



# Corporate Presentation

NASDAQ: ABUS

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

August 6, 2024



# 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' expectations regarding its technology licensed to third parties; the expected timing and payments associated with strategic and/or licensing agreements; the patent infringement lawsuits; and other statements relating to Arbutus' future operations, future financial performance, 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 pre-clinical 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 patent litigation matters. 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; uncertainties associated with litigation generally and patent litigation specifically; market shifts may require a change in strategic focus; and the parties may never realize the expected benefits of the collaborations. 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](http://www.sec.gov) and at [www.sedar.com](http://www.sedar.com). All forward-looking statements herein are qualified in their entirety by this cautionary statement, and Arbutus disclaims any obligation to revise or update any such forward-looking statements or to publicly announce the result of any revisions to any of the forward-looking statements contained herein to reflect future results, events or developments, except as required by law.

# Our Strategy for Value Creation

Leverage the proven track record of success established with our team's expertise in understanding and treating viral infections by discovering and developing a differentiated pipeline of therapies targeting chronic HBV.



Develop a **combination therapy that includes antivirals and immunologics** to provide a finite duration treatment for people with cHBV that results  $\geq 20\%$  functional cure rate.

# Investment Highlights



**Indications with significant unmet medical need & large market opportunities**

Focused on developing a functional cure for HBV



**Team with virology expertise and proven track record**

Discovered, developed & commercialized multiple drugs



**Portfolio of internally discovered assets with distinct MOAs**

RNAi therapeutic PD-L1 inhibitor



**Lead HBV compound – imdusiran (AB-729) RNAi therapeutic in multiple Phase 2a combination clinical trials**

Data shows imdusiran is generally safe and well-tolerated and has shown meaningful suppression of HBsAg while on- or off-treatment



**Strong financial position**

Cash runway into Q4 2026



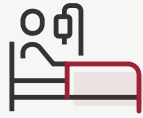
**Patented LNP technology**

Receiving licensing royalties arising from Alnylam's Onpattro® and seeking damages from patent litigation suits filed against Moderna & Pfizer/BioNTech for COVID-19 vaccine sales

# Pipeline

		Phase 1	Phase 2	Phase 3	Marketed
RNAi Therapeutic	Imdusiran (AB-729) cHBV	IM-PROVE I Combo trial (imdusiran + Peg-IFN $\alpha$ -2a + NA)			
		IM-PROVE II Combo trial (imdusiran + vaccine + NA +/- nivolumab)			
PD-L1 Inhibitor	AB-101 cHBV	AB-101-001 single- /multiple-ascending dose			

# HBV Overview



## Cause & Symptoms

- Life-threatening liver infection caused by hepatitis B virus (HBV)
- Transmitted through body fluids and from mother to child
- Long-term chronic infection (cHBV) leads to higher risk of cirrhosis and/or liver cancer



## Diagnosis

- HBsAg detection
- Additional biomarkers necessary to determine stage of disease



## Treatments

- NA therapy – lifelong daily therapy, aimed at reducing HBV DNA and risk of cirrhosis and/or HCC
- Peg-IFN $\alpha$  – administered weekly; poorly tolerated over 48 weeks of treatment
- <5% of patients achieve functional cure



## Rationale

- Need for finite and more efficacious HBV treatments that further improve long-term outcomes and increase functional cure rate
- Combination therapy with different MOAs will be required to reduce HBsAg, suppress HBV DNA, and boost immune system

Sources for all data on slide:

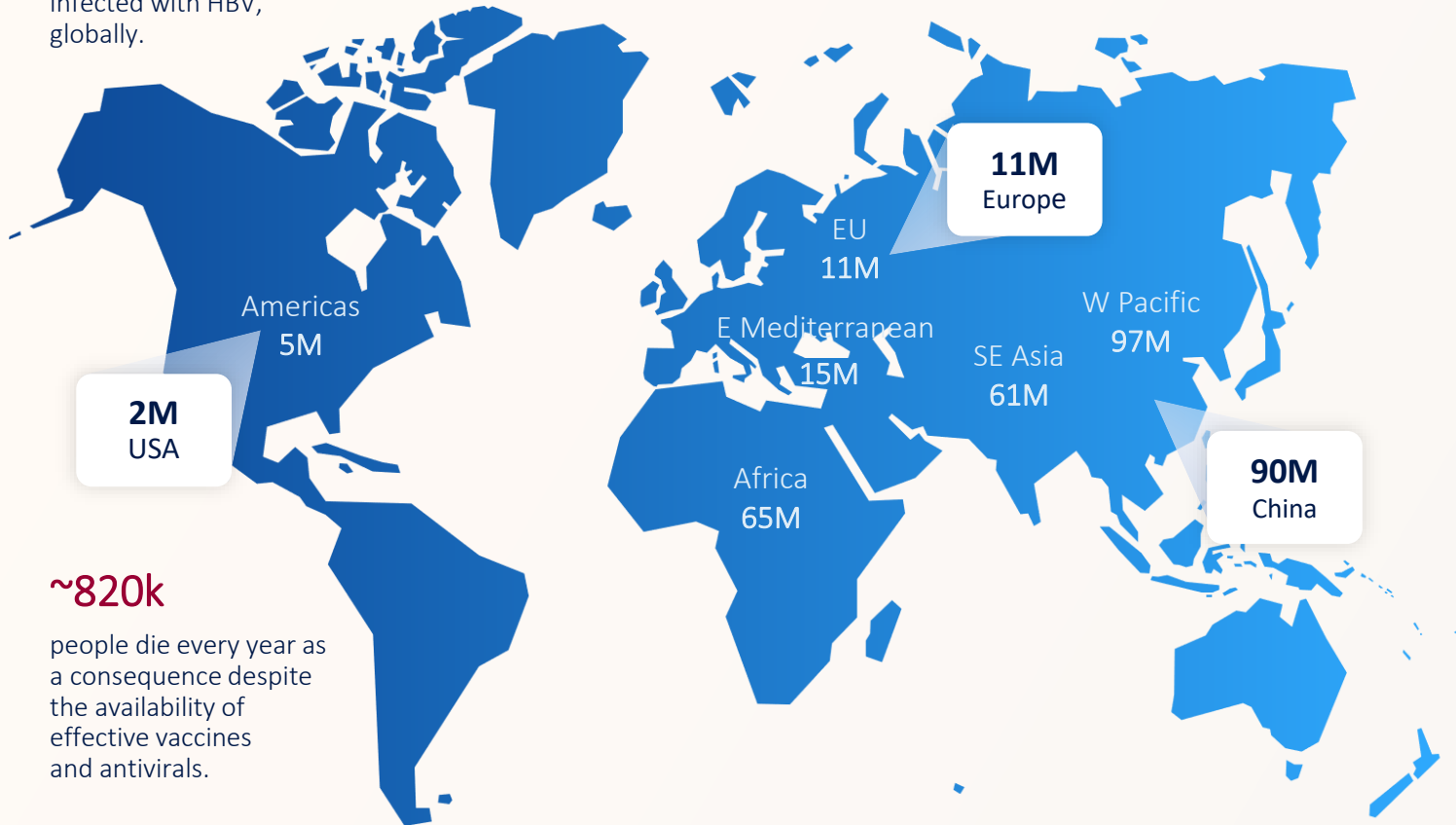
1 Hepatitis B Fact Sheet, WHO <https://www.who.int/news-room/fact-sheets/detail/hepatitis-b> ; Hep B Foundation link <https://www.hepb.org/what-is-hepatitis-b/what-is-hepb/facts-and-figures/> ; Kowdley et al. Hepatology (2012) Prevalence of Chronic Hepatitis B Among Foreign-Born Persons Living in the US by Country of Origin

