PLIANT

Developing Novel Treatments for Fibrotic Diseases

MARCH **2023**

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

- Inhibition of integrin-mediated TGF-β activation resulting in antifibrotic effect and shown to be well-tolerated
- Proprietary drug discovery platform - In-house compound library of integrin binders

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

- Bexotegrast (PLN-74809) in Phase 2a development in IPF and PSC
  - Well tolerated with clear treatment effect on FVC and lung fibrosis (QLF) in IPF patients
- IND cleared for PLN-101095 – potential first-in-class small molecule dual $\alpha_V\beta_8/\alpha_V\beta_1$ inhibitor addressing ICI resistance

Strong Financial Position

- Over $895M raised to date including 2020 IPO (Nasdaq: PLRX), $230M follow on (July 2022), $287.5M million follow on (January 2023)
- $601M proforma cash[1] balance as of December 31, 2022
- Operations funded into second half 2026 together with loan agreement and follow on proceeds

1 – Proforma for January 2023 $287.1M equity offering. Includes cash, cash equivalents and short-term investments.

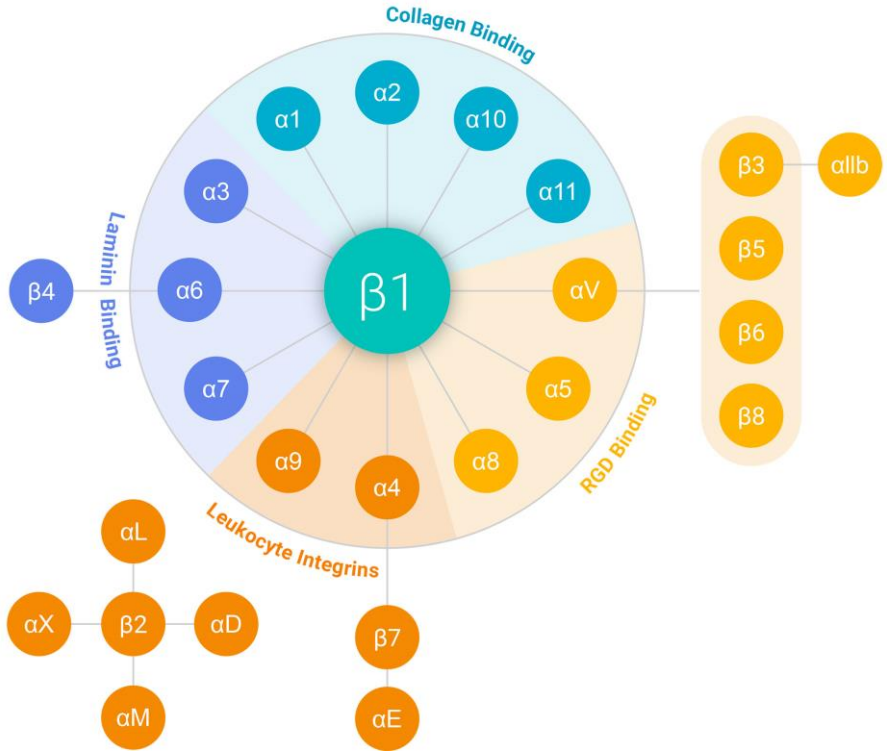
Pliant Development Pipeline

Program	Indication	Preclinical	Clinical			Anticipated Milestone	Global Rights
			Phase I	Phase II	Phase III		
Bexotegrast (PLN-74809) Dual selective inhibitor of $\alpha_v\beta_6$ /$\alpha_v\beta_1$	Idiopathic Pulmonary Fibrosis			→		Phase 2a 320 mg 24-Week Data Expected 2Q 2023	PLIANT
	Primary Sclerosing Cholangitis			→		Phase 2a Data Expected 3Q 2023	PLIANT
PLN-101095 Inhibitor of $\alpha_v\beta_8$ /$\alpha_v\beta_1$	Solid Tumors		→			Phase 1 Initiation 2Q 2023	PLIANT
PLN-101325 Anti-integrin mAb of $\alpha_7\beta_1$	DMD Other Muscular Dystrophies		→			IND Filing Expected 2023	PLIANT
PLN-1474 Selective inhibitor of $\alpha_v\beta_1$	NASH-Associated Liver Fibrosis			→		Phase 2 Ready	PLIANT

