



Developing Novel Treatments for Fibrotic Diseases

40th Annual J.P. Morgan Healthcare Conference

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 inhibition (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 cash¹ balance as of September 30, 2021
- Company funded into 2H 2023

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

Pliant's Integrin Focused Library

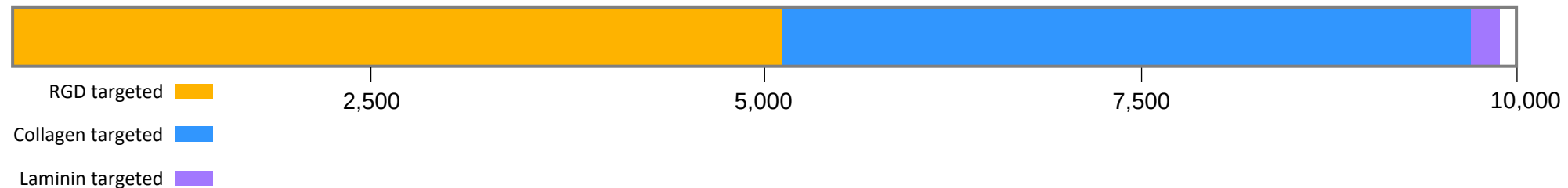
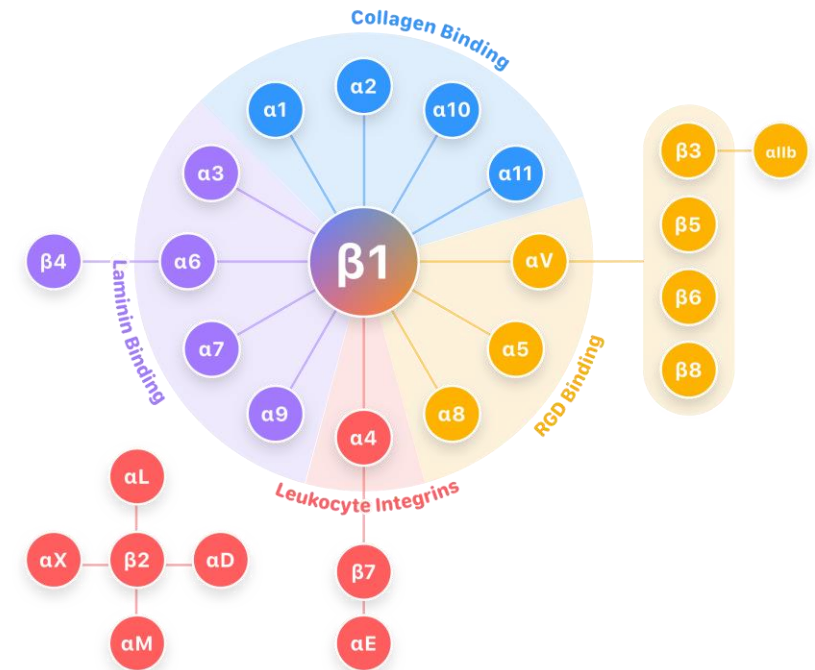
Core Platform for Novel Pipeline and Partner Programs

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

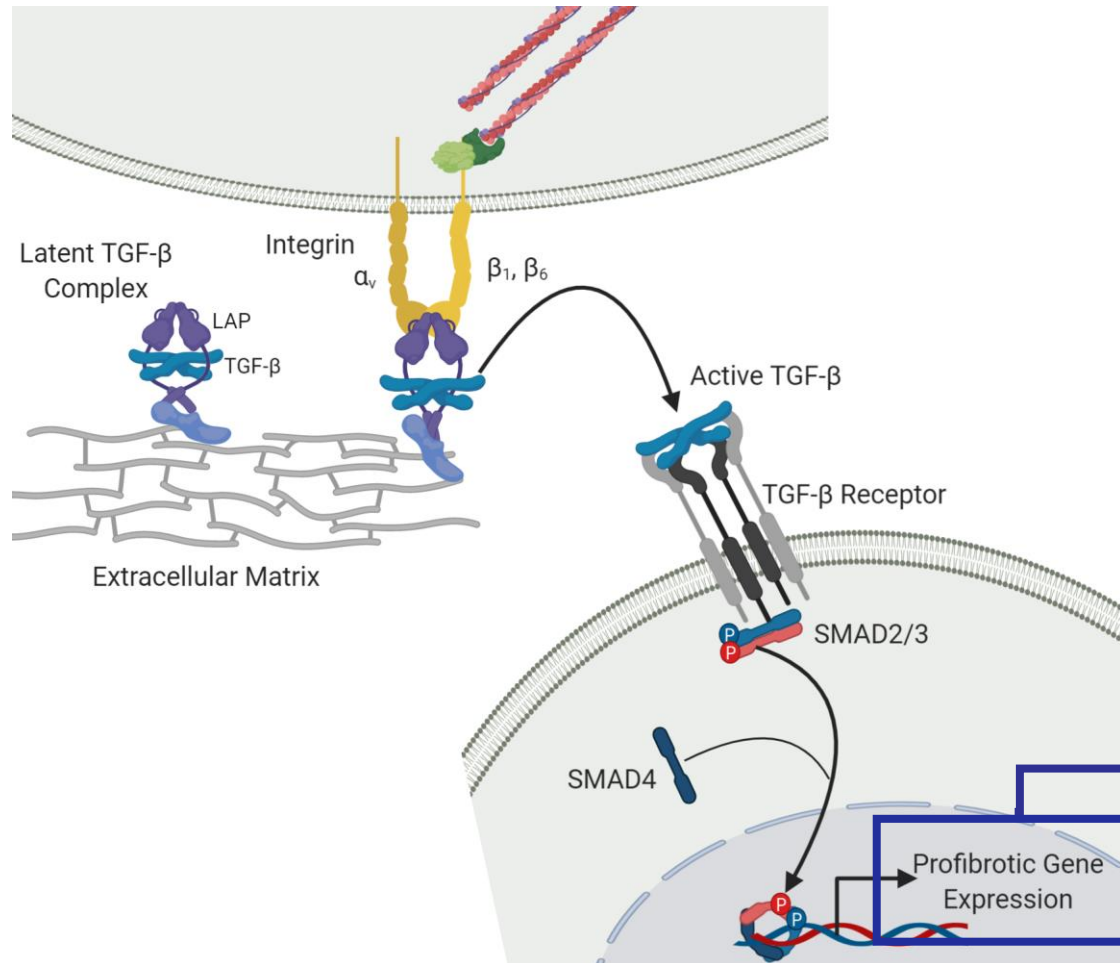


Pliant Development Pipeline

	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

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

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

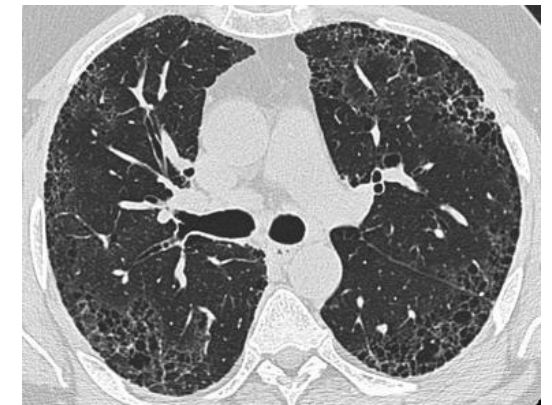


- TGF- β is central mediator of fibrosis
- $\alpha_v\beta_6$ / $\alpha_v\beta_1$ Integrins activate latent TGF- β only in fibrotic tissue
- Systemic TGF- β blockade carries toxicity risks

