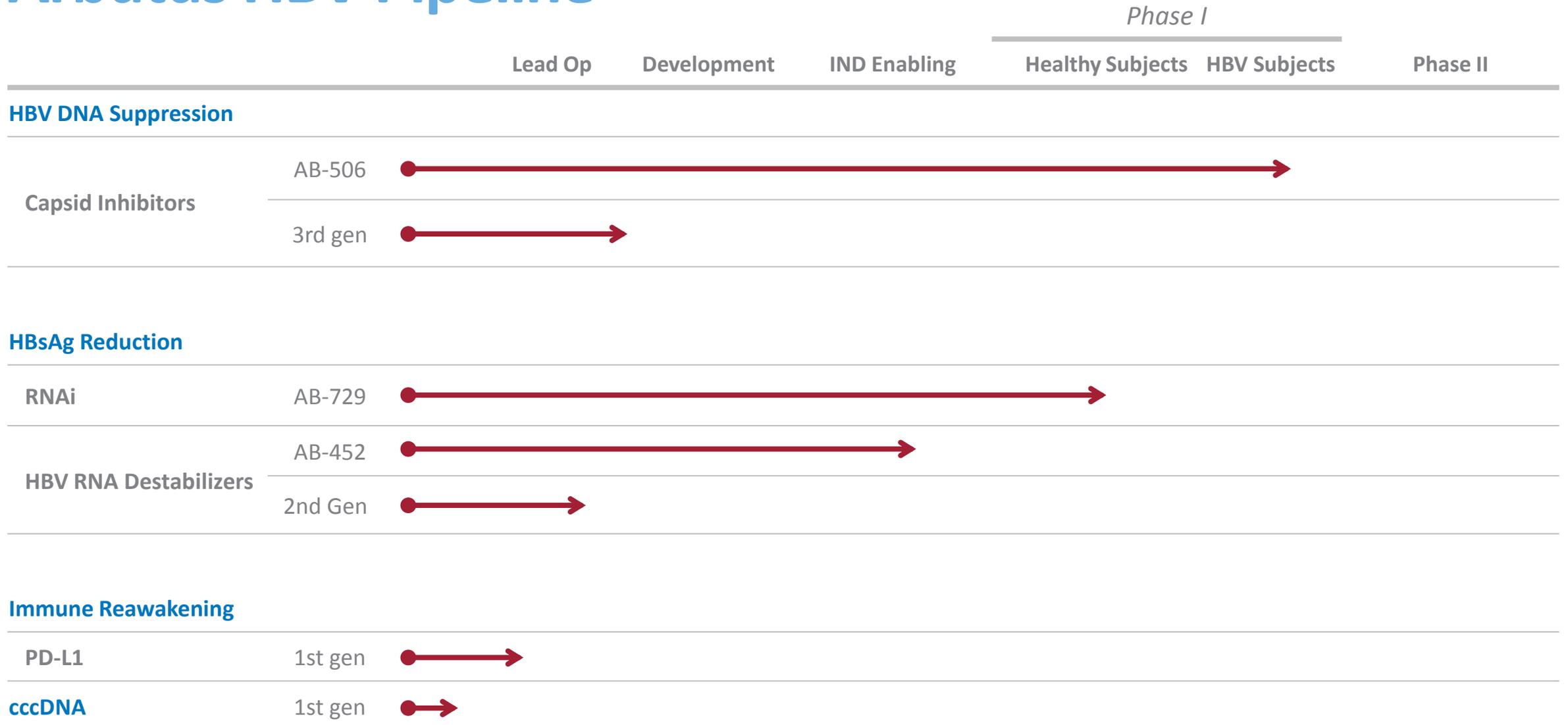
Suppress HBV DNA and viral antigens

Reawaken host immune response

Therapeutic success will require a combination of agents with complementary MOAs.



