Aileron Therapeutics Announces Positive Topline Data from Cohort 2 of the Phase 1b Clinical Trial of LTI-03 in Idiopathic Pulmonary Fibrosis (IPF)

November 13, 2024

High-dose LTI-03 (5 mg BID), a Caveolin-1 related peptide, reduced expression of multiple profibrotic proteins in both pathological basal-like cells and fibroblasts and decreased the expression of a biomarker indicative of epithelial health and lung function decline, suggesting potential therapeutic effect

Positive trend observed in seven out of eight IPF biomarkers in Cohort 2, with four biomarkers statistically significant in the combined Cohort 1 and Cohort 2 data set, and dose dependent movement of five biomarkers compared to low dose LTI-03 indicative of active LTI-03 pharmacodynamics

High-dose LTI-03 was well-tolerated, with no safety signals observed

Planning is underway for a Phase 2 clinical trial

Company to host conference call today at 8:30 am ET

WALTHAM, Mass., Nov. 13, 2024 /PRNewswire/ -- 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 topline data from Cohort 2 of its 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 modulates both pro-fibrotic activity and sustain critical alveolar epithelial cells.

Following inhaled administration of high dose LTI-03 (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 four biomarkers that were statistically significant in the combined data set of Cohort 1 and Cohort 2, and data from five biomarkers that showed dose dependence relative to the data from those biomarkers in Cohort 1. Overall, the collective findings from this Phase 1b clinical trial provide the Company with strong confidence that LTI-03 has the potential to improve lung function and reverse the course of IPF.

"We are extremely pleased with the results achieved by high dose LTI-03, including measuring statistical significance in three biomarkers in Cohort 2, with the combined data sets showing even stronger results, with four statistically significant biomarkers," said Brian Windsor, Ph.D., President and

Chief Executive Officer of Aileron. "Additionally, we saw dose dependent effects in five biomarkers which provides evidence of active LTI-03 pharmacodynamics. We believe that this data, including the 5% decrease in surfactant protein D, a biomarker for epithelial cell health, at 14 days of treatment, reinforces LTI-03's potential for disease stabilization or even reversal. We look forward to evaluating LTI-03 in a Phase 2 study."

"I am delighted with the Cohort 2 data as it confirms previous results obtained with LTI-03 in cell experiments, animal studies and ex-vivo studies employing human IPF high precision cut lung slices. In these studies, the evaluated biomarkers were found to be downregulated by LTI-03. These observations have now been reproduced in IPF patients upon inhalative application of LTI-03 vs placebo," said Prof. Andreas Gunther, M.D., Head of the Center for Interstitial and Rare Lung Diseases of the Justus Liebig University in Giessen, Germany. "Moreover, the profile of the statistically significant changes in the biomarkers in response to LTI-03 treatment also suggests that LTI-03 may not only act on fibroblasts, but also on epithelial cells, which would represent a novel therapeutic principle in the IPF treatment landscape. IPF is a devastating disease with worsening quality of life over time, and LTI-03 has the potential to meaningfully impact the current treatment paradigm. I look forward to further evaluating LTI-03´s potential in a Phase 2 study."

Summary of Cohort 2 Analysis

Twelve patients were enrolled in Cohort 2 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 high dose of LTI-03 (5mg BID) twice a day for 14 days, followed by a bronchoscopy on day 14 and seven days of post-treatment follow-up. Cohort 2 findings include:

- Reduced expression of multiple profibrotic proteins active in both pathologic basal-like cells and fibroblasts, with four biomarkers (IL-11, CXCL7, TSLP and GAL-7) showing statistically significant decreases in the combined data set supporting the potential of LTI-03 to reduce fibrosis, inflammation and associated functional changes in the lung.
- Dose dependent trends were observed in five biomarkers, including COL1A1, CXCL7, TSLP, GAL-7, and Surfactant protein D (SPD) which provide evidence of active LTI-03 pharmacodynamics.
- SPD, an indicator of epithelial cell health that is significantly linked to decline in lung function, decreased by 5% in Cohort 2 at 14 days of treatment, while current standard of care for IPF reduced SPD by 4% at 12-weeks in precedent trials[1, 2].
- LTI-03 did not induce inflammation in peripheral blood mononuclear cells (PBMCs) in either Cohort, measured by pAKT, a safety marker for inflammation in this trial.
- LTI-03 was generally well-tolerated, and there were no drug-related adverse events that resulted in a discontinuation of the trial.

Conference Call Information

Aileron will host a conference call on Wednesday, November 13th at 8:30 am ET to discuss the topline results from Cohort 2 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: 951-8768-4226 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 1b 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[3]. IPF typically presents in adults 65 or older and is usually fatal within two to five years after diagnosis[4].

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. LTI-03 completed a Phase 1b clinical trial for the treatment of idiopathic pulmonary fibrosis. 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]Jenkins RG, Cottin V, Nishioka Y, et al. Effects of nintedanib on circulating biomarkers of idiopathic pulmonary fibrosis. ERJ Open Res 2024; in press (https://doi.org/10.1183/23120541.00558-2023).

[2]The biomarker data regarding change in SPD in this trial and the data from the INMARK trial of nintedanib compares two clinical trials with different trial designs, patient enrollment criteria and treatment regimens. In addition, the applicable measurements were observed over different time periods. As a result, the data from these trials may not be directly comparable.

[3]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.

[4]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 a Phase 2 trial of LTI-03; future expectations, plans and prospects for the Company, the sufficiency of the Company's cash resources; 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 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, including in a Phase 2 trial of LTI-03, or that partial results of a 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. Food and Drug Administration 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 and the Quarterly Report on Form 10-Q for the quarter ended June 30, 2024, which are 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.

Investor Relations & Media Contact:
Argot Partners
aileron@argotpartners.com
212-600-1902

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