Arbutus BIOPHARMA

Curing Chronic Hepatitis B

Update on AB-729 and AB-836, an siRNA and capsid inhibitor currently in development for the treatment of chronic hepatitis B infection

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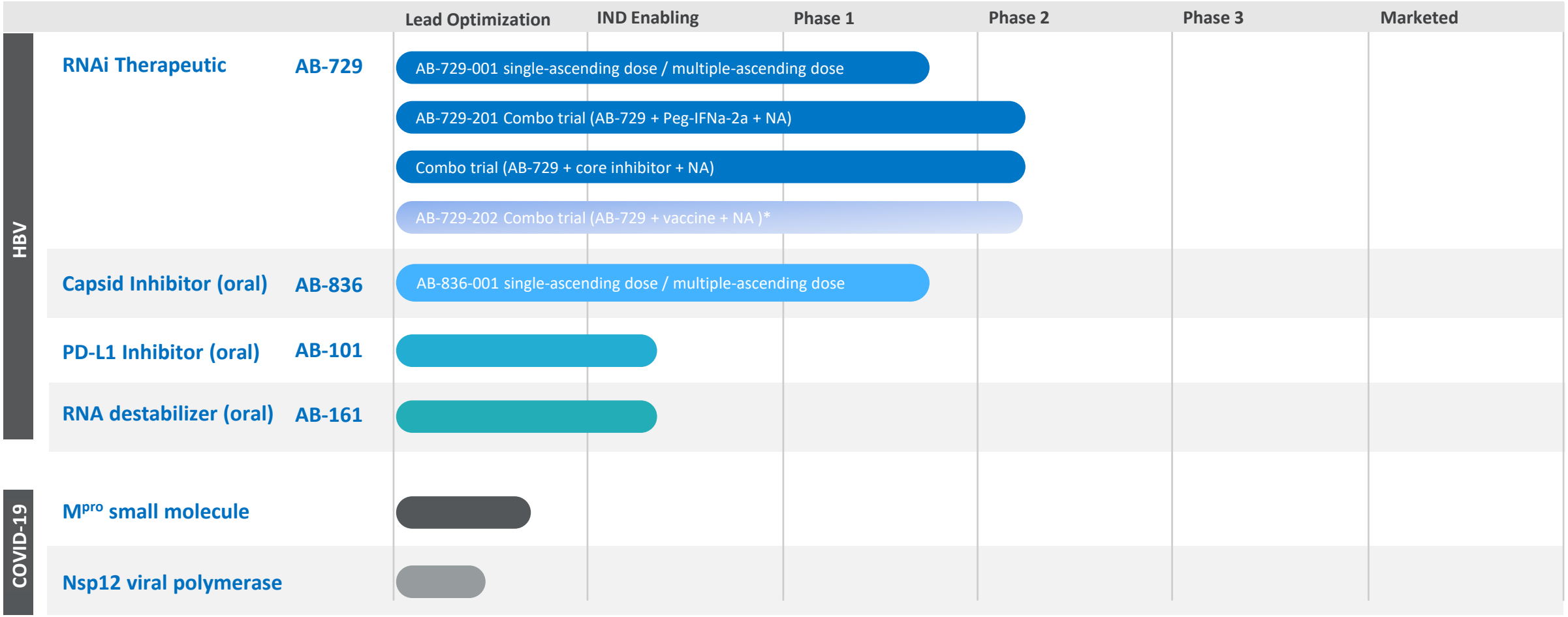
Singapore HBV Cure Meeting