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



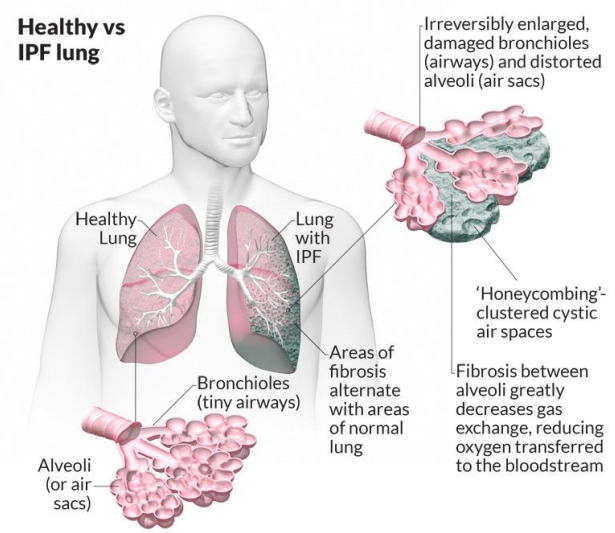
Pliant's Proprietary Library of 10,000+ Integrin Binding Compounds

- Emphasis on optimal pharmacokinetic and selectivity profile
- Broad spectrum of receptor subfamilies including α_V integrins, collagen and laminin binders

Fibrosis – A Silent Killer

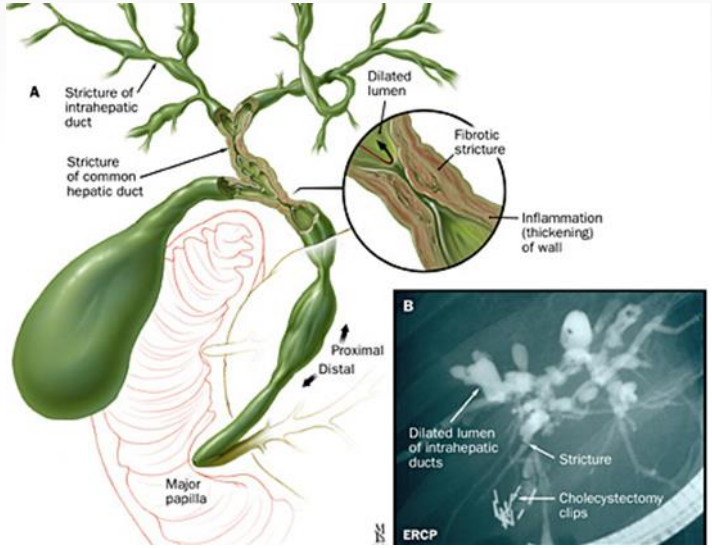
Idiopathic Pulmonary Fibrosis (IPF) is a lethal pathological process with limited therapeutic options

- 140k patients in the U.S.; 30k-40k new cases/year; 40k deaths/year
- **Median survival: 3–5 years -** Worse than some common cancers



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

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



Bexotegrast
Understanding the IPF commercial opportunity

CURRENT COMMERCIAL LANDSCAPE IN IPF

- Two marketed agents – Esbriet® and Ofev® with **>$3 billion total global revenues** in 2021
- Growing market with positive tailwinds
  - Increasing incidence of IPF with aging population
  - New therapies expanding treatable population

CHANGING TREATMENT LANDSCAPE

- Near-term patent expiry of current treatments
  - Esbriet: First generic sold May 2022
  - Ofev: Loss of US market exclusivity projected in 2025

SIGNIFICANT NEED FOR NEW THERAPEUTIC OPTIONS

- Esbriet and Ofev display modest slowing of IPF progression
  - No improvement on patient quality of life or survival benefit
  - **Significant tolerability issues**

Esbriet® is a trademark of Genentech/Roche
Ofev® is a trademark of Boehringer Ingelheim International

PLIANT

Bexotegrast
A Potential Preferred Treatment Option

ANTI-FIBROTIC MoA

- Targeted inhibition of fibrotic process– tissue specific inhibition of TGF-β
- Dose-dependent FVC benefit in INTEGRIS-IPF study

