24-Week Safety and Efficacy of Brelovitug Monotherapy for the Treatment of Chronic Hepatitis D: Data From Phase 2b of AZURE-1

Poster LBP-021

Tatyana Kushner,[1] David Yardeni,[2] Marta Dobryanska,[3] Alina Jucov,[4] Douglas T. Dieterich,[5] Jordan J. Feld,[6] Maia Butsashvili,[7] Ekaterine Dolmazashvili,[8] Dragomir Gerov,[9] Tamar Khuchua,[10] Tarek Saadi,[11] David Kaplan,[12] James Park,[13] Dimitar Pavlov,[14] Mariana Penkova Radicheva,[9] Carla S. Coffin,[15] Edward J. Gane,[16] Sébastien Poulin,[17] Ira Jacobson,[18] Miriam Levy,[19] Mark S. Sulkowski,[20] Norah Terrault,[21] Karen Doucette,[22] Nancy S. Reau,[23] Simone Strasser,[24] Tomohiro Tanaka,[25] Ashley Duzik,[26] Susanna K. Tan,[27*] Sue Naim,[27] Will Garner,[27] Craig S. Pace,[27] Hassan Javanbakht,[27*] Nancy Shulman,[27*] Saeed Sadiq Hamid,[28] Cihan Yurdaydin[29]

[1]Weill Cornell Medicine, New York, New York, United States; [2]Soroka University Medical Center, Beersheva, Israel; [3]Arensia Exploratory Medicine GmbH, Kyiv, Ukraine; [4]Arensia Exploratory Medicine GmbH and Nicolae Testemitanu State University of Medicine and Pharmacy, Chişinău, Moldova; [5]Icahn School of Medicine at Mount Sinai, New York, New York, United States; [6]Toronto Centre for Liver Disease, University Health Network, Toronto General Hospital, Toronto, Canada; [7]Clinic NeoLab, Tbilisi, Georgia; [8]Hepatology Clinic Hepa, Tbilisi, Georgia; [9]University Multiprofile Hospital For Active Treatment, Plovdiv, Bulgaria; [10]Geo Hospitals Tbilisi Multiprofile Medical Center, Tbilisi, Georgia; [11]Rambam Health Care Campus, Haifa, Israel; [12]University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, United States; [13]Northwell Health Center for Liver Disease and Transplantation, New York, New York, United States; [14]Multiprofile Hospital for Active Treatment, Plovdiv, Bulgaria; [15]University of Calgary, Cumming School of Medicine, Calgary, Canada; [16]New Zealand Clinical Research (NZCR), Auckland, New Zealand; [17]CMU du Quartier Latin, Montreal, Canada; [18]NYU Grossman School of Medicine, New York, New York, United States; [19]Liverpool Hospital, Liverpool, Australia; [20]Johns Hopkins Hospital, Baltimore, Maryland, United States; [21]Keck School of Medicine of the University of Southern California, Los Angeles, California, United States; [22]University of Alberta, Edmonton, Canada; [23]Rush University System for Health, Chicago, Illinois, United States; [24]AW Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital, Sydney, Australia; [25]University of Iowa, Iowa City, Iowa, United States; [26]Long Beach Research Institute, Long Beach, California, United States; [27]Mirum Pharmaceuticals, Inc., Foster City, California, United States; [28]Aga Khan University, Karachi, Pakistan; [29]Koc University Hospital, Istanbul, Türkiye

*Previously at Bluejay Therapeutics, Inc., Redwood City, California, United States

Introduction

- Chronic hepatitis D (CHD) is the most severe form of viral hepatitis, affecting >12 million people worldwide.[1]
- Patients with CHD have a higher risk of cirrhosis, liver cancer, and death compared to those with chronic hepatitis B (CHB) alone.[2,3]
- Brelovitug is an investigational fully human immunoglobulin G1 (IgG1) neutralising monoclonal antibody administered subcutaneously, that targets the hepatitis B virus surface antigen (HBsAg) with pan-genotypic activity.[4]
  - In *in vitro* assays, brelovitug potently binds to HBsAg to neutralise both hepatitis D virus (HDV) and hepatitis B virus (HBV), preventing new infection of hepatocytes.[4,5]
  - Brelovitug also rapidly clears circulating HDV and HBV virions and subviral particles.[4,5]
- In a phase 2 clinical trial, brelovitug demonstrated parallel reductions in HDV RNA and ALT over time across all regimens tested and was well tolerated in individuals with CHD with and without cirrhosis.[5]