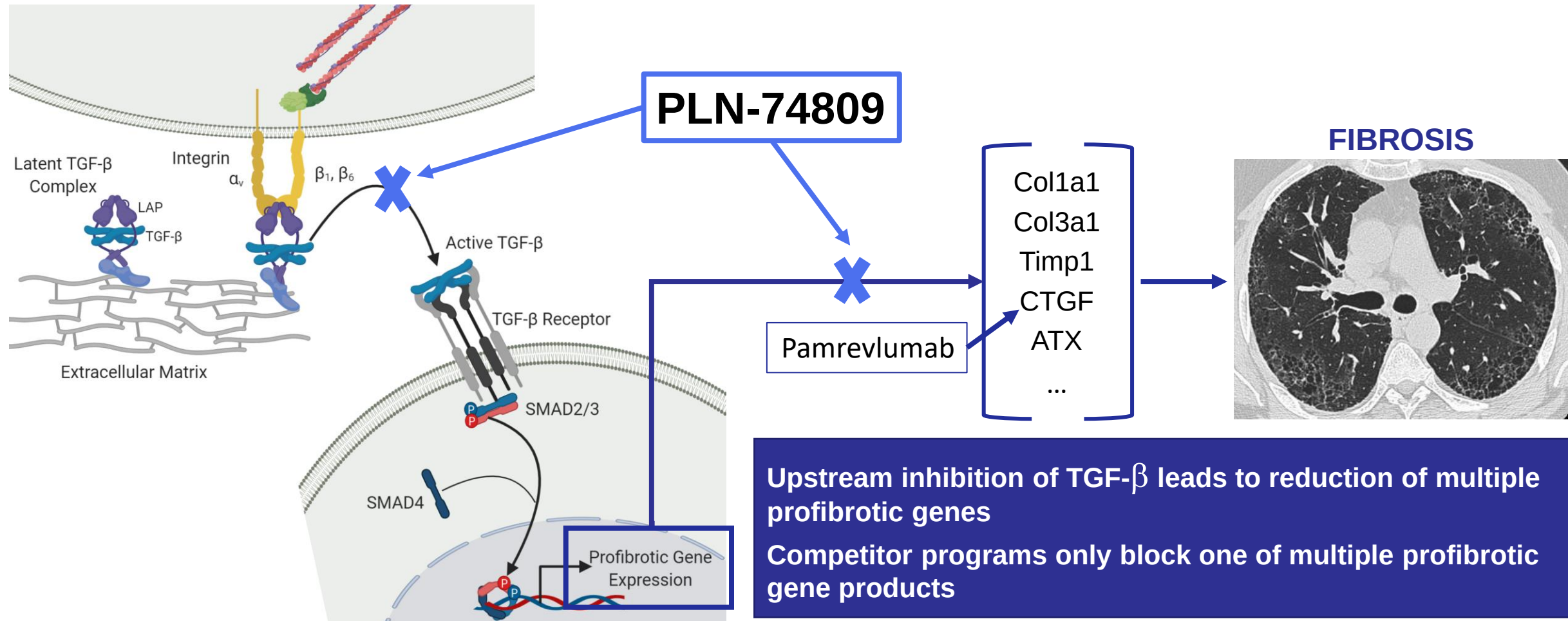
Selectively blocking TGF- β in fibrotic tissues may provide a low risk, effective antifibrotic approach

Col1a1
Col3a1
Timp1
CTGF
ATX
...

FIBROSIS



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



Pliant Compounds Have Not Shown Adverse Effects of Systemic Inhibition of TGF- β Pathways¹

By targeting integrins that are upregulated specifically in fibrotic tissues, Pliant's small molecule compounds may **avoid toxicities associated with systemic TGF- β blockade¹**

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

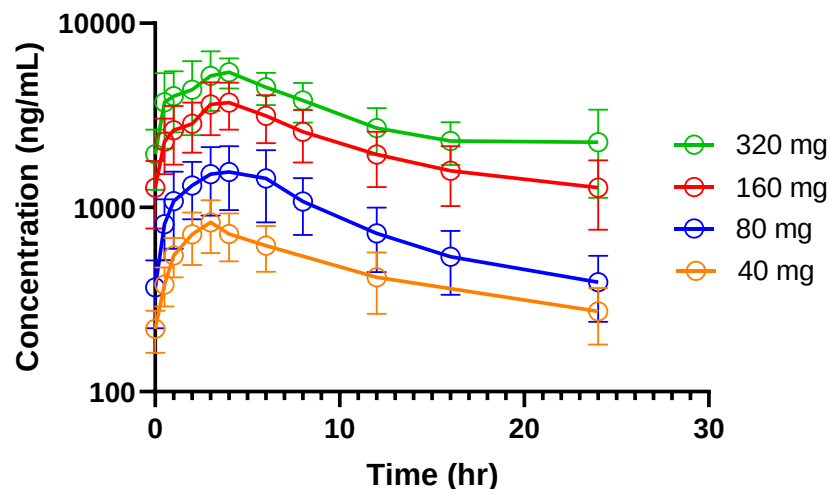
1 - Based on preclinical GLP tox studies as well as clinical trials to date.

PLN-74809 – Extended Phase 1a Data Summary

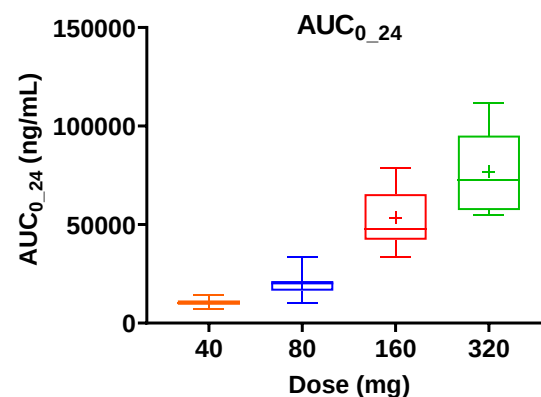
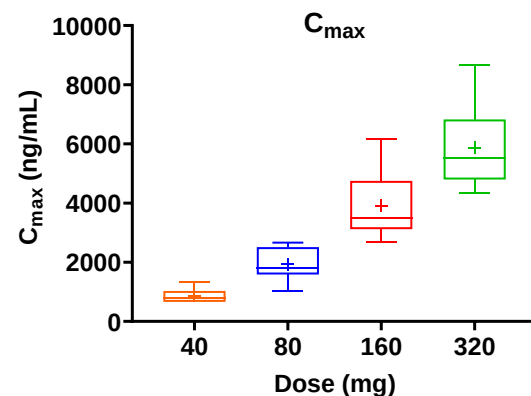
Pharmacokinetics

