



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

JULY 11, 2022

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Today's Speakers



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



Éric Lefebvre, M.D.
Chief Medical Officer



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



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



Toby Maher, M.D., Ph.D.
Director of ILD,
Keck School of Medicine,
USC



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

Welcome and Opening Remarks

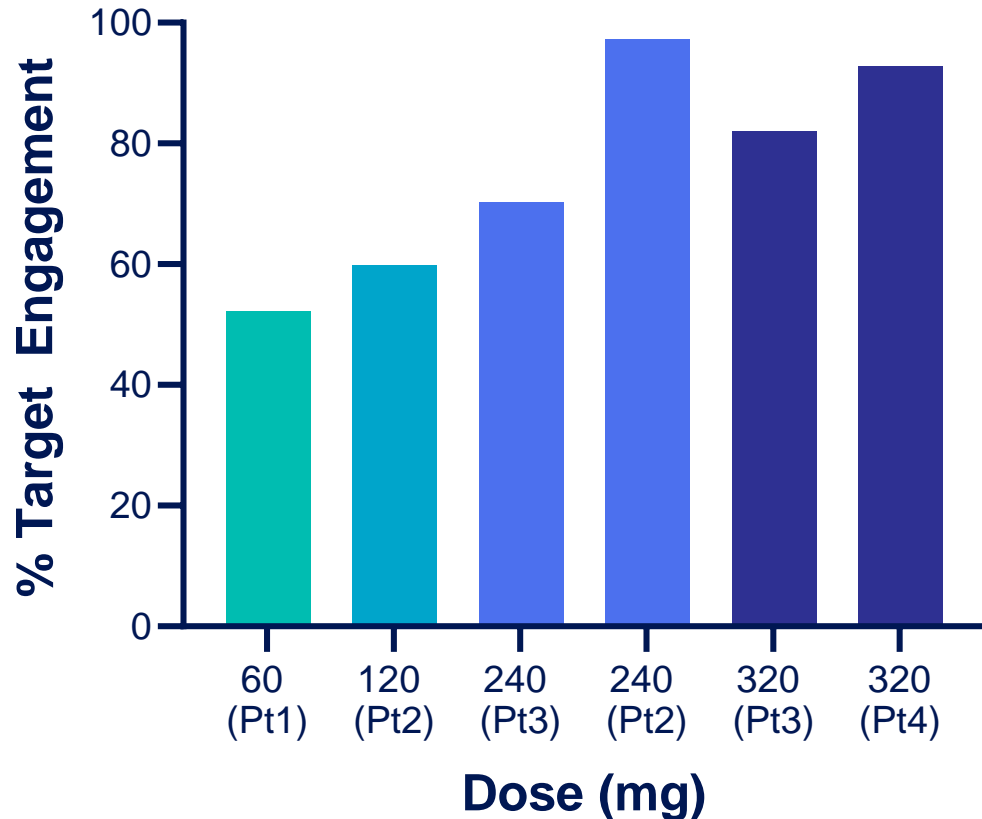


Éric Lefebvre, M.D.
Chief Medical Officer

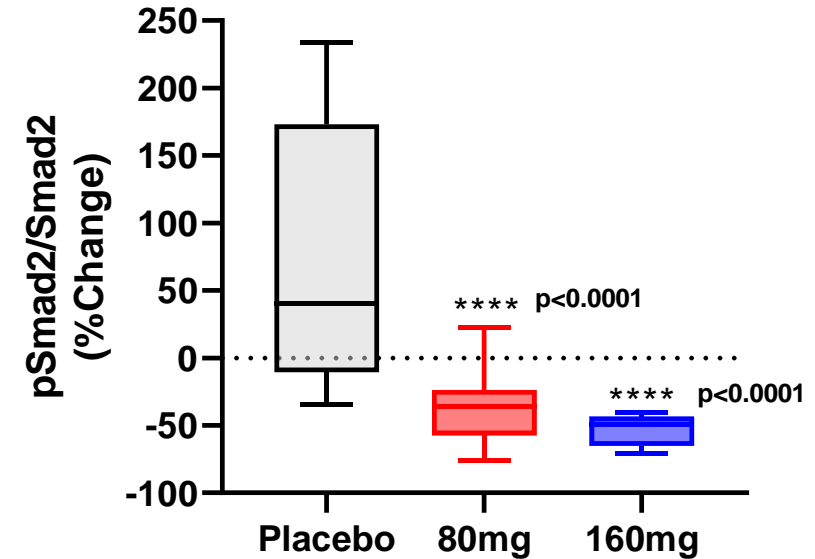
Executive Summary

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

Target Engagement After a Single Dose of PLN-74809



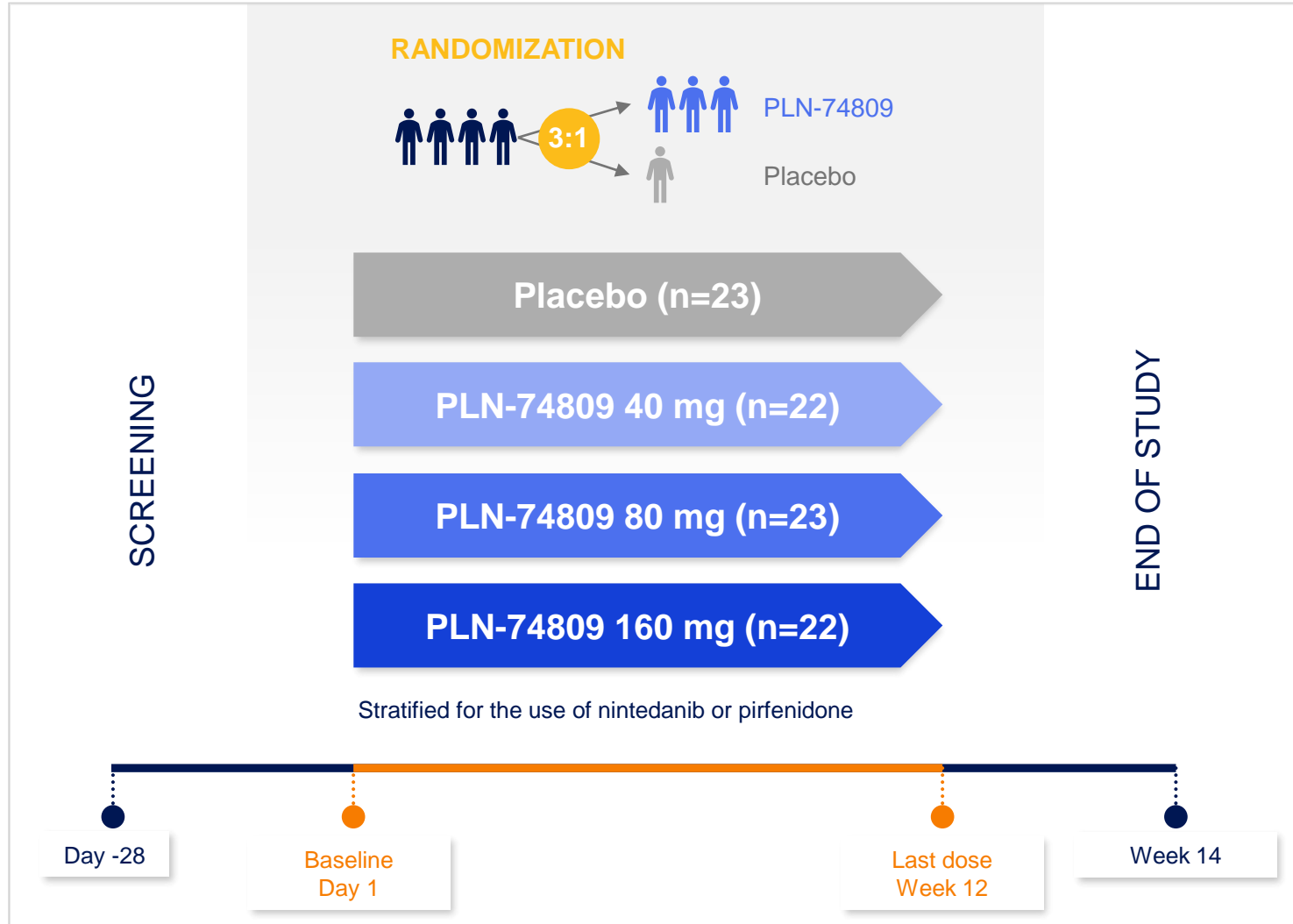
Alveolar pSmad2/Smad2 Percentage Change from Baseline at 24 Hours



