Avalyn PHARMA

Improved Therapies for
Interstitial Lung Disease (ILD)

# ATS Respiratory Innovation Summit

May 2022

# Avalyn Pharma

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| **Mission** | • Develop inhaled therapies for restrictive lung diseases that improve efficacy and safety |
| **Areas of Focus** | • IPF and PFILD<br>• CLAD (Chronic lung allograph dysfunction)<br>• Post Covid-19 lung fibrosis |
| **Programs** | • AP01 (Pirfenidone Solution for Inhalation) Phase 3 start up ongoing<br>• AP02 (Inhaled Nintedanib) Phase 1 completing 6/22 |

# AP01 (inhaled pirfenidone)

- Pirfenidone formulated for inhaled aerosol lung delivery
- Nebulizer developed by PARI for fast delivery to peripheral lung
- Patents issued in US, Canada, Japan and EU

## Formulation

- 12.5 mg/mL pirfenidone
- 4 mL (50 mg) blow fill seal plastic ampoules
- 3-year room temperature stability
- Trace saccharin used to mask bitterness

## Nebulizer

- PARI eFlow® electronic vibrating mesh nebulizer
- High-efficiency device marketed with other approved products
- Particle size 3-4 microns for deep lung delivery
- Approximately 40% efficient in delivery to lung

# AP01 Preclinical Toxicology and Phase 1 SAD Study

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| **Preclinical Toxicology** | • Preclinical inhaled toxicology studies:<br>  • 28-day dog and rat, 6-month rat study<br>  • No lung findings in any study<br>  • 30-60 fold safety margin based on liver findings |
| **Phase 1 Clinical Study** | • SAD study (Khoo, JK et al, JAMPDD, 2019 32:1-6)<br>• Dose escalation to 100 mg in nebulizer<br>• No bronchospasm or decreased oxygen saturation in any volunteer or IPF patient<br>• BAL cohort showed 35-fold higher epithelial lining fluid pirfenidone levels with 100 mg dose than estimated for oral 801 mg dose<br>• 100 mg dose has 1/15 systemic exposure than 801 mg dose |

