

Curing Chronic Hepatitis B

Corporate Presentation

January 24, 2022

NASDAQ: ABUS

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 market opportunity for HBV; Arbutus' ability to meet a significant unmet medical need; the sufficiency of Arbutus' cash and cash equivalents for the anticipated durations; the expected cost, timing and results of Arbutus' clinical development plans and clinical trials, including its clinical collaborations with third parties; the potential for Arbutus' product candidates to achieve their desired or anticipated outcomes; Arbutus' expectations regarding the timing and clinical development of Arbutus' product candidates, including its articulated clinical objectives; the timeline to a combination cure for HBV; Arbutus' coronavirus strategy; Arbutus' expectations regarding its technology licensed to third parties; the expected timing and payments associated with strategic and/or licensing agreements; and other statements relating to Arbutus' future operations, future financial condition, prospects or other future events.

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 including uncertainties and contingencies related to the ongoing COVID-19 pandemic. 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; changes in Arbutus' strategy regarding its product candidates and clinical development activities; Arbutus may not receive the necessary regulatory approvals for the clinical development of Arbutus' products; economic and market conditions may worsen; market shifts may require a change in strategic focus; the parties may never realize the expected benefits of the collaborations; and the ongoing COVID-19 pandemic could significantly disrupt Arbutus' clinical development programs. A more complete discussion of the risks and uncertainties facing Arbutus appears in Arbutus' Annual Report on Form 10-K, Quarterly Report on Form 10-Q and Arbutus' periodic disclosure filings which are available at www.sec.gov and at www.seclar.com. All forward-looking statements



Investment Highlights

Significant
Unmet
Medical
Need in HBV

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

Goal of HBV Functional Cure

Undetectable HBV
DNA and HBsAg
delivered through
finite duration
treatment with a
combination of
drugs with different
modes of action

Broad HBV Portfolio

HBV compounds include:

RNAi

Capsid Inhibitors

PD-L1 Inhibitors

HBV RNA
Destabilizer

Coronavirus Research Initiative

Focused on direct acting antivirals targeting the viral polymerase and protease

Team with
Antiviral
Expertise &
Proven Track
Record

Extensive
knowledge gained
from HIV and HCV
success being
applied to
HBV and
Coronaviruses

16 % Ownership in Genevant

Rights to potential future royalties and sublicense revenues for patented LNP Technology



Proven Leadership Team

Successful track records in the discovery, development, and commercialization of multiple antivirals including 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



