Aerovate Therapeutics Presents Phase 1 Data for AV-101, A Novel Dry Powder Inhaled Formulation of Imatinib Being Developed for the Treatment of Patients with Pulmonary Arterial Hypertension (PAH)

May 16, 2022

AV-101 is being developed to address cellular hyperproliferation and resistance to apoptosis in the pulmonary vasculature, which are key features of the pathophysiology of PAH

PAH is an area of high unmet need, and currently approved therapies are limited by acting primarily through vasodilation

These Phase 1 results show that AV-101 delivered by dry powder inhalation was generally well tolerated and significantly reduced systemic exposure compared with oral imatinib in healthy adult participants

WALTHAM, Mass., May 16, 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 presents Phase 1 results at the American Thoracic Society (ATS) International Conference in San Francisco. Aerovate's data show that AV-101, a novel inhaled dry powder formulation of imatinib, was generally well-tolerated by healthy adult volunteers with no serious adverse events reported.

"We are pleased these Phase 1 data showed that AV-101 was generally well-tolerated in this trial of healthy adult volunteers across a dose range we believe may overlap or exceed lung exposures from 400 mg of oral imatinib, the dose used in the Novartis global Phase 3 IMPRES trial, while simultaneously reducing systemic exposure," said Timothy Noyes, Chief Executive Officer at Aerovate. "These findings represent an important step forward in our clinical development of AV-101, and support the selection of doses being evaluated in our ongoing Phase 2b/Phase 3 IMPAHCT trial."

Imatinib 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 oral imatinib for PAH was discontinued. Aerovate designed AV-101, a dry powder inhaled formulation of imatinib, to target imatinib's anti-proliferative activity in the pulmonary vasculature by direct delivery to the lungs while potentially avoiding the treatment-limiting systemic toxicities seen with oral imatinib.

Aerovate's Phase 1 trial evaluated single and multiple ascending doses of AV-101 administered by inhalation for safety, tolerability, and pharmacokinetics in healthy adult volunteers. The single ascending dose (SAD) portion of Aerovate's trial included 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 consisted of 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. Only the morning dose was delivered on Day 7 so pharmacokinetics could be followed. Due to its known tolerability profile, the predicted steady-state exposure data for multiple doses of oral imatinib were obtained using a population pharmacokinetics model and data for oral imatinib 400 mg from the SAD study. At all doses, AV-101 demonstrated lower systemic exposure than 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.

"Formulated as a dry powder for inhalation, AV-101 is designed to deliver high concentrations of imatinib throughout the airways and straight to diseased blood vessels," said Hunter Gillies, M.B.Ch.B., Chief Medical Officer at Aerovate. "By limiting systemic exposure and directly targeting the disease process of hyperproliferation in the pulmonary vasculature, AV-101 has the potential to make a meaningful difference for the PAH community."

A copy of the conference presentation will be available in the "Presentations > Events" section of Aerovate's website at ir.aerovatetx.com.

Session: B106 – Union Square: Observational Studies and Clinical Trials in Pulmonary Hypertension
Poster: A Phase 1 Single and Multiple Ascending Dose (SAD/MAD) Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of AV-101, a Novel Inhaled Dry Powder Formulation of Imatinib in Healthy Adults
Poster number: 610
Presenting author: Hunter Gillies, M.B.Ch.B
Date: May 16, 2022
Time: 2:15-3:45 pm PT

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. 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
Pulmonary arterial hypertension (PAH) is a rare, progressive disease characterized by cellular hyperproliferation 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 portion of the trial will evaluate three doses of AV-101 compared to placebo to identify an optimal dose based on the primary endpoint, change in pulmonary vascular resistance (PVR) over 24 weeks versus placebo, and safety, tolerability, and other clinical measures. The Phase 3 portion of the trial will compare patients taking the optimal dose selected in Phase 2b of AV-101 with 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 clinical trial, 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," "potential," 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 of AV-101; our expectations regarding site initiation, patient enrollment and potential outcomes for our Phase 2b/Phase 3 trial of AV-101 in PAH and timing of top-line results; our business plans and objectives for AV-101, including expectations regarding the timing and success of our Phase 2b/Phase 3 clinical trial, including the timing of top-line results, the therapeutic potential and clinical benefits of AV-101 and 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 site activation, patient recruitment, initiation and continuation of our Phase 2b/Phase 3 trial of AV-101 in PAH patients and timing of top-line results; the impact of the ongoing COVID-19 pandemic on our business, clinical trial, 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