



Enanta Announces Results of INTREPID Study of EDP-305 for the Treatment of Primary Biliary Cholangitis

May 6, 2020

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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 topline results from its INTREPID Phase 2 study of EDP-305, a Farnesoid X receptor (FXR), in subjects with primary biliary cholangitis (PBC).

The INTREPID study was a 12-week, randomized, double-blind, placebo-controlled study evaluating the safety, tolerability, pharmacokinetics and efficacy of EDP-305 in subjects with PBC, with or without an inadequate response to ursodeoxycholic acid. The primary endpoint of the study was to evaluate the proportion of subjects with at least 20% reduction in alkaline phosphatase (ALP) from pre-treatment value (ALP response), or normalization of ALP, at week 12.

In the intent-to-treat (ITT) analysis, EDP-305 1 mg and 2.5 mg treatment arms resulted in 45% (n=14/31, p=0.106) and 46% (n=13/28, p=0.063) ALP response, respectively, compared to 11% (n=1/9) in the placebo arm. Absolute changes from baseline in ALP at week 12 in both the EDP-305 1 mg arm (p=0.017) and the 2.5 mg arm (p=0.021) compared to the change from baseline in the placebo arm were statistically significant. In a post-hoc analysis, the proportions of ALP responders among those who completed treatment with no missing value at week 12 were 50% (n=14/28, p=0.039) and 62% (n=13/21, p=0.011), respectively, compared to 11% in placebo (n=1/9).

In the ITT analysis, key secondary endpoints, which included changes from baseline in liver enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gamma-glutamyl transferase (GGT) at week 12, were met with a statistically significant difference compared to placebo in both the EDP-305 1 mg arm and the 2.5 mg arm. Absolute changes from baseline at week 12 in these key secondary endpoints in the EDP-305 1 mg and 2.5 mg arms compared to placebo were respectively: ALT (p=0.001, p=0.009), AST (p=0.000, p=0.001) and GGT (p=0.000, p=0.000). A statistically significant difference in the percent change from baseline of these key biomarkers at week 12 was also observed in both EDP-305 arms compared to placebo.

Overall, EDP-305 was generally safe in subjects with PBC, with the majority of treatment-emergent adverse events (TEAEs) being mild to moderate. Five patients in the 2.5 mg arm experienced severe pruritus. The most common ($\geq 10\%$ or >1 subject/arm) TEAEs included pruritus, gastrointestinal-related symptoms (abdominal pain, diarrhea, gastro-esophageal reflux), headache and insomnia. These TEAEs are consistent with the safety profile observed across more than 400 subjects exposed to EDP-305 for up to 12 weeks. The incidence of treatment discontinuation due to pruritus in INTREPID was approximately 3% for the 1 mg EDP-305 treatment group and 18% for the 2.5 mg EDP-305 treatment group. Treatment with EDP-305 had no apparent effect on lipids, including cholesterol, low-density lipoproteins, high-density lipoproteins and triglycerides.

"While INTREPID did not meet the primary endpoint in subjects with PBC, as defined by at least a 20% reduction in ALP in the ITT set analysis, there were numerically higher response rates with 1 mg and 2.5 mg compared to placebo," said Jay Luly, Ph.D., President and Chief Executive Officer of Enanta Pharmaceuticals. "In addition, as shown in the completer analysis, those subjects who finished treatment had a significant ALP response. We were also able to obtain actionable data from this study to help us advance EDP-305 and were encouraged that the lower dose of 1 mg could achieve much better tolerability, in terms of pruritus, without reducing the number of ALP responders or key biomarkers of target engagement also achieved at the 2.5 mg dose. This is an encouraging finding, particularly for the intermediate doses of 1.5 mg and 2.0 mg that we plan to take into our ARGON-2 study in non-alcoholic steatohepatitis (NASH) patients. One of those two doses in NASH could potentially achieve an efficacy and tolerability profile acceptable in NASH patients."

Dr. Luly continued, "Rather than conducting further dose selection studies with EDP-305 in PBC, a disease for which there is already an approved second-line FXR agonist therapy, we intend to focus our future efforts with EDP-305 on NASH, a disease where FXR agonists like EDP-305 have the potential to be important components of drug combinations designed to give maximum benefit to patients. Our ARGON-2 study in NASH will explore new intermediate doses with the potential to optimize efficacy and tolerability, thereby maximizing the opportunity to develop EDP-305 in combination with other mechanisms of action against NASH."

"Based on these data, it's clear that EDP-305 demonstrated evidence of target engagement with robust reductions in markers of liver injury," said Kris Kowdley, M.D., FACP, FACC, AGAF, FAASLD, Director, Liver Institute Northwest and Clinical Professor, Elson S. Floyd College of Medicine, Washington State University, the Principal Investigator for the study. "These data suggest that a dose between 1.0 mg and 2.5 mg could hit an optimal level of efficacy and tolerability, which could bode well for future studies in NASH. I look forward to seeing future data on EDP-305."

About Primary Biliary Cholangitis

Primary biliary cholangitis (PBC) is a chronic disease of the liver that slowly destroys the medium-sized bile ducts within the liver. Bile is a digestive liquid that is made in the liver. It travels through the bile ducts to the small intestine, where it helps digest fats and fatty vitamins.

In patients with PBC, the bile ducts are destroyed by inflammation. This causes bile to remain in the liver, where its increased levels gradually damage liver cells and cause cirrhosis or scarring of the liver. As cirrhosis progresses and the amount of scar tissue in the liver increases, the liver loses its ability to function, leading to potential liver failure, liver transplantation or hepatocellular carcinoma. PBC affects mostly women, but more men are now being diagnosed. The disorder usually becomes apparent during middle age, initially affecting most individuals between the ages of 45 to 65 years. However, the disorder has been diagnosed in females as young as 22 years of age and in females in their early 90s. It has been estimated that PBC is one of the most common autoimmune diseases, affecting nearly 1 in 1000 women over the age of 40.¹

About EDP-305, a Farnesoid X Receptor Agonist

EDP-305 is a potent Farnesoid X receptor (FXR) agonist and Enanta's lead product candidate being developed primarily for the treatment of NASH. FXR is a nuclear receptor and a main regulator of bile acid levels in the liver and small intestine. It responds to bile acids by regulating gene transcription of key enzymes and transporters, many of which play important roles in lipid metabolism, insulin resistance, inflammation, and fibrosis. EDP-305 represents a class of FXR agonists that has been designed to take advantage of increased binding interactions with the receptor. This non-bile acid class contains steroid and non-steroid components and does not contain the carboxylic acid group normally present in other classes of FXR agonists and natural bile acids that can lead to the formation of taurine and glycine conjugates.

About Enanta Pharmaceuticals, Inc.

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), non-alcoholic steatohepatitis (NASH) and hepatitis B virus (HBV). Enanta is also conducting research in human metapneumovirus (hMPV) and emerging coronaviruses, including SARS-CoV-2.

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 and now marketed by AbbVie as part of its leading treatment for chronic HCV infection, is sold under the brand names 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-305. 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 NASH; the impact of development, regulatory and marketing efforts of others with respect to competitive treatments for NASH; 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 fiscal quarter ended December 31, 2019 and any 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://rarediseases.org/rare-diseases/primary-biliary-cholangitis/>



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Source: Enanta Pharmaceuticals, Inc.