Arbutus BIOPHARMA

Curing Chronic Hepatitis B

Safety and pharmacodynamics of the GalNAc-siRNA AB-729 in subjects with chronic hepatitis B infection

MF Yuen[1], E Berliba[2], YJ Kim[3], J Holmes[4], Y-S Lim[5], S Strasser[6], C Schwabe[7], A Jucov[2], ACH Lee[8], EP Thi[8], T Harasym[8], GR Pamulapati[8], P Wattamwar[8], J Kunta[8], M Sofia[8], H Sevinsky[9], K Gray[9], T Eley[9], G Picchio[9], KD Sims[9], E Gane[7]

The Liver Meeting, November 2020

NASDAQ: ABUS | www.arbutusbio.com

[1] Queen Mary Hospital, Hong Kong; [2] Arensia Exploratory Medicine, Moldova; [3] Seoul National University Hospital, South Korea; [4] St. Vincent's Hospital, Melbourne, Australia; [5] Asan Medical Center, Seoul, South Korea; [6] Royal Prince Alfred Hospital, Sydney, Australia; [7] Auckland Clinical Studies, New Zealand; [8] Arbutus Biopharma Discovery, Warminster, PA, USA; [9] Arbutus Biopharma Clinical Development, Warminster, PA, USA

Arbutus BIOPHARMA

Man-Fung Yuen, D.Sc., M.D., Ph.D.

- Chief of Division of Gastroenterology and Hepatology, Department of Medicine, The University of Hong Kong, Hong Kong
- A therapeutic expert and pioneering clinical researcher leading numerous studies on novel antiviral and immunomodulatory agents for the treatment of chronic hepatitis B virus infection
- Research includes prevention, natural history, virology, treatment of chronic hepatitis B and C and hepatocellular carcinoma and is actively involved with cutting-edge research on novel markers for hepatitis B infection and occult hepatitis B infection
- One of the top international researchers in the field of hepatitis B, with more than 450 papers published in world-renowned medical journals

