Enanta Pharmaceuticals Reports Positive Data from Phase 1b Study of EDP-514, a Hepatitis B Virus (HBV) Core Inhibitor, in Viremic Chronic HBV Patients

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Positive 28-Day Data from First Two EDP-514 Dose Cohorts: 200 mg and 400 mg

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

Patients Dosed with 400 mg EDP-514 Showed a Mean Reduction of 3.3 Logs in HBV DNA

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 its Phase 1b study of EDP-514 in viremic chronic HBV patients who were not being treated with a nucleoside reverse transcriptase inhibitor (NUC). The data demonstrated that EDP-514, Enanta's novel class II oral HBV core inhibitor, was safe and well-tolerated through 28 days of treatment, displayed pharmacokinetics (PK) supportive of once-daily dosing, and resulted in mean HBV DNA reductions of 2.9 and 3.3 logs at 28 days for the 200 mg and 400 mg cohorts, respectively.

"We are extremely pleased with these promising clinical results for EDP-514, which are comparable to the best antiviral effects reported for any core inhibitor to date and also extend the compound's excellent safety and tolerability profile," said Jay R. Luly, Ph.D., President and Chief Executive Officer of Enanta Pharmaceuticals. "In particular, we are encouraged by the rapid and robust declines in HBV DNA, which position EDP-514 to be a key component of a combination regimen for HBV. We believe EDP-514, in combination with a NUC and other mechanisms, could provide a foundation for an all-oral treatment approach to achieve functional cures in patients with chronic HBV infection. We look forward to progressing EDP-514 in combination with our oral HBV RNA destabilizer, EDP-721, a compound that has demonstrated significant reductions in HBsAg preclinically and which we expect to advance into the clinic mid-year. Ultimately, our all-oral, triple combination approach could provide potent suppression of multiple key steps in HBV replication, including HBV DNA, HBV RNA and HBsAg, to achieve our goal of developing a functional cure for HBV patients."

The randomized, double-blind, placebo-controlled Phase 1b study is evaluating the safety, pharmacokinetics, and antiviral activity of three doses of EDP-514 in viremic patients with chronic HBV infection, either HBeAg-positive or HBeAg-negative, and without cirrhosis. Patients were randomized to receive 200 mg (n=6), 400 mg (n=6), or 800 mg (n=6) of EDP-514 or placebo (n=6) daily for 28 days with an 8-week follow-up period. The 800 mg cohort is ongoing and final study results will be presented at a future scientific conference.

Of the sixteen patients randomized in the first two dose cohorts (6 active and 2 placebo per cohort), majorities were male (56%), Asian (100%) and HBeAg-negative (94%), with a mean age of 45 years, mean baseline HBV DNA of 4.87 logs IU/mL, and mean baseline HBV RNA of 3.45 logs IU/mL. Overall, six patients reported treatment emergent adverse events (TEAEs) and all were mild except for 4 moderate events (2 in placebo and 2 in the 200 mg cohort) both of which were considered unlikely related to drug. No grade 3 TEAEs or serious adverse events, grade 3/4 clinical laboratory abnormalities, ALT/AST elevations or clinically relevant electrocardiogram (ECG) or vital sign changes were observed in the EDP-514 groups. EDP-514 exposure increased linearly with dose, with concentrations up to approximately 20-fold the protein-adjusted EC50 (9-fold for 200 mg, 20-fold for 400 mg).

At Day 28, mean reductions in HBV DNA were 2.9, 3.3, and 0.2 logs IU/mL in the 200 mg, 400 mg and placebo groups, respectively, with a maximum reduction of 4.2 logs vs. 0.5 log in placebo. HBV DNA was below the lower level of quantitation (LLOQ) in 4 patients treated with EDP-514 compared to none in the placebo group. Mean HBV RNA reductions of 2.9, 2.4 and 0.3 logs IU/mL were observed in the 200 mg, 400 mg and placebo groups, respectively, with a maximum reduction of 4.8 logs vs. 1.9 logs in placebo. HBV RNA was undetectable at Day 28 in 8 patients treated with EDP-514 vs. none in placebo. As expected, no clinically significant changes in levels of HBsAg, HBeAg, or HBcrAg were observed.

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 a 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 SARS-CoV-2 (COVID-19) and human metapneumovirus (hMPV).

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 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 risks of early stage development 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, 2021 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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