- 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)

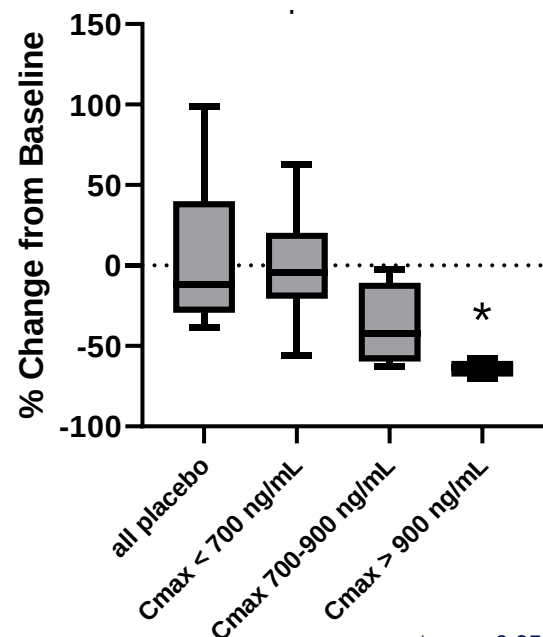
Multiple Ascending QD Doses						
	10 mg (N=9)	20 mg (N=9)	40 mg (N=9)	80 mg (N=8)	160 mg (N=16)	320 mg (N=8)
AE SEVERITY						
Mild	--	11%	--	13%	19%	25%
Moderate	--	--	--	25%	6%	--
Severe	--	--	--	--	--	--

PLN-74809 – Phase 1b Proof of Biological Mechanism

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

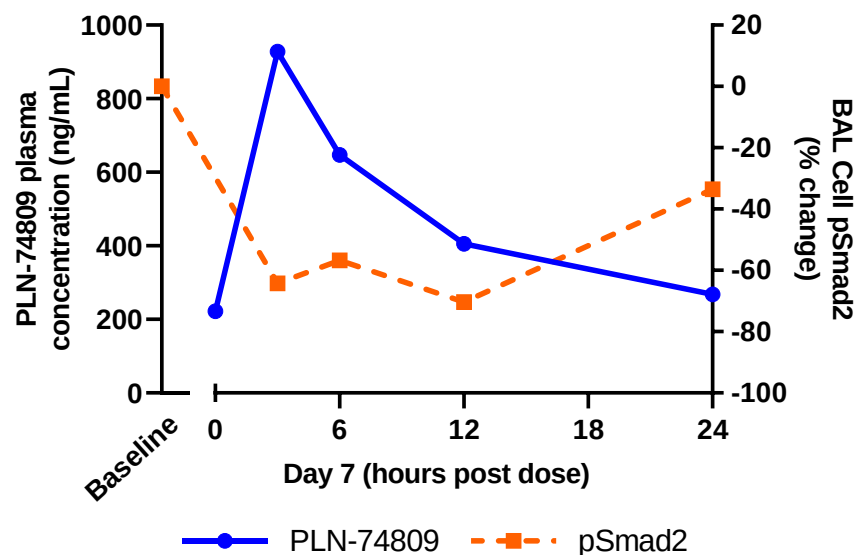
Data Presented June 2019

Alveolar pSMAD2/SMAD2
(all time points)