ARQULE





Elizabeth Howard, PhD, JD

EVP, General Counsel and Chief Compliance Officer





Michael J. McElhaugh

Chief Business Officer

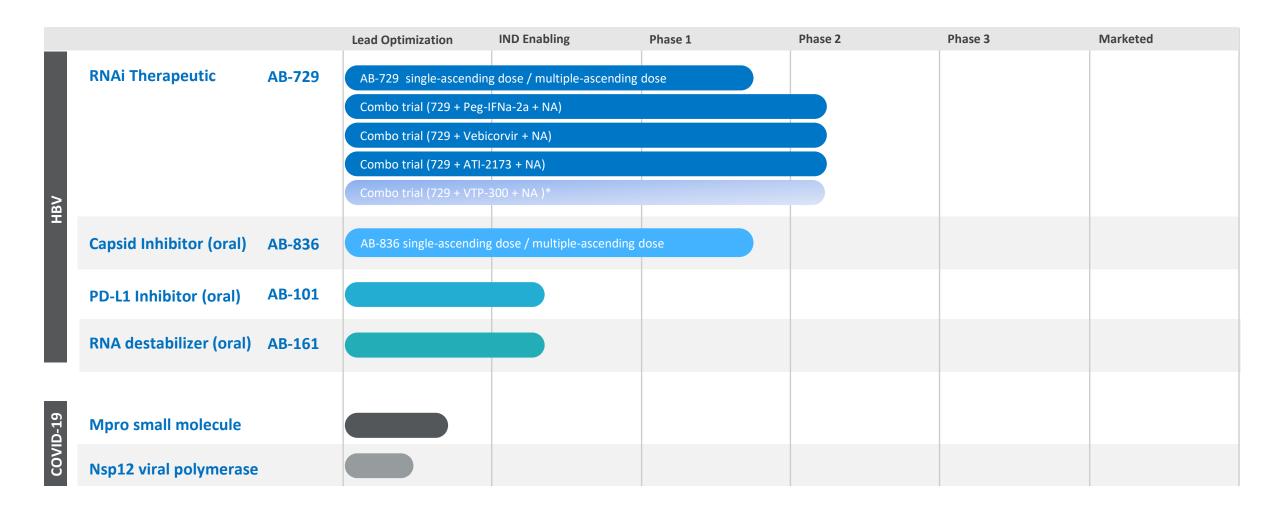


Bristol-Myers Squibb





Pipeline





*Clinical trial to initiate in 1H 2022

HBV Presents a Significant Unmet Medical Need

>257M

people are chronically infected with HBV, globally.

2M United States EU 15M Europe

E Mediterranean SE Asia 39M

African 60M

115M

~900k

people die every year as a consequence despite the availability of effective vaccines and antivirals.



90M

China

Significant Opportunity

to Improve HBV Cure Rates

HBV cures are achievable with today's SOC in <5% of patients.

Sustained HBsAg and HBV DNA loss after end-of-treatment* is rare.

*undetectable HBsAg and HBV DNA 6 months after end-of-treatment accepted as a functional cure.

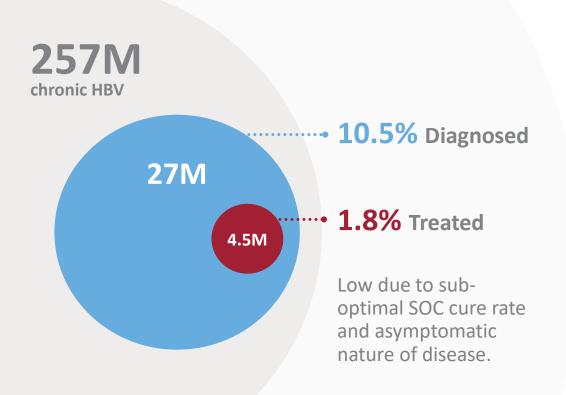
STANDARD OF CARE THERAPIES FOR CHRONIC HBV

	PegIFN	Entecavir	Tenofovir	Therapies
Dosing Duration	48-weeks	Chronic	Chronic	rate of Undetectable HBV DNA
HBV DNA Undetectable (<60-80 IU/ml)	7-19%	67-90%	76-93%	rate of HBsAg Loss
HBsAg Loss	~3-7%	~1-2%	~1-3%	HIGHER CURES RATES

Achievable HBV Cure Rates with Current SOC

New HBV

Compelling Growth Opportunity in the HBV Market



An HBV curative regimen

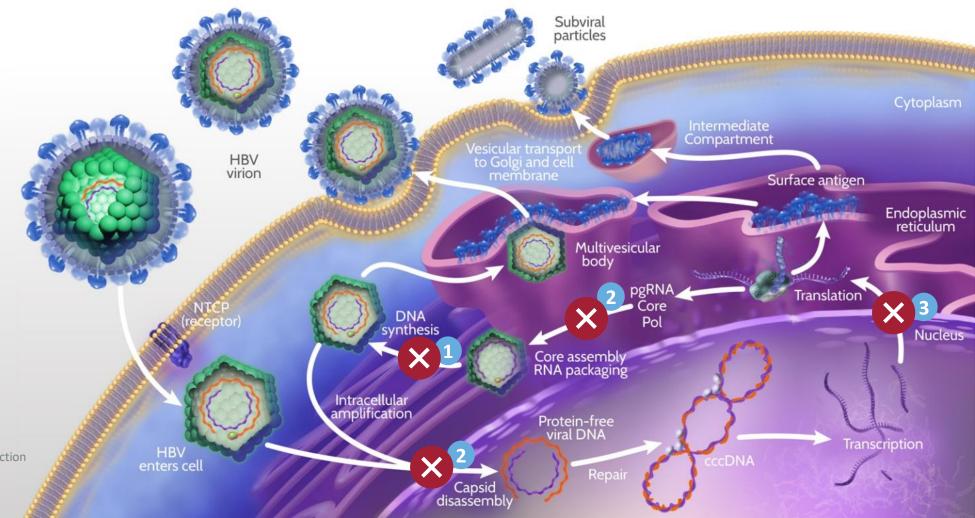
would substantially increase diagnosis and treatment rates to unlock significant market growth opportunities.



