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Curing Chronic Hepatitis B

Update on AB-729, an RNAi therapeutic in Phase 2 development as a key component of a functional cure strategy for cHBV

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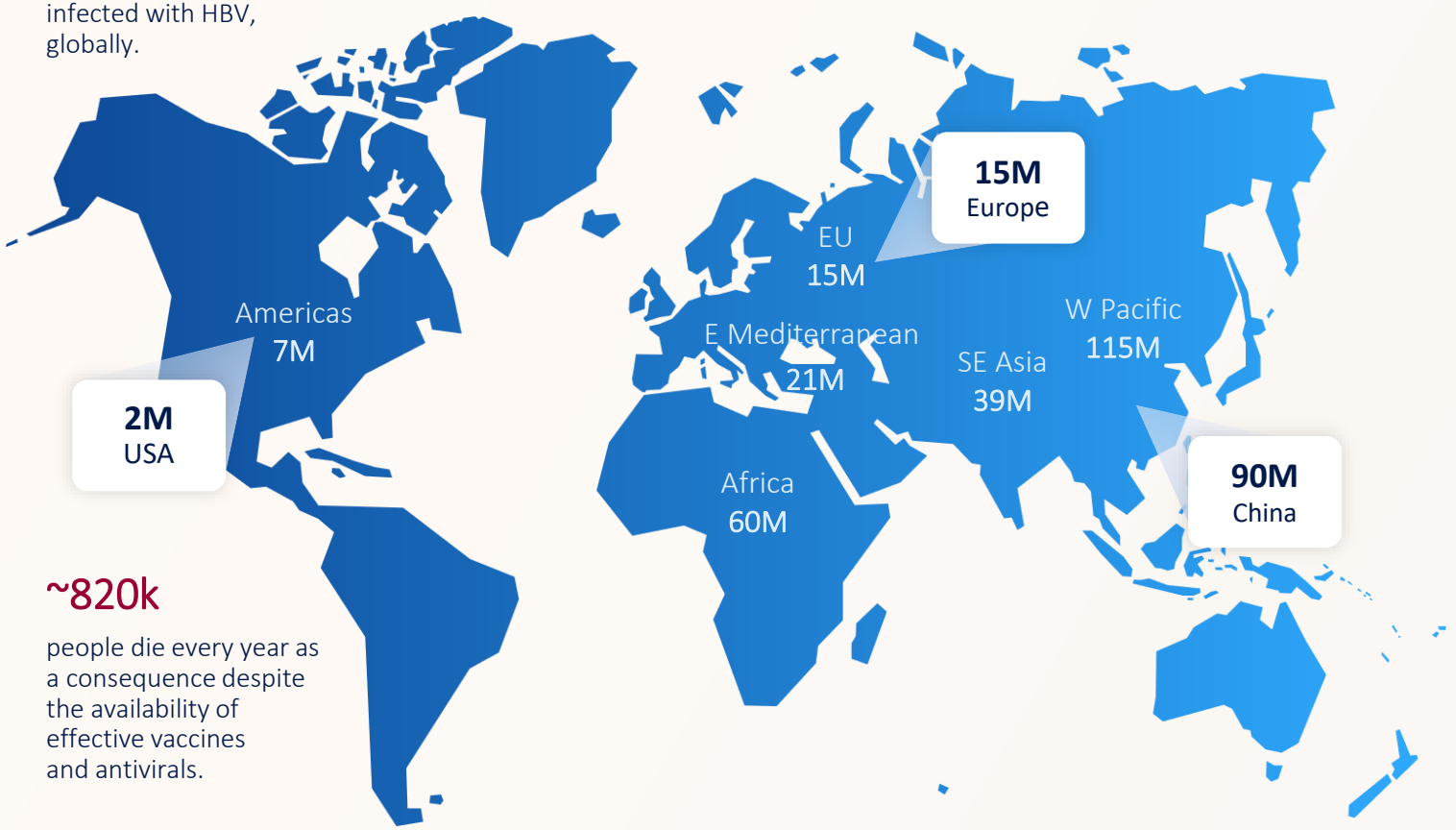
HBV Presents a Significant Unmet Medical Need