* = $p < 0.05$ vs placebo
and $C_{\max} < 700$ ng/mL group

Mean PK/PD Response in Subjects with
 $C_{\max} > 700$ ng/mL



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

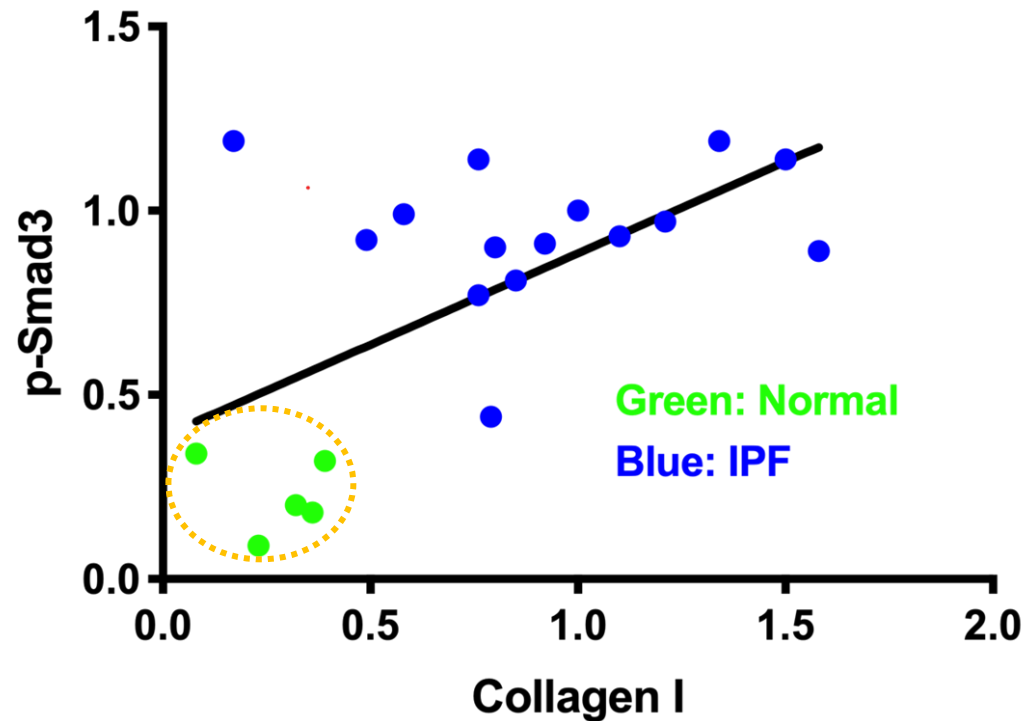
PLN-74809 target engagement

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



Pearson Correlation: $r=0.6004$
 p (two-tailed) = 0.0051

- 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

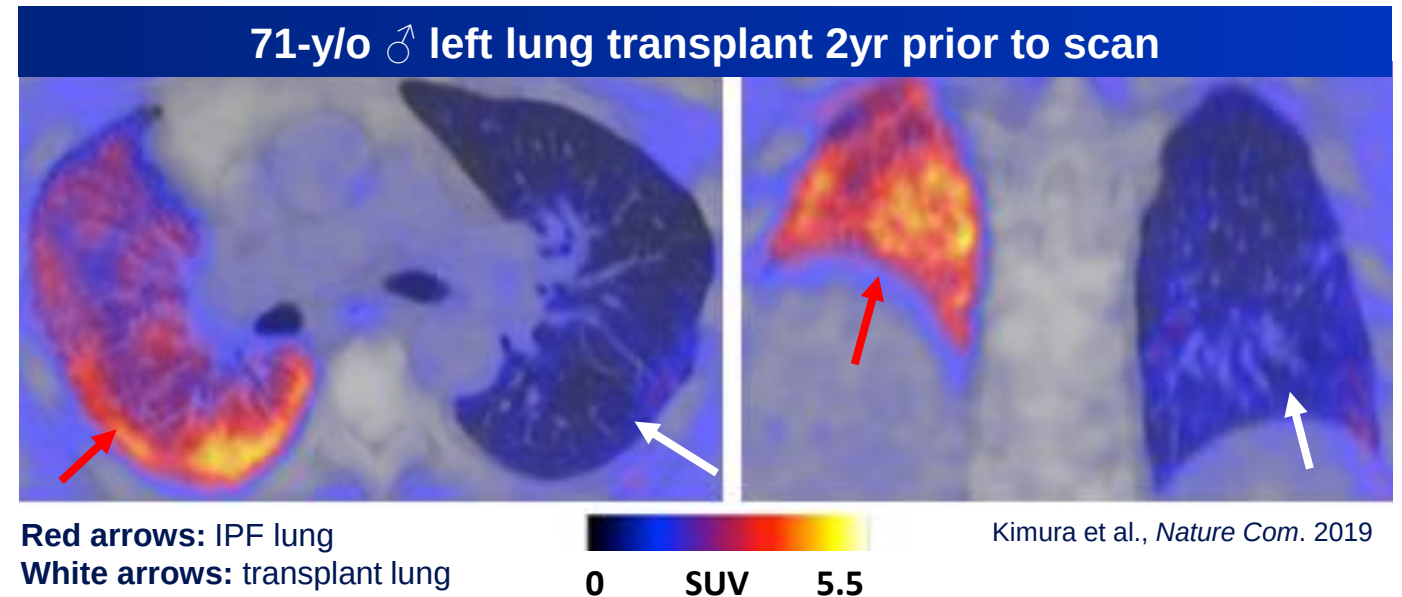
Phase 2a PET Trial – $\alpha_v\beta_6$ Expression Measured by a PET Ligand is Correlated with Extent of Fibrosis in IPF

TRIAL DESIGN

- Single-site open-label trial at Stanford University
- Adults with IPF diagnosis (n=12) and FVC $\geq$ 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

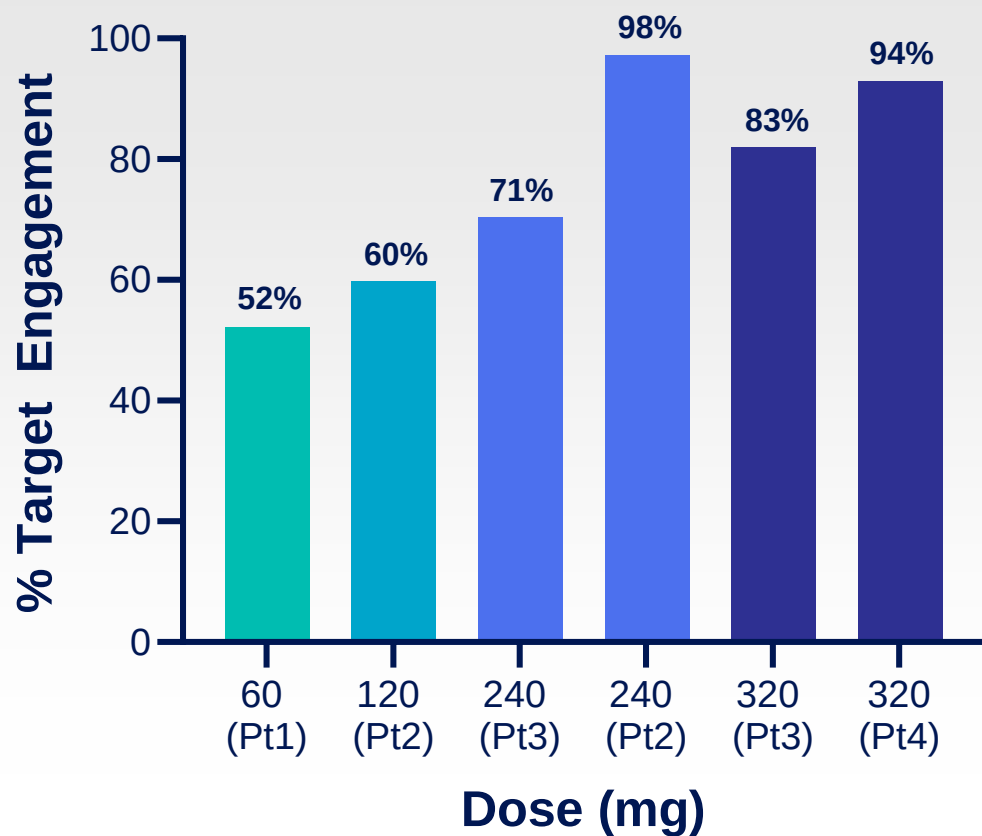
- **Primary:** Evaluation of $\alpha_v\beta_6$ target engagement by PLN-74809 assessed by change in PET tracer uptake following a single oral dose
- **Secondary:** Assessment of safety and tolerability of PLN-74809 in IPF patients
- **Exploratory:** Relationship between PLN-74809 systemic exposure and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



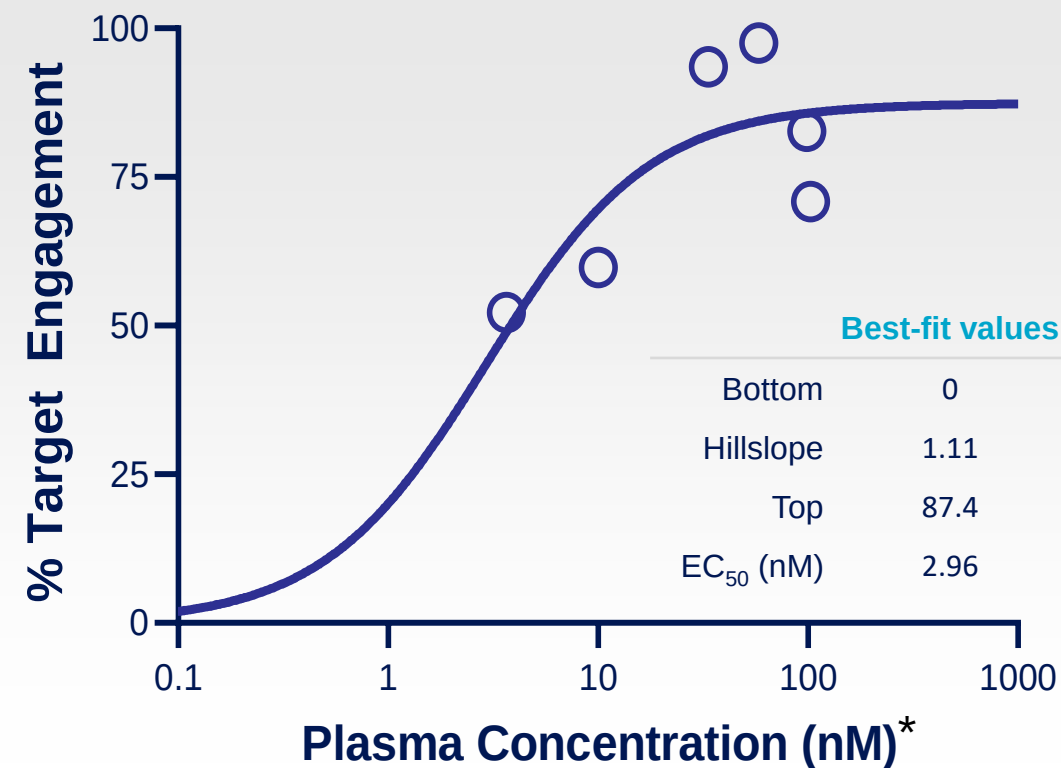
PET Ligand Uptake Confined to IPF Lung in Unilateral Lung Transplant Patient