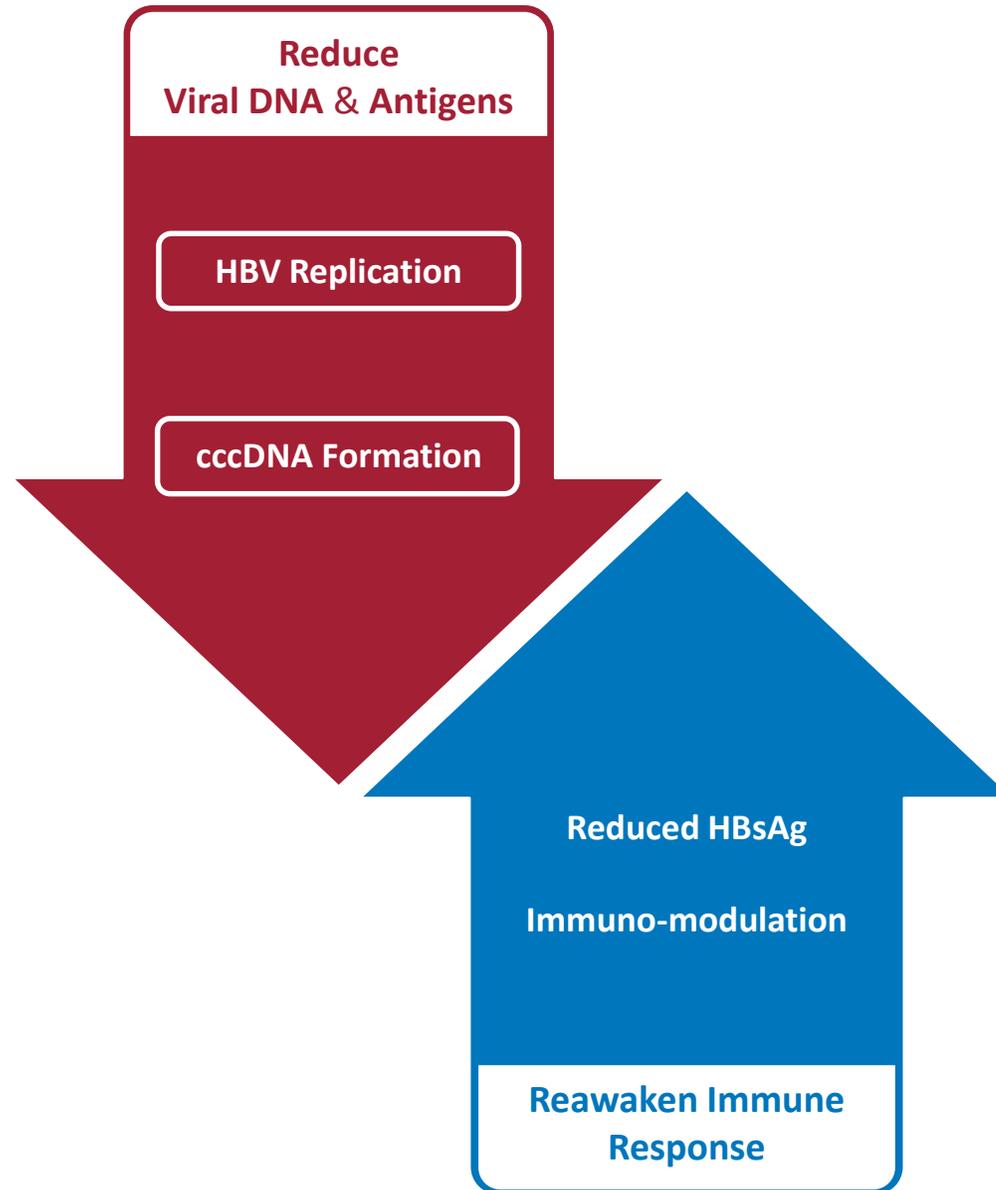
# Arbutus HBV Pipeline



# Capsid Inhibitor:

## Blocking HBV Replication

Driving HBV DNA to undetectable, in the serum **and in the liver** is a key to therapeutic success in HBV



# AB-506

## Capsid Inhibitor

AB-506 shows **preclinical and clinical potency and PK profile** consistent with best in class agents

Active against all genotypes & NA resistant variants

Once daily dosing

Complementary with HBsAg reducing agents

## Clinical Development: Preliminary Phase 1a/1b Results

### Efficacy: 160mg and 400mg Cohorts

- Mean HBV DNA and RNA declines (Day 28) from -2.0 log (160 mg dose) to -2.8 log (400 mg dose) and -2.4 log (both doses), respectively
- One Grade 4 ALT flare (400 mg) was associated with notable declines in HBsAg (-1.4 log) and HBeAg (-2.0 log) and serum IFN gamma increase suggesting an immune mediated response

