



Avalyn Showcases Clinical Data Across Multiple Pulmonary Fibrosis Programs at ATS 2025

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Topline results for AP02 (inhaled nintedanib) confirmed safety and tolerability with limited systemic exposure and substantially improved lung exposure compared to oral nintedanib

AP01 (inhaled pirfenidone) treatment demonstrated long-term antifibrotic effects and continued favorable safety out to over 4.5 years

CAMBRIDGE, Mass., May 20, 2025 (GLOBE NEWSWIRE) -- [Avalyn Pharma Inc.](#), a clinical-stage biopharmaceutical company developing inhaled therapies for the treatment of life-threatening pulmonary diseases, presented positive clinical data on both of its lead programs. AP01 and AP02, optimized inhaled formulations of pirfenidone and nintedanib, respectively, are in development for the treatment of patients with pulmonary fibrosis. The findings were shared in multiple poster presentations and featured events during the American Thoracic Society (ATS) International Conference 2025 being held May 16-21, 2025, in San Francisco, CA.

Results from the Phase 1 single-ascending dose (SAD) and multiple-ascending dose (MAD) clinical trials of AP02 in healthy adult volunteers and patients with idiopathic pulmonary fibrosis (IPF) demonstrated favorable safety and tolerability at all dose levels evaluated. Importantly, AP02 treatment had significantly lower systemic exposures compared to historical data with oral nintedanib, the current standard-of-care antifibrotic therapy for patients with IPF. Systemic delivery with oral nintedanib is associated with multiple serious side effects that affect its tolerability, frequently leading to treatment discontinuation. Further, compared to oral nintedanib, AP02 demonstrated significantly improved exposure in the lungs, indicating that inhaled delivery can achieve clinically meaningful lung exposure at substantially lower doses relative to oral administration. The data suggest that AP02 has the potential to offer superior efficacy and an improved tolerability profile over oral nintedanib.

"As a pulmonologist, I've witnessed firsthand how the current standard-of-care oral treatments for pulmonary fibrosis are challenging for many patients, and the urgent need in the community for new treatment options that both slow fibrosis progression and are tolerable for patients to take long-term," said Joyce Lee, M.D., Professor of Pulmonary Sciences and Critical Care Medicine, Director of the Interstitial Lung Disease Program, University of Colorado School of Medicine and an AP02 Steering Committee member. "These Phase 1 results for AP02 demonstrate its potential to deliver pulmonary drug concentrations and antifibrotic benefits directly to the lungs, with a considerably lower dose than oral nintedanib to minimize the common, burdensome side effects seen with the oral dosing. I look forward to a continued collaboration with Avalyn as they advance this important potential new treatment."

Avalyn also presented long-term data from the ongoing ATLAS open-label extension (OLE) of AP01, demonstrating continued antifibrotic effects and favorable safety up to 240 weeks, or 4.5 years, in patients with different forms of pulmonary fibrosis. Furthermore, Avalyn, in collaboration with Qureight, presented results from two deep learning-based analyses of high-resolution computed tomography (HRCT) scans and patient data from the ATLAS trial, exploring the utility of novel imaging biomarkers and synthetic study arms in validating treatment efficacy in patients with IPF.

"We are pleased to share our clinical findings for both AP02 and AP01 with the respiratory community at ATS, which add to the growing body of evidence that our inhaled approach can offer enhanced treatment alternatives to systemic oral treatments," said Melissa Rhodes, Ph.D., D.A.B.T, chief operating officer of Avalyn Pharma. "AP02 has been well-tolerated up to the highest evaluated dose, and the data reaffirm our belief that AP02 has the potential to meaningfully improve outcomes for patients with IPF. In addition, we are thrilled to share new long-term data on AP01 from our ATLAS OLE trial that demonstrates continued antifibrotic effects out to 4.5 years, representing a major milestone in the treatment of pulmonary fibrosis. We are grateful to the investigators and medical teams, and the study participants, who all make our research possible. With these encouraging results, we are excited to rapidly advance AP02 into a Phase 2 clinical trial in IPF, alongside our ongoing global Phase 2b trial of AP01 in progressive pulmonary fibrosis."