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 $\geq 10\%$, a well-established predictor of death and disease progression in IPF

Other Exploratory Endpoints

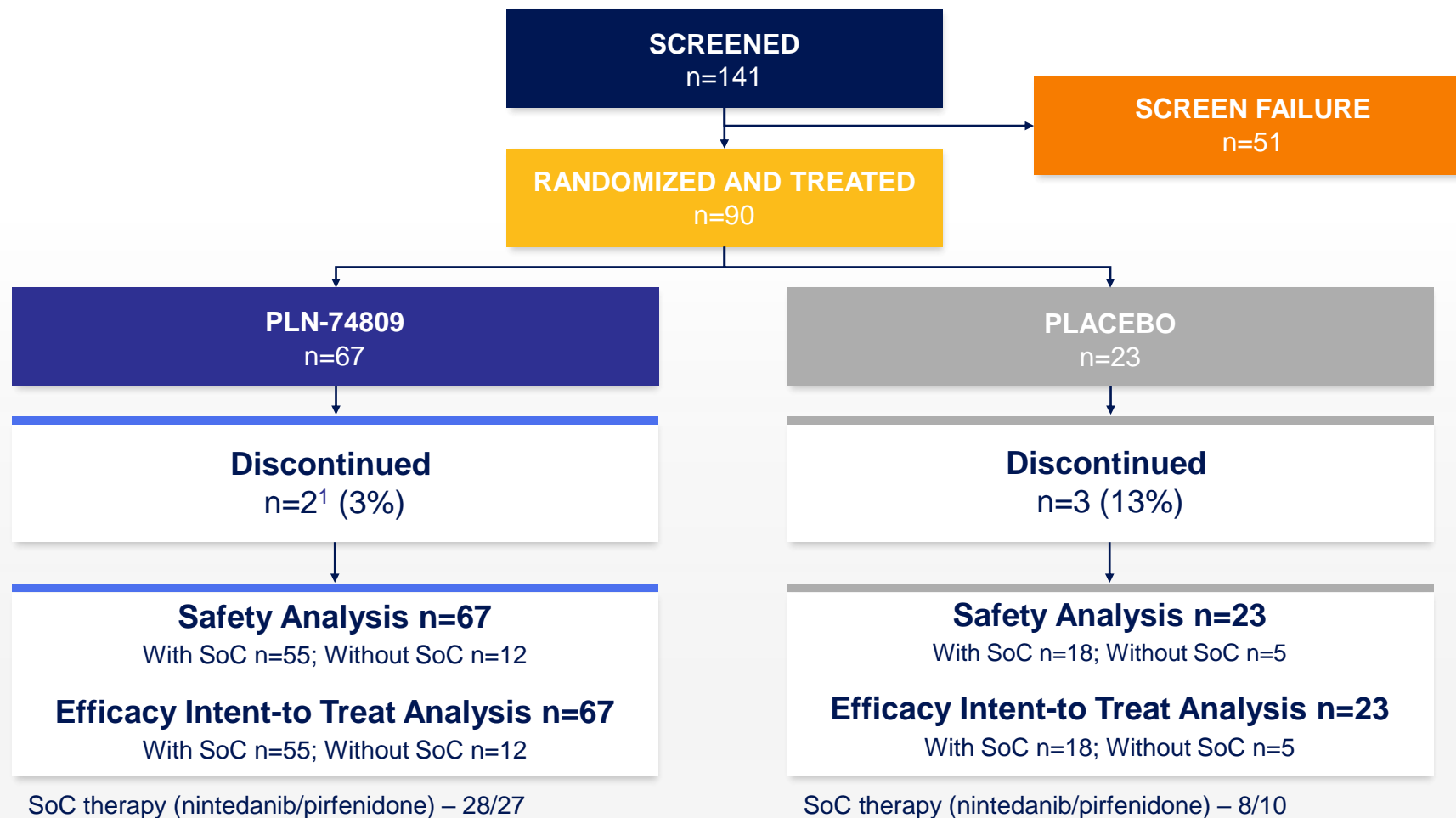
- Dose-dependent antifibrotic effect seen on QLF Imaging, with no progression in 160 mg group at Week 12
- PLN-74809 decreased serum biomarkers of collagen synthesis (PRO-C3 and PRO-C6) relative to placebo



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/m²), 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.

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.

