Aileron Therapeutics Announces Positive Data from Cohort 1 of the Phase 1b Clinical Trial of LTI-03 in Idiopathic Pulmonary Fibrosis (IPF)

May 1, 2024

Low-dose LTI-03 (2.5 mg BID), a Caveolin-1 related peptide, reduced expression of multiple profibrotic proteins in both pathological basal-like cells and fibroblasts and increased the expression of a biomarker indicative of epithelial health, suggesting potential therapeutic effect

Positive trend was observed in seven of eight IPF biomarkers evaluated

Low-dose LTI-03 was well-tolerated, with no safety signal observed

Data from Cohort 2 evaluating high-dose LTI-03 (5 mg BID) is expected in the third quarter of 2024

Company to host conference call on Wednesday, May 1st at 9:00 am ET

WALTHAM, Mass., May 01, 2024 (GLOBE NEWSWIRE) -- Aileron Therapeutics, Inc. ("Aileron") (NASDAQ: ALRN), a biopharmaceutical company advancing a novel pipeline of first-in-class medicines to address significant unmet medical needs in orphan pulmonary and fibrosis indications, today announced positive data from Cohort 1 of the ongoing Phase 1b clinical trial evaluating the safety and tolerability of inhaled LTI-03 in patients diagnosed with idiopathic pulmonary fibrosis (IPF). LTI-03 is a novel, Caveolin-1-related peptide that addresses both inhibition of pro-fibrotic signaling and survival of critical epithelial cells.

Following inhaled administration of low dose LTI-03 (2.5 mg BID), a positive trend was observed in seven out of eight biomarkers with evidence of reduced expression among profibrotic proteins produced by basal-like cells and fibroblasts that contribute to the progression of IPF, including data from several biomarkers that were statistically significant, reinforcing the potential of LTI-03 to improve lung function and reverse the course of IPF.

"We find it encouraging that low dose LTI-03 achieved statistical significance in three out of eight biomarkers evaluated in the trial" said Brian Windsor, Ph.D., President and Chief Executive Officer of Aileron. "This, paired with the positive trends observed in several of the other biomarkers, strengthens our belief that LTI-03 has the potential for disease stabilization or even reversal. We look forward to continuing to evaluate LTI-03 in the ongoing Phase 1b study and sharing results from the high-dose cohort later this year."

Summary of Cohort 1 Analysis

Twelve patients were enrolled in Cohort 1 of the ongoing Phase 1b clinical trial, three in the placebo arm and nine in the active arm. Patients had a bronchoscopy at baseline, received a low dose of LTI-03 (2.5mg BID) twice a day for 14 days, followed by a bronchoscopy on day 14 and seven days of follow-up. Cohort 1 findings include:

- Reduced expression of multiple profibrotic proteins in both pathologic basal-like cells and fibroblasts, with statistically significant decreases observed in GAL-7, TSLP and Col-1α1 biomarkers, supporting the potential of LTI-03 to reduce fibrosis, inflammation and associated changes in the lung.
- Stimulated production of solRAGE, a factor indicative of type I epithelial cell health that is a critically important aspect of IPF and has gone largely unaddressed.
- LTI-03 did not induce inflammation in peripheral blood mononuclear cells (PBMCs).
- Results show LTI-03 to be generally well-tolerated with no serious adverse events (SAEs) reported.

The Phase 1b study is ongoing, with topline results from the high-dose cohort expected in the third quarter of 2024.

"We are pleased with the Cohort 1 data as it seems to confirm LTI-03's mode of action in patients with IPF" said Andreas Gunther, M.D., Head of the Center for Interstitial and Rare Lung Diseases of the Justus Liebig University in Giessen, Germany. "Importantly, the statistical significance observed in collagen deposition, inflammation and cellular processes underscores the potential of LTI-03 to act on both, fibroblasts as well as epithelial cells, the latter of which are believed to be causative in onset and aggravation of the disease. These findings underscore the promise of LTI-03 to combat the devastating effects of IPF and improve lung function and quality of life for those living with the disease. I look forward to further evaluating LTI-03's potential, particularly at the higher dose, in the ongoing study."

Conference Call Information

Aileron will host a conference call on Wednesday, May 1st at 9:00am ET to discuss the initial results from Cohort 1 of the Phase 1b clinical trial of LTI-03 in IPF. To access the call, please dial +1 646-876-9923 (domestic) or +44 330 088 5830 (international) and reference meeting ID: 970 4548 0706 when prompted by the operator. A live webcast of the event can be accessed at **https://investors.aileronrx.com/events-presentations/investor-events**. A replay of the webcast will be available following the completion of the event.

