Enanta Pharmaceuticals Reports Positive Topline Results from its Phase 2b Study of Zelicapavir for the Treatment of Respiratory Syncytial Virus (RSV) in High-Risk Adults

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- *6.7-Day Improvement in Time to Complete Resolution of All RSV Symptoms for Patients with Chronic Obstructive Pulmonary Disease (COPD), Congestive Heart Failure (CHF), or Age ≥75*
- *Statistically Significant Improvement in Patient Global Impression of Severity Score*
- *Lower Hospitalization Rate for Patients Treated with Zelicapavir (1.7%) vs. Placebo (5%)*
- *4- to 5-Day Faster Median Time to Undetectable Viral Load with Zelicapavir vs. Placebo*
- *Management to Host Conference Call and Webcast Today at 8:30 a.m. ET*

WATERTOWN, Mass.--(BUSINESS WIRE)--Sep. 29, 2025-- Enanta Pharmaceuticals, Inc. (NASDAQ: ENTA), a clinical-stage biotechnology company dedicated to creating small molecule drugs for viral infections and immunological diseases, today announced positive topline data from RSVHR, a Phase 2b, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of zelicapavir in outpatient adults with acute RSV infection who are at high risk of complications including the elderly and/or those with congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD) or asthma. 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. This proof-of-concept study was designed to understand the antiviral treatment effect on symptom endpoints measured using the Respiratory Infection Intensity and Impact Questionnaire (RiiQ^{TM}) patient reported outcome tool, as well as other clinically meaningful endpoints, in a broad patient population.

A clinically meaningful improvement in time to complete resolution of all 13 RSV symptoms was observed for zelicapavir compared to placebo, with a benefit of 2.2 days for the overall efficacy population and 6.7 days for patients with CHF, COPD or age ≥75, termed the HR3 population, which comprised the majority (81%) of the efficacy population. Zelicapavir also showed an improvement in time to complete resolution on the 29-parameter total RiiQ™ symptom scale of 3.6 days for the efficacy population and 7.2 days for the HR3 population compared to placebo. Additionally, there was a 3.0-day faster time to complete resolution of lower respiratory tract disease (LRTD) symptoms in the HR3 population; however, no effect was observed on the time to resolution of the LRTD subset of four symptoms to mild, which was the primary endpoint. The study met the secondary endpoint of time to improvement in the Patient Global Impression of Severity (PGI-S) score, with a statistically significant 2-day faster resolution with zelicapavir compared to placebo. Importantly, a lower hospitalization rate was observed for patients treated with zelicapavir compared to placebo. The study met key secondary virology endpoints showing a robust antiviral effect. The study also showed that zelicapavir demonstrated a favorable safety profile and was well-tolerated.

“We are highly encouraged by these results from our Phase 2b trial of zelicapavir in high-risk adults infected with RSV. This represents the first time an RSV antiviral treatment has demonstrated a clinically meaningful benefit in these high-risk adult outpatients. These data demonstrate the potential for zelicapavir to reduce the duration of RSV symptoms in high-risk adults who face an increased risk of hospitalization or death from this virus,” said Scott T. Rottinghaus, M.D., Chief Medical Officer of Enanta Pharmaceuticals. “Building on the previously reported antiviral activity and favorable safety from our first-in-pediatrics study, we believe these findings continue to validate zelicapavir’s mechanism of action and reinforce its potential as a broadly effective, first-in-class RSV treatment. We believe the totality of these data provides strong rationale for further clinical advancement of zelicapavir. Importantly, we identified multiple potential registrational endpoints for a Phase 3 trial. We wish to thank the patients, family members and staff from all the sites who participated in the study. These results would not have been possible without their trust and involvement.”

“The patients enrolled in this study are particularly vulnerable to complications of RSV infection, often facing prolonged symptoms and heightened risk of hospitalization. Currently, there are no safe and effective antiviral RSV treatments available,” said Mohamed Fayed, M.D., UCSF School of Medicine Regional Campus at Fresno (UCSF Fresno), a Principal Investigator in the study. “The RSV symptom benefit observed in this study is compelling and could significantly improve outcomes for high-risk adults.”

Zelicapavir RSVHR Phase 2b Study Topline Results
RSVHR was a Phase 2b, randomized, double-blind, placebo-controlled study of RSV infection in non-hospitalized adults who are at high risk of complications, including the elderly and/or those with CHF, COPD or asthma. The proportion of patients aged 65-74 years or those with asthma was capped at 20% of the total population. Patients were enrolled within 72 hours of symptom onset and received 800mg of zelicapavir or placebo once daily for 5 days. The goal of this proof-of-concept, signal finding study was to inform the design of a Phase 3 trial, including populations and endpoints, as well as give an indication of a treatment effect on symptoms that could be confirmed in a larger registrational study. Symptoms were measured using the RiiQ^{TM} scale, which evaluates a total of 29 parameters, including 13 RSV symptoms, four of which are LRTD symptoms, and three other impact of disease components (daily activities, emotions, and social relationships). The primary endpoint evaluated the time to resolution of the LRTD subset of four symptoms to mild. Predefined analyses of complete resolution, defined by all symptoms absent, were also conducted. Multiple secondary endpoints, including all 13 RSV symptoms, total RiiQ^{TM} score, additional patient reported outcomes (e.g.; PGI-S), virology, safety, and hospitalization rate, were assessed.

