Developing Novel Treatments for Fibrotic Diseases

RBC Biotech Expert Insight Series
Pulmonary / Lung Disease

OCTOBER 2022

Disclaimers

This presentation has been prepared by Pliant Therapeutics, Inc. ("we," "us," "our," "Pliant" or the “Company”). The information set forth herein does not purport to be complete or to contain all of the information you may desire. Statements contained herein are made as of the date of this presentation unless stated otherwise, and this presentation shall not under any circumstances create an implication that the information contained herein is correct as of any time after such date or that information will be updated or revised to reflect information that subsequently becomes available or changes occurring after the date hereof.

This presentation includes forward-looking statements regarding Pliant’s proprietary drug candidates, the timing of the start and conclusion of ongoing or planned clinical trials, including the timing of, and our ability to achieve, anticipated milestones, the sufficiency of our cash, cash equivalents and short-term investments, the timing and outcome of regulatory decisions, future availability of clinical trial data, our collaborations for our product candidates and the maintenance of those collaborations; business and results from operations; and other matters. Actual results could differ materially from those contained in any forward-looking statements as a result of various factors, including without limitation: that Pliant’s drug candidates do not advance in development or result in approved products on a timely or cost effective basis or at all; the cost, timing and results of clinical trials; our ability to manage and mitigate the impact of the ongoing COVID-19 pandemic; that many drug candidates that have completed early-stage trials do not become approved drugs on a timely or cost effective basis or at all; the ability to enroll patients in clinical trials; possible safety and efficacy concerns; regulatory developments; the ability of Pliant to protect its intellectual property rights, and unexpected costs, charges or expenses that reduce cash runway. Pliant’s pipeline programs are in various stages of pre-clinical and clinical development, and the process by which such pre-clinical or clinical therapeutic candidates could potentially lead to an approved therapeutic is long and subject to significant risks and uncertainties. Pliant undertakes no obligation to update forward-looking statements as a result of new information or otherwise. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled “Risk Factors” and elsewhere in the Company's most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q on file with the Securities and Exchange Commission (the "SEC") and our other filings with the SEC.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

This presentation concerns drugs that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration (the “FDA”). They are currently limited by Federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

Pliant – Company Highlights

Industry-Leading Fibrosis Platform

- Built on integrin-mediated inhibition of TGF-β pathway resulting in antifibrotic effect and shown to be safe
- Proprietary drug discovery platform based on novel in-house compound library of integrin binders
- Lead molecule PLN-74809 is highly antifibrotic in lung and liver while well tolerated at highest doses tested

Programs Targeting High Unmet Medical Need with High-Impact, Near-Term Catalysts

- PLN-74809 in Phase 2a development in IPF and PSC
  - Phase 2a topline data in IPF showed PLN-74809 was well tolerated with strong treatment effect on FVC and QLF
  - 320 mg: positive DSMB review; interim data early 2023
  - IND submissions in oncology and muscular dystrophies expected by YE 2022

Strategic Partnership with Novartis Validates Platform

- Largest ($80M) upfront for a preclinical NASH program
- Significant expense offset to pipeline programs
- Broad multi-target research collaboration
  - Next generation anti-fibrotic molecules targeting novel integrins

Strong Financial Position

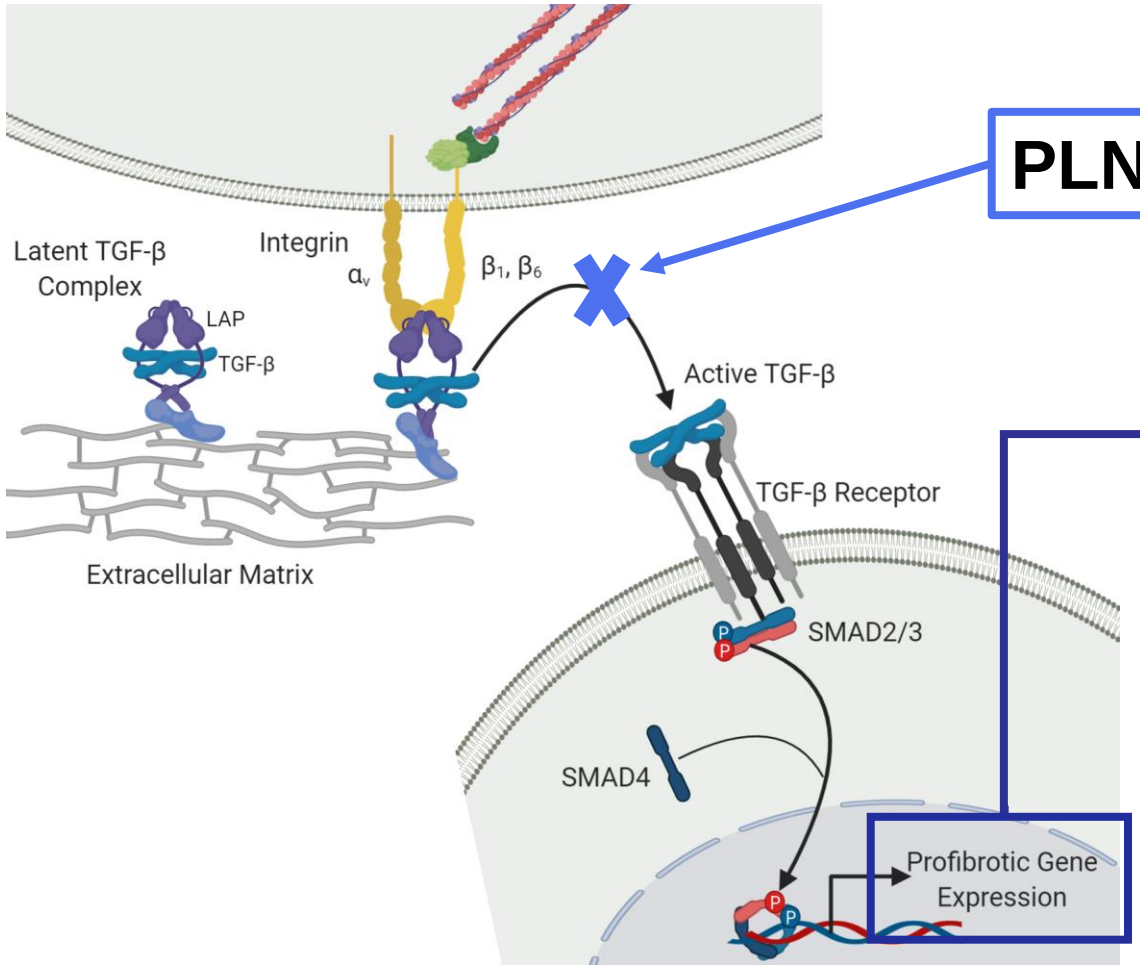
- Over $625 million raised to date including June 2020 IPO (Nasdaq: PLRX) and $230 million follow on July 2022
- $379.8 million proforma cash[1] balance as of June 30, 2022
- $100 million loan facility ($10 million drawn)
- Operations funded to mid-2025

1 – Proforma for July 2022 $230M equity offering. Includes cash, cash equivalents and ST investments.

