Aerovate Therapeutics Presents Nonclinical Pharmacokinetic Data in Support of AV-101, a Novel Dry Powder Inhaled Formulation of Imatinib, at the American Thoracic Society (ATS) 2023 International Conference

May 22, 2023

Direct delivery of imatinib to the lungs in nonclinical species demonstrated increased lung exposure compared with oral or IV dosing

Formulation impacted lung exposure with dry powder demonstrating greater lung exposure than suspension or solution and greater lung exposure vs oral or IV delivery

The potential for a novel dry powder formulation of inhaled imatinib (AV-101), to lower the human dose necessary for an improved therapeutic profile in the treatment of pulmonary arterial hypertension is being explored in the currently recruiting IMPAHCT Phase 2b / Phase 3 trial

WALTHAM, Mass., May 22, 2023 (GLOBE NEWSWIRE) -- Aerovate Therapeutics, Inc. (Nasdaq: AVTE), a clinical-stage biopharmaceutical company focused on developing drugs that meaningfully improve the lives of patients with rare cardiopulmonary disease, today presents results from a series of studies in nonclinical species assessing the pharmacokinetics of different formulations of imatinib at the American Thoracic Society (ATS) 2023 International Conference in Washington, D.C. Aerovate is developing inhaled imatinib as AV-101 for the treatment of pulmonary arterial hypertension (PAH). While oral imatinib has previously demonstrated clinically significant efficacy in PAH patients in the global Phase 3 IMPRES trial conducted by Novartis, the oral formulation was poorly tolerated due to adverse events.

“The results from these nonclinical studies further support our development of AV-101, a dry powder formulation of imatinib administered by inhalation for the treatment of PAH,” said Ralph Niven, Ph.D., Chief Scientific Officer at Aerovate Therapeutics. “Direct pulmonary delivery of imatinib demonstrates greater lung and lower systemic exposure than can be achieved with oral imatinib.”

The studies investigated the pharmacokinetics of imatinib in nonclinical models, including mice, rats, and cynomolgus monkeys, following delivery of imatinib formulations directly into the lungs compared to other routes of administration. Data showed that lung exposure in mice and rats following dry powder inhaled delivery was substantially higher versus oral delivery, and the dry powder formulation of imatinib enhanced lung exposure in rats over direct delivery of suspension or solution, and improved lung exposure versus oral or intravenous delivery. Repeat dosing of dry powder aerosol to rats and monkeys also suggested concentrations were maintained in the lungs after 24 hours. Measurements of the active imatinib metabolite, N-desmethyl imatinib, showed no apparent contribution to imatinib metabolism arising from the lungs. Plasma time course profiles of imatinib after direct dry powder or suspension dosing in rats were indicative of dissolution-controlled absorption. These nonclinical results suggest that the AV-101 formulation and inhaled delivery of imatinib can enhance lung exposure at a lower dose versus oral administration.

A previous Phase 1 study of AV-101 in healthy volunteers demonstrated significantly lower systemic exposure compared to oral imatinib. AV-101 was generally well-tolerated, suggesting that lower systemic exposure can potentially decrease the side-effects associated with oral imatinib for the treatment of PAH.

Aerovate continues to enroll IMPAHCT, a multi-national, placebo-controlled Phase 2b/Phase 3 trial that is evaluating the safety and efficacy of AV-101 in adults with PAH. Aerovate expects to report topline data from the Phase 2b portion of the trial in the second quarter of 2024.

A copy of the conference poster presentation will be available in the “Presentations & Events” section of Aerovate’s website at ir.aerovatetx.com.

