PLIANT

Developing Novel Treatments for Fibrotic Diseases

Corporate Presentation

JANUARY 2022

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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 expected mid-2022
  - Significant clinical derisking: target engagement (PET) and TGF-β pathway inibition (pSmad)
- 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 $385 million raised to date in four financing rounds including June 2020 IPO (Nasdaq: PLRX)
- $221 million cash[1] balance as of September 30, 2021
- Company funded into 2H 2023

1 - Includes cash, cash equivalents and ST investments.

Recent Company Highlights

- **PLN-74809 Phase 2a INTEGRIS-IPF trial enrollment complete**
  - PLN-74809 has been administered to over 450 subjects to date and shown to be well tolerated
  - INTEGRIS-IPF topline data expected mid-2022
- **Positive interim data from PLN-74809 PET imaging target engagement study**
  - PLN-74809 showed target engagement up to 98% in lungs of IPF patients
  - All doses tested achieved target engagement above threshold for predicted antifibrotic activity
- **FDA authorized evaluation of long-term treatment with PLN-74809 at doses up to 320 mg in IPF**
  - No safety concerns identified to date at doses up to 640 mg single dose and 320 mg multiple dose
  - No treatment-related effects in chronic GLP tox, NOAEL set at the highest dose tested
  - Expected 1H 2022 initiation of 6-month Phase 2a trial of PLN-74809 at 320 mg in IPF patients
- **PLN-74809 Phase 2a INTEGRIS-PSC trial on track for full enrollment by mid-2022**
  - INTEGRIS-PSC topline data expected late 2022 / early 2023
- **Early-stage programs in Oncology and DMD advancing toward IND**
  - INDs expected in both indications by YE 2022

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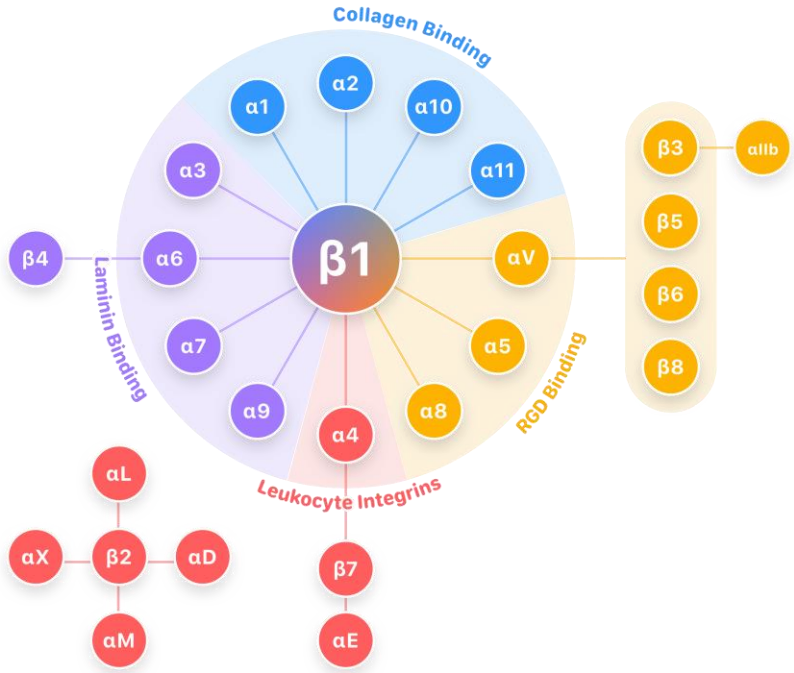
Pliant's Integrin Focused Library
Core Platform for Novel Pipeline and Partner Programs

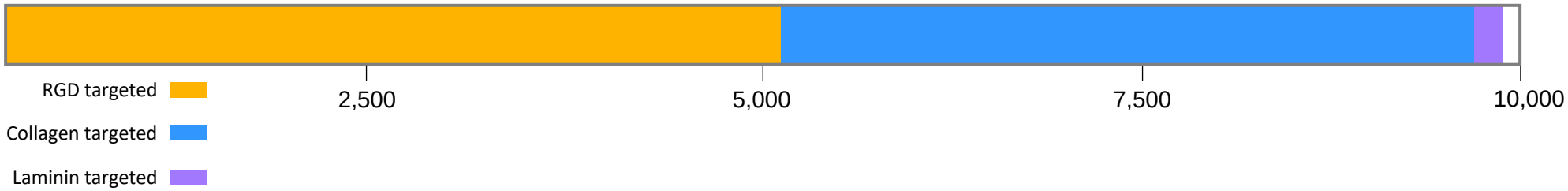
Integrins

- Cell surface receptors that facilitate cell-cell and cell-extracellular matrix adhesion and interaction
- A major path of communication between the extracellular matrix, inflammatory cells, fibroblasts
- Closely involved in signaling processes governing tissue fibrosis

Pliant's proprietary library of integrin binding compounds

- Emphasis on structural diversity
- Broad spectrum of receptor subfamilies including α_V integrins, collagen and laminin binders





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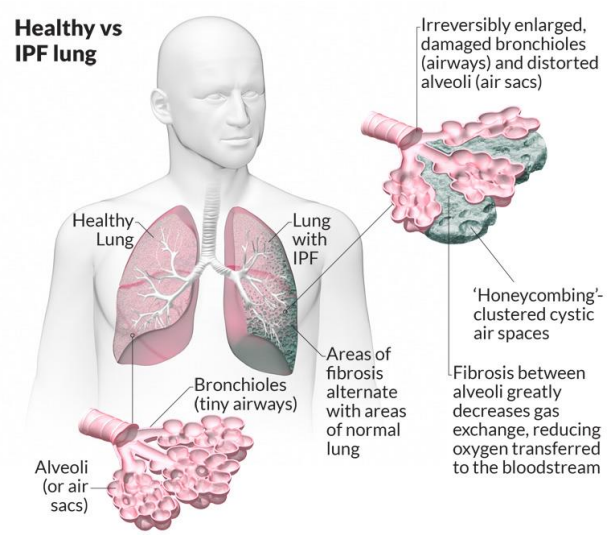
Pliant Development Pipeline

	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	INTEGRIS-IPF Enrollment Complete				Phase 2a Topline Data Expected Mid-2022	PLIANT
		Primary Sclerosing Cholangitis					Phase 2a Enrollment Complete Expected Mid-2022	PLIANT
	Oncology Inhibitor of $\alpha_V\beta_8$	Solid Tumors					IND Filing Expected YE 2022	PLIANT
	Muscular Dystrophies Anti-integrin mAb	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

Fibrosis: The Silent Killer

Idiopathic Pulmonary Fibrosis (IPF) is a lethal pathological process with limited therapeutic options

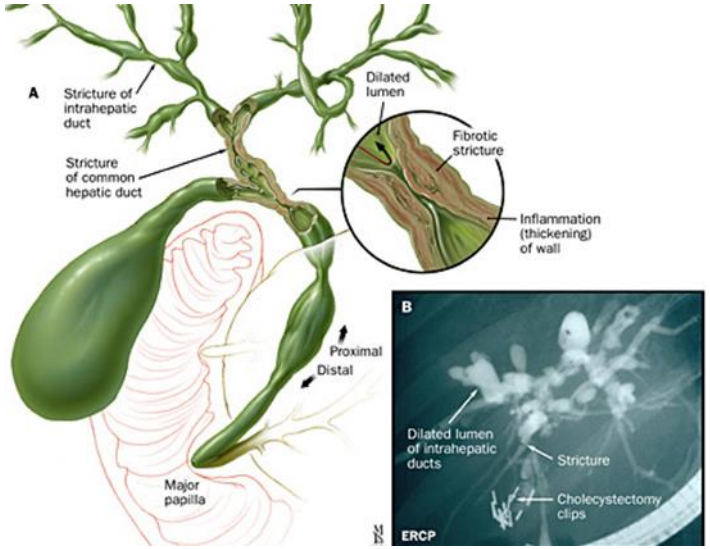
- 140k patients in the U.S.; 30k-40k new cases/year; 40k deaths/year
- **Median survival: 3–5 years -** Worse than some common cancers
- 2 FDA approved therapeutics generate **annual revenues >$3.6 billion** despite significant remaining unmet medical need



https://www.lungsandyou.com/ipf

Primary Sclerosing Cholangitis (PSC) is a progressive inflammatory liver disease resulting in scarring of bile ducts, and cirrhosis

