# Aridis Receives Agreement from the FDA on a Single Confirmatory Phase 3 Study of AR-301 and the Clinical Study Design

LOS GATOS, Calif., May 31st, 2023 /GlobeNewswire/ -- Aridis Pharmaceuticals, Inc. (Nasdaq: ARDS) today announced positive feedback from the FDA on the Company's proposed single confirmatory Phase 3 study of investigational monoclonal antibody candidate AR-301, which is being developed as an adjunctive therapy in combination with standard of care (SOC) antibiotics for the treatment of pneumonia caused by Gram-positive bacteria *Staphylococcus aureus* (*S. aureus*) in mechanically ventilated hospitalized patients.

**Key agreements with FDA:**

- FDA agreed on the design of the single confirmatory Phase 3 superiority study required to support the submission of a Biologics License Application (BLA).
- FDA agreed to the proposed expansion of the confirmatory Phase 3 study in *S. aureus* ventilator associated pneumonia (VAP) patients to include ventilated hospital acquired pneumonia (HAP) and ventilated community acquired pneumonia (CAP) patients.
- The clinical efficacy endpoint will be the same endpoint of Clinical Cure of pneumonia on Day 21 used in the previous Phase 3 superiority trial AR-301-002. However, the primary efficacy endpoint will be in older adults ≥65 years of age - given that the absolute efficacy in the AR-301-002 Phase 3 study was higher in older adults than the overall population, i.e., +34% improvement on Day 21 (p= 0.057) and by +38% on Day 28 (p= 0.025) in older adults versus +11% improvement (p=0.24) in the overall population.
- The confirmatory AR-301-003 Phase 3 superiority study will be powered for efficacy in both the primary efficacy endpoint in adults ≥65 years of age, and for the key secondary efficacy endpoint in all study subjects (≥65 and <65 years of age)

"We are particularly gratified to reach concurrence with the FDA on the overall study design, endpoints, and patient populations," said Aridis CEO Vu Truong. "This provides a clear clinical and regulatory pathway to bring AR-301 to patients with high unmet medical needs and enhances the opportunity for potential pharma partners."

**About the Confirmatory AR-301-003 Phase 3 Study**

AR-301-003 will be the second and final of two planned superiority Phase 3 studies evaluating the efficacy and safety of AR-301 for adjunctive treatment of pneumonia caused by *S. aureus* in critically ill hospitalized patients. The study is a randomized, double-blind, superiority trial with the primary efficacy endpoint of Clinical Cure of pneumonia in adults 65+ years old at Day 21

post-treatment. The secondary endpoints will include Clinical Cure rates of pneumonia in study subjects ≥65 and <65 years of age, safety including all-cause mortality, and healthcare utilization. Approximately 200 clinical sites in 20+ countries are expected to participate in the study, including US, Latin and S. America, Europe, and Asia Pacific.

**About AR-301**

AR-301 is a fully human IgG1 monoclonal antibody that specifically targets *S. aureus* alpha-toxin, an important virulence factor that is secreted by both methicillin-resistant *S. aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA). AR-301 is designed to protect against alpha-toxin mediated destruction of host cells, preserving a functional host immune response. AR-301's mode of action is independent of the antibiotic resistance profile of *S. aureus* and it is active against infections caused by both MRSA and MSSA. Previously in the AR-301-002 Phase 3 superiority study, an improvement trend in absolute improvement in Clinical Cure rate at Day 21 of 11.3%, [p= 0.23] was observed in treated patients as compared to placebo. An improvement in Clinical Cure rate (or absolute efficacy) ≥10% is considered a clinically meaningful improvement by many key opinion leaders. In the prespecified older adult population of 65+ years, the absolute efficacy (improvement in Clinical Cure rate) on Day 21 was increased to 34% (p= 0.057), and to 38% on Day 28 (p= 0.025). The increase in absolute efficacy was particularly remarkable given the lower efficacy of SOC antibiotics in older adults 65+ years old compared to adults less than 65 years old (30% vs. 75*%,* respectively). In the methicillin resistant *S. aureus* (MRSA) patients, the Day 21 absolute efficacy trend was 28% higher than SOC alone (p=0.831). The increase in absolute efficacy was also driven primarily by the lower efficacy of SOC antibiotics in MRSA patients compared to methicillin susceptible *S. aureus* (MSSA) patients (38% vs. 63%, respectively). Furthermore, treatment with AR-301 was associated with reduction trends in key secondary outcome measures of duration of hospitalization (median 19 vs. 28 days, difference: 9 days), time in ICU (median 13 vs. 20 days, difference: 7 days) and mechanical ventilation days (median 6 vs. 8 days, difference: 2 days). Consistent positive efficacy trends were observed in favor of AR-301 treatment in other key secondary efficacy outcomes (e.g., Clinical Cure rates at days 7, 14, 28).

Primary outcome measures of safety and tolerability of AR-301 were achieved. AR-301 intravenous (IV) infusion was well tolerated. Adverse Events (AEs) and Serious Adverse Events (SAEs) reported over the 28-day study period for the single IV infusion were similar across the active and placebo treatment groups, with no SAEs deemed drug-related.

***Staphylococcus aureus* Ventilator Associated Pneumonia (VAP), Hospital Acquired Pneumonia (HAP), and Community Acquired Pneumonia (CAP)**

VAP, ventilated HAP, and ventilated CAP caused by *S. aureus* poses serious challenges in the hospital setting, as standard of care antibiotics are becoming inadequate in treating infected patients. There are approximately 251,600 cases of hospital acquired pneumonia reported in the U.S. annually caused by *S. aureus* (Decision Resources Group 2016 data base). These patients are typically at high risk of mortality, which is compounded by other life-threatening co-morbidities and the rise in antibiotic resistance. Epidemiology studies estimate that the probability of death attributed to *S. aureus* ranges from 29% to 55%. In addition, pneumonia infections can prolong

patient stays in ICUs (intensive care units) and the use of mechanical ventilation, creating a major economic burden on patients, hospital systems and payors.

**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 *S. aureus* alpha-toxin and is being evaluated in a global Phase 3 superiority clinical study as an adjunctive treatment of VAP, HAP, and CAP caused by *S. aureus*.
**AR-320** (VAP). AR-320 is a fully human IgG1 mAb targeting *S. aureus* alpha-toxin that is being developed 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, 2022 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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