Aridis Meets Primary and Secondary Endpoints in Phase 2a Study of AR-501 in Cystic Fibrosis Patients

The study achieved high uptake of AR-501 in the respiratory tract at levels that were more than 50-fold higher than required for inhibition of the target bacteria P. aeruginosa

LOS GATOS, Calif., March 13, 2023 /GlobeNewswire/ -- Aridis Pharmaceuticals, Inc. (Nasdaq: ARDS) today announced preliminary top-line results from the randomized, double blinded, placebo-controlled Phase 2a study of AR-501, which evaluated the safety and pharmacokinetics of three ascending doses of AR-501 administered as an inhaled aerosol in cystic fibrosis (CF) patients with confirmed *Pseudomonas aeruginosa* bacterial and other potential infections. The study was conducted with funding support from the Cystic Fibrosis Foundation. AR-501 is being developed as a once-per-week inhaled dosing regimen that is self-administered using a commercially available nebulizer device.

Key findings:

- The study's primary and secondary endpoints of safety and pharmacokinetics (PK) were met
- Three weekly inhaled doses of AR-501 at 6.4mg, 20mg, and 40mg dose levels were well tolerated in CF patients. No drug related serious adverse events (SAEs) were observed. The majority of treatment emergent adverse events (TEAEs) were respiratory in nature and mostly mild to moderate in severity
- CF patients achieved high uptake of AR-501 in the respiratory tract, as measured by sputum concentrations, at levels that were more than 50-fold higher than required for inhibition of the target bacteria *P. aeruginosa*
- Inhaled delivery achieved more than 10-fold higher respiratory uptake of gallium (AR-501) than past clinical studies of intravenous (IV) gallium which resulted in lung function improvement and *P. aeruginosa* reduction.

"We are very pleased to see the safety and tolerability that we had observed in healthy volunteers also confirmed in CF patients," said Hasan Jafri, MD, Aridis' Chief Medical Officer. "The high drug level achieved in the lungs along with low systemic exposure from inhaled delivery effectively overcome the limitations of conventional intravenous delivery, and provide a strong basis for a large efficacy study in CF and other lung infections."

"The data from this study are encouraging and the results align with the expectations for the outcomes in safety and bioavailability. These data certainly warrant the continued evaluation of this drug in CF patients," said Dr. Noah Lechtzin, the study's lead principal clinical investigator, Director of the Adult Cystic Fibrosis Program and Associate Professor of Medicine at Johns Hopkins University.

The study was primarily designed as a safety and PK trial in clinically stable cystic fibrosis subjects and due to the heterogeneity of concurrent medicine use (CFTR channel modulators and antibiotics) in the study subjects, exploratory objectives, such as microbiological burden of *P. aeruginosa* and lung function (FEV1), were not established in this study.

"Having met the primary and secondary endpoints of this study, we thank the Cystic Fibrosis Foundation for the tremendous support they've provided to help us complete this study" said Aridis' CEO Vu Truong, PhD. **"**The attractive safety profile of AR-501, combined with the recent results from our AR-301 mAb Phase 3 program in older adults with ventilator associated pneumonia provide Aridis with two promising first-in-class, novel anti-infectives. We look forward to discussing the results from these two programs with the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) to plan the definitive next study for each program to support the filing of a license application."

About AR-501 Phase 2a

The Phase 2a study of AR-501 enrolled 42 adults, ages 18–80, with CF and confirmed *P. aeruginosa* bacterial colonization to evaluate the safety and pharmacological properties of three (3) weekly doses of AR-501 administered as a liquid aerosol at 6.4mg (low dose cohort), 20mg (mid dose cohort), and 40mg (high dose cohort). Dose related increase in blood serum level of gallium was observed, reaching 0.6ug/mL AR-501 after the third inhaled dose at day 14 for the high dose cohort. Sputum levels of gallium, a surrogate for level in lung fluids, were well over 50 ug/mL, which is greater than 50-fold required to inhibit *P. aeruginosa*. Prior Phase 1 & 2 studies of 5-day continuous intravenous (IV) infusion of gallium resulted in statistically significant lung function improvements and reductions of *P. aeruginosa* in CF patients, despite low sputum uptake (~1ug/mL) and high blood serum exposures (2-3 ug/mL) [see Goss, CH et al. Sci Transl Med. 2018 September 26; 10(460). doi:10.1126/scitranslmed.aat7520]. The current pharmacokinetics data of inhaled delivery showed >10-fold higher respiratory uptake of gallium (AR-501) and ~5-fold lower blood serum exposure as compared to IV delivery.

Inhaled AR-501 was found to be well tolerated. The majority of adverse events (AEs) were non-serious and deemed not related to the study drug by the blinded study investigator. Most AEs were Grade 1 or Grade 2 in severity. Most common treatment emergent adverse events (TEAEs) were respiratory in nature (e.g., cough, throat irritation), with one Grade 3 TEAE of dry throat and cough that occurred in the first of the 3 inhaled doses. An independent data and safety monitoring board (DSMB) consisting of CF physicians has reviewed the safety data and authorized the escalation to the 80 mg (highest) dose cohort. Aridis received approval by the FDA and support from the CF Foundation to continue the study with the 80mg cohort to explore the drug candidate's potential at a higher dose. Data from the highest cohort are expected in the second half of 2023.

AR-501's once weekly inhaled formulation of gallium, given in either a single ascending dose or a multiple ascending dose regimen (5 weekly doses), was found to be safe and well-tolerated in 48 healthy adults participating in the Phase 1 part of Aridis' Phase 1/2a study (NCT03669614).

AR-501 has received Orphan Drug designation in the US and in Europe, Fast Track and Qualified Infectious Diseases Product (QIDP) designations from the US FDA as a potential treatment of CF-related lung infections.

