

# Developing Breakthrough Treatments for Fibrotic Diseases

May 2019

**PLIANT**  
THERAPEUTICS

# Pliant – The Fibrosis Company

## Unique Fibrosis Platform with Clinical Stage Products

Program	Discovery		Preclinical		Clinical	
	<i>In vitro</i>	<i>In vivo</i>	<i>Lead Op</i>	<i>IND Enabling</i>	<i>Phase I</i>	<i>Phase II</i>
<b>PLN-74809</b> <i>Dual selective inhibitor of <math>\alpha_v\beta_6/\alpha_v\beta_1</math></i> <i>IPF, PSC</i>	IPF					
	PSC					
<b>PLN-1474</b> <i>Selective inhibitor of <math>\alpha_v\beta_1</math></i> <i>NASH/liver fibrosis</i>						
<b>TGF-<math>\beta</math>1 Target</b> <i>Multiple fibrotic diseases</i>						
<b>Undisclosed Programs</b> <i>Multiple</i>						

Unique integrin chemistry and screening platform  
 >4,500 compound library &  
 broad multi-integrin screening platform

- Pre-Efficacy de-risking capabilities and development strategy: human fibrotic tissue assays, advanced imaging (PET), BMx

**Strong Balance Sheet with Over \$120 Million Raised To Date (Series A: \$56M / Series B: \$68M)**



COWEN