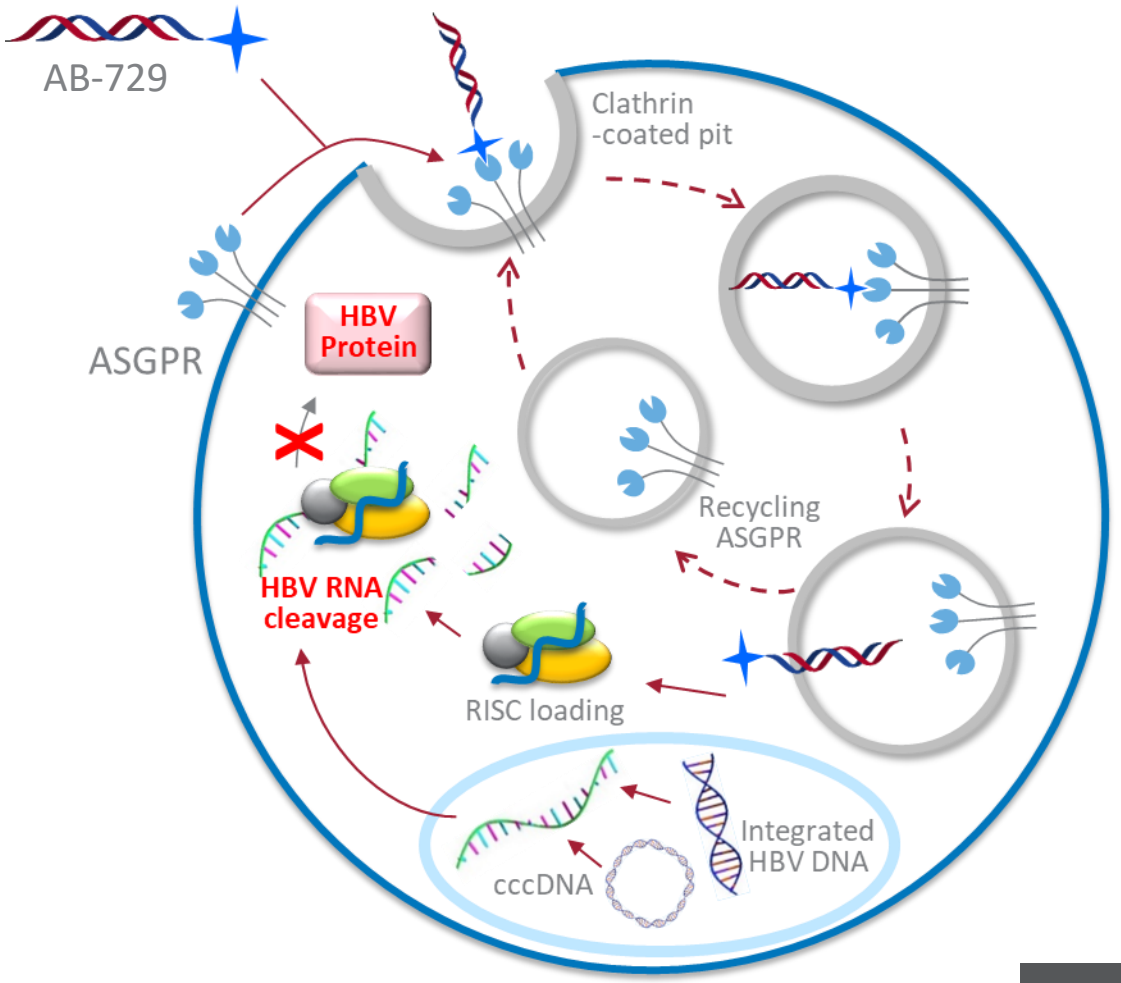
Arbutus BIOPHARMA

Disclosures

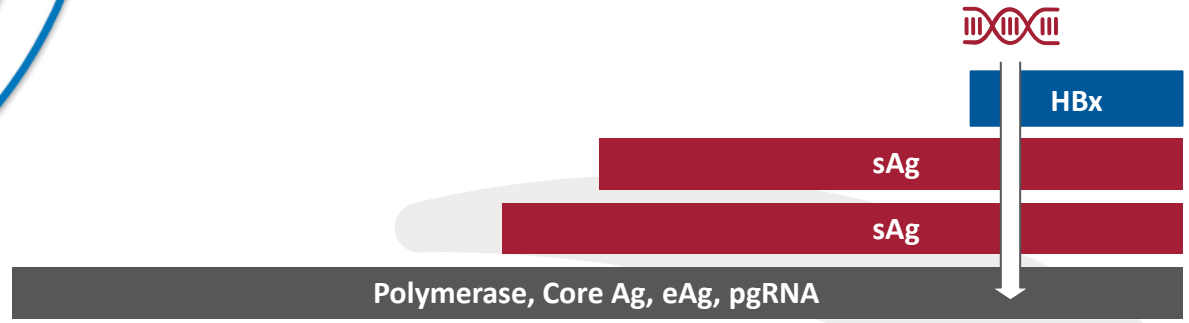
MFY acted as a consultant for AbbVie, Arbutus Biopharma, Bristol-Myers Squibb, Dicerna Pharmaceuticals, GlaxoSmithKline, Gilead Sciences, Janssen, Merck Sharp and Dohme, Clear B Therapeutics, Springbank Pharmaceuticals and Assembly Biosciences, and received grant/research support from Assembly Biosciences, Arrowhead Pharmaceuticals, Bristol-Myers Squibb, Fujirebio Incorporation, Gilead Sciences, Merck Sharp and Dohme, Springbank Pharmaceuticals, Sysmex Corporation.