Pliant Development Pipeline

	Program	Indication	Preclinical	Clinical			Anticipated Milestone	Global Rights
				Phase I	Phase II	Phase III		
WHOLLY OWNED	PLN-74809 Dual selective inhibitor of $\alpha_v\beta_6$ /$\alpha_v\beta_1$	Idiopathic Pulmonary Fibrosis					Phase 2a 320 mg Data Expected Early 2023	PLIANT
		Primary Sclerosing Cholangitis					Phase 2a Data Expected 1H 2023	PLIANT
	Oncology Inhibitor of $\alpha_v\beta_8$ /$\alpha_v\beta_1$	Solid Tumors					IND Filing Expected YE 2022	PLIANT
	PLN-101325 Anti-integrin mAb of $\alpha_7\beta_1$	DMD Other Muscular Dystrophies					IND Filing Expected YE 2022	PLIANT
PARTNERED	PLN-1474 Selective inhibitor of $\alpha_v\beta_1$	NASH-Associated Liver Fibrosis					Phase 2 Initiation	NOVARTIS

PLN-74809 Provides Profound Antifibrotic Activity through Upstream Inhibition of TGF-β Activation

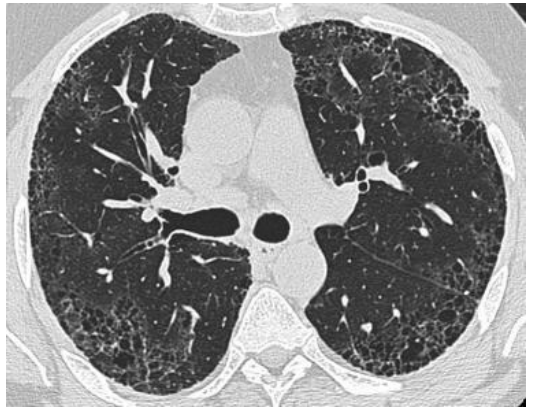


PLN-74809

Pamrevlumab

Col1a1
Col3a1
Timp1
CTGF
ATX
…

FIBROSIS



- **Upstream inhibition of TGF-β leads to reduction of multiple profibrotic genes**
- **Competitor programs only block one of multiple profibrotic gene products**

PLIANT

PLN-74809 Nonclinical Toxicology Studies
No Effects of Concern for Clinical Advancement

GLP Study Category	Studies Completed	Findings with PLN-74809
Repeat Dose Toxicology	• 1-Month IND-enabling NHP and mouse • 3-Month Sub-chronic NHP and mouse • 9-Month Chronic NHP • 6-Month Chronic Mouse	**No findings limiting clinical advancement including** • No pulmonary infiltrates NOAEL[1] in sub-chronic and chronic GLP tox studies at the highest dose tested in NHPs
Safety Pharmacology	• Standard cardiac ion channel panel • Cardiovascular/respiratory in telemetered NHP	**No findings:** • No effect on respiratory or cardiovascular parameters
Genetic Toxicology	• Ames • *In vitro* micronucleus • *In vivo* micronucleus	**No genotoxic findings:** • Ames negative • Micronucleus negative
Reproductive Toxicology	• Mouse Embryofetal Development • Rabbit Embryofetal Development • Mouse Fertility	**No findings:** • No embryofetal effects • No effects on fertility

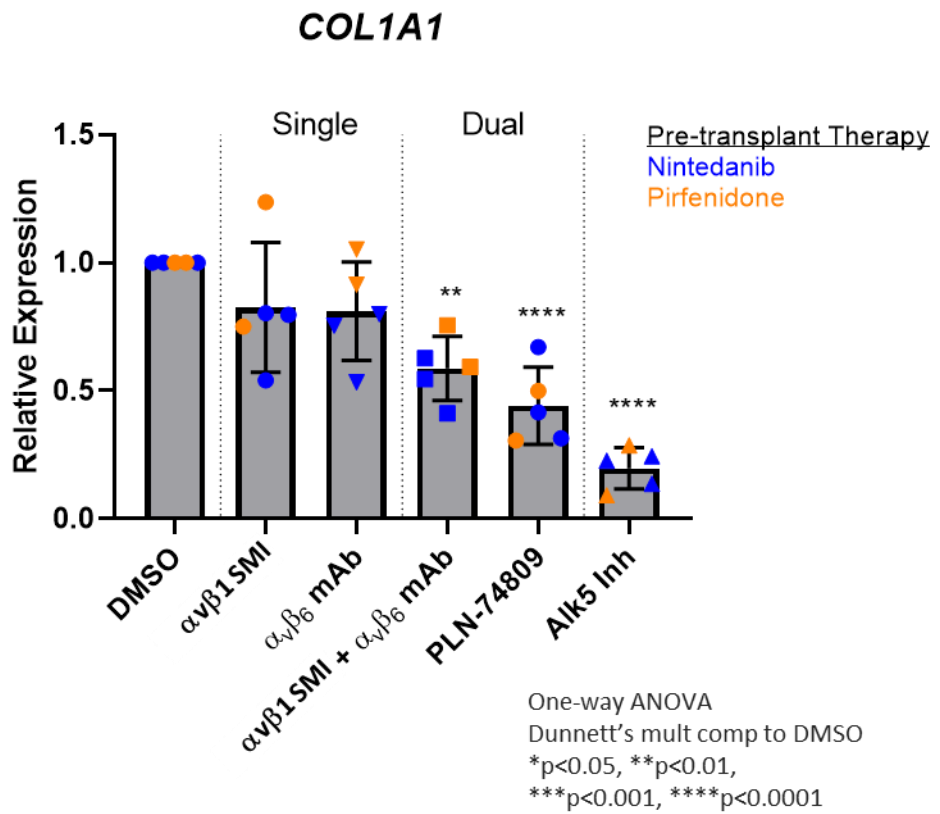
450+ human subjects dosed to date with no safety concerns identified at doses up to 640 mg

1 – No observed adverse effect level.