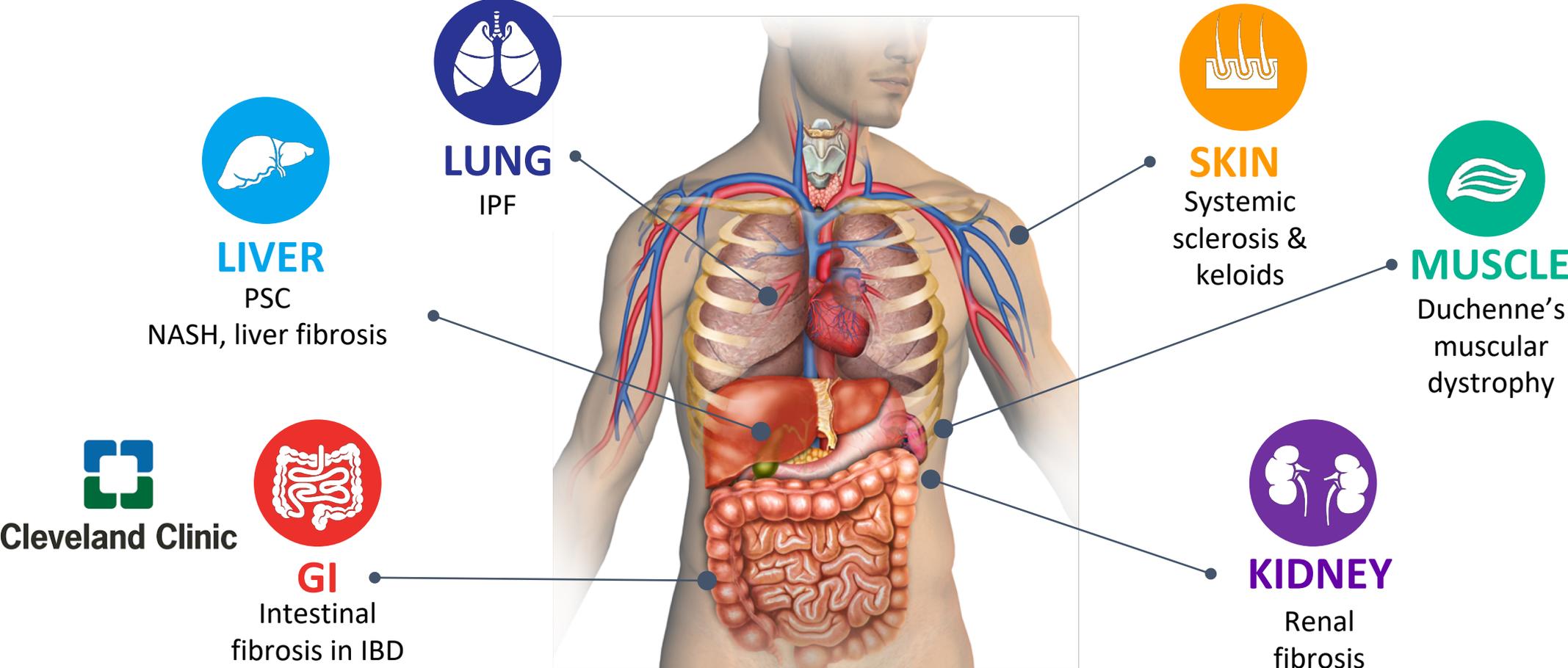


Schroder Adveq



# Pliant's Pipeline Covers Wide Spectrum of High Value Diseases

## Discovery Platform Powers Growing Franchise



**PLN-74809**

**A Dual Selective  $\alpha_v\beta_6/\alpha_v\beta_1$  Inhibitor for  
the Treatment of IPF and PSC**

# PLN-74809 – Dual Selective $\alpha_v\beta_6$ / $\alpha_v\beta_1$ inhibitor

## Program Summary

### Multiple Target Indications

- Efficacy in multiple disease models: IPF, PSC, renal fibrosis
- ***Profound antifibrotic effect in human IPF and PSC tissue***

### Favorable Drug Properties & Pharmacokinetics

- Highly potent ( $IC_{50} < 5$  nM) and selective (>100-fold vs other integrins)
- High **oral bioavailability** and exposure at low starting dose (15 mg) in humans
- Long  $T_{1/2}$  (20 hrs) – **Once daily dosing**

### Reduced Developmental Risk Profile

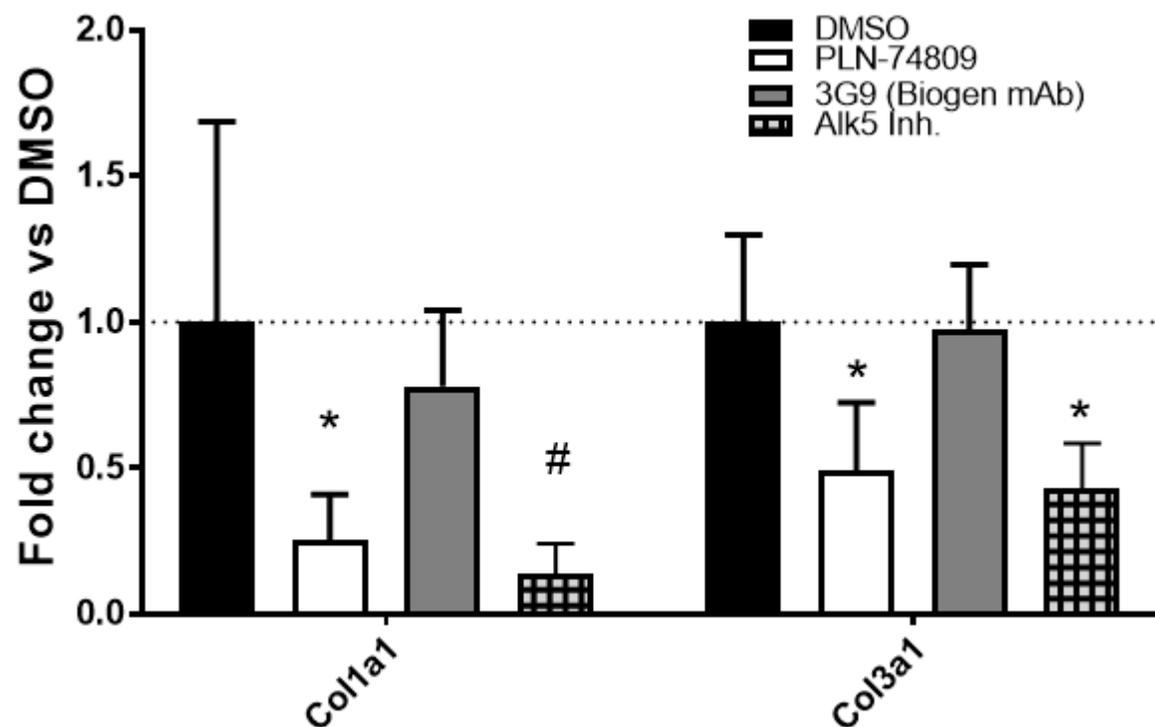
- Biomarker for target inhibition: **reduction of alveolar pSMAD**
- $\alpha_v\beta_6$  **PET ligand** for target engagement in Phase 2a study in IPF (Stanford)

