# INTEGRIS-IPF: A Phase 2a Clinical Trial of PLN-74809 in Patients with IPF

JULY 11, 2022

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# Today's Speakers

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**Bernard Coulie, M.D., Ph.D., M.B.A.**
President & CEO

# Welcome and Opening Remarks

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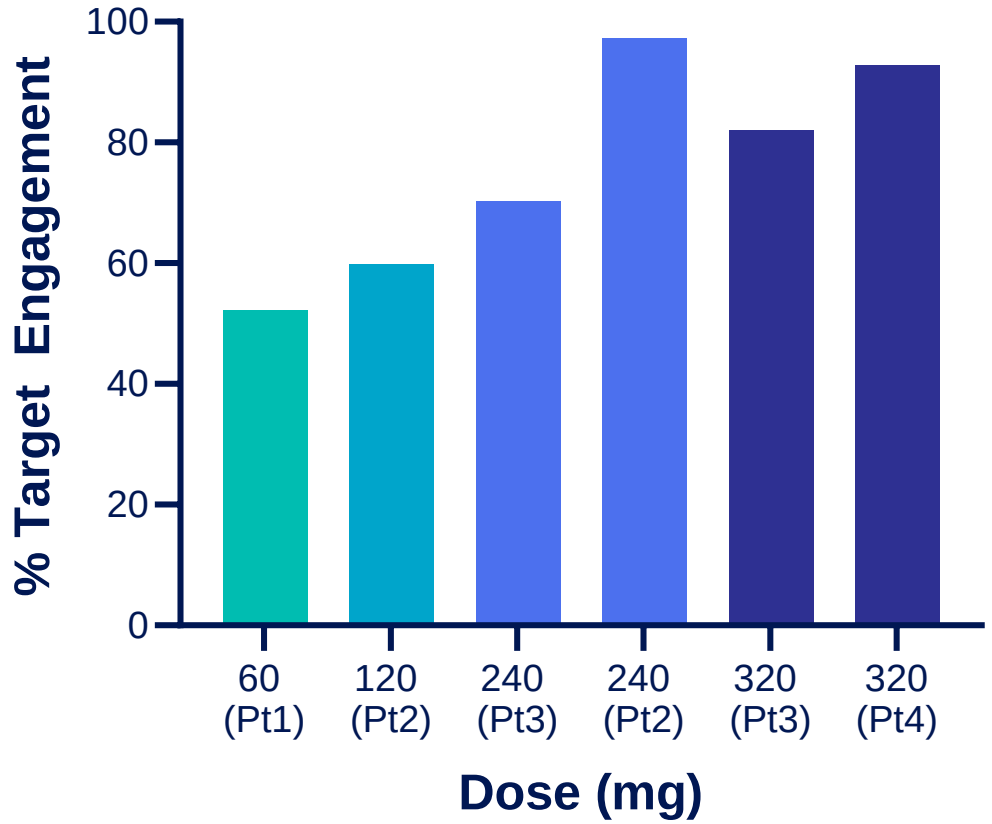
**Éric Lefebvre, M.D.**
Chief Medical Officer

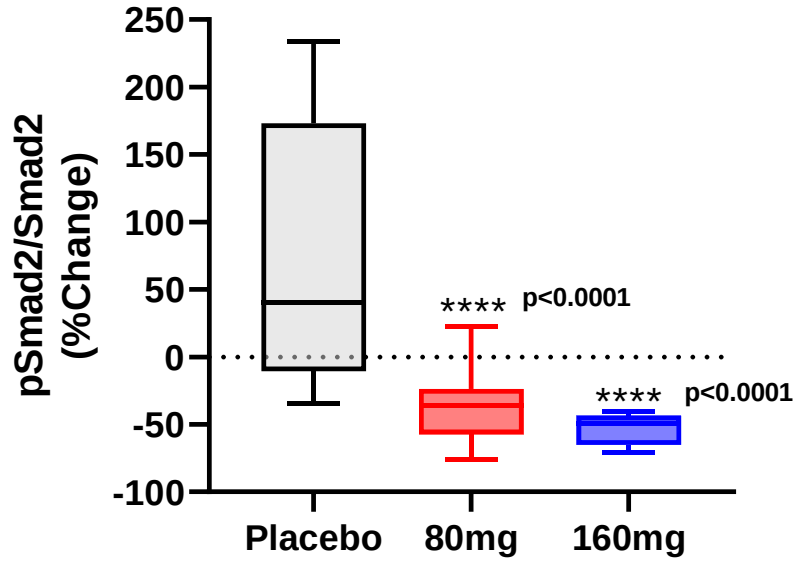
# Executive Summary

# PLN-74809 Achieved Dose Dependent Target Engagement and TGF-β Suppression in Prior Studies

## Target Engagement After a Single Dose of PLN-74809



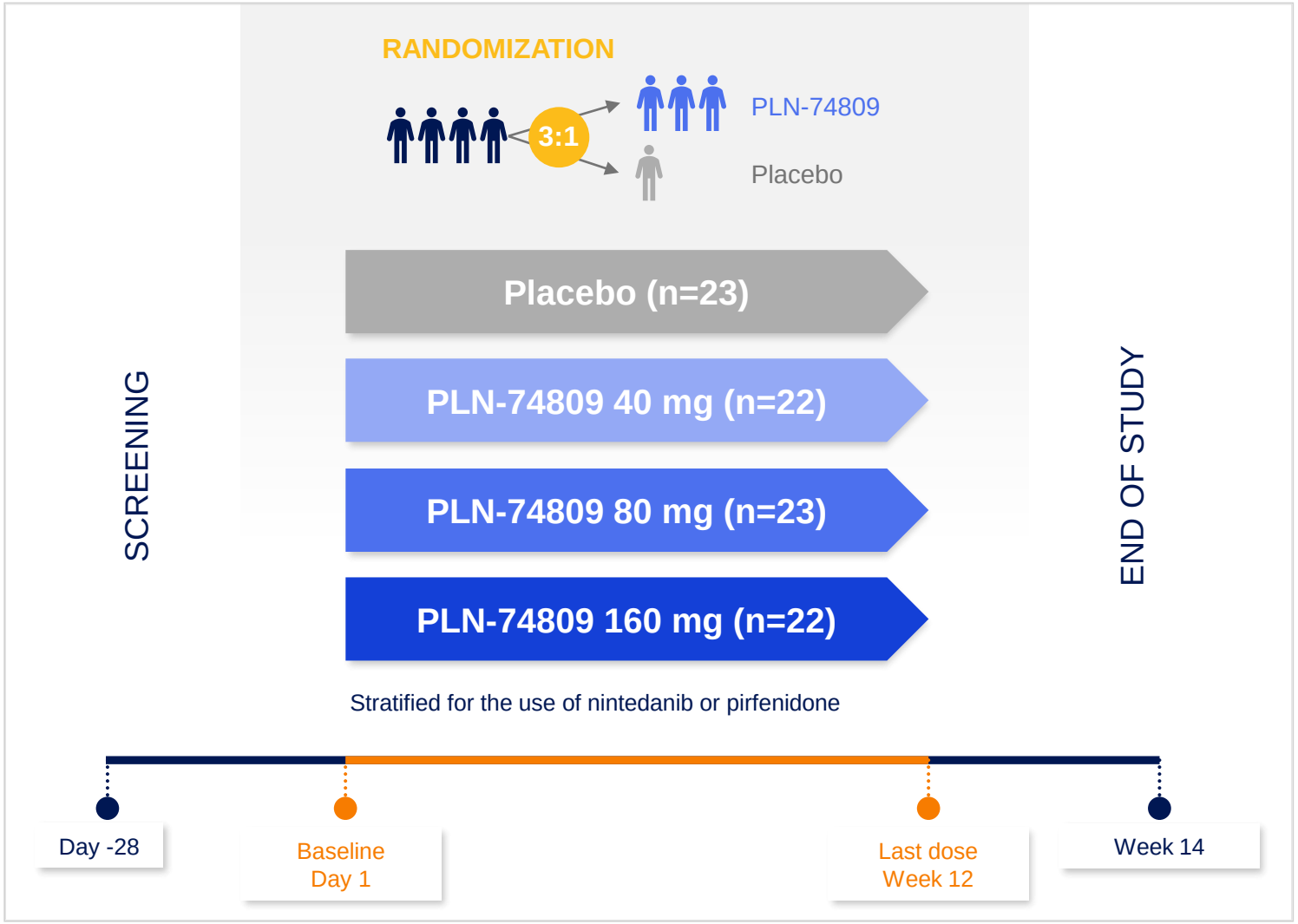

## Alveolar pSmad2/Smad2 Percentage Change from Baseline at 24 Hours




**Percent change pSmad2/Smad2 was statistically significant at both doses of PLN-74809 vs. placebo (p<0.0001)**

BAL – bronchoalveolar lavage; pSmad2/Smad2 – ratio of phosphorylated Smad2 to total Smad2; QD – once daily