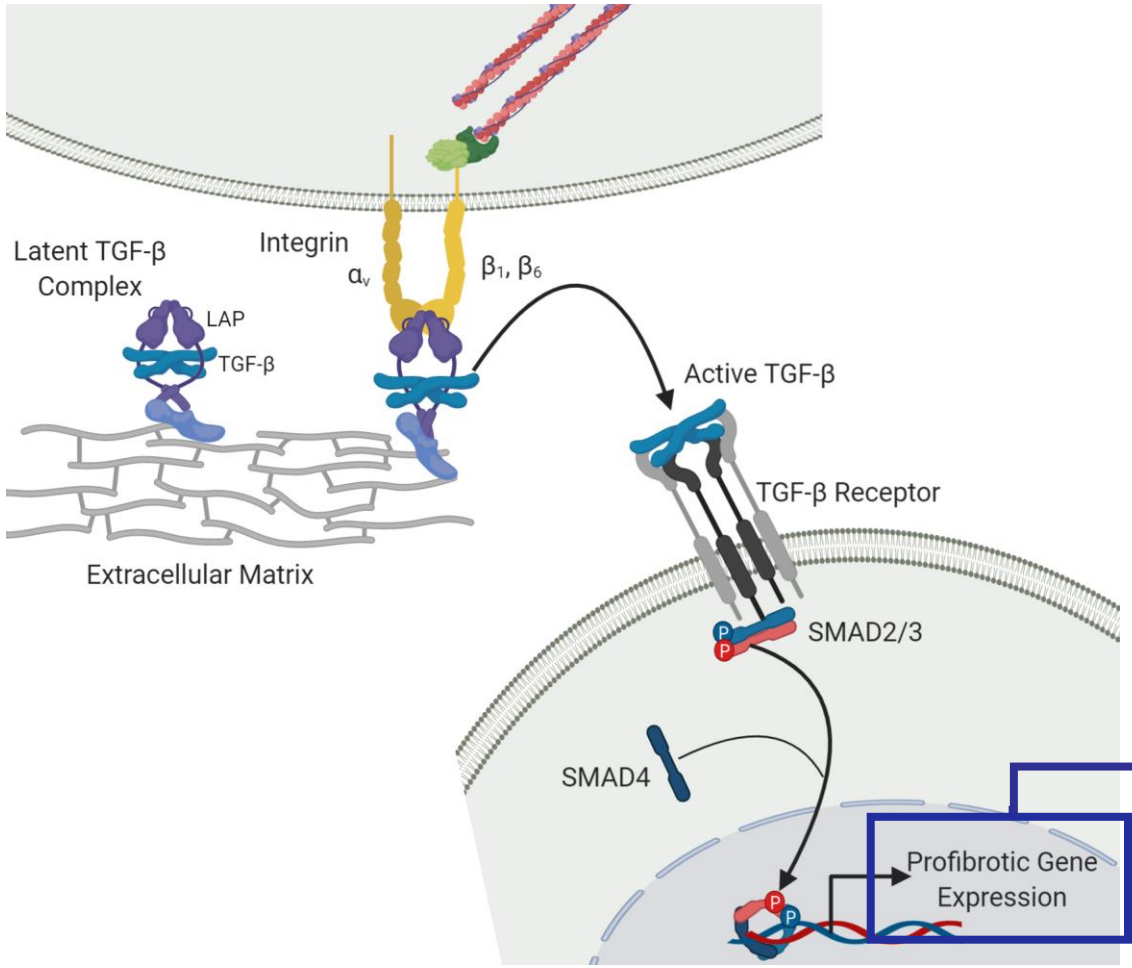
- Currently **no FDA approved therapeutics**
- 30k-45k patients in the U.S.
- **Median survival: 10-12 years** without intervention



www.jhmicall.org

$\alpha_V\beta_6$ / $\alpha_V\beta_1$ Integrins Drive Cell-Matrix Interactions in Fibrosis

$\alpha_V\beta_6$ / $\alpha_V\beta_1$ Integrins promote fibrosis by TGF-β activation

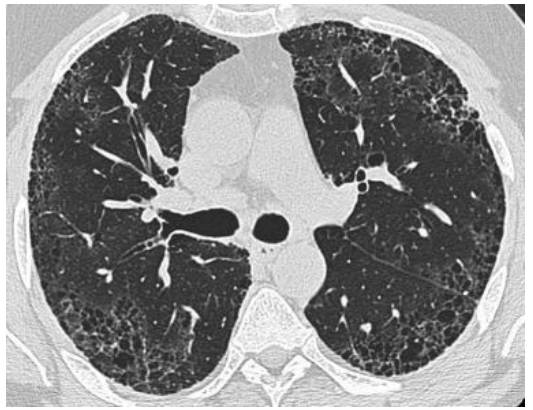


- TGF-β is central mediator of fibrosis
- $\alpha_V\beta_6$ /$\alpha_V\beta_1$ Integrins activate latent TGF-β only in fibrotic tissue
- Systemic TGF-β blockade carries toxicity risks

Selectively blocking TGF-β in fibrotic tissues may provide a low risk, effective antifibrotic approach

Col1a1
Col3a1
Timp1
CTGF
ATX
…

FIBROSIS



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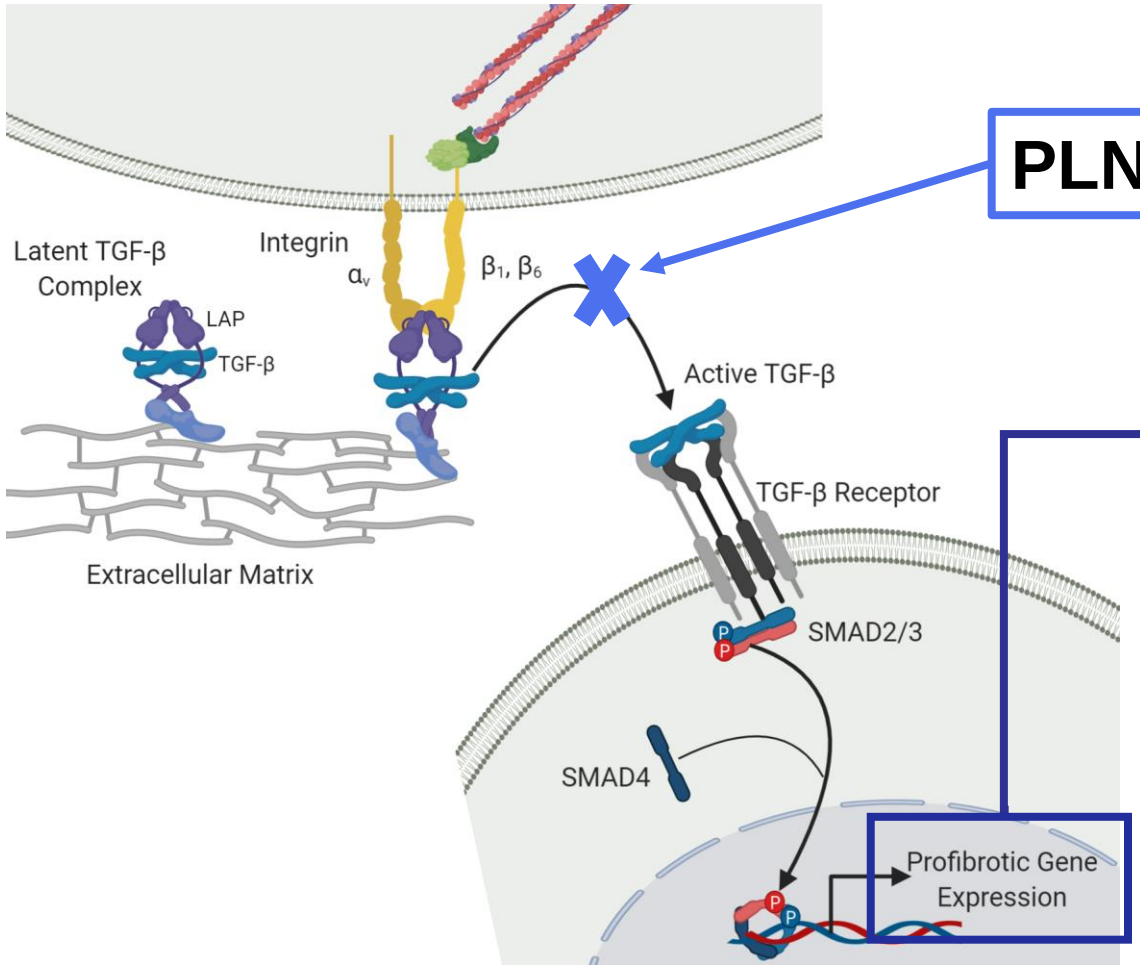
PLN-74809 Provides Profound Antifibrotic Activity through Upstream Inhibition of TGF-β Activation

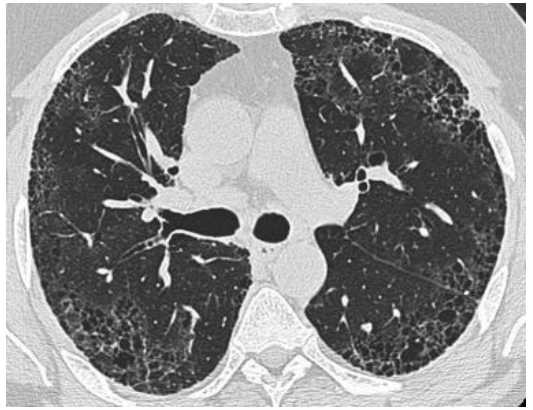


PLN-74809

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 Compounds Have Not Shown Adverse Effects of Systemic Inhibition of TGF-β Pathways[1]

By targeting integrins that are upregulated specifically in fibrotic tissues, Pliant's small molecule compounds may avoid toxicities associated with systemic TGF-β blockade[1]

Affected Organ System	Systemic TGF-β Blockade	Observed with Pliant Compounds?[1]
Cardiovascular System	Cardiotoxicity	No
Immune System	Autoimmunity/Inflammation	No
GI System	Autoimmunity/Inflammation	No
Skin	Keratoacanthomas/SCC	No
Hematology	Thrombocytopenia/Anemia	No

1 - Based on preclinical GLP tox studies as well as clinical trials to date.