### Regulatory Status

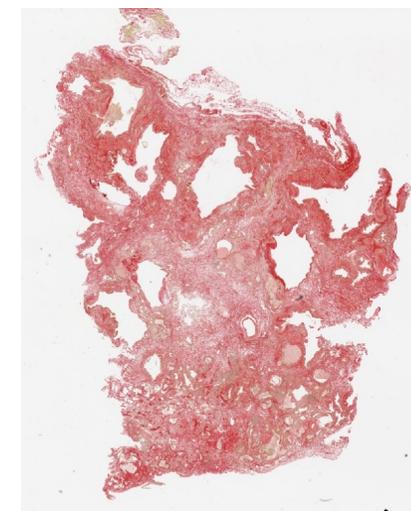
- **Orphan Drug Designation** for IPF and PSC granted

# PLN-74809 Decreases the Expression of Pro-Fibrotic Genes in Fresh Human IPF Tissue

## Combined Inhibition of $\alpha_v\beta_6$ and $\alpha_v\beta_1$ Provides Increased Antifibrotic Activity versus $\alpha_v\beta_6$ Inhibition Alone



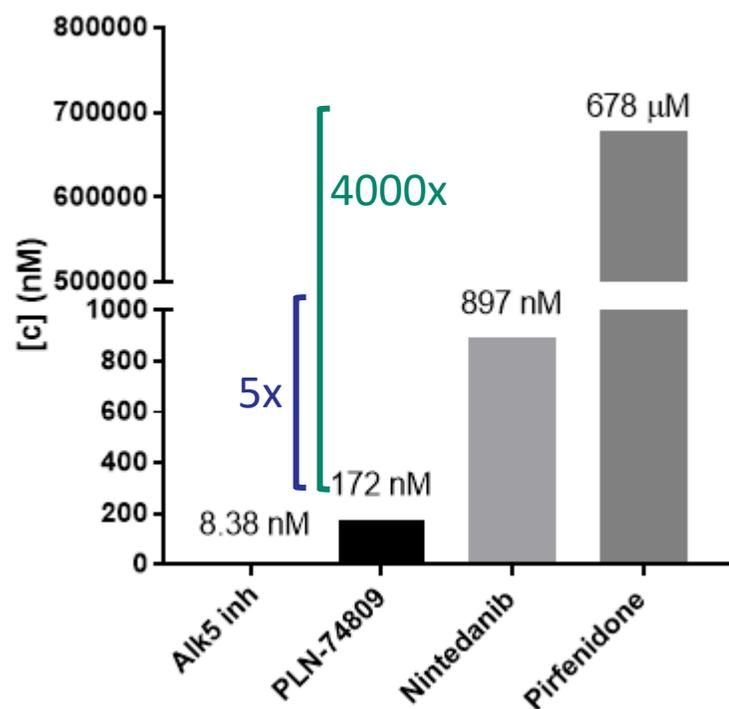
- Fresh human lung from **IPF patient**
- **500  $\mu\text{m}$**  thick precision cut tissue slices
- **3 day culture** and treatment



n = 3  
Std Dev  
\* p < 0.05  
# p < 0.01

Compound	Dose	Target
PLN-74809	10x IC50	$\alpha_v\beta_6/\alpha_v\beta_1$
3G9 Biogen mAb	10x IC50	$\alpha_v\beta_6$
Alk5 inhibitor	100x IC50	TGF- $\beta$ receptor