# INTEGRIS-IPF Study Design and Objectives




## PRIMARY AND SECONDARY ENDPOINTS

- Safety, tolerability, PK

## EXPLORATORY ENDPOINTS

- Change in Forced Vital Capacity (FVC) over 12 weeks
- High Resolution CT-based Quantitative Lung Fibrosis (QLF) imaging
- Patient-reported outcome (PRO): VAS-cough severity
- Effect on selected biomarkers

# Executive Summary

## PLN-74809 Well Tolerated Over 12 Weeks of Treatment

- Most TEAEs were mild or moderate in severity
- No discontinuations due to adverse events
- No deaths or drug-related SAEs

## PLN-74809-Treated Patients Experienced an 80% Reduction in FVC Decline Over 12 Weeks (-15.1 mL, Pooled Active Groups) Compared to Placebo (-74.1 mL)

- PLN-74809 treatment effect was evident with and without use of standard-of-care agents
- An improvement in FVC (+24.6 mL) was observed in PLN-74809 80 mg dose cohort
- Dose-dependent reduction in proportion of patients with percent predicted FVC (FVCpp) decline of ≥10%, a well-established predictor of death and disease progression in IPF

## Other Exploratory Endpoints

- Dose-dependent antifibrotic effect seen on QLF Imaging, with no progression in 160 mg group at Week 12
- PLN-74809 decreased serum biomarkers of collagen synthesis (PRO-C3 and PRO-C6) relative to placebo

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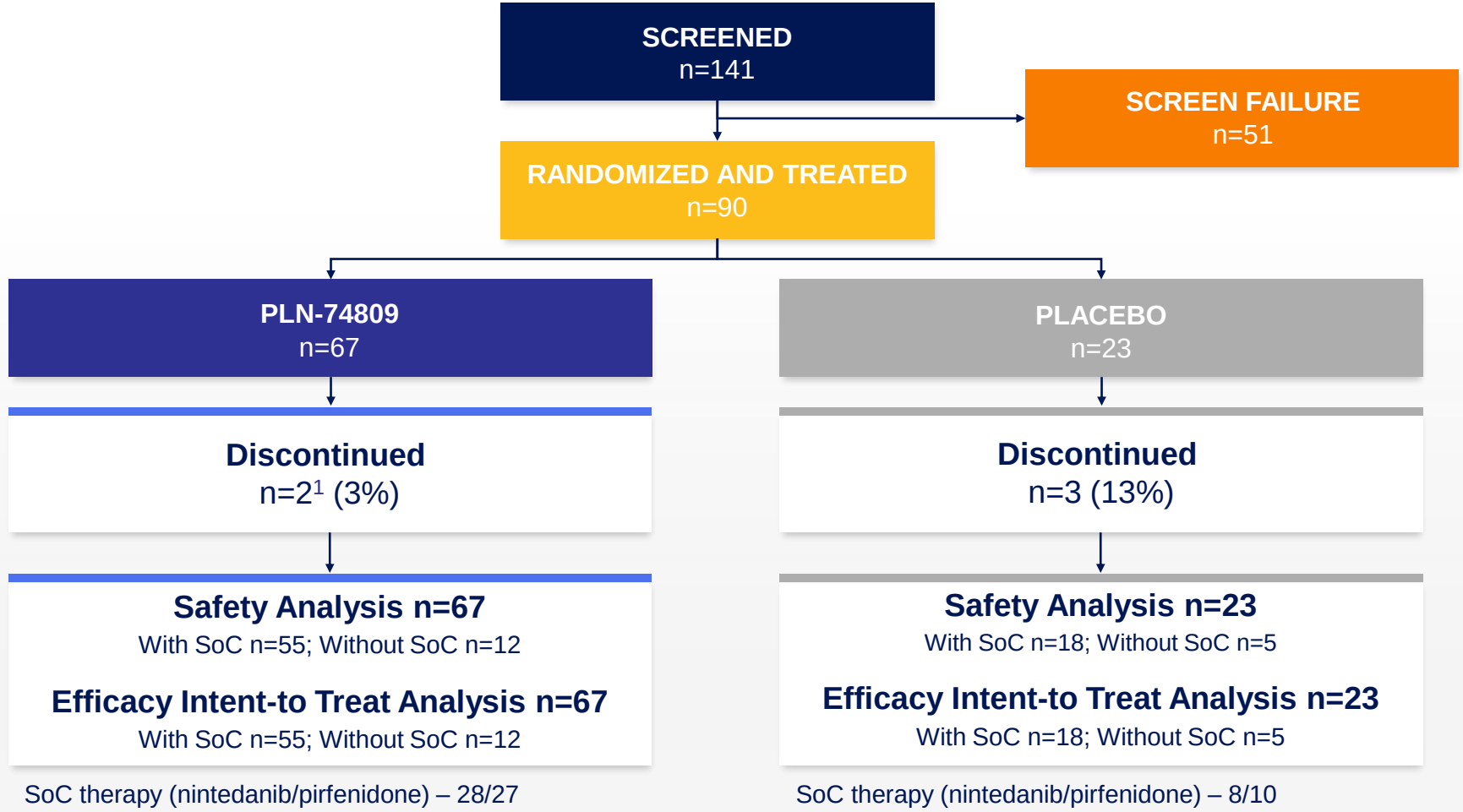
**Greg Cosgrove, M.D., FCCP**
Vice President,
Clinical Development

# INTEGRIS-IPF Study Results

# Participant Disposition




1 - Withdrawal of consent (n=1); Physician decision (n=1)

SoC = Standard of Care

# Baseline Demographics

| Characteristic | PLN-74809 40mg (n=22) | PLN-74809 80mg (n=23) | PLN-74809 160mg (n=22) | PLN-74809 All (n=67) | Placebo (n=23) |
|---|---|---|---|---|---|
| **Male sex—no. (%)** | 18 (81.8) | 19 ( 82.6) | 16 ( 72.7) | 53 ( 79.1) | 22 ( 95.7) |
| **Female sex-no. (%)** | 4 (18.2) | 4 (17.4) | 6 (27.3) | 14 (20.9) | 1 (4.3) |
| **Age—yr (SD)** | 69.2 (7.11) | 74.2 (4.70) | 71.5 (6.63) | 71.7 (6.45) | 71.7 (5.61) |
| **Race—no. (%)** | | | | | |
| White | 22 (100.0) | 21 ( 91.3) | 22 (100.0) | 65 ( 97.0) | 22 ( 95.7) |
| Asian | 0 | 1 (4.3) | 0 | 1 ( 1.5) | 1 ( 4.3) |
| Not Reported / Unknown | 0 | 1 (4.3) | 0 | 1 ( 1.5) | 0 |
| **Weight—kg, Mean (SD)** | 86.09 (18.223) | 85.89 (14.949) | 85.37 (13.507) | 85.79 (15.437) | 85.23 (10.743) |
| **Body-mass index (kg/m$^2$), Mean (SD)** | 27.67 (4.205) | 28.54 (5.790) | 29.28 (4.663) | 28.50 (4.915) | 27.43 (2.488) |

SD = Standard deviation; BMI = Body Mass Index; FVC = Forced Vital Capacity; DLCO = Diffusing capacity for carbon monoxide; Duration since diagnosis at screening is calculated from the first reported date for preferred terms of Idiopathic Pulmonary Fibrosis,Pulmonary Fibrosis or Interstitial Lung Disease.
Percentages are based on the number of participants in the Safety Population by treatment group.
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# Baseline Disease Characteristics