A Combination of Agents with Complementary MOA is Needed for HBV Cure

HBV lifecycle illustrates key points for intervention

- 1. Nucleoside Analogue
- 2. Capsid Inhibitor
- 3. RNAi & RNA Destabilizer





MOA: Mechanism of Action

DUTUS NASDAQ: ABUS
BIOPHARMA www.arbutusbio.com

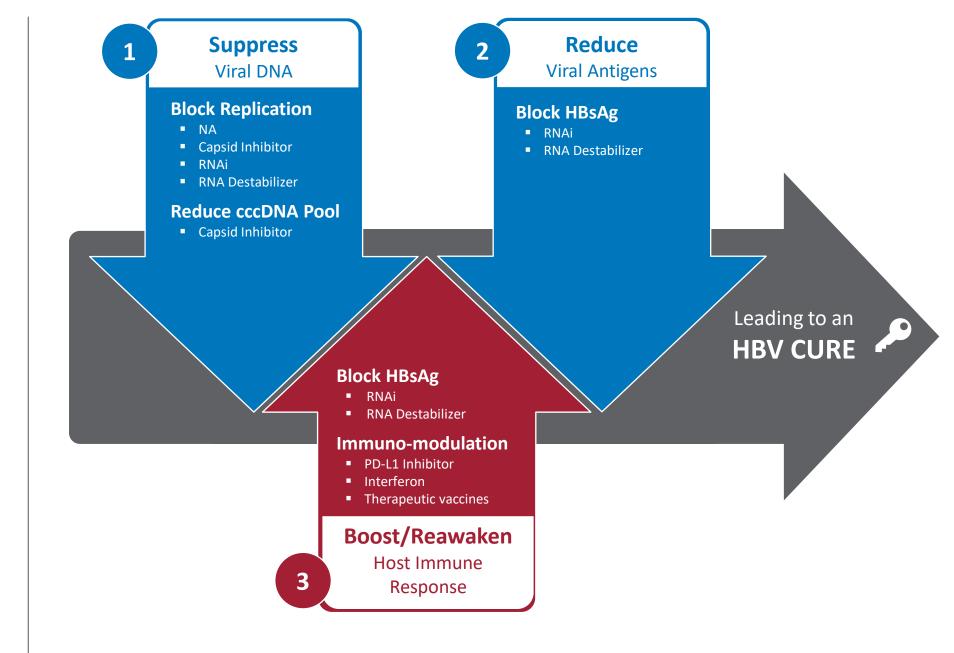
3-Pronged Approach to Therapeutic Success

Suppress viral antigens

Reduce HBV DNA

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

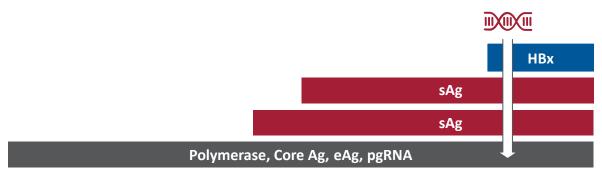
Pan-genotypic activity across HBV genotypes

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





Clinical Trial Key Takeaways

- Clinical data continues to support evaluating AB-729 60 mg every 8 weeks in Phase 2a combination trials
- 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 monotherapy (90 mg single-dose) resulted in robust HBsAg and HBV DNA declines in HBV DNA + patients
- AB-729 was safe and well-tolerated through 40-48 weeks of dosing



*Data presented at EASL 2021

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

Part 1 & 2: Single-Ascending Dose
Dosing Completed

	Healthy Subjects	cHBV Patients
Doses	60 mg / 180 mg / 360 mg	180 mg / 60 mg / 90 mg DNA-/ 90 mg DNA+
n=	6 per cohort	6 per cohort
Results	Up to 180 mg AB-729 was safe and well-tolerated	Single doses of AB-729 result in comparable mean HBsAg declines at week 12 followed by a sustained plateau phase