# AP01-002 ATLAS Study

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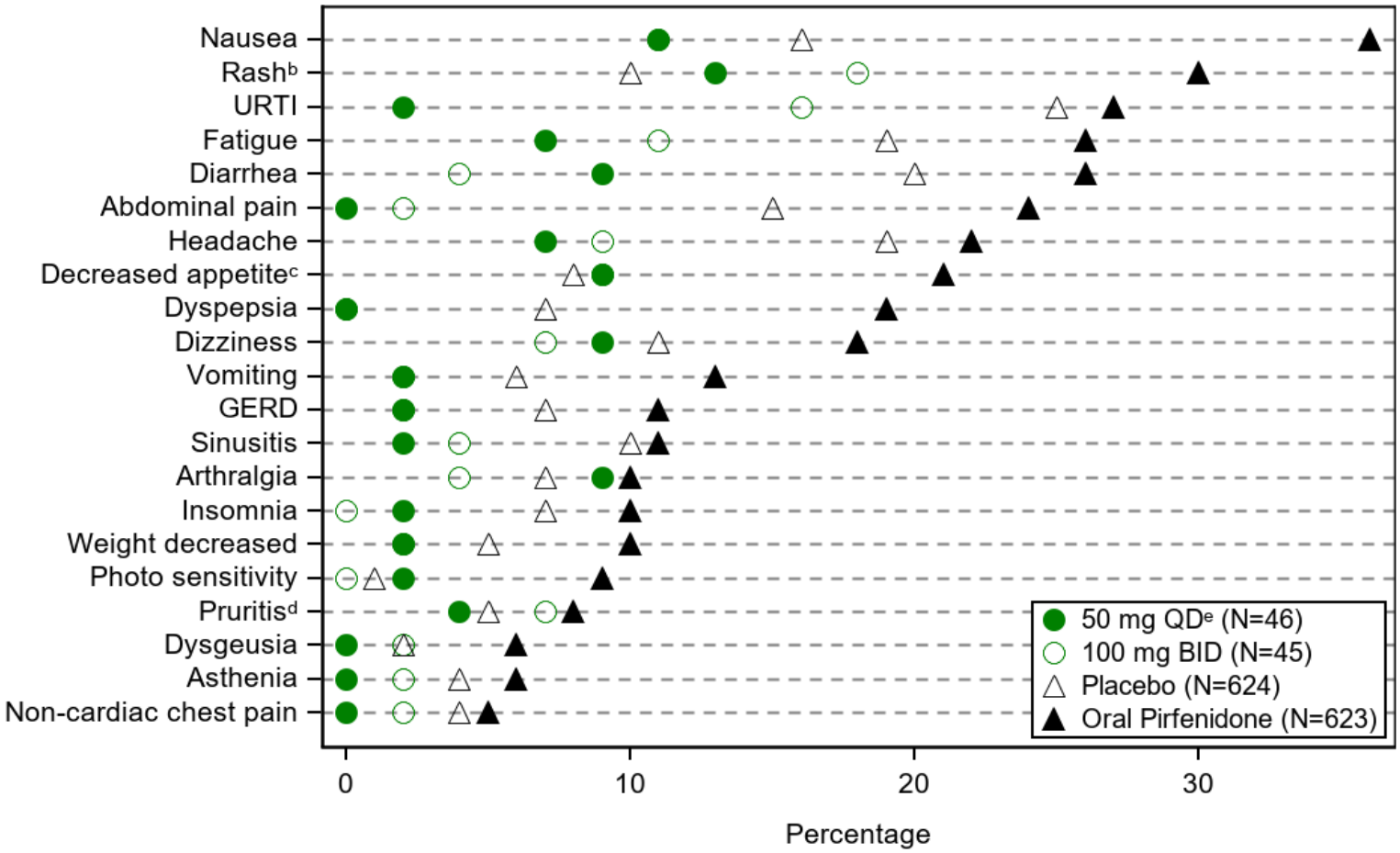
| **Eligibility** | • Confident diagnosis of IPF<br>• Not eligible for oral pirfenidone/nintedanib per national formulary restrictions OR intolerant to or unwilling to start oral pirfenidone and nintedanib, if previously offered<br>• 40 ≤ FVC ≤ 90% predicted (40 - 50% capped at 20 patients) |
| **Design** | • 25 sites in 6 countries<br>• 100 patients, randomized, 2 arm, open-label<br>• 50 mg QD or 100 mg BID<br>• Visits every month through Week 24 - no nintedanib allowed<br>• Visits every 3 months through Week 72 - nintedanib allowed at physician's discretion |
| **Objective** | • Confirm multidose safety<br>• Estimate effect size and variability for dose selection<br>• Endpoints: Safety/tolerability, FVC, cough, PRO, lung fibrosis/volumes per HRCT |
| **Conduct** | • Enrollment July 2019 – April 2020<br>• Baseline characteristics similar to oral pirfenidone Phase 3 studies<br>• COVID-19 impacted patients' ability to attend site visits<br>  – Enrollment halted at 91 patients<br>• DSMB Review in Oct 2020 recommended convert to single dose 100 mg BID |

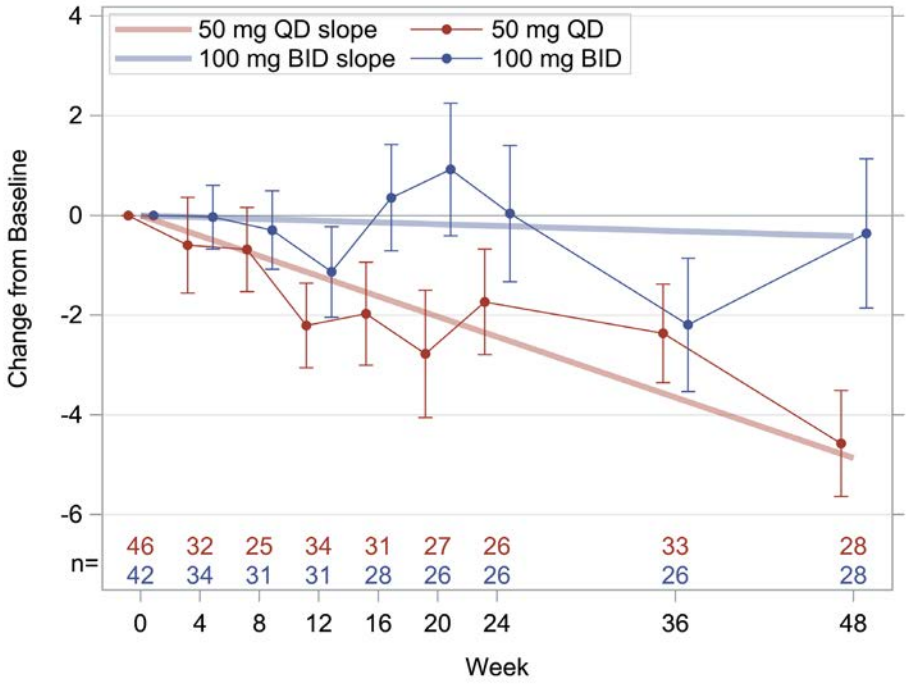
# AP01 Has Substantially Improved AE Profile Compared to Oral Pirfenidone