### Safety: 160mg and 400mg Cohorts

- No SAEs or ALT elevations in healthy subjects
- No SAEs in CHB subjects
- Four CHB subjects experienced Grade 4 ALT flares (2 in the 160 mg cohort and 2 in the 400 mg cohort); none met DILI criteria and all occurred while HBV DNA was declining (>2.0 log)
- Two CHB subjects experienced Grade 2 flares in the 160 mg Cohort

# AB-506 Capsid Inhibitor

## Clinical Development **Next Steps**

**Phase 1a** healthy subject study investigating dosing of AB-506 for 28 days

Results expected later this year

Continue with **Phase 1b** study in CHB subjects investigating longer dosing of AB-506

Establish longer term safety (with and w/o NA)

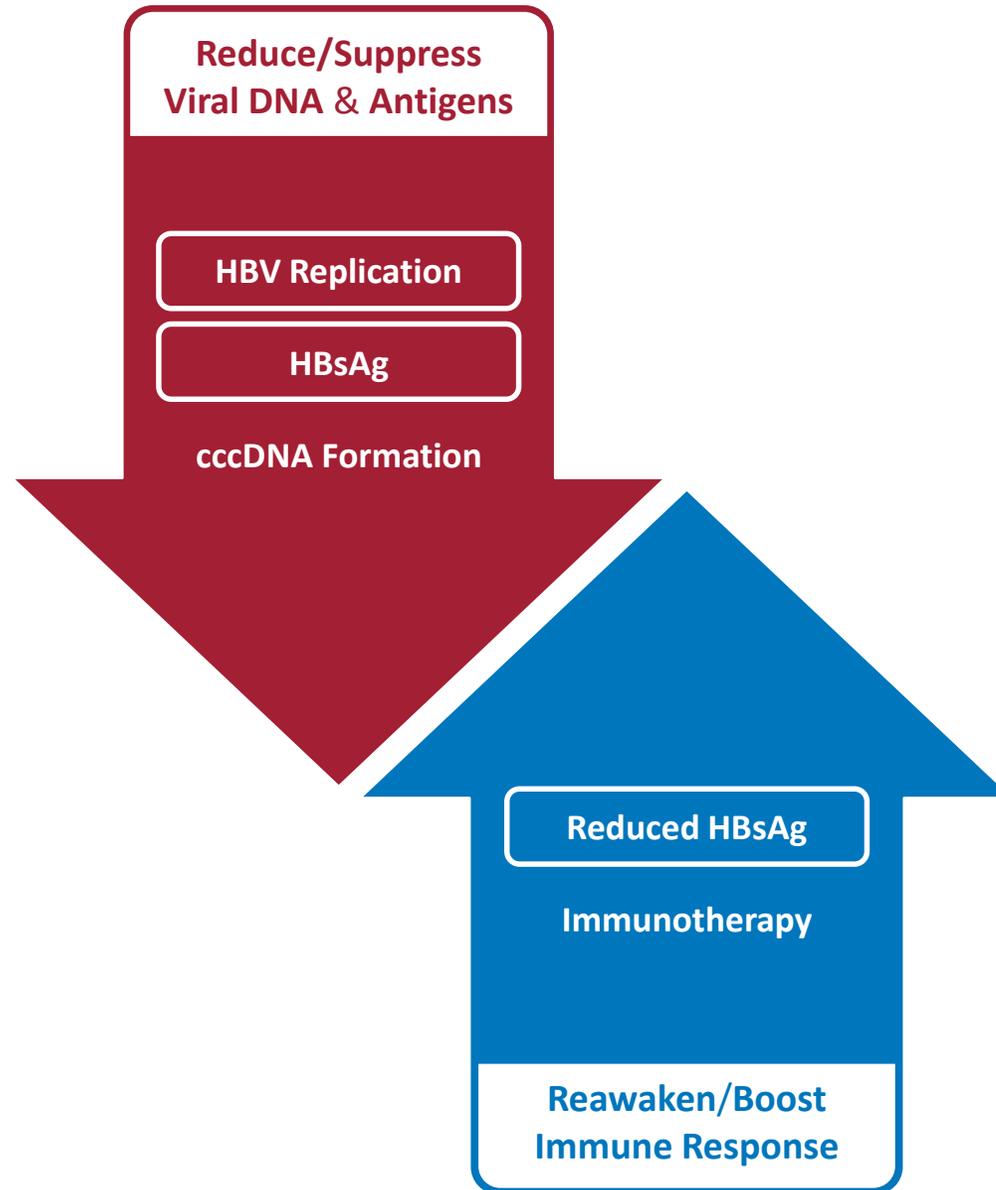
Inclusion with **AB-729** in a combination regimen