Part 3: Multiple Doses In cHBV Patients (n=7) - Ongoing

E: 60 mg Q4W HBV DNA -

F: 60 mg Q8W HBV DNA -

G: 90 mg Q8W + TDF HBV DNA +

I: 90 mg Q8W HBV DNA -

J: 90 mg Q12W HBV DNA -

K: 90 mg Q8W HBV DNA -, HBeAg+ only

Baseline Characteristics

	HBV DNA-				HBV DNA+
Baseline Measure#	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)



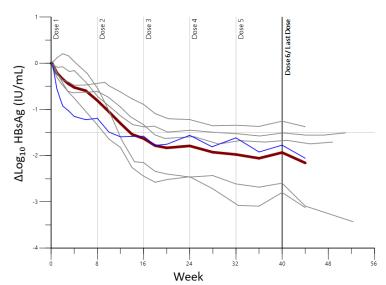
Mean (SE) Baseline HBsAg Response Similar Regardless of AB-729 Dose and Dosing Intervals to Date

	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 (# w	Off Treatment (# weeks post last dose)				
Week 16	-1.74 -1.76 (0.20) (0.19)				
Week 20	-1.61 (0.20)	-1.55* (0.28)			
Week 24	-1.54 (0.19)				



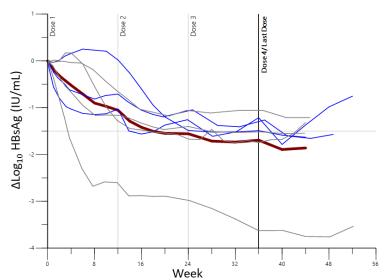
AB-729 dosed at 90mg Q8W or Q12W Reduces HBsAg in both DNA- and DNA+ Patients





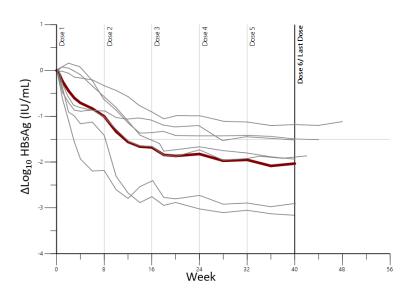
Cohort J: 90mg Q12W DNA- (n=7)





Cohort G: 90mg Q8W DNA+ (n=7)

5/7 < 100 IU/mL*



*at time of last visit

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

MeanIndividual HBeAg-Individual HBeAg+

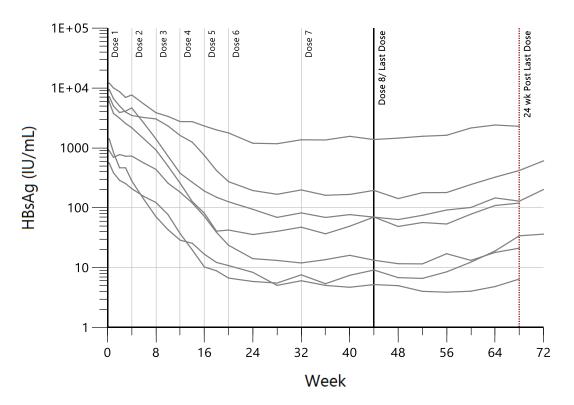


Data presented at AASLD 2021

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

Cohort E

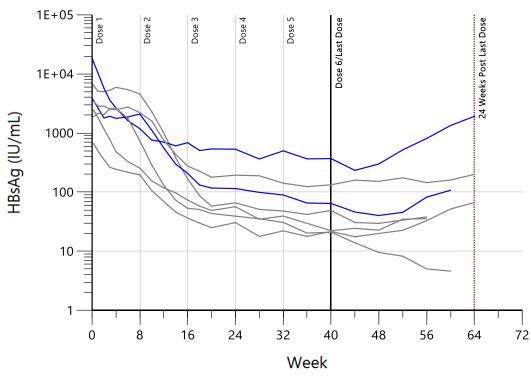
AB-729 60 mg every 4 Wks⁺ HBV DNA- patients