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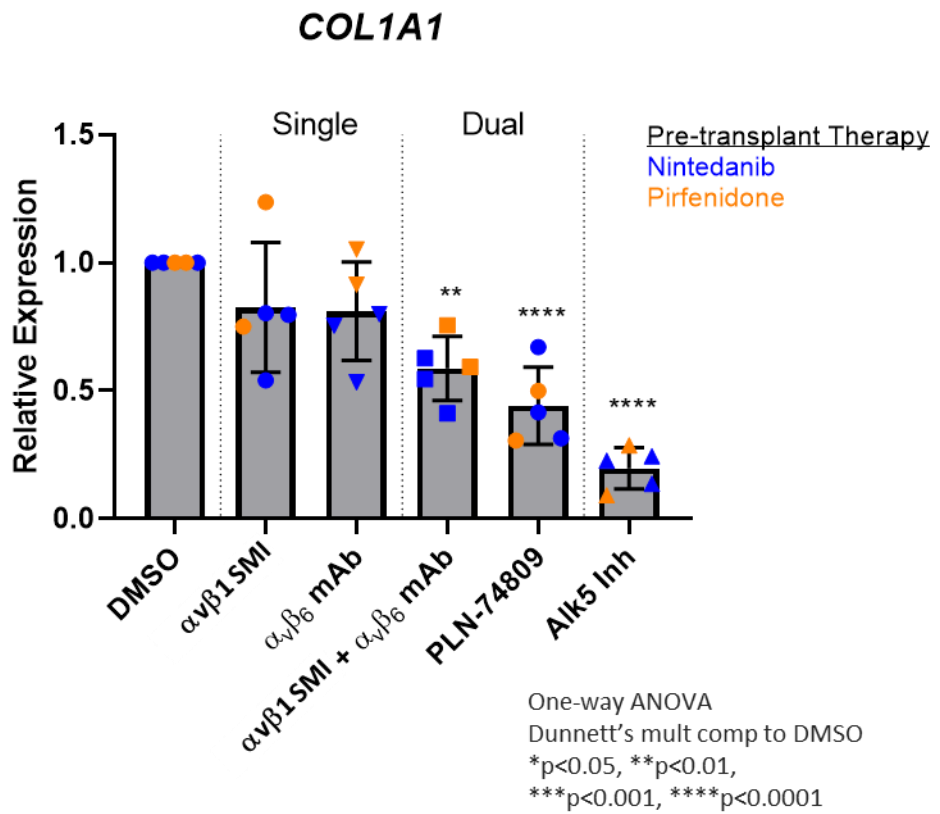
Dual $\alpha_v\beta_6/\alpha_v\beta_1$ Inhibition Blocks COL1A1 Gene Expression More than Single Inhibition in Human IPF Tissue

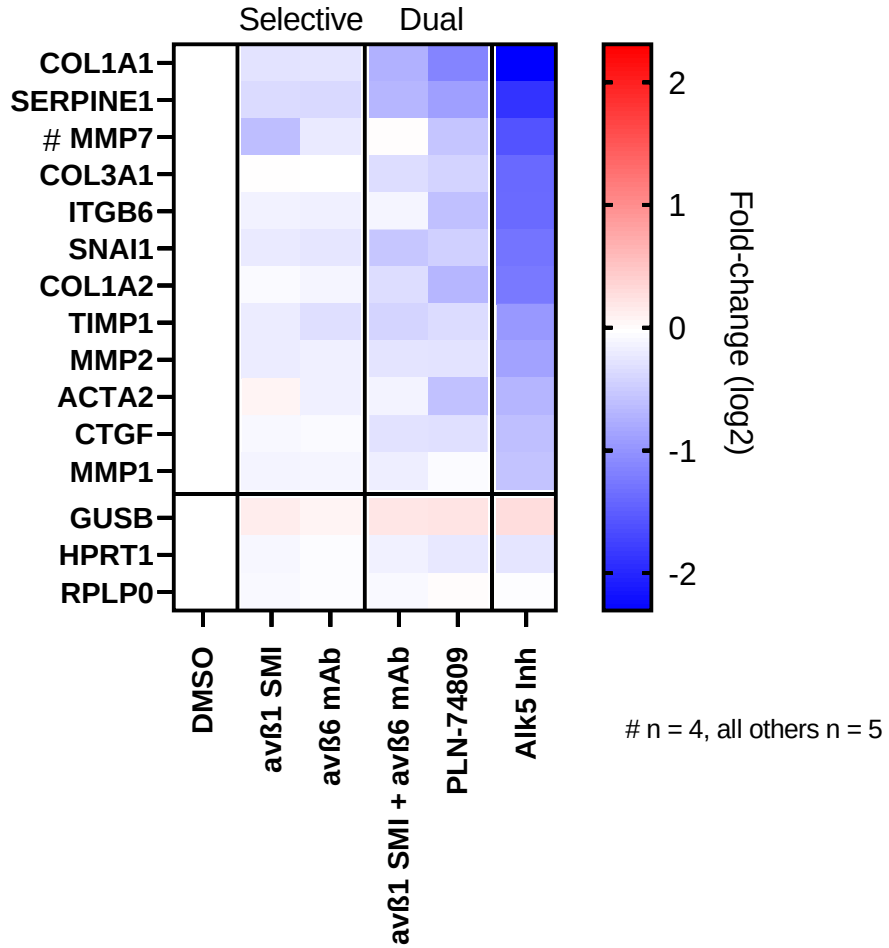
- Ex-planted lungs from 5 IPF patients
- Sliced and cultured for 7 days



One-way ANOVA
Dunnett's mult comp to DMSO
*p<0.05, **p<0.01,
***p<0.001, ****p<0.0001

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

Profibrotic Gene Expression Panel



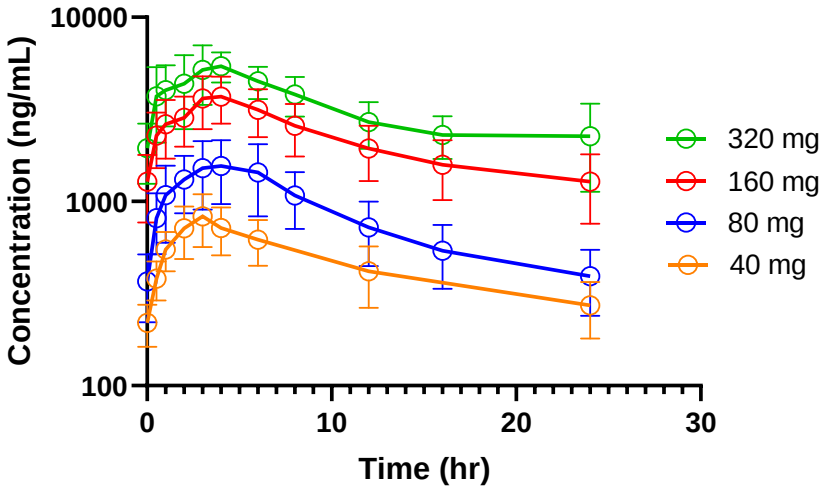
n = 4, all others n = 5

PLN-74809 – Extended Phase 1a Data Summary

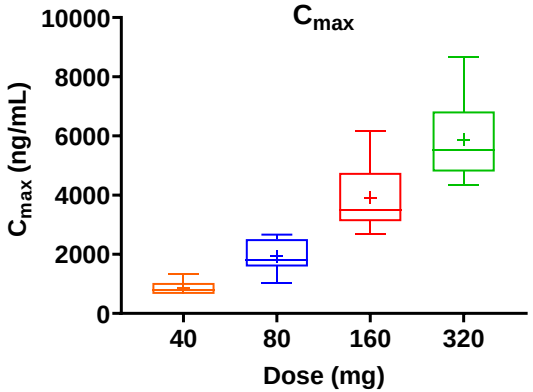
Pharmacokinetics

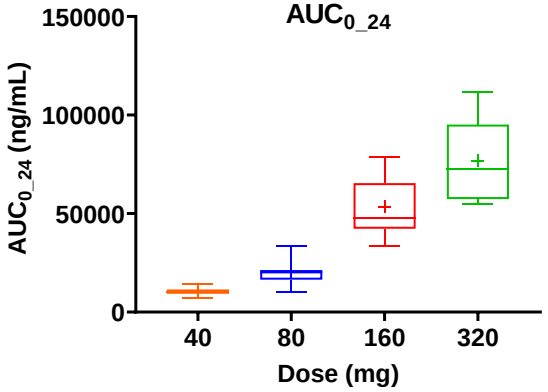
- Well absorbed, orally bio-available
- Long $T_{1/2}$: ~50 hrs – QD dosing

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.