| Characteristic | PLN-74809 40mg (n=22) | PLN-74809 80mg (n=23) | PLN-74809 160mg (n=22) | PLN-74809 All (n=67) | Placebo (n=23) |
|---|---|---|---|---|---|
| **Time since diagnosis of IPF—yr, Mean (SD)** | 1.78 (0.925) | 2.39 (1.422) | 2.13 (1.083) | 2.10 (1.176) | 2.62 (1.378) |
| **Standard of Care Use** | 17 (77.3) | 19 ( 82.6) | 19 ( 86.4) | 55 ( 82.1) | 18 ( 78.3) |
| None | 5 (22.72) | 4 (17.39) | 3 (13.63) | 12 (17.91) | 5 (21.74) |
| Nintedanib | 12 ( 54.5) | 9 ( 39.1) | 7 ( 31.8) | 28 ( 41.8) | 8 ( 34.8) |
| Pirfenidone | 5 ( 22.7) | 10 ( 43.5) | 12 ( 54.5) | 27 ( 40.3) | 10 ( 43.5) |
| **Duration of Standard of Care at Randomization (months), Mean, (SD)** | 19.47 (11.527) | 20.21 (11.523) | 20.07 (11.632) | 19.93 (11.350) | 24.12 (17.295) |
| **FVC** | | | | | |
| Mean—mL (SD) | 2976.5 (861.01) | 3128.7 (814.20) | 2863.0 (725.39) | 2991.5 (797.76) | 3211.7 (792.68) |
| Median—mL | 2937.0 | 2929.0 | 2702.5 | 2806.0 | 3282.0 |
| Percent of predicted value, Mean (SD) | 74.81 (14.698) | 82.67 (13.471) | 78.75 (16.356) | 78.80 (14.995) | 78.30 (15.859) |
| **Percent of predicted DLCO, corrected for the hemoglobin level, Mean (SD)** | 57.200 (14.7434) | 51.782 (14.6690) | 48.615 (15.1082) | 52.521 (15.0362) | 50.335 (16.2161) |
| **GAP Stage** | | | | | |
| GAP Stage I, n (%) | 11 ( 50.0) | 8 ( 34.8) | 7 ( 31.8) | 26 ( 38.8) | 7 ( 30.4) |
| GAP Stage II, n (%) | 10 ( 45.5) | 15 ( 65.2) | 13 ( 59.1) | 38 ( 56.7) | 13 ( 56.5) |
| GAP Stage III, n (%) | 1 ( 4.5) | 0 | 2 ( 9.1) | 3 ( 4.5) | 3 ( 13.0) |

SD = Standard deviation; BMI = Body Mass Index;
Duration since diagnosis at screening is calculated from the first reported date for preferred terms of Idiopathic Pulmonary Fibrosis,Pulmonary Fibrosis or Interstitial Lung Disease.
Percentages are based on the number of participants in the Safety Population by treatment group.
GAP Stage I = GAP Index 0-3; GAP Stage II = GAP Index 4-5; GAP Stage III = GAP Index 6-8.
GAP Index score (0-8) derived from Gender, Age, FVC, % Predicted and DLCO, % Predicted.

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# Safety Analyses – Primary Objective

# Safety Summary

| AE, n (%) of Participants Reporting | PLN-74809 40mg (n=22) | PLN-74809 80mg (n=23) | PLN-74809 160mg (n=22) | PLN-74809 All (n=67) | Placebo (n=23) |
|---|---|---|---|---|---|
| **Any AEs** | 16 ( 72.7) | 15 ( 65.2) | 15 (68.1) | 46 ( 68.7) | 14 ( 60.9) |
| **TEAE** | 16 ( 72.7) | 15 ( 65.2) | 14 ( 63.6) | 45 ( 67.2) | 14 ( 60.9) |
| Related to study drug | 4 ( 18.2) | 7 ( 30.4) | 4 ( 18.2) | 15 ( 22.4) | 8 ( 34.8) |
| **Serious TEAE** | 1 ( 4.5) | 0 | 2 ( 9.1) | 3 ( 4.5) | 2 ( 8.7) |
| Related to study drug | 0 | 0 | 0 | 0 | 0 |
| **TEAE of CTCAE Grade 3 or Higher** | 2 ( 9.1) | 0 | 2 ( 9.1) | 4 ( 6.0) | 1 ( 4.3) |
| Related to study drug | 0 | 0 | 1 ( 4.5) | 1 ( 1.5) | 0 |
| **TEAE Leading to Interruption of Study Drug** | 0 | 0 | 1 ( 4.5) [1] | 1 ( 1.5) [1] | 0 |
| **TEAE Leading to Withdrawal of Study Drug** | 0 | 0 | 0 | 0 | 2 ( 8.7) |
| **TEAE Leading to Early Termination from Study** | 0 | 0 | 0 | 0 | 1 ( 4.3) |
| **TEAE Leading to Death** | 0 | 0 | 0 | 0 | 0 |

1 – COVID-19

AE = Adverse Event; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Events. Adverse events coded using MedDRA v. 24.0.
TEAE is defined as any AE starting (or worsening) on or after the date of first dose.

# Safety Summary by SOC Use in Pooled PLN-74809 Groups

| | Without Background SoC (n=17) | | With Background SoC (n=73) | |
|---|---|---|---|---|
| **AE, n (%) of Participants Reporting** | **PLN-74809 (n=12)** | **Placebo (n=5)** | **PLN-74809 (n=55)** | **Placebo (n=18)** |
| **Any AEs** | 8 ( 66.7) | 3 ( 60.0) | 38 ( 69.1) | 11 ( 61.1) |
| **TEAE** | 8 ( 66.7) | 3 ( 60.0) | 37 ( 67.3) | 11 ( 61.1) |
| Related to study drug | 2 ( 16.7) | 2 ( 40.0) | 13 ( 23.6) | 6 ( 33.3) |
| **Serious TEAE** | 0 | 0 | 3 ( 5.5) | 2 ( 11.1) |
| Related to study drug | 0 | 0 | 0 | 0 |
| **TEAE of CTCAE Grade 3 or Higher** | 0 | 0 | 4 ( 7.3) | 1 ( 5.6) |
| Related to study drug | 0 | 0 | 1 ( 1.8) | 0 |
| **TEAE Leading to Interruption of Study Drug** | 1 ( 8.3) | 0 | 0 | 0 |
| **TEAE Leading to Withdrawal of Study Drug** | 0 | 1 ( 20.0) | 0 | 1 ( 5.6) |
| **TEAE Leading to Early Termination from Study** | 0 | 1 ( 20.0) | 0 | 0 |
| **TEAE Leading to death** | 0 | 0 | 0 | 0 |

TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Events. Adverse events coded using MedDRA version 24.0.
TEAE is defined as any AE starting (or worsening) on or after the date of first dose.
SOC = standard of care, nintedanib or pirfenidone

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# Most Frequent TEAEs – Any Causality

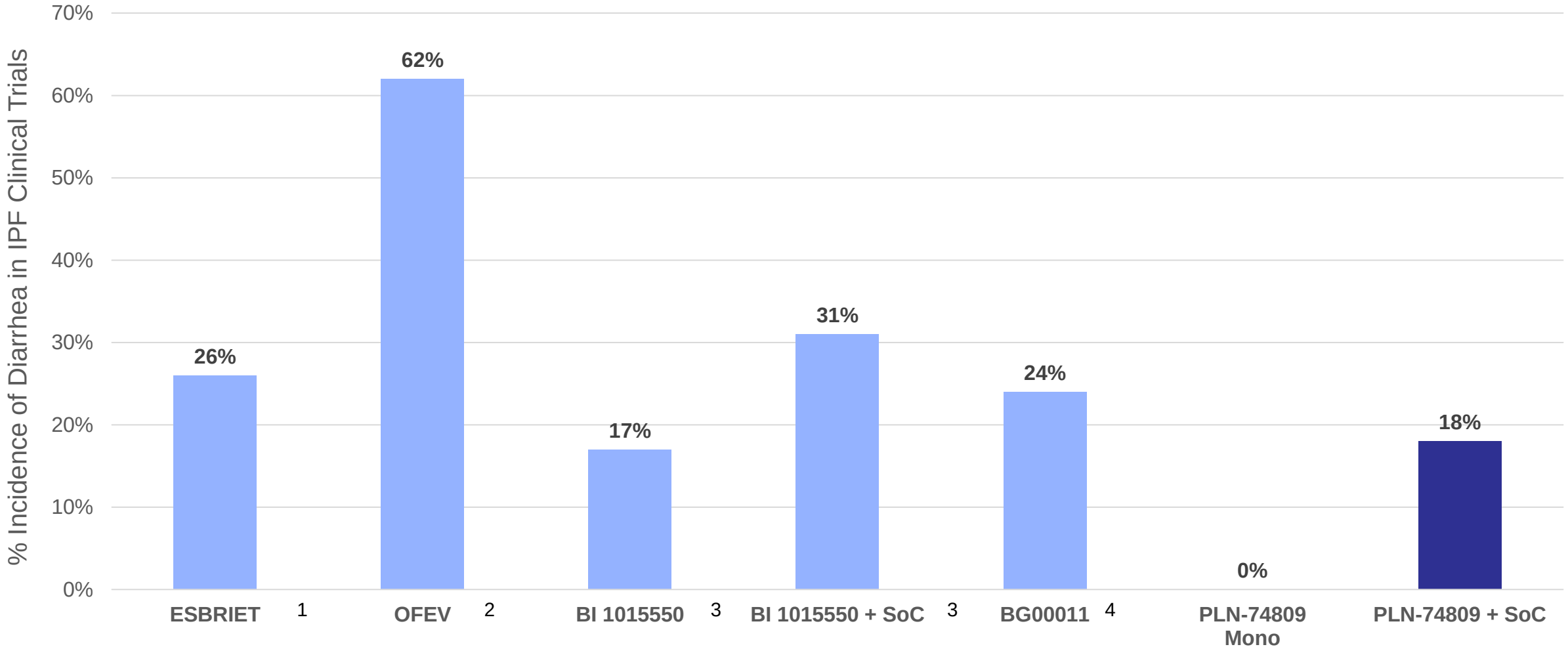
| AE, n (%) of Participants Reporting | PLN-74809 40mg (n=22) | PLN-74809 80mg (n=23) | PLN-74809 160mg (n=22) | PLN-74809 All (n=67) | Placebo (n=23) |
|---|---|---|---|---|---|
| **Most frequent TEAEs (≥ 10% in at least one arm)** | | | | | |
| Diarrhea | 2 ( 9.1) | 5 ( 21.7) | 5 ( 22.7) | 12 ( 17.9) | 1 ( 4.3) |
| Related to study drug | 1 (4.5) | 3 (13.0) | 4 (18.2) | 8 ( 11.9) | 1 ( 4.3) |