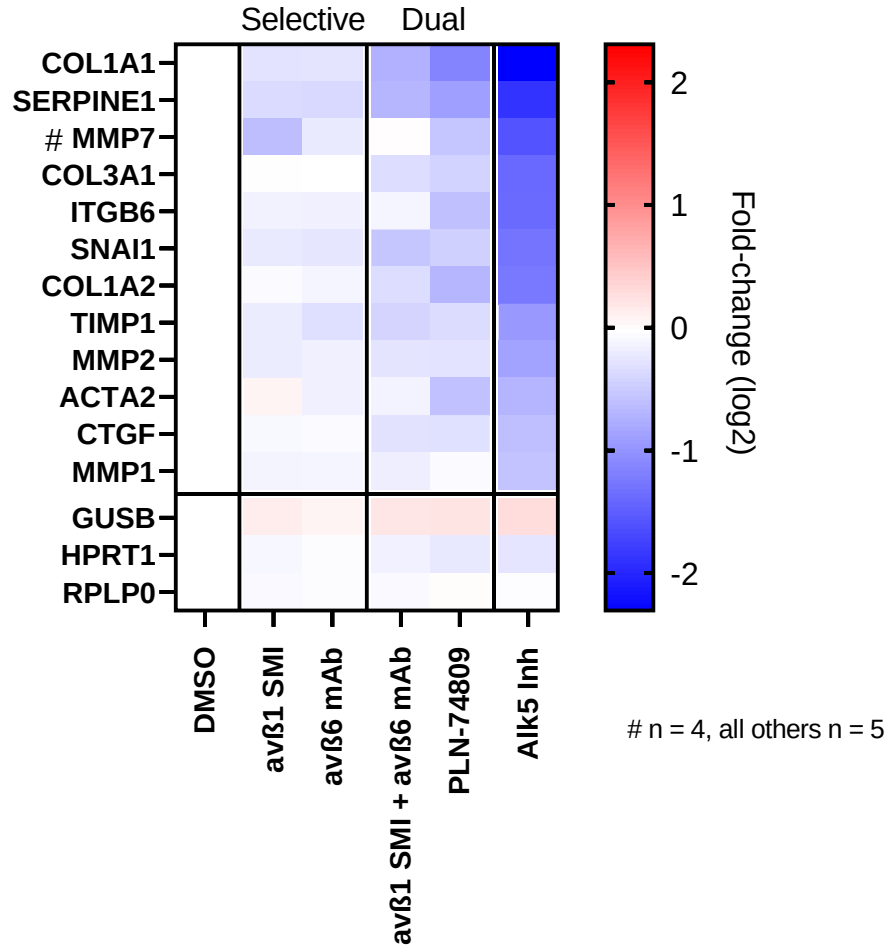
PLIANT

Dual $\alpha_v\beta_6/\alpha_v\beta_1$ Inhibition Blocks COL1A1 Gene Expression More Than Single Inhibition in Human IPF Tissue

- Ex-planted lungs from 5 IPF patients
- Sliced and cultured for 7 days



Profibrotic Gene Expression Panel



n = 4, all others n = 5

BMC Respiratory Research

Decaris et al. *Respir Res* (2021) 22:265

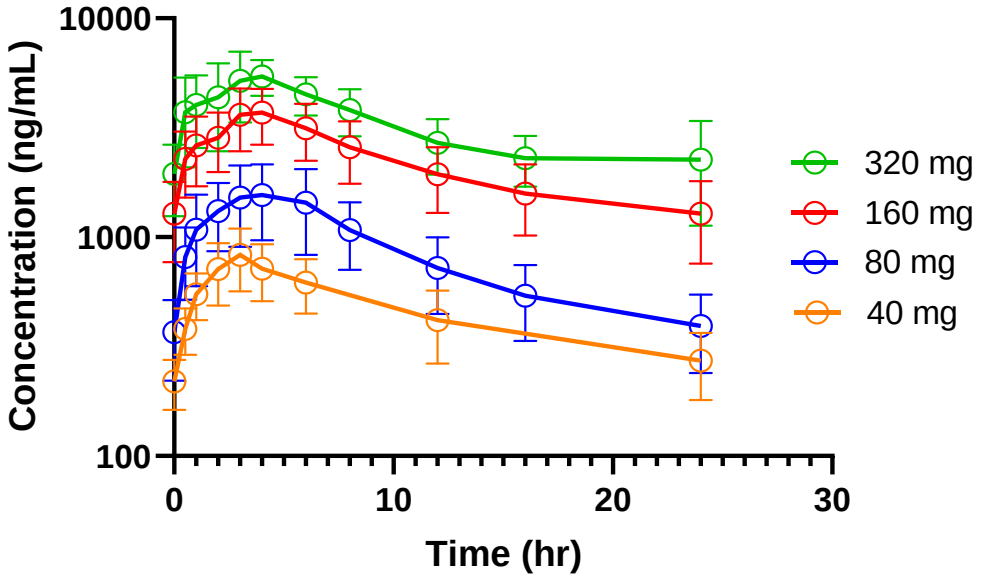
PLIANT

PLN-74809: Phase 1a Data Summary - Pharmacokinetics

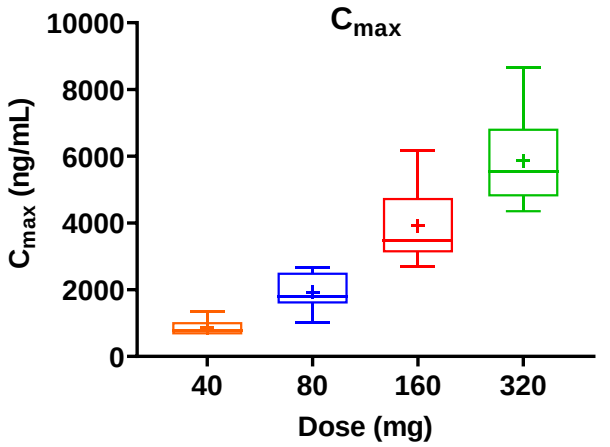
Pharmacokinetics

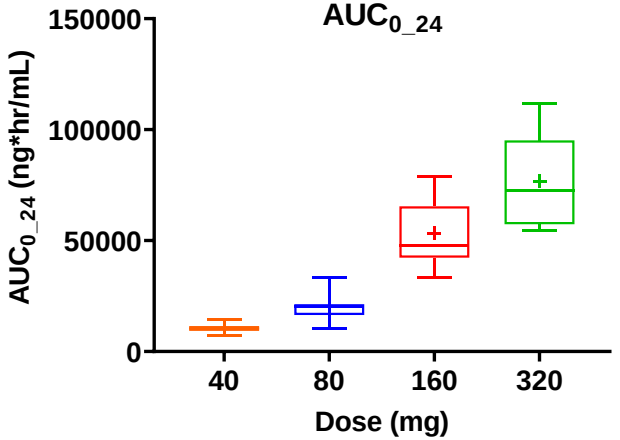
- Well absorbed, orally bio-available
- Long $T_{1/2}$: ~50 hrs – QD dosing

Summary PK Curves by Cohort at Steady State



PK sampling up to 144h; only 0-24hr plotted.
Doses 10mg to 40mg from Study PLN-74809-P1-01, Day 14.
Doses 80mg, 160mg and 320mg from Study PLN-74809-104, Day 7.