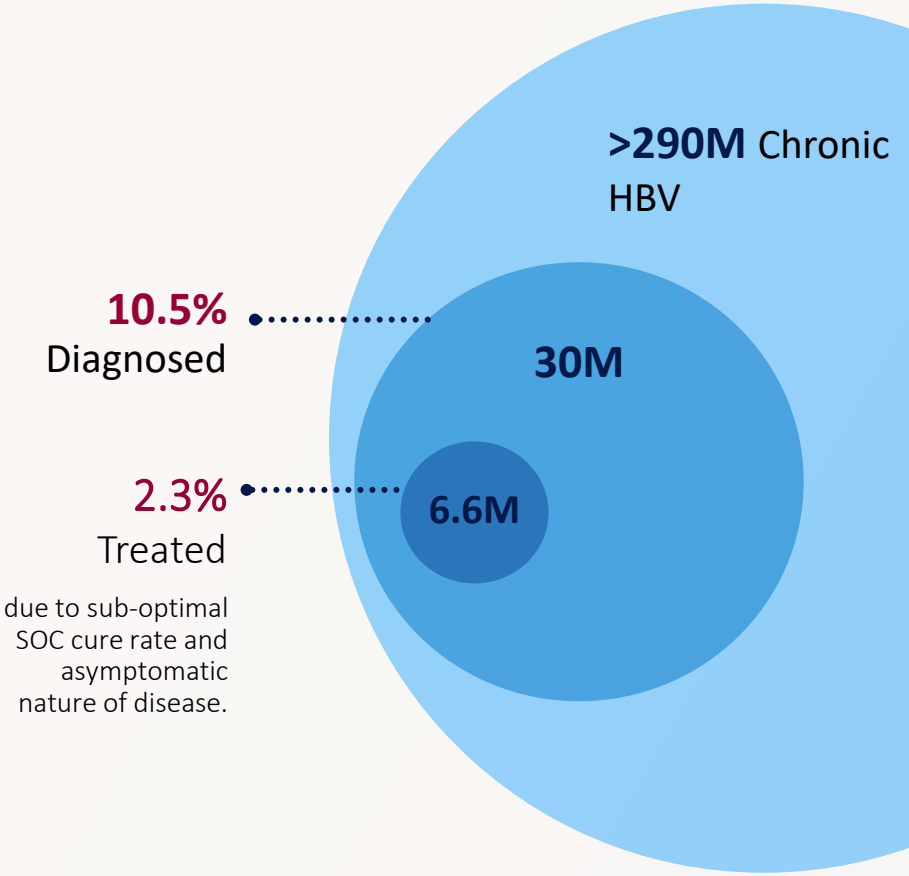
>290M

people are chronically infected with HBV, globally.