Arbutus BIOPHARMA

AB-729 GalNAc-siRNA Therapeutic



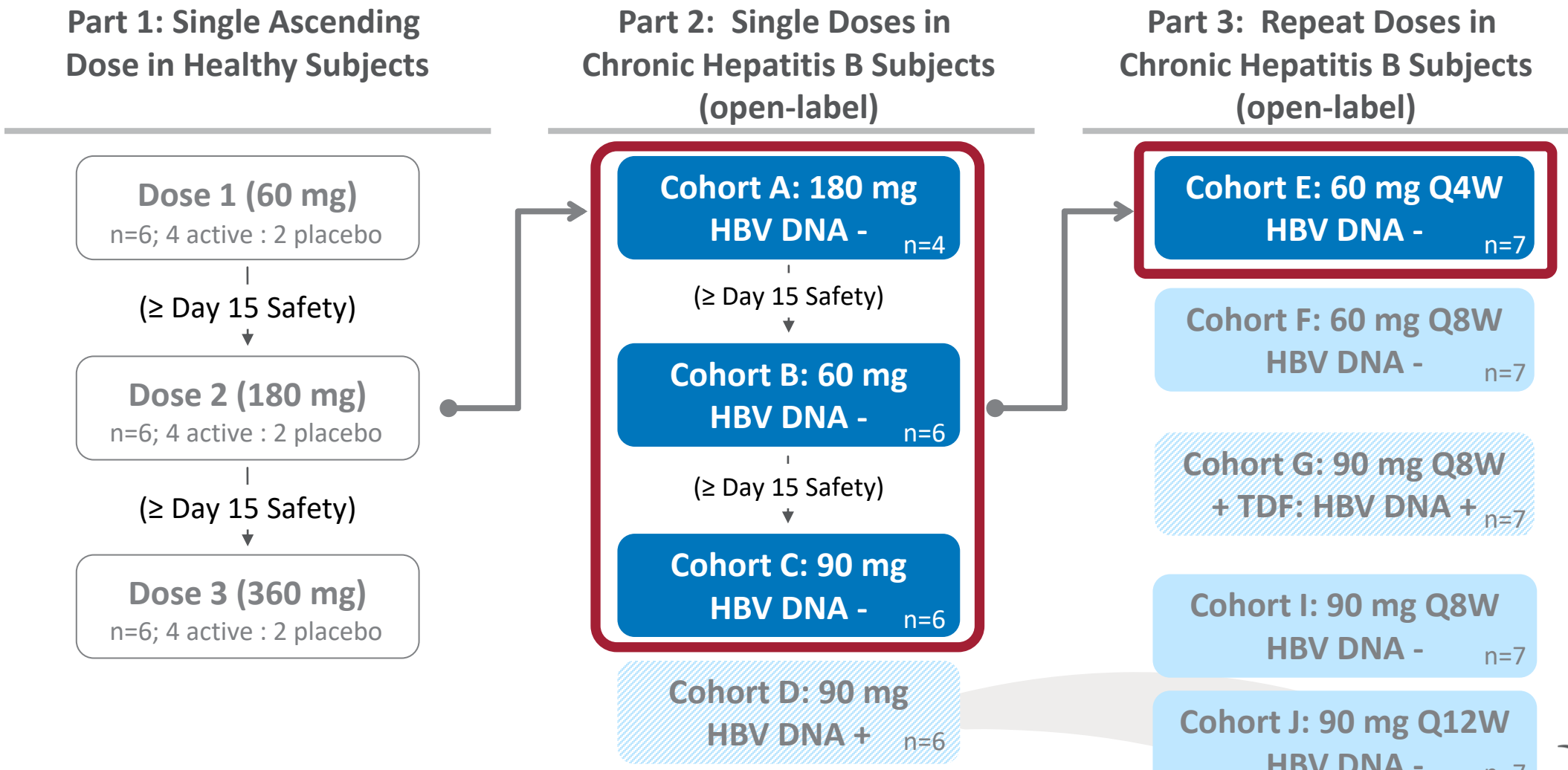
- Single trigger RNA interference agent administered subcutaneously
- Proprietary liver targeting technology based on GalNAc ligand interaction with ASGPr
- Inhibits HBV replication, reduces all HBV transcripts, and lowers all HBV antigens
- Pan-genotypic activity across HBV genotypes



Arbutus BIOPHARMA

AB-729-001 Study Overview

presentation includes data available through 06-Oct-2020



HBV: Hepatitis B Virus | TDF: tenofovir disoproxil fumarate

Key Inclusion Criteria

- **Cohorts A, B, C and E**
  - Age 18 – 65 years old
  - At least 6 months of stable nucleos(t)ide analogue (NA) therapy (ETV, TDF, TAF) prior to Screening
  - HBeAg positive or negative
  - HBV-DNA < LLOQ and HBsAg ≥ 250 IU/mL at Screening
  - Non-cirrhotic, Fibroscan® result of ≤10 kPa
  - ALT/AST at Screening:
    - Part 2 (Cohorts A, B, and C): ≤ 5x ULN
    - Part 3 (Cohort E): ≤ 2x ULN