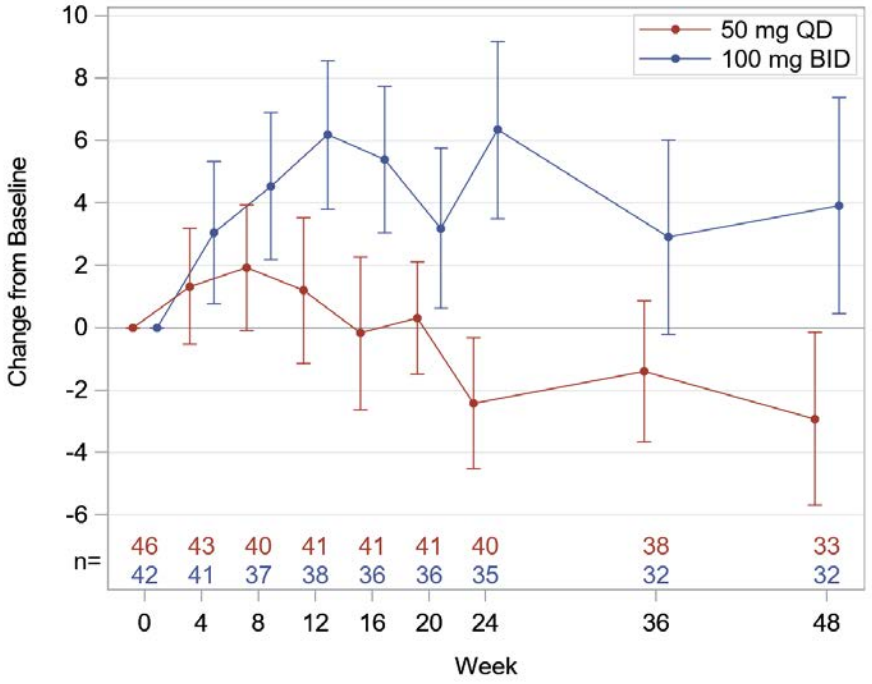

a. Occurring in ≥ 5% of Esbriet® patients and more commonly than placebo in CAPACITY and ASCEND
b. For ATLAS, rash includes rash, rash macular, rash papular, rash erythematous, and rash pruritic
c. Per MedDRA updates anorexia now codes to decreased appetite
d. For ATLAS, pruritis includes pruritis and pruritis generalized
e. 50 mg QD patients transitioned to 100 mg BID: After transition nausea, diarrhea, and rash from patient; weight increased from 1 patient are reported in 50 mg QD