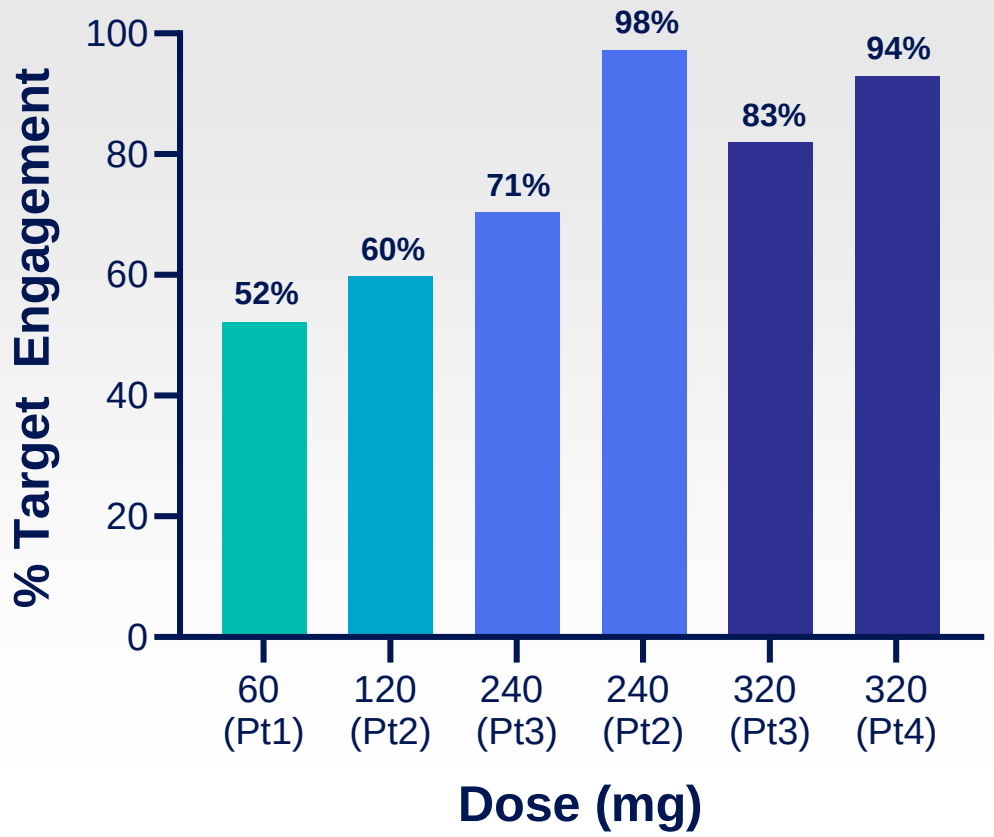




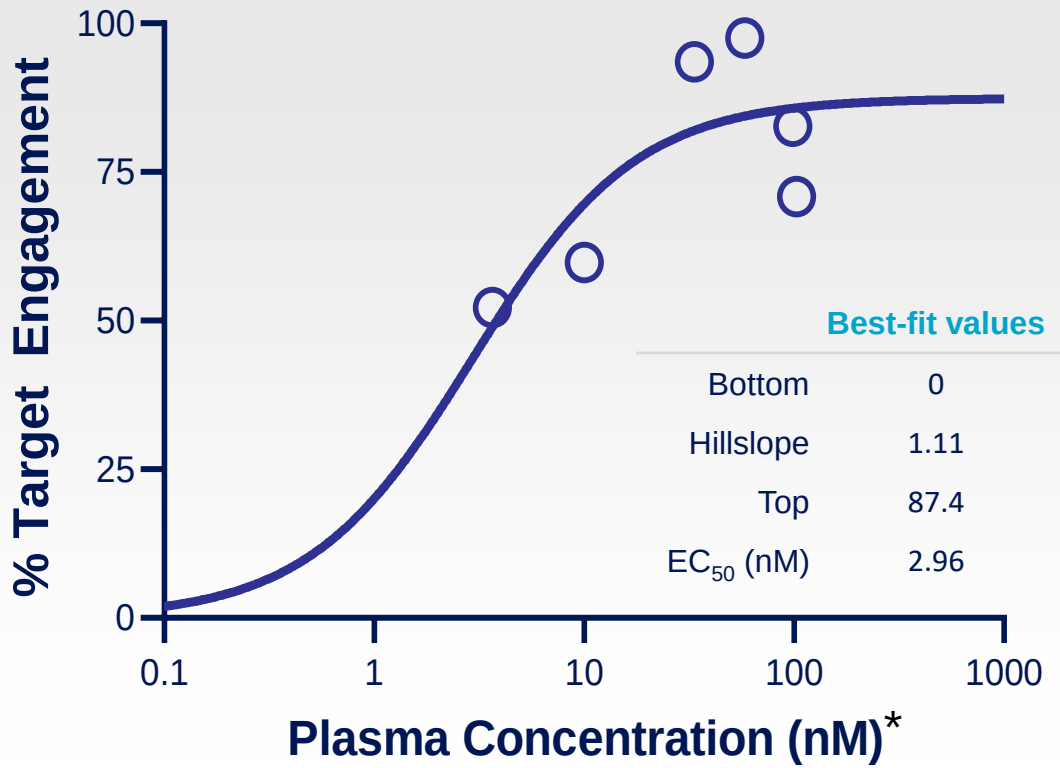
Data presented as box plots (max to min)
with line at median and + at mean.