Dose and Plasma Concentration Dependent Target Engagement

Dose-Dependent Target Engagement



Plasma Conc-Dependent Target Engagement

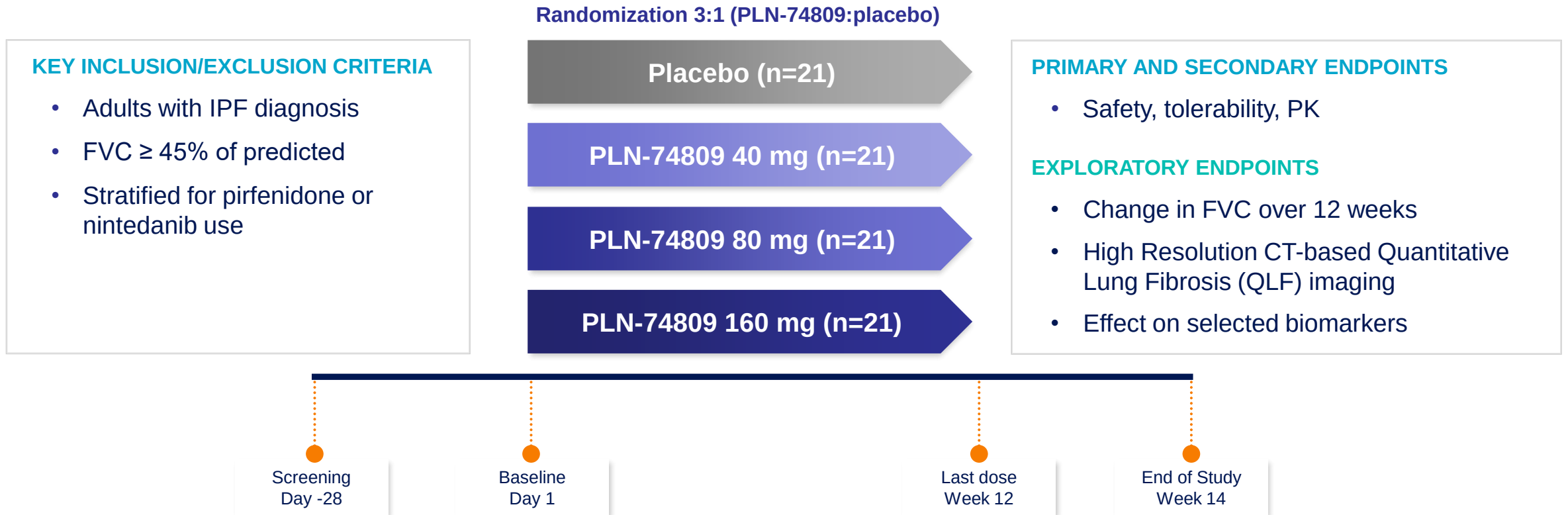


* Free plasma concentration

PLN-74809-IPF-202 [INTEGRIS-IPF]

Phase 2a Global Safety-PK-Exploratory Efficacy Trial in IPF

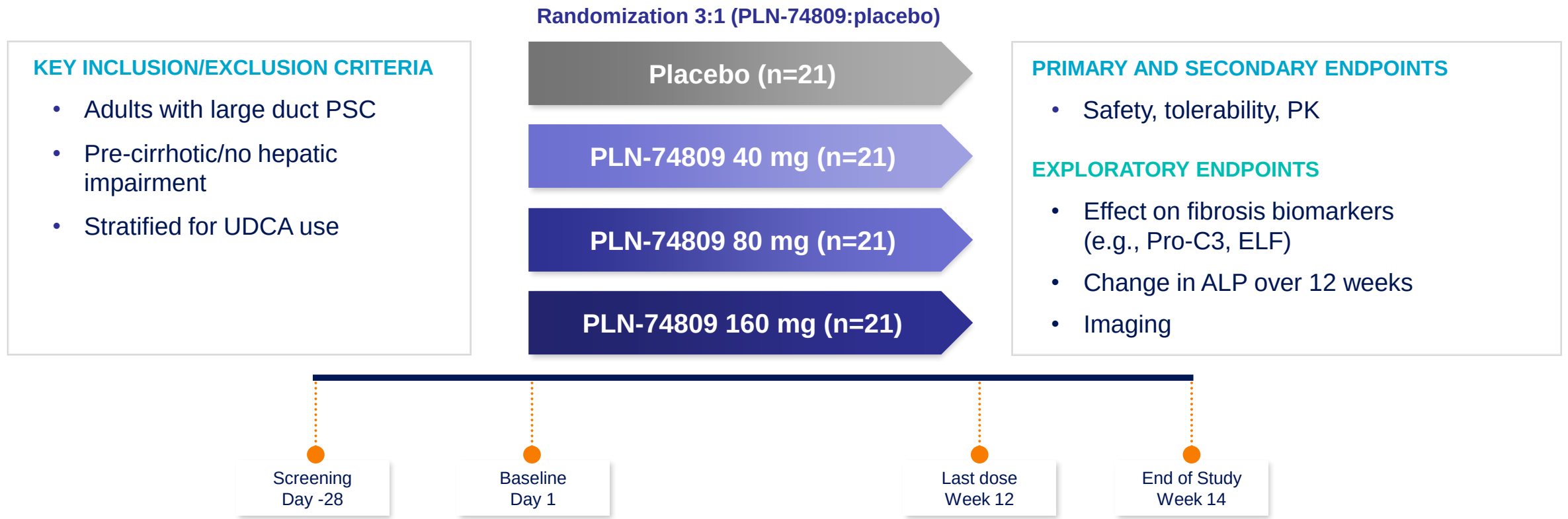
Enrollment Complete with Topline Data Expected Mid-2022