Arbutus BIOPHARMA

Baseline Characteristics

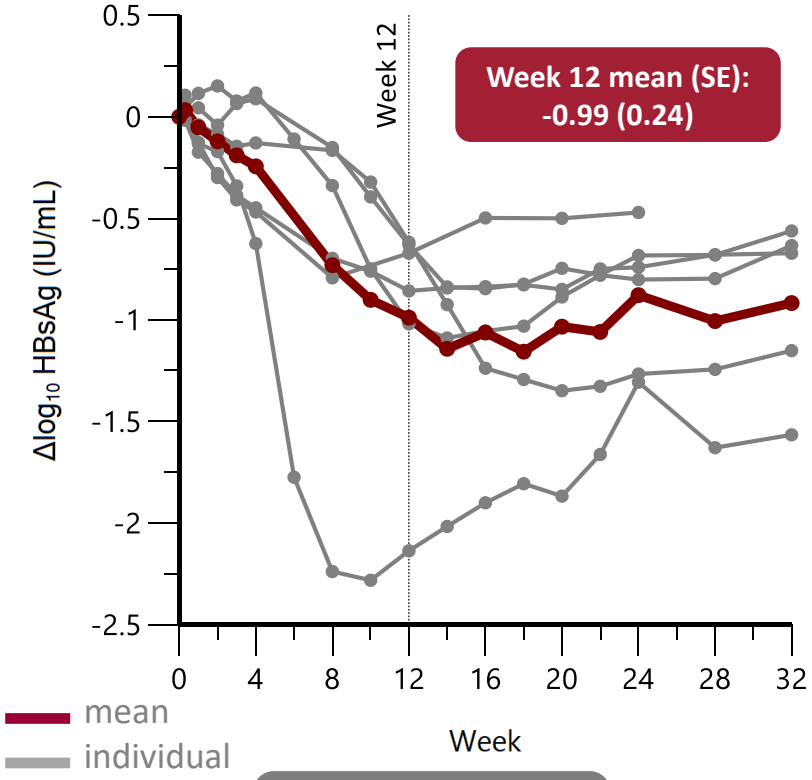
Baseline Measure	Cohort A 180 mg (N=4)	Cohort B 60 mg (N=6)	Cohort C 90 mg (N=6)	Cohort E 60 mg Q4Wk (N=7)
Age in years, mean (range)	42.8 (35-53)	48.2 (33-56)	54.8 (47-62)	45.1 (33-63)
Male gender, n (%)	3 (75%)	3 (50%)	6 (100%)	4 (57%)
BMI, mean (SD)	23.7 (3.62)	26.6 (3.23)	25.2 (1.96)	27.7 (5.01)
Race, n (%)				
Asian	0	3 (50%)	6 (100%)	1 (14%)
White	4 (100%)	3 (50%)	0	6 (86%)
ALT (U/L), mean (SD)	39.3 (35.36)	20.0 (6.52)	25.5 (9.23)	22.4 (10.52)
HBV eAg negative, n (%)	3 (75%)	6 (100%)	6 (100%)	7 (100%)
HBsAg (IU/mL), mean (range)	8577 (4720 – 10,289)	2095 (405 – 5110)	822 (261 – 1400)	5372 (584 – 11761)

- All subjects were virologically suppressed on an NA (ETV, TDF or TAF) with HBV DNA < LLOQ (20 IU/mL)
- HBV genotype was not determined

Arbutus BIOPHARMA

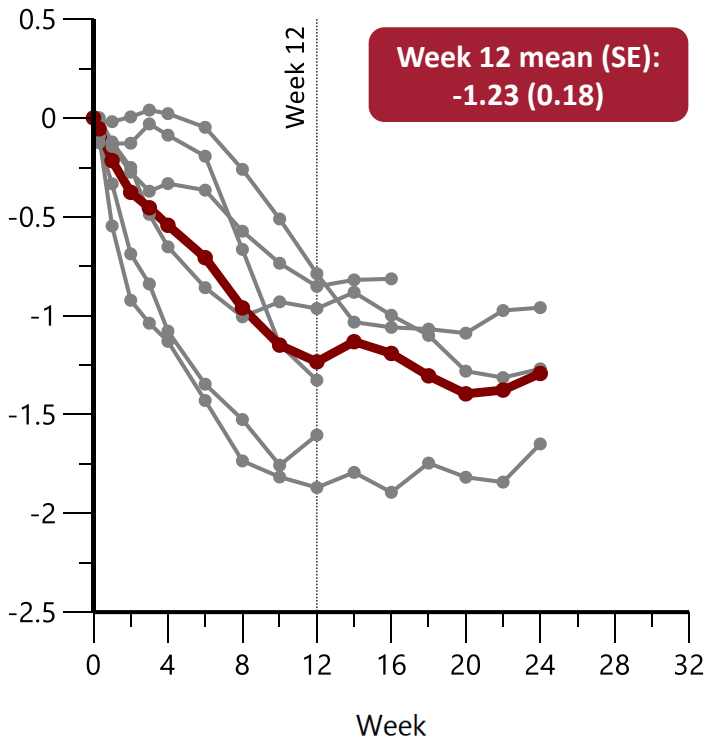
Single doses of AB-729 result in comparable mean HBsAg declines at Week 12 followed by a sustained plateau phase

