Aerovate Therapeutics Publishes Results of Phase 1 Study Evaluating AV-101 for the Treatment of Pulmonary Arterial Hypertension in ERJ Open Research

November 17, 2022

Phase 1 results showed that AV-101 was generally well tolerated with significantly reduced systemic exposure compared to oral imatinib in healthy adult participants

WALTHAM, Mass., Nov. 17, 2022 (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 announced the publication of Phase 1 study results evaluating AV-101, a novel dry powder inhaled formulation of imatinib, in *ERJ Open Research*. The results showed that AV-101 was generally well tolerated and inhaled administration significantly reduced systemic exposure compared to orally dosed imatinib with no serious adverse events reported. AV-101 is being developed to address abnormal cellular proliferation and resistance to apoptosis in the pulmonary vasculature, which are key features of the pathophysiology of pulmonary arterial hypertension (PAH).

Imatinib is an anti-proliferative drug initially approved for the treatment of chronic myeloid leukemia. It has previously demonstrated a statistically significant and clinically meaningful benefit in PAH patients in the global Phase 3 IMPRES trial, conducted by Novartis, when administered orally as a tablet but was poorly tolerated due to adverse events. The development of imatinib for PAH was discontinued. Aerovate designed AV-101 to deliver imatinib throughout the airways to more directly access the diseased blood vessels in the lung, at or above concentrations observed with the oral dose while limiting systemic exposure. This allows for the potential to maximize efficacy while limiting the adverse events observed with oral imatinib.

“Our objective was direct delivery of imatinib to the lung using lower doses to limit systemic exposure, and our Phase 1 findings demonstrate that inhaled AV-101 limited systemic exposure compared to oral imatinib and was generally well tolerated,” said Dr. Hunter Gillies, M.B.Ch.B., Chief Medical Officer at Aerovate and lead author. “There continues to be a high unmet need for new medications to treat PAH, and these results reaffirm our confidence in AV-101 as a potential option for people living with the condition. We look forward to further investigation of AV-101 in our Phase 2b/Phase 3 trial.”

The Phase 1, placebo-controlled trial, with topline results previously reported at the American Thoracic Society 2022 International Conference, evaluated single and multiple ascending doses of AV-101, self-administered twice daily with an easy-to-use pocket-sized inhaler in 82 healthy adults. The single ascending dose (SAD) portion of Aerovate’s trial included 40 patients divided into 5 cohorts of 8 subjects each (6 randomized to AV-101, 2 placebo), who were administered a planned progression of 1 mg, 3 mg, 10 mg, 30 mg, and 90 mg single doses of inhaled AV-101 or placebo, compared to an additional cohort of 8 participants receiving 400 mg oral imatinib, the dose used in the IMPRES trial. The multiple ascending dose (MAD) portion included 34 patients divided into 3 cohorts of up to 12 subjects each (9 randomized to AV-101, 3 placebo) who received AV-101 or placebo at either 10 mg, 30 mg, or 90 mg twice daily for 7 days. At all doses, AV-101 demonstrated only moderate plasma accumulation and significantly lower systemic exposure compared to oral imatinib.

No serious treatment-emergent adverse events (TEAEs) were reported in either the SAD or the MAD cohorts. In the SAD portion of the trial, the most common TEAEs were dizziness and headache, whereas in the MAD portion of the trial, the most common TEAEs were short periods of cough and headache, primarily in the 90 mg cohort.

Aerovate’s Phase 2b/Phase 3 trial, called IMPAHCT (Inhaled iMatinib Pulmonary Arterial Hypertension Clinical Trial), is underway to evaluate the safety and efficacy of inhaled AV-101 in adults with PAH. Enrollment is ongoing and topline data are expected from the Phase 2b portion of the trial in the fourth quarter of 2023 or first quarter of 2024.

About AV-101
AV-101 is an investigational, proprietary dry powder inhaled formulation of the anti-proliferative drug imatinib. Developed specifically for pulmonary arterial hypertension (PAH), 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 presented at the 2022 American Thoracic Society (ATS) annual meeting 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 different doses of AV-101 in adults with PAH.

About PAH
PAH is a rare, progressive disease characterized by abnormal cellular proliferation of the pulmonary vasculature that affects approximately 70,000 people in the United States and Europe. The disease process involves remodeling, constriction and occlusion of the small pulmonary arteries resulting in elevated blood pressure in the pulmonary circulation. PAH can cause strain on the heart, leading to limitation of physical activity, heart failure and reduced life expectancy. Existing vasodilator drugs fail to treat the underlying cellular proliferation causing the disease.

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 part 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 and 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 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 belief that we will have capital to fund Aerovate into the second half of 2025; our expectations regarding the strength of our intellectual property portfolio globally; 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 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.

Media Contact
info@aerovatetx.com

Investor Contact
ir@aerovatetx.com