Enanta Pharmaceuticals Announces Positive Data From a Phase 1 Clinical Study of EDP-323, an Oral, L-Protein Inhibitor in Development for the Treatment of Respiratory Syncytial Virus

June 20, 2023

- Generally Safe and Well-Tolerated up to 800 mg for Seven Days with Pharmacokinetics Supportive of Once-Daily Dosing

- All Doses Resulted in Strong Exposure Multiples Against Both RSV A and B Strains

- Human Challenge Study to be Initiated by Early Fourth Quarter 2023

WATERTOWN, Mass.--(BUSINESS WIRE)--Jun. 20, 2023-- Enanta Pharmaceuticals, Inc. (NASDAQ: ENTA), a clinical-stage biotechnology company dedicated to creating novel, small molecule drugs for viral infections, today announced positive topline data from a Phase 1 study assessing the safety, tolerability, and pharmacokinetics (PK) of orally administered single ascending doses (SAD) and multiple ascending doses (MAD) of EDP-323 in healthy adult subjects. EDP-323, which received Fast Track designation from the U.S. Food and Drug Administration (FDA), is a novel L-protein inhibitor in development as a once-daily oral treatment for respiratory syncytial virus (RSV). Data from the Phase 1 study demonstrated favorable safety, tolerability, and PK supportive of once-daily dosing, with good exposure multiples, thereby supporting further clinical advancement of EDP-323.

“With the significant unmet need for effective antivirals to treat patients with RSV, we are pleased to report positive Phase 1 results for EDP-323. These data demonstrate that EDP-323 was generally safe and well-tolerated up to 800 mg, with a PK profile supportive of once-daily dosing and strong exposure multiples across both RSV A and B strains” said Scott T. Rottinghaus, M.D., Senior Vice President and Chief Medical Officer of Enanta Pharmaceuticals. “EDP-323 is an inhibitor of the L-protein, a distinct mechanism of action from EDP-938, our potent N-protein inhibitor, which allows the potential for each compound to be used alone or in combination therapy. With these positive results, we are advancing EDP-323 into a human challenge study by early fourth quarter of 2023 and we look forward to continuing to build upon our leadership in the RSV field.”

This first-in-human, randomized, double-blind, placebo-controlled, Phase 1 study enrolled healthy volunteers to evaluate the safety, tolerability, and PK of oral EDP-323 for seven days. The study evaluated a range of single and multiple doses in fasted and fed states. The SAD phase enrolled a total of six dose cohorts (doses ranging from 50 to 800 mg), one of which was a two-part food effect (FE) cohort. The MAD phase enrolled four dose cohorts (doses ranging from 200 to 800 mg). All SAD and MAD cohorts enrolled eight participants who were randomized to receive EDP-323 or placebo in a 3:1 ratio. The 200 mg SAD/FE cohort enrolled ten subjects randomized in a 4:1 ratio.

A total of 82 subjects (n=50 in SAD; n=32 in MAD) received at least one dose of EDP-323 or placebo. Overall, EDP-323 was generally safe and well-tolerated in healthy subjects up to 800 mg for up to seven days. Among participants receiving EDP-323, most adverse events (AEs) were mild, and there were no serious or severe AEs. There was one study discontinuation due to syncope, in the SAD/FE group, which was deemed unlikely to be related to EDP-323. In the MAD phase, three AEs deemed possibly related to EDP-323 were mild, with two headaches and one gastrointestinal event. There were no discontinuations due to AEs in the MAD phase.

EDP-323 exposure increased with increasing single and multiple dosing up to 600 mg with a half-life ranging from 11-17 hours, supporting once daily dosing. No food effect was observed with a high fat meal during the 200 mg SAD FE cohort, suggesting that EDP-323 can be administered without regard to food.

EDP-323 doses ranging from 200 to 800 mg once-daily resulted in strong EC_{90} multiples against both RSV A and B strains. Specifically, EDP-323 administered once daily for seven days resulted in C_{24} (C_{trough}) concentrations at steady state of 11- to 44-fold over the protein adjusted EC_{90} (0.3 nM) against both RSV A and B strains.

Based on these positive data, Enanta plans to initiate a human challenge study evaluating EDP-323 by early fourth quarter of 2023.

About Respiratory Syncytial Virus
RSV is the most common cause of bronchiolitis (inflammation of the small airways in the lung) and pneumonia in children under one year of age in the United States and a significant cause of respiratory illness in older adults and immunocompromised individuals.[1] According to the Centers for Disease Control and Prevention, virtually all children in the United States get an RSV infection by the time they are two years old and one to two out of every 100 children younger than six months of age with an RSV infection may need to be hospitalized.[2] Globally, there are an estimated 33 million cases of RSV annually in children less than five years of age, with about 3 million hospitalized and up to approximately 120,000 dying each year from complications associated with the infection.[3] RSV represents a significant health threat for adults older than 65 years of age, with an estimated 177,000 hospitalizations and 14,000 deaths associated with RSV infections annually in the United States.[4]

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. Enanta’s research and development programs include clinical candidates for the following disease targets: respiratory syncytial virus (RSV), SARS-CoV-2 (COVID-19) and hepatitis B virus (HBV). Enanta is also conducting research on a single agent targeting both RSV and human metapneumovirus (hMPV).

Enanta receives royalties from hepatitis C virus (HCV) products developed under its collaboration with AbbVie. Glecaprevir, a protease inhibitor discovered by Enanta, is part of one of the leading treatment regimens for curing chronic HCV infection and is sold by AbbVie in numerous countries 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 advancement of EDP-323 for treatment of RSV. 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 impact of development, regulatory and marketing efforts of others with respect to competitive treatments for RSV; the development risks of Enanta's program for RSV; the competitive impact of development, regulatory and marketing efforts of others in this disease area; any continuing impact of the COVID-19 pandemic on clinical trials; Enanta's lack of clinical development experience; Enanta's need to attract and retain senior management and key research and development 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 Form 10-K for the fiscal year ended September 31, 2022, 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. Centers for Disease Control & Prevention – Respiratory Syncytial Virus
2. Centers for Disease Control & Prevention – RSV in Infants and Young Children
3. Shi et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. *Lancet*. 2017 Sep 2; 390(10098): 946–958:
4. Falsey AR, et al. Respiratory syncytial virus infection in elderly and high-risk adults. *New Engl J Med*. 2005;352(17):1749-59.

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