AB-729 60 mg single dose (N=6)*



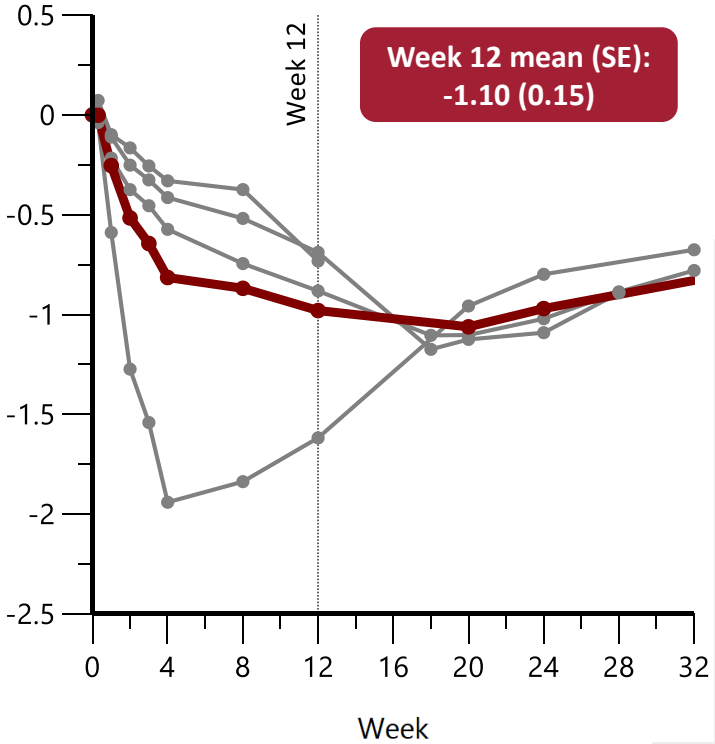
3/6 HBsAg <100 IU/mL
1/6 HBsAg <10 IU/mL

AB-729 90 mg single dose (N=6)**



5/6 HBsAg <100 IU/mL
1/6 HBsAg <10 IU/mL

AB-729 180 mg single dose (N=4)#



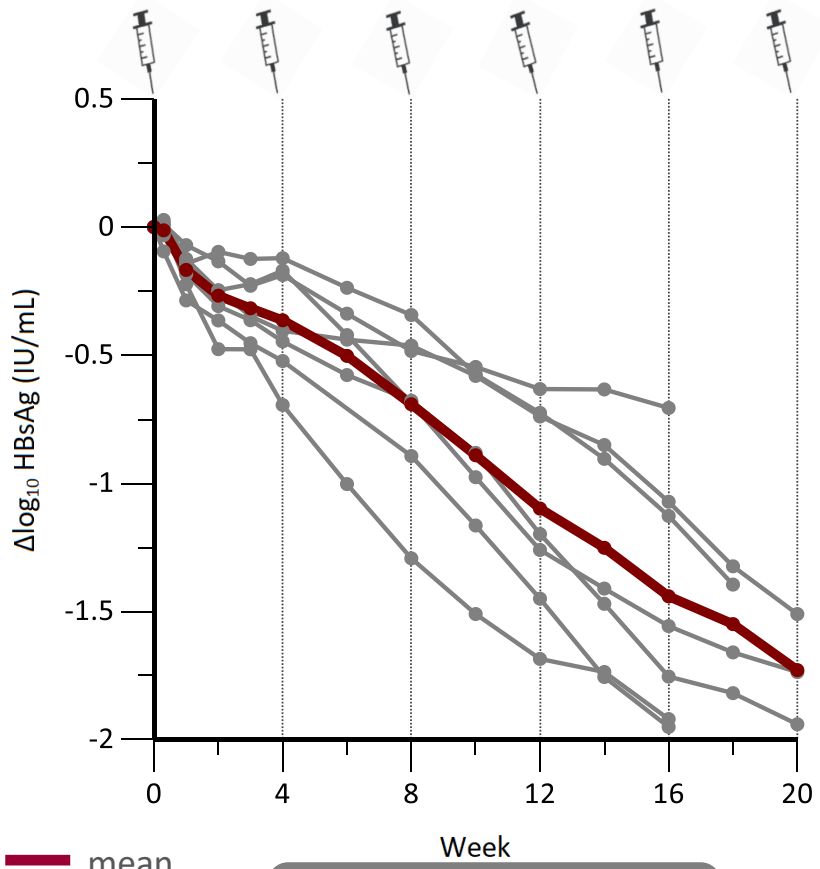
0/4 HBsAg <100 IU/mL

*N=5 at Week 10, 14, 18, 22, 28, and 32
**N=4 at Week 14 and 16; N=3 at Weeks 18 – 24
#N=3 after Week 12; nominal visits ± 7 days

Arbutus BIOPHARMA

Repeat dosing of AB-729 60 mg every 4 weeks results in continuous HBsAg declines beyond Week 12