Safety

- Administered to over 450 subjects to date including healthy volunteers and patients
- Generally well tolerated
- Most frequently reported AE in healthy volunteers was headache with no drug-related severe AEs reported

Safety Summary (Participants with drug-related TEAEs)

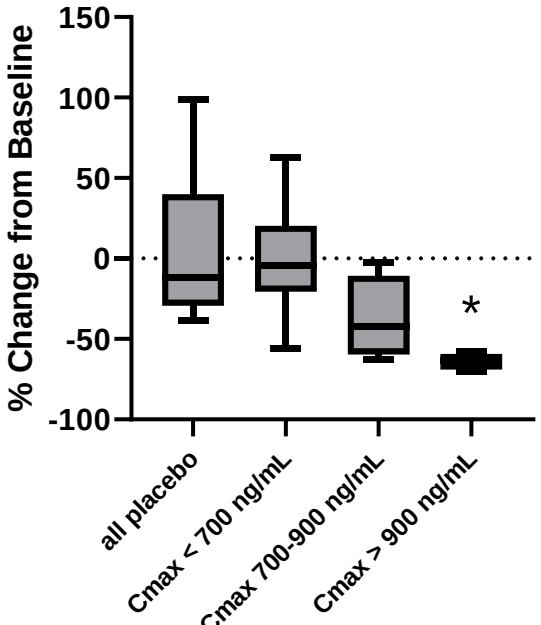
Multiple Ascending QD Doses						
	10 mg (N=9)	20 mg (N=9)	40 mg (N=9)	80 mg (N=8)	160 mg (N=16)	320 mg (N=8)
AE SEVERITY						
Mild	--	11%	--	13%	19%	25%
Moderate	--	--	--	25%	6%	--
Severe	--	--	--	--	--	--

PLN-74809 – Phase 1b Proof of Biological Mechanism

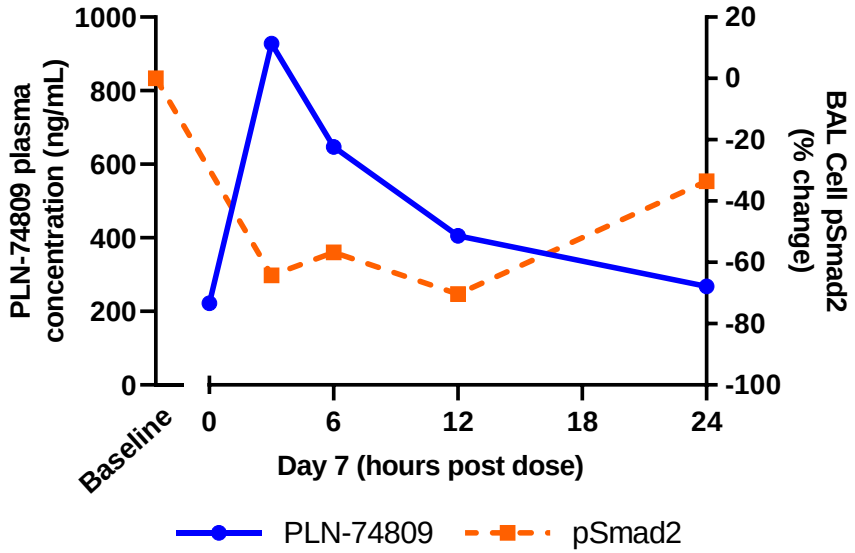
Strong PK/PD Relationship – C_{max} above IC_{50} Results in Predicted Biological Effect

Data Presented June 2019

Alveolar pSMAD2/SMAD2 (all time points)



Mean PK/PD Response in Subjects with Cmax > 700ng/mL



* = p < 0.05 vs placebo and Cmax < 700 ng/mL group

Phase 1b Study Investigating Higher Doses – Data Expected in 1Q2022

Data from this study and the PET target engagement trial evaluate 80, 160 or 320 mg to demonstrate the relationship between:

PLN-74809 plasma exposure

▼

PLN-74809 target engagement

▼

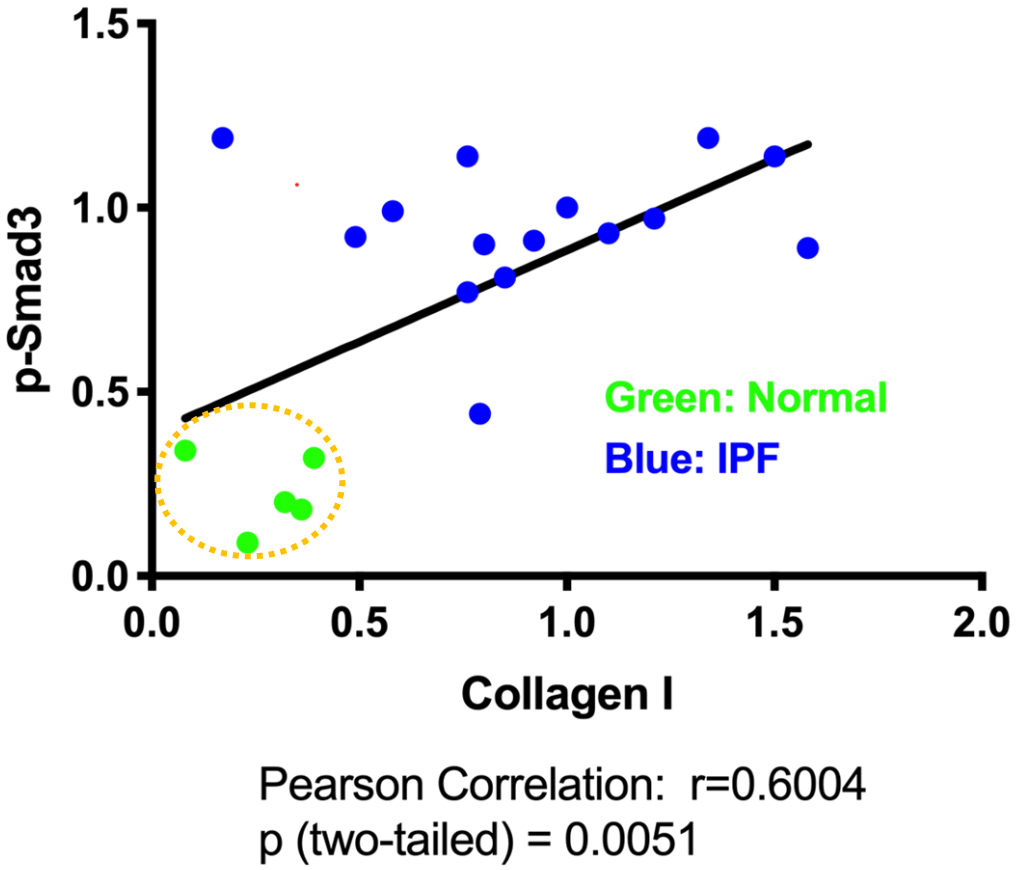
TGF-β signaling inhibition

▼

Antifibrotic activity

Tissue pSMAD Levels Are Highly Significantly Correlated with Extractable Collagen Levels in Normal and Fibrotic Lungs

Reduction in Pulmonary pSMAD Appears to Be a Marker for Reduction of Fibrosis



- Diagnostic open lung biopsies from 10 patients with ILD and suspected IPF
- 2-3 distinct lung regions sampled from each patient
- 5 controls (non-transplanted lungs)
- Total pSMAD3 had a strong correlation vs. extractable Collagen I (Western Blot)

Adapted from Chapman HA et al. March 12, 2020; 382:1068-1070

The NEW ENGLAND JOURNAL of MEDICINE

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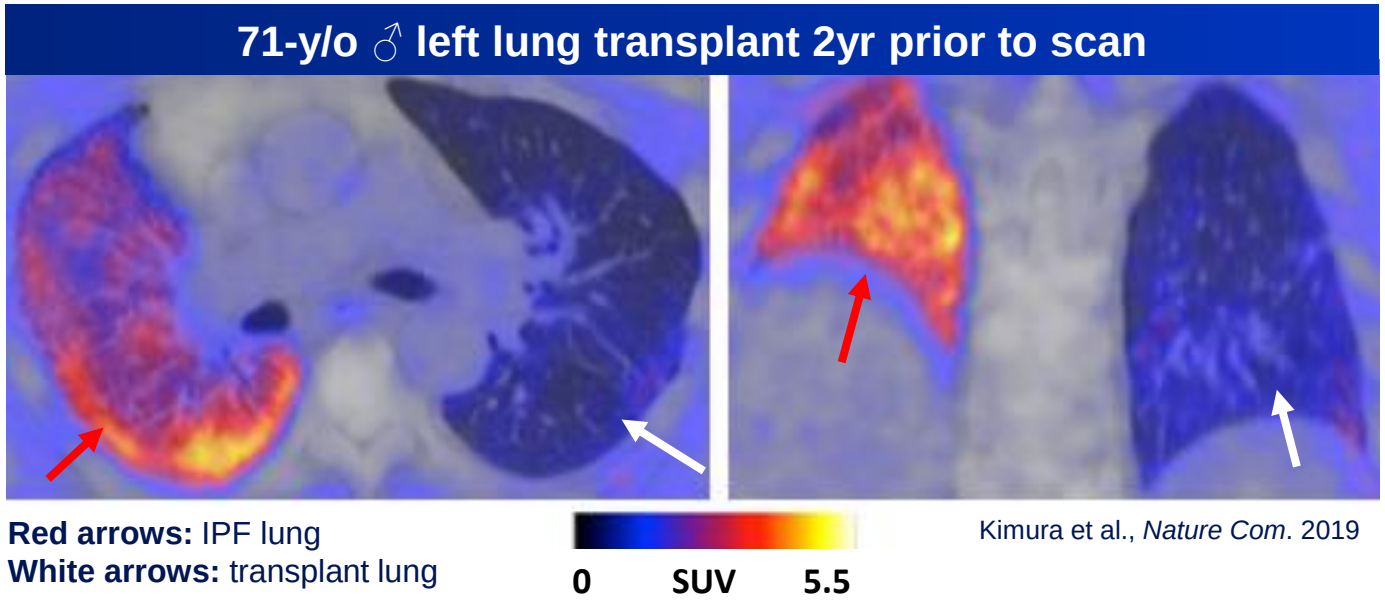
Phase 2a PET Trial – $\alpha_v\beta_6$ Expression Measured by a PET Ligand is Correlated with Extent of Fibrosis in IPF

