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Creating Best In Class Antivirals In Post-COVID China: Interview with Huahui Health CSO Li Wenhui

by **Brian Yang**

COVID-19 has highlighted the need for potent, safe and effective antiviral therapies for infectious diseases and now one well-known Chinese researcher is tackling hepatitis B and D through a homegrown drug discovery approach. He talks to *Scrip* in this wide-ranging audio interview.

With severe acute respiratory syndrome (SARS) in 2003 and then COVID-19, China has seen two pandemics originate and spread fast in the country, which has also become known for its large scientific talent pool and boom in research papers.

A virology researcher by training, Li Wenhui was among the first in 2003 to identify the cellular receptor for SARS virus. In 2002, Li had opened his own lab at the prestigious Institute of Biotech in Beijing (NIBS), led by [BeiGene, Ltd.](#) co-founder Wang Xiaodong.

Li now serves as the leading scientific officer of Huahui Health, a biotech startup founded in 2015 and devoted to hepatology and anti-infectious drug development, located in the Zhongguancun Life Science Park in the outskirts of Beijing. It currently has five drugs in its pipeline including HH-003 and HH-006 for hepatitis B and D dual infection and HH120 for COVID-19, as well as HH-101 in the immuno-oncology space. The HBV drug and COVID-19 antibodies are now entering Phase II development.

In 2017, Li and researchers at NIBS published research on the entry of HBV and its satellite hepatitis D virus through sodium taurocholate co-transporting polypeptide (NTCP).

The paper, “*NTCP is a functional receptor of hepatitis B and D virus*” paved the way for Li's deeper move into drug discovery and led to him being selected as the recipient of the 2022 Future Science Prize.

'Best In Class' Potential

There is already one drug approved in Europe for HDV, Hepcludex (bulevirtide), a small molecule antiviral from [Gilead Sciences, Inc.](#) However, last October the US Food and Drug Administration issued a Complete Response Letter to Gilead citing concerns regarding the manufacture and delivery of bulevirtide. No new studies to evaluate the safety and efficacy have been requested and there are currently no other approved products for HDV in the US.

China has also not yet approved any therapies for the infection and elsewhere companies large and small are racing to get one to market, including the entry level inhibitors which Huahui is developing.

Data compiled by *Citeline* show there are only four other drugs other than HH-103 currently in the clinical pipeline. [Assembly Pharmaceuticals](#)' AB-543 is a same-class HBV/HDV entry inhibitor, while the development of [AstraZeneca PLC](#)'s AZD-3409, a small molecule farnesyltransferase inhibitor, has been halted.

The other two being studied for HBV/HDV are [Alnylam Pharmaceuticals Inc.](#)'s ALN-HDV, a small interfering RNA targeting the HDV genome under development for chronic infections, while [Bristol Myers Squibb Company](#)'s BMS-914143 is an interleukin-29 and recombinant PEG-interferon lambda-type therapy, under development by [Eiger BioPharmaceuticals, Inc.](#) for HDV.

Despite the time-consuming process of translating basic research to drug discovery and the costly development process for antibodies, Li believes the relatively smaller field gives the Chinese company hopes of being the best in the class, based on solid basic research.

Small molecule drugs currently marketed for HBV can't cure the viral infection and Li believes antibodies can address the relevant proteins and reduce or eliminate infection and re-infections, thus "killing two birds with one stone."

Aside from antibodies, Xiamen-based [Xiamen Innovax Biotech Co Ltd](#) has been successful in developing a vaccine for hepatitis E, which has received World Health Organization prequalification.

COVID-19 Nasal Spray Progresses

Li's company is also developing HH-120 for COVID-19, which is moving close to the Phase III stage. The nasal spray product aims to neutralize dependent mutating virus, addressing the need to combat emerging new mutations. Being locally administered and rapidly effective, it also has high potency and a good safety profile, the executive noted.

However, given China's sudden U-turn in its previously tough COVID-19 restrictions, domestic demand for antivirals and antibodies has dropped. [Brii Biosciences](#), one local developer, has since

ceased manufacturing its approved antibody combination therapy due to the situation.

How does Li view antiviral development post-COVID? How are the company's hepatitis drugs differentiated from others? Why does Li believe that antiviral development remains vital? He sat down with *Scrip* to discuss these and other key issues in this audio interview.

During the 50-minute discussion, Li first outlined why HBV is a tough nut to crack, while HDV, a rare form of hepatitis, only affects people who are already infected by HBV. There are an estimated 300 million people living with HBV globally and 15 million live with both HBV and HDV, which is much more severe and potentially leads to rapid progression of serious conditions such as liver fibrosis, hepatic cirrhosis, hepatic decompensation and an increased risk of liver cancer and death.

Interview timestamps:

0002-0004: Background introduction

0004-0006: Founding of Huahui Health and its goals

0006-0008: Entry level inhibitors for HBV/HDV

0008-0010: Mode of action of HH-103 for HBV/HDV

0010-0012: Limitations of small molecules for hepatitis infections

0012-0014: Translating target discovery to founding the firm and new drugs, a long process

0014-0016: HBV a "hard nut to crack" due to mini chromosome reservoirs and reactivation by re-infection

0016-0020: Need for antibodies to treat hepatitis and why antivirals/antibodies have big potential

0018—0020: Antibody-dependent cellular cytotoxicity and antibody-dependent cellular phagocytosis

0020-0024: Antibodies to "kill two birds with one stone"

0024-0026: Antibodies will exist side-by-side with small molecules

0027-0029: Next milestones in clinical development of HH-103

0030-0031: Suppress, block ongoing infections and engage/bolster the immune system

0032-0034: Two Phase II trials with NIBS on interferon combination, results expected this year. Hepatitis antibodies back on track post-COVID, HBV a bigger challenge delayed over past three years

0035-0037: HH-120, a nasal spray fusion protein which blocks S-protein and binds to viral protein, now close to Phase III

0038-0049: HH-120 results so far

0040-0046 : Prevention and mitigation of severe symptoms

0047-0050: Competitive landscape in antibodies for hepatitis and differentiation strategies

0051- 0052: 'Made in China' research, how homegrown innovation can be applied globally

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