AB-729 60 mg Q4weeks



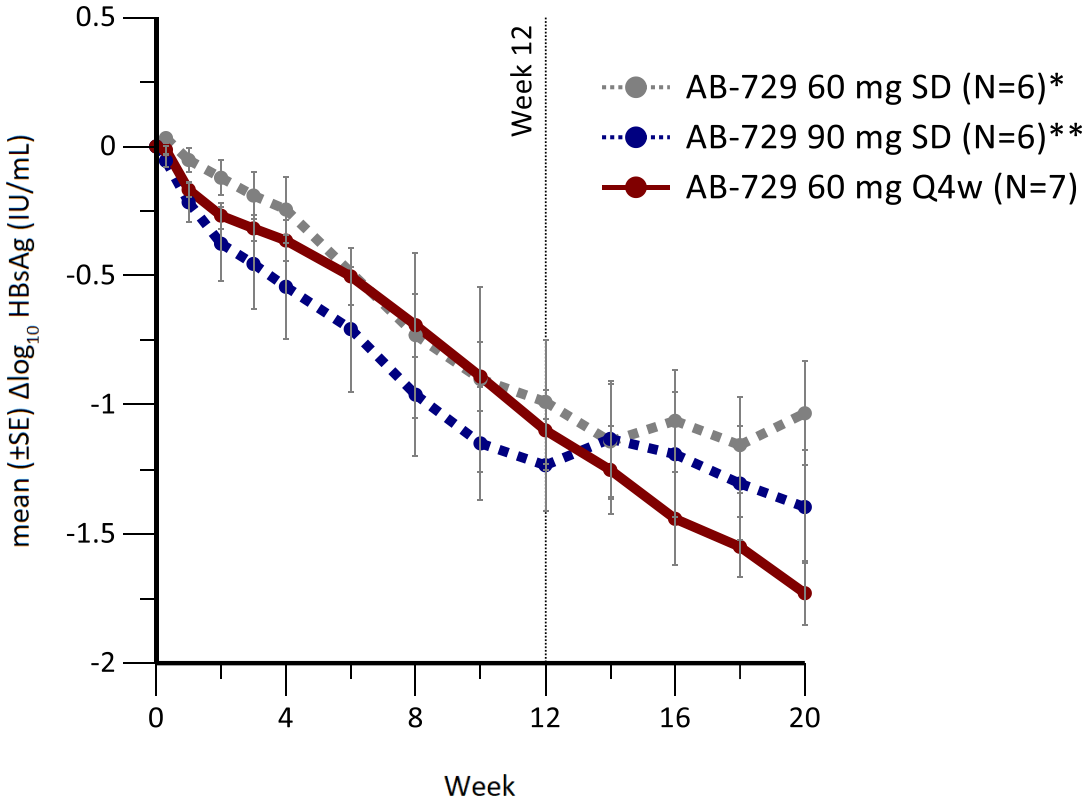
4/7 HBsAg <100 IU/mL
1/7 HBsAg <10 IU/mL

Mean (SE) Week 12:
-1.10 (0.15)

Mean (SE) Week 16:
-1.44 (0.18)

Mean (SE) Week 20:
-1.73 (0.12) [N=3]