2 Pegasys, PEG-Intron, Baraclude and Viread Package Inserts

# HBV Presents a Significant Unmet Medical Need

>250M

people are chronically infected with HBV, globally.



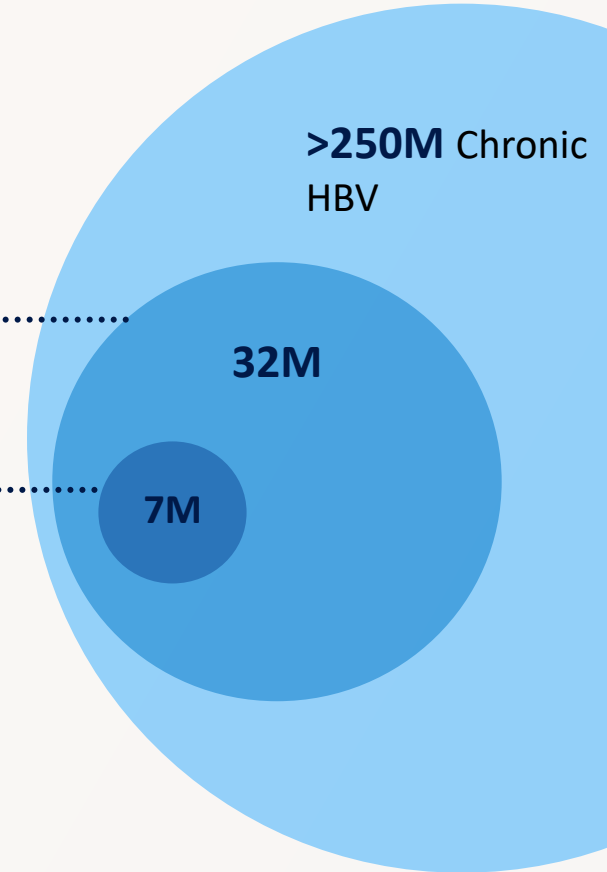
~820k

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

13%  
Diagnosed

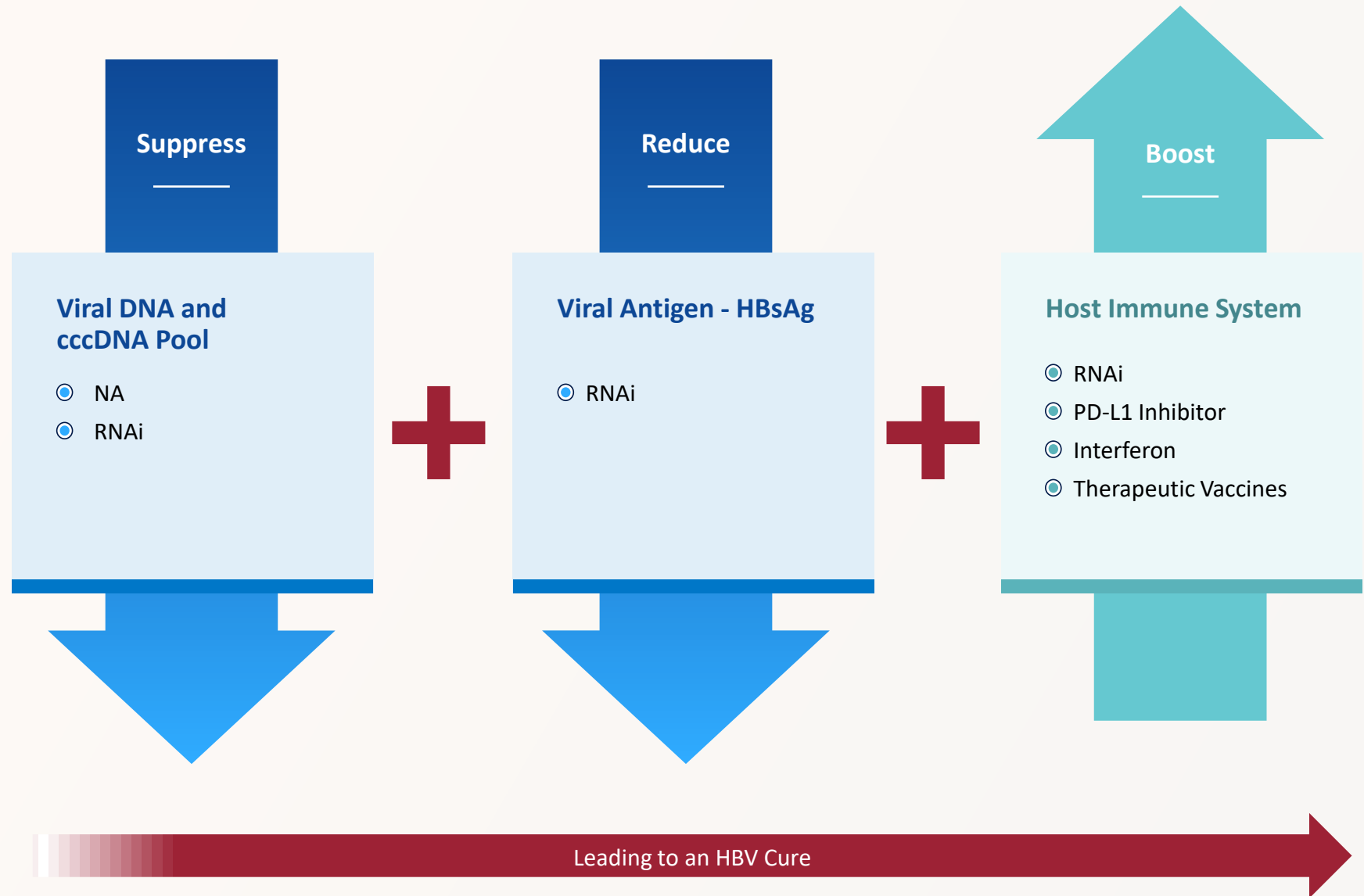
3%  
Treated

Low due to sub-optimal SOC cure rate and asymptomatic nature of disease.



