



Enanta Pharmaceuticals Reports Positive Data from Part 2 of its Phase 1b Study of EDP-514 in Chronic Hepatitis B Virus Patients on Treatment with a Nucleoside Reverse Transcriptase Inhibitor

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Positive Data from First Two Dose Cohorts: 200 mg and 400 mg of EDP-514

EDP-514 was Safe and Well-Tolerated with Pharmacokinetics Supportive of Once Daily Dosing

Patients Dosed with EDP-514 for 28 Days Showed a Mean Reduction in HBV RNA of 1 Log

WATERTOWN, Mass.--(BUSINESS WIRE)-- Enanta Pharmaceuticals, Inc. (NASDAQ:ENTA), a clinical stage biotechnology company dedicated to creating small molecule drugs for viral infections and liver diseases, today announced positive data from the first two dose cohorts of Part 2 of its Phase 1b study of EDP-514 in chronic hepatitis B virus (HBV) patients already being treated with a nucleoside reverse transcriptase inhibitor (NUC). The data demonstrated that EDP-514, the Company's novel class II oral HBV core inhibitor, was safe and well-tolerated, displayed pharmacokinetics (PK) supportive of once-daily dosing, and resulted in a mean reduction in HBV RNA of 1 log.

"These positive clinical trial results from the 200 mg and 400 mg cohorts are very encouraging and support the continued advancement of EDP-514 as a potential treatment for HBV," said Nathalie Adda, M.D., Senior Vice President and Chief Medical Officer of Enanta Pharmaceuticals. "We are particularly encouraged by the emerging safety and tolerability profile of EDP-514 in combination with NUC treatment, which could provide a foundation for a combination therapy approach to achieve functional cures in patients with chronic HBV infection. We look forward to progressing our clinical program for EDP-514 and completing the 800 mg cohort, as well as reporting data on our ongoing Phase 1b study in viremic patients later this quarter, which will provide key information about the impact of EDP-514 on HBV DNA levels.

The randomized, double-blind, placebo-controlled Phase 1b study is Part 2 of a Phase 1a/1b study assessing the safety, tolerability, PK and antiviral activity of three doses of EDP-514 in 24 NUC-suppressed chronic HBV patients who were either HBeAg-positive or HBeAg-negative. Patients were randomized to receive 200 mg (n=6), 400 mg (n=6), 800 mg (n=6) of EDP-514 or placebo (n=6) daily for 28 days. The 800 mg cohort is ongoing and final study results will be presented at a future scientific conference.

In the 16 patients randomized in the first two dose cohorts, the majority of patients were HBeAg-negative and treated with tenofovir. EDP-514 was safe and well-tolerated and pharmacokinetics were supportive of once daily dosing, consistent with what was observed in Part 1 in healthy subjects. EDP-514 exposure increased linearly with dose, achieving trough concentrations up to 18-fold the protein-adjusted EC50. No liver enzyme elevations or other laboratory abnormalities were reported and no grade 3 or serious adverse events (AEs) occurred during the treatment period and the 4-week follow-up. Six of 12 patients given EDP-514 had at least one grade 1 or 2 AE during treatment. One patient dosed with 200 mg of EDP-514 had upper abdominal pain, a grade 2 AE, that led to study drug discontinuation.

A mean reduction in HBV RNA of 1 log was observed in patients dosed with EDP-514 compared to 0.3 log in the placebo group after 28 days of treatment, which is similar to reported results for other HBV core inhibitors. A maximum reduction of 2.3 log (HBeAg-negative) and 2.8 log (HBeAg-positive) was observed in patients receiving EDP-514 as compared with a maximum 1.2 log reduction in those receiving placebo. As expected, the HBV DNA assessment did not show any change from baseline as these patients already had suppressed HBV DNA levels from NUC therapy. Additionally, no virologic failure or breakthrough was observed and as expected there were no changes in HBsAg, HBeAg, or HBcrAg levels.