Dose- and Plasma Concentration-Dependent Target Engagement

Dose-Dependent Target Engagement

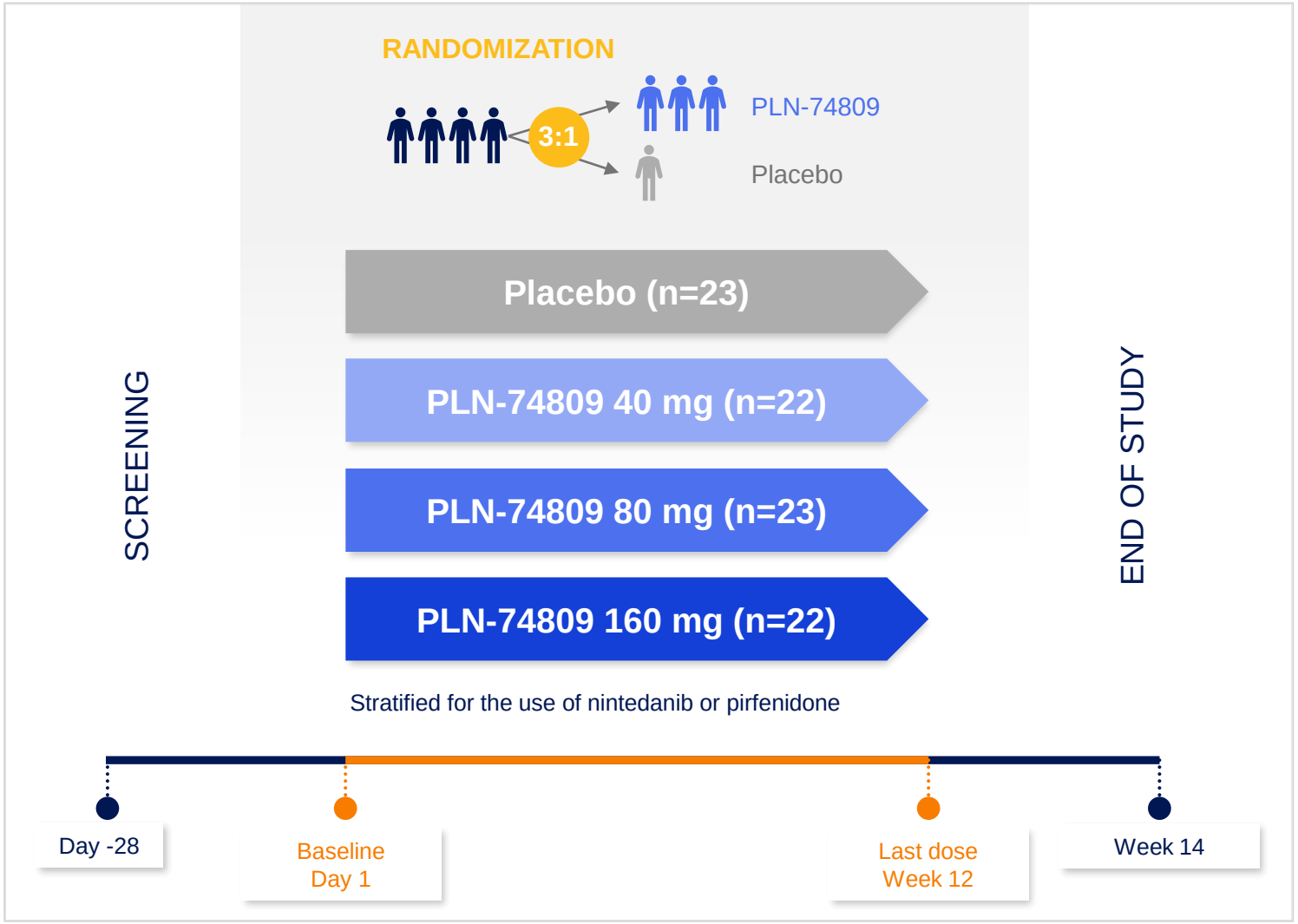


Plasma Conc-Dependent Target Engagement



* Free plasma concentration

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

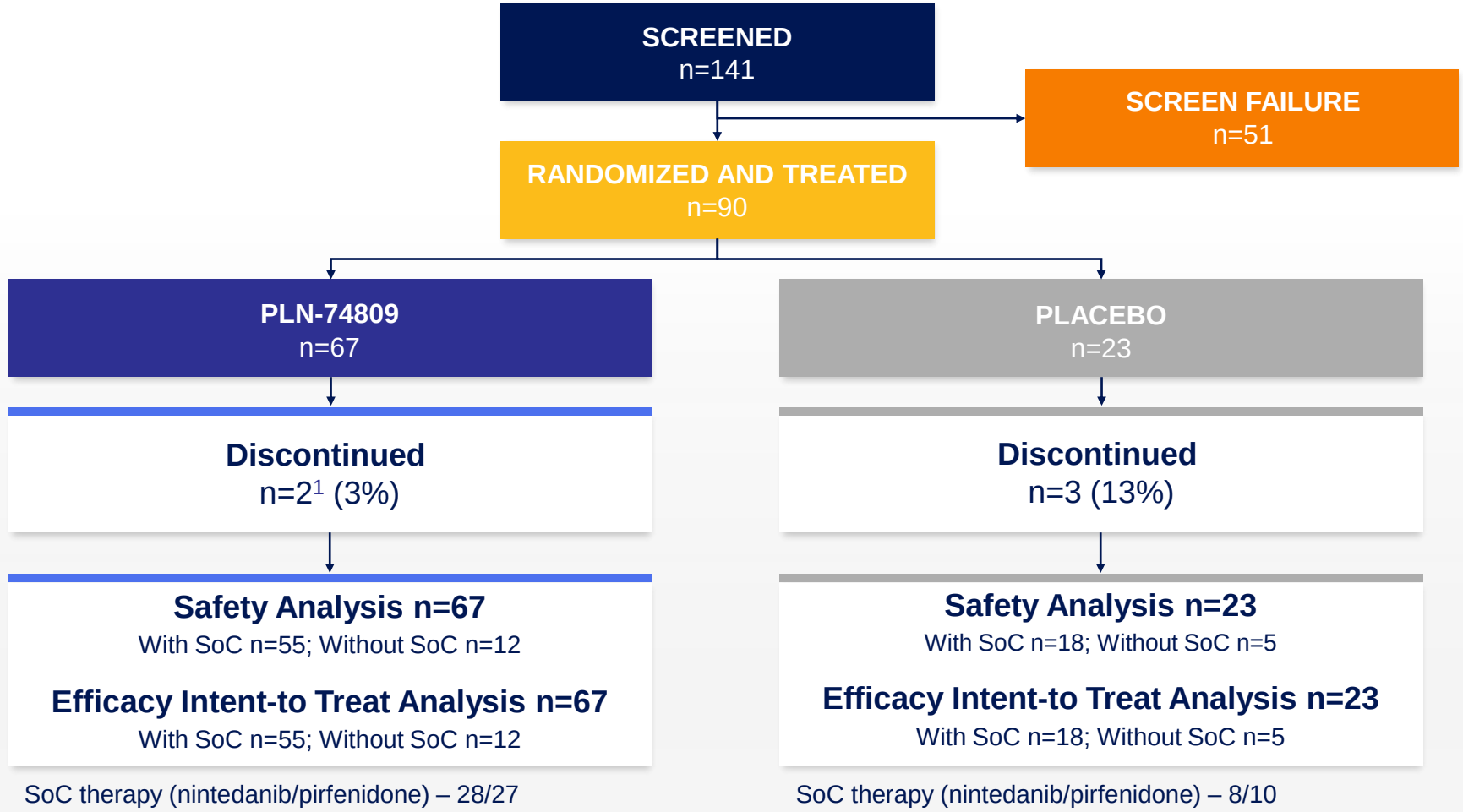
PLN-74809-Treated Patients Experienced an 80% Reduction in FVC Decline Over 12 Weeks (-15.1 mL, Pooled Active Groups) Compared to Placebo (-74.1 mL)

- 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

Participant Disposition



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

SoC = Standard of Care

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.

PLIANT

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.

Most Frequent TEAEs – Any Causality

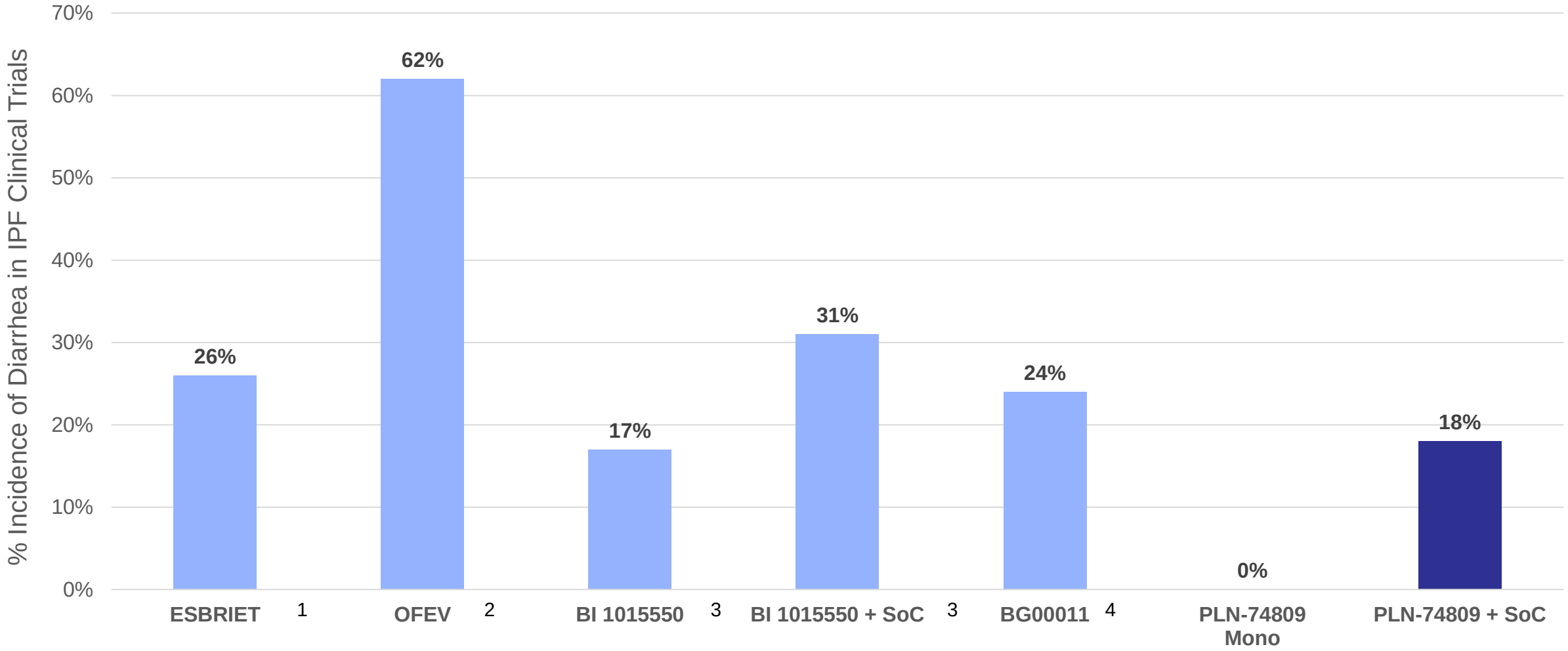
AE, n (%) of Participants Reporting	PLN-74809 40mg (n=22)	PLN-74809 80mg (n=23)	PLN-74809 160mg (n=22)	PLN-74809 All (n=67)	Placebo (n=23)
Most frequent TEAEs (≥ 10% in at least one arm)					
Diarrhea	2 (9.1)	5 (21.7)	5 (22.7)	12 (17.9)	1 (4.3)
Related to study drug	1 (4.5)	3 (13.0)	4 (18.2)	8 (11.9)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

