

## Dicerna announces start of Ph1 clinical trial of DCR-HBVS

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Dicerna Pharmaceuticals, a leading developer of RNA interference (RNAi) therapeutics, today announced the dosing of the first human volunteer in its Phase 1 clinical trial of DCR-HBVS, the Company's investigational GalXC-based therapy for the treatment of chronic hepatitis B virus (HBV) infection in adults. The Company anticipates human proof-of-concept data from the Phase 1 trial, which is known as DCR-HBVS-101, in the second half of 2019.

"The dosing of the first human in the DCR-HBVS-101 trial brings us a step closer to the potential availability of an innovative therapy for patients with chronic hepatitis B, a serious liver infection that can lead to advanced hepatic disease or liver cancer if not treated effectively," said Ralf Roskamp, M.D., chief medical officer of Dicerna. "We are hopeful that this three-part Phase 1 trial will validate RNA interference as a viable clinical strategy against chronic hepatitis B infection, based upon our encouraging preclinical data on DCR-HBVS."

DCR-HBVS is comprised of a single GalXC molecule that targets HBV messenger RNAs (mRNAs) within the hepatitis B surface antigen (HBsAg) gene sequence region. Preclinical studies with a standard mouse model of HBV infection showed DCR-HBVS led to greater than 99% reduction in circulating HBsAg, suggesting superior HBsAg suppression (both in magnitude and duration of suppression), compared to targeting within the X gene sequence region.

"RNAi-based therapy has the potential to change the treatment paradigm for patients with chronic HBV infection. By silencing not only the S antigen but also other viral genes, through a powerful and long-acting mechanism, RNAi-based therapy could tip the balance toward allowing the patient's own immune system to mount an effective immune response. This approach could help eradicate HBV and remove the need for life-long therapy," said principal investigator Edward Gane, MBChB, M.D., deputy director and hepatologist of the New Zealand Liver Transplant Unit at Auckland City Hospital and clinical professor of Medicine at the University of Auckland School of Medicine. "Given the encouraging inhibitory activity of DCR-HBVS in animal studies, as well as its favorable preclinical safety profile, we eagerly anticipate the first results from healthy volunteers in the DCR-HBVS-101 trial, and then in the second part of the study, from patients with chronic hepatitis B."

## About the DCR-HBVS-101 Trial

The DCR-HBVS-101 clinical trial is a randomized, placebo-controlled study designed to evaluate the safety and tolerability of DCR-HBVS in normal healthy volunteers (NHVs) and in patients with non-cirrhotic chronic HBV. Secondary objectives are to characterize the pharmacokinetic (PK) profile of DCR-HBVS and to evaluate preliminary pharmacodynamics (PD) and antiviral efficacy on plasma levels of HBsAg and HBV in blood. The study is divided into three phases or groups:

- In Group A, 30 NHVs are to receive a single ascending-dose of DCR-HBVS (0.1, 1, 1.5, 3, 6, or 12 mg/kg), with a four-week follow-up period.
- Group B is a single-dose study of DCR-HBVS (3 mg/kg) in eight patients with HBV who are naïve to nucleoside analog therapy; these patients will be followed for at least 12 weeks. The Company expects to initiate Group B dosing in the third quarter of 2019.
- Group C is a multiple ascending-dose study of DCR-HBVS (1.5, 3, or 6 mg/kg) in 18 patients with HBV previously treated with nucleoside analogs with a follow-up period of 24 weeks or more. The Company expects to initiate Group C dosing in the second quarter of 2019.