~820k

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



10.5%
Diagnosed

2.3%
Treated

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

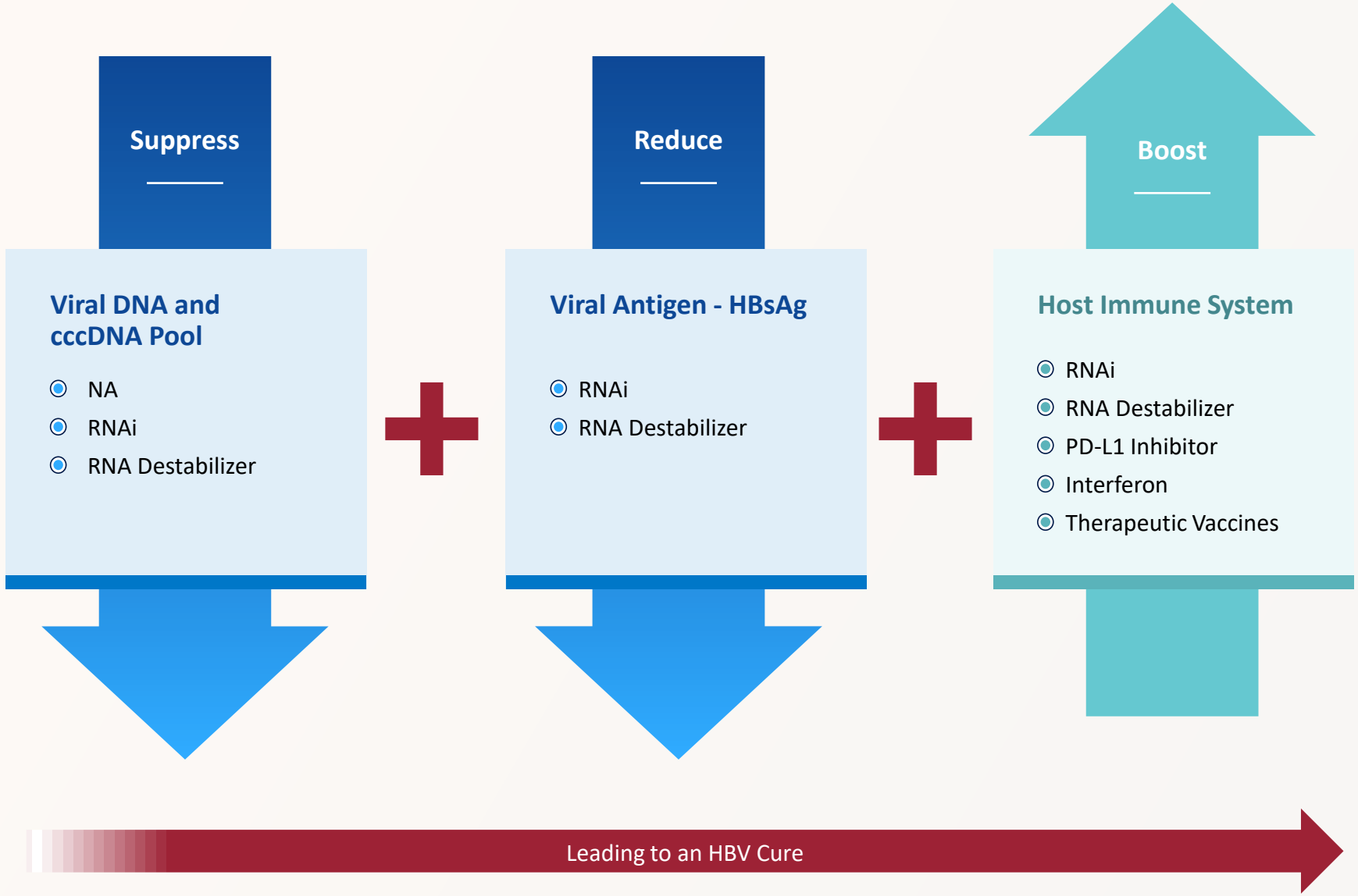
SOC: Standard of Care

Sources: https://www.who.int/news-room/fact-sheets/detail/hepatitis-b

https://www.hepb.org/what-is-hepatitis-b/what-is-hepb/facts-and-figures/

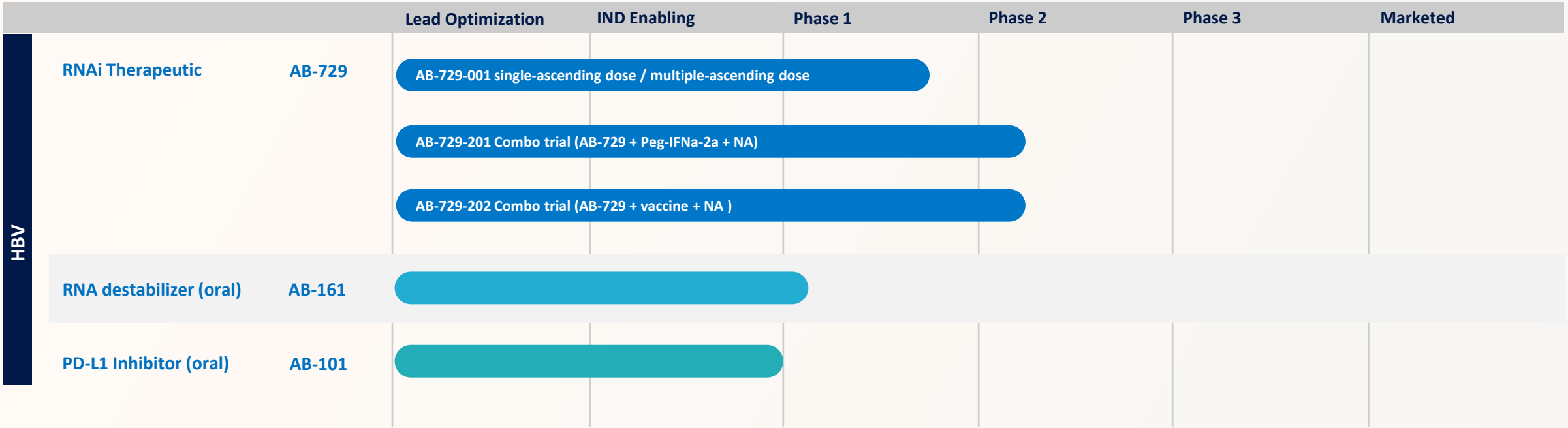
3-Pronged Approach to Therapeutic Success

- **Suppress** HBV DNA
- **Reduce** viral antigens
- **Boost** host immune response



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

Arbutus' HBV Pipeline



- AB-161:
  - Preclinical AB-161 data presented at Global Hepatitis Summit, April 27, 2023
  - Currently in Phase 1 clinical trial
- AB-101
  - Preclinical AB-101 data presented at AASLD, Nov 4-8, 2022
  - Currently Phase 1 ready

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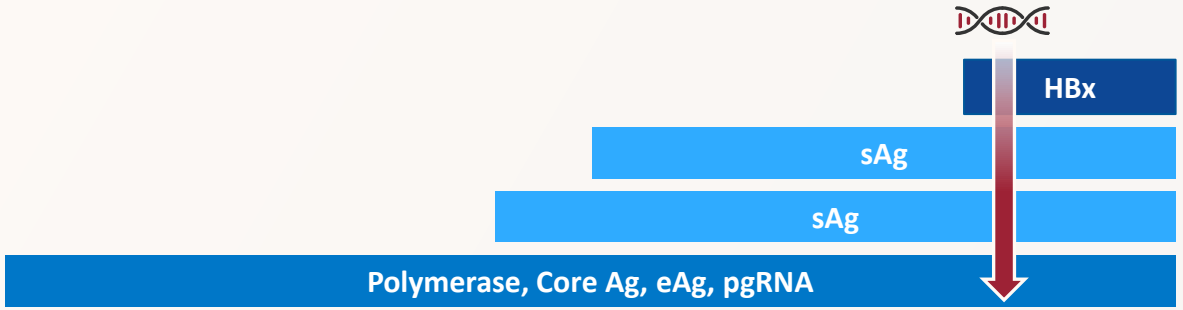
NA: Nucleoside Analogue

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 other agents
- Actively targets the liver
- Active against cccDNA derived and integrated HBsAg transcripts
- Clean profile in long term preclinical safety studies



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

Part 1 & 2:
Single ascending doses in healthy subjects and cHBV subjects

AB-729 single dose conclusions:

- Robust HBsAg declines across all cohorts
- HBV DNA declines in HBV DNA+ patients
- Dosing intervals > 4 weeks possible

Part 3: Multiple Ascending Doses in cHBV Patients (48 weeks)

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

- AB-729 dosing complete in all Cohorts
- Part 3 subjects who completed 48 weeks of AB-729 treatment and met protocol-defined NA stopping criteria (assessed at least 24 weeks after the last dose of AB-729) were permitted to stop NA therapy
  - ALT <2 × ULN,
  - Undetectable (target not detected, TND) HBV DNA,
  - HBeAg negative, and
  - HBsAg <100 IU/mL at two consecutive visits

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HBeAg: HBV e-antigen | TDF: tenofovir disoproxil fumarate | NA: nucleos(t)ide analogue

Data presented at EASL 2022

Robust HBsAg Declines Irrespective of Dose, Dosing Schedule, HBeAg or HBV DNA Status