TRIAL DESIGN

- Single-site open-label trial at Stanford University
- Adults with IPF diagnosis (n=12) and FVC ≥ 45% of predicted
- Patients receive single oral dose of PLN-74809 with PET scans prior to dosing and at T_{max} post dose
- Dose cohorts being evaluated: 60 mg, 120 mg, 240 mg, and 320 mg

ENDPOINTS

- **Primary**: Evaluation of $\alpha_v\beta_6$ target engagement by PLN-74809 assessed by change in PET tracer uptake following a single oral dose
- **Secondary**: Assessment of safety and tolerability of PLN-74809 in IPF patients
- **Exploratory**: Relationship between PLN-74809 systemic exposure and positron emission tomography (PET) imaging and biomarkers in IPF participants



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

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Phase 2a PET Trial in IPF – Interim Analysis Methodology

- **PET scan acquisitions at baseline (no drug) and after drug administration (4 hours post-dose)**
  - 1 week interval between baseline and post-dose PET scan acquisition
- **Administration of a single dose of PLN-74809: 60 mg – 120 mg – 240 mg – 320 mg**
- **Interim PK and target engagement data from 6 dose administrations in 4 patients**
  - 2 out of 4 patients received one single dose
  - 2 out of 4 patients received two single doses with at least a 2-week washout interval between doses

	60 mg	120 mg	240 mg	320 mg
Patient 1	x			
Patient 2		x	x	
Patient 3			x	x
Patient 4				x

- **All patients on standard of care therapy (nintedanib)**
- **Image analysis for target engagement in highly fibrotic regions of the lungs**

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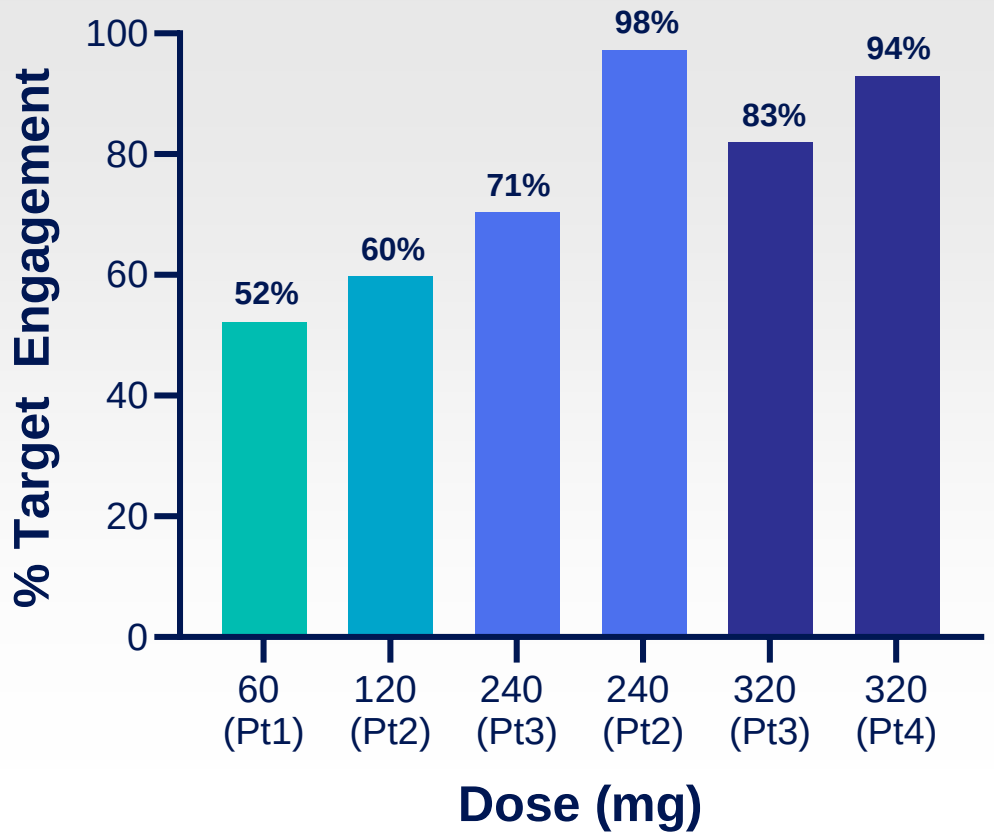
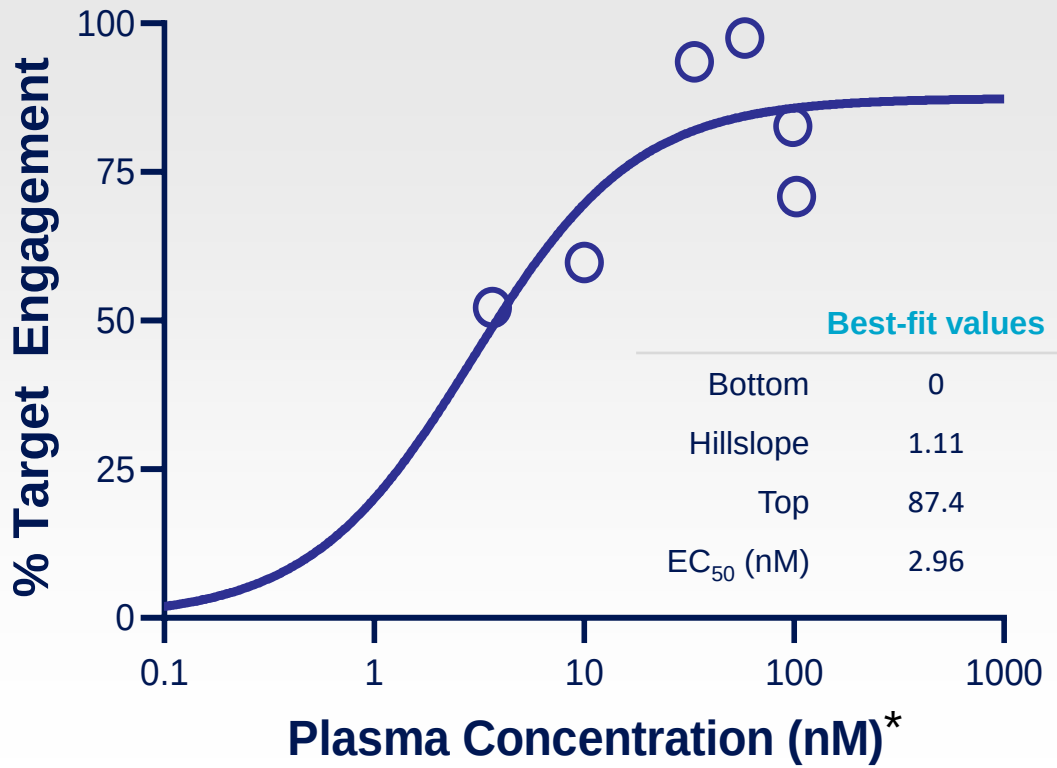
Dose and Plasma Concentration Dependent Target Engagement

Dose-Dependent Target Engagement



Plasma Conc-Dependent Target Engagement



* Free plasma concentration

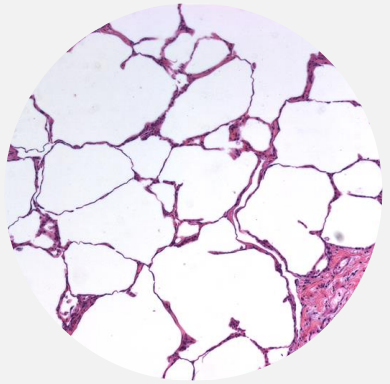
Putting the Interim Phase 2a PET Data into Perspective

Target engagement above the threshold for predicted anti-fibrotic activity across all doses (>50% target engagement)

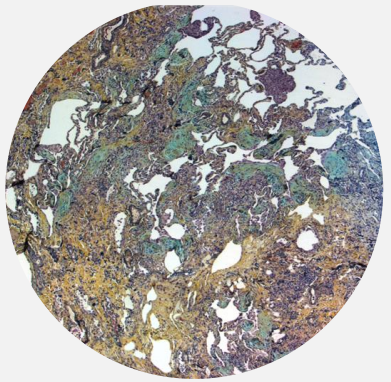
Dose- and plasma concentration-dependent response approaching target saturation at the two highest doses

- PLN-74809 penetrates highly fibrotic areas of the lung
- Potential anti-fibrotic activity of PLN-74809 at clinical doses
- Informs dose selection in Phase 2b trials and beyond
- Provides robust PK/PD model to predict exposure-response relationship

NORMAL LUNG



IPF LUNG



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PLN-74809-IPF-202 [INTEGRIS-IPF]
Phase 2a Global Safety-PK-Exploratory Efficacy Trial in IPF

Enrollment Complete with Topline Data Expected Mid-2022

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=21)
- PLN-74809 40 mg (n=21)
- PLN-74809 80 mg (n=21)
- PLN-74809 160 mg (n=21)

PRIMARY AND SECONDARY ENDPOINTS

- Safety, tolerability, PK

EXPLORATORY ENDPOINTS

- Change in FVC over 12 weeks
- High Resolution CT-based Quantitative Lung Fibrosis (QLF) imaging
- Effect on selected biomarkers

