Enanta Pharmaceuticals Presents Preclinical Data for its Respiratory Syncytial Virus (RSV) and Human Metapneumovirus (hMPV) Programs at the 12th International RSV Symposium

September 29, 2022

- *EDP-323 Demonstrates Potent Inhibition of RSV Replication and Associated Pathology*
- *3D Airway Model Provides Accurate Insight into the Dynamics of RSV Infection*
- *Advances in hMPV Virology Methods Improve In Vitro Characterization of Direct-Acting Antivirals*

WATERTOWN, Mass.--(BUSINESS WIRE)--Sep. 29, 2022-- Enanta Pharmaceuticals, Inc. (NASDAQ: ENTA), a clinical-stage biotechnology company dedicated to creating small molecule drugs for viral infections and liver diseases, today announced new preclinical data related to its RSV program, as well as new virology methods used for its RSV and hMPV programs, will be presented during the 12th International RSV Symposium at ICC Belfast in Northern Ireland, United Kingdom.

An oral presentation and poster highlight the preclinical characteristics and the *in vivo* efficacy of EDP-323, a novel non-nucleoside RSV L-inhibitor. Additional posters characterize a 3D culture model for studying RSV, as well as outline methods for improved *in vitro* characterization of hMPV, another acute viral respiratory infection in which Enanta is conducting research.

"We are very pleased with the progress we have made to date in the infectious disease space, including in RSV and hMPV," said Jay R. Luly, Ph.D., President and Chief Executive Officer of Enanta Pharmaceuticals. "These data continue to demonstrate our leadership in the respiratory virology field, and support and facilitate continued development of our RSV and hMPV programs. By characterizing and understanding viral dynamics and identifying advanced treatment mechanisms that potently block RSV replication without generating resistance, we continue to demonstrate our robust science enabling the advancement of our pipeline."

ORAL PRESENTATION

October 1, 2022, 09:45 – 10:00 BST

"EDP-323, a Novel L-Protein Inhibitor for the Treatment of Respiratory Syncytial Virus," Michael Rhodin, Ph.D., United States

In a preclinical study, EDP-323 inhibited RSV L RNA polymerase activity *in vitro*, measured by an enzyme-coupled luminescence assay, with an IC_{50} of 14 nM. EDP-323 also inhibited virus-induced cytopathic effect of RSV-A and RSV-B strains and clinical isolates with EC_{50}s of 0.044-0.36 nM in HEp-2 cells. In differentiated primary human airway epithelial cells cultured at an airway-liquid interface (pHAEC-ALI), EDP-323 inhibited the replication of RSV-A Long with an EC_{90} of 0.16 nM. A CC_{50} of 18 µM (HEp-2 cells) was observed, which provides a selectivity index >30,000. Importantly, in a mouse RSV infection model, treatment was associated with improved lung histopathology and dose-dependent reductions in pro-inflammatory cytokines such as TNFα, IL1β, and MCP-1. Results demonstrate potent inhibition of RSV replication and associated pathology in a rodent infection model, supporting continued advancement of EDP-323 as an oral therapy for RSV.

POSTER PRESENTATIONS

September 30, 2022, 18:00 – 20:00 BST

"Evaluation of a Human 3D Airway Tissue Culture Model for the Study of Respiratory Syncytial Virus Infection and the Development of Antiviral Drugs," Nicole McAllister, United States

EDP-323, a novel non-nucleoside RSV L-inhibitor, and EDP-938, a non-fusion RSV replication inhibitor, were evaluated against RSV-A and -B isolates in a 3D pseudostratified epithelium (EpiAirway) model designed to simulate *in vivo* conditions. EDP-938 and EDP-323 displayed potent anti-RSV activity with EC_{50}s below 30 nM and 1 nM, respectively. Further, RSV infection was isolated to the ciliated cells of the EpiAirway model, and a viral load reduction was observed in compound-treated tissues. Data support using the EpiAirway tissue to accurately reflect dynamics of RSV infection.

"An Improved Toolkit for *In Vitro* hMPV Characterization," Joyce Sweeney Gibbons, Ph.D., United States

Data highlights several advances in virus detection, quantification and growth methods for the generation of an improved toolkit for *in vitro* characterization of multiple hMPV strains across each of the four hMPV genetic subgroups. The universal P RT-qPCR primer-probe set detected all hMPV clinical isolates across all four subgroups. Virus quantification for TN/1501/A1, TN/94-49/A2, and TN/98-242/B1 strains were successfully determined. Additionally, improved growth conditions yielded a 32-fold increase in viral titers for TN/94-49/A2 strain, compared to prior growth conditions. 3D airway tissues were also successfully employed for hMPV infections with a considerable increase in viral amplification over initial viral load for both the A2 and B2 strains. This expanded *in vitro* characterization of genetically distinct hMPV strains catalyzes the advancement of hMPV virology and the development of direct-acting antivirals.

"*In Vivo* Efficacy of EDP-323, a Novel L-Protein Inhibitor for the Treatment of Respiratory Syncytial Virus," Rachel Levene, Ph.D., United States

In vivo and *in vitro* studies demonstrate that EDP-323 significantly reduced RSV replication. In a mouse model of infection, EDP-323 was associated

with reduced lung immunopathology and dose-dependent decreases in pro-inflammatory cytokines, including IFNγ, TNFα, and IL1β. Interestingly, no viruses were isolated in any group with variants at residues that were identified through *in vitro* drug resistance generation as conferring EDP-323 drug resistance. These data suggest that EDP-323 effectively blocks RSV replication and pathology in the mouse model without generating mutations consistent with *in vitro* EDP-323 resistance, further supporting advancement of the program as a potential oral therapy for RSV.

About Enanta

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 and liver diseases. Enanta's research and development programs include clinical candidates currently in development for the following disease targets: respiratory syncytial virus (RSV), SARS-CoV-2 (COVID-19) and hepatitis B virus (HBV). Enanta is also conducting research in human metapneumovirus (hMPV).

Enanta's research and development activities are funded by 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

This press release contains forward-looking statements, including statements with respect to the prospects for advancement of Enanta's programs in RSV and hMPV. 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 Enanta's programs in RSV and hMPV; the competitive impact of development and regulatory efforts of others in these disease areas; any continuing impact of the COVID-19 pandemic on Enanta's business operations and 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-Q for the fiscal quarter ended June 30, 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20220929005108/en/

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

Source: Enanta Pharmaceuticals, Inc.