# 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.



# RNAi Therapeutic

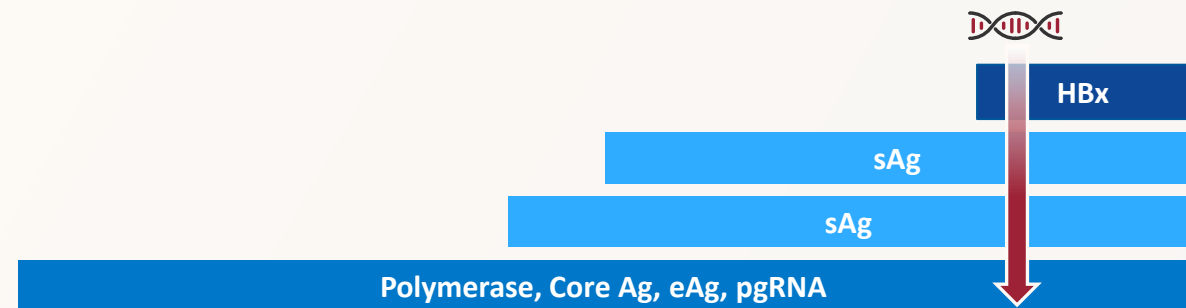
## Imdusiran

# 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 other agents
- 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: **Key Takeaways**

**Imdusiran was generally safe and well-tolerated after completing dosing in over 40 CHB patients**

**Imdusiran provided robust and comparable HBsAg declines regardless of dose, dosing interval, HBeAg or DNA status**

**A reduction in HBsAg and HBV DNA was sustained in the majority of patients that stopped all treatments**

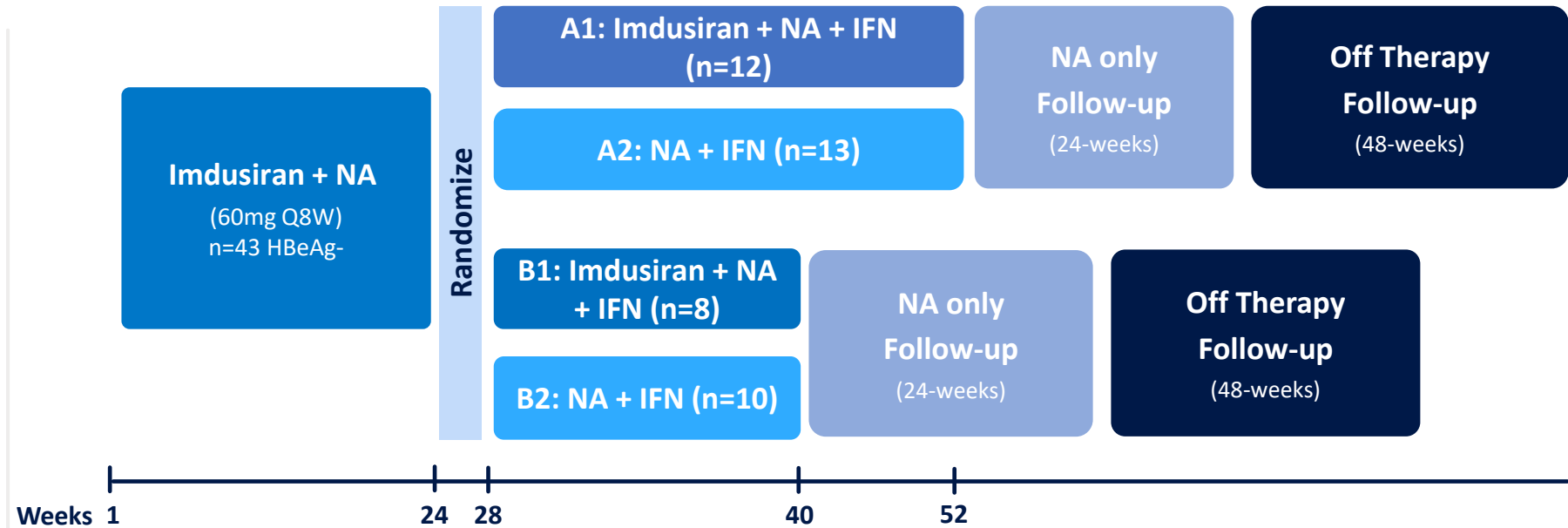
**Imdusiran results in HBV-specific T-cell immune restoration and decrease of exhausted T-cells in some patients**

Imdusiran 60 mg every 8 weeks for 24 to 48 weeks selected for Phase 2 trials

## IM-PROVE I:

# Phase 2a POC Clinical Trial

Imdusiran in combination with ongoing NA therapy and short courses of Peg-IFN $\alpha$ -2a in cHBV patients



### Multi-center, open-label Phase 2a

**Primary objective:** evaluate safety and tolerability of imdusiran in combination with Peg-IFN $\alpha$ -2a in patients with NA-suppressed cHBV

After completing IFN treatment and the 24-week NA only follow-up period, patients are assessed to stop NA therapy. Those patients that stop NA therapy will be followed for an additional 48 weeks

Data presented at EASL Congress 2024 showed that 48 weeks of imdusiran plus 24 weeks of IFN therapy was generally safe, well-tolerated and achieved sustained undetectable HBsAg in 33% of patients after completion of IFN treatment, which were maintained in 100% of these patients 24 weeks after completing imdusiran and IFN treatment

