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AASLD 2024: Tune Therapeutics Shows Near-Complete HepB Virus Repression with Tune-401 Epigenetic Silencer

Preclinical data shows strong, durable, and precise repression of HBV DNA across in vitro and in vivo models, offering a possible pathway to a functional cure

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DURHAM, N.C. & SEATTLE--(BUSINESS WIRE)--Leading epigenome editing company Tune Therapeutics showcased new data yesterday at the American Association for the Study of Liver Diseases (AASLD) conference, in support of its drive to develop a lasting, functional cure for chronic Hepatitis B Virus (HBV).

Tune unveiled its lead HBV program at the 2023 AASLD event with preclinical data showing strong and durable effect in targeted human hepatocytes. This year, Tune Therapeutics Principal Scientist Brian Cosgrove shared new *in vitro* and *in vivo* data, showcasing Tune's clinically optimized liver-targeting LNP-RNA epi-silencing drug (Tune-401) – which enabled the near-complete repression of HBV RNA in human cells, and in a 'true infection' FRG mouse model.

The challenge behind targeting chronic HBV infection, explained Cosgrove, is two-fold: HBV DNA integrates into the host genome, but it also exists as copies of extrachromosomal cccDNA (covalently closed circular DNA) in hepatocyte nuclei. This makes functional cure very rare with current standard-of-care treatments (less than 1-3% of patients achieve this), as no existing or pipeline therapy can effectively inactivate both integrated DNA (intDNA) and cccDNA.

"Our groundbreaking approach addresses the dual challenges of HBV by targeting both integrated viral DNA and the source of viral latency – cccDNA – which current therapies do not target," said Cosgrove. "The data we've gathered strengthens the case for epi-editing as a uniquely powerful treatment modality for HBV – and gives us confidence as we move into human clinical trials."

Tune-401 is a novel epigenetic silencing therapeutic that is designed to target both types of HBV DNA, in an effort to shut down viral transcription and suppress the production of new viral particles. As Cosgrove explained, the approach has achieved highly promising results in preclinical studies, including:

- Up to 99.99% repression of 3.5 kb HBV RNA from cccDNA of infected primary human hepatocytes (PHHs)
- Corresponding reduction in PHHs of extracellular Hepatitis B surface antigen (HBsAg) – the primary indicator of Hepatitis B infection

- In Hep3B cell lines, strong repression of total HBV RNA and extracellular HBsAg from intDNA.
- Definitive inverse correlation between HBV DNA methylation and HBV RNA production – presenting a clearly defined mechanism of action for Tune-401
- Durability of virus silencing beyond 550 days following transient delivery to a cell line harboring HBV – which represents the persistence of repressive epigenetic marks through over 275 rounds of cell division

“Tune-401 offers a unique opportunity to show the impact of epi-editing,” said Blythe Sather, Vice President, Head of Research. “Chronic Hepatitis B affects more than 250 million people worldwide – each one facing the daily reality of living with this devastating disease. I truly believe that our innovative epi-silencing approach, which targets *all* HBV viral reservoirs, could be the scientific advance we so sorely need – a new strategy that could meaningfully change the treatment paradigm for this disease.”

About Tune Therapeutics

Armed with its powerful and innovative genetic tuning platform (TEMPO), Tune Therapeutics aims to bring gene, cell, and regenerative therapies into a new era of human medicine – expanding their range of application to common, chronic, and age-related diseases that are straining healthcare systems and limiting human healthspan on a global scale.

About Tune-401

Tune-401 is a first-in-class investigational product candidate for treating Hepatitis B (HBV) infection. Tune-401 utilizes the company’s TEMPO platform to epigenetically silence viral HBV intDNA and cccDNA necessary for sustained HBV infection. Lipid nanoparticle technology for Tune-401 has been provided by Acuitas Therapeutics Inc.

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