## All TEAEs of Diarrhea Occurred in Patients on Standard of Care

- 12 of 13 participants with diarrhea were taking nintedanib
- All but one event were mild to moderate in severity
- Diarrhea infrequently reported in PLN-74809 Phase 1 trials

TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Events. Adverse events coded using MedDRA version 24.0.
TEAE is defined as any AE starting (or worsening) on or after the date of first dose

# Incidence of Diarrhea in IPF Randomized Clinical Trials




[1]ESBRIET USPI, [2] OFEV USPI, [3] Richeldi et al, 2022, [4] Raghu et al, 2022

# No Treatment-Emergent SAEs Were Related to Study Drug

| Treatment Group | Preferred Term | Standard Toxicity Grade | Any alternative cause or confounding factors? | Action Taken | Outcome |
|---|---|---|---|---|---|
| **PLN-74809 40mg** | Acute respiratory failure | Grade 3 (Severe) | No | Dose not changed | Recovered / Resolved |
| | Pneumonia | Grade 2 (Moderate) | Removed carpet from home without a mask | Dose not changed | Recovered / Resolved |
| **PLN-74809 160mg** | Idiopathic pulmonary fibrosis | Grade 3 (Severe) | Underlying disease and atrial fibrillation | Not applicable - hospitalization | Not Recovered / Not Resolved |
| **PLN-74809 160 mg** | Atrial flutter | Grade 3 (Severe) | Underlying disease | Not applicable - hospitalization | Recovered / Resolved |
| **Placebo** | Bladder dilatation | Grade 2 (Moderate) | No | Dose not changed - Foley catheter placed | Recovered / Resolved with Sequelae |
| **Placebo** | Respiratory failure | Grade 3 (Severe) | Coronary artery disease with triple vessel disease | Not applicable - early termination from the study | Recovered / Resolved with sequelae |

Adverse events coded using MedDRA version 24.0

# Safety Evaluation – Conclusions

- PLN-74809 was well tolerated with no dose relationship for adverse events
- No deaths or treatment related SAEs
- No participants discontinued PLN-74809 due to TEAE
- Most frequent TEAE seen was diarrhea, but only seen in patients on standard of care

**Éric Lefebvre, M.D.**
Chief Medical Officer

# Pharmacokinetic Analyses: A Secondary Endpoint

# Pharmacokinetics – Conclusions

- Based on sparse sampling, overall PLN-74809 pharmacokinetics and % unbound in IPF consistent with that of previous studies
- Concentrations in IPF participants increased approximately proportionally with dose
- Overall % unbound was ~0.3 to 0.5%
- Full PK curve will be predicted using population PK model to project $AUC_{0\_24}$ and $C_{max}$

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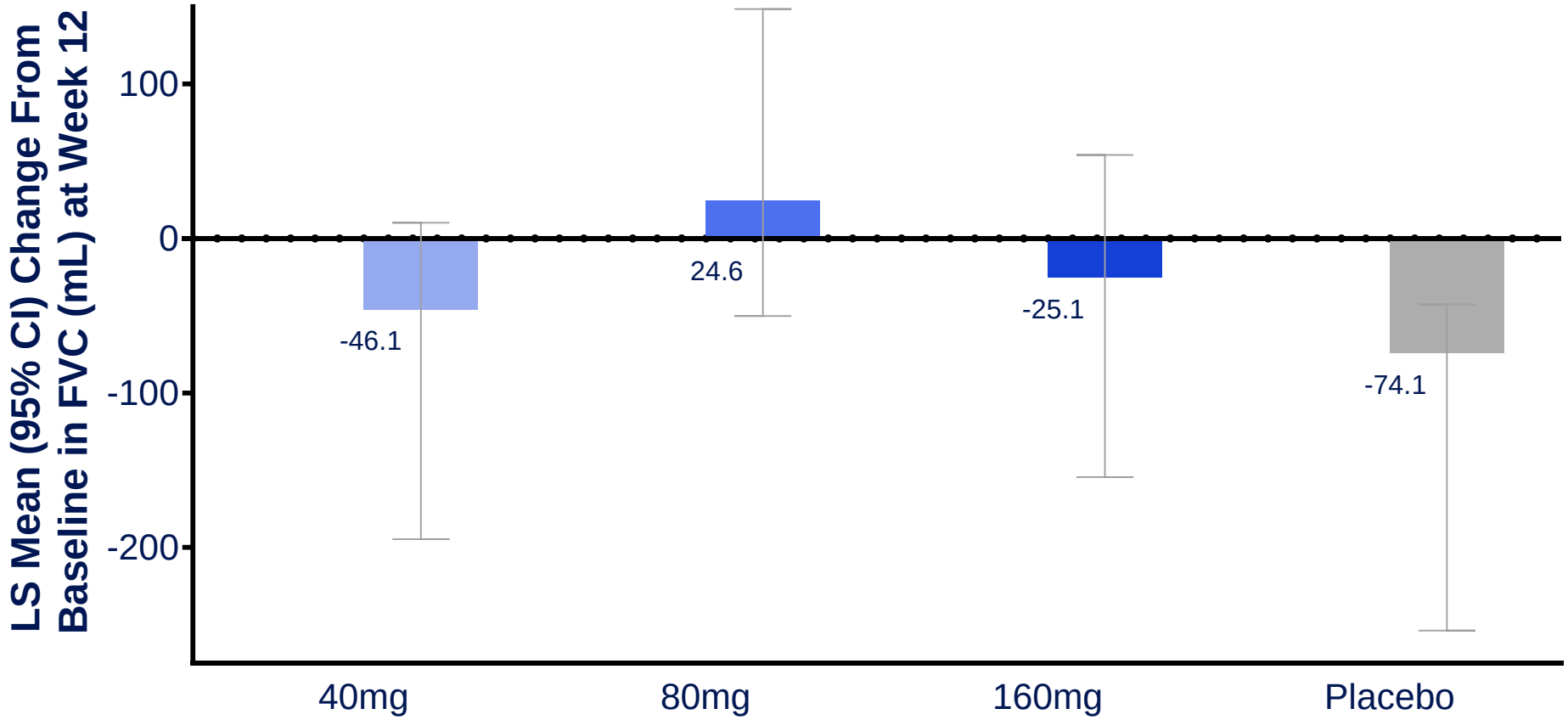
**Greg Cosgrove, M.D., FCCP**
Vice President,
Clinical Development

# Analyses of FVC: An Exploratory Endpoint

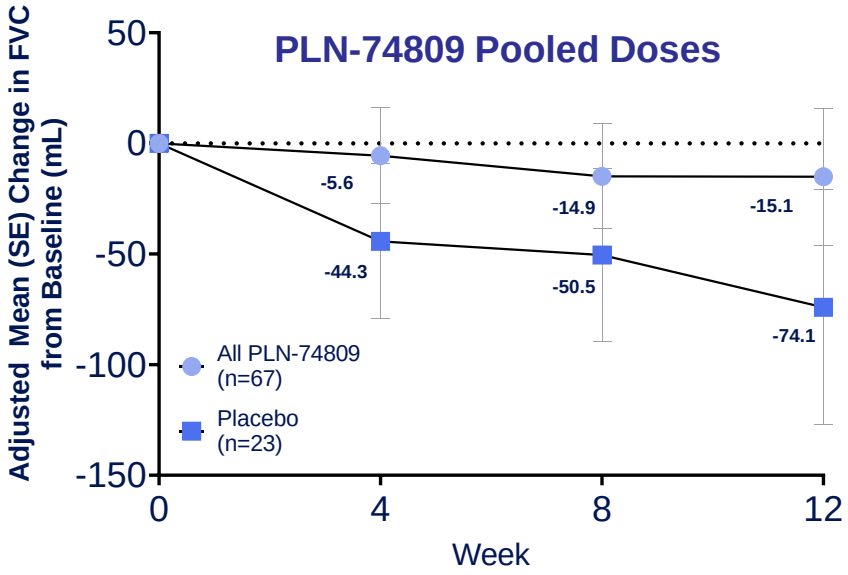
# Change in FVC from Baseline to Week 12
## MMRM Analysis - ITT Population