# IM-PROVE I: Imdusiran with Short Courses of IFN Leads to Undetectable HBsAg and Sustained HBsAg Loss

## Number of Patients with Undetectable HBsAg at Key Timepoints

Achieved HBsAg ≤ LLOQ (0.05 IU/mL)	Cohort A1: IDR x 6 + NA + IFN x 24W (N = 12)	Cohort A2: IDR x 4 + NA + IFN x 24W (N = 13)
Anytime during treatment	6/12 (50%)	3/13 (23%)
EOT (W52)	4/12 (33.3%)	3/13 (23%)
	7/25 (28%)	
Next Assay negative	4/4	2/3
24 weeks post-EOT (NA therapy only)	4/12 (33.3%)	2/13 (15.4%)
	6/25 (24%)	
Next Assay negative	2*/4 (*1 subject pending testing)	2/2
Discontinued NA therapy	9/12 (75%)	3/13 (23%)

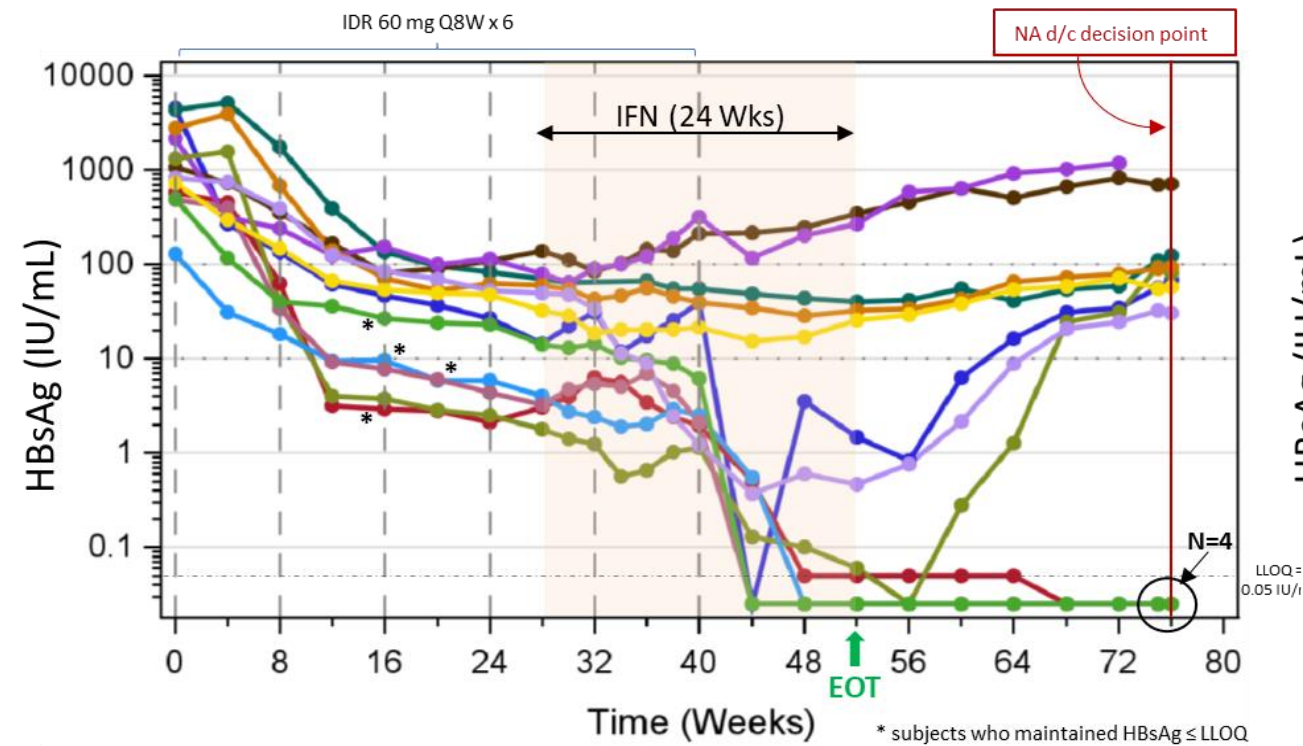
W: week; EOT: end-of-treatment; Next Assay LLOD=0.005 IU/mL

## Key Findings:

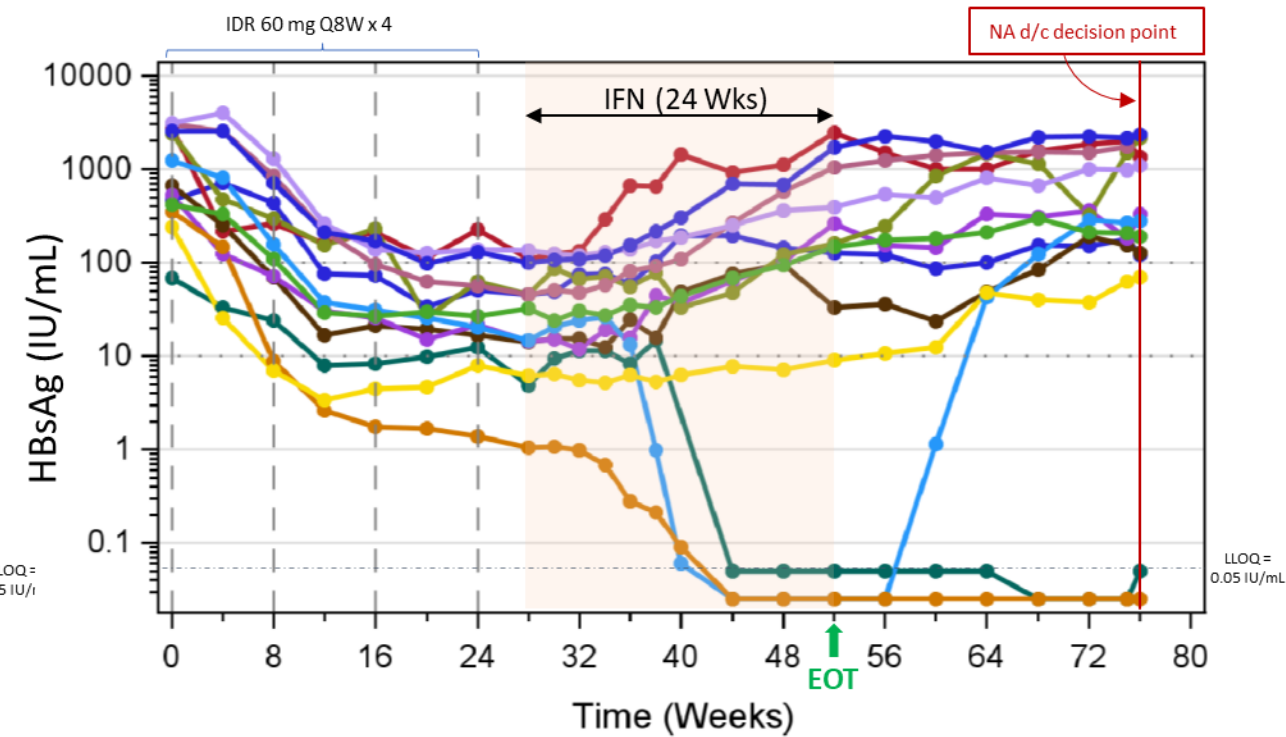
- 33% of patients in Cohort A1 reached and maintained undetectable HBsAg for 24 weeks after completing imdusiran and IFN treatment
- Undetectable HBsAg was achieved in 67% of those patients in Cohort A1 with HBsAg less than 1000 IU/mL at baseline
- Patients with sustained HBsAg loss had corresponding high anti-HBs levels (43.8 to >1000 mIU/mL)
- Imdusiran and 24 weeks of IFN was generally safe and well-tolerated
  - No related-SAEs and no AEs leading to discontinuation
- All 6 undetectable patients (plus an additional 15 from all 4 Cohorts, n=21 total) discontinued NA therapy after the 24 weeks post-EOT visit
  - 2/6 undetectable patients have reached 12 weeks off all therapy remain undetectable
  - 1 patient in Cohort B2 achieved functional cure during the NA discontinuation period