Mean log_{10} (SE) Baseline and Δ log_{10} HBsAg by Visit

Visit	HBV DNA-					HBV DNA+
	Cohort E (N=7)	Cohort F (N=7)	Cohort I (N=6)	Cohort J (N=7)	Cohort K (N=7)	Cohort G (N=7)
Baseline	3.51 (0.20)	3.53 (0.17)	3.36 (0.23)	3.37 (0.28)	3.23 (0.14)	3.14 (0.14)
Treatment Week 12	-1.10 (0.15)	-1.02 (0.11)	-1.30 (0.19)	-1.06 (0.31)	-1.63 (0.39)	-1.56 (0.32)
Treatment Week 24	-1.84 (0.16)	-1.57 (0.09)	-1.79 (0.22)	-1.56 (0.25)	-1.99 (0.35)	-1.82 (0.29)
Treatment Week 48	-1.89 (0.18)	-1.90 (0.14)	-1.91 (0.32)	-1.80 (0.41)	-2.57 (0.61)	-2.05 (0.31)
Follow Up Week 12	-1.74 (0.20)	-1.59 (0.23)	-1.42 (0.26)	-1.52 (0.40)	-2.38 (0.75)	-1.50 (0.13)
Follow Up Week 24	-1.43 (0.18)	-1.26 (0.21)	-1.37 (0.39)	-1.49 (0.35)	-1.82 (0.63)	-1.53 (0.29)
Follow Up Week 48	-1.55 (0.56)	-1.01 (0.24)	-0.88 (0.33)	-1.04 (0.20)	-1.86 (0.70)	-1.10 (0.27)

Data shown as mean (SE) log_{10} IU/mL; minimum of 5 subjects/timepoint. Last AB-729 dose Cohort E: Week 44, Cohorts F, I, G, K: Week 40, Cohort J: Week 36; HBsAg Assay LLOQ = 0.07 IU/mL; *N=6; #N=5

- All Cohorts achieved at least a -1.8 log_{10} decline in mean HBsAg at the end of the treatment period (Week 48)
- Mean HBsAg levels remained below baseline values at Follow Up Week 48
- There were no significant differences in mean HBsAg declines between the 60 mg and 90 mg doses or between different dosing intervals

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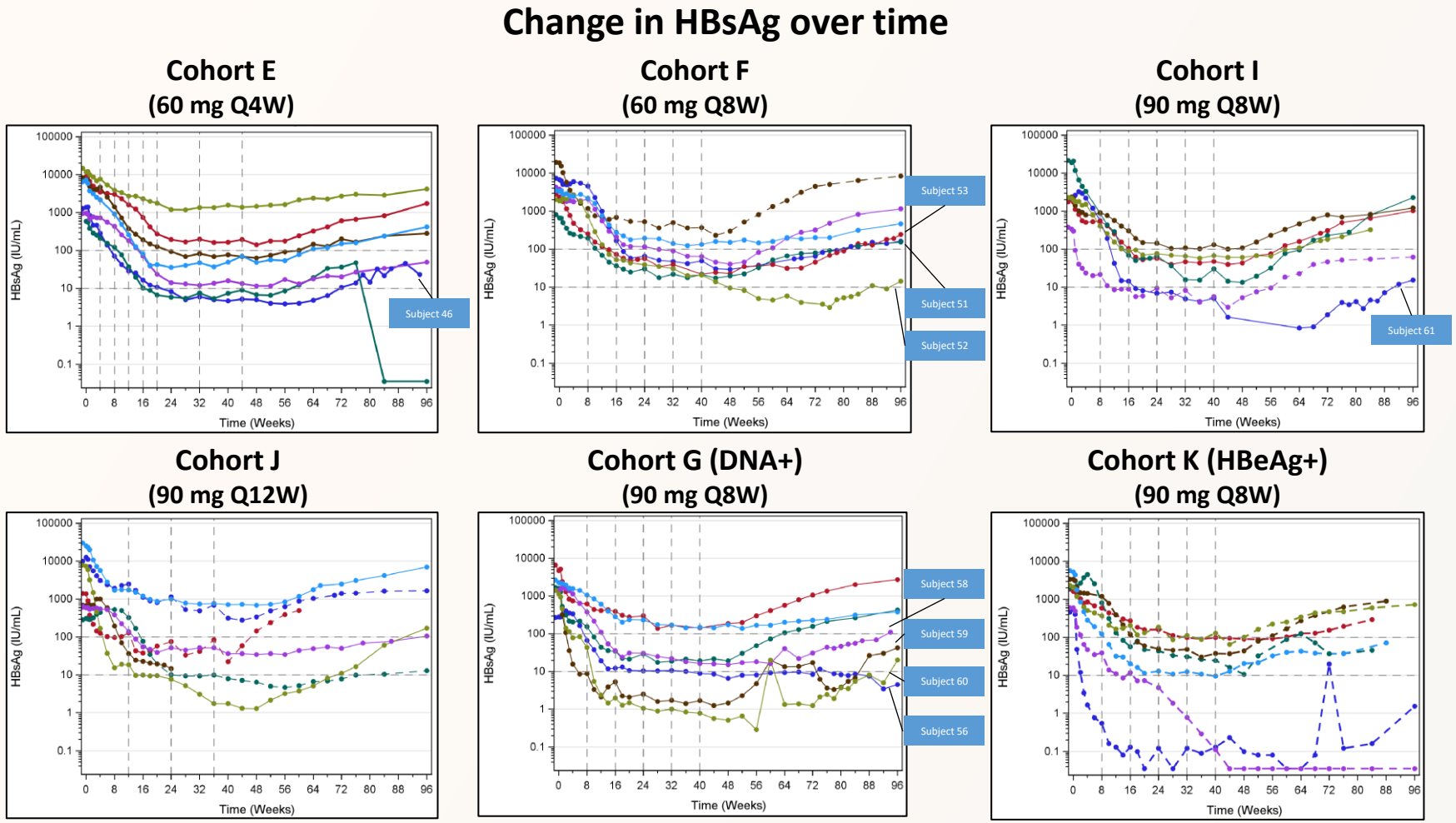
SE: standard error