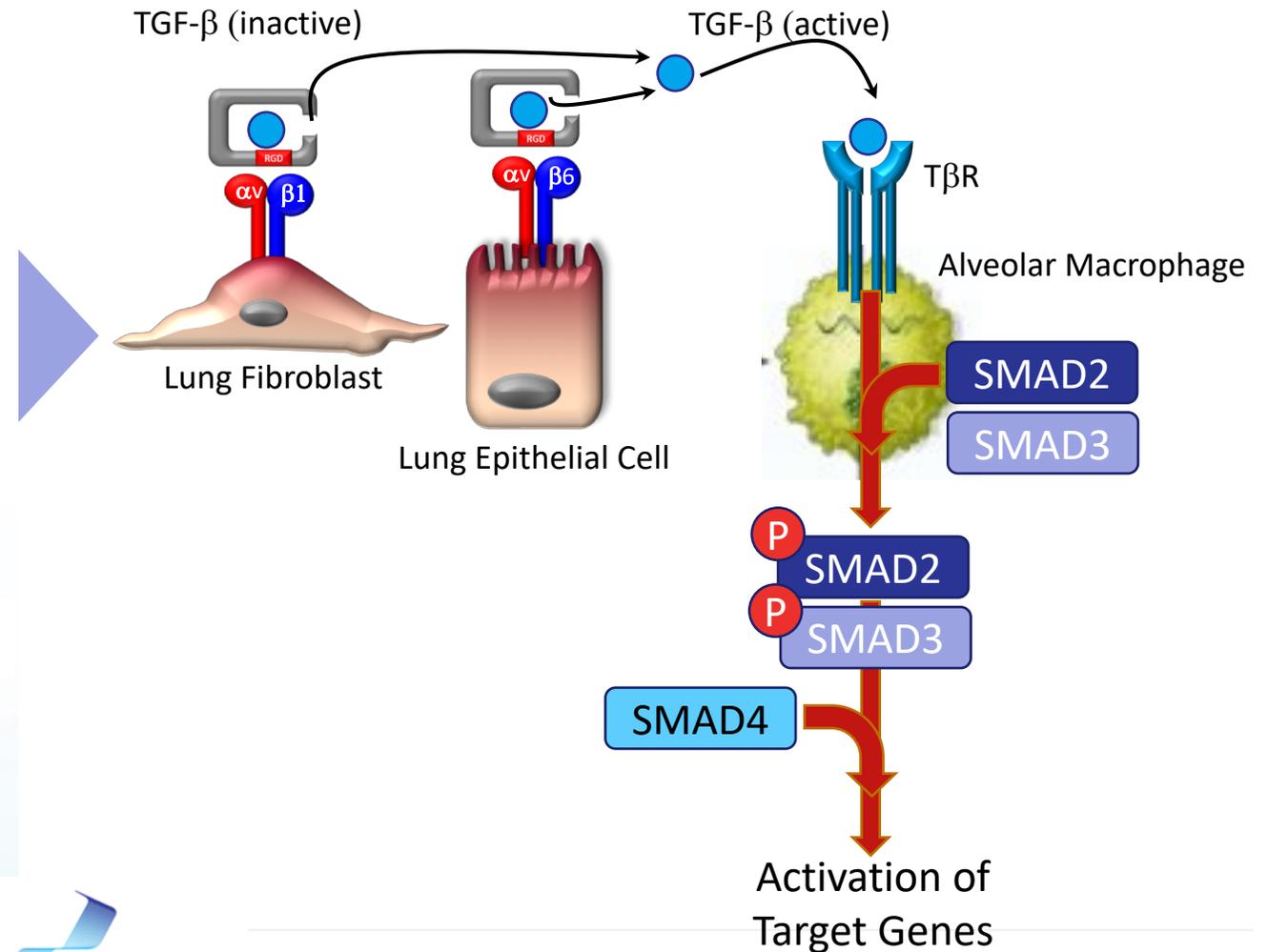
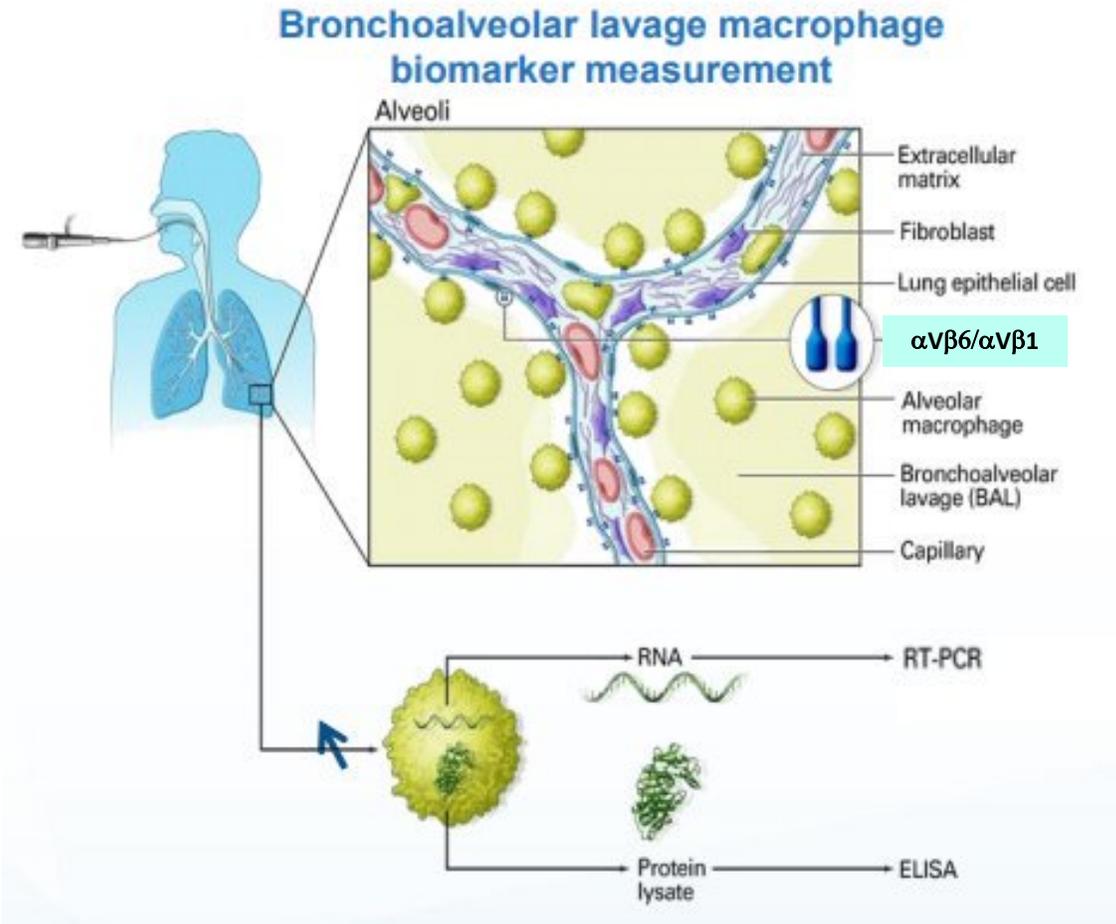
# Murine Bleo Lung Data Suggest PLN-74809 is a More Potent Antifibrotic than Current IPF Standard of Care