# IM-PROVE I: Imdusiran with 24 Weeks of IFN Reduces HBsAg Levels to Undetectable in 6 patients

**Cohort A1: HBsAg Level by Visit**



**Cohort A2: HBsAg Level by Visit**





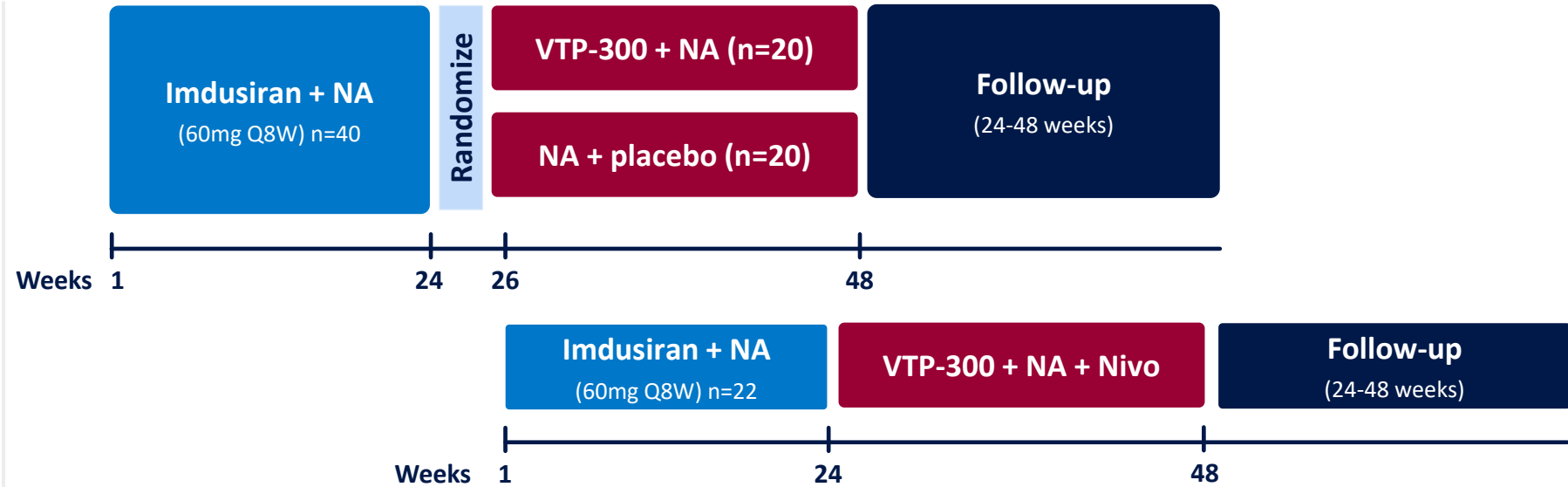
## IM-PROVE II:

# Phase 2a POC Clinical Trial



### POC Phase 2a clinical trial

evaluating imdusiran in combination with Barinthus Bio's immunotherapeutic, VTP-300, and NA with or without low dose nivolumab



**Primary objective:** evaluate safety and reactogenicity of imdusiran followed by VTP-300 or placebo

At Week 48 all participants who are eligible to discontinue NA therapy will be followed for an additional 48 weeks