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



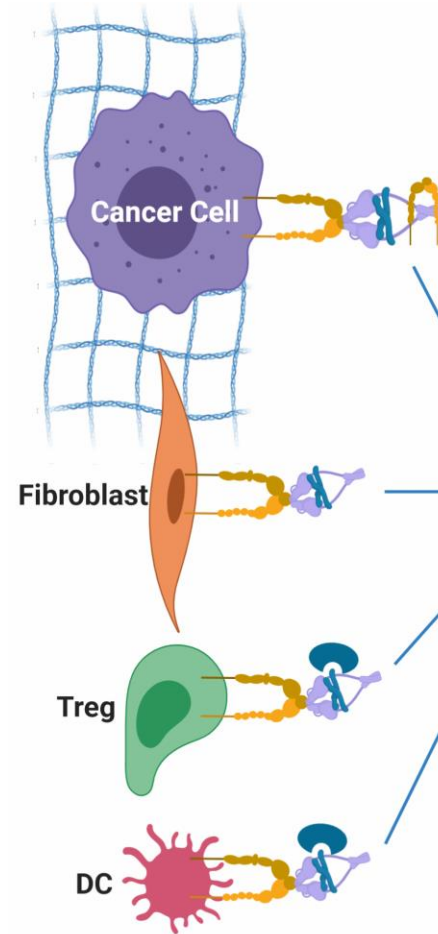


Pliant's Integrin-Based Oncology Program

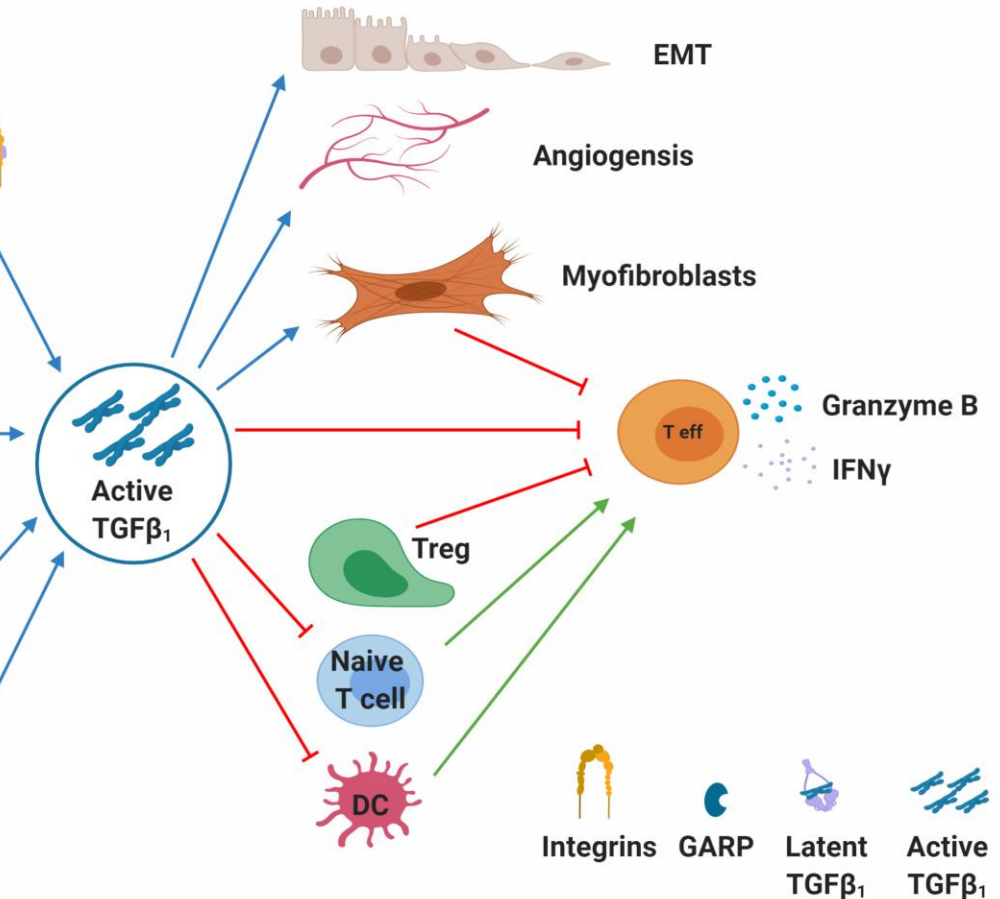
Activated TGF- β Contributes to Immune Exclusion & Evasion, Tumor Metastasis and Angiogenesis