ATS 2025 Poster Presentations:

Title: [A Double-blind, Placebo-controlled, Randomized Phase 1 Study to Evaluate Safety, Tolerability, and Pharmacokinetics After Single or Repeat Twice-daily Doses of AP02, a Nebulized Formulation of Nintedanib](#) (Thematic Poster Session: A57, Poster #: P1007)

Avalyn presented a late-breaking poster presentation on the recently completed Phase 1 trial of AP02. The study enrolled a total

of 60 healthy volunteers (HVs) and consisted of a single-ascending dose (SAD) portion, a multi-ascending dose (MAD) portion, and a bronchoalveolar lavage (BAL) portion, which assessed lung exposure following a single 4.0 mg AP02 dose across three different time points.

AP02 was well-tolerated following single doses and 7 days of twice daily (BID) doses, up to the highest dose (8 mg BID). The most common treatment-emergent adverse events were throat irritation and dizziness, all of which were mild and mostly resolved during the study. There were no cases of bronchospasm, cough, or diarrhea observed in the study. Notably, AP02 treatment had substantially lower systemic exposures than historical data with oral nintedanib, the current standard-of-care antifibrotic therapy for patients with IPF.

AP02 also demonstrated significantly improved exposure in the lungs as measured by BAL compared to oral nintedanib. Compared to the 150 mg oral dose, a single 4.0 mg AP02 dose delivered greater than 20-fold higher lung exposure. The data suggest that AP02 has the potential to offer superior efficacy and an improved tolerability profile over oral nintedanib.

Title: [Inhaled Nintedanib \(AP02\) for the Treatment of IPF: Safety, Tolerability, and Pharmacokinetics After Single Ascending Doses to Healthy Subjects and IPF Patients](#) (Thematic Poster Session: A101, Poster #: 112)

Avalyn's Phase 1a trial of AP02 assessed clinical tolerability and pharmacokinetic profiles in three SAD cohorts, up to a maximum 2.0 mg dose in HVs; two BAL cohorts in HVs; and one cohort of patients with IPF.

AP02 was well-tolerated at all doses explored in this study. The most common treatment-emergent adverse events were headache, nausea, and cough, all of which were mild, except for one, and all resolved during the study. There were no serious adverse events, bronchospasm, or decreased oxygen saturation observed.

AP02 demonstrated a dose-related increase in systemic exposure. Between HVs and patients with IPF, there was no difference in systemic exposure with inhaled dosing. Notably, inhaled dosing resulted in approximately 15-fold lower C_{max} and 68-fold lower AUC_{0-24} than the oral nintedanib approved dosage. Additionally, AP02 demonstrated approximately 9-fold higher bronchoalveolar lavage fluid (BALF) exposure than oral administration, highlighting that inhaled delivery has the potential to improve efficacy and tolerability of oral nintedanib through increasing lung exposure and decreasing systemic exposure.

Title: [Long-term Safety and Efficacy Data with Inhaled Pirfenidone \(AP01\) in the ATLAS Open-label Extension Study Up to 240 Weeks](#) (Thematic Poster Session: A101, Poster #: 103)

Avalyn's open-label extension (OLE) trial enrolled a total of 100 patients, including 41 patients rolled over from the ATLAS study, 31 AP01-naïve patients with IPF, and 28 AP01-naïve patients with progressive pulmonary fibrosis (PPF). All patients received 100 mg twice daily (BID) in the OLE.

Data from roll-over patients from the ATLAS study had an FVC change of -69 ml/year; naïve IPF patients had a FVC change of -120 ml/year, while naïve PPF patients had a FVC change of +11 ml/year. AP01 has continued to demonstrate a well-tolerated profile, with no new safety signals seen during weeks 144 to 240. These positive findings, demonstrating durable efficacy and stable safety up to approximately 4.5 years, are unprecedented as the median survival of pulmonary fibrosis is 3-5 years after diagnosis. Many patients are unable to remain on oral antifibrotic therapies for this length of time, often due to tolerability challenges or because they succumb to disease progression, limiting long-term follow-up. Patients in the ATLAS OLE study have been alive for up to 6.5 years since diagnosis.

These data indicate that AP01 demonstrates durable efficacy with a stable safety profile over the long-term, providing further support for the development of AP01.