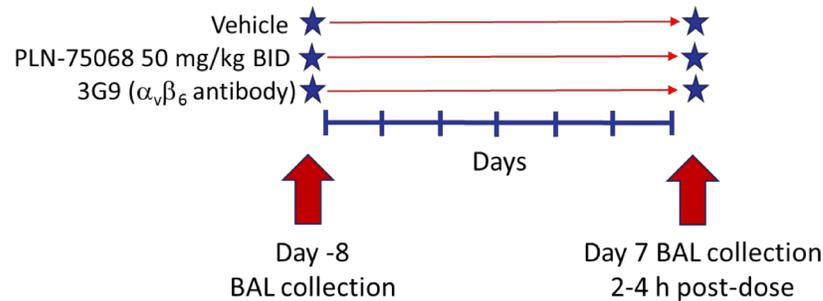
[c] for 50% inhibition of *Col1a1* expression is extrapolated from the dose response curve generated by plotting mean ddCT (to DMSO) versus log([c])

SMI	N	[c]
Alk5 inhibitor	11	1.5 nM – 1 μM
PLN-74809	9	16 pM – 10 μM
Nintedanib (Ofev)	5	2 nM – 10 μM
Pirfenidone (Esbriet)	4	50 μM – 2 mM

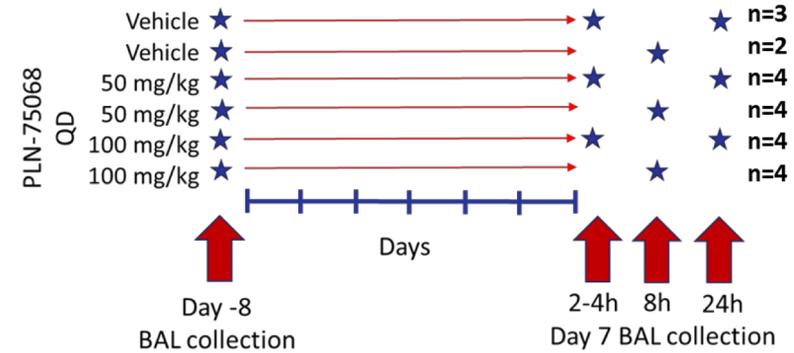
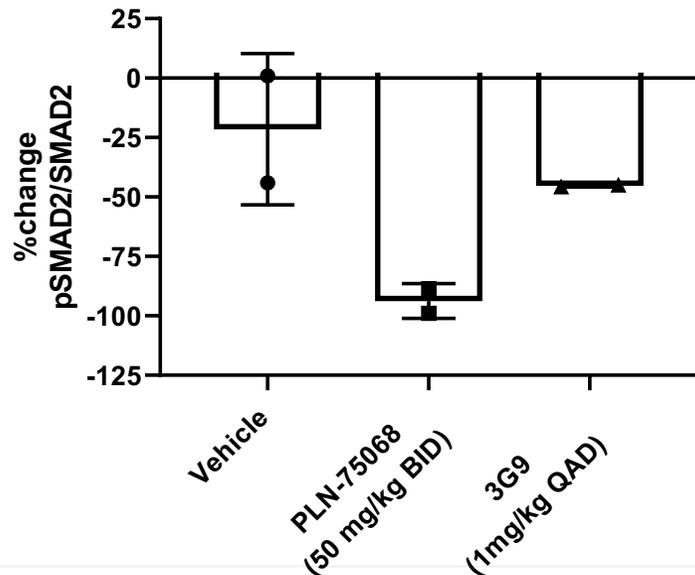
# Suppression of Alveolar pSMAD2 Biomarker for Biological Activity of Integrin Inhibitor