June 1, 2022

Broad Pipeline



*Clinical trial expected to initiate in 1H 2022

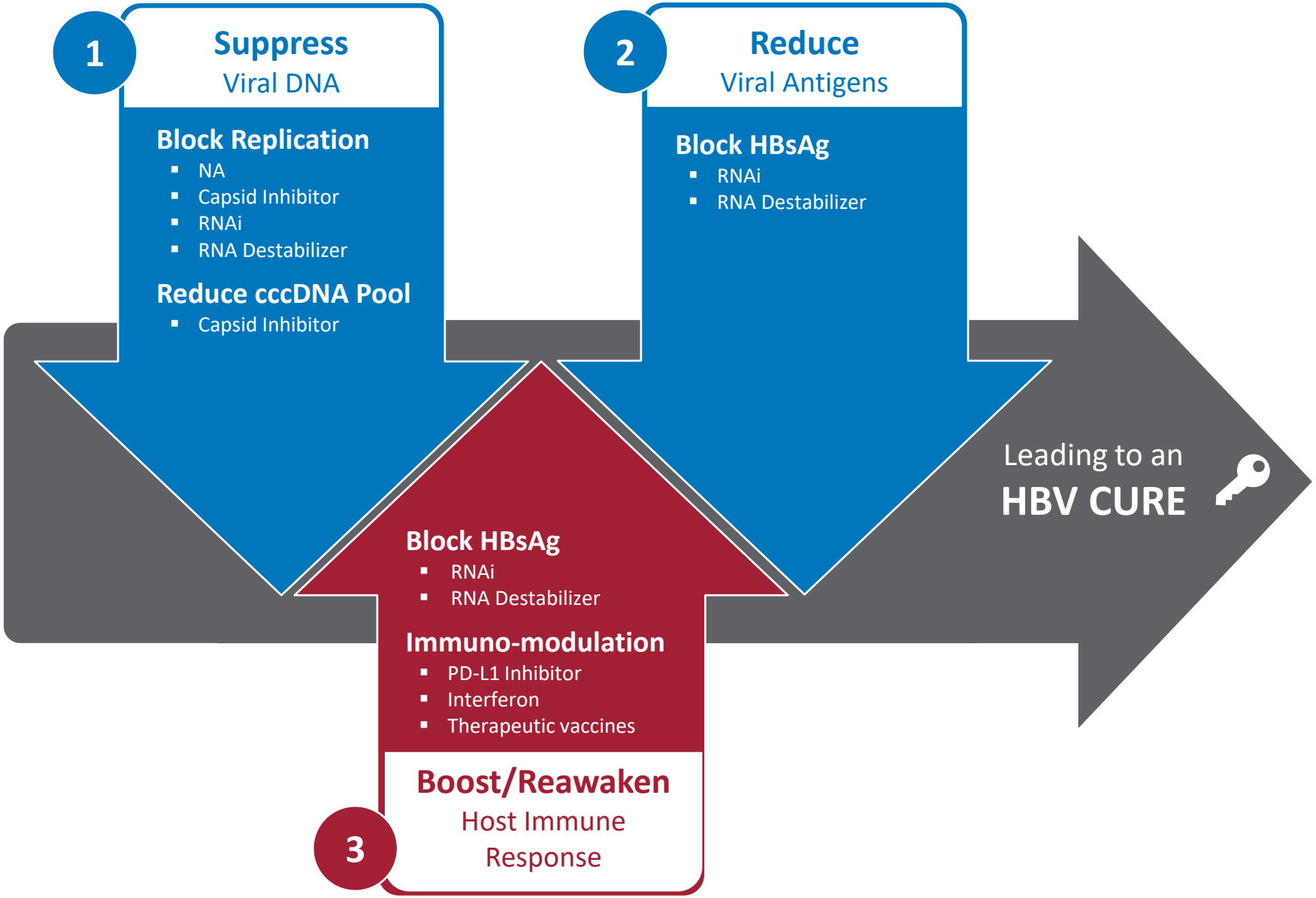
3-Pronged Approach to Therapeutic Success

Suppress HBV DNA

Reduce viral antigens

Boost host immune response

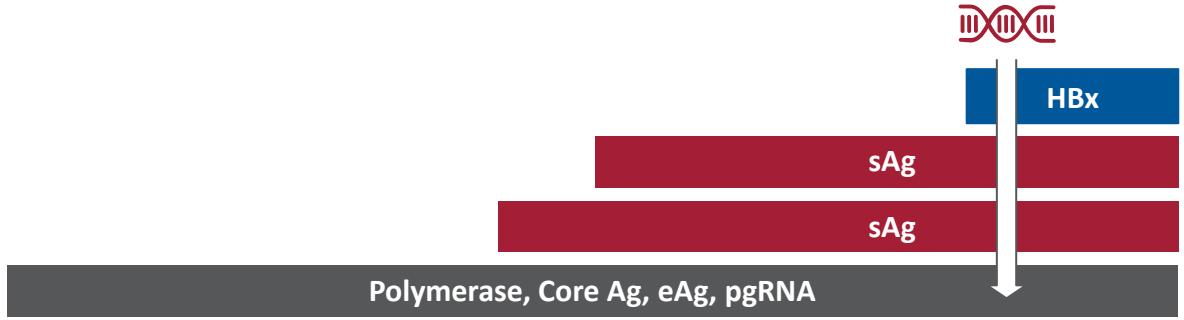
Therapeutic success will **require a combination of agents** with complementary MOAs



