Enanta Pharmaceuticals Announces Positive Topline Results for EDP-323 in a Phase 2a Human Challenge Study of Healthy Adults Infected With Respiratory Syncytial Virus (RSV)

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- *Treatment With Once-Daily EDP-323 Met Primary and Secondary Endpoints, Achieving Highly Statistically Significant Reductions in Both Viral Load and Clinical Symptoms Compared to Placebo*
- *Favorable Safety and Tolerability Observed*
- *Conference Call and Webcast to Discuss Data at 8:30 a.m. ET Today*

WATERTOWN, Mass.--(BUSINESS WIRE)--Sep. 26, 2024-- Enanta Pharmaceuticals, Inc. (NASDAQ:ENTA), a clinical-stage biotechnology company dedicated to creating best-in-class small molecule drugs for virology and immunology indications, today announced positive topline results from a Phase 2a human challenge study of EDP-323 in healthy adults infected with respiratory syncytial virus (RSV). These data demonstrated that EDP-323 was generally safe and well-tolerated and achieved an 85-87% reduction in viral load area under the curve (AUC) by qRT-PCR ($p<0.0001$), a 97-98% reduction in infectious viral load AUC by viral culture ($p<0.0001$), and a 66-78% reduction of total clinical symptoms score AUC ($p<0.0001$) compared to placebo. 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 RSV.

“We are excited about these impressive data that demonstrate a rapid and sustained reduction in viral load. These results are among the strongest ever reported in an RSV challenge study, raising the high bar set by zelicapavir. The significant antiviral activity and symptom alleviation observed in this study highlight EDP-323’s potential as a safe, highly effective, direct-acting antiviral for the treatment of RSV,” said Scott T. Rottinghaus, M.D., Chief Medical Officer of Enanta Pharmaceuticals.

“These EDP-323 results represent a meaningful advancement toward achieving our longstanding goal of developing new medicines to treat respiratory infections such as RSV, as there remains a substantial need for safe and effective oral treatments. Enanta has the leading portfolio of potent RSV replication inhibitors, with EDP-323, our L-protein inhibitor, and zelicapavir, our N-protein inhibitor, both in Phase 2 development. These distinct mechanisms have the potential to be developed as once-daily single agents or in combination for specific patient populations,” added Jay R. Luly, Ph.D., President and Chief Executive Officer of Enanta Pharmaceuticals.

EDP-323 Phase 2a Challenge Study Topline Results

This Phase 2a study was a randomized, double-blind, placebo-controlled, human challenge study of 142 healthy adult participants inoculated with RSV. Randomized participants (n=141) received either a once-daily (QD) 600 mg dose of EDP-323 for five days [high dose, n=47], a single 600 mg loading dose on day one followed by a 200 mg once-daily (QD) dose of EDP-323 for four days [low dose, n=47], or placebo for five days [n=47]. The intent-to-treat-infected population (ITT-I) was defined as all randomized participants receiving challenge virus and at least one dose of study drug with confirmed RSV infection.

EDP-323 demonstrated a rapid and sustained antiviral effect. A highly statistically significant reduction ($p<0.0001$) was observed for the primary efficacy endpoint of AUC for viral load as measured by qRT-PCR in the ITT-I population for each of the EDP-323 dosing groups as compared with placebo. Specifically, EDP-323 lowered viral load AUC by 85% in the high dose arm and 87% in the low dose arm compared to placebo. There was no statistically significant difference between the two EDP-323 dosing groups.

A highly statistically significant reduction ($p<0.0001$) was observed for the secondary efficacy endpoint of AUC for infectious viral load as measured by quantitative culture in the ITT-I population for each of the EDP-323 dosing groups, with a reduction in viral culture AUC by 98% in the high dose arm and 97% in the low dose arm compared to placebo. There was no statistically significant difference between the two EDP-323 dosing groups.

For the secondary efficacy endpoint of AUC for total symptom score, a highly statistically significant reduction ($p<0.0001$) was observed in the ITT-I population for each of the EDP-323 dosing groups, with a symptom reduction of 66% in the high dose arm and 78% in the low dose arm compared to placebo. There was no statistically significant difference between the two EDP-323 dosing groups.

EDP-323 demonstrated favorable pharmacokinetics, supportive of once-daily dosing. Mean trough plasma concentrations were maintained at 16-fold above the protein-adjusted EC_{90} with the low dose, and 35-fold above the protein-adjusted EC_{90} with the high dose, for both RSV A and B strains.

Overall, EDP-323 demonstrated a favorable safety profile over a 5-day dosing period and through 28 days of follow-up. Adverse events were similar between EDP-323 dosing groups and placebo. There were no serious adverse events, no severe adverse events, and no adverse events leading to treatment discontinuation or study withdrawal.

Full data from the study will be presented at a future medical conference or in a peer-reviewed publication.

Conference Call and Webcast Information
Enanta will host a conference call and webcast today at 8:30 a.m. ET. The live webcast can be accessed at "Events & Presentations" in the investors section of Enanta’s website. To participate by phone, please register for the call here. It is recommended that participants register a minimum of 15 minutes before the call. Once registered, participants will receive an email with the dial-in information. The archived webcast will be available on Enanta’s website for approximately 30 days following the event.

About EDP-323

EDP-323, a novel, oral, direct-acting antiviral selectively targeting the RSV L-protein, has received Fast Track designation by the U.S. Food and Drug Administration. In a Phase 1 study, EDP-323 was found to be generally safe and well-tolerated in healthy subjects up to 800 mg for up to seven days, with a pharmacokinetic profile supporting once-daily dosing and all doses achieving target exposures. In addition to its Phase 1 profile, EDP-323 is also supported by *in vitro* data demonstrating a significant reduction in RSV replication with picomolar potency in primary human bronchial epithelial cells infected with RSV A and B, and across a range of RSV clinical isolates and various cell types. In a mouse model of RSV infection, EDP-323 treatment was associated with dose-dependent decreases in viral load in the lung, reductions in lung immunopathology and decreases in pro-inflammatory cytokines, including IFNγ, TNFα, and IL1β.

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 with an emphasis on indications in virology and immunology. Enanta's research and development programs are currently focused on respiratory syncytial virus (RSV) and chronic spontaneous urticaria (CSU) and the company has previously advanced clinical-stage compounds for SARS-CoV-2 (COVID-19) and chronic hepatitis B virus (HBV) infection.

Glecaprevir, a protease inhibitor discovered by Enanta, is part of one of the leading treatment regimens for curing chronic hepatitis c virus (HCV) infection and is sold by AbbVie in numerous countries under the tradenames MAVYRET® (U.S.) and MAVIRET® (ex-U.S.) (glecaprevir/pibrentasvir). A portion of Enanta's royalties from HCV products developed under its collaboration with AbbVie contribute ongoing funding to Enanta's operations. 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 and advancement of EDP-323 for the 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 development risks of early stage discovery efforts in the disease areas in Enanta's research and development pipeline, such as RSV; the impact of development, regulatory and marketing efforts of others with respect to vaccines and competitive treatments for RSV; Enanta's limited clinical development experience; Enanta's need to attract and retain senior management and 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 30, 2023 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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