Study initiation expected 2H 2020

# Driving Down HBsAg Is A Key to Therapeutic Success in HBV

HBsAg is responsible for  
immune exhaustion

Replication inhibitors do not  
block HBsAg production



# AB-729

## RNAi

## Therapeutic

**Proprietary GalNAc-conjugate delivery technology** provides liver targeting and enables **subcutaneous dosing**

Single trigger RNAi agent targeting all HBV transcripts

Inhibits HBV replication and lowers all HBV antigens

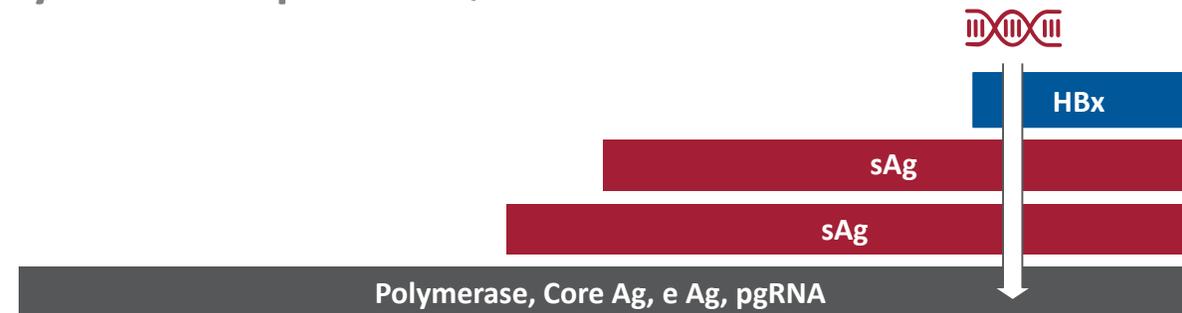
- Potent HBsAg reduction in preclinical models