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
- Pan-genotypic activity across HBV genotypes
- Demonstrated complementarity with capsid inhibitors
- Actively targets the liver
- Active against cccDNA derived and integrated HBsAg transcripts
- Clean profile in long term preclinical safety studies



AB-729-001 Phase 1a/1b Clinical Trial

Part 1 & 2: Single-ascending dose

AB-729 monotherapy (90mg single-dose) resulted in robust HBsAg and HBV DNA declines in HBV DNA+ patients

Part 3: Multiple Doses In cHBV Patients - Ongoing

- **E: 60mg Q4W HBV DNA-**
- **F: 60mg Q8W HBV DNA-**
- **G: 90mg Q8W + TDF HBV DNA+**
- **I: 90mg Q8W HBV DNA-**
- **J: 90mg Q12W HBV DNA-**
- **K: 90mg Q8W HBV DNA-, HBeAg+ only**

Baseline Measure[#]	HBV DNA-				HBV DNA+
	Cohort E[‡] (N=7)	Cohort F (N=7)	Cohort I (N=6)[^]	Cohort J (N=7)	Cohort G (N=7)
Age in years, mean (range)	45.1 (33 – 63)	44.0 (31 – 59)	45.7 (38 – 54)	44.3 (35 – 61)	43.9 (34 – 50)
Male gender, n (%)	4 (57%)	4 (57%)	4 (67%)	5 (71%)	3 (43%)
BMI, mean (SD)	27.7 (5.0)	23.7 (2.2)	25.5 (3.1)	28.7 (4.8)	23.8 (4.0)
Race, n (%)					
Asian	1 (14%)	5 (71%)	5 (83%)	4 (57%)	6 (86%)
Black	0	1 (14%)	0	0	0
White	6 (86%)	1 (14%)	1 (17%)	3 (43%)	1 (14%)
ALT (U/L), mean (SD)	22.4 (10.5)	23.4 (15.2)	26.0 (10.2)	20.1 (7.2)	32.7 (15.8)
HBV eAg negative, n (%)	7 (100%)	6 (71%)[◊]	5 (83%)	4 (57%)	7 (100%)
HBsAg (IU/mL), mean (range)	5,372 (584 – 11,761)	5,354 (667 – 18,605)	4,691 (338 – 19,017)	6,911 (309 – 25,345)	1,818 (277 – 4,723)