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

AE, n (%) of Participants Reporting	Without Background SoC (n=17)		With Background SoC (n=73)	
	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

Most Frequent TEAEs – Any Causality

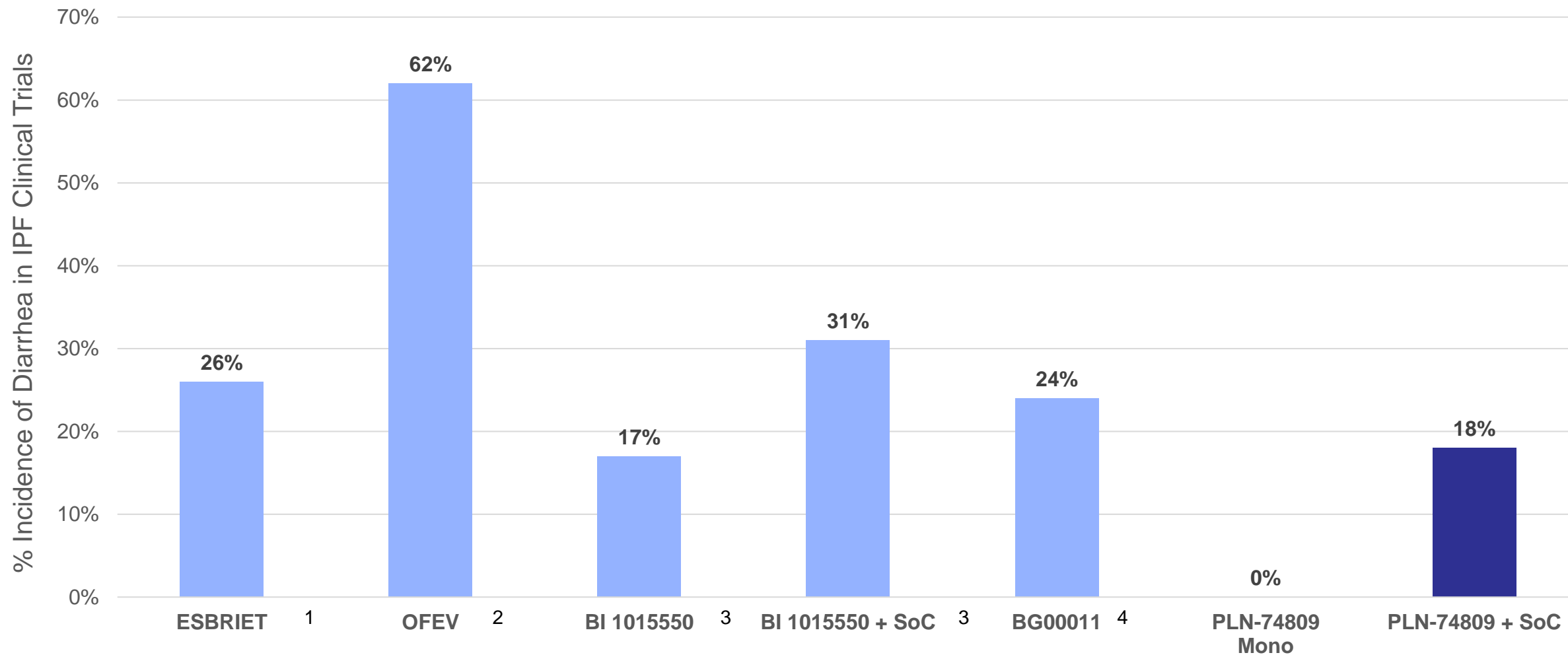
AE, n (%) of Participants Reporting	PLN-74809 40mg (n=22)	PLN-74809 80mg (n=23)	PLN-74809 160mg (n=22)	PLN-74809 All (n=67)	Placebo (n=23)
Most frequent TEAEs (≥ 10% in at least one arm)					
Diarrhea	2 (9.1)	5 (21.7)	5 (22.7)	12 (17.9)	1 (4.3)
Related to study drug	1 (4.5)	3 (13.0)	4 (18.2)	8 (11.9)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



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

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

Pharmacokinetic Analyses: A Secondary Endpoint



Éric Lefebvre, M.D.
Chief Medical Officer

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}

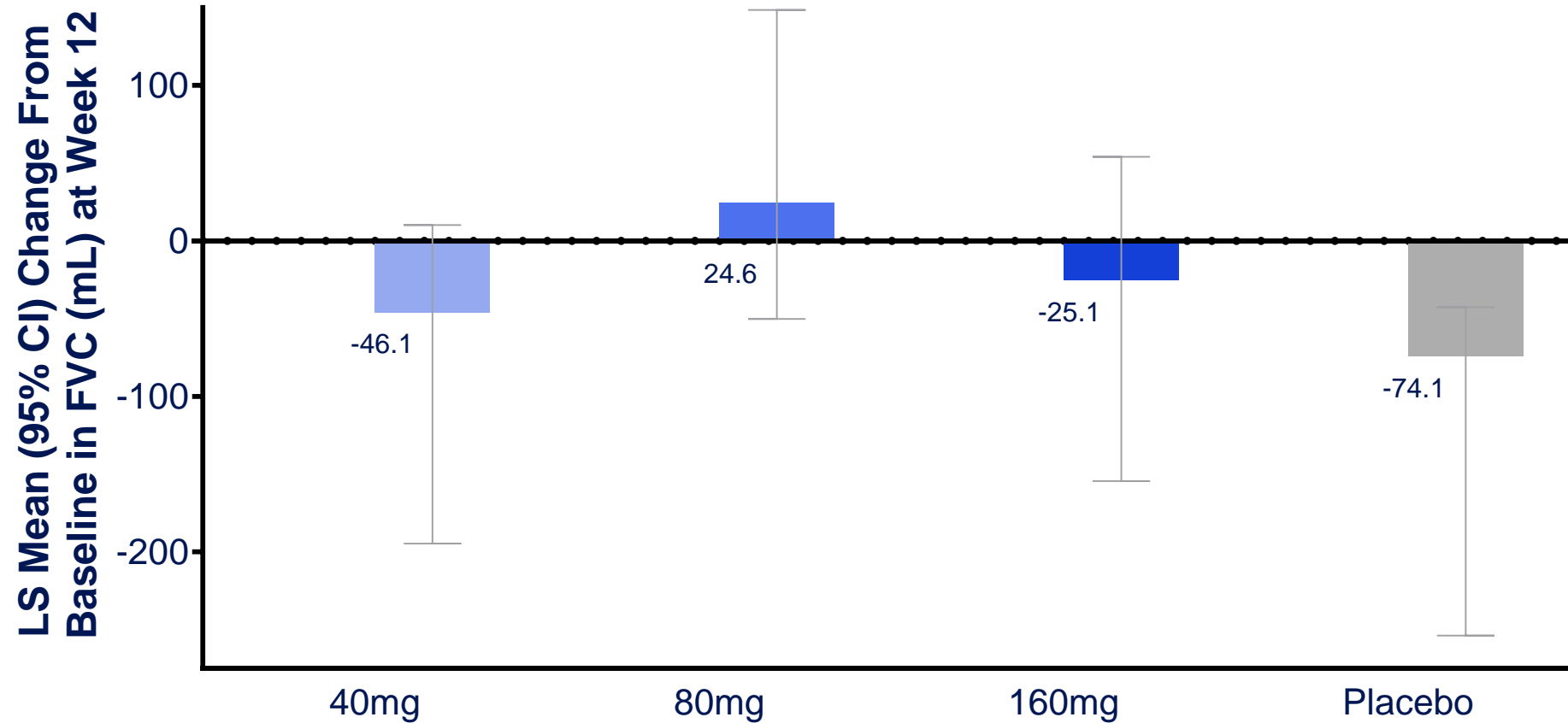
Analyses of FVC: An Exploratory Endpoint