Objective

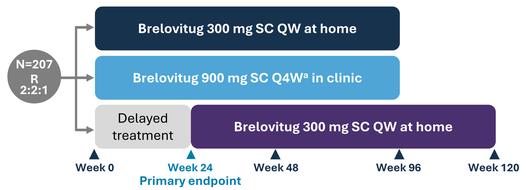
- To evaluate the efficacy and safety of brelovitug compared to delayed treatment in individuals with CHD.

Methods

- AZURE-1 (NCT06907290) is a global, randomised, controlled, seamless phase 2b/3 study of brelovitug vs delayed treatment in participants with CHD that is being conducted in 10 countries, including the United States.[6]
- The phase 2b portion comprises the first ~50 patients.

Key Inclusion Criteria:
- Aged ≥18 years
- HDV RNA >500 IU/mL and ALT >ULN
- Child-Pugh score <7
- Taking or willing to take nucleos(t)ide treatment

Key Exclusion Criteria:
- Clinical hepatic decompensation
- Hepatocellular carcinoma
- Presence of other liver diseases
- Platelet count <50,000/µL
- No exclusion criteria for liver stiffness, portal hypertension, HIV coinfection, bilirubin, albumin, INR, or maximum ALT



Primary Endpoint
- Composite of virologic response (HDV RNA ≥2 $\log_{10}$ reduction or <LLOQ or undetectable) and ALT normalisation at Week 24

Select Secondary Endpoints
- Safety and tolerability vs delayed treatment
- Efficacy at Week 48 and Week 96
- Change from Baseline in liver stiffness

[a]With a loading dose at Week 2.

Results

- Of 54 participants who were randomised, 53 were evaluated: 300 mg QW (n=21), 900 mg Q4W (n=20), and delayed treatment (n=12).
  - One participant who was randomised to the 300 mg QW cohort was never dosed and was excluded from efficacy and safety analyses.

Table 1. Demographics and Baseline Characteristics

Parameter[a]	300 mg QW (n=21)[b]	900 mg Q4W (n=20)[c]	Delayed treatment (n=12)[d]	Total (N=53)
Age, years	45.8 (7.0), 37-61	44.8 (8.4), 26-58	49.0 (9.9), 34-65	46.1 (8.2), 26-65
Sex, male, n (%)	13 (62)	15 (75)	9 (75)	37 (70)
Race, White, n (%)	19 (90)	19 (95)	11 (92)	49 (92)
Cirrhosis, n (%)[e]	10 (48)	11 (55)	7 (58)	28 (53)
Child-Pugh score, n (%)[f]				
A5	9 (90)	9 (82)	6 (86)	24 (86)
A6	1 (10)	2 (18)	1 (14)	4 (14)
Liver stiffness, kPa	16.4 (12.7), 4.9-57.3	16.8 (9.6), 6.0-40.9	16.6 (8.6), 6.7-39.2	16.6 (10.5), 4.9-57.3
Liver stiffness ≥25 kPa, n (%)	3 (14)	4 (20)	1 (8)	8 (15)
ALT, U/L	116 (91), 25-357	132 (106), 47-492	124 (91), 35-273	124 (95), 25-492
ALT ≥5 × ULN, n (%)	4 (19)	3 (15)	4 (33)	11 (21)
Platelet count, n (%)				
<110,000/µL	5 (24)	5 (25)	4 (33)	14 (26)
<150,000/µL	7 (33)	9 (45)	6 (50)	22 (42)
HBsAg, $\log_{10}$ IU/mL	4.0 (0.4), 2.9-4.7	4.1 (0.5), 2.8-4.7	3.9 (0.8), 2.0-4.9	4.0 (0.5), 2.0-4.9
HBeAg+, n (%)	6 (29)	4 (20)	3 (25)	13 (25)
HIV coinfection, n (%)	0	0	1 (8)	1 (2)
HDV RNA, $\log_{10}$ IU/mL	5.4 (1.0), 2.9-6.6	5.6 (0.6), 4.6-6.9	5.5 (0.9), 3.7-6.4	5.5 (0.8), 2.9-6.9
HBV genotype D, n (%)	18 (86)	18 (90)	10 (83)	46 (87)
HDV genotype 1, n (%)	19 (90)	20 (100)	12(100)	51 (96)