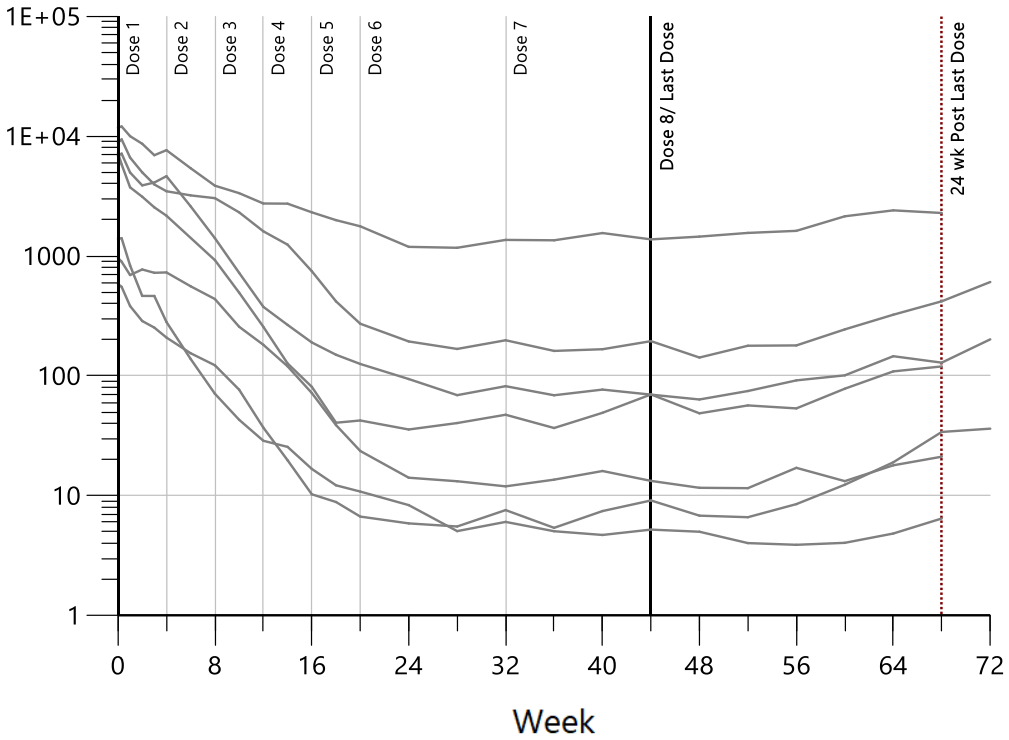
[#] Genotype not determined; [‡] Subjects switched to AB-729 60 mg Q12W for the extension phase; ^ N = 6 due to one subject meeting exclusion criteria on Day 1 and a replacement subject receiving an incorrect dose on Day 1; both entered follow up and were excluded from the analysis; [◊] One subject counted as HBeAg negative was identified as "HBeAg borderline" (baseline HBeAg = 0.18 IU/mL, LLOQ = 0.11 IU/mL)

HBsAg Suppression at levels <100 IU/mL Maintained up to 28 Weeks off AB-729 Treatment

Cohort E

AB-729 60mg every 4 Wks[+]

