Enanta Pharmaceuticals Announces Positive Topline Results from First-in-Pediatrics Phase 2 Study Evaluating Zelicapavir for the Treatment of Respiratory Syncytial Virus (RSV)

December 9, 2024

- *Observed an antiviral effect for the primary and secondary virology endpoints in the overall population, with a viral load decline of 1.4 log at the end of treatment in Part 2*
- *Demonstrated a viral load decline of 1.2 log compared to placebo at the end of treatment in prespecified analysis of patients randomized within 3 days of symptom onset*
- *Zelicapavir was well-tolerated with a favorable safety profile*
- *Conference call and webcast to discuss data at 8:30 a.m. ET today*

WATERTOWN, Mass.--(BUSINESS WIRE)--Dec. 9, 2024-- Enanta Pharmaceuticals, Inc. (NASDAQ:ENTA), a clinical-stage biotechnology company dedicated to creating small molecule drugs for virology and immunology indications, today announced positive topline results from the first-in-pediatrics Phase 2 study evaluating zelicapavir in hospitalized and non-hospitalized children aged 28 days to 36 months with respiratory syncytial virus (RSV). An antiviral effect was observed for the primary and secondary virology endpoints in the overall pooled efficacy population. The primary endpoint in Part 2 of the study, which focused on virology, showed a pronounced antiviral effect with a 1.4 log decline in viral load at Day 5 compared to placebo. Additionally, a rapid and robust virologic effect was observed in a prespecified subset of patients who were randomized within 3 days of symptom onset, with a 1.2 log decline in viral load at Day 5 compared to placebo. The study also showed that zelicapavir demonstrated a favorable safety profile and was well-tolerated in this pediatric population. Zelicapavir, which received Fast Track designation from the U.S. Food and Drug Administration (FDA), is a novel N-protein inhibitor in development as a once-daily oral treatment for RSV.

“We are excited to share these positive results from our first-in-pediatric Phase 2 study of zelicapavir, which we believe confirm a strong profile for our lead RSV antiviral and strengthen Enanta’s position as a leader in developing treatments for RSV. Zelicapavir demonstrated an antiviral effect on both primary endpoints, as well as secondary virology endpoints. Furthermore, patients who joined the study within 3 days of symptom onset showed a robust 1.2 log reduction in viral load at Day 5. These data provide us with continued confidence in zelicapavir and valuable insights to inform the design of a potential registration enabling trial,” said Scott T. Rottinghaus, M.D., Chief Medical Officer of Enanta Pharmaceuticals. “There is a substantial need for safe and effective oral treatments for RSV, and we believe that these important antiviral data along with the favorable safety profile observed in this young, vulnerable population support further clinical evaluation of zelicapavir.”

“In my practice, I see many children requiring hospitalization for severe RSV infection during the RSV season. The impact of RSV is felt not only by patients and caregivers, but also broadly by public health. I believe that a safe and effective antiviral therapeutic is critical in addressing this significant and unmet need,” said Jaime Deville, MD, FAAP, a Principal Investigator in the Phase 2 pediatric clinical trial of zelicapavir and Professor of Clinical Infectious Diseases in the Department of Pediatrics at the David Geffen School of Medicine, University of California, Los Angeles and UCLA Mattel Children’s Hospital. “These results support further evaluation of zelicapavir and suggest the potential for zelicapavir to improve patient outcomes. I’m excited to see this compound move forward, to possibly deliver the first safe and effective antiviral to treat children with RSV infection.”

Zelicapavir Phase 2 Study Topline Results

This Phase 2 study was a randomized, double-blind, dose ranging, placebo-controlled study in hospitalized and non-hospitalized pediatric patients with RSV aged 28 days to 36 months. The primary objective of Part 1 of the study was to evaluate the safety and pharmacokinetics of zelicapavir and to determine the optimal dosing for Part 2 of the study. The primary objective of Part 2 of the study was to evaluate the antiviral activity of zelicapavir, with assessment of symptom severity as an exploratory objective. Because exposure was similar across all cohorts and doses, and all patients received a therapeutic dose, primary efficacy analyses were able to be performed across all dosed patients from Parts 1 and 2.

A total of 96 patients received zelicapavir (n=70) or placebo (n=26). Part 1 evaluated multiple doses and patients were treated with zelicapavir (n=36) or placebo (n=16) once-daily (QD) for 5 days. In Part 2, patients received the selected dose of zelicapavir (n=34) or placebo (n=10) QD for 5 days. Demographics and baseline characteristics were balanced across treatment groups, with the majority of patients being hospitalized at enrollment, and a mean duration of RSV symptoms prior to randomization of 4 days.