[a]Data are mean (SD), range unless otherwise indicated. [b]One participant was randomised to the 300 mg QW cohort and received 1 dose, then discontinued (not due to an AE) and had no efficacy follow-up; they were not included in the efficacy analyses. [c]One participant in the 900 mg Q4W cohort was lost to follow-up and withdrawn from study after Week 12; they were included in all analyses. [d]One participant in the delayed treatment cohort withdrew from the study after Week 12 due to a move out of the country; they were included in all analyses. [e]Defined as liver stiffness ≥12.5 kPa. [f]Child-Pugh score is n (%) of participants with cirrhosis.

AZURE-1 Phase 2b Week 24 Data Met the Primary Endpoint

Table 2. Virologic Response and ALT Normalisation[a,b]

Parameter, n/N (%)	300 mg QW (n=20)	900 mg Q4W (n=20)[c]	Delayed treatment (n=12)
Virologic response (HDV RNA ≥2 $\log_{10}$ reduction or undetectable)	20/20 (100)	15/20 (75)	0/12 (0)
HDV RNA <LLOQ	9/20 (45)	2/20 (10)	0/12 (0)
HDV RNA undetectable	6/20 (30)	1/20 (5)	0/12 (0)
ALT normalisation	9/20 (45)	8/20 (40)	1/12 (8)
Primary endpoint[d] (Virologic response + ALT normalisation)	9/20 (45) ***P*=0.003**	7/20 (35) ***P*=0.024**	0/12 (0)

[a]Data were analysed for participants who had at least one post-Baseline efficacy assessment. [b]HDV RNA levels were assessed using an RT-qPCR assay (Victorian Infectious Disease Reference Laboratory, Melbourne) in which LLOQ was 10 IU/mL and LOD was 5 IU/mL. [c]One participant in the 900 mg Q4W who was lost to follow-up and withdrawn from study after Week 12 had HDV RNA decline of -2.6 $\log_{10}$ at Week 12 but was considered a non-responder at primary analysis. [d]*P* values compare each treatment group against delayed treatment using a stratum-adjusted Cochran-Mantel-Haenszel test.

- Normalisation of ALT at any time up to and including Week 24 was observed in 60% (12/20) and 50% (10/20) of the 300 mg QW and 900 mg Q4W cohorts, respectively.

In a Previous Phase 2 Trial (BJT-778-001), Brelovitug Demonstrated Antiviral Activity and ALT Normalisation at Week 24

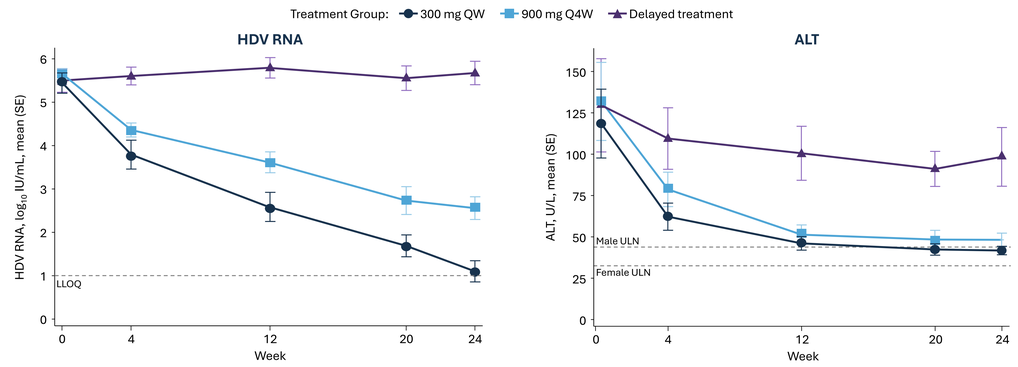
Table 3. Virologic Response and ALT Normalisation[a]