HBV DNA- patients

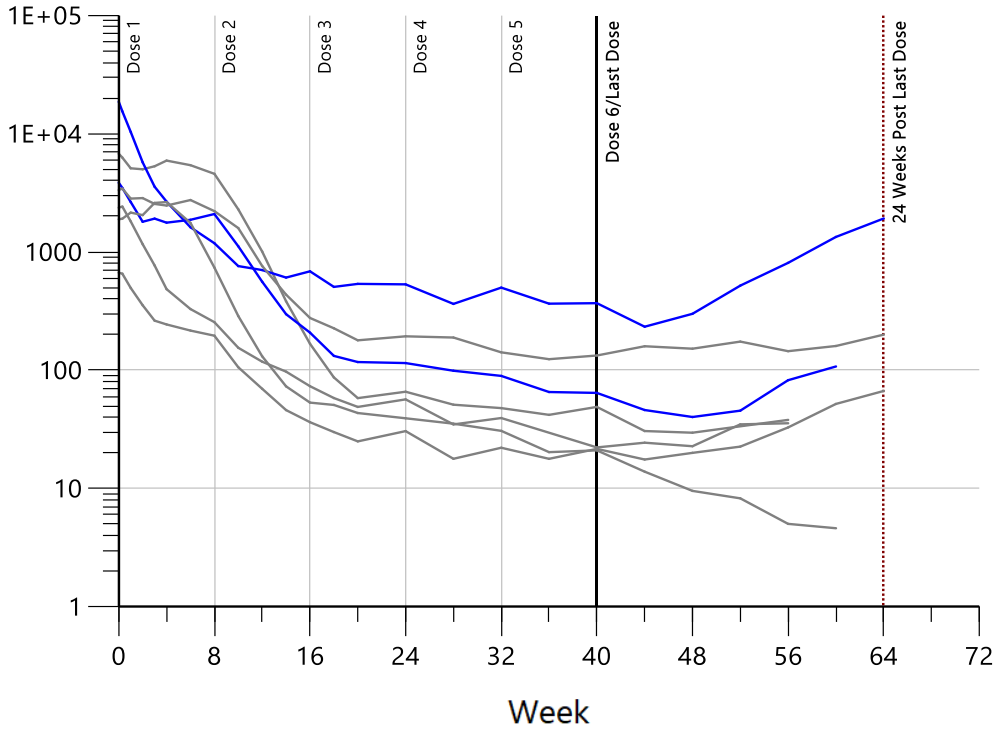


HBV DNA-		
Visit	Cohort E 60mg Q4W[ǂ] (n=7)	Cohort F 60mg Q8W (n=7)
Baseline	3.51 (0.20)	3.53 (0.17)
Week 12	-1.10 (0.15)	-1.02 (0.11)
Week 24	-1.84 (0.16)	-1.57 (0.09)
Week 40	-1.84 (0.19)	-1.78 (0.10)
Week 44	-1.81 (0.17)	-1.88 (0.13)
Week 48	-1.89 (0.18)	-1.90 (0.14)
Off Treatment (# weeks post last dose)		
Week 16	-1.74 (0.20)	-1.76 (0.19)
Week 20	-1.61 (0.20)	-1.55* (0.28)
Week 24	-1.54 (0.19)	---