About AR-501 and Cystic Fibrosis

AR-501 is an inhaled formulation of gallium citrate that is being developed to treat chronic lung infections in cystic fibrosis patients. It is a non-antibiotic, broad acting antimicrobial with a mechanism of action involving interference with iron acquisition in microbes and disruption of microbial iron-dependent metabolic pathways distinct from current antibiotics. AR-501 acts as an iron analog and is believed to disrupt multiple iron dependent pathways in microbes, leading to growth inhibition. AR-501 has antimicrobial activities against a number of gram-negative and gram-positive bacteria, including antibiotic resistant strains. Preclinical efficacy and safety data have demonstrated that AR-501 works synergistically with multiple antibiotics, is effective against antibiotic resistant strains, and has a low intrinsic resistance profile.

Cystic fibrosis patients often suffer from severe, persistent secondary bacterial lung infections due to their underlying lung disease which results in an immune-compromised state. Current standard of care antibiotics approved for lung infections in cystic fibrosis patients are inhaled tobramycin (TOBI®) and inhaled aztreonam (Cayston®). Both are administered daily 2 to 3 times per day. AR-501 is being developed as a self-administered, inhaled once-a-week treatment. Separately, an intravenous (IV) formulation of gallium nitrate citrate has been evaluated in Phase 1 and Phase 2 clinical studies as a single, 5-day infusion in moderate and severe cystic fibrosis patients by researchers at the University of Washington (Seattle, WA). Both clinical studies of IV gallium demonstrated safety and efficacy as measured by improvement in lung function.

About Aridis Pharmaceuticals, Inc.

Aridis Pharmaceuticals, Inc. discovers and develops anti-infectives to be used as add-on treatments to standard-of-care antibiotics.

The Company is advancing multiple clinical stage mAbs targeting bacteria that cause life-threatening infections such as ventilator associated pneumonia (VAP) and hospital acquired pneumonia (HAP), in addition to preclinical stage antiviral mAbs. The use of mAbs as anti-infective treatments represents an innovative therapeutic approach that harnesses the human immune system to fight infections and is designed to overcome the deficiencies associated with the current standard of care which is broad spectrum antibiotics. Such deficiencies include, but are not limited to, increasing drug resistance, short duration of efficacy, disruption of the normal flora of the human microbiome and lack of differentiation among current treatments. The mAb portfolio is complemented by a non-antibiotic novel mechanism small molecule anti-infective candidate being developed to treat lung infections in cystic fibrosis patients. The Company's pipeline is highlighted below:

Aridis' Pipeline

AR-301 (VAP). AR-301 is a fully human IgG1 mAb targeting gram-positive *Staphylococcus aureus* (*S. aureus)* alpha-toxin that has recently completed the first of two planned Phase 3 superiority clinical studies as an adjunctive treatment of *S. aureus* ventilator associated pneumonia (VAP).

AR-320 (VAP). AR-320 is a fully human IgG1 mAb targeting *S. aureus* alpha-toxin that is being evaluated in a Phase 3 clinical study as a preventative treatment of *S. aureus* colonized mechanically ventilated patients who do not yet have VAP.
AR-501 (cystic fibrosis). AR-501 is an inhaled formulation of gallium citrate with broad-spectrum anti-infective activity being developed to treat chronic lung infections in cystic fibrosis (CF) patients. This program is currently in Phase 2a clinical development in CF patients.
AR-701 (COVID-19). AR-701 is a cocktail of fully human mAbs discovered from convalescent COVID-19 patients that are directed at multiple protein epitopes on the SARS-CoV-2 virus. It is formulated for delivery via intramuscular injection or inhalation using a nebulizer.
AR-401 (blood stream infections). AR-401 is a fully human mAb preclinical program aimed at treating infections caused by gram-negative *Acinetobacter baumannii*.
AR-101 (HAP). AR-101 is a fully human immunoglobulin M, or IgM, mAb in Phase 2 clinical development targeting *Pseudomonas aeruginosa* (*P. aeruginosa)* liposaccharides serotype O11, which accounts for approximately 22% of all *P. aeruginosa* hospital acquired pneumonia cases worldwide.
AR-201 (RSV infection). AR-201 is a fully human IgG1 mAb out-licensed preclinical program aimed at neutralizing diverse clinical isolates of respiratory syncytial virus (RSV).

For additional information on Aridis Pharmaceuticals, please visit https://aridispharma.com/.

Forward-Looking Statements
Certain statements in this press release are forward-looking statements that involve a number of risks and uncertainties. These statements may be identified by the use of words such as "anticipate," "believe," "forecast," "estimated" and "intend" or other similar terms or expressions that concern Aridis' expectations, strategy, plans or intentions. These forward-looking statements are based on Aridis' current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, the need for additional financing, the timing of regulatory submissions, Aridis' ability to obtain and maintain regulatory approval of its existing product candidates and any other product candidates it may develop, approvals for clinical trials may be delayed or withheld by regulatory agencies, risks relating to the timing and costs of clinical trials, risks associated with obtaining funding from third parties, management and employee operations and execution risks, loss of key personnel, competition, risks related to market acceptance of products, intellectual property risks, risks related to business interruptions, including the outbreak of COVID-19 coronavirus, which could seriously harm our financial condition and increase our costs and expenses, risks associated with the uncertainty of future financial results, Aridis' ability to attract collaborators and partners and risks associated with Aridis' reliance on third party organizations. While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various important factors, including, without limitation, market conditions and the factors described under the caption "Risk Factors" in Aridis' 10-K for the year ended December 31, 2021 and Aridis' other filings made with the Securities and Exchange Commission. Forward-looking

statements included herein are made as of the date hereof, and Aridis does not undertake any obligation to update publicly such statements to reflect subsequent events or circumstances.

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