Mean (±SE) HBsAg declines across Cohorts

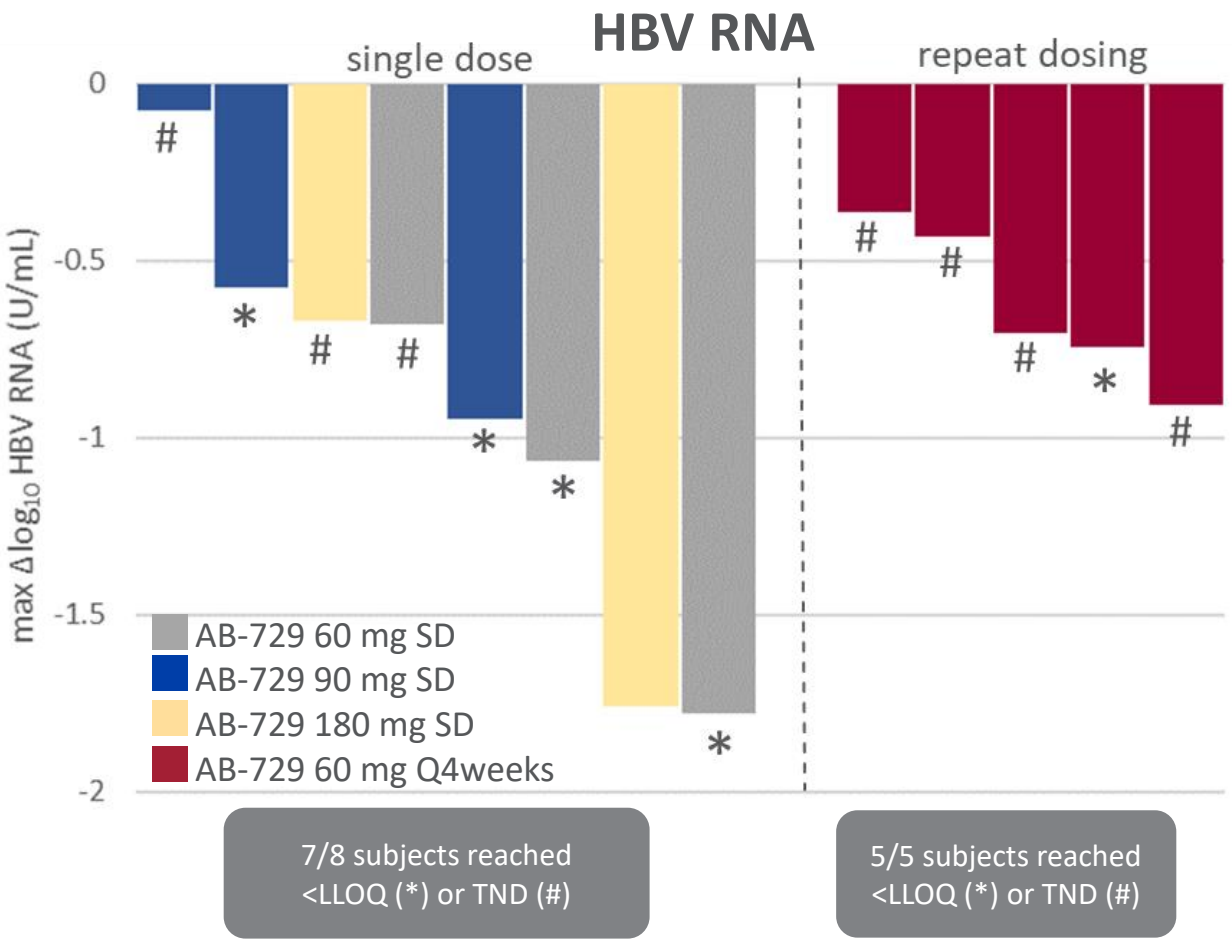


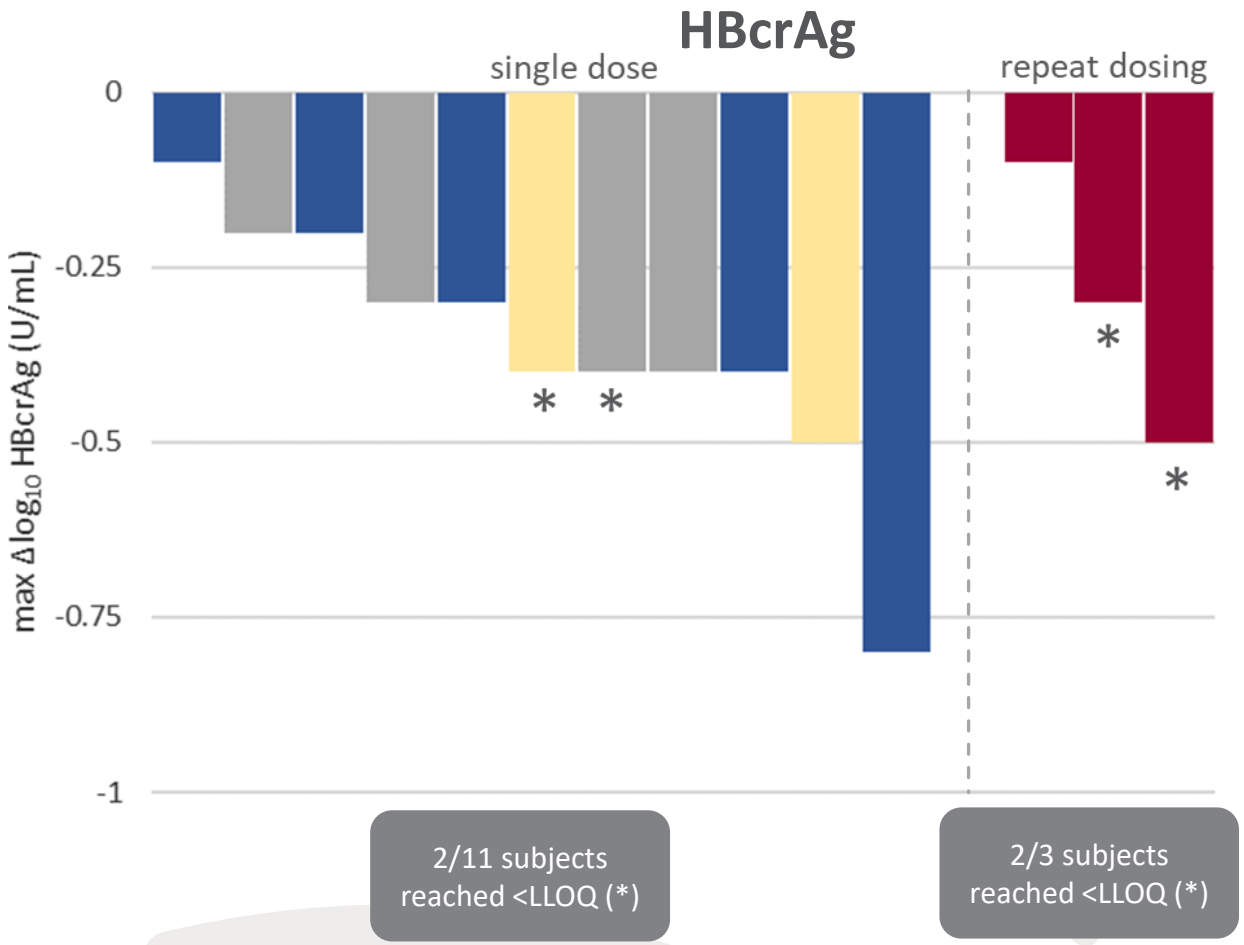
*N=5 at Week 10 and 14
**N=4 at Weeks 14 and 16; N=3 at Weeks 18 and 20
SD: single dose; Q4w: every 4 weeks