Cohort F

AB-729 60mg every 8 Wks

HBV DNA- patients

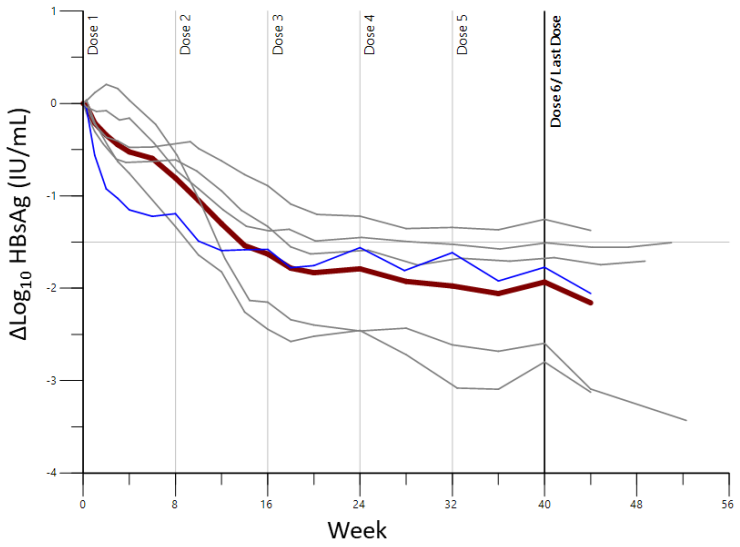


[+] patients switched to AB-729 60 mg Q12W after Week 20 dose

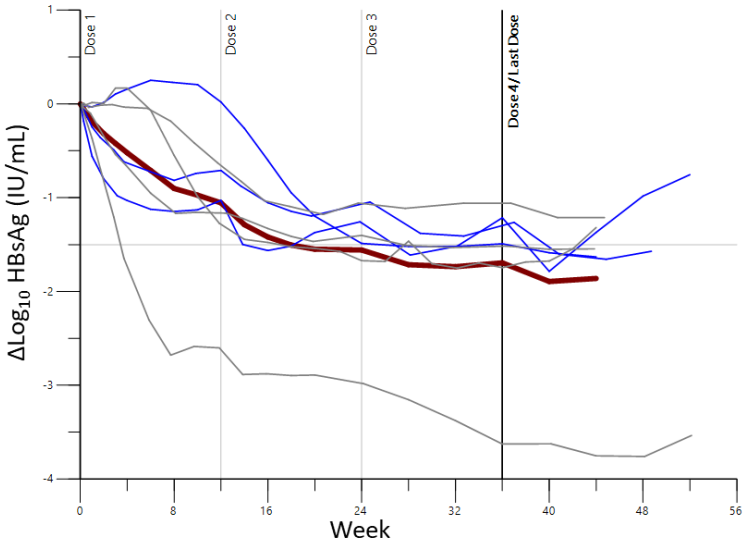
*Data presented at AASLD 2021

AB-729 dosed at 90mg Q8W or Q12W Reduces HBsAg in both DNA- and DNA+ Patients

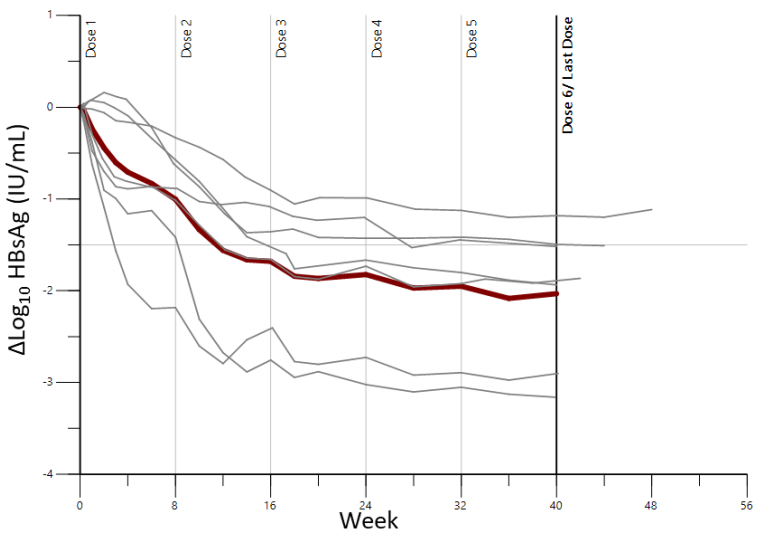
Cohort I: 90mg Q8W DNA- (n=6)
6/6 < 100 IU/mL*



Cohort J: 90mg Q12W DNA- (n=7)
4/7 < 100 IU/mL*



Cohort G: 90mg Q8W DNA+ (n=7)
5/7 < 100 IU/mL*



*at time of last visit

Mean
Individual HBeAg-
Individual HBeAg+

Key Findings:

- The magnitude of HBsAg suppression (1.8-2.0 log reduction at wk 40) was similar across both dosing intervals
- Some patients achieved HBsAg <100 IU/mL
- HBsAg reduction is sustained over time

Mean (SE) Baseline HBsAg Response Similar Regardless of AB-729 Dose and Dosing Intervals to Date

	HBV DNA-				HBV DNA+
Visit	Cohort E 60mg Q4W‡ (n=7)	Cohort F 60mg Q8W (n=7)	Cohort I 90mg Q8W (n=6)	Cohort J 90mg Q12W (n=7)	Cohort G 90mg Q8W (n=7)
Baseline	3.51 (0.20)	3.53 (0.17)	3.36 (0.23)	3.37 (0.28)	3.14 (0.14)
Week 12	-1.10 (0.15)	-1.02 (0.11)	-1.30 (0.19)	-1.06 (0.31)	-1.56 (0.32)
Week 24	-1.84 (0.16)	-1.57 (0.09)	-1.79 (0.22)	-1.56 (0.25)	-1.82# (0.29)
Week 40	-1.84 (0.19)	-1.78 (0.10)	-1.93 (0.25)	-1.89^ (0.35)	-2.03+ (0.33)
Week 44	-1.81 (0.17)	-1.88 (0.13)	-2.16 (0.31)	-1.86^ (0.38)	---
Week 48	-1.89 (0.18)	-1.90 (0.14)	---	---	---
Off Treatment (# weeks post last dose)					
Week 16	-1.74 (0.20)	-1.76 (0.19)	---	---	---
Week 20	-1.61 (0.20)	-1.55* (0.28)	---	---	---
Week 24	-1.54 (0.19)	---	---	---	---

NOTE: Mean (SE) values presented only if n>3; there are no statistically significant differences between cohorts (data not shown); *n=5; ^n=6, one patient in Cohort J chose not to extend treatment; #6 of 7 patients had HBV DNA <LLOQ by Week 8, the 7th patient became <LLOQ at Week 16; +n=6
Data Presented at AASLD 2021

AB-729-001 Safety Summary

- **AB-729 generally safe and well-tolerated after single and repeat doses**
- **No treatment-related SAEs or discontinuations due to AEs**
- **No treatment-related Grade 3 or 4 AEs***
- **No treatment-related Grade 3 or 4 laboratory abnormalities***
  - Grade 1 and Grade 2 ALT elevations have improved or stabilized with continued treatment
- **Injection site TEAEs were mostly mild (erythema, pain, bruising, pruritis)**
- **No clinically meaningful changes in ECGs or vital signs**