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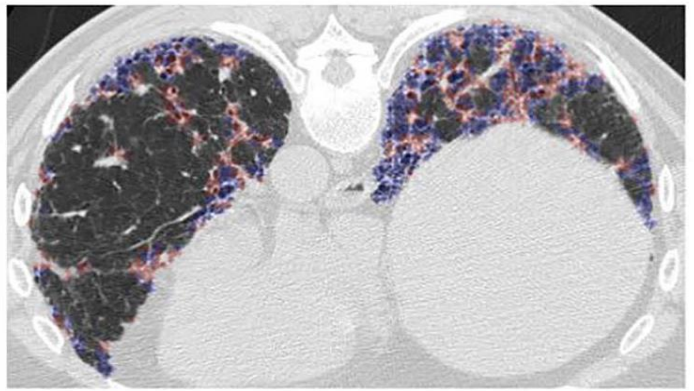
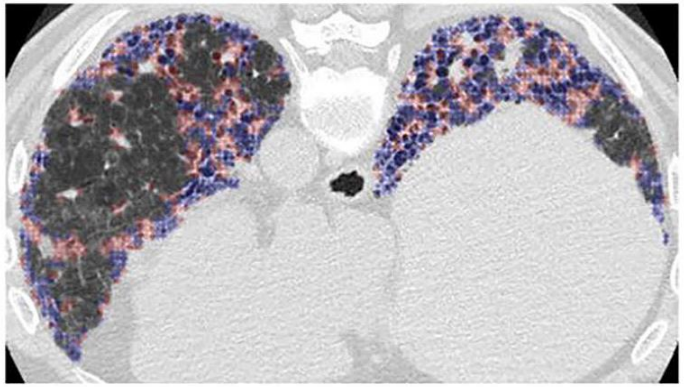
Quantitative Lung Fibrosis (QLF): A Sensitive Measure of FVC Change Over Time in IPF

- **QLF: a computed tomography (CT) biomarker**
  - Assessment via high resolution CT imaging
    - Standardized and centralized image analysis
  - QLF is an automated quantification of lung fibrosis
    - 94.4% sensitivity and 94.7% specificity
    - Fibrosis presence/ absence detected at threshold level of 1%[1]
- **QLF is a sensitive measure of change over time in IPF**
  - A change of 2% in QLF from baseline correlates with a clinically meaningful worsening or improvement of FVC
  - Moreover, clinically meaningful changes in FVC are associated with statistically significant changes in QLF[2,3]
- **Inverse correlation with:**
  - Percent predicted FVC at 6 & 12 months[3,4]
  - Percent predicted DLCO
  - Progression Free Survival (PFS)

Screening



Week 26



ΔFVC= -24%; ΔQLF= 7.8%; ΔSOBQ= 30

Representative coronal and axial HRCT images from a placebo arm participant in the BMS-986020 P2a study at screening and week 26. Change over 26 weeks: FVC: −24%; QLF score: 7.8%. Classification overlay for QLF score is in blue and red.[3]

DLCO – diffusion capacity for carbon monoxide; FVC, forced vital capacity

[1] H.Kim and J Goldin et al. *Acad Radiol*;22:70-80; 2015
[2] Kafaja et al. *AJRCCM*;197:644–652, 2018
[3] Kim et al.*Ther Adv Respir Dis;* 15: 1–11, 2021
[4] Richeldi et al. *Lancet Respir Med* 2020; 8: 25–33

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PLN-74809-PSC-203 [INTEGRIS-PSC]
Phase 2a Global Safety-PK-Fibrosis and Cholestasis Biomarker Trial in PSC

Enrollment Expected to be Completed by Mid-2022

KEY INCLUSION/EXCLUSION CRITERIA

- Adults with large duct PSC
- Pre-cirrhotic/no hepatic impairment
- Stratified for UDCA use

Randomization 3:1 (PLN-74809:placebo)

- Placebo (n=21)
- PLN-74809 40 mg (n=21)
- PLN-74809 80 mg (n=21)
- PLN-74809 160 mg (n=21)

PRIMARY AND SECONDARY ENDPOINTS

- Safety, tolerability, PK

EXPLORATORY ENDPOINTS

- Effect on fibrosis biomarkers (e.g., Pro-C3, ELF)
- Change in ALP over 12 weeks
- Imaging

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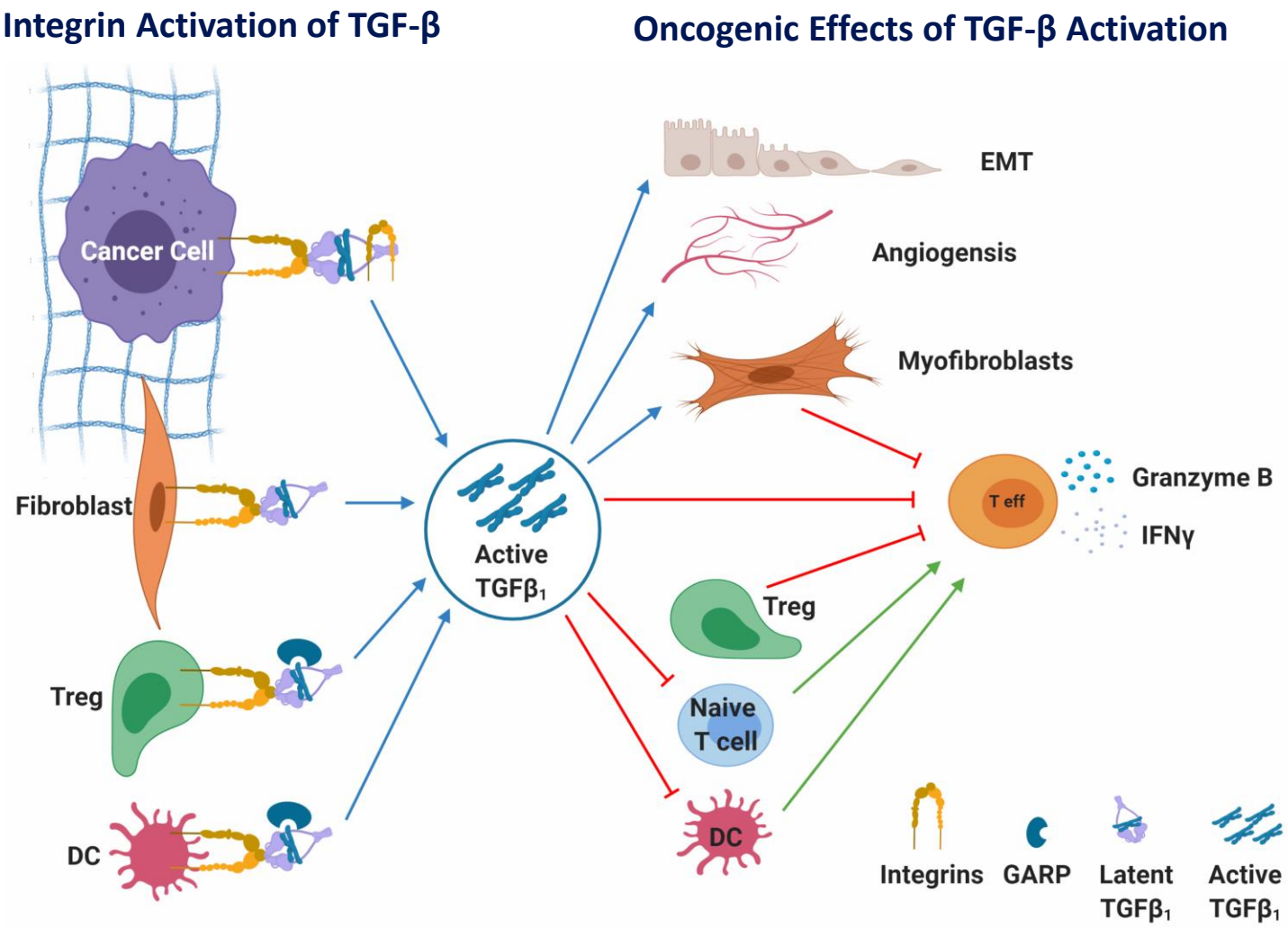
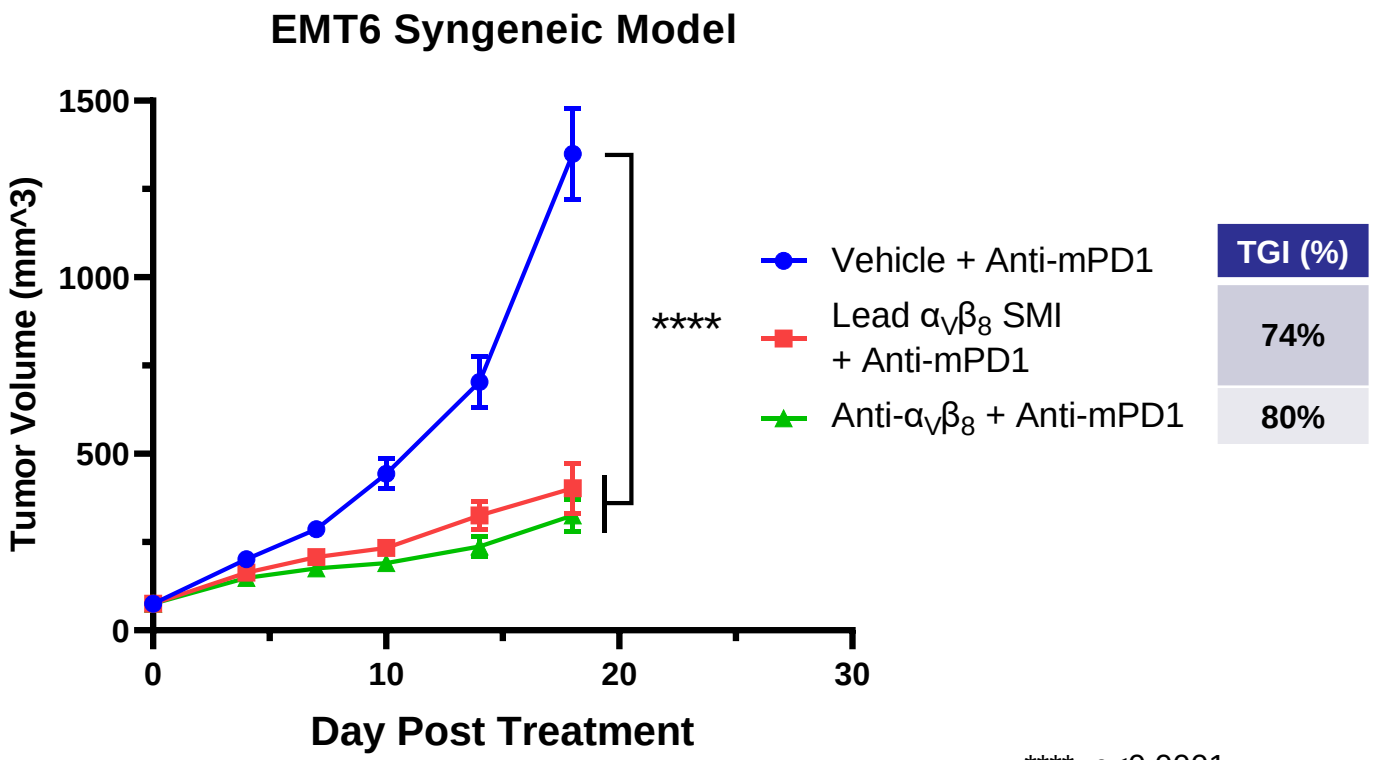
Pliant’s Integrin-Based Oncology Program