- 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

Integrin Activation of TGF- β

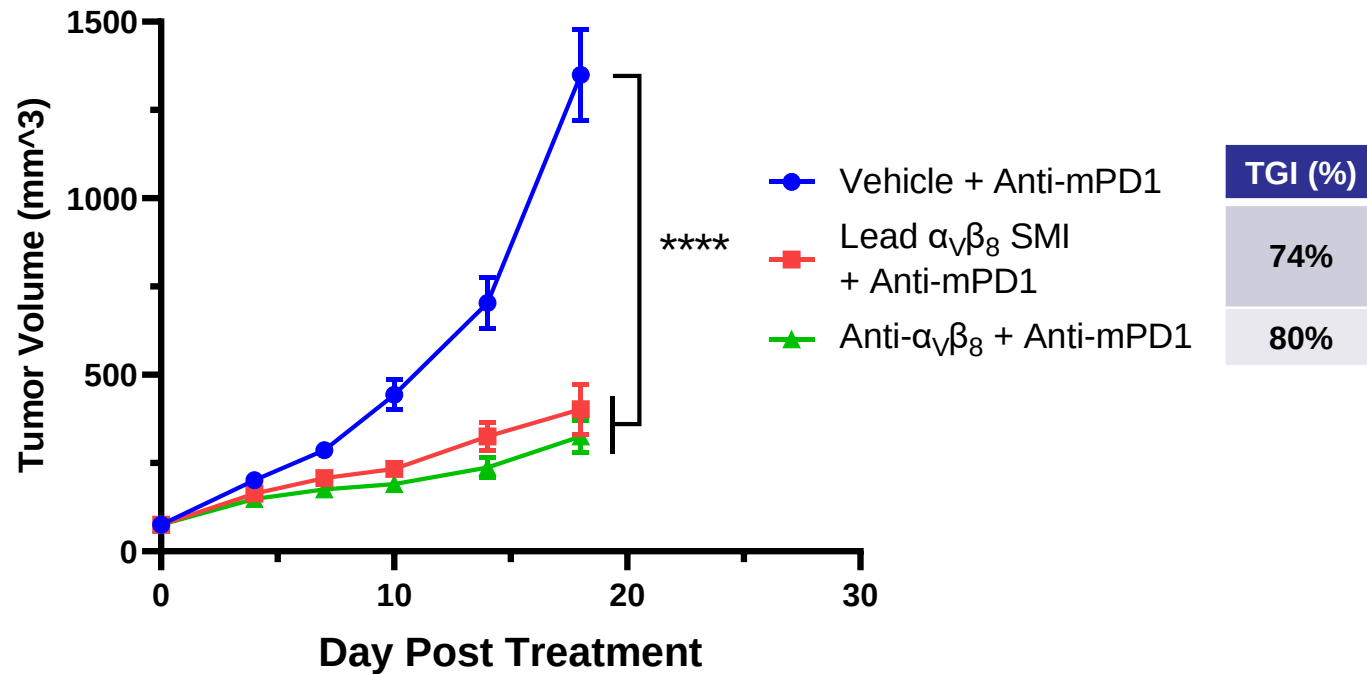


Oncogenic Effects of TGF- β Activation



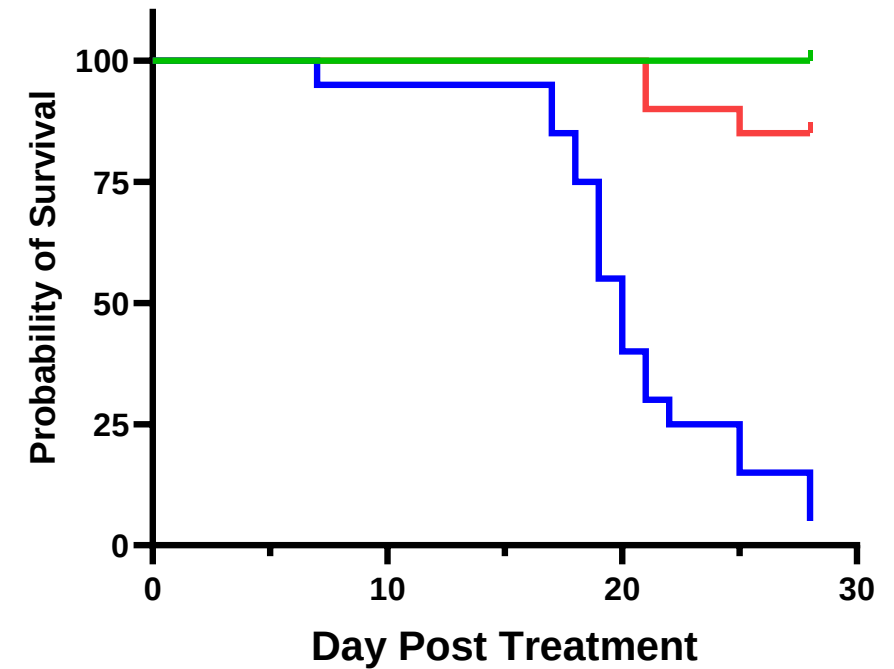
$\alpha_v\beta_{8/1}$ Inhibitor/ Anti-PD-1 Combo Reduced Tumor Burden and Increased Survival in Preclinical Models vs. Anti-PD-1 Alone