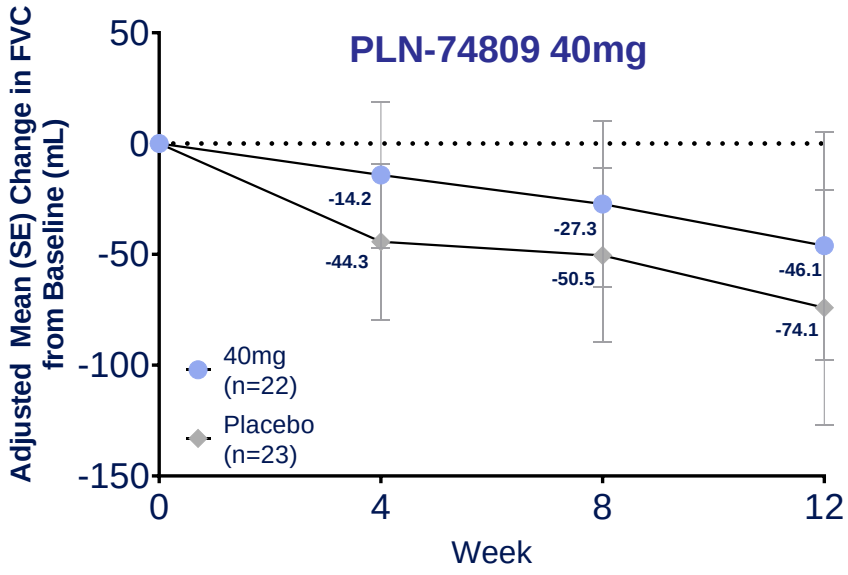


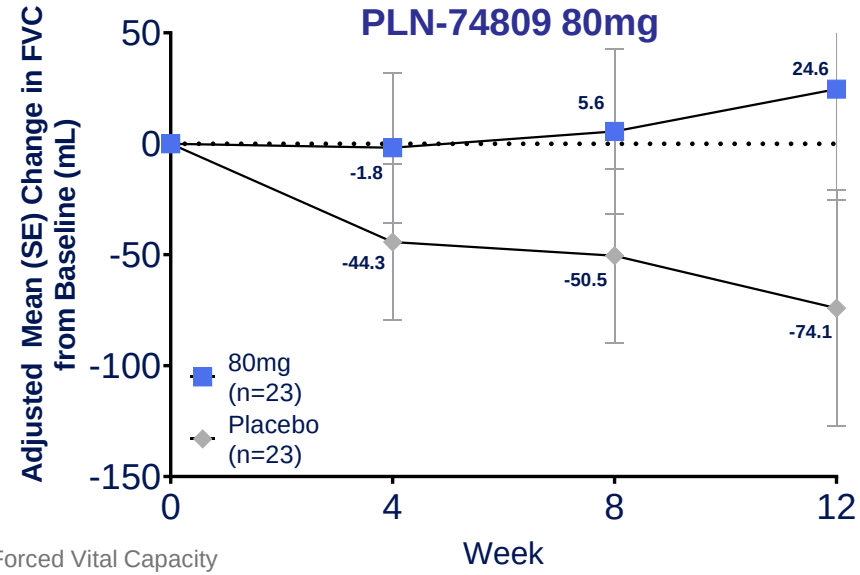

Change from baseline analyzed using a mixed model for repeated measures with terms for treatment group, SOC (Y/N), visit, baseline value, and treatment-by-visit interaction. An unstructured covariance (UN) structure was used.

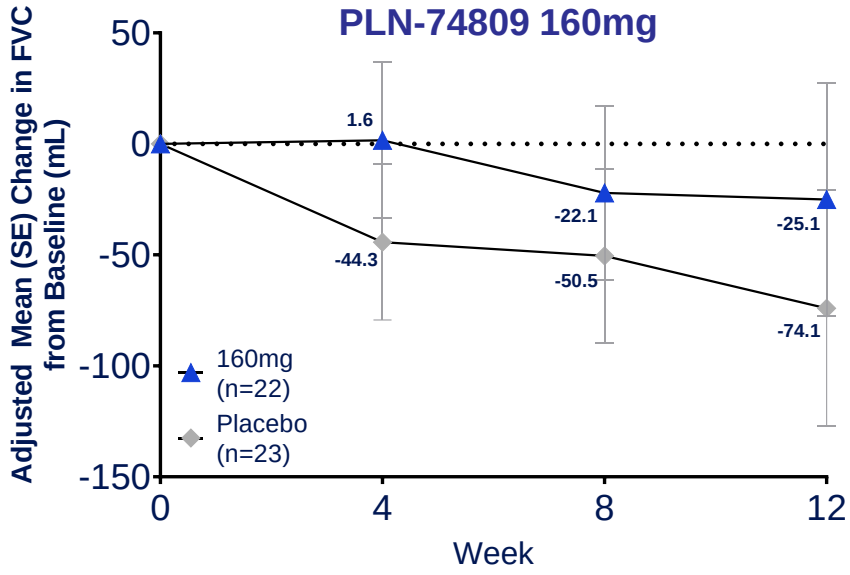
# Change in FVC over 12 Weeks in INTEGRIS-IPF

## MMRM Analysis - ITT Population



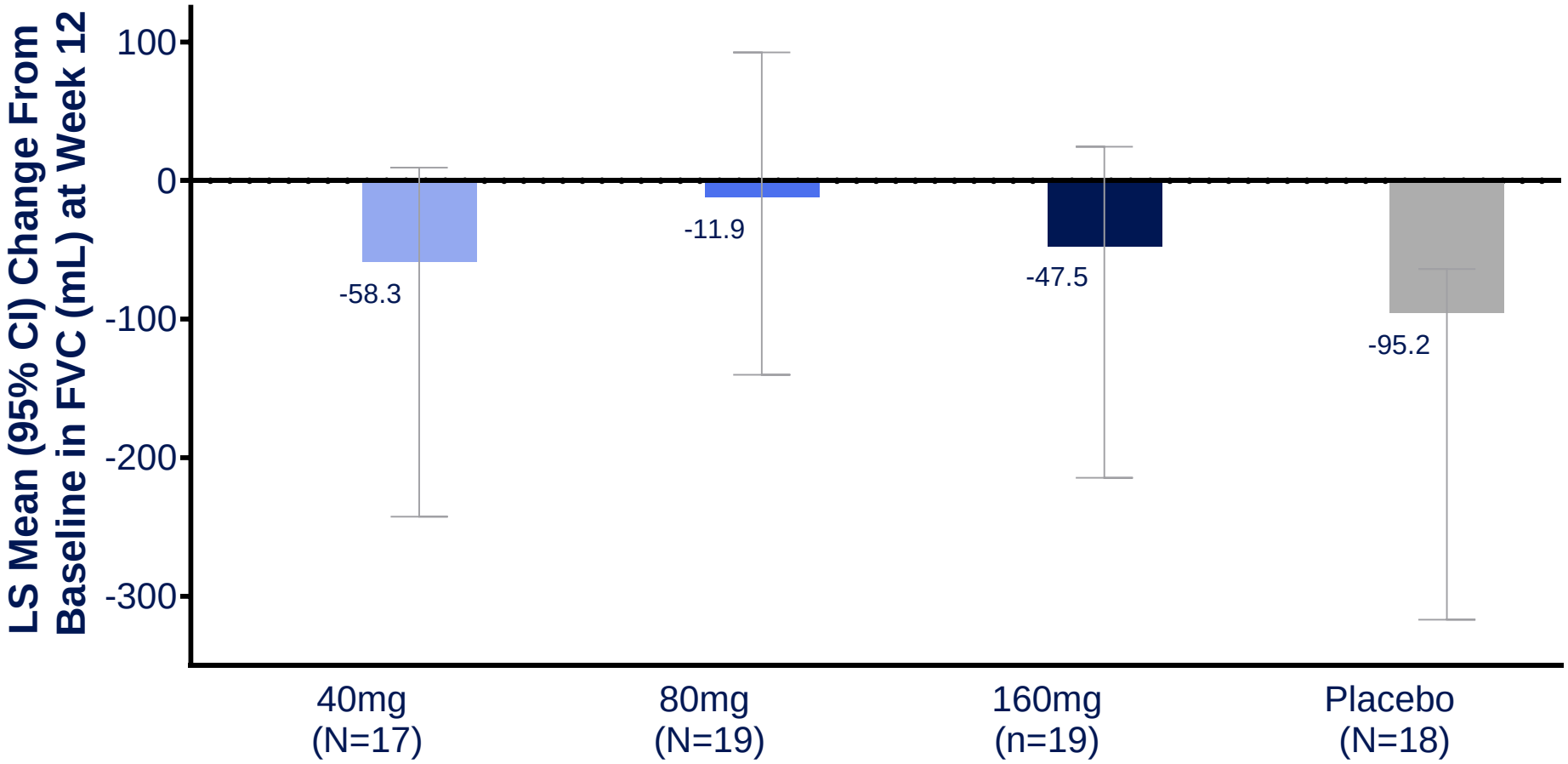




FVC = Forced Vital Capacity
MMRM = Mixed Model Repeat Measures.