*Data presented at AASLD 2021

Cohort F

AB-729 60 mg every 8 Wks HBV DNA- patients





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
- All but 1 patient to date has consented to an additional 6 months of dosing in the Extension period



Next Steps – Combine AB-729 with Different Compounds in Phase 2a to Inform Future Clinical Trials

- Enrollment on-going in a Phase 2a combination trial with ongoing NA therapy and short courses of Peg-IFNα-2a in cHBV patients
- Three Phase 2a proof-of-concept clinical collaborations are on-going or expected to initiate shortly to accelerate key combination data
 - Assembly Biosciences, Inc. enrolling patients in Phase 2a
 - Antios Therapeutics, Inc. additional cohort with AB-729 added to clinical trial in 2H 2021
 - Vaccitech plc clinical trial expected to initiate in early 2022



Phase 2a POC Clinical Trial

AB-729 in combination with ongoing NA therapy and short courses of Peg-IFNα-2a in cHBV patients

n=40 stably NA-suppressed, HBeAg negative, non-cirrhotic cHBV patients

After a 24-week dosing period of AB-729 (60 mg every 8 weeks), patients will be randomized into one of 4 groups:

- A1: AB-729 + NA + weekly Peg-IFN α -2a for 24 weeks (n=12)
- A2: NA + weekly Peg-IFN α -2a for 24 weeks (n=12)
- B1: AB-729 + NA + weekly Peg-IFN α -2a for 12 weeks (n=8)
- B2: NA + weekly Peg-IFN α -2a for 12 weeks (n=8)

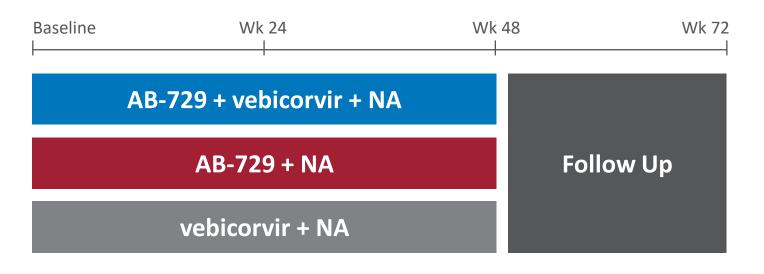
After completion of the assigned Peg-IFN α -2a treatment period, all patients will remain on NA therapy for the initial 24-week follow up period, and then will discontinue NA treatment if treatment stopping criteria are met



AB-729 Clinical Collaboration



Provides accelerated
AB-729 combination
proof-of-concept (POC)
with Assembly's capsid
inhibitor and a NA



Phase 2 clinical trial enrolling

n= ~60 virologically-suppressed patients with chronic HBV infection

Equal sharing of expertise and costs for this POC open-label trial



NA: Nucleoside Analogue 21

AB-729 Clinical Collaboration



POC Phase 2a clinical trial

Evaluating AB-729 in combination with Vaccitech's immunotherapeutic, VTP-300, and a NA

Evaluate safety, pharmacokinetics, immunogenicity and anti-viral activity of triple combination - AB-729, VTP-300 and an NA compared to double combinations of AB-729 with an NA and VTP-300 with an NA

Expected to initiate clinical trial in first half of 2022

Full rights retained by the Companies of their respective product candidates and all costs split equally

Assuming positive results parties intend to undertake a larger Phase 2b clinical trial



AB-729 Clinical Collaboration



POC Phase 2a clinical trial

AB-729 in combination with Antios' proprietary active site polymerase inhibitor nucleotide (ASPIN), ATI-2173, and a NA Evaluate AB-729, ATI-2173 and a NA in a single cohort in the ongoing Antios Phase 2a ANTT201 clinical trial

First patient dosed in December 2021

Trial cohort includes 10 patients with chronic HBV assigned 8:2 to active drug or matching placebos in combination with an NA

Antios responsible for costs and Arbutus responsible for supply of AB-729



AB-729 Strategic Collaboration



Exclusive Licensing* and Strategic Partnership

Develop, manufacture and commercialize AB-729 in mainland China, Hong Kong, Macau and Taiwan