Data presented at Global Hepatitis Summit 2023

AB-729-001: Robust & Sustained HBsAg Declines While On- or Post-Treatment with AB-729



- 33 of 41 patients had HBsAg <100 IU/mL at some point during the trial
- 1 patient in Cohort E (baseline HBsAg = 583.5 IU/mL) who qualified but declined to participate in NA discontinuation seroconverted at Week 84 (HBsAg < LLOQ and HBsAb = 189 IU/mL at last visit); liver enzymes remained within normal limits.
- 2 patients in Cohort K reached HBsAg <LLOQ on multiple visits with detectable HBsAb levels, 1 also reached HBeAg <LLOQ

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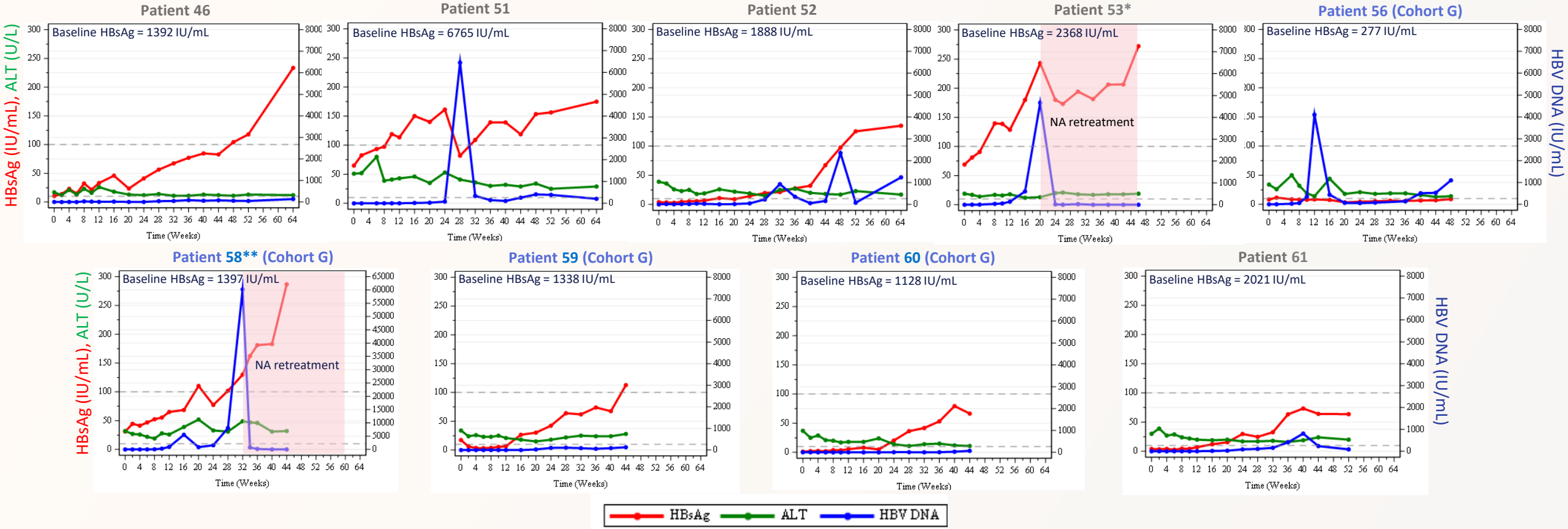
Data presented at EASL 2022, AASLD 2022, GHS 2023

AB-729-001: AB-729 Shows Low Levels of HBV Markers Persisting in cHBV Patients While Off-Treatment



- 7 of 9 (78%) subjects remain off NA therapy for 44-64 weeks and all completed AB-729 treatment over 1½ years ago
- Most subjects have maintained low HBV DNA levels off treatment
- HBsAg remains between -0.8 and -1.6 $\log_{10}$ IU/mL below baseline values
- NA discontinuation post-AB-729 treatment appears well tolerated with no ALT flares

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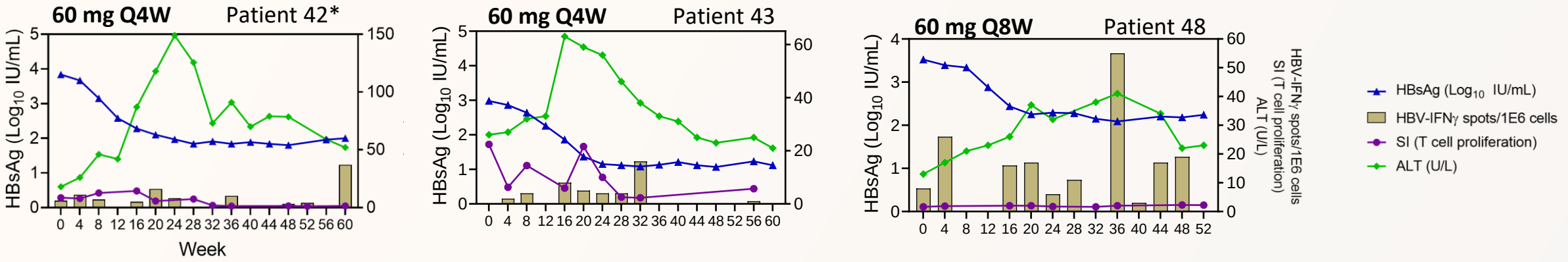
Data presented at GHS 2023