A total of 186 subjects received 800mg of zelicapavir (n=121) or placebo (n=65) orally, once daily for 5 days and were evaluated for 28 days thereafter (safety population). An efficacy population of 175 patients was further defined as those who were PCR positive for RSV at a central laboratory. An HR3 population was defined as those who had CHF, COPD, or age ≥75 (81% of the efficacy population). Demographics and baseline characteristics were balanced across treatment groups, with the majority of patients being enrolled within 48 hours of symptom onset.

Zelicapavir demonstrated a favorable safety profile over the initial 5-day dosing period and through 28 days of follow-up, with adverse events (AEs)

being similar between zelicapavir and placebo. No AEs led to treatment discontinuation or study withdrawal in the zelicapavir group. The majority of AEs were mild with diarrhea and asthma being the most common AEs on zelicapavir at 3.3% and 2.5%, respectively.

A clinically meaningful improvement in time to complete resolution (defined as all symptoms absent) of all 13 RSV symptoms and in the total RiiQ™ was observed for zelicapavir compared to placebo in both the efficacy and HR3 populations. There was also a faster time to complete resolution of the subset of four LRTD symptoms in the HR3 population.

Improvement in Time to Complete Resolution of Symptoms for Zelicapavir Compared to Placebo

	LRTD 4 Symptoms	**All RSV 13 Symptoms**	**Total RiiQ™ All 29 Parameters**
Efficacy Population	0.5 days	2.2 days	3.6 days
HR3 Population	3.0 days	6.7 days	7.2 days

No effect was observed on the time to resolution of symptoms (defined as mild), including the primary endpoint of time to resolution of the LRTD subset of four symptoms in the efficacy population.

Additionally, a statistically significant improvement in RiiQ^{TM} RSV 13-symptom score in the HR3 population at Days 9 (p=0.0403) and 14 (p=0.0247) was observed in a post-hoc analysis for zelicapavir compared to placebo.

Furthermore, the study met a key secondary endpoint with zelicapavir treatment resulting in a statistically significant 2-day faster improvement in a Patient Global Impression of Severity (PGI-S) score compared to placebo in both the efficacy population (p=0.0446) and the HR3 population (p=0.0465).

Importantly, a lower hospitalization rate was observed for patients treated with zelicapavir (1.7%) compared to placebo (5.0%). Blinded attribution by investigators judged none (0%) of the hospitalizations on zelicapavir and all (5.0%) of the hospitalization on placebo to be related to RSV. Post-hoc attribution suggested RSV-relatedness of 0.9% for the patients on zelicapavir compared to 5.0% on placebo.

The study met key secondary virology endpoints showing a robust antiviral effect, with a statistically significantly greater proportion of zelicapavir patients having an undetectable viral load at the end of treatment compared with placebo. In the efficacy population undetectable viral load at the end of treatment was 23.5% vs. 10.0% in placebo (p=0.0198), and in the HR3 population was 23.9% vs. 10.0% in placebo (p=0.0292). Treatment with zelicapavir resulted in a 4- or 5-day faster median time to undetectable viral load and a 0.6 or 0.7 log decline in viral load at the end of treatment compared to placebo for the efficacy and HR3 populations, respectively.

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 under "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. 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 was safe and well-tolerated, with infrequent adverse events. In a Phase 2 randomized, double-blind, placebo-controlled study of pediatric RSV patients aged 28 days to 3 years old, 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. Zelicapavir has a favorable and consistent safety profile in over 600 people exposed to date.

About Respiratory Syncytial Virus in Older Adults
RSV is a common respiratory virus that infects the lungs and respiratory tract. Older adults are at significantly increased risk of severe illness due to the natural weakening of the immune system with age. This risk is even greater for individuals with underlying health conditions such as chronic obstructive pulmonary disease (COPD), asthma, or chronic heart failure. Those conditions can also be exacerbated by RSV, potentially lead to serious complications such as pneumonia, hospitalization, or even death. For adults aged 65 years and older, annually there are approximately 1.7 million medically attended visits, with 120K emergency room visits and between 160K-177K hospitalizations.[1,2]

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 and acute 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

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. McLaughlin, John M et al. "Rates of Medically Attended RSV Among US Adults: A Systematic Review and Meta-analysis." *Open forum infectious diseases* vol. 9,7 ofac300. 17 Jun. 2022, doi:10.1093/ofid/ofac300
2. 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

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