* 1 patient (Cohort A) with rapid decline in HBsAg of ~2.0 log10 IU/mL had an unrelated Gr 2 AE of food poisoning resulting in unrelated transient Grade 3 AEs of ALT/AST elevation (without bilirubin changes)

AB-729-001 Clinical Trial Key Takeaways

- **AB-729 dosed 60mg every 4 wks and every 8 wks and 90mg every 8 wks and 12 wks resulted in robust and comparable HBsAg declines**
  - AB-729 monotherapy (90mg single-dose) resulted in robust HBsAg and HBV DNA declines in HBV DNA + patients
- **Long-term dosing with AB-729 resulted in 74% of patients reaching <100 IU/mL of HBsAg, a clinically relevant threshold which could inform when to stop all therapies**
  - HBsAg suppression at levels of <100 IU/mL maintained up to 28 weeks off AB-729 treatment
- **Preliminary data suggest that long-term suppression of HBsAg with AB-729 results in increased HBV-specific immune response***
- **AB-729 was safe and well-tolerated through 40-48 weeks of dosing**

*Data presented at EASL 2021

AB-836

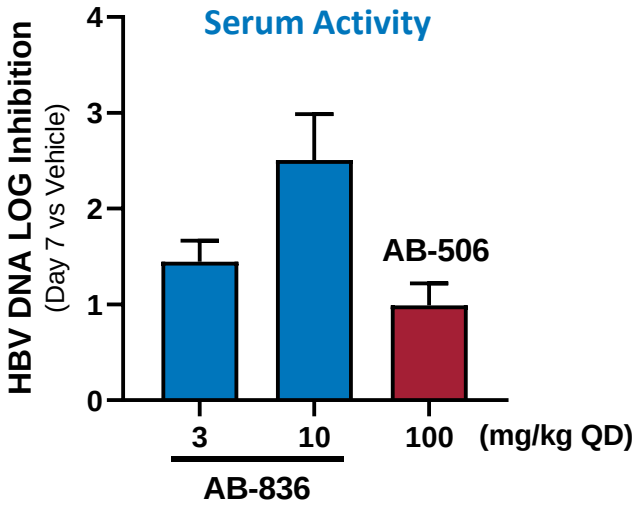
Next Generation Capsid Inhibitor

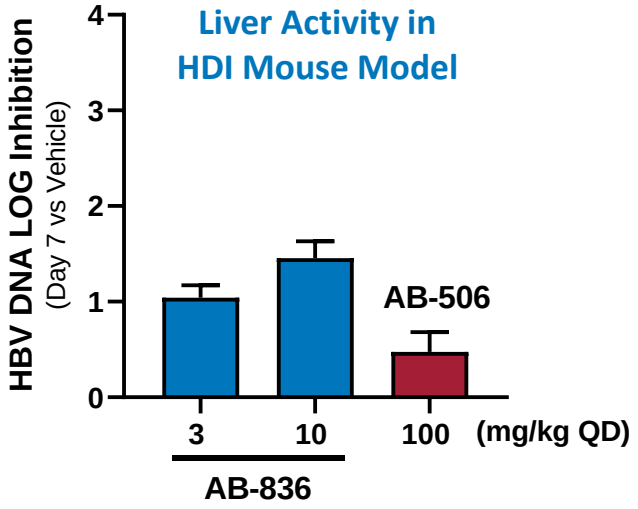
Potential for increased efficacy and enhanced resistance profile relative to earlier generation capsid inhibitors