Pan-genotypic activity across HBV genotypes

**Duration of HBsAg reduction supports once per month dosing**

Demonstrated complementarity with capsid inhibitors

**Phase I initiated in July 2019;**  
**preliminary results expected Q1 2020**



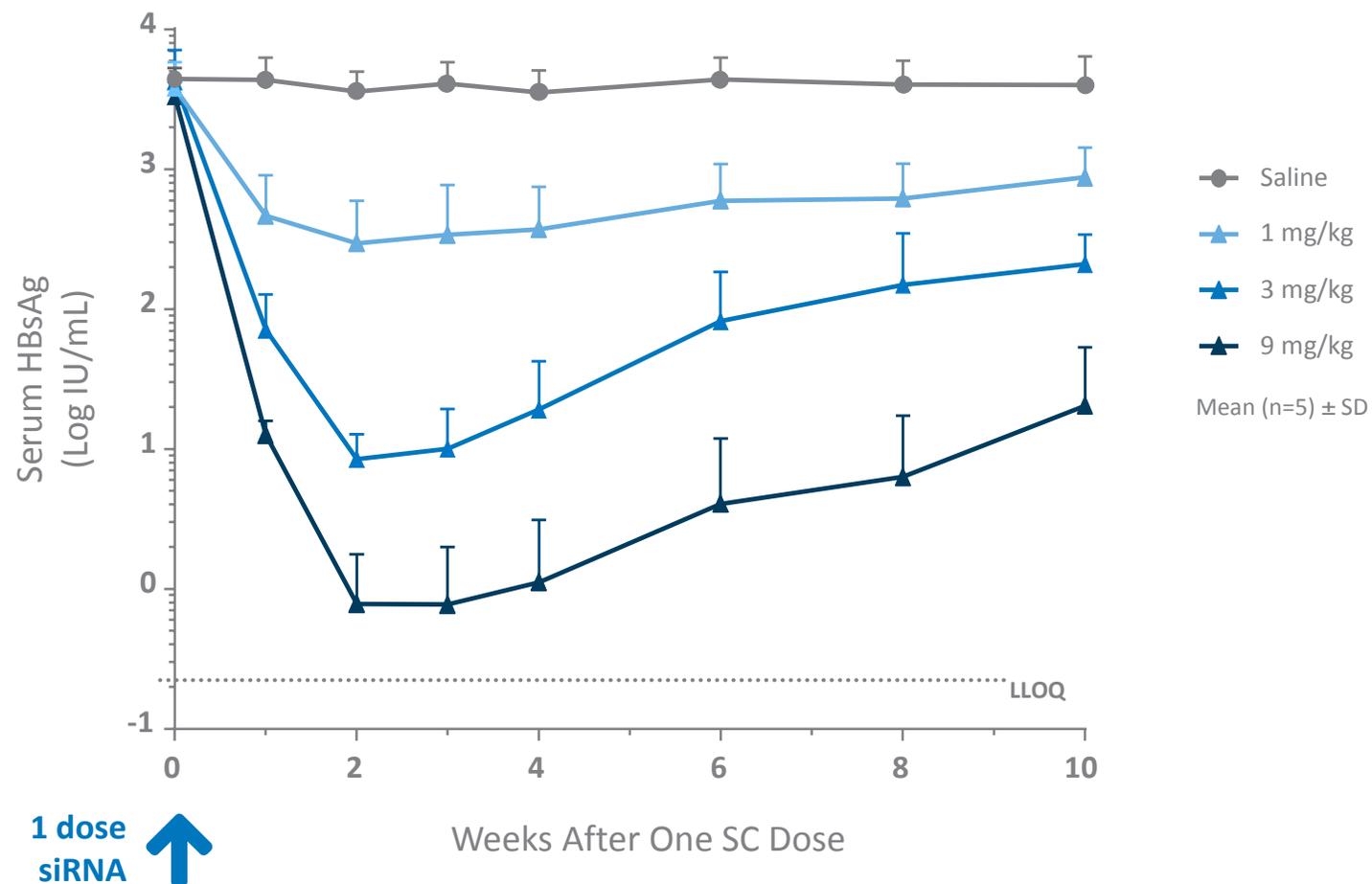
# AB-729

## In Vivo Single Dose Response & Duration

Clear dose response in AAV mouse model

Achieves maximum HBsAg reduction possible in this model

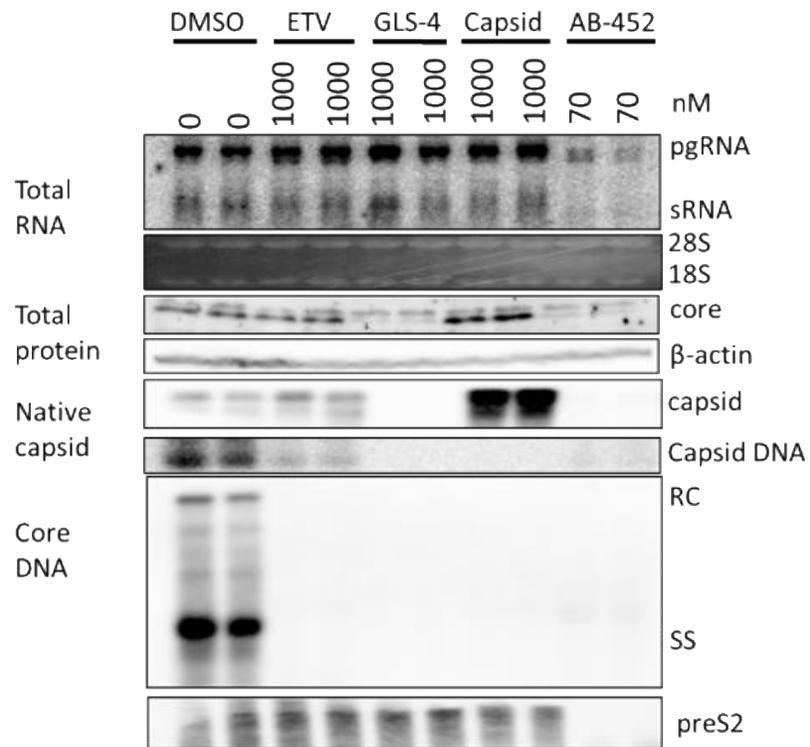
Duration supports a clinical dosing frequency of **once per month**