# Change in FVC from Baseline to Week 12 in On SoC Subgroup

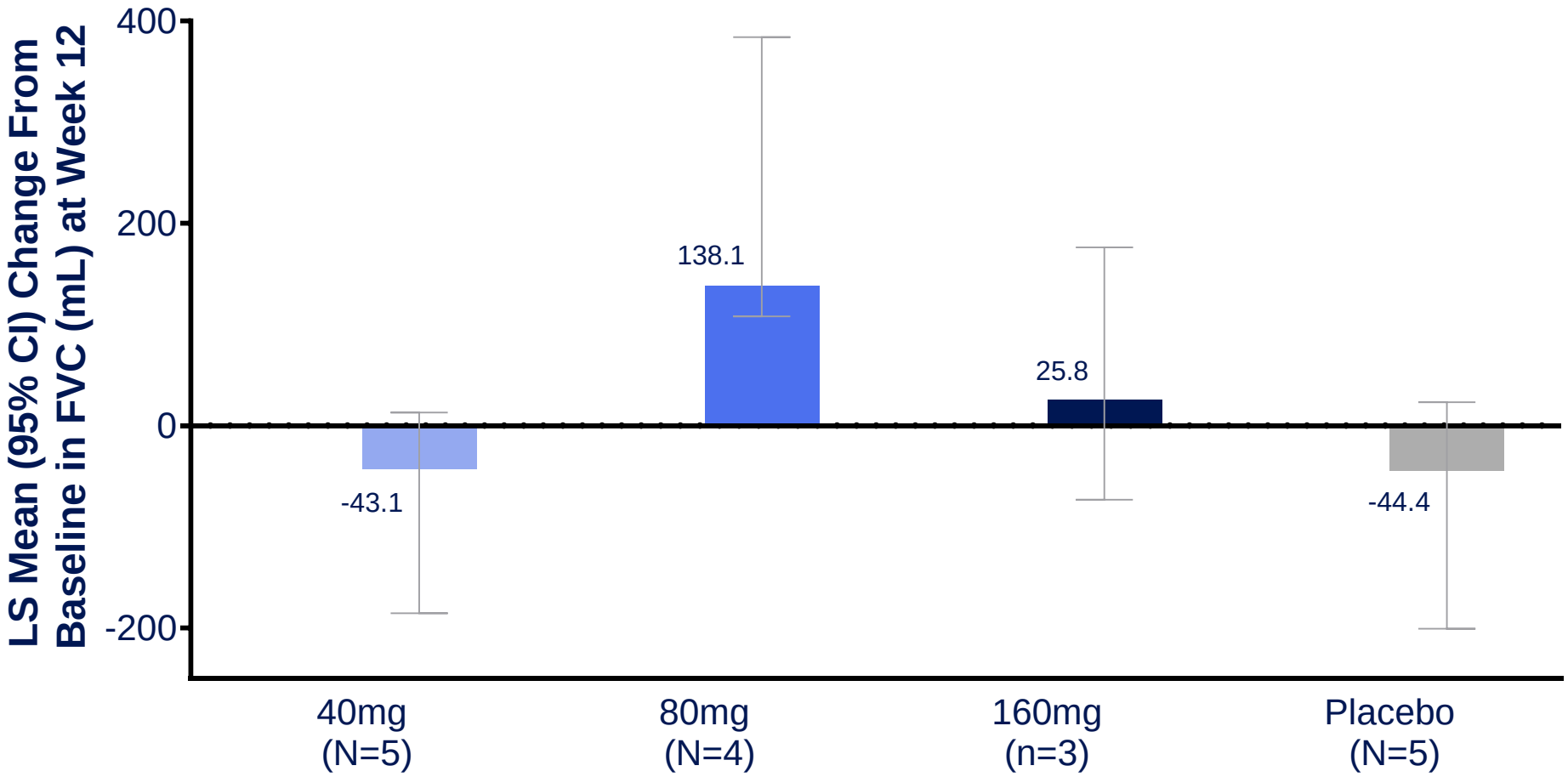
## MMRM Analysis - ITT Population




Change from baseline analyzed using a mixed model for repeated measures with terms for treatment group, SOC (Y/N), visit, baseline value, and treatment-by-visit interaction. An unstructured covariance (UN) structure was used. FVC = Forced Vital Capacity

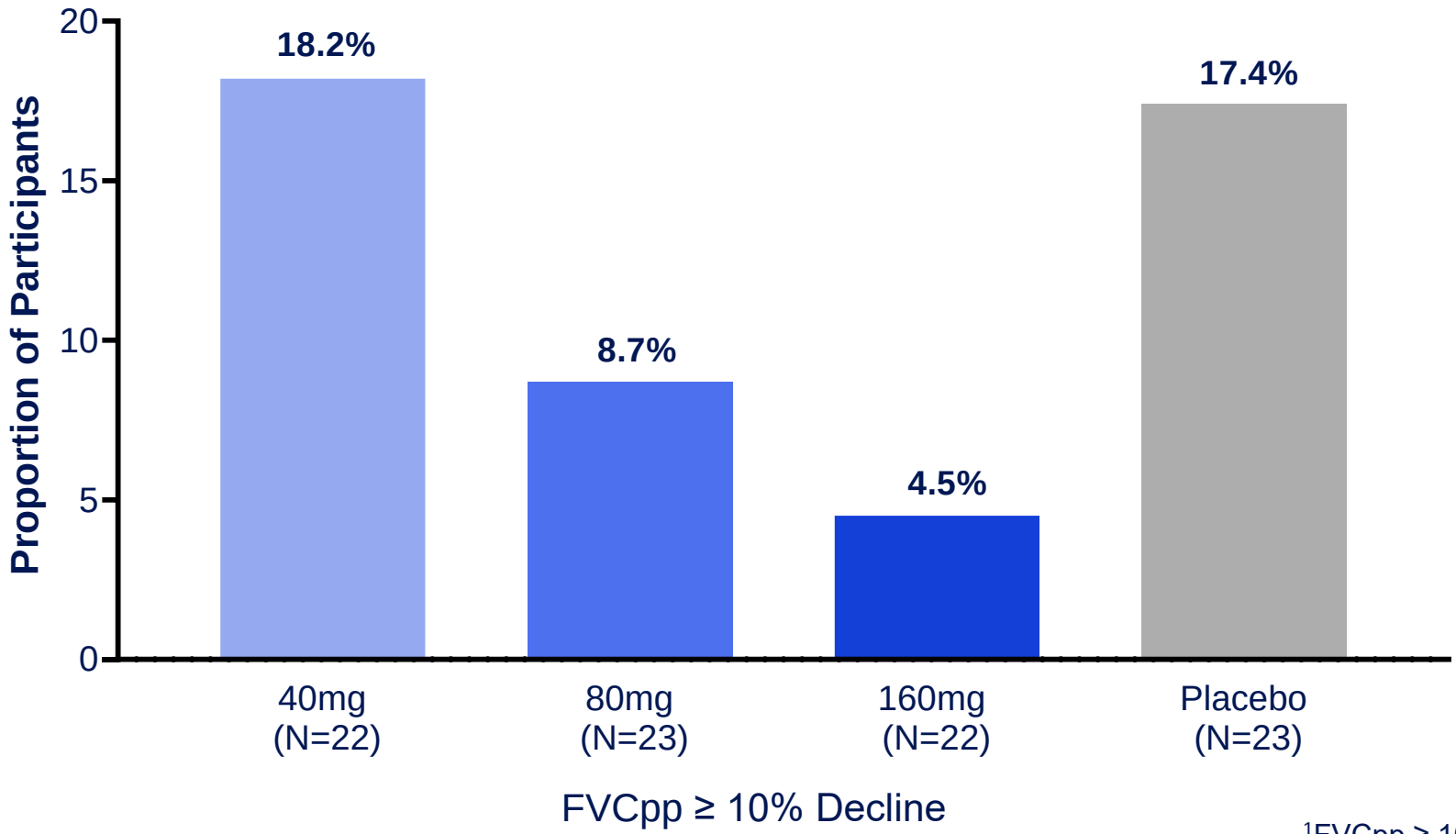
# Change in FVC from Baseline to Week 12 in Not on SoC Subgroup

## MMRM Analysis - ITT Population




Change from baseline analyzed using a mixed model for repeated measures with terms for treatment group, SOC (Y/N), visit, baseline value, and treatment-by-visit interaction. An unstructured covariance (UN) structure was used. FVC = Forced Vital Capacity

# Proportion of Participants with FVCpp Decline ≥10% - ITT Population




[1]FVCpp ≥ 10%: strong predictor of disease progression and mortality

FVCpp = Forced vital capacity, percent predicted

[1]Ann Am Thorac Soc. 2017 Sep;14(9):1395-1402.

