Hepatitis D breakthrough: Chinese-built antibody Libevitug offering hope for cirrhosis reversal

Editorial Team*

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The therapeutic landscape for chronic hepatitis D virus (HDV) infection, long considered the most severe form of viral hepatitis, has remained largely static for decades. With the recent conditional approval of Libevitug (HH-003) by China's National Medical Products Administration in January 2026, a new class of therapy—a fully human monoclonal antibody targeting viral entry—has entered clinical practice. It is now reaching patients in China, with the first clinical prescription written at Beijing Friendship Hospital on March 16, 2026, marking the official start of its real-world application.

This first-in-class biologic was developed by Huahui Health, a biotechnology company co-founded by Dr. Wenhui Li in China to translate fundamental discoveries into therapies. It represents a significant advance in treating HDV patients and brings new hope for cirrhosis reversal.

HDV is a defective RNA virus that requires hepatitis B virus (HBV) surface proteins for assembly, release, and transmission. The resulting HBV/HDV co-infection accelerates liver disease progression, with affected individuals facing a 2- to 5-fold higher risk of developing cirrhosis and hepatocellular carcinoma compared to those with HBV monoinfection.

Until recently, treatment options were limited to off-label pegylated interferon-alpha (PEG-IFNα), which achieves sustained virological response in only 20-30% of patients and is poorly tolerated. The entry inhibitor bulevirtide (Hepcludex®) received marketing authorization in the European Union in 2023 and has since been approved in several other countries. However, its availability remains geographically restricted.

MECHANISM OF ACTION AND PRECLINICAL DEVELOPMENT

The foundation of Libevitug is based on a landmark scientific discovery. In

Figure 1. Libevitug approved in China as first-in-class treatment for hepatitis D

2012, a research team led by Dr. Wenhui Li at the National Institute of Biological Sciences(NIBS), Beijing, identified the sodium taurocholate cotransporting polypeptide (NTCP) as the long-sought functional receptor for both HBV and HDV.[1] This breakthrough, which solved a decades-old mystery, revealed the precise "keyhole" the viruses use to unlock and enter liver cells. Building on this, Dr. Li and his team, in collaboration with antibody expert Dr. Jianhua Sui, co-founded the biotechnology company Huahui Health in 2015 to translate this fundamental discovery into a therapeutic.

Libevitug targets the preS1 domain of the HBV large envelope protein, which is also present on the HDV envelope. This domain mediates virus attachment to NTCP. By binding to preS1, Libevitug acts as a precise "molecular lock," sterically blocking the virus-receptor interaction and preventing de

novo infection or reinfection of hepatocytes. Preclinical studies demonstrated that the antibody, derived from a parental clone designated 2H5-A14, neutralizes HBV and HDV with picomolar potency in cell culture systems. In humanized mouse models, prophylactic administration prevented HDV infection, while therapeutic dosing reduced established HBV infection in an Fc-dependent manner, suggesting that antibody-dependent cellular cytotoxicity and phagocytosis may contribute to viral clearance beyond simple entry blockade.[2]

"The teams at Huahui Health and NIBS have worked together to complete the full-cycle of biomedical innovation from 'uncovering fundamental mechanism' to 'developing effective drugs', positioning us at the leading edge of this field and demonstrating our capability and commitment to tackling critical challenges in human health." Dr. Li said.

CLINICAL EFFICACY: PHASE IIA AND IIB FINDINGS

The proof-of-concept Phase IIa trial, conducted at a single center in China, enrolled nine participants with chronic HBV/HDV coinfection who received 20 mg/kg Libevitug intravenously every two weeks, followed by 24 weeks of follow-up. At week 24, eight of nine participants (88.9%) achieved a ≥1 $\log_{10}$ reduction in HDV RNA from baseline, with four (44.4%) attaining undetectable levels. Virological response, defined as undetectable HDV RNA or ≥2 $\log_{10}$ decline, was achieved in 77.8% of participants. Among those with elevated baseline ALT, three of five (60.0%) achieved Alanine aminotransferase (ALT) normalization. Importantly, six of nine participants (66.7%) maintained virological response through week 48, indicating durability of effect following treatment cessation.