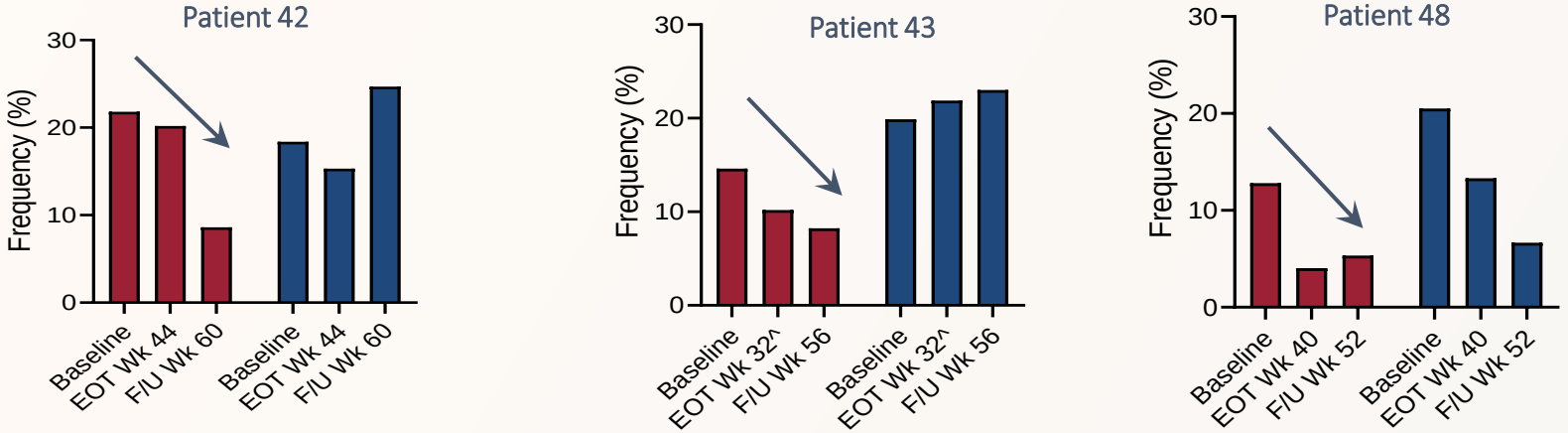
* Patient 53 restarted NA therapy at Investigator's request after the NA d/c FU W20 visit (pink shaded area).
** Patient 58 restarted therapy after the NA d/c FU W36 visit (pink shaded area).

AB-729-001: Treatment with AB-729 Reactivates HBV Specific Immunity in Some Patients

AB-729 Increased HBV-Specific T-Cell Activation



AB-729 Decreased Exhausted T-Cells



^ Last on-treatment PBMC sample available prior to last dose at Wk 44

- Upregulation of HBV-specific T-cell activation markers observed in all 7 patients assessed to date
- Two profiles of HBV-specific T cell IFN-γ responses observed
  - Elevation between Wk 16-28 which coincides with nadir of HBsAg reduction
  - *Elevation after AB-729 dosing completed, between Wk 48-60
- Reduction of exhausted T cells also evident

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Data presented at EASL 2022

AB-729-001 Safety Summary

- AB-729 is generally safe and well-tolerated after repeat dosing for up to 48 weeks
- 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 observed have improved or stabilized with continued treatment
- Injection site AEs were all Grade 1 (erythema, pain, bruising)
- No clinically meaningful changes in ECGs or vital signs
- After NA treatment discontinuation, no ALT flares have been observed

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SAE: Serious Adverse Event | AE: Adverse Event

AB-729-001 Clinical Trial Key Takeaways

AB-729 provided robust and comparable HBsAg declines regardless of dose, dosing interval, HBeAg or DNA status

Discontinuation of both AB-729 and NA-therapy results in sustained reduction in HBsAg and HBV DNA in 7 of 9 patients

AB-729 results in HBV-specific T-cell immune restoration and decrease of exhausted T-cells in some patients

AB-729 was generally safe and well-tolerated after completing dosing in 41 patients