Activated TGF-β Contributes to Immune Exclusion & Evasion, Tumor Metastasis and Angiogenesis

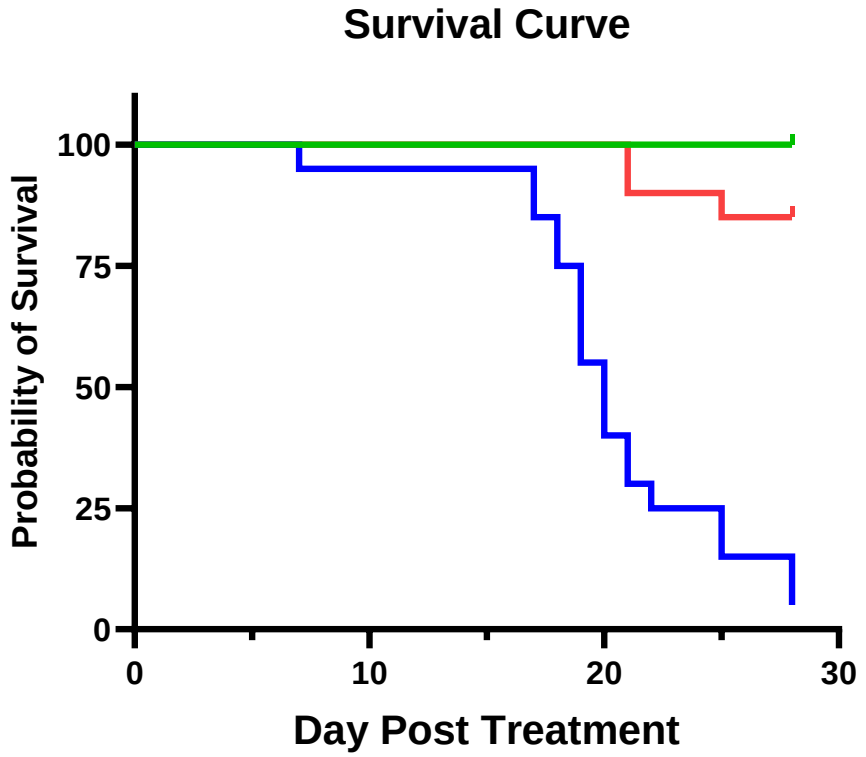
- **Integrins activate TGF-β on cancer cells and multiple cell types in the tumor micro-environment**
- **This leads to immune suppression and resistance to I/O therapies**
- **Selectively inhibiting integrin binding to latent TGF-β complex has potential to:**
  - Safely block TGF-β activation
  - Enhance efficacy of multiple checkpoint inhibition pathways



$\alpha_V\beta_{8/1}$ Inhibitor/ Anti-PD-1 Combo Reduced Tumor Burden and Increased Survival in Preclinical Models vs. Anti-PD-1 Alone