*ABUS retains the non-exclusive right to develop and manufacture in the Qilu territory for exploiting AB-729 in the rest of the world Goal - to bring AB-729 to the largest HBV patient population and to tap into one of the largest and most promising healthcare markets worldwide

Arbutus has received \$40M upfront payment and \$15M equity investment, and is eligible for up to \$245M in commercialization and milestone payments and double-digit tiered royalties up to low twenties percent on annual sales

Qilu Pharmaceutical – one of the leading pharmaceutical companies in China, provides development, manufacturing and commercialization expertise to this partnership

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 ≤ 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

Projected to be once daily dosing

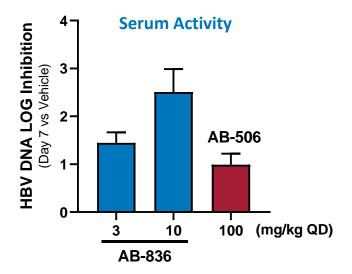
Pan-genotypic

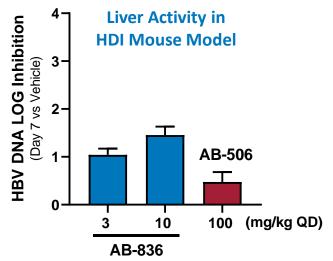
Combinable with other MOA agents

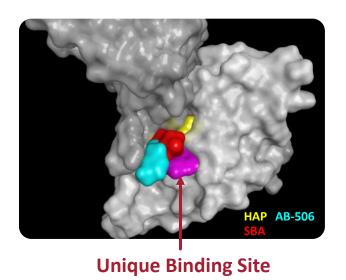


AB-836: Next Generation Capsid Inhibitor

		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









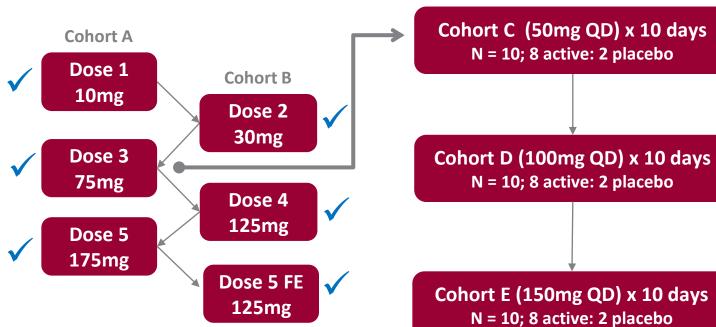
AB-836-001 Phase 1a/1b Clinical Trial

Part 1: Single Ascending
Dose In Healthy Subjects

Part 2: Multiple Ascending Dose in Healthy Subjects

Part 3: Multiple Doses In Chronic Hepatitis B Patients

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



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



*

*

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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) log10 change from baseline of -3.1 (0.5) at Day 28 (n=4)



AB-161: Next Generation Oral RNA Destabilizer

Next generation small molecule that circumvents non-clinical safety findings with first generation molecule Offers a novel
mechanism of action
to reduce HBsAg and
other viral proteins and
viral RNA

We believe
this approach offers
potential for an **oral HBsAg reducing agent**and all oral combination
therapy



AB-101: Oral PD-L1 Inhibitor for HBV Immune Reactivation

Rationale

- HBV immune tolerance is a critical driver of cHBV infection
- PD-1:PD-L1 checkpoint axis plays a key role in immune tolerization in cHBV
- PD-L1 expression upregulated during HBV infection
- PD-1 upregulated on HBVspecific T- and B-cells
- Inhibition associated with HBsAg loss in some cHBV patients

Small-Molecule Inhibitor Approach

- Allows controlled checkpoint blockade
- Enables oral dosing
- Designed to reduce systemic safety issues seen with Abs

AB-101

- Blocks PD-L1/PD1 interaction at sub-nM concentrations
- Activates HBV-specific immune responses in T-cells from CHB patients in <u>vitro</u>
- Novel MOA identified
- Demonstrates a robust checkpoint mediated in vivo effect
- Improves HBV-specific T- and B-cell responses ex vivo