# Forced Vital Capacity Evaluation – Conclusions

**PLN-74809-treated participants experienced a benefit in FVC change from Baseline to Week 12 (-15.1 mL for pooled PLN-74809 group) compared to those on placebo (-74.1 mL)[1]**

**PLN-74809 treatment effect was evident with and without use of standard of care**

**PLN-74809 80 mg dose demonstrated an improvement in FVC (+24.6 mL)**

**Dose-dependent reduction in proportion of participants with FVCpp decline of ≥10%**

[1] MMRM analysis ITT population

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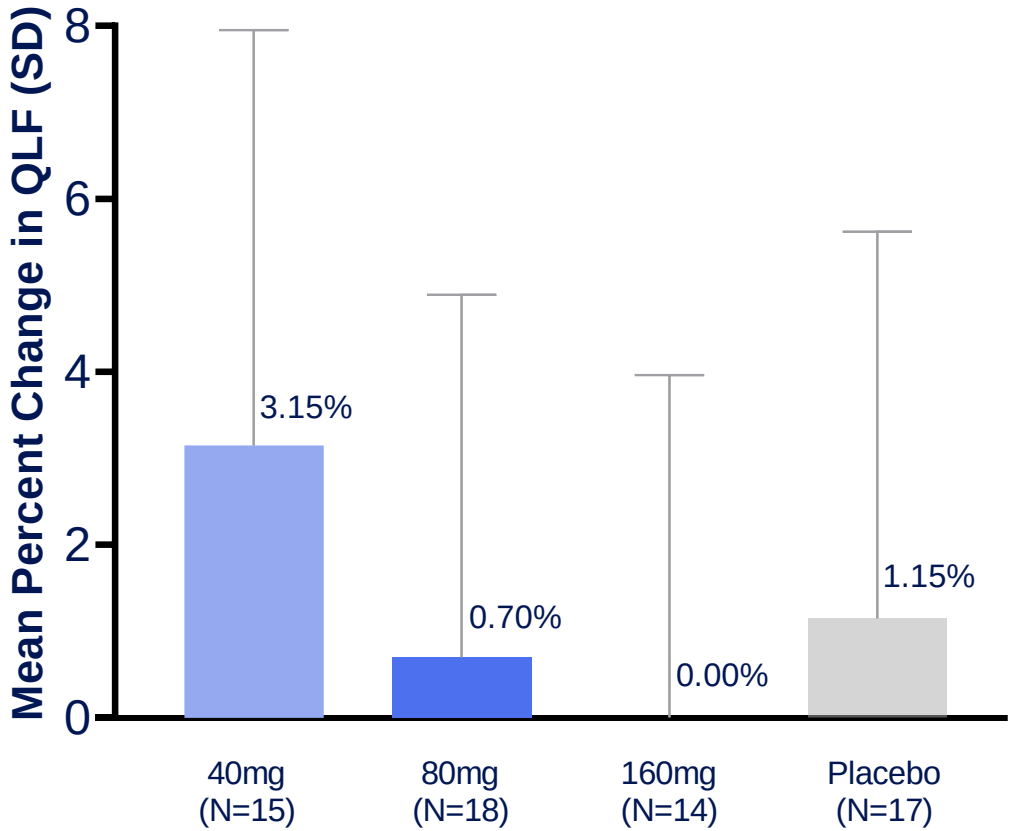
# Quantitative Lung Fibrosis (QLF) imaging

High-resolution Computed Tomography (HRCT) based Quantitative Lung Fibrosis (QLF) imaging

# Mean Percent Change in QLF Extent From Baseline to Week 12

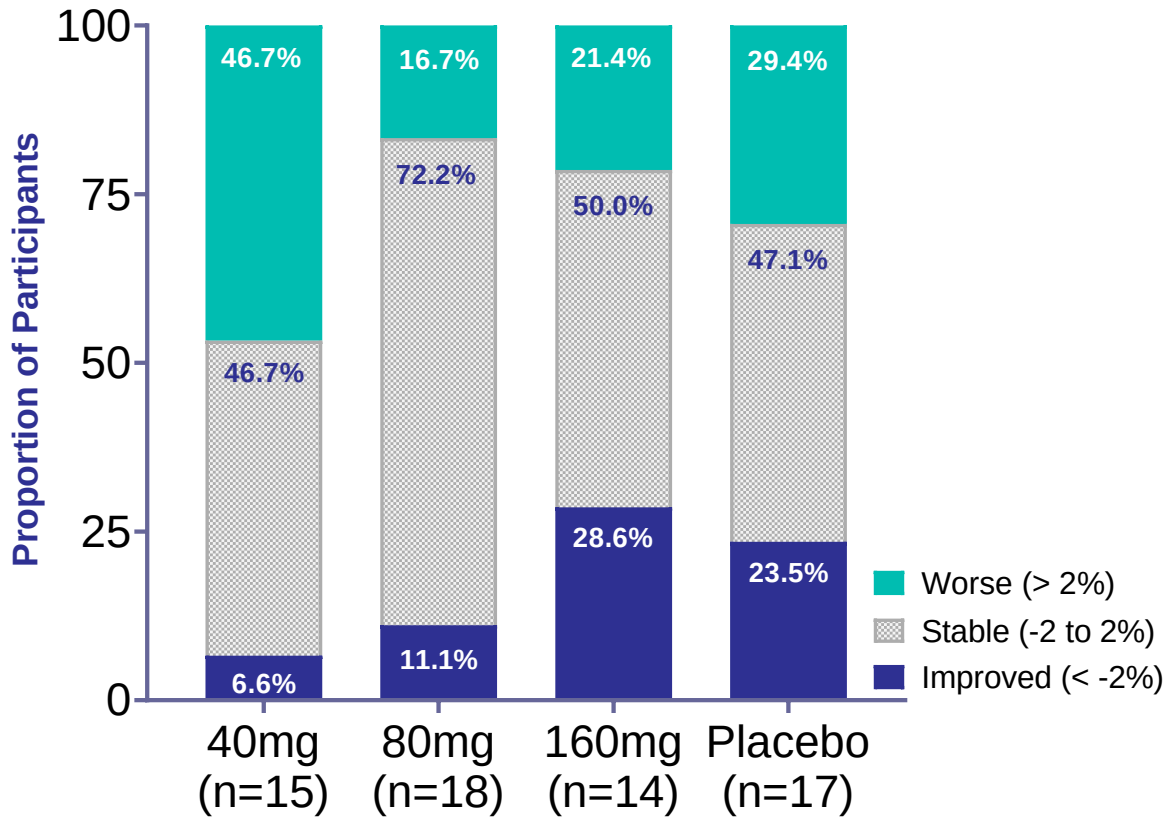
## CT Protocol Population within Screening Window