MONO & COMBO TREATMENT

- Will be evaluated as backbone therapy to be used as monotherapy, and with current treatments
- Flexibility in optimizing therapy for each patient

ORAL 1X DAILY DOSING

- Improvement over current multi-pill, multiple times a day options
- No added burden of monthly liver function monitoring

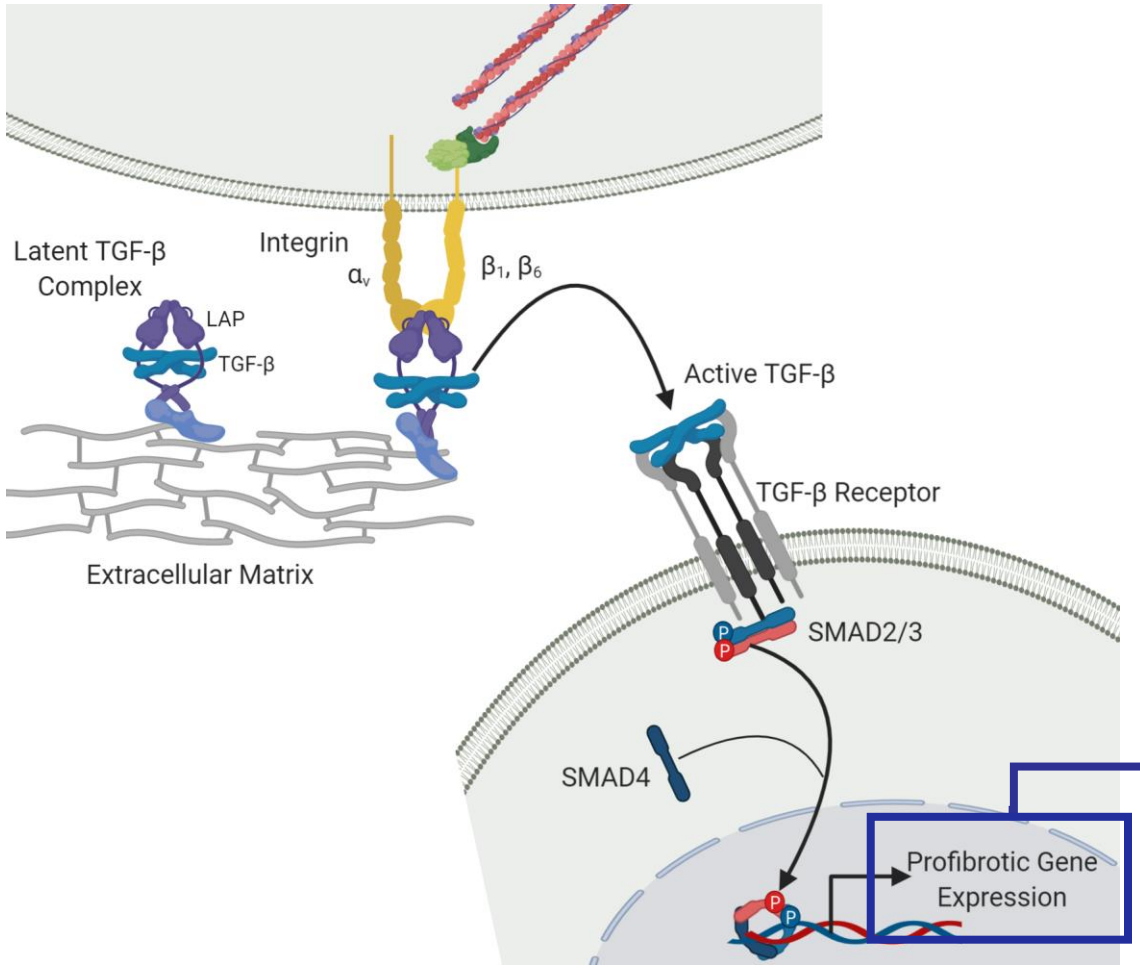
SAFETY / TOLERABILITY

- Well tolerated
- Low frequency of GI-related AEs in monotherapy setting

PLIANT

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

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