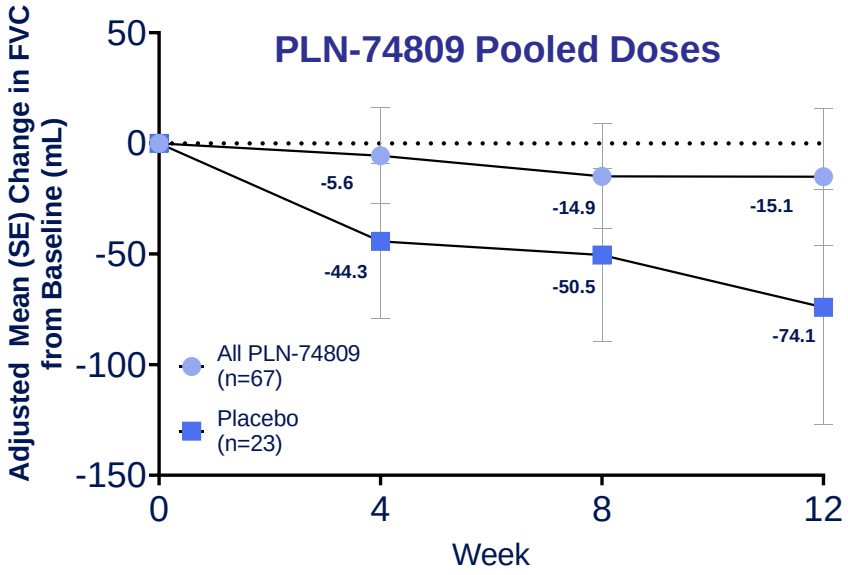
Incidence of Diarrhea in IPF Randomized Clinical Trials

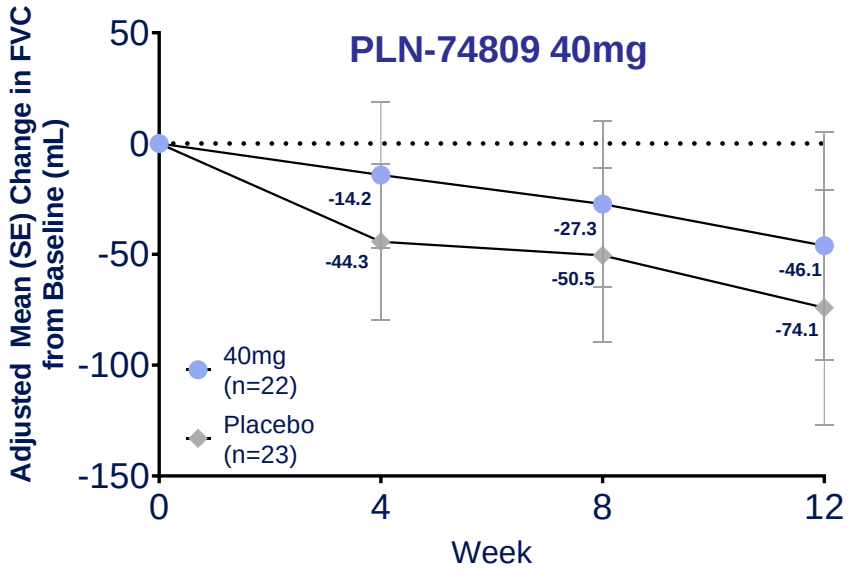


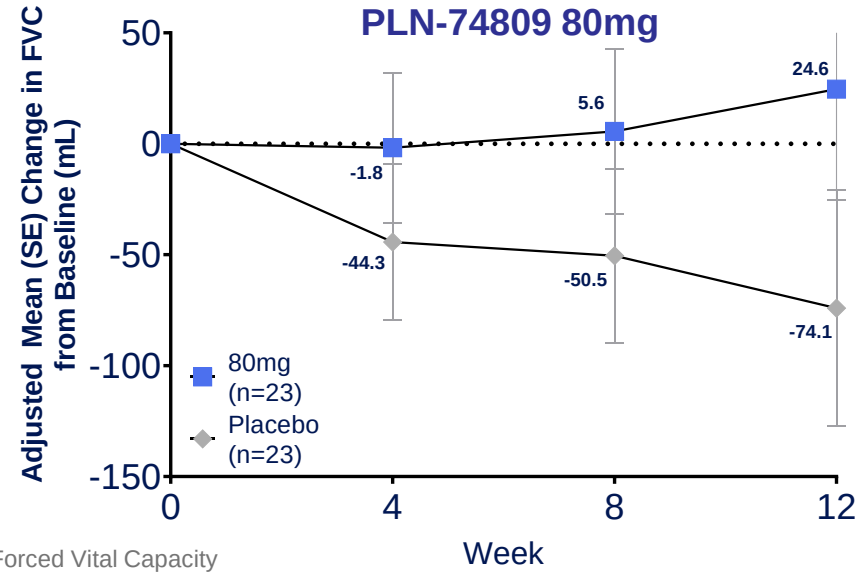
[1]ESBRIET USPI, [2] OFEV USPI, [3] Richeldi et al, 2022, [4] Raghu et al, 2022

