AP01-007 (MIST Study) *ClinicalTrials.gov Identifier:* NCT06329401 ***RECRUITING**

Sponsor: Avalyn Pharma Inc.
A Randomized, Double-Blind, Placebo-Controlled, Phase 2b Study Evaluating the Safety and Efficacy of Pirfenidone Solution for Inhalation (AP01) in Subjects with Progressive Pulmonary Fibrosis (PPF)

Primary Objective:
To evaluate the effect of AP01 high dose twice a day (BID) or AP01 low dose twice a day (BID) compared to placebo twice a day (BID)

Primary Endpoint:
Change from baseline in FVC (mL) at Week 52

Secondary Endpoint:
Living with Pulmonary Fibrosis (L-PF) Questionnaire Dyspnea and Cough domain scores at Week 52
Time to disease progression (absolute FVC percent predicted decline of ≥10% prior to Week 52)
Change in lung fibrosis score based on HRCT from Baseline to Week 52

Inclusion criteria:
- Diagnosis of PPF
- Physiologic evidence of progression within at least 1 of the following criteria:
  - Relative decline in FVC ≥ 10% predicted within the previous 24 months compared to Screening visit 1
  - Relative decline in FVC ≥ 5% to < 10% predicted within the previous 24 months compared to Screening visit 1 with at least 1 of the 2 following criteria:
    - Worsening respiratory symptoms OR Radiological HRCT evidence of disease progression
    - Worsening of respiratory symptoms AND radiological HRCT evidence of disease progression per a local or central radiologist
- Must have been on Nintedanib ≥ 6 months, discontinuing must have been ≥ 12 weeks & can initiate if progression occurs
- Treated for non-pulmonary manifestations of RA/CTD must have been on standard of care ≥ 12 weeks
- Use of MMF, TOCI, MTX, Azathioprine, (prednisone ≤20 mg or eq. allowed) or RTX, must have been on these medications ≥ 12 weeks prior to Screening (6 months for RTX)

Exclusion criteria:
- Diagnosis of IPF (UIP that is not idiopathic, for example related to RA, is not exclusionary)
- Significant clinical worsening of PPF during screening
- Previous or current treatment with oral pirfenidone within 3 months prior to screening
- Extent of emphysema is greater than the extent of fibrosis according to central review of the HRCT
- Acute respiratory exacerbation requiring hospitalization within 12 weeks prior to screening
- FVC ≤ 45% or DLco ≤ 30%
- Significant liver or kidney disease
- Significant non PPF disease such as cancer, very high blood pressure or a heart attack or unstable angina within the previous 6 months

Trial schedule:
12 on-site visits (screening visit 1 & 2, baseline, weeks 2, 4, 8, 12, 18, 26, 38, 48 & 52).

Dosing:
Patients will be randomized 2:1:2 to 1 of 3 treatment arms: AP01 100 mg BID, AP01 50 mg BID, or placebo BID by oral inhalation using the investigational eFlow Nebulizer.

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