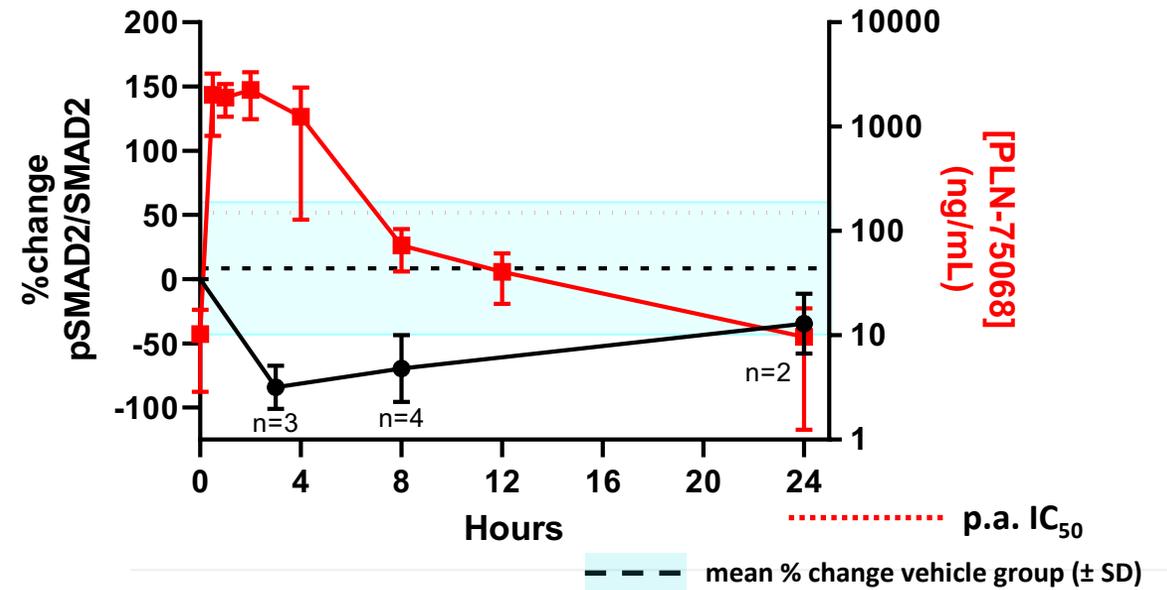
# PLN-75068 Dosed QD Exceeds IC<sub>50</sub> Levels in Plasma and Suppresses BALF Cell pSMAD2/SMAD2 Ratio for > 8 hrs



Day 7 - BALF Cell Results  
 (measurement acquired from n=2 per group)



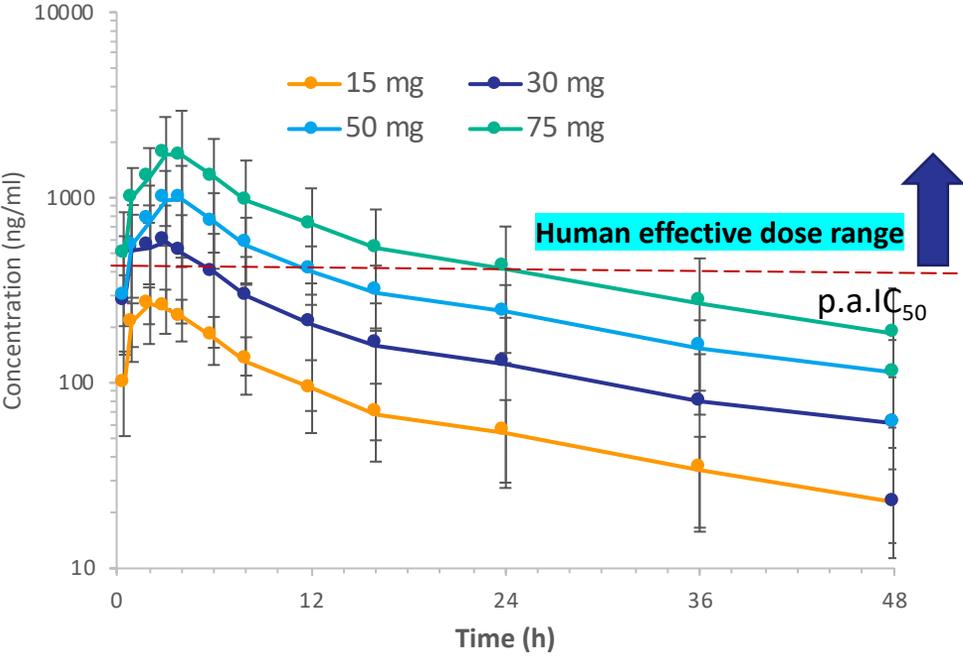
PLN-75068 QD 50 mg/kg  
 Day 7 - BALF Cell Results