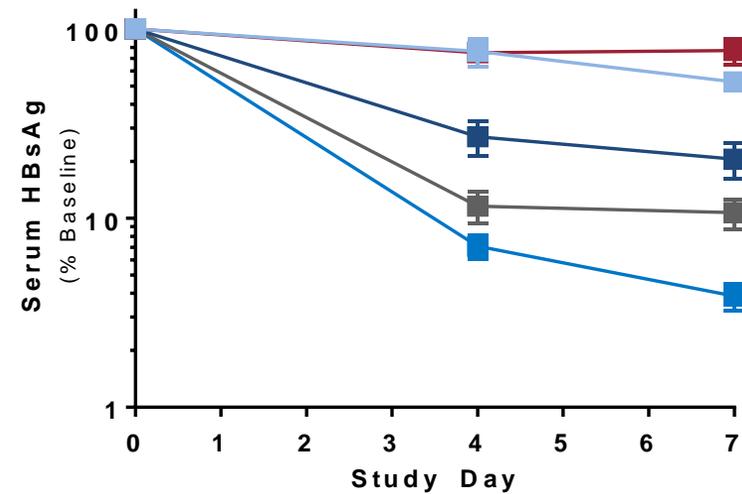
AB-729 also reduces HBV RNA, HBV DNA and e-antigen

# Small Molecule HBV RNA Destabilizers

HBV RNA reduction leads to interference in viral gene expression, DNA replication, and virion assembly

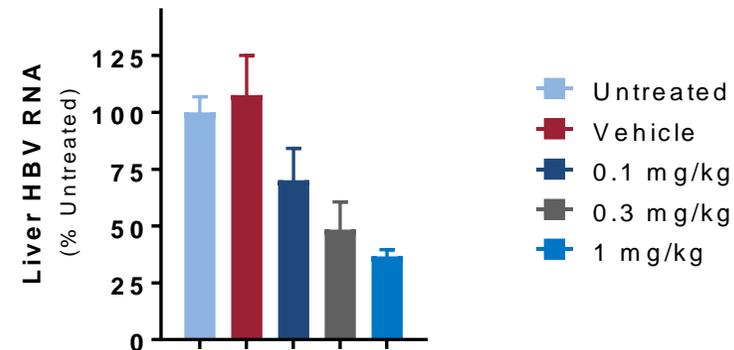


AAV mouse model  
PO dosing



Dose-dependent reduction in HBsAg

HBsAg reduction correlates with reductions in liver HBV RNAs



# AB-452 and RNA Destabilizer Program

## Multiple evaluations underway to support AB-452 and RNA destabilizer program next steps

### Completed

- ✓ IND enabling studies and 28 day toxicology
- ✓ AB-452 mechanism of action studies demonstrating AB-452 causes HBV mRNA poly A tail shortening
- ✓ Host protein knock out causes no cellular tox
- ✓ Host gene expression studies indicating that AB-452 has no detectable effect on host cell mRNAs