*Data presented at EASL 2021

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* Data previously presented

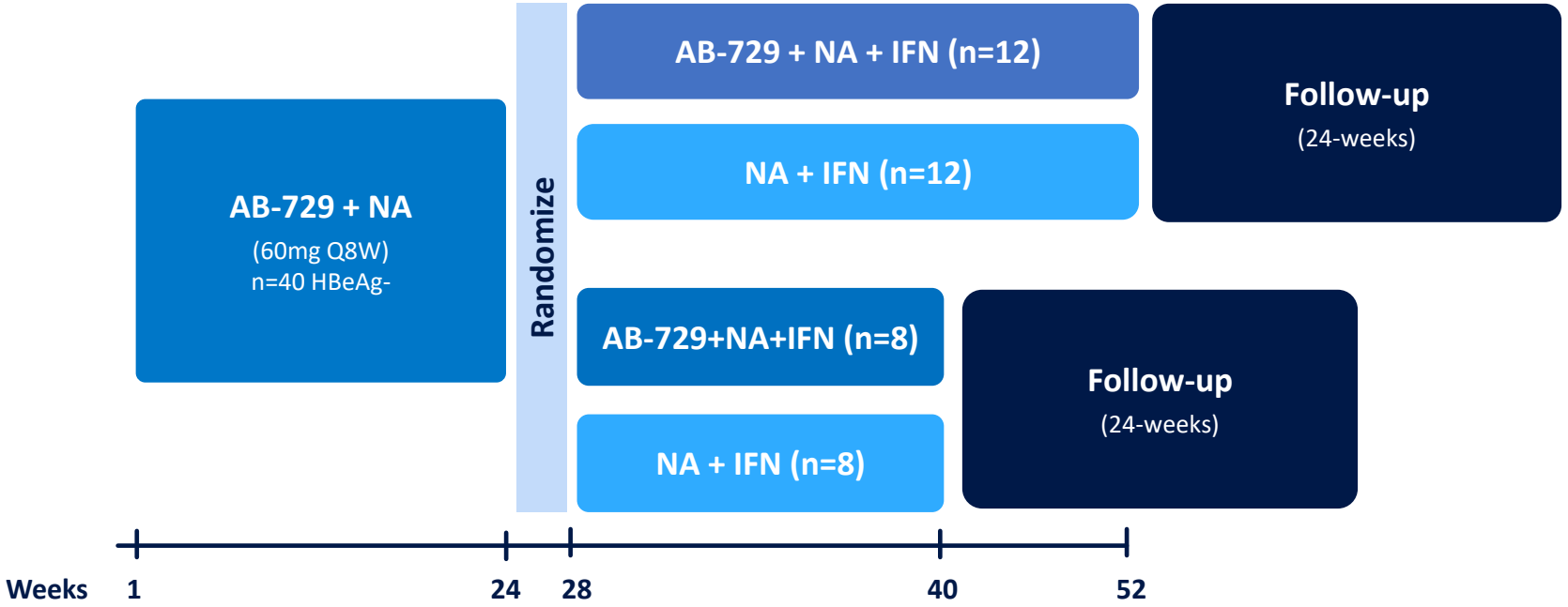
Phase 2 AB-729 Studies

AB-729-201:

Phase 2a POC Clinical Trial

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

Enrollment complete. Additional preliminary data including IFN data will be presented at **EASL 2023**



Multi-center, open-label Phase 2a

Primary objective: evaluate safety and tolerability of AB-729 in combination with Peg-IFNa-2a in patients with NA-suppressed cHBV

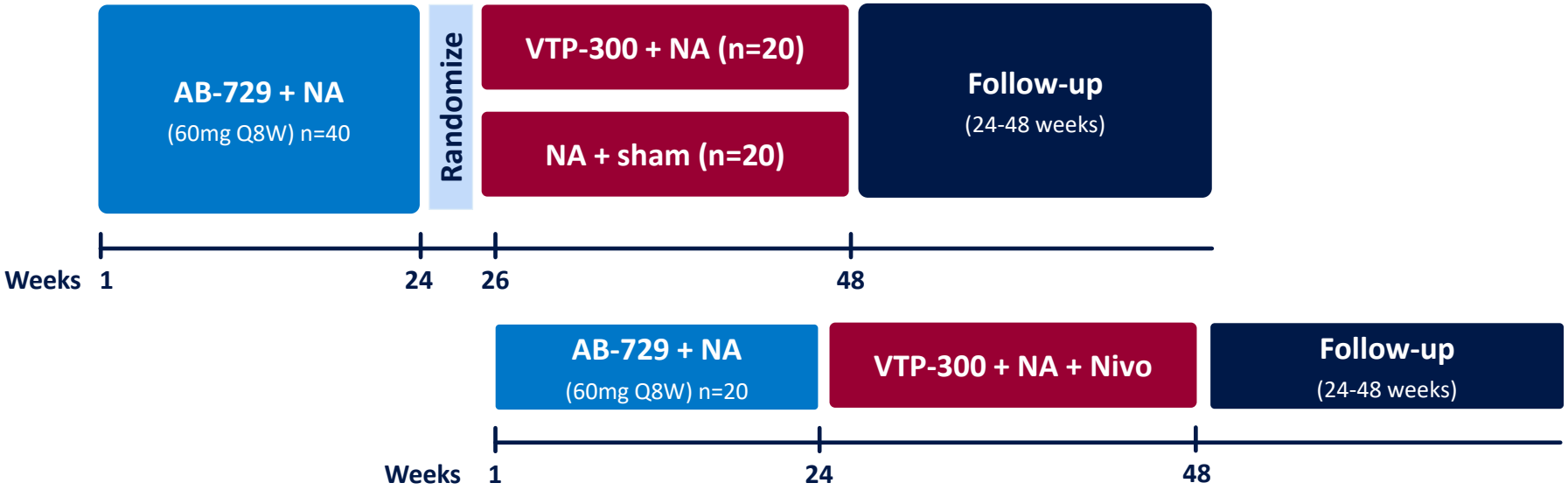
Preliminary results: First 15 patients reached Week 16 (two doses of AB-729) with a mean HBsAg decline of -1.51 log

After 24-weeks follow-up, patients will be evaluated to stop NA therapy. Those patients that stop NA therapy will be followed for an additional 48 weeks.