# AP01 Change from Baseline in Lung Function and Quality of Life

## Change from Baseline in FVC % Predicted

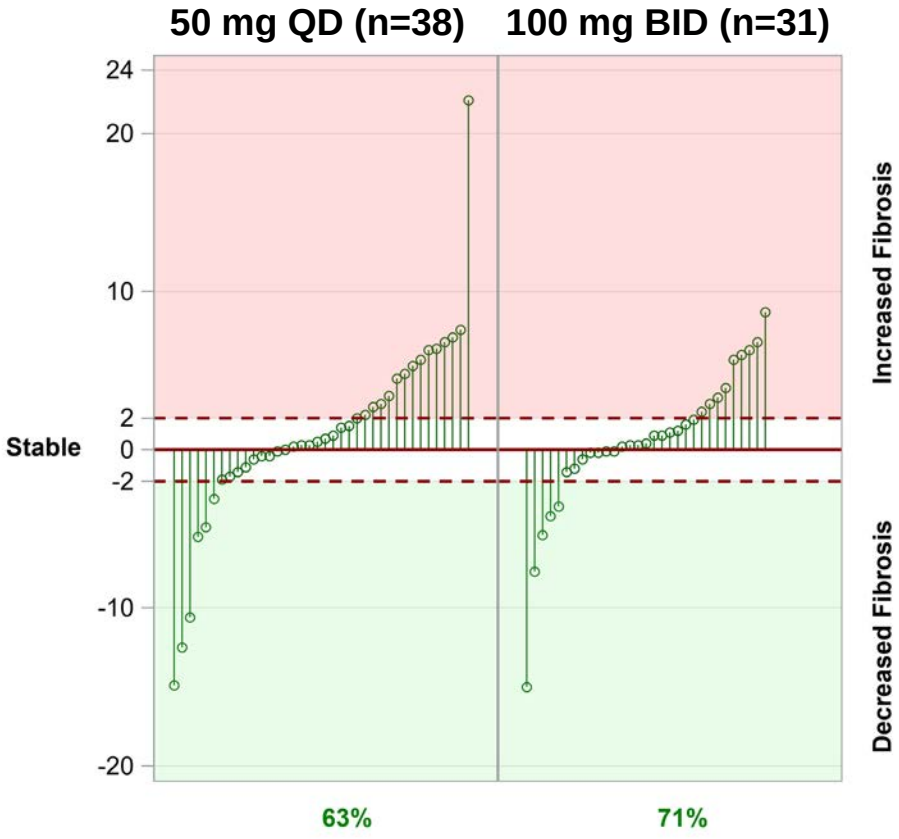



## Change from Baseline in KBILD Breathlessness and Activities



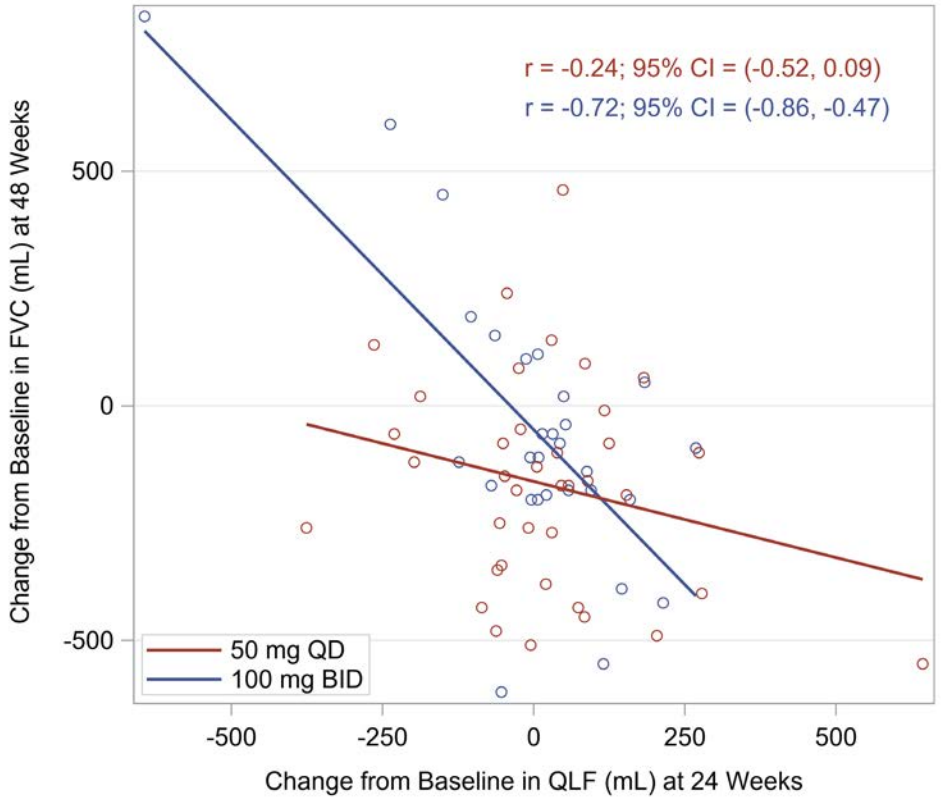
# AP01 24 Week Change from Baseline in Whole Lung Quantitative Lung Fibrosis using HRCT Scans

## Change from Baseline in Percent of Lung with Fibrosis




**Percent of Patients Stable or Improved**

## Change in QLF and FVC Correlated Well



# Future Plans

AP01 (Pirfenidone Solution for Inhalation)

- In IPF, test the hypothesis that AP01 is superior to oral pirfenidone in both efficacy and safety
  - Phase 2/3, 52-week, head-to-head, double-dummy
  - 100 mg BID AP01 vs 801 mg TID oral pirfenidone
- In PFILD, test the hypothesis that AP01 is better than placebo
  - Phase 2/3, 52-week, placebo-controlled

AP02 (Inhaled Nintedanib)

- Complete Phase 1
  - Characterize inhaled benefit and determine whether nintedanib effective dose may be possible with a dry powder inhaler

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