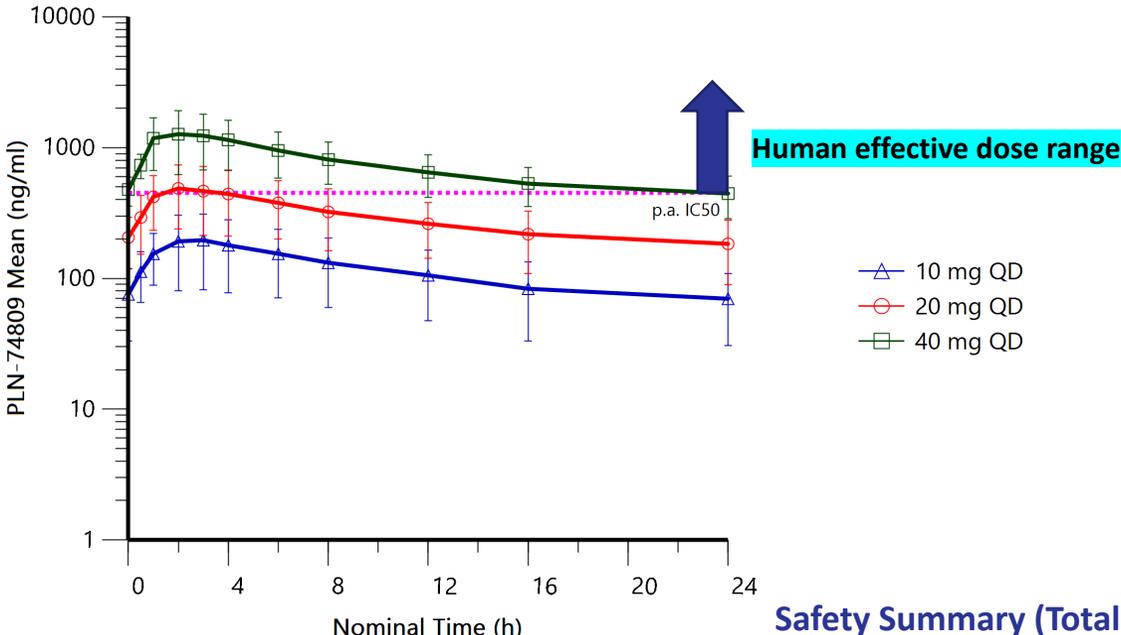
# PLN-74809 – Phase 1a Safety/PK Summary

## High Exposures at Low Doses – Once Daily Dosing

SAD - Summary PK Curves by Cohort



MAD - Summary PK Curves by Cohort



**40 mg QD provides 24 hrs exposure in human effective dose range**

Safety Summary (Total AE's)