Parameter, n/N (%)	300 mg QW (N=18)[b]	900 mg Q4W (N=18)[b]
Virologic response (HDV RNA ≥2 $\log_{10}$ reduction or undetectable)	16/18 (89)	18/18 (100)
HDV RNA <LLOQ (10 IU/mL)	9/18 (50)	8/18 (44)
HDV RNA undetectable	5/18 (28)	6/18 (33)
ALT normalisation	9/17 (53)	13/17 (76)
Virologic response + ALT normalisation	9/17 (53)	13/17 (76)

[a]Registered trials: ACTRN12623000075684, ACTRN12623000078651, ACTRN12623000105640, and ACTRN12623000111673. [b]One participant had normal ALT at Baseline.

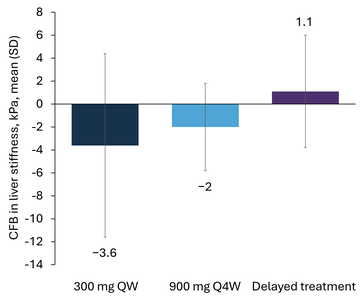
Reductions in Both HDV RNA and ALT Were Observed After Treatment With Brelovitug

Figure 1. Change in HDV RNA and ALT Levels From Baseline Through Week 24



- Decline in both HDV RNA and ALT levels were observed from Baseline through Week 24 for both brelovitug 300 mg QW and 900 mg Q4W arms versus delayed treatment arm.
- No virologic breakthrough observed to date.

Figure 2. Change in Liver Stiffness From Baseline at Week 24



Brelovitug Treatment was Safe and Well Tolerated

Table 4. Summary of AEs

Parameter, n (%)	300 mg QW (n=21)	900 mg Q4W (n=20)	Delayed treatment (n=12)
AEs			
Any	11 (52)	10 (50)	3 (25)
Related to treatment	7 (33)	7 (35)	0
AE grade ≥3			
Any	1 (5)[a]	0	0
Related to treatment	0	0	0
Serious AE			
Any	0	1 (5)[b]	0
Related to treatment	0	0	0
AE leading to discontinuation of study drug	0	0	0
Injection site reactions	3 (14)	4 (20)	0
Flu-like syndrome	0	1 (5)	0

[a]Grade 3 AE of musculoskeletal pain, not related. [b]Hospitalisation for liver cirrhosis, class B, in a participant with recent history of ascites and hypoalbuminaemia, not related and resolved.

- Both regimens of brelovitug were well tolerated; flu-like syndrome was uncommon.
- Most common adverse event related to brelovitug was injection site reaction; all were mild grade 1 events.

Conclusions

- In participants with chronic hepatitis D, improvements in HDV RNA and ALT levels, key markers of disease activity, were observed with brelovitug treatment.
- A statistically significant difference in the primary endpoint (composite of virological response and ALT normalisation at Week 24) was observed for both doses of brelovitug evaluated, compared with delayed treatment.
- Brelovitug was safe and well tolerated, with the most common adverse events being injection site reactions.
- Multiple phase 3 trials are ongoing (NCT06907290; NCT07200908; NCT07454837; NCT07298330).