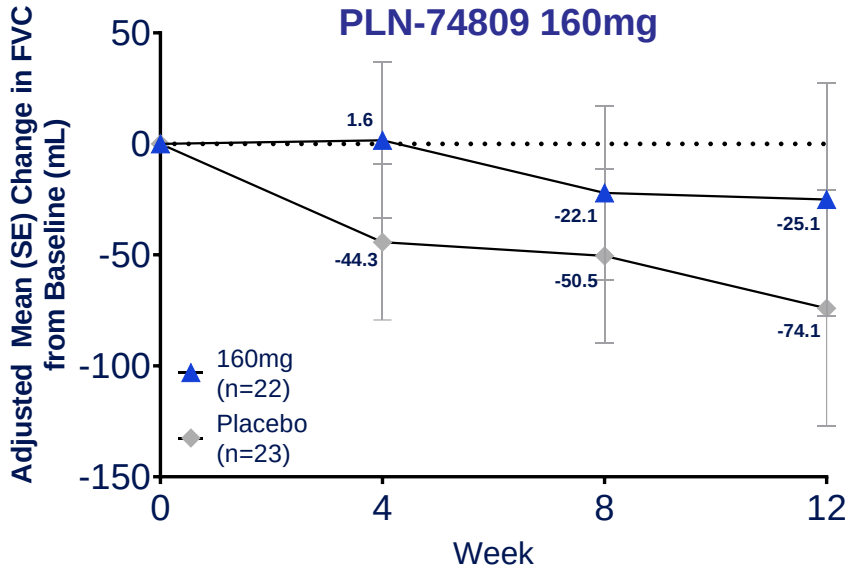
Change in FVC over 12 Weeks in INTEGRIS-IPF

MMRM Analysis - ITT Population



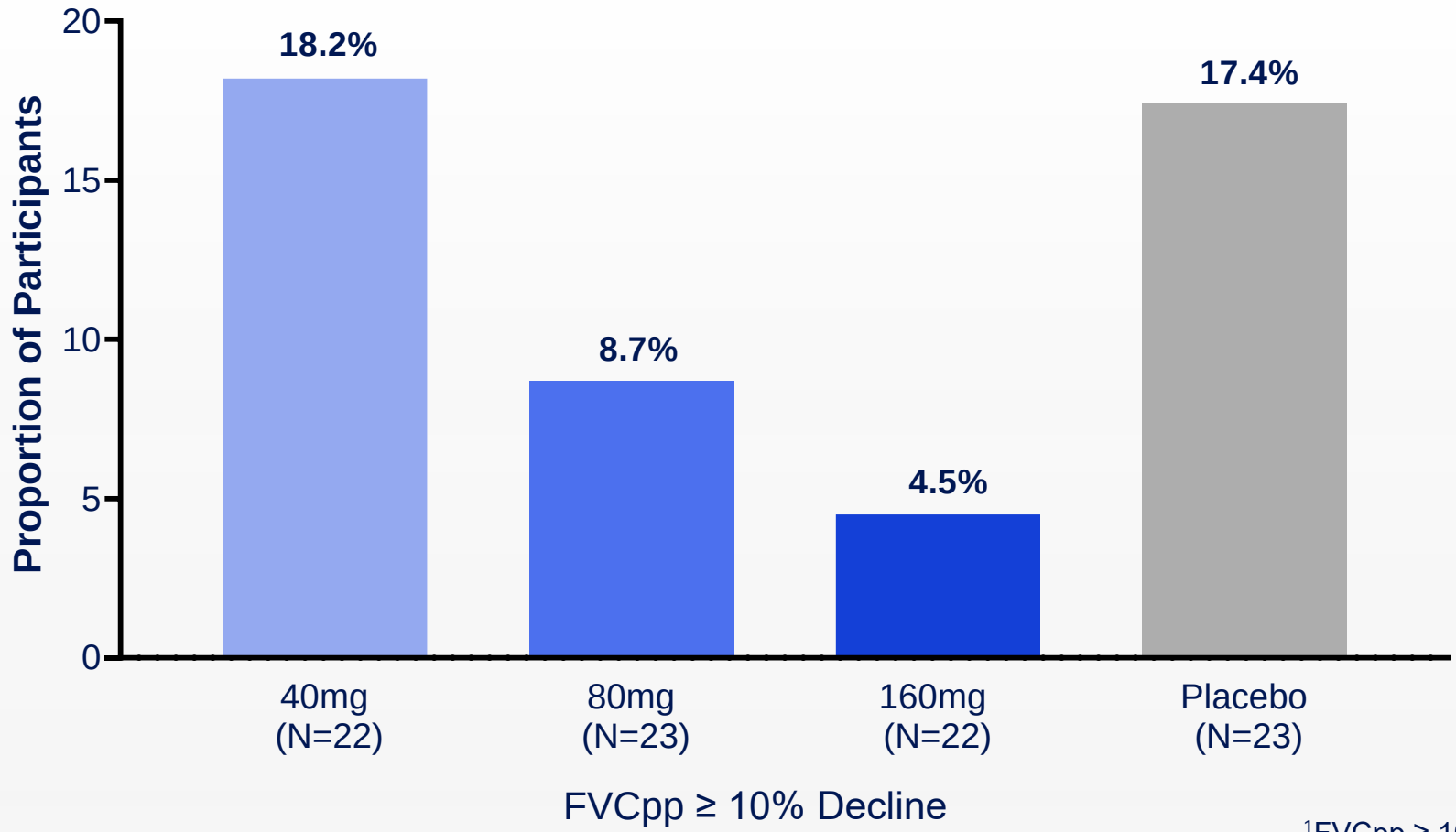






FVC = Forced Vital Capacity
MMRM = Mixed Model Repeat Measures.

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



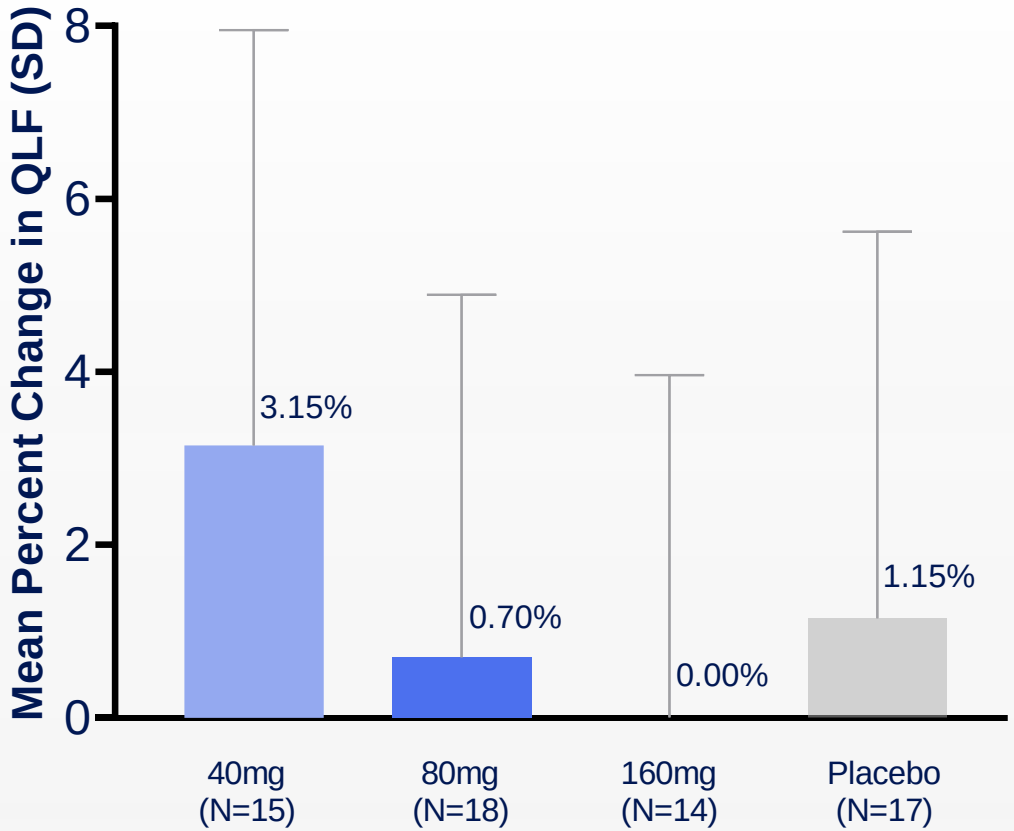
[1]FVCpp ≥ 10%: strong predictor of disease progression and mortality