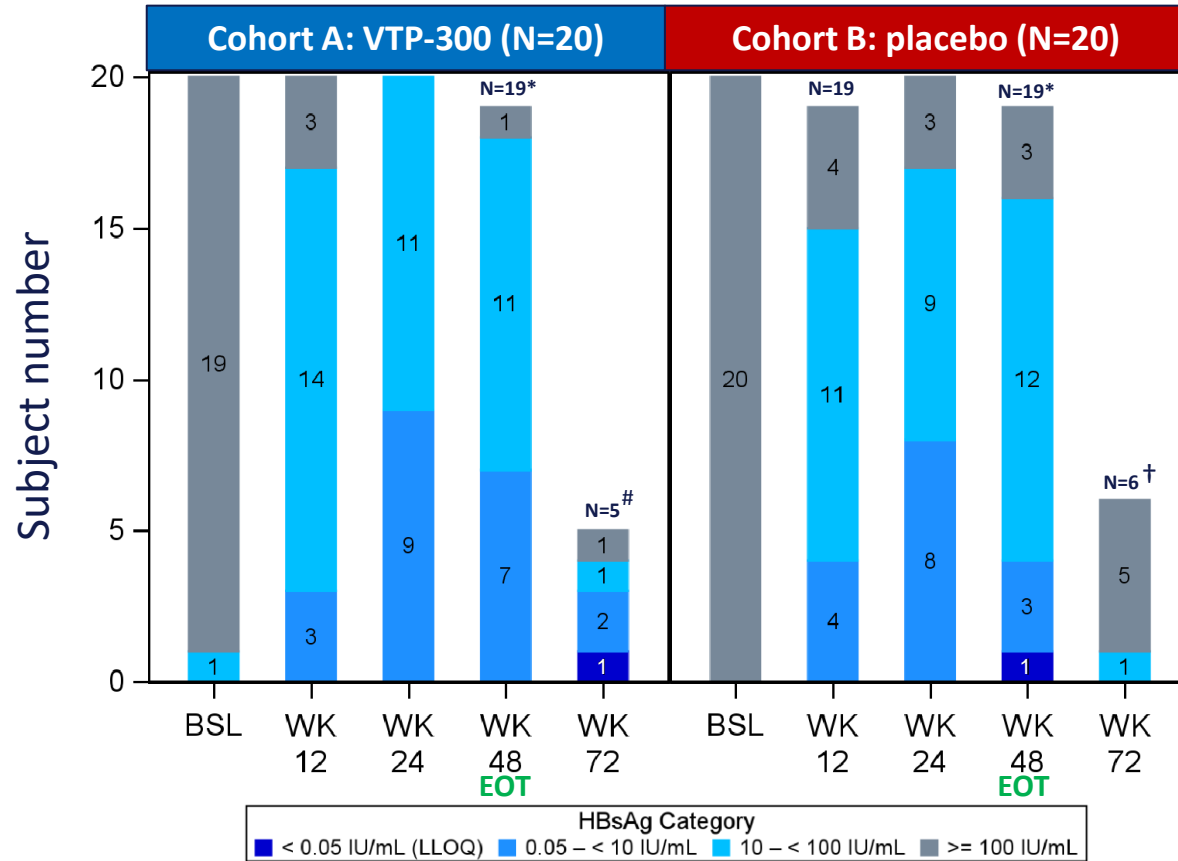
Results presented at EASL Congress 2024 showed that imdusiran followed by VTP-300 was generally safe and well-tolerated and led to maintenance of lower HBsAg levels during the post-treatment follow-up period

Clinical trial expanded to include an additional arm with nivolumab (Opdivo®) with preliminary data expected in 2H 2024

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

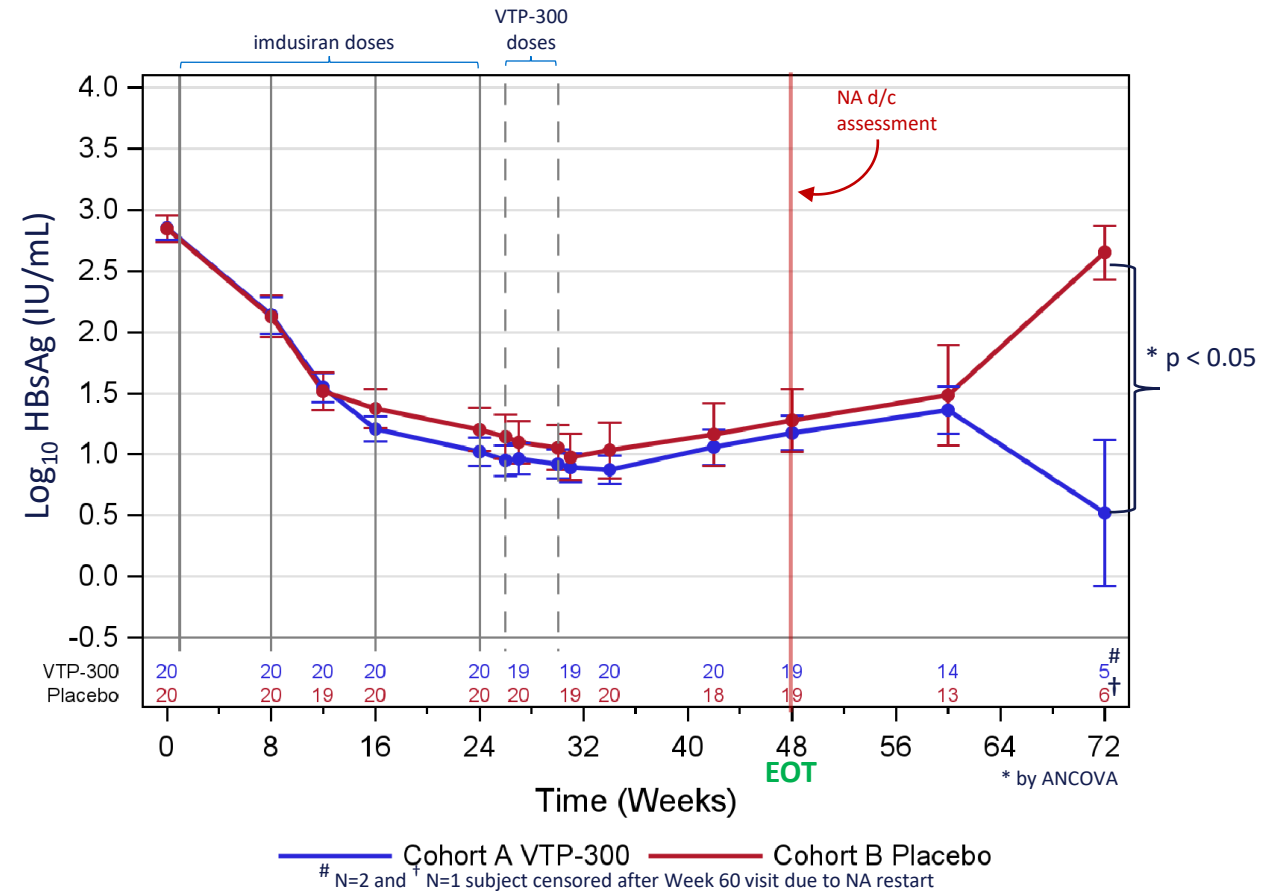
# IM-PROVE II: Imdusiran and VTP-300 Achieve Statistical Significance in Lowering HBsAg Levels

### HBsAg Thresholds Achieved by Visit



BSL=baseline; WK=week; EOT=end of treatment; \* 2 subjects did not reach timepoint by datacut; # N=2 and † N=1 subject censored after Week 60 visit due to NA restart