Zelicapavir demonstrated a favorable safety profile over the initial 5-day dosing period and through 23 days of follow-up. Adverse events (AEs) were similar between zelicapavir and placebo and there were no AEs leading to treatment discontinuation or study withdrawal. Furthermore, zelicapavir achieved target drug exposure levels across all age groups and dosing cohorts. Exposure was similar across cohorts and doses, and all patients received a therapeutic dose. A dose of 5 mg/kg was selected for age ≥ 28 days to <12 months, and a dose of 7.5 mg/kg was selected for age ≥12 months to ≤36 months.

An antiviral effect was observed for the primary and secondary virology endpoints in the overall pooled efficacy population, with the viral load decline peaking at 0.7 log on Day 9 compared to placebo. The primary endpoint for Part 2 of the study showed a more pronounced effect, with a viral load decline of 1.0 log at Day 3 and 1.4 log at Day 5 compared to placebo. Additionally, a rapid and robust antiviral effect was observed in the prespecified subset of patients who were randomized within 3 days of symptom onset, which represents about 40% of patients in the study (n=38/96). In these patients, a viral load decline of 0.9 log at Day 3 and 1.2 log at Day 5 was observed compared to placebo. Furthermore, zelicapavir treatment resulted in a greater proportion of patients having undetectable viral load at Days 5 and 9 compared to placebo and improvements in AUC of change from baseline for viral load at all timepoints. Qualitative improvement in time to undetectable viral load was observed at early timepoints, although median

time to undetectable was similar between groups. Overall, virology results were similar regardless of age or whether patients were enrolled from a hospitalized or outpatient setting.

As there are no validated symptom tools approved by regulatory agencies for pediatric RSV, multiple methods were used to assess symptoms. ReSViNET (REspiratory Syncytial VIrus NETwork), a publicly available pediatric tool with caregiver assessments, was used as an exploratory endpoint in all patients. This tool was originally designed primarily for prophylaxis studies to assess disease severity at a single timepoint. There was no difference in symptoms between zelicapavir and placebo using ReSViNET. RESOLVE-P (RESpiratory ObservabLE Reported Outcome-Pediatric), a proprietary tool being developed by Enanta in alignment with regulatory agency input, was specifically designed to assess the severity of pediatric RSV infection change over time based on observations by the child's caregiver. As this tool was finalized and introduced late in the study, data are only available from a small number of patients (n=15). In this dataset, a trend toward greater symptom reduction in patients treated with zelicapavir was observed.

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 Zelicapavir

Zelicapavir, Enanta's lead N-protein inhibitor, is being developed for the treatment of RSV infection, and has been granted Fast Track designation by the U.S. Food and Drug Administration. Zelicapavir is a nanomolar inhibitor of both RSV-A and RSV-B activity. Zelicapavir is differentiated from RSV fusion inhibitors as the N-protein inhibitor targets the virus' replication machinery and has demonstrated a high barrier to resistance in vitro. In preclinical studies, Zelicapavir maintained antiviral potency across all clinical isolates tested and was active against viral variants resistant to other mechanisms. Zelicapavir demonstrated a favorable safety, pharmacokinetic and drug-drug interaction profile in an extensive Phase 1 program. In a Phase 2 challenge study, zelicapavir achieved highly statistically significant ($p<0.001$) reductions in RSV viral load and clinical symptoms compared to placebo, and demonstrated a favorable safety profile and was well-tolerated, with infrequent adverse events. Zelicapavir is currently being evaluated in RSVHR, a Phase 2b study in the elderly and/or those with congestive heart failure, chronic obstructive pulmonary disease (COPD) or asthma.

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 100,000 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 clinical programs are currently focused on respiratory syncytial virus (RSV) and its earlier-stage immunology pipeline aims to develop treatments for inflammatory diseases by targeting key drivers of the type 2 immune response, including KIT and STAT6 inhibition.

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 with respect to the prospects for further development and advancement of zelicapavir 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 competitive treatments for RSV; 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 Annual Report on Form 10-K for the fiscal year ended September 30, 2024 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. All forward-looking statements contained in this release speak only as of the date on which they were made and are based on management's assumptions and estimates as of such date. Enanta undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

1. Centers for Disease Control & Prevention – Respiratory Syncytial Virus Last accessed: December 2024.
2. Centers for Disease Control & Prevention – RSV in Infants and Young Children Last accessed: December 2024.

3. Shi, Ting 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 (London, England)* vol. 390,10098 (2017): 946-958. doi:10.1016/S0140-6736(17)30938-8
4. Falsey, Ann R et al. “Respiratory syncytial virus infection in elderly and high-risk adults.” *The New England Journal of Medicine* vol. 352,17 (2005): 1749-59. doi:10.1056/NEJMoa043951

View source version on businesswire.com: https://www.businesswire.com/news/home/20241209611449/en/

Media and Investors:
Jennifer Viera
617-744-3848
jviera@enanta.com

Source: Enanta Pharmaceuticals, Inc.