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

Change in FVC from Baseline to Week 12

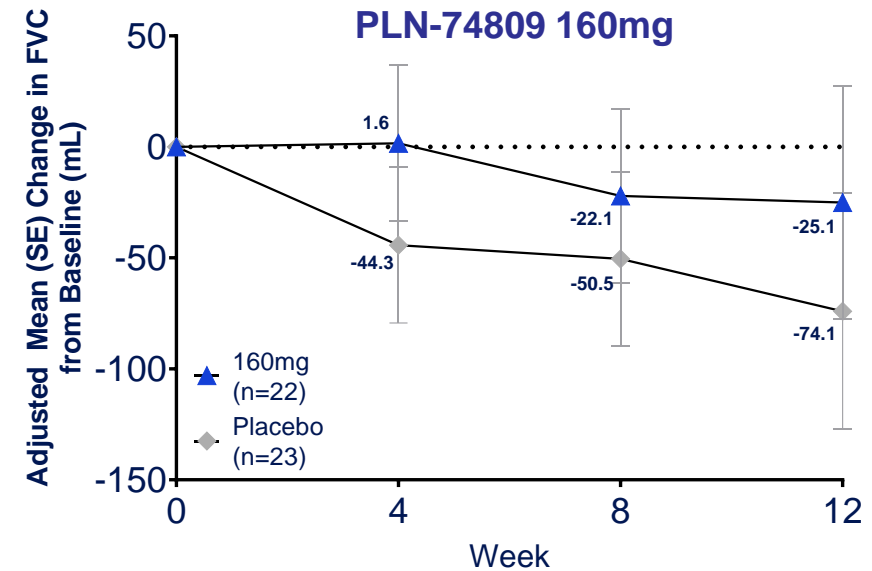
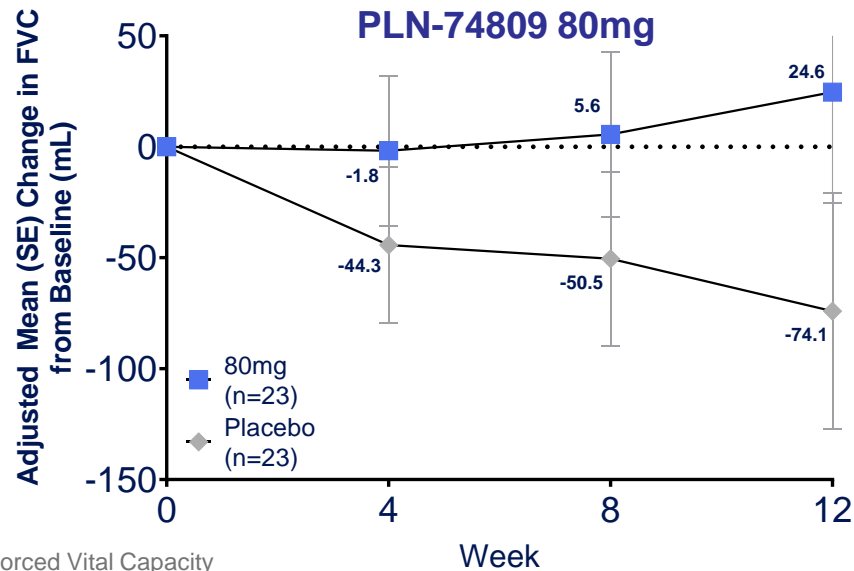
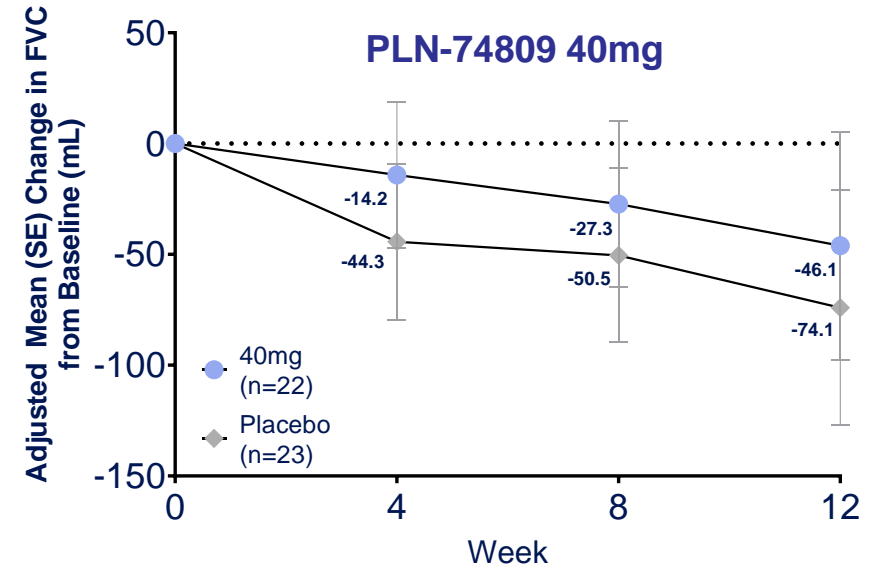
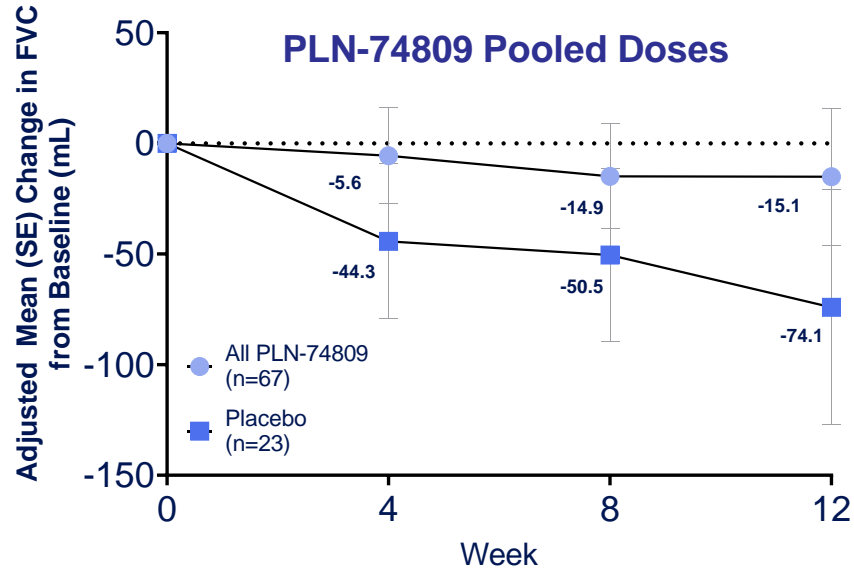
MMRM Analysis - ITT Population