In Part 1 of the Phase 1a/1b study, EDP-514 was studied in healthy subjects who received single or multiple doses for up to 14 days. EDP-514 was well tolerated and demonstrated a favorable safety profile. Treatment-emergent AEs were infrequent and mild in intensity. No patients discontinued EDP-514 due to an AE. Additionally, the pharmacokinetic profile was supportive of once-daily dosing.

About EDP-514

EDP-514 is Enanta's lead HBV core inhibitor candidate. Core inhibitors, also known as capsid assembly modulators or core protein allosteric modulators, are a novel class of HBV replication inhibitors that have been shown to act at multiple steps in the HBV lifecycle. Preclinical data demonstrate that EDP-514 is a potent inhibitor of HBV replication and prevents the *de novo* formation of new HBV cccDNA in primary human hepatocytes when given early during HBV infection. *In vitro* data also show that EDP-514 is pan-genotypic, and that combinations of EDP-514 with a NUC, the current anti-viral therapy for HBV, or with a class I core inhibitor, result in additive to synergistic antiviral effects. *In vivo* models of EDP-514 demonstrate excellent efficacy with greater than 4-log viral load reduction in HBV-infected PxB mice.

About Hepatitis B Virus

Hepatitis B is a viral infection that attacks the liver and can cause both acute and chronic disease. The virus is most commonly transmitted from mother to child during birth and delivery, as well as through contact with blood or other body fluids. It is estimated that over 290 million people worldwide have chronic HBV infection.¹ Current approaches to treatment include interferon therapy and/or NUCs. Treatment with interferon offers poor cure rates and is accompanied by serious side effects.² NUCs can be very effective at suppressing the virus but rarely result in full eradication of the virus from the liver.³

About Enanta

Enanta is using its robust, chemistry-driven approach and drug discovery capabilities to become a leader in the discovery and development of small molecule drugs for the treatment of viral infections and liver diseases. Enanta's research and development efforts have produced clinical candidates for the following disease targets: respiratory syncytial virus (RSV), hepatitis B virus (HBV) and non-alcoholic steatohepatitis (NASH). Enanta is also conducting research in human metapneumovirus (hMPV) and SARS-CoV-2 (COVID-19).

Enanta's research and development activities are funded by royalties from hepatitis C virus (HCV) products developed under its collaboration with AbbVie. Glecaprevir, a protease inhibitor discovered by Enanta, is sold by AbbVie in numerous countries as part of its leading treatment for chronic HCV infection under the tradenames MAVYRET® (U.S.) and MAVIRET® (ex-U.S.) (glecaprevir/pibrentasvir). Please visit www.enanta.com for more information.

Forward Looking Statements Disclaimer

This press release contains forward-looking statements, including statements with respect to the prospects for further development of EDP-514 for hepatitis B virus (HBV). Statements that are not historical facts, are based on management's current expectations, estimates, forecasts and projections about Enanta's business and the industry in which it operates and management's beliefs and assumptions. The statements contained in this release are not guarantees of future performance and involve certain risks, uncertainties and assumptions, which are difficult to predict. Therefore, actual outcomes and results may differ materially from what is expressed in such forward-looking statements. Important factors and risks that may affect actual results include: the development risks of early stage discovery efforts in the disease areas in Enanta's research and development pipeline, such as HBV; the impact of development, regulatory and marketing efforts of others with respect to competitive treatments for HBV; Enanta's limited clinical development experience; Enanta's need to attract and retain senior management and key scientific personnel; Enanta's need to obtain and maintain patent protection for its product candidates and avoid potential infringement of the intellectual property rights of others; and other risk factors described or referred to in "Risk Factors" in Enanta's most recent Form 10-Q for the quarter ended March 31, 2020 and other periodic reports filed more recently with the Securities and Exchange Commission. Enanta cautions investors not to place undue reliance on the forward-looking statements contained in this release. These statements speak only as of the date of this release, and Enanta undertakes no obligation to update or revise these statements, except as may be required by law.

¹ <https://pubmed.ncbi.nlm.nih.gov/29599078/>

² <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5401664/>

³ <https://pubmed.ncbi.nlm.nih.gov/30342034/>

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