Enanta Pharmaceuticals Announces Positive Phase 1 a/b Clinical Results for its Lead FXR Agonist, EDP-305

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- EDP-305 was generally safe and well tolerated over a broad range of single and multiple doses with pharmacokinetic (PK) data supporting once daily oral dosing
- EDP-305 exhibited strong engagement of the FXR receptor as evidenced by increased FGF19 levels and reduced C4 levels
- Results support the ability to administer EDP-305 in future trials at doses that neither elicit clinically significant changes in lipids nor result in pruritus

WATERTOWN, Mass.--(BUSINESS WIRE)--Oct. 23, 2017-- Enanta Pharmaceuticals, Inc. (NASDAQ:ENTA), a chemistry-driven biotechnology company dedicated to creating small molecule drugs for viral infections and liver diseases, today announced positive results from its Phase 1 clinical study of EDP-305, Enanta's lead FXR agonist for non-alcoholic steatohepatitis (NASH) and primary biliary cholangitis (PBC). The objective of this double-blind, placebo-controlled study in adult healthy volunteer (HV) subjects and subjects with presumed non-alcoholic fatty liver disease (NAFLD) (PN)* was to evaluate the safety, tolerability and pharmacokinetics of single ascending dose (SAD) and multiple ascending dose (MAD) levels of EDP-305. Pharmacodynamic (PD) markers of FXR activity (FGF19, C4) and lipids were measured in all dose groups.

Summary of results:

- A total of 146 subjects received at least one dose of EDP-305 (n=110) or placebo (n=36) including 50 HV subjects in SAD and 96 (48 HV, and 48PN) in the MAD phases of the study. Overall, mean BMI in the PN cohort was 32 (29,35). SAD had 6 cohorts at doses of 1, 5, 10, 20, 40 and 80 mg EDP-305/placebo, and MAD had 6 cohorts at doses of 0.5, 1, 2.5, 5, 10 and 20 mg EDP-305/placebo for 14 days.
- Strong FXR target engagement was demonstrated, with doses of EDP-305 > 1 mg increasing FGF19 and reducing C4 in all subjects, while PN subjects were even more sensitive with significant effects also observed in both parameters at the lowest multiple doses of 0.5 and 1 mg.
- Pharmacokinetic analysis revealed a PK profile suitable for once daily oral dosing.
    - Dose proportional increases in exposure were observed, with median $t_{1/2}$ from 11-23 hours in HV and from 10-18 hours in PN subjects following multiple doses.
    - Longer $t_{1/2}$ (2-fold) and more drug accumulation (~3 to 4-fold) were observed following the multiple 20 mg dose compared to lower doses.
- No serious adverse events (SAEs) were reported, and EDP-305 was generally well tolerated at all doses tested.
    - Treatment-emergent adverse events occurring in ? 2 EDP-305 treated subjects in MAD cohorts were: headache and pruritus in HV subjects, and constipation and pruritus in PN subjects.
    - Of the cases of pruritus noted (9% for EDP-305, 3% in placebo), the majority were mild or moderate and occurred at multiple doses of 20 mg, with no cases below 10mg. Notably, EDP-305 demonstrated potent engagement of the FXR receptor across the lower dose range where there was no pruritus.
    - Two subjects discontinued treatment in the MAD phase at the 20 mg dose level, one for a transient grade 2 ALT/AST elevation, and one for moderate pruritus.
- No dose-related changes in lipids were observed in HV subjects at any doses; and no dose-related changes in lipids were observed in PN subjects except for reductions of total cholesterol and HDL cholesterol at the multiple 20mg dose, with no concomitant increase in LDL cholesterol.
- These results support further clinical evaluation of EDP-305 in NASH and PBC patients.
- Enanta plans to present detailed results at a future scientific conference.

"We are very encouraged by our Phase 1 a/b results demonstrating a good safety profile as well as strong target engagement in our PN subjects in the lower multiple dose range of 0.5 to 5 mg," stated Jay R. Luly, Ph.D., President and CEO, Enanta. "Enanta plans to initiate a Phase 2 dose-ranging study in PBC patients by the end of 2017 and a Phase 2 dose-ranging study in NASH patients by early 2018 utilizing doses in that dose range."

***** Presumed NAFLD (PN) subjects are obese, with or without pre-diabetes or type 2 diabetes mellitus.

About EDP-305, a Farnesoid X Receptor (FXR) Agonist

EDP-305 is a potent FXR agonist and Enanta's lead product candidate being developed for the treatment of NASH and PBC. EDP-305 represents a new class of FXR agonists that has been designed to take advantage of increased binding interactions with the receptor. Further, this non-bile acid class contains steroidal and non-steroidal components, and does not contain the carboxylic acid group that can lead to the formation of taurine and glycine conjugates normally associated with bile acids, which may also be present in other classes of FXR agonists.

About NAFLD, NASH, and FXR

Non-alcoholic fatty liver disease (NAFLD) is the accumulation of excessive fat in the form of triglycerides in patients' liver cells (steatosis) that is not caused by alcohol. NAFLD is widely considered to be the liver expression of metabolic disease associated with type 2 diabetes, insulin resistance, obesity, and hyperlipidemia. A subgroup of NAFLD patients has liver cell injury and inflammation in addition to excessive fat (steatohepatitis). Progression of this condition leads to non-alcoholic steatohepatitis (NASH). Patients with NASH can develop fibrosis and ultimately cirrhosis of the liver, potentially leading to hepatocellular carcinoma (HCC) or requiring a liver transplant. Farnesoid X receptor (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.

About Enanta

Enanta Pharmaceuticals has used its robust, chemistry-driven approach and drug discovery capabilities to become a leader in the discovery of small molecule drugs for the treatment of viral infections and liver diseases. Two protease inhibitors, paritaprevir and glecaprevir, discovered and developed through Enanta's collaboration with AbbVie, have now been approved in jurisdictions around the world as part of AbbVie's direct-acting antiviral (DAA) regimens for the treatment of hepatitis C virus (HCV) infection, including the U.S.-marketed regimens MAVYRET™ (glecaprevir/pibrentasvir) and VIEKIRA PAK® (paritaprevir/ritonavir/ombitasvir/dasabuvir).

Royalties and milestone payments from the AbbVie collaboration are helping to fund Enanta's research and development efforts, which are currently focused on the following disease targets: non-alcoholic steatohepatitis (NASH)/ primary biliary cholangitis (PBC), respiratory syncytial virus (RSV) and hepatitis B virus (HBV). Please visit www.enanta.com for more information.

Forward Looking Statements

This press release contains forward-looking statements, including statements with respect to the prospects for development of EDP-305 for the treatment of NASH and PBC. 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 discovery and development risks of early stage development efforts in disease areas such as NASH that currently have no therapeutic treatment; potential competition from the development efforts of others in this disease area; Enanta's level of 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-K for the fiscal year ended September 30, 2016 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.

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