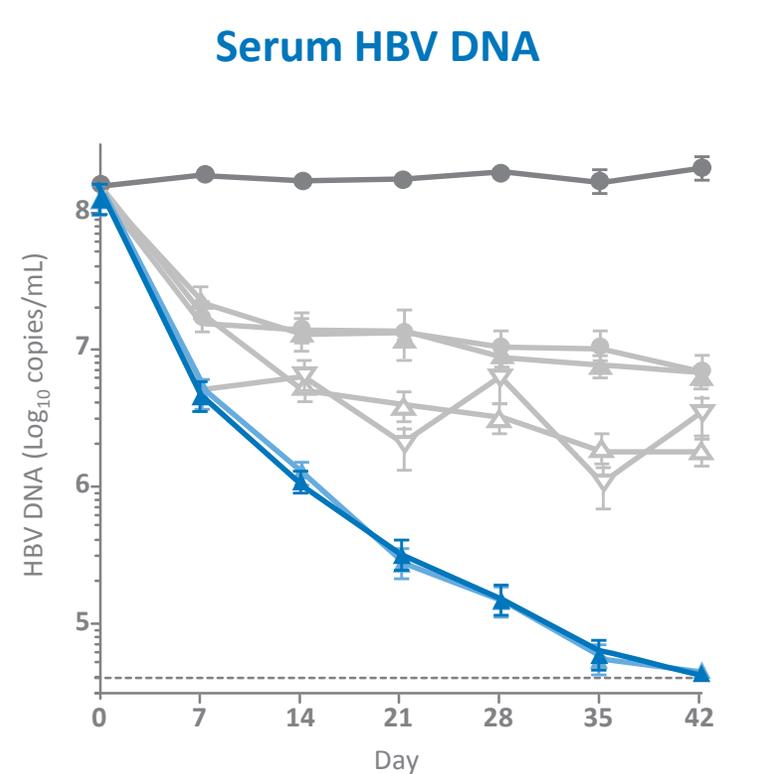
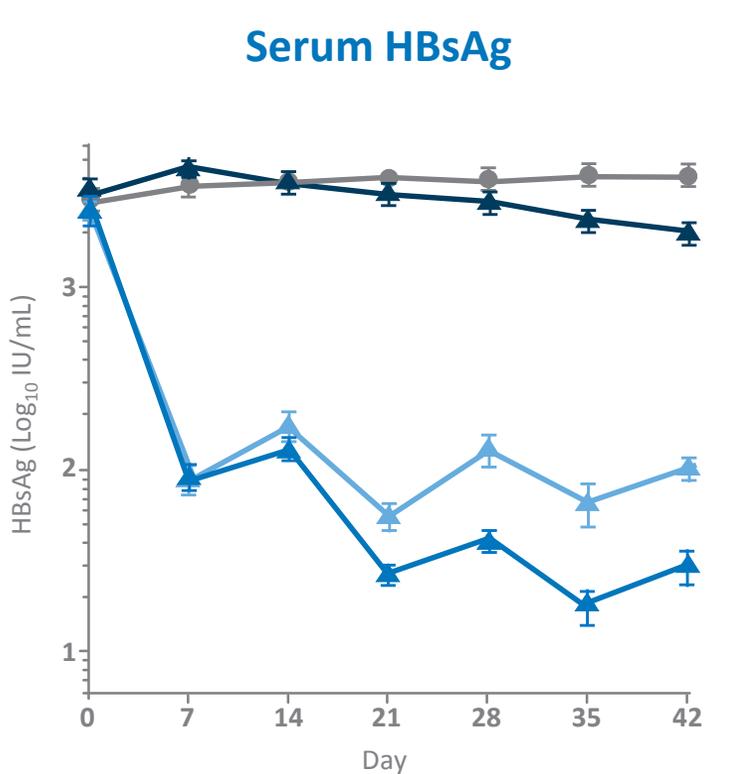
### Ongoing

- *In vitro* target engagement and target-based cell viability evaluations
- Additional, specialized *in vitro* and *in vivo* non-clinical safety assessments
- In depth DMPK evaluations
- 90 day toxicology studies, two species

Multiple small molecule chemotypes under investigation to **maximize program opportunity**

# Preclinical Combination In **Humanized Mouse Model**

RNAi + Capsid inhibitor containing regimens result in HBV DNA and HBsAg reductions



### Treatment for 6 weeks

|                  | Dosage    | Route | Frequency |
|------------------|-----------|-------|-----------|
| Capsid Inhibitor | 100 mg/kg | PO    | BID       |
| ETV              | 1.2 µg/kg | PO    | QD        |
| PegIFN           | 30 µg/kg  | SQ    | 2x/wk     |
| RNAi             | 3 mg/kg   | IV    | biweekly  |