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

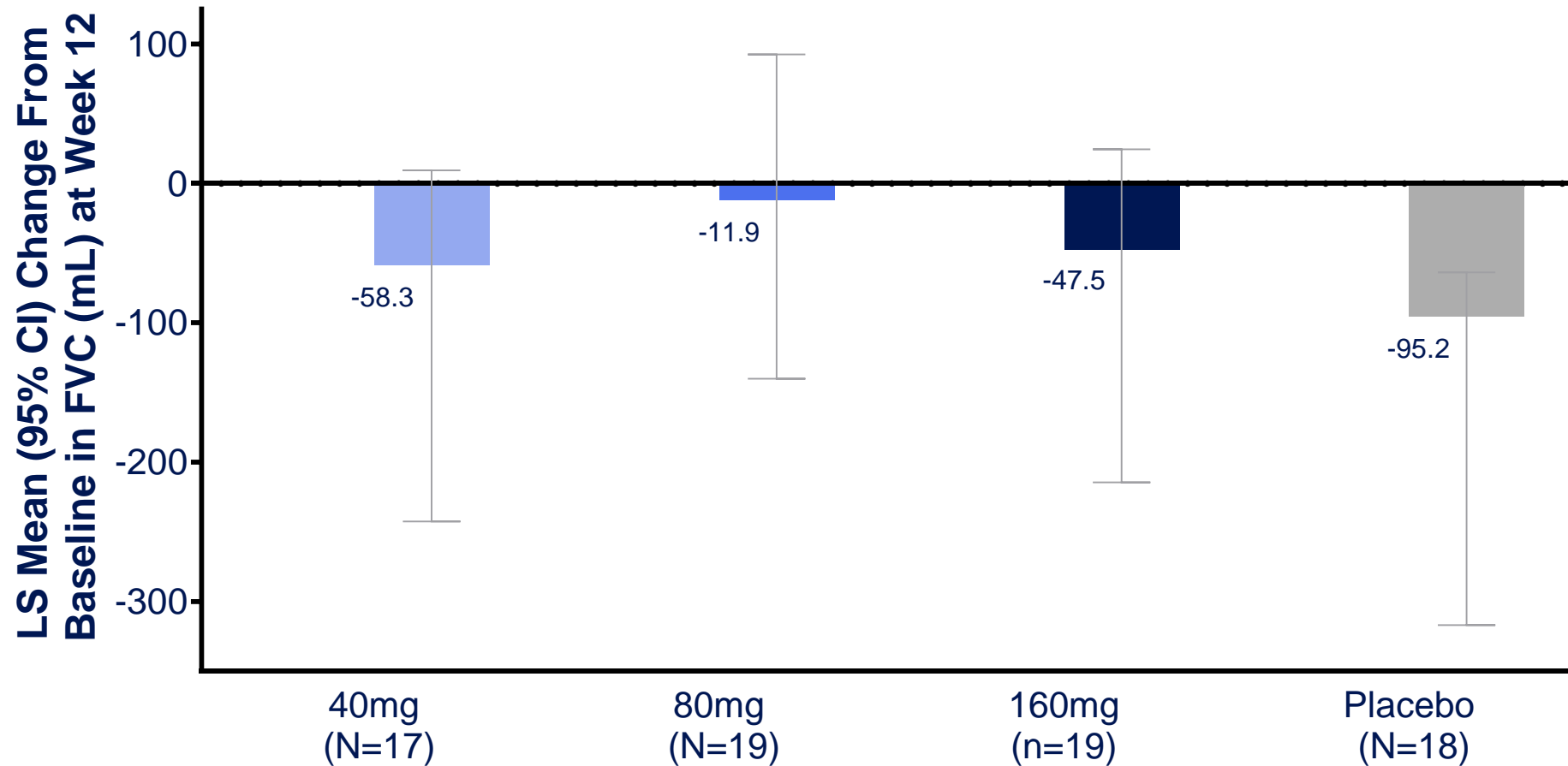
MMRM Analysis - ITT Population



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

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

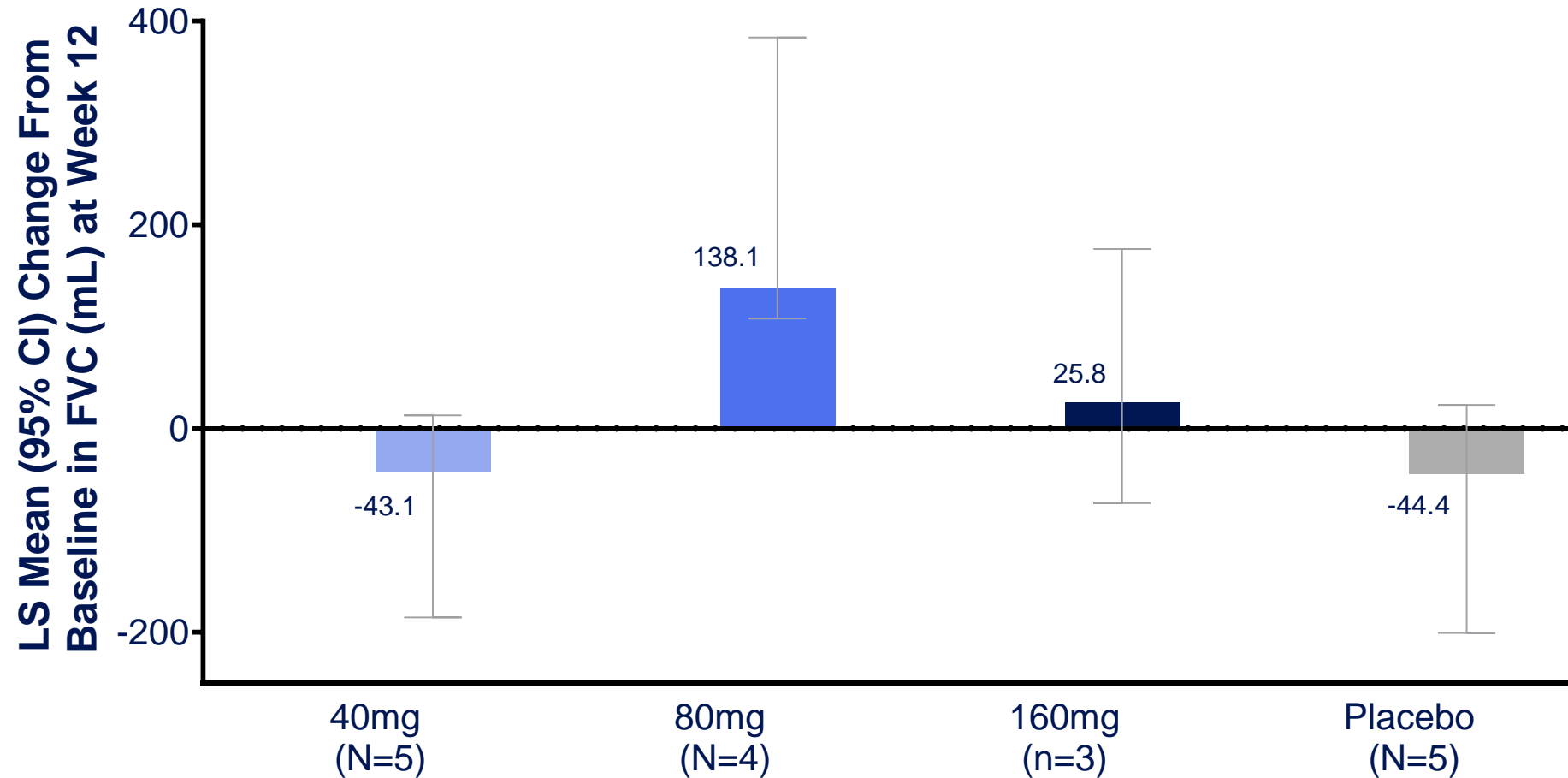
MMRM Analysis - ITT Population



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