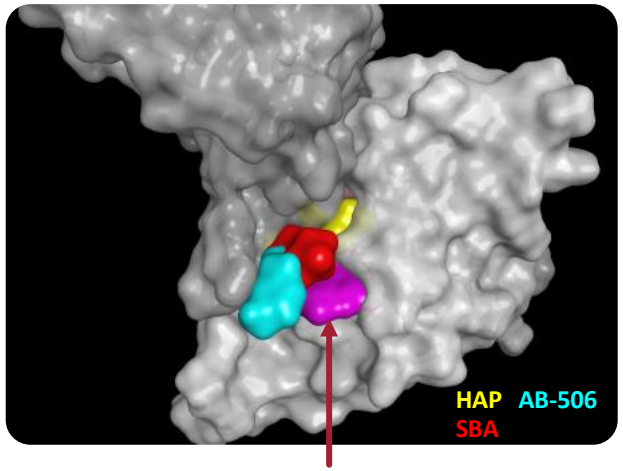
- Novel chemical series differentiated from AB-506 and other competitor compounds in the Class II capsid inhibitor space
- Leverages a novel binding site within the core protein dimer-dimer interface
- Improved intrinsic potency with EC50 $\leq$ 10 nM
- Active against NA-resistant variants
- Potential to address known capsid resistant variants T33N and I105T
- Provides the potential for low dose and wide therapeutic window
- Demonstrates high liver concentrations in multiple species
- Once daily dosing
- Pan-genotypic
- Combinable with other MOA agents

AB-836: Next Generation Capsid Inhibitor

	HBV DNA / 1° Mechanism				cccDNA Formation / 2° Mechanism	Human Serum Shift
Compound	HepDE19 (EC_{50} µM)	HBV infected PHH (EC_{50} µM)	HBV infected HepG2-NTCP-C4 (EC_{50} µM)	Core I105T Mutation (EC_{50} µM)	HBV infected HepG2-NTCP-C4 (HBsAg EC_{50} µM)	(FC in EC_{50} in 40% Human Serum)
AB-506	0.077	0.032	0.101	1.26	1.430	6x
AB-836	0.010	0.002	0.012	0.118	0.196	2x







Unique Binding Site

HAP: Heteroaryldihydropyrimidine | **SBA:** Sulfamoylbenzamide I **PHH:** Primary Human Hepatocytes

AB-836-001 Phase 1a/1b Clinical Trial

Part 1: Single Ascending Dose In Healthy Subjects

Alternating Cohorts A and B
n=8/cohort; 6 active: 2 placebo

Cohort A

- ✓ Dose 1 10mg
- ✓ Dose 3 75mg
- ✓ Dose 5 175mg

Cohort B

- ✓ Dose 2 30mg
- ✓ Dose 4 125mg
- ✓ Dose 5 FE 125mg

Part 2: Multiple Ascending Dose in Healthy Subjects

- Cohort C (50mg QD) x 10 days ✓
  N = 10; 8 active: 2 placebo
- Cohort D (100mg QD) x 10 days ✓
  N = 10; 8 active: 2 placebo
- Cohort E (150mg QD) x 10 days ✓
  N = 10; 8 active: 2 placebo

Part 3: Multiple Doses In Chronic Hepatitis B Patients

- Cohort F 50 mg QD x 28 days DNA + *
  N = 12; 10 active: 2 placebo
- Cohort G 100 mg QD x 28 days DNA+ *
  N = 12; 10 active: 2 placebo
- Cohort H 200 mg QD x 28 days DNA+ *
  N = 12; 10 active: 2 placebo
- Cohort I (Dose TBD) + NA x 28 days DNA-
  N = 12; 10 active: 2 placebo
- Cohort J (Dose TBD) + TDF x 28 days DNA+
  N = 12; 10 active: 2 placebo

FE: with Food

* ongoing

AB-836 Phase 1a/1b Clinical Trial Preliminary Data

Parts 1 & 2: Single and multi-doses of AB-836 in healthy subjects

- **Safety:**
  - No deaths or SAEs
  - 1 subject (50mg once daily) discontinued on day 13 due to AE of agitation
  - All but 3 AEs were mild (Grade 2 headache, agitation and bronchitis), one assessed as drug related (Grade 1 rash)
  - No clinically significant abnormalities in clinical laboratory tests, ECGs, vital signs or physical exams noted.

Part 3: 50mg and 100mg of AB-836 once daily for 28 days in patients with cHBV

- **Safety:**
  - No deaths or AEs
  - 1 patient had transient increase in ALT from baseline Grade 1 to Grade 3 that resolved with continued dosing
  - No clinical abnormalities in ECGs, vital signs or physical exams
- **Efficacy (Cohort G - 100 mg QD):**
  - Provides robust antiviral activity - mean (SE) $\log_{10}$ change from baseline of -3.1 (0.5) at Day 28 (n=4)

Part 3 of the trial continues to enroll patients

Thank You

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