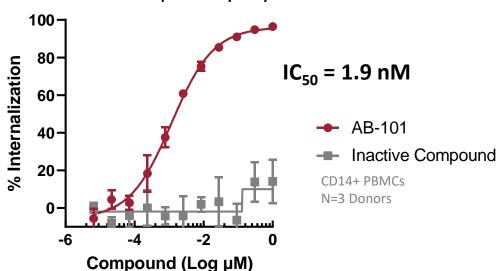
AB-101 is currently in IND-enabling studies



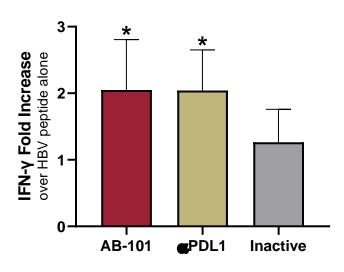
AB-101: Small-Molecule Oral PD-L1 Inhibitor for HBV

AB-101 is highly potent with demonstrated activity against cells from chronic HBV patients

AB-101 reduces PD-L1 on the surface of human primary myeloid cells



AB-101 reinvigorates HBV-specific cHBV patient T-cells

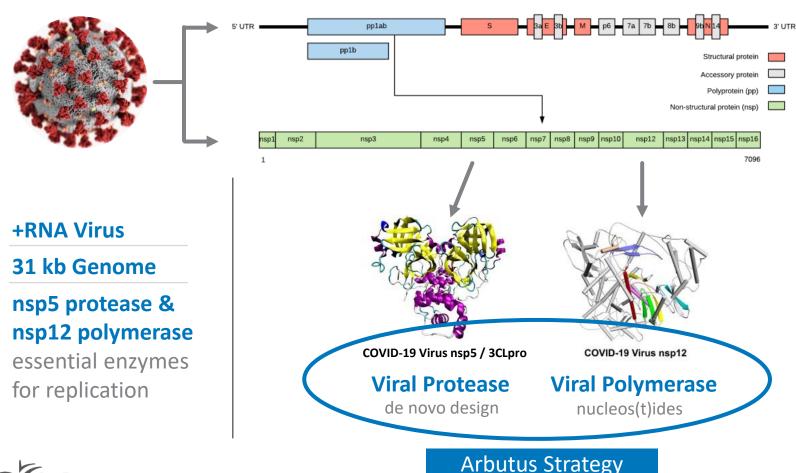


PBMCs N= cells from 9 cHBV patients *p<-0.05



Coronavirus Strategy

Leveraging our proven expertise and capabilities in antiviral drug discovery and development



Pan-Coronavirus Focused

Long Term Commitment

Small Molecule Direct-Acting Antivirals

X-Chem/Proteros Collaboration

- Proprietary DEL library screening and structural biology for M^{PRO} inhibitor discovery
- First milestone reached; several unique compound series that inhibit nsp5 protease identified
- Advancing to lead optimization stage



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2022 Key Objectives

Proforma cash balance of \$245M (unaudited) as of December 31, 2021*, cash runway into 2Q 2024

Objective	Timing 2022
AB-836, next generation oral capsid inhibitor: Full data set from Phase 1a/1b clinical trial in patients with chronic HBV	1H
AB-729, RNAi therapeutic: initiate a triple combination Phase 2a POC clinical trial with VTP-300 (Vaccitech) and a NA	1H
AB-729: Follow-up data (long-term on- and off-treatment) from Phase 1a/1b, evaluating multiple doses and dosing schedules	1H/2H
AB-729: Initial data from Phase 2a combination trial with NA therapy and Peg-IFNα-2a	2H
AB-729: Initial data from Phase 2a combination trial with VBR (Assembly) and a NA	2H
AB-729: Initial data from Phase 2a combination trial with ATI-2173 (Antios) and Viread	2H
AB-101, oral PD-L1 inhibitor compound: complete IND-enabling studies	2H
AB-161, next generation oral RNA destabilizer: complete IND-enabling studies	2H
COVID M ^{pro} : Advance clinical candidate that inhibits the SARS-CoV-2 nsp5 main protease into IND-enabling	211



studies

Anticinated

2H

Thank You