Arbutus BIOPHARMA

AB-729 reduces HBV RNA to the limits of quantification or detection in most subjects; HBcrAg also declines

Maximum reductions shown through Week 12 in subjects with quantifiable data at baseline





LLOQ = lower limit of quantitation; TND = target not detected; SD = single dose
HBcrAg samples <LLOQ (3.0 $\log_{10}$ IU/mL) assigned a value of 2.9 $\log_{10}$ IU/mL
HBV RNA samples <LLOQ (1.65 $\log_{10}$ IU/mL) or target not detected assigned a value of 1.64 $\log_{10}$ IU/mL

Arbutus BIOPHARMA

AB-729 was safe and well tolerated after single and repeat doses

- No SAEs or discontinuations due to AEs
- No treatment-related Grade 3 or 4 AEs or laboratory abnormalities
  - 1 subject (Cohort A) with rapid decline in HBsAg of ~2.0 $\log_{10}$ 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)
- Injection site TEAEs were mild (erythema, pain, pruritis, bruising) or moderate (pain) and transient
- No clinically meaningful changes in ECGs or vital signs

Subjects, n (%)	Cohort A (180 mg) N=4	Cohort B (60 mg) N=6	Cohort C (90 mg) N=6	Cohort E (60 mg Q4Wk) N=7	Total N=23
Subjects with any TEAE	4 (100)	4 (67)	5 (83)	4 (57)	17 (74)
Subjects with related TEAEs	3 (75)	2 (33)	5 (83)	3 (43)	13 (57)
Grade 1	1 (25)	2 (33)	2 (33)	2 (29)	7 (30)
Grade 2	2 (50)	0	3 (50)	1 (14)	6 (26)
Grade 3	0	0	0	0	0
Grade 4	0	0	0	0	0
Most common related TEAEs (in ≥ 2 subjects):					
Injection site pain	0	0	5 (83)†	0	5 (9)‡
Injection site erythema	0	1 (17)	0	2 (29)	4 (7)‡
ALT elevation	2 (50)	0	0	3 (43)	5 (22)
AST elevation	1 (25)	0	0	1 (14)	2 (9)
Headache	2 (50)	0	0	0	2 (9)

Grading criteria based on Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, Corrected Version 2.1., July, 2017
ALT and AST elevations were all Grade 1 excepting one Grade 2 ALT, all were asymptomatic without bilirubin changes
† 4/5 subjects from same site; 2 Gr 2 TEAEs had AB-729 dose erroneously split into 2 injections, all TEAEs lasted <1 hour
‡ n, % is number of events out of 54 total AB-729 doses administered

Arbutus BIOPHARMA

Key Take-Aways

- Across all single-dose cohorts, mean HBsAg concentrations continuously declined up to Week 12 before reaching a plateau
  - No clear dose response was observed based on HBsAg decline at Week 12; however the duration of the plateau phase may be dose dependent
  - This finding supports dosing of AB-729 less frequently than every 4 weeks
- The kinetics of HBsAg decline were similar between the single dose and repeat dose cohorts up to Week 12
- Upon repeat dosing, HBsAg continued to steadily decline beyond Week 12 with no plateau in response observed to date
- HBV RNA and HBcrAg declined upon AB-729 administration
- The doses and dose frequencies of AB-729 explored were generally safe and well tolerated

Arbutus BIOPHARMA

Acknowledgements

We express our gratitude to the patients who participated in this study as well as investigators, study site staff, Andreas Kroemer and the Novotech team, Covance, DDL, PharStat Inc., and Mark Anderson and Gavin Cloherty of Abbott Diagnostics for their contributions to this study. The authors also thank other Arbutus staff, including Michael Child, Maksym Chernyakhovskyy, Deana Antonello, Joanne Brown, Julia Williams, Laura Maile as well as the AB-729 Discovery team.

Arbutus BIOPHARMA