### Key

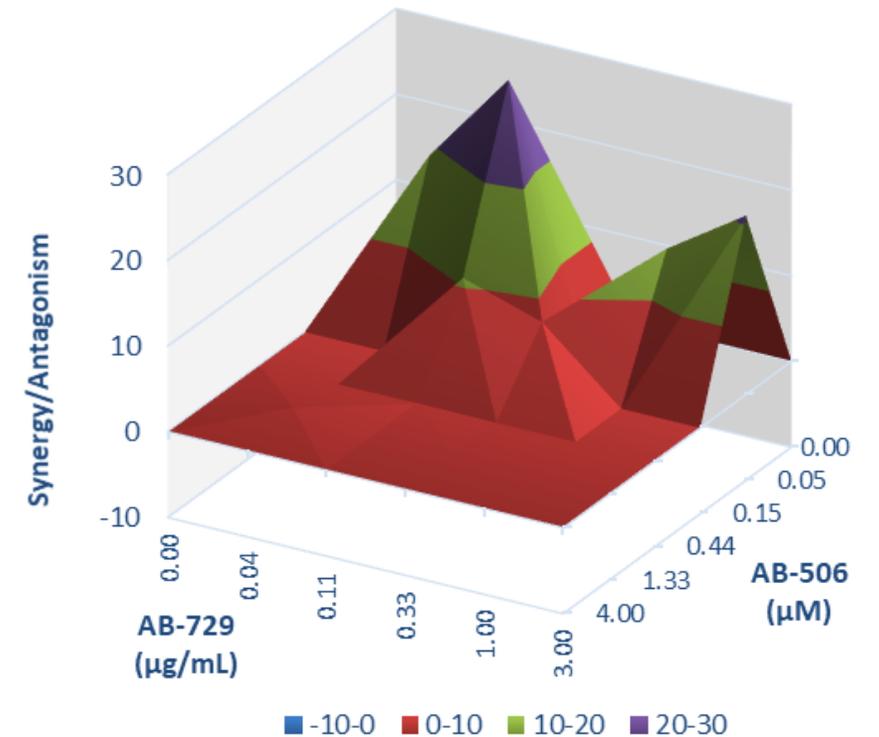
- ▲ RNAi + Capsid Inhibitor + ETV
- ▲ RNAi + Capsid Inhibitor + PegIFN
- Vehicle
- ▲ Capsid Inhibitor + PegIFN

# Drug Combination Analysis of AB-506 + AB-729

Capsid Inhibitor + Antigen Inhibitor

| Assayed Marker | Inhibitor A            | Inhibitor A EC <sub>50</sub> | AB-729 EC <sub>50</sub> (µg/mL) | Synergy Volume (%) | Antagonism Volume (%) | Conclusion                   |
|----------------|------------------------|------------------------------|---------------------------------|--------------------|-----------------------|------------------------------|
| HBV-DNA        | TAF (µM)               | 0.08                         | <0.12                           | 88.42, 2.46        | -1.1, -2.33           | Additive to Moderate Synergy |
| HBsAg          |                        | 4.12                         | <0.12                           | 0, 0               | -2.46, -1.74          | Additive                     |
| HBV-DNA        | PegIFN-alpha2a (IU/mL) | 1.19                         | <0.12                           | 0, 8.59            | -15.53, -0.19         | Additive                     |
| HBsAg          |                        | 12.91                        | <0.12                           | 0, 0.02            | 0, -2.74              | Additive                     |
| HBV-DNA        | AB-506 (µM)            | 0.08                         | <0.12                           | 106.05, 17.24      | 0, 0                  | Additive to Strong Synergy   |
| HBsAg          |                        | >4.00                        | <0.12                           | 2.33, 0            | 0, 0                  | Additive                     |
| HBV-DNA        | AB-452 (µM)            | 0.01                         | <0.12                           | 45.01, 4.55        | 0, 0                  | Additive to Minor Synergy    |
| HBsAg          |                        | 0.01                         | <0.12                           | 0, 0               | -22.78, -16.16        | Additive                     |

## Serum HBV DNA



# Key Catalysts for 2H 2019 - 2020

2H 2019



**AB-729**  
Initiation  
of Phase  
1 study



**AB-506**  
Preliminary  
Phase  
1a/1b data

**AB-506**  
28 day healthy  
volunteer  
study results

2020

**AB-729**  
Preliminary  
Phase 1a/1b  
data

**AB-506**  
Final Phase  
1b data

**Combination  
Proof-of-  
Concept  
Clinical Trial**  
AB-729 +  
AB-506  
w/ NA in  
HBV pts