About the Phase 1 Clinical Trial of LTI-03

The Phase 1b clinical trial of LTI-03 is a randomized, double-blind, placebo controlled, multi-center, dose escalation study in patients recently diagnosed with IPF that have not received prior treatment with anti-fibrotic agents for at least two months (NCT05954988). Eligible patients are randomly assigned (3:1) to receive one of two doses of LTI-03 or placebo. The primary objective of the study is to investigate the safety and tolerability of LTI-03 in patients with IPF after treatment for 14 consecutive days, with multiple biomarker concentration as exploratory endpoints.

About IPF

IPF is a chronic lung disease characterized by progressive tissue scarring that prevents proper lung function. It is a progressive, fatal, age-associated lung disease affecting approximately 100,000 people in the United States[1]. IPF typically presents in adults 65 or older and is usually fatal within two to five years after diagnosis[2].

About LTI-03 and Caveolin-1 (Cav1)

LTI-03 is a seven amino acid peptide, the sequence of which is derived from the caveolin scaffolding domain (CSD), an important binding region of the Cav1 protein. Cav1 normally serves a critical function in the prevention of fibrosis by maintaining a balance between pathways that both initiate and arrest lung repair and cell movement. Through the CSD, caveolin interacts with a large number of signaling molecules, all of which possess a caveolin binding domain region. Cav1 expression is decreased in IPF lung tissues and has been demonstrated to decrease during the fibrotic phase of bleomycin, or BLM, lung injury in mice. Restoring the balance of important biological signals in the lung may not only slow lung function decline but could also restore healthy lung function through the protection of healthy epithelial cells.

About Aileron Therapeutics

Aileron Therapeutics is a biopharmaceutical company advancing a novel pipeline of first-in-class medicines to address significant unmet medical needs in orphan pulmonary and fibrosis indications. Aileron's lead product candidate, LTI-03, is a novel, synthetic peptide with a dual mechanism targeting alveolar epithelial cell survival as well as inhibition of profibrotic signaling. Currently, LTI-03 is being evaluated in a Phase 1b clinical trial for the treatment of idiopathic pulmonary fibrosis, with Cohort 2 results expected to be reported in the third quarter this year. Aileron's second product candidate, LTI-01, is a proenzyme that has completed Phase 1b and Phase 2a clinical trials for the treatment of loculated pleural effusions. LTI-01 has received Orphan Drug Designation in the US and EU and Fast Track Designation in the US.

References

[1] Pergolizzi, Jr., J., LeQuang, J., Varrassi, M., Breve, F., Magnusson, P., Varrassi, G., (2023). What Do We Need to Know About Rising Rates of Idiopathic Pulmonary Fibrosis? A Narrative Review and Update. Springer Nature, Published online 2023 Jan 24. Doi: 10.1007/s12325-022-02395-9.

[2] Nathan et al. "Long-term Course and Prognosis of Idiopathic Pulmonary Fibrosis in the New Millennium". Chest Journal Volume 140, ISSUE 1, P221-229, July 2011.

Forward-Looking Statements

This press release may contain forward-looking statements of Aileron Therapeutics, Inc. ("Aileron", the "Company", "we", "our" or "us") within the meaning of the Private Securities Litigation Reform Act of 1995, including statements with respect to: the timing and expectation of the results of the Phase 1b study of LTI-03; future expectations, plans and prospects for the Company, the sufficiency of the Company's cash resources; certain milestones of the Company; the projected cash runway of the Company; the status and plans for clinical trials, including the timing of data; future product development; and the potential commercial opportunity of LTI-03 and LTI-01. We use words such as "anticipate," "believe," "estimate," "expect," "hope," "intend," "may," "plan," "predict," "project," "target," "potential," "would," "can," "could," "should," "continue," and other words and terms of similar meaning to help identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including risks and uncertainties related to, the ability to maintain the listing of the common stock of the Company on The Nasdaq Stock Market, changes in applicable laws or regulations, the possibility that the Company may be adversely affected by other economic, business, and/or competitive factors, including risks inherent in pharmaceutical research and development, such as: adverse results in the Company's drug discovery, preclinical and clinical development activities, the risk that the results of preclinical studies and early clinical trials may not be replicated in later clinical trials or that partial results of a trial such as the Cohort 1 results from the Company's ongoing Phase 1b trial will be indicative of the full results of the trial, the Company's ability to enroll patients in its clinical trials, and the risk that any of its clinical trials may not commence, continue or be completed on time, or at all; decisions made by the U.S. FDA and other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies with respect to our development candidates; our ability to obtain, maintain and enforce intellectual

property rights for our platform and development candidates; competition; uncertainties as to the sufficiency of the Company's cash resources to fund its planned activities for the periods anticipated and the Company's ability to manage unplanned cash requirements; and general economic and market conditions; as well as the risks and uncertainties discussed in the "Risk Factors" section of the Company's Annual Report on Form 10-K for the year ended December 31, 2023, which is on file with the United States Securities and Exchange Commission (the "SEC"), and in subsequent filings that the Company files with the SEC. These forward-looking statements should not be relied upon as representing the Company's view as of any date subsequent to the date of this press release, and we expressly disclaim any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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