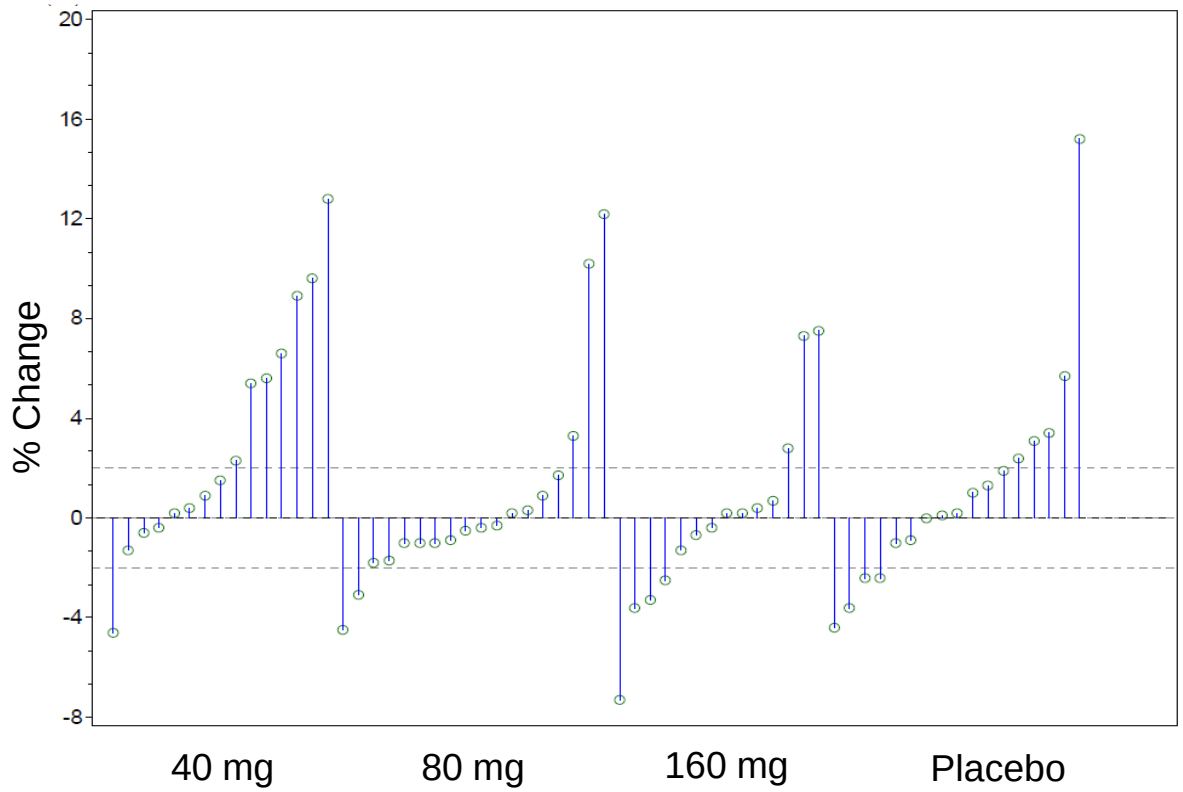

QLF = quantitative lung fibrosis

# Mean Percent Change in QLF Extent From Baseline to Week 12 CT Protocol Population

## Proportion of Participants with "Improved," "Stable" or "Worse" QLF Score at 12 Weeks




## Drop Line Plot of Change in Individual QLF Scores at Week 12 for PLN-74809 and Placebo Groups




QLF = quantitative lung fibrosis

# Quantitative Lung Fibrosis Evaluation – Conclusions

**Dose-dependent antifibrotic effect as evidenced by QLF Imaging**

**No progression in 160 mg group at Week 12 based on mean change from baseline**

**Higher proportion of participants remained stable or improved in the 80 mg and 160 mg groups versus placebo**

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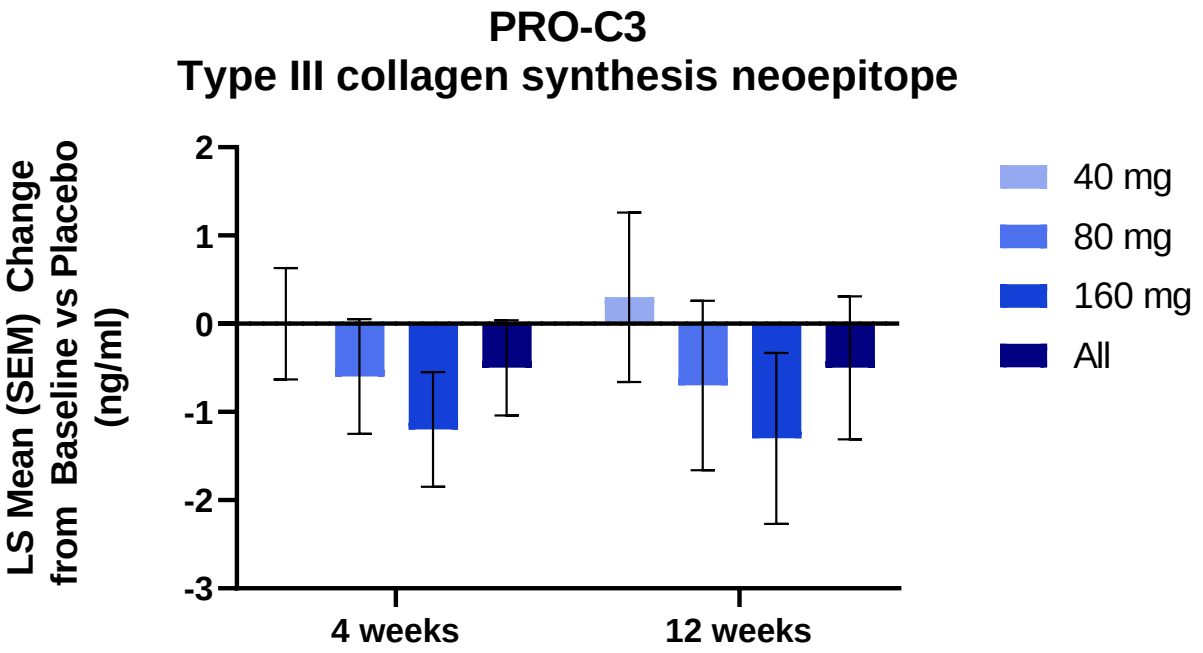
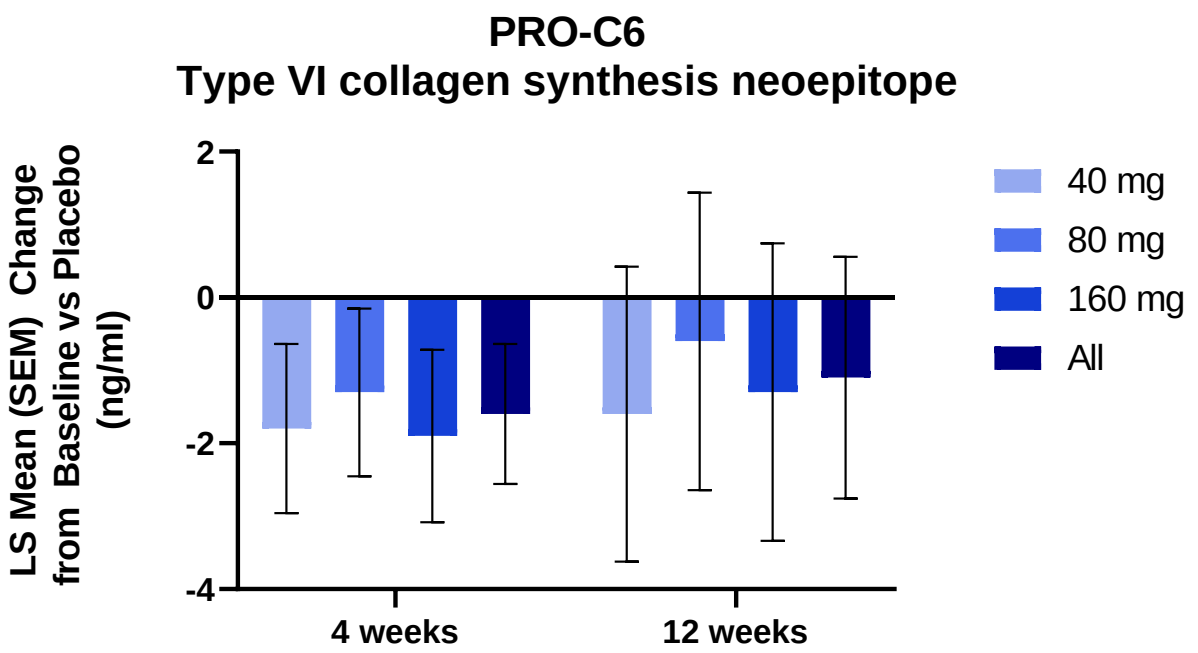
**Scott Turner, Ph.D.**
Senior Vice President,
Research

# Analyses of Serum Biomarkers

# Serum Biomarkers of Collagen Synthesis were Reduced in Participants Receiving PLN-74809 (Change from Baseline after 4 and 12 Weeks vs Placebo)




**PRO-C3 and PRO-C6, serum biomarkers of type III and VI collagen synthesis, respectively, have previously been shown to be elevated in patients with IPF and associated with progressive disease (Organ et al Respir Res 2019)**

Change from baseline analyzed using a mixed model for repeated measures with terms for treatment group, visit, baseline value, and treatment-by-visit interaction.

LS = Least Squares; SE = Standard Error

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# KOL Perspective

# Conclusion and Next Steps

- **Results from the INTEGRIS-IPF trial exceeded our expectations showing a favorable safety and tolerability profile and a treatment effect on FVC and QLF**

  **Importantly, the fact the treatment effect was also observed on top of standard of care therapy gives us confidence that PLN-74809 has the potential to advance the treatment of IPF**

- **Pliant recently completed enrollment in the 320 mg cohort of the INTEGRIS-IPF Phase 2a trial. Interim data from this trial is anticipated in early 2023**

- **Pliant intends on sharing today's data with regulatory authorities in the near term to discuss the late-stage development plan for PLN-74809**

# Questions