Title: [Monte Carlo External Control Arm Generation Utilizing Real-world Patient Data and Deep Learning-based Quantitative CT Metrics Demonstrates Treatment Effect in the ATLAS IPF Trial](#) (Thematic Poster Session: A57, Poster #: P1009)

Avalyn, in collaboration with Qureight, presented a late-breaking poster presentation on findings from a Monte Carlo Cross Validation (MCCV) approach to generate external placebo control arms using real-world data of treatment-naïve IPF patients. The approach produced well-matched external placebo control arms for both treatment groups. The results, comparing the change in FVC between these external placebo control arms and the treatment arms, demonstrated a significant treatment effect for 100 mg BID over 48 weeks. This represents the first known application of quantitative HRCT in creating a matched external placebo control arm, signaling a potential paradigm shift in the investigation of novel drug candidates for IPF in clinical trials.

Title: [Dose-Dependent Change of Inhaled Pirfenidone Seen in Lung Volume and Fibrosis Quantification in Patients With IPF: A Deep Learning Image-Based Analysis of Data from the ATLAS Phase 1b Trial](#) (Thematic Poster Session: C23, Poster #: 601)

Together with Qureight, Avalyn presented results from deep learning-based analyses of HRCT scans and patient data from the completed ATLAS trial of AP01. The Qureight platform analyzed HRCT scans from patients with IPF from the ATLAS study to quantify the volumes of the lungs, airways, pulmonary vessels, and fibrosis. Across all visits, HRCT-derived total lung volume strongly correlated with the forced vital capacity (FVC).

Between the 50 mg QD and 100 mg BID cohorts, patients on the higher dose showed a smaller lung volume reduction at week 36 and reduced fibrosis progression at week 24 compared to the 50 mg QD dose. These data demonstrate dose-dependent effects of

AP01 on anatomy through Qureight's deep learning-based imaging biomarkers and efficacy as measured by FVC.

About AP01

AP01 is an optimized formulation of pirfenidone, a small molecule inhibitor with anti-inflammatory and anti-fibrotic effects through modulation of cytokines and growth factors. AP01 is administered using the PARI eFlow® Nebulizer System that delivers the medication to the lungs in less than 10 minutes. AP01 has been extensively studied in over 150 clinical trial participants with over 3,000 months of patient exposure. In the completed Phase 1b trial (ATLAS), AP01 demonstrated a markedly improved tolerability profile, with significantly fewer gastrointestinal and skin-related side effects compared to historical data with oral pirfenidone. AP01 continues to demonstrate long-term safety and efficacy in the ongoing open label extension trial, outperforming historical data of oral pirfenidone, with some patients surviving more than 4.5 years. A Phase 2b trial (MIST) is underway to further evaluate AP01 in patients with Progressive Pulmonary Fibrosis (PPF).

About AP02

AP02 is an optimized formulation of nintedanib in clinical development for idiopathic pulmonary fibrosis (IPF). Nintedanib is a small molecule inhibitor of multiple tyrosine kinases, known to disrupt the cellular processes that lead to lung fibrosis. Oral nintedanib is associated with significant tolerability challenges, including diarrhea, hyperbilirubinemia, and drug-induced liver injury. Avalyn's AP02 provides optimal delivery to the lung with limited systemic exposure. The company has completed single-ascending dose (SAD) and multiple-ascending dose (MAD) Phase 1 clinical trials in healthy adult volunteers and patients with IPF.

About Avalyn Pharma

Avalyn is reimagining the future of pulmonary fibrosis treatment with a pipeline of new inhaled formulations of approved medicines. Pulmonary fibrosis is characterized by scarring of lung tissue, decline in lung function, reduced exercise capacity, and quality of life, and is associated with increased mortality. Currently approved therapeutic options slow pulmonary fibrosis progression but are associated with significant toxicities that restrict their use and dosing. Avalyn's [inhaled approach](#) tackles the underlying pathophysiology of pulmonary fibrosis at its source by safely delivering treatments directly into the lungs, thereby improving tolerability by decreasing systemic exposure and improving efficacy by increasing lung exposure. Avalyn's AP01 is an optimized inhaled formulation of pirfenidone, currently being studied in the ongoing MIST Phase 2b study in progressive pulmonary fibrosis (PPF). AP01 has been assessed in over 150 individuals with different forms of pulmonary fibrosis and demonstrated clinical proof-of-concept with improved efficacy and safety compared to historical data with existing therapies. The company completed two Phase 1 studies for AP02, inhaled nintedanib, for the treatment of idiopathic pulmonary fibrosis (IPF). For more information, please visit avalynpharma.com and follow us on [LinkedIn](#).

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