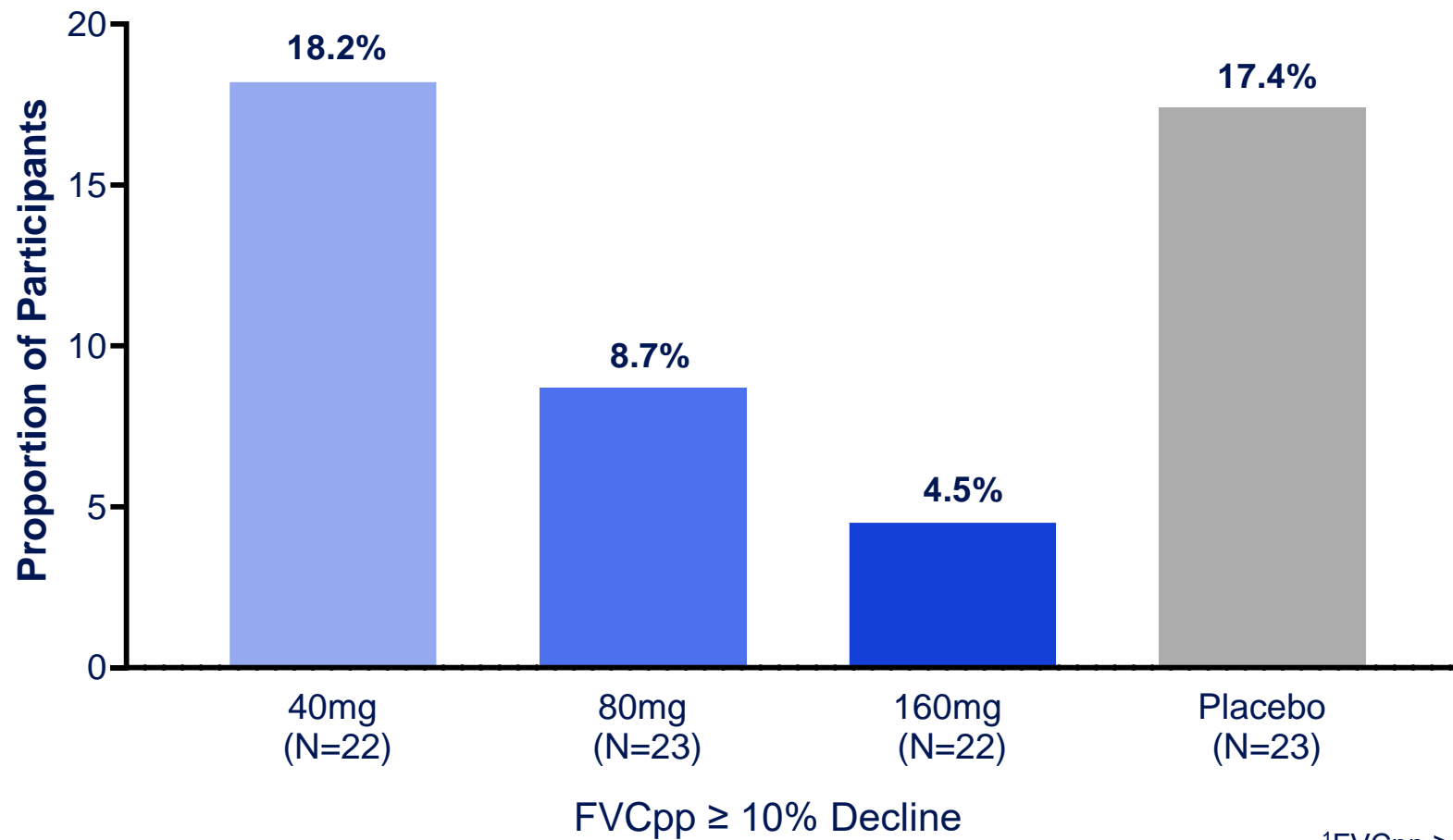
Change in FVC from Baseline to Week 12 in Not on SoC Subgroup

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 $\geq 10\%$ - ITT Population



¹FVCpp $\geq 10\%$: strong predictor of disease progression and mortality

FVCpp = Forced vital capacity, percent predicted
¹Ann 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 $\geq 10\%$