### Mean [SE] Log<sub>10</sub> HBsAg Level by Visit



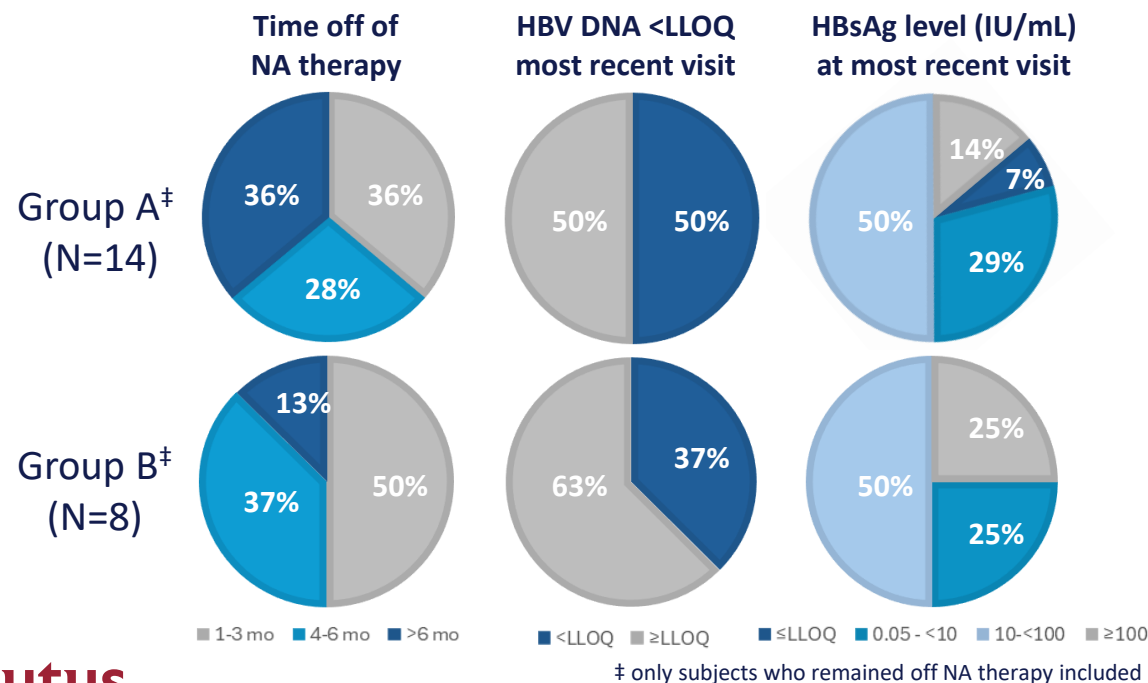
- Imdusiran led to declines of -1.8 log<sub>10</sub> by Week 26, 95% of subjects had HBsAg <100 at time of VTP-300 or placebo dosing
- More subjects maintained HBsAg thresholds of <100 IU/mL and <10 IU/mL when administered VTP-300 vs placebo
- At 24 weeks post-EOT (Week 72, N=11), there was a significant difference in HBsAg levels between groups, which may reflect the delayed effect of VTP-300 on HBsAg levels observed in other trials



# IM-PROVE II: More patients Treated with Imdusiran and VTP-300 stopped NA treatment

- 84% of patients in Group A/VTP-300 met NA discontinuation criteria and stopped treatment after W48
  - More Group A/VTP-300 subjects (50%) have maintained HBV DNA <LLOQ off NA therapy than placebo subjects (37.5%)
  - Group A/VTP-300 subjects have maintained lower HBsAg levels after NA discontinuation
    - 1 Group A/VTP-300 subject reached HBsAg <LLOQ at Week 72, another has >1.5 log<sub>10</sub> HBsAg decline between Week 60 and 68

- Imdusiran and VTP-300 was generally safe and well-tolerated when administered sequentially
  - No SAEs, Grade 3 or 4 adverse events (AEs) or treatment discontinuations due to AEs
  - Most common treatment-related AEs in 2 or more patients (all Grade 1 or 2):
    - Imdusiran: injection site-related (bruising and/or swelling in 2 subjects), ALT increased in 2 subjects
    - VTP-300: injection site-related (redness, pain and/or injection reaction in 2 subjects)



## Imdusiran

# Strategic Collaboration



### Exclusive Licensing\* and Strategic Partnership

Develop, manufacture and commercialize imdusiran 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

### Deal economics for Arbutus:

<b>\$40M</b>	Upfront payment (received in 2022)
<b>\$15M</b>	Equity investment (received in 2022)
<b>Up to \$245M</b>	Commercialization and milestone payments
<b>Double-digit up to low twenties %</b>	Tiered royalties on annual sales

#### Qilu Pharmaceutical:

One of the leading pharmaceutical companies in China, provides development, manufacturing, and commercialization expertise to this partnership



# Oral PD-L1 Inhibitor

# 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 HBV-specific 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

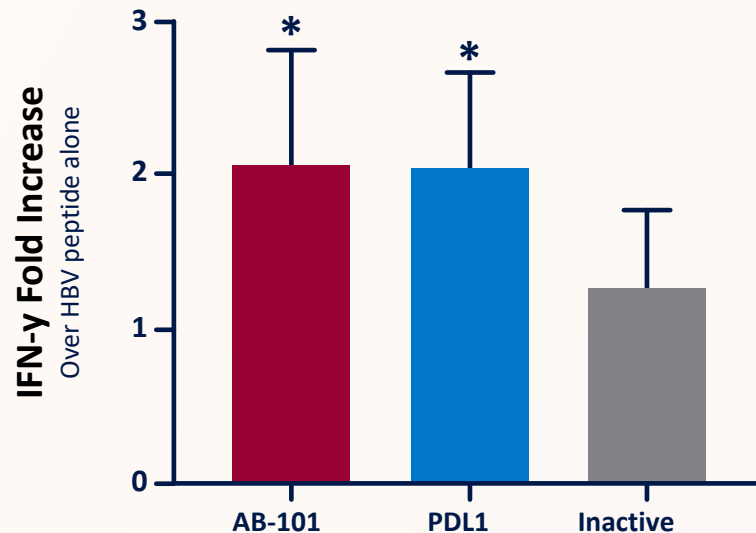
- Blocks PD-L1/PD-1 interaction at sub-nM concentrations
- Activates HBV-specific immune responses in T-cells from cHBV patients *in vitro*
- Novel MOA identified
- Demonstrates a robust checkpoint mediated *in vivo* effect
- Improves HBV-specific T- and B-cell responses *ex vivo*