Session: B59 – Union Square: Breaking Bad: New Drugs and Formulations for Pulmonary Hypertension and RV Failure
Poster: The Influence of Route of Delivery and Formulation on the Pulmonary Pharmacokinetics of Imatinib in Nonclinical Species
Poster number: P220
Presenting author: Ralph Niven, Ph.D.
Date: May 22, 2023
Time: 11:30am – 1:15pm ET

About AV-101

AV-101 is an investigational, proprietary dry powder inhaled formulation of the antiproliferative drug imatinib. Developed specifically for pulmonary arterial hypertension (PAH), AV-101 targets cellular hyperproliferation and resistance to apoptosis, driven by improper signaling in cells of the distal pulmonary arteries. By targeting the proliferation and accumulation of cells in the arteries of the lungs, we believe AV-101 has the potential to provide meaningful improvements for patients beyond the capabilities of currently approved therapies. AV-101 is designed for delivery by an easy-to-use dry powder inhaler, directly into the lungs to maximize potential clinical benefit and limit systemic adverse effects. Phase 1 results published in ERJ Open Research showed that AV-101 delivered by dry powder inhalation was generally well-tolerated by healthy adult volunteers with no serious adverse events reported. Aerovate is enrolling patients in the IMPAHCT Phase 2b/Phase 3 clinical trial to evaluate the safety and efficacy of AV-101 in adults with PAH.

About PAH

PAH is a rare, progressive orphan disease with unmet medical need that affects approximately 70,000 people in the United States and Europe. PAH can cause strain on the heart, leading to limitation of physical activity, heart failure and reduced life expectancy.

About the IMPAHCT Trial

IMPAHCT (Inhaled iMatinib Pulmonary Arterial Hypertension Clinical Trial) is a multi-national, placebo-controlled Phase 2b/Phase 3 trial in adults with PAH that will continuously enroll patients as the study progresses from Phase 2b to Phase 3. The Phase 2b portion of the trial will evaluate three doses of AV-101 over 24 weeks, compared to placebo, to identify an optimal dose based on the primary endpoint, change in pulmonary vascular resistance (PVR), and safety, tolerability, and other clinical measures. The Phase 3 portion of the trial will compare patients taking the optimal dose of AV-101, selected from the Phase 2b data, to placebo. The primary endpoint of the Phase 3 portion of the trial will be change in six-minute walk distance (6MWD) over 24 weeks versus placebo. More information about this trial is available at https://clinicaltrials.gov/ct2/show/NCT05036135.

About Aerovate Therapeutics, Inc.

Aerovate is a clinical-stage biopharmaceutical company focused on developing drugs that meaningfully improve the lives of patients with rare cardiopulmonary disease. Aerovate's initial focus is on advancing AV-101, its proprietary dry powder inhaled formulation of the drug imatinib for the treatment of patients with PAH. Learn more at aerovatetx.com or follow the company on Twitter and LinkedIn.

Available Information

Aerovate announces material information to the public about the Company, its products and services, and other matters through a variety of means, including filings with the U.S. Securities and Exchange Commission (SEC), press releases, public conference calls, webcasts, the investor relations section of the Company website at ir.aerovatetx.com, and the Company's Twitter account @AerovateTx in order to achieve broad, non-exclusionary distribution of information to the public and for complying with its disclosure obligations under Regulation FD.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements can be identified by words such as "anticipate," "believe," "continue," "could," "estimate," "expect," "future," "goal," "intend," "look forward to," "may," "plan," "potential," "predict," "project," seek," "strategy," "should," "target," "will," "would" and similar expressions regarding future periods. These forward-looking statements include, but are not limited to, statements regarding the therapeutic potential, tolerability and clinical benefits of AV-101; our expectations regarding clinical site activation and patient enrollment for our Phase 2b/Phase 3 trial; our anticipated timing for the release of topline data from the Phase 2b portion of our clinical trial; our business plans and objectives for AV-101, including expectations regarding timing and success of our Phase 2b/Phase 3 clinical trial, potential regulatory submissions and approvals for AV-101; and our growth and goals as a company.

Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, those risks and uncertainties related to the therapeutic potential, tolerability and clinical benefits of AV-101; the timing associated with the identification and activation of clinical sites, patient enrollment, initiation, delivery of drug supply and continuation of our Phase 2b/Phase 3 trial of AV-101 in PAH patients; the impact of the COVID-19 pandemic on our business, clinical trials, operations and goals; positive results from a clinical study may not necessarily be predictive of the results of future or ongoing clinical studies; regulatory developments in the United States and foreign countries; as well as those risks and uncertainties set forth more fully under the caption "Risk Factors" in our most recent Annual Report on Form 10-K filed with the SEC and subsequent filings with the SEC. We caution you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. We disclaim any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this press release represent our views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date.

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