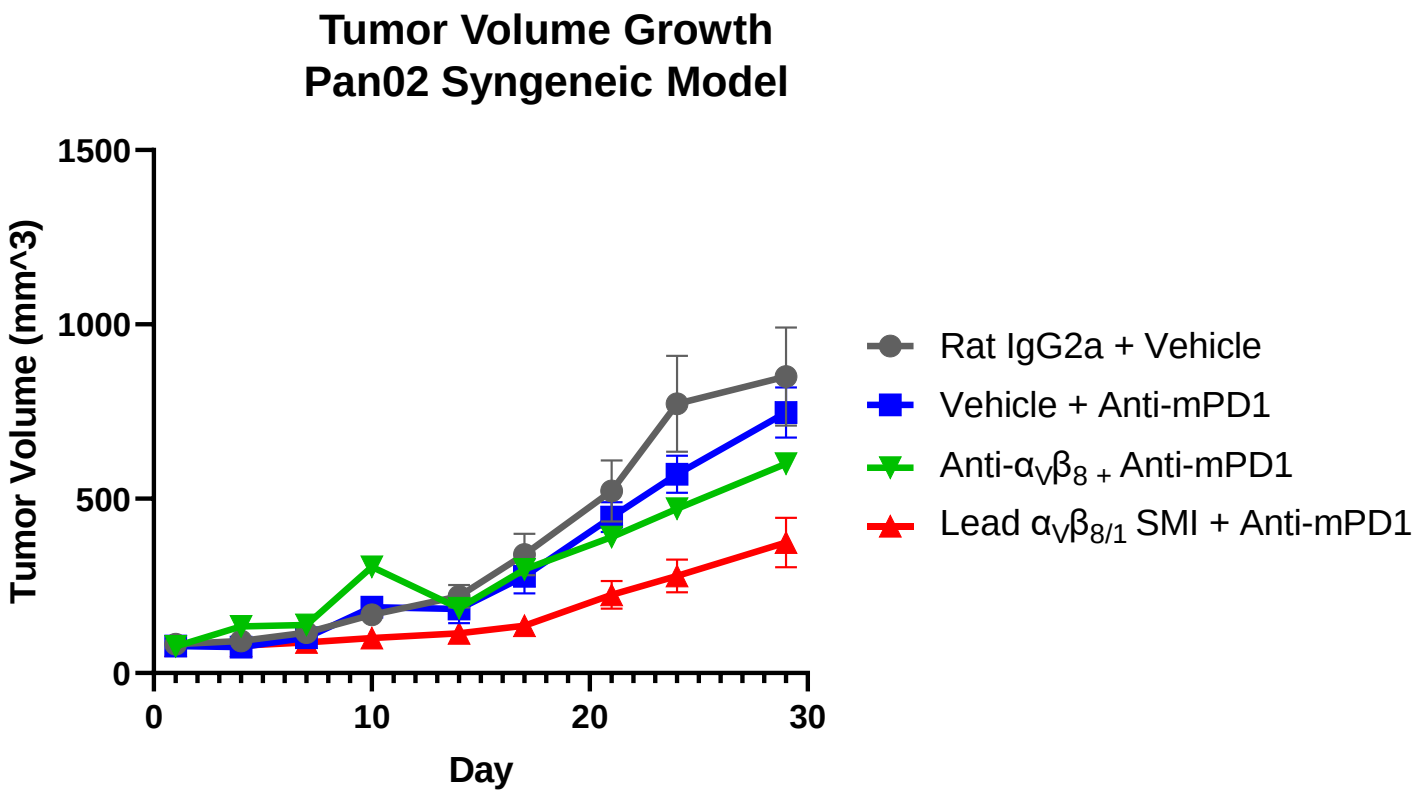


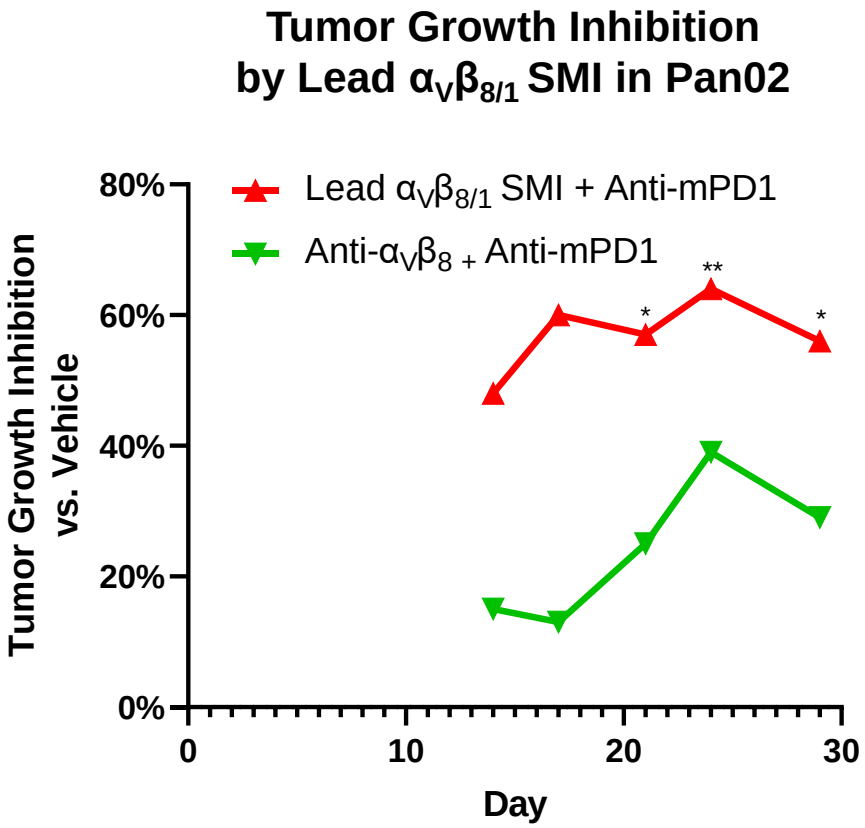
**** p<0.0001



EMT6 Model, N=20 per arm

Lead $\alpha_V\beta_{8/1}$ Inhibitor Superior to Clinical-stage $\alpha_V\beta_8$ Antibody in Pan02 Pancreatic Mouse Syngeneic Model





* p<0.05 vs. vehicle + rat IgG2a
** p<0.01 vs. vehicle + rat IgG2a

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Selective Muscle Cell Integrin Agonism for the Treatment of Muscular Dystrophies

Pliant's Muscular Dystrophy Program – Overview

Targeting an integrin receptor on the muscle cell surface

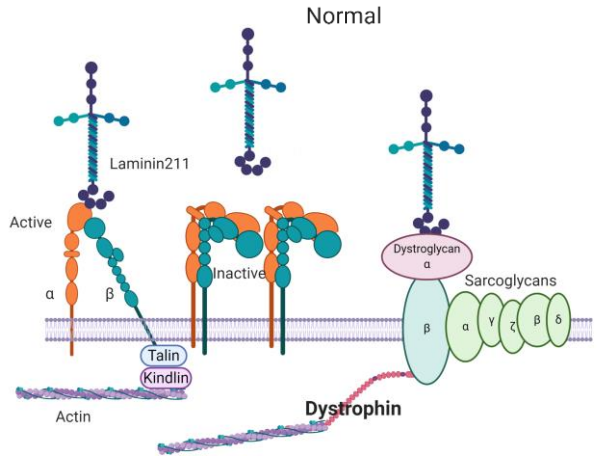
- Integrin target is upregulated as a **compensatory mechanism** in **different types of muscular dystrophy**
- Acts as a **substitute for dystrophin**, helping to stabilize the muscle membrane, decreasing muscle damage
- **Mutations in the target result in human congenital myopathy**

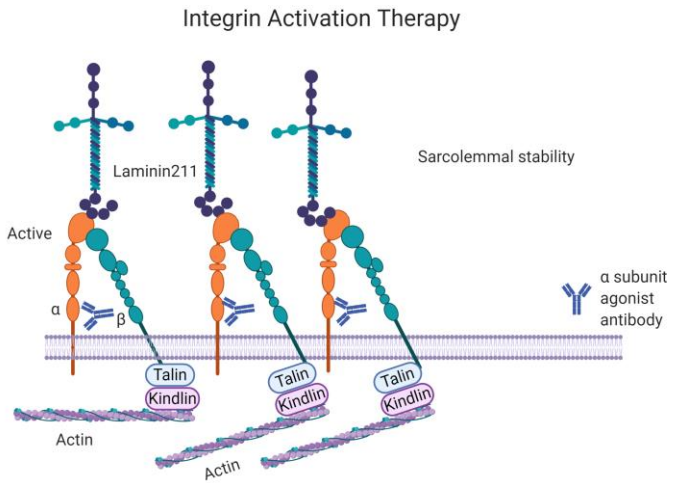
Allosteric agonistic monoclonal antibody

- Activates the target to **augment the compensatory mechanism**

Potential to combine across multiple muscular dystrophy indications

- Target is **upregulated across different forms of muscular dystrophy**
- Mechanism is unrelated to underlying gene mutation
- May be **combined with existing therapies** as well as new modalities (CRISPR, gene therapy,…)





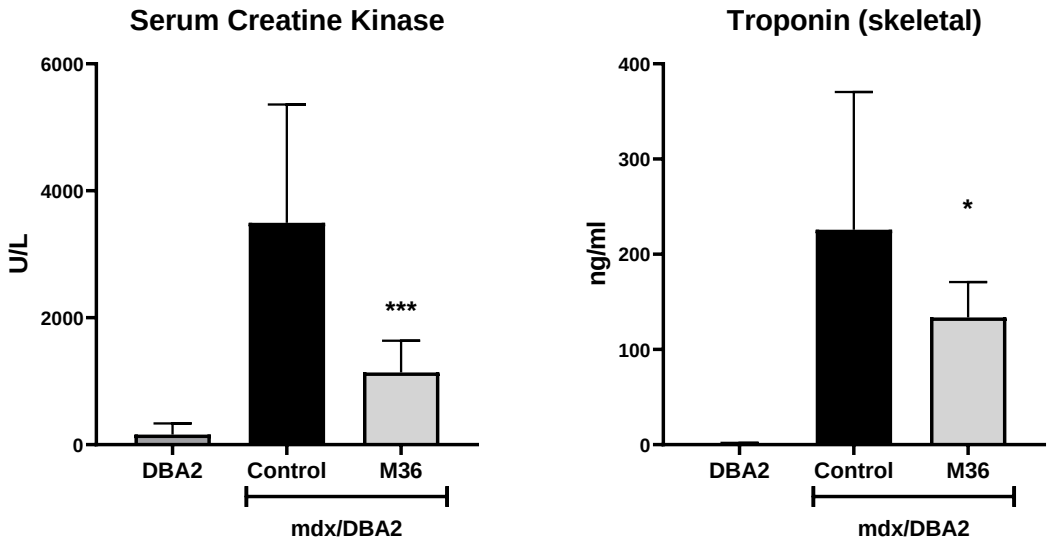
Pliant's mAb Demonstrated Improved Muscle Membrane Integrity and Diaphragm Function in Mouse DMD Model

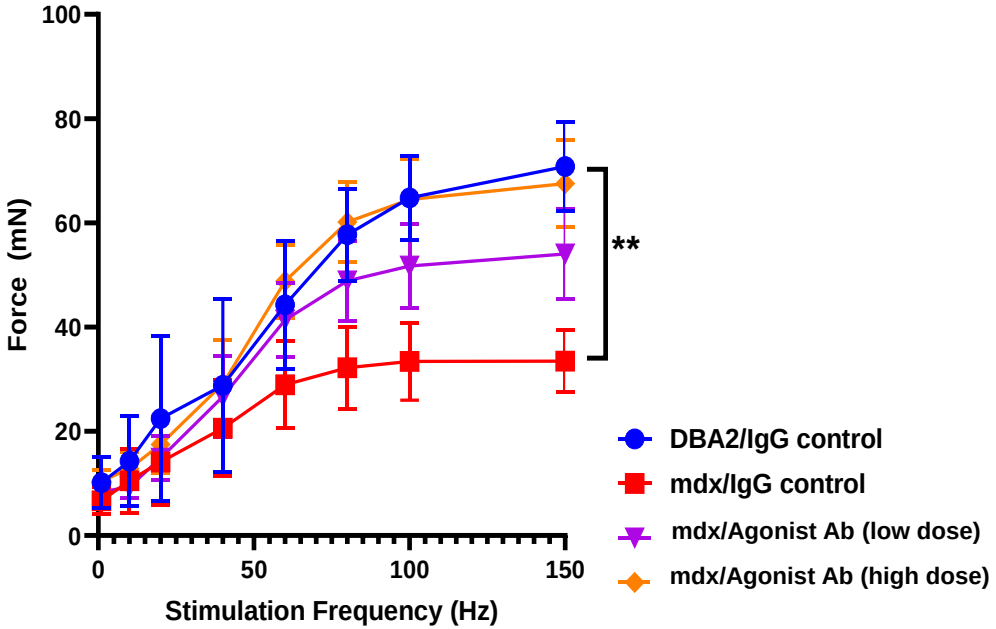
Antibody treatment protected against muscle damage

- Reduction of clinical biomarkers including serum creatine kinase and skeletal troponin

Duchenne muscular dystrophy (DMD) causes progressive wasting of cardiac and respiratory muscles (main cause of death)

- Improvement in diaphragm function is expected to significantly improve patient pulmonary function





Mean +/- SD n=10/group

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	INTEGRIS-IPF Enrollment Complete				Phase 2a Topline Data Expected Mid-2022	PLIANT
		Primary Sclerosing Cholangitis					Phase 2a Enrollment Complete Expected Mid-2022	PLIANT
	Oncology Inhibitor of $\alpha_V\beta_8$	Solid Tumors					IND Filing Expected YE 2022	PLIANT
	Muscular Dystrophies Anti-integrin mAb	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

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Developing Novel Treatments for Fibrotic Diseases

Corporate Presentation

JANUARY 2022