Currently in a Phase 1a/1b clinical trial

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

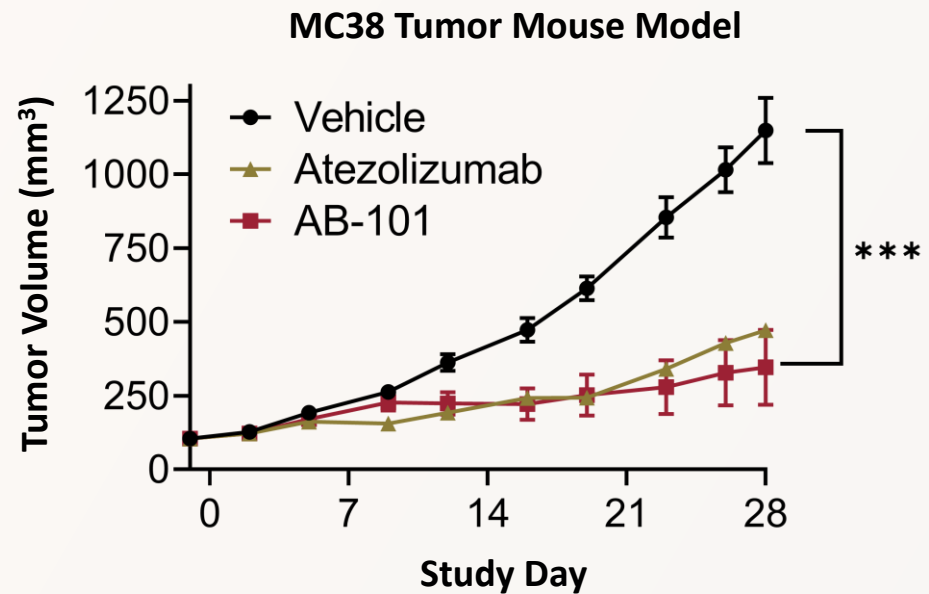
AB-101 is highly potent and activates HBV specific immune cells from chronic HBV patients

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



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

Once daily oral administration of AB-101 resulted in  
profound tumor reduction



Data presented at EASL 2022

# AB-101-001: Phase 1a/1b Clinical Trial with AB-101

## Parts 1 & 2 – Healthy Subjects

Part 1: SAD  
(n=8/cohort – 6:2)

1A: Dose 1



1B: Dose 2



1C: Dose 3



1D: Dose 4 \*



Part 2: MAD  
(n=10/cohort – 8:2)

2A: Dose ≤ dose tested in  
Part 1; interval TBD

2B:  
Dose/interval TBD

Dosing initiated with preliminary  
data from MAD portion expected  
in 2H 2024.

Additional optional dose panels  
may be used.

Part 3 – cHBV Patients  
(n=12/cohort – 10:2)  
Virally suppressed

3A: Dose ≤ dose tested in Part 2;  
interval TBD x 28d

3B: Dose/interval TBD x 28d

3C: Dose/interval TBD x 28d

\* Preliminary data shows AB-101 is well tolerated and binds to the receptor target. In the 25mg cohort, all 5 evaluable subjects showed evidence of receptor occupancy between 50-100%.

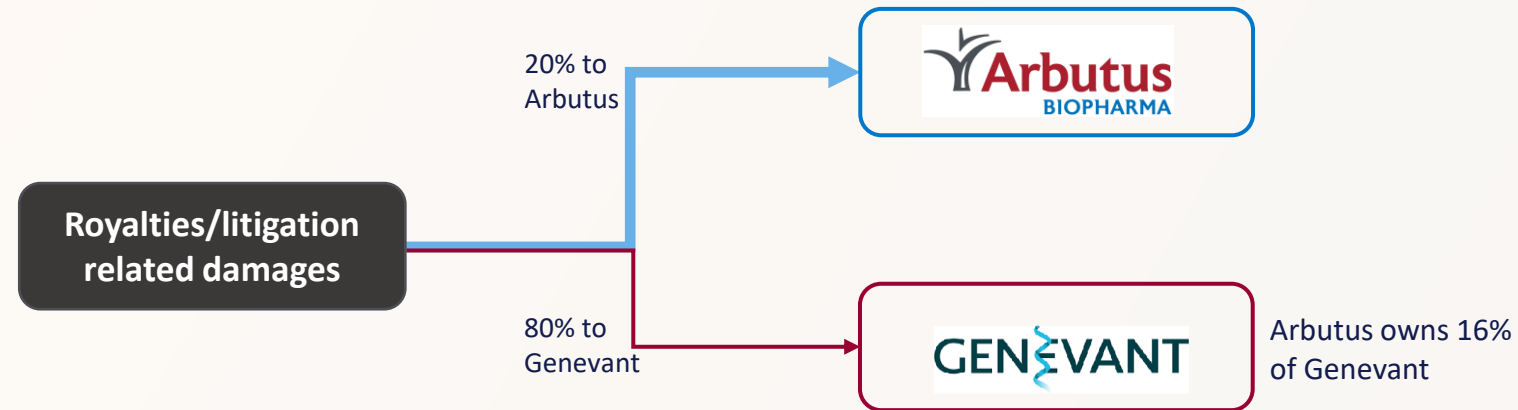
# LNP Litigation: Update

## ● Moderna - Trial date September 24, 2025\*

- Markman Hearing occurred February 8, 2024 – judge heard arguments on claim construction.
  - Court provided ruling on April 3 and agreed with Arbutus’s position on the majority of the claims
- Next Steps
  - Expert reports / depositions

## ● Pfizer

- Lawsuit ongoing
- Date for claim construction hearing has not been set



\*Above referenced date is included in the 8/5/2024 Stipulation to Extend Time and is pending Court’s approval.

# 2024 Key Milestones

Cash balance\* of \$148.5M as of June 30, 2024, cash runway into Q4 2026; 2024 cash burn between \$63M and \$67M

Milestone	Anticipated Timing 2024
IM-PROVE I Phase 2a (imdsiran + IFN): End-of-treatment data	1H ✓
IM-PROVE II Phase 2a (imdsiran + VTP-300): End-of-treatment data	1H ✓
AB-101-001: Preliminary data from healthy subject cohorts	1H ✓
AB-729-202 Phase 2a (imdsiran + VTP-300 + nivolumab): End-of-treatment data	2H
AB-101-001: Preliminary data from multiple-ascending dose healthy subject cohorts	2H

\*Consists of cash, cash equivalents and marketable securities



# Thank You