FVCpp = Forced vital capacity, percent predicted

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

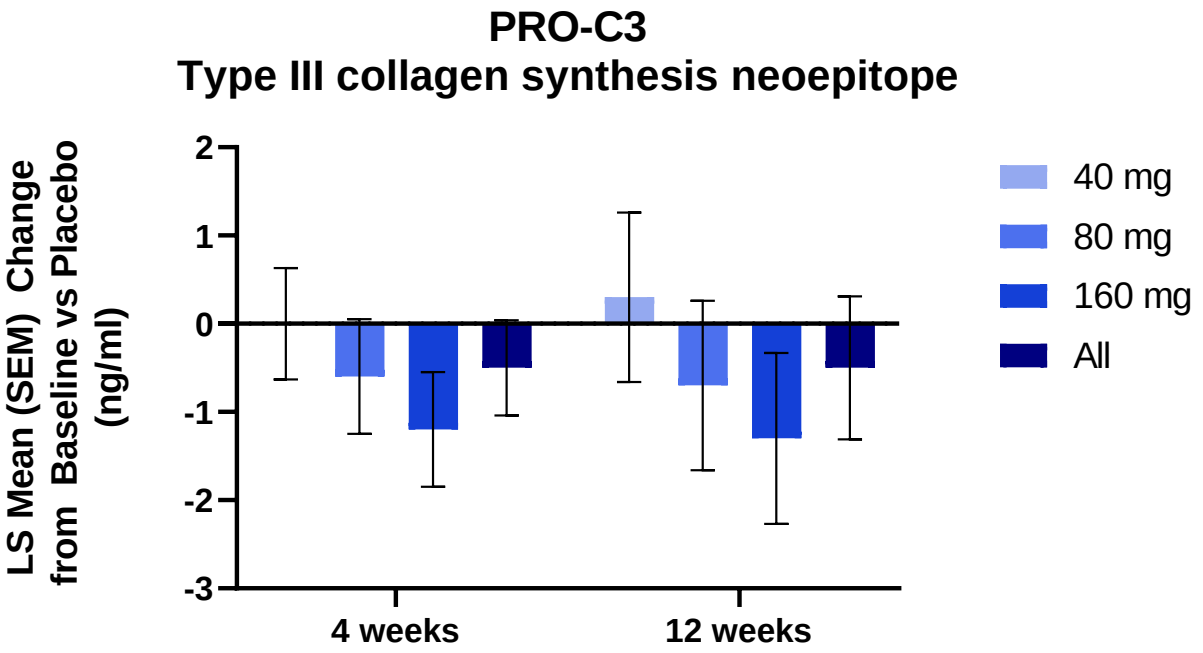
Mean Percent Change in QLF Extent From Baseline to Week 12

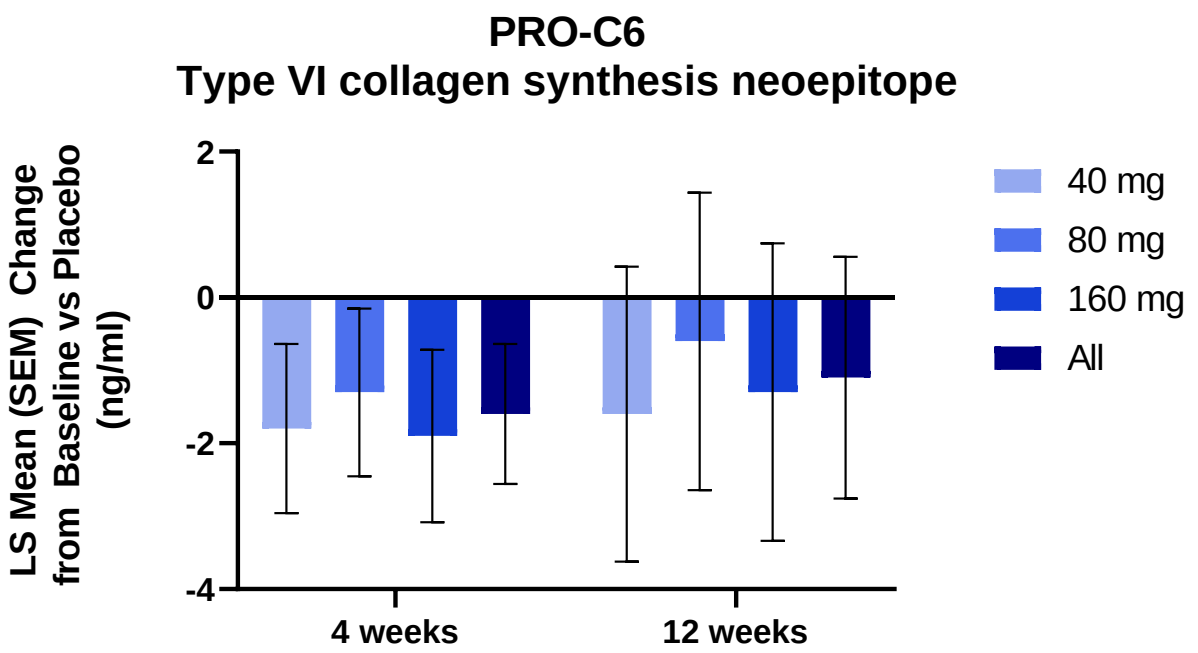
CT Protocol Population within Screening Window



QLF = quantitative lung fibrosis

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

PLN-74809 Phase 2a 320 mg Dose Global Safety-PK-Exploratory Efficacy Trial in IPF

Enrollment Complete; 12-Week Interim Data Expected in Early 2023

KEY INCLUSION/EXCLUSION CRITERIA

- Adults with IPF diagnosis
- FVC ≥ 45% of predicted
- Stratified for pirfenidone or nintedanib use

Randomization 3:1 (PLN-74809:placebo)

- Placebo (n=7)
- PLN-74809 320 mg (n=21)

PRIMARY AND SECONDARY ENDPOINTS

- Safety, tolerability, PK

EXPLORATORY ENDPOINTS

- Change in FVC at wk 24 and up to 48 wks
- High Resolution CT-based Quantitative Lung Fibrosis (QLF) imaging
- Effect on selected biomarkers

*Trial will complete once the last trial participant enrolled reaches 24 weeks of treatment

PLIANT

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 the INTEGRIS-IPF Phase 2a data with regulatory authorities in the near term to discuss the late-stage development plan for PLN-74809**