EMT6 Syngeneic Model



**** p<0.0001

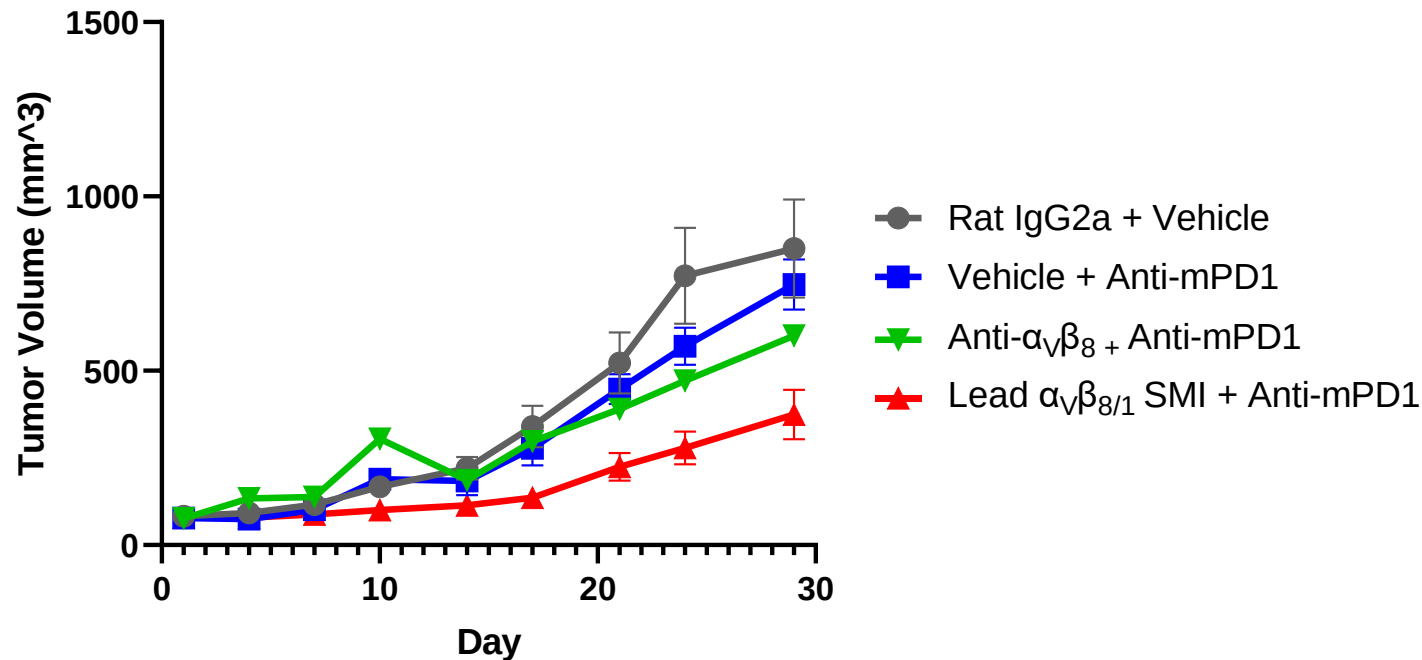
Survival Curve



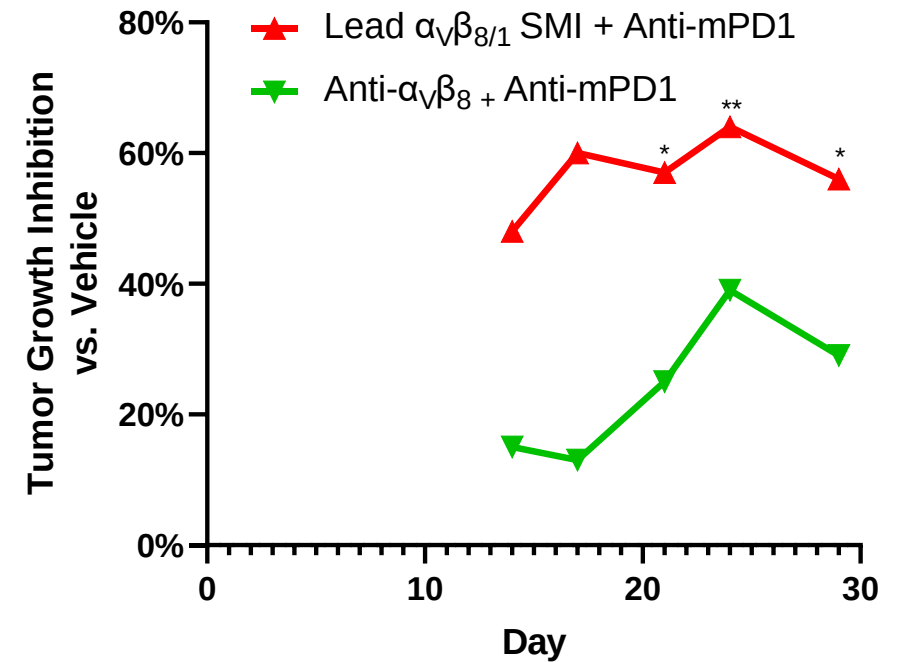
EMT6 Model, N=20 per arm

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

Tumor Volume Growth
Pan02 Syngeneic Model



Tumor Growth Inhibition
by Lead $\alpha_v\beta_{8/1}$ SMI in Pan02



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



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

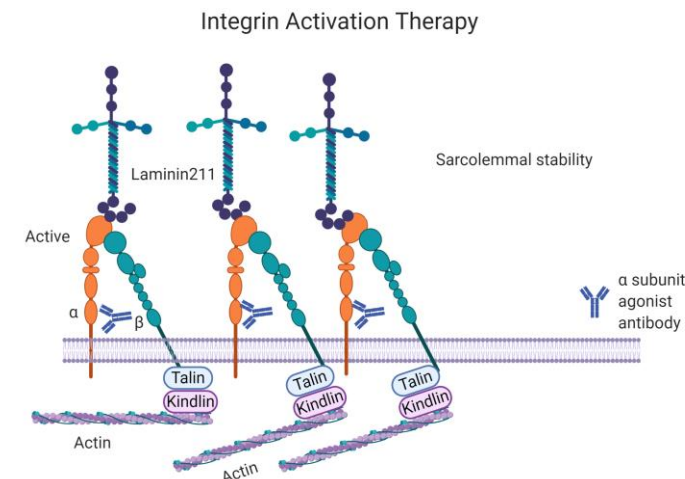
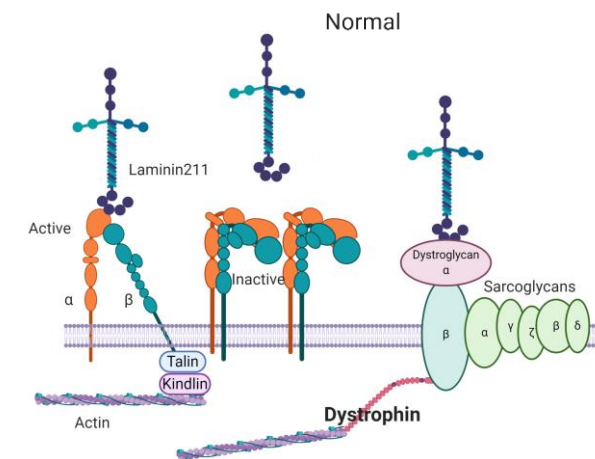
- Integrin target is upregulated as a **compensatory mechanism** in **different types of muscular dystrophy**
- Acts as a **substitute for dystrophin**, helping to stabilize the muscle membrane, decreasing muscle damage
- **Mutations in the target result in human congenital myopathy**

Allosteric agonistic monoclonal antibody

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

Potential to combine across multiple muscular dystrophy indications

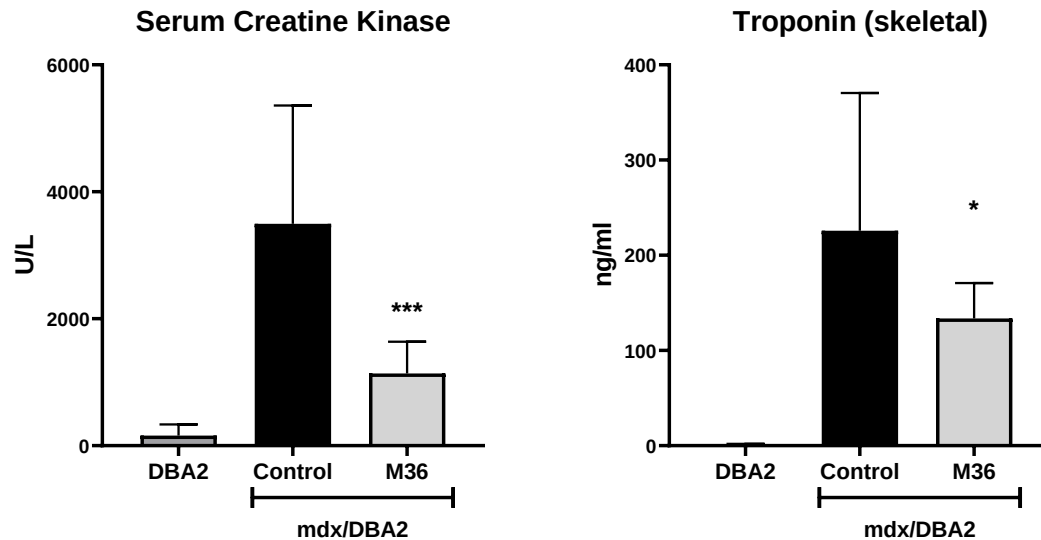
- Target is **upregulated across different forms of muscular dystrophy**
- Mechanism is unrelated to underlying gene mutation
- May be **combined with existing therapies** as well as new modalities (CRISPR, gene therapy,...)



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

Antibody treatment protected against muscle damage

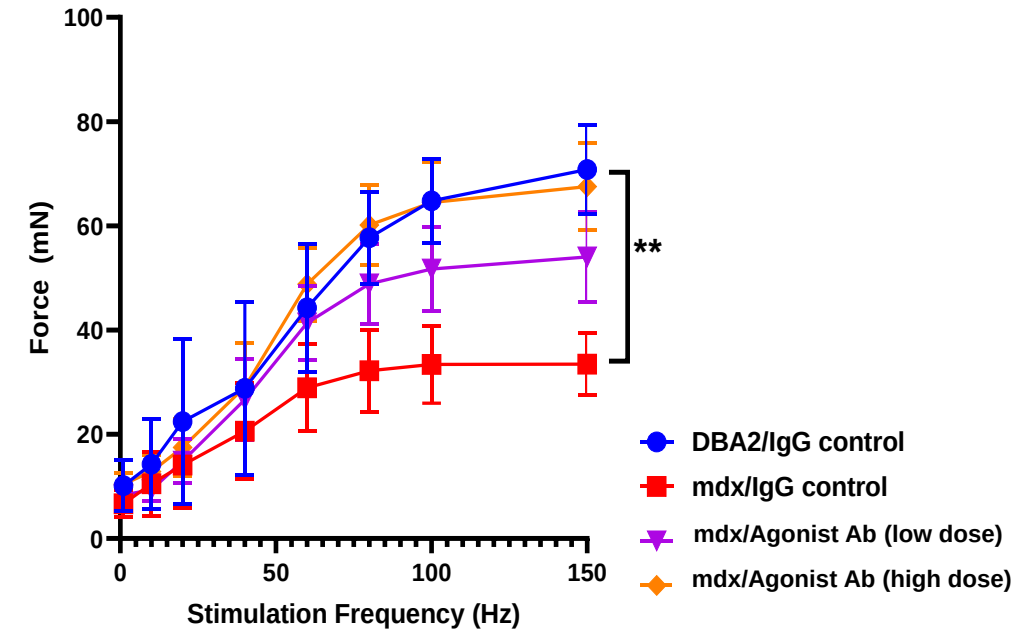
- Reduction of clinical biomarkers including serum creatine kinase and skeletal troponin



Mean +/- SD n=10/group

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



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