The subsequent Phase IIb trial (NCT05861674), conducted in China and Pakistan, was multi-center, randomized, controlled and open-label. It randomized 94 patients with abnormal baseline ALT across three arms: Libevitug 20 mg/kg plus tenofovir alafenamide (TAF), Libevitug 10 mg/kg plus TAF, or TAF alone. At week 24, combined response rates (HDV RNA < lower limit of quantification or ≥2 $\log_{10}$ decline plus ALT normalization) were 35.0% and 32.4% in the 20 mg/kg and 10 mg/kg groups, respectively, compared to 5.0% in controls. By week 48, combined response rates increased to 42.5% and 44.1% in the active arms. Treatment was also associated with improvements in liver stiffness measurements, suggesting potential fibrosis regression. Notably, in the 20mg/kg group, HDV virological suppression was achieved in 60% of patients, and a high ALT normalization of 70%.[3]

Perhaps most striking was the drug's impact on liver stiffness, a non-invasive measure of fibrosis. The data suggest Libevitug can not only halt disease progression but actively improve liver hardness, indicating potential reversal of cirrhosis—a clinical endpoint that matters immensely to patients.

Safety data from the Phase IIb trial indicated favorable tolerability. No serious adverse events related to Libevitug or treatment discontinuations were reported. Adverse events were predominantly mild to moderate, with treatment-related events occurring in a minority of participants.

LIMITATIONS AND KNOWLEDGE GAPS

Despite encouraging efficacy signals, some critics argue that both trials enrolled relatively small numbers of patients, and the Phase IIa study lacked a control group. They further point out that the optimal treatment duration remains undefined. As an entry inhibitor, Libevitug blocks infections but does not directly eliminate the virus from already infected cells. Its success is tied to the persistent presence of its target, the large envelope protein of HBV. The observed plateau in viral decline and potential for relapse upon treatment cessation, challenges familiar from the bulevirtide experience, will need to be addressed.

COMPARATIVE CONSIDERATIONS AND SAFETY PROFILE

Mechanistically, Libevitug and bulevirtide both block NTCP-mediated entry but differ in their molecular format and interaction with the receptor. Bulevirtide is a synthetic N-acylated preS1 peptide that directly engages NTCP, whereas Libevitug is a full-length IgG1 antibody targeting the viral preS1 domain. A notable distinction is their effect on bile acid homeostasis: bulevirtide inhibits NTCP's bile salt transport function, leading to consistent elevations in serum bile acids. In contrast, Libevitug demonstrated minimal impact on bile acid levels in clinical trials, potentially due to its mechanism of viral blockade without receptor occupancy.

GLOBAL FUTURE

Regulatory authorities outside China have not yet approved Libevitug. However, the US Food and Drug Administration granted it Breakthrough Therapy Designation in 2024. Discussions regarding Phase III trials and potential partnerships are reportedly underway in regions with high HDV prevalence, including Pakistan and parts of Eastern Europe and Central Asia, where prevalence rates among HBV carriers can exceed 20%.

Several unanswered questions will shape the drug's future role. The potential for combination therapy—with PEG-IFNα, or emerging agents targeting HBV cccDNA or HBV mRNAs—remains to be explored. Furthermore, long-term outcomes, including cirrhosis regression, HCC incidence, and survival, require extended follow-up.

According to the World Health Organization, approximately 12 million people worldwide are infected with HDV, affecting nearly 5% of all chronic HBV carriers. Geographical hotspots include Mongolia, the Republic of Moldova, and countries in western and central Africa. In Pakistan alone, officials estimate over one million individuals may be affected, with approximately 20% of hepatitis B patients potentially co-infected. In July 2025, the International Agency for Research on Cancer (IARC) officially classified HDV as carcinogenic to humans, underscoring the urgency of effective intervention. WHO recommends screening and testing for hepatitis D in all hepatitis B surface antigen (HBsAg)-positive individuals.

Until Libevitug was conditionally approved by the Chinese regulator in January, aside from Europe, no drugs for chronic HDV infection had been approved in China or the United States. It now joins the limited armamentarium as the first monoclonal antibody-based therapy for HDV. Its entry into clinical use provides a novel mechanism of action and a favorable safety profile, though its ultimate contribution will depend on confirmatory studies and broader geographic availability.

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DECLARATION OF INTERESTS

The author declares no competing interests.