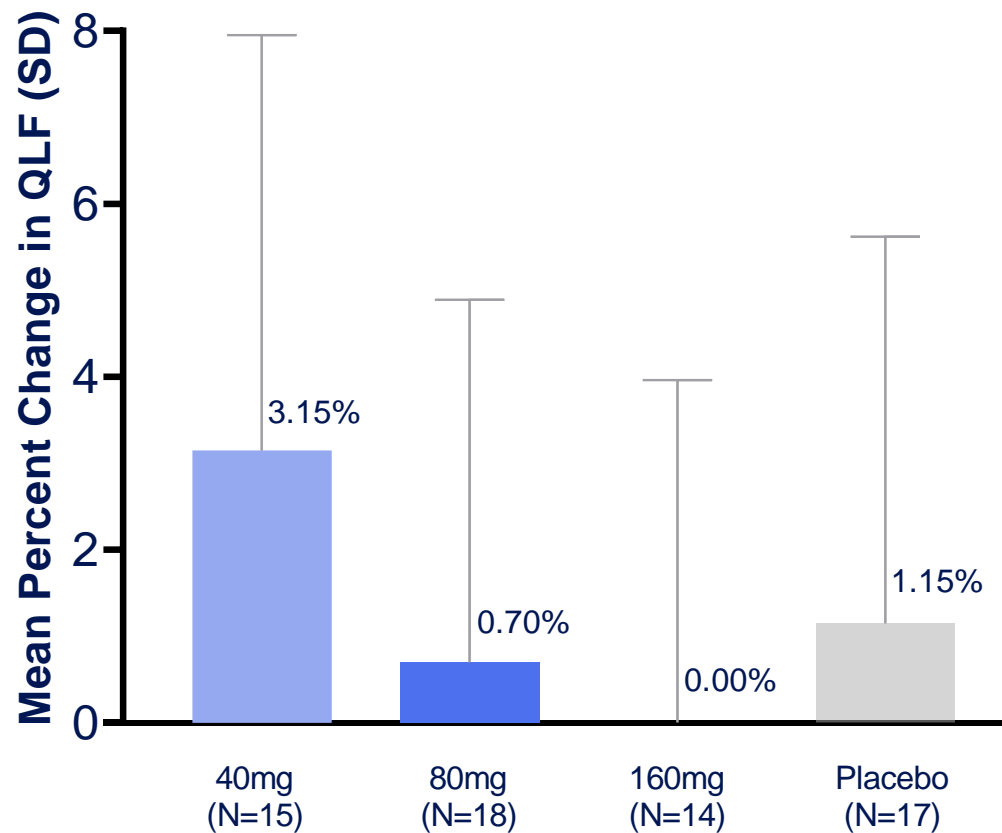
¹ MMRM analysis ITT population

Quantitative Lung Fibrosis (QLF) imaging

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

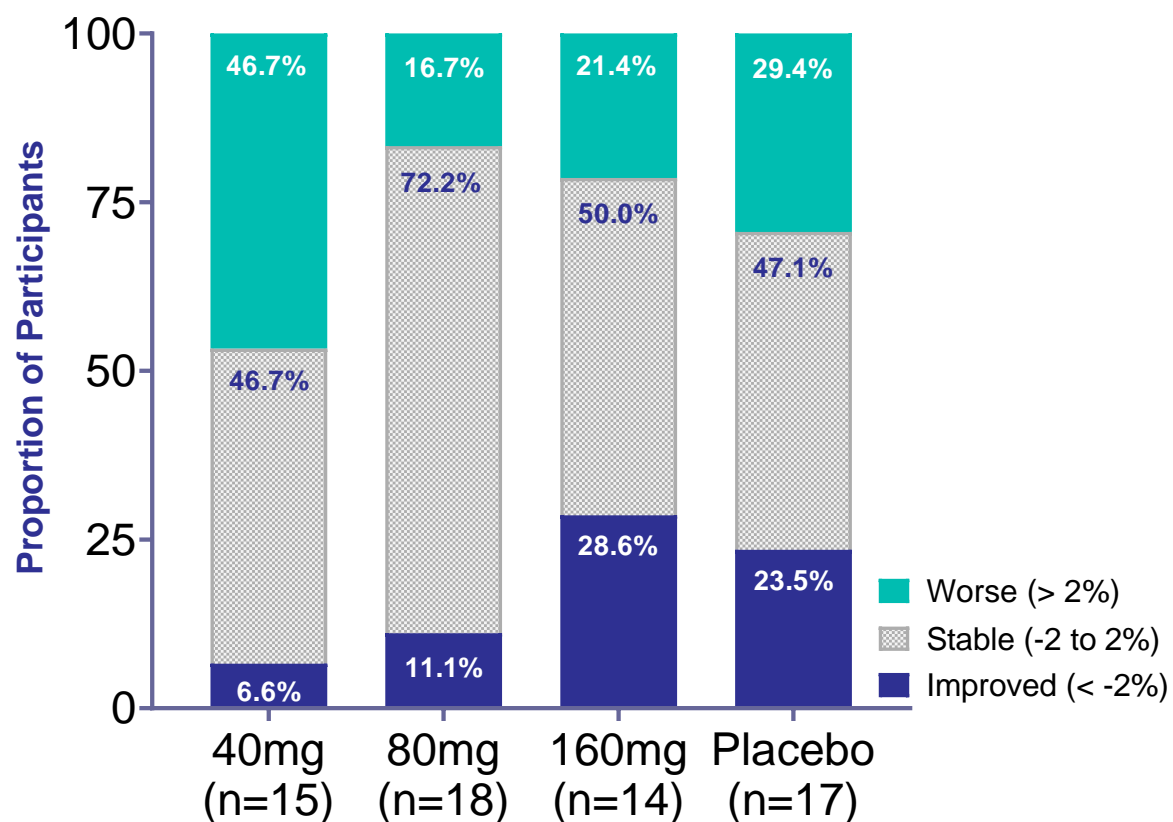
Mean Percent Change in QLF Extent From Baseline to Week 12