POC: Proof of Concept

AB-729-202:

Phase 2a POC Clinical Trial



POC Phase 2a clinical trial evaluating AB-729 in combination with Vaccitech's immunotherapeutic, VTP-300, and a NA

Preliminary data expected in 2H '23

Primary objective: evaluate safety and reactogenicity of AB-729 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

Expanded the clinical trial to include an additional arm with nivolumab (Opdivo®), and dose first patient in this arm in the first half of 2023

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

AB-729

Clinical Collaboration

assembly bio

Primary objective: evaluate safety and tolerability of vebicorvir (VBR) in combination with AB-729 in patients with cHBV receiving NA therapy

Preliminary results: Adding VBR to AB-729+NA:

- Does not result in greater on-treatment improvements in HBV biomarkers as compared to AB-729+NA alone.
- Does not have a negative impact on reducing sAg.

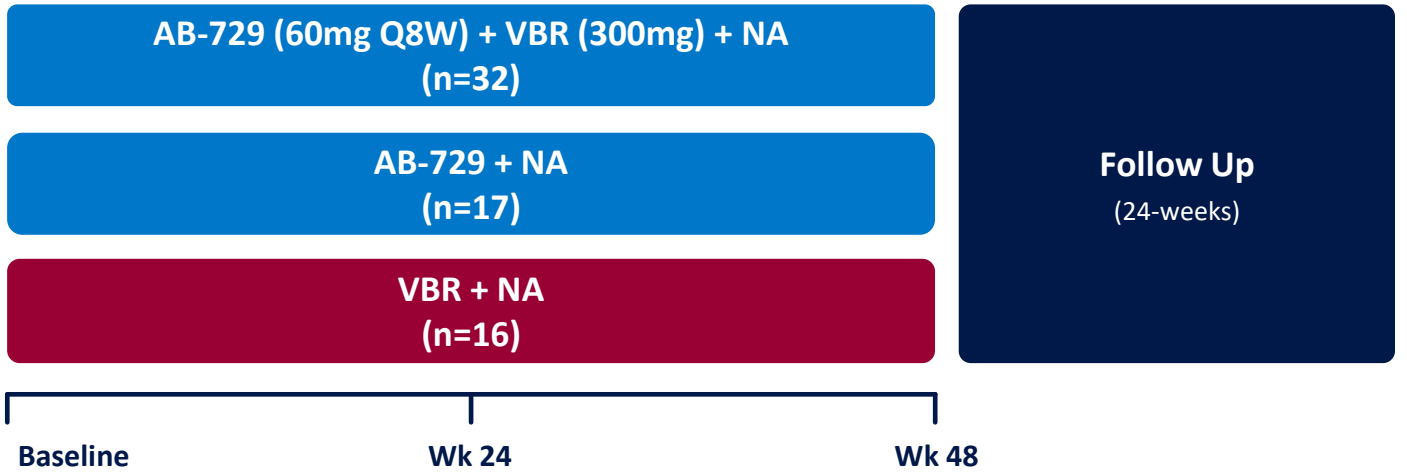
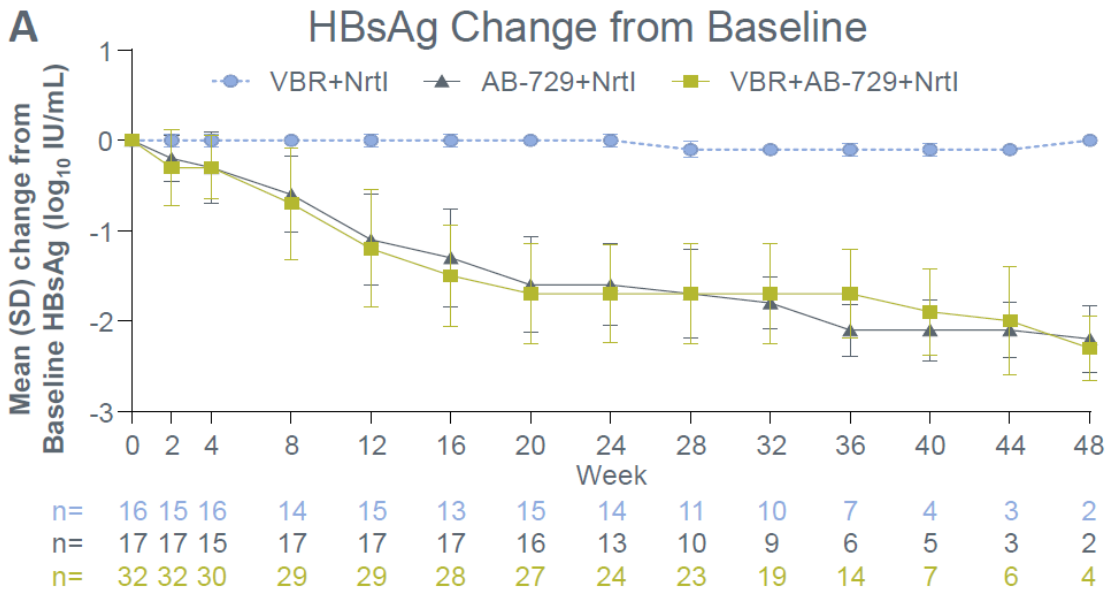


Figure 2. Changes in Virologic Parameters (On-Treatment)



Data presented at AASLD 2022

Acknowledgements

Arbutus Biopharma thanks all participating study subjects and their families, our Investigators and site staff, our CRO and laboratory partners, and the AB-729 Research and Development Teams.

Thank you!

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