Abbreviations

A5, Child-Pugh A5; A6, Child-Pugh A6; AE, adverse event; ALT, alanine aminotransferase; CFB, change from baseline; CHB, chronic hepatitis B; CHD, chronic hepatitis D; HBeAg+, hepatitis B virus e antigen positive; HBsAg, hepatitis B virus surface antigen; HBV, hepatitis B virus; HDV, hepatitis D virus; HIV, human immunodeficiency virus; IgG1, immunoglobulin G1; INR, international normalised ratio; IU, international units; kPa, kilopascals; LLOQ, lower limit of quantitation; LOD, limit of detection; Q4W, every 4 weeks; QW, weekly; R, randomisation; RNA, ribonucleic acid; RT-qPCR, reverse transcription quantitative polymerase chain reaction; SC, subcutaneous; SD, standard deviation; SE, standard error; ULN, upper limit of normal.

Disclosures

T. Kushner is an advisor to and received research support from Gilead, Mirum Pharmaceuticals, Inc., Madrigal, and Ipsen and is an advisor to GSK, VIR, AbbVie, and Argo. AJ reports a relationship with Vir Biotechnology, Tune Therapeutics, and Mirum Pharmaceuticals, Inc. (previously BlueJay Therapeutics, Inc.). MB reports a relationship with Health Research Union (HRU), The Partnership for International Vaccine Initiatives - boosting influenza vaccine uptake among healthcare workers in Georgia. DK received support to his institution from Bausch, AstraZeneca, and Mirum Pharmaceuticals, Inc. (previously Bluejay Therapeutics, Inc.). JP received research funding (paid to Northwell Health) from Aligos and Bluejay Therapeutics, Inc. and is a consultant for VIR, Mirum Pharmaceuticals, Inc. (previously Bluejay Therapeutics, Inc.), Gilead, GSK, Orphalan, and IPSEN. CSC reports relationships with GSK, Gilead, VIR, and AusperBio, and received funding from BlueJay Therapeutics, Inc. (paid to the University of Calgary). SP is a consultant for and received grants from Gilead and is a consultant for AbbVie, GSK, Merck, and ViiV. NT is an advisor for and received grant support from Mirum Pharmaceuticals, Inc. (previously Bluejay Therapeutics, Inc.). KD is an advisor of and received research funding from Gilead and GSK and received research funding from Janssen and Bluejay Therapeutics, Inc. NSR received research funding from VIR (paid to Rush University), Gilead, and Bluejay Therapeutics, Inc. and is a consultant for VIR, Mirum Pharmaceuticals, Inc. (previously Bluejay Therapeutics, Inc.), and Gilead. SS reports a relationship with CSL Behring, CSL Seqirus, Roche, Ipsen, Dr Falk, Novo Nordisk, Norgine, Gilead Sciences, AstraZeneca, Sirtex, and Chiesi. SKT, SN, WG, CSP, HJ, and NS are employees of and shareholders in Mirum Pharmaceuticals, Inc. DY, MD, DTD, JJF, ED, DG, T. Khuchua, TS, DP, MPR, EJG, IJ, ML, MSS, TT, AD, SSH, and CY declare no conflicts of interest.

Acknowledgements

The authors would like to thank the clinical trial participants, their families, and the investigators for their participation in this study. Brelovitug is owned by Mirum Pharmaceuticals, Inc. This analysis was funded by Mirum Pharmaceuticals, Inc. Medical writing and editorial support for the development of this poster was provided by Precision AQ in Bethesda, Maryland, USA, and was funded by Mirum Pharmaceuticals, Inc.

References

1. Stockdale AJ, et al. *J Hepatol*. 2020;73:523-532. 2. Fattovich G, et al. *Gut*. 2000;46:420-426. 3. Wranke A, et al. *Hepatol Int*. 2023;17:1359-1367. 4. Ramos HJ, et al. Presented at EASL 2024. 5. Agarwal K, et al. Presented at AASLD 2025. 6. ClinicalTrials.gov identifier: NCT06907290. Updated March 2, 2026. Accessed May 8, 2026. https://clinicaltrials.gov/study/NCT06907290.

Presented at the European Association for the Study of the Liver (EASL) Congress; 27-30 May 2026; Barcelona, Spain