CT Protocol Population within Screening Window

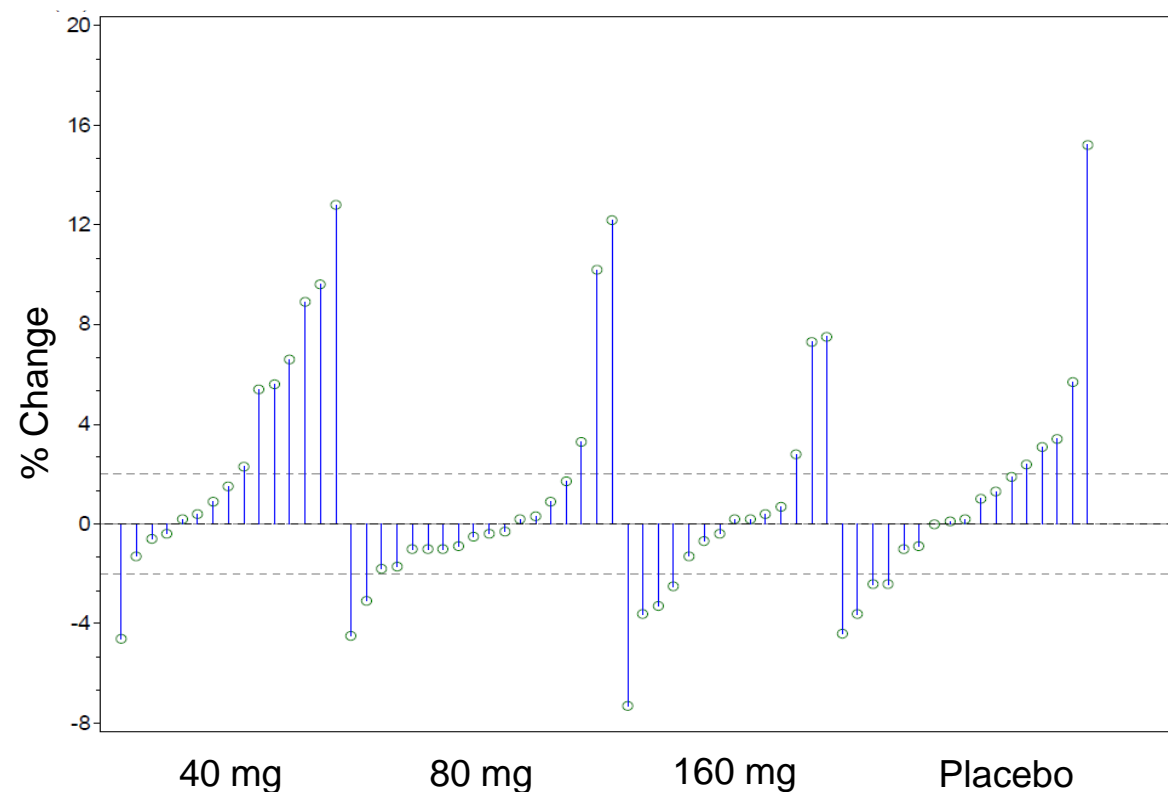


Mean Percent Change in QLF Extent From Baseline to Week 12 CT Protocol Population

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



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

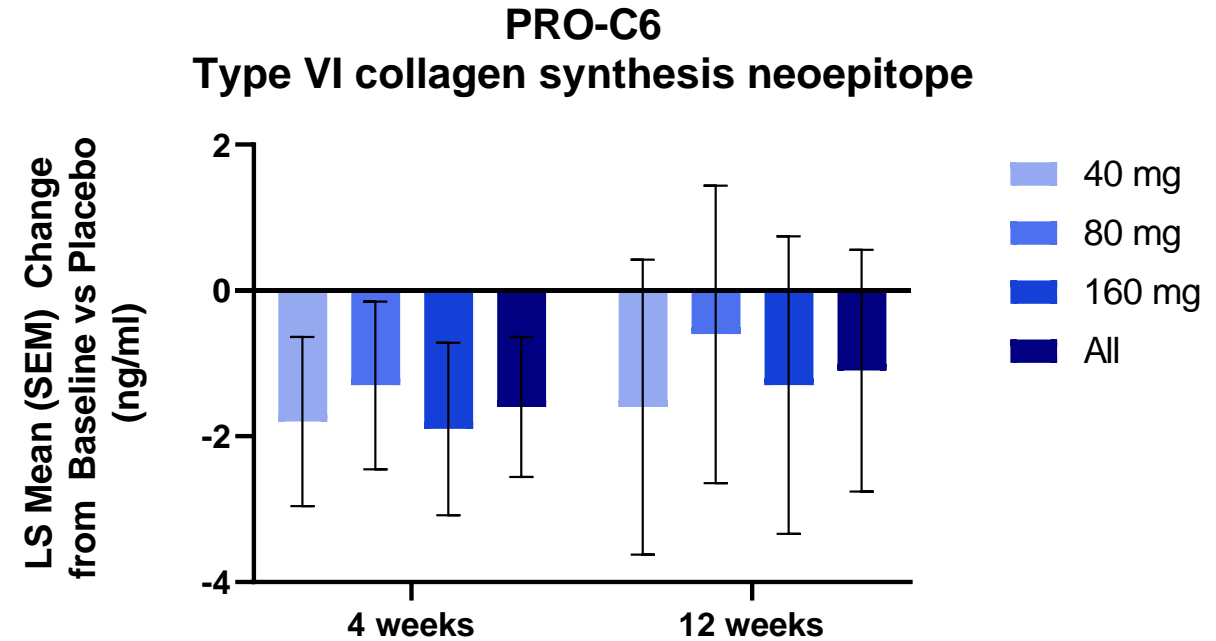
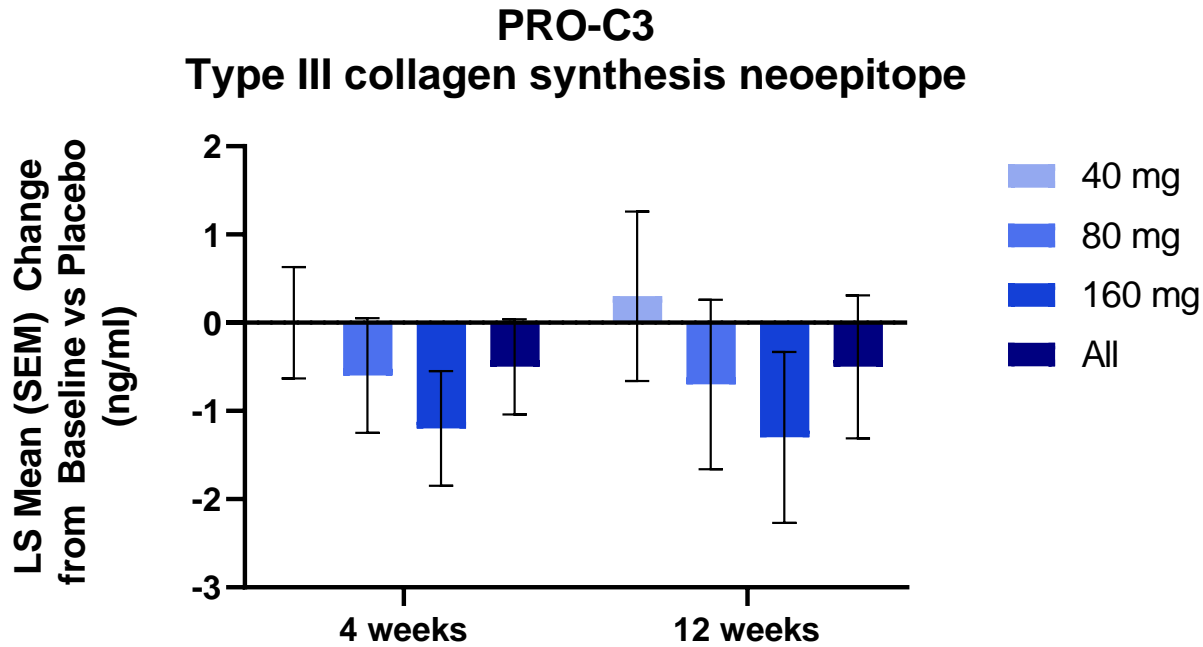
Higher proportion of participants remained stable or improved in the 80 mg and 160 mg groups versus placebo



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

KOL Perspective



Toby Maher, M.D.
Director of ILD,
Keck School of Medicine,
USC

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