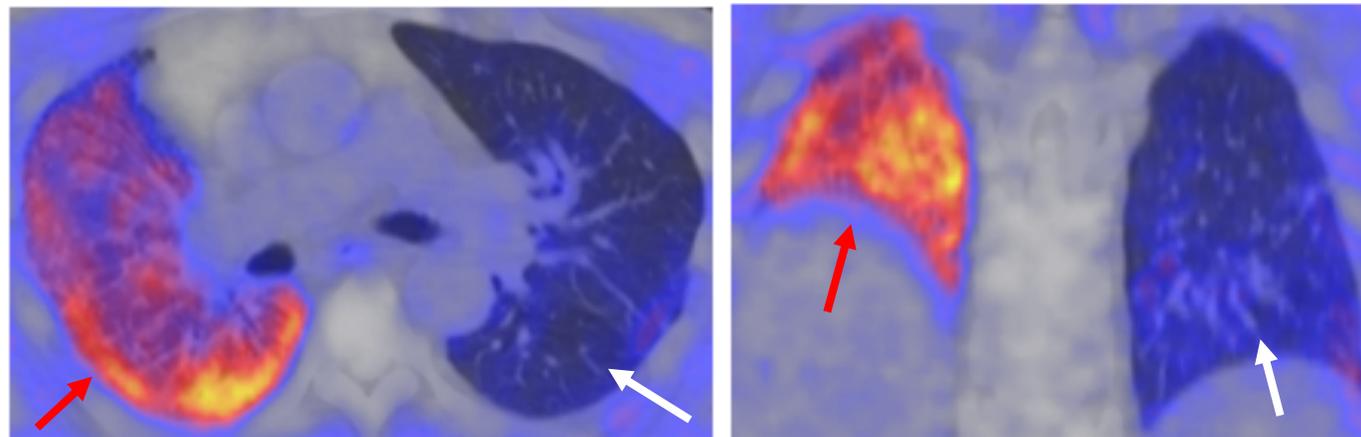
AE	15mg	30mg	50mg	75mg
Grade 1	--	3*	--	--
Grade 2	--	--	--	--
Grade 3	--	--	--	--
Grade 4	--	--	--	--
Grade 5	--	--	--	--

# Pulmonary $\alpha_v\beta_6$ PET Ligand Uptake in IPF Patients

## PET Ligand Uptake Confined to IPF Lung in Unilateral Lung Transplant Patient

71-y/o ♂ left lung tx 2016

FEV1 = 1.86 (68%), FVC = 2.31 (56%),

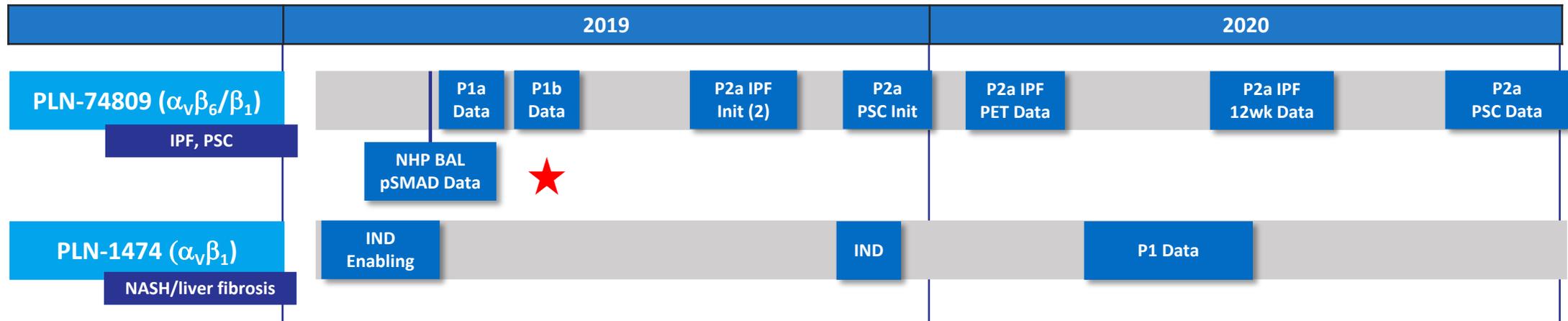


Red arrow: IPF lung  
White arrow: transplant lung

0 SUV 5.5

120' acquisition - 7.5 mCi of [18F]FP-R01-MG-F2

# Key Value Inflection Points 2019 - 2020



## Key Data PLN-74809

- Phase 1a (April/May 2019): safety/tolerability; pharmacokinetic profile - **COMPLETED**
- Phase 1b (May/June 2019): proof of biological mechanism - predictive biomarker for anti-fibrotic effect - **ONGOING**
- Phase 2a in IPF (1Q2020): safety/tolerability; target engagement (PET); biomarkers (2 separate studies)
- Phase 2a in PSC (4Q2020): safety/tolerability; effect on fibrosis and cholestasis biomarkers

The background is a gradient of blue, transitioning from a lighter shade on the left to a darker shade on the right. There are several abstract white shapes: a large, soft-edged wave-like shape on the left, and a series of parallel lines on the right that curve and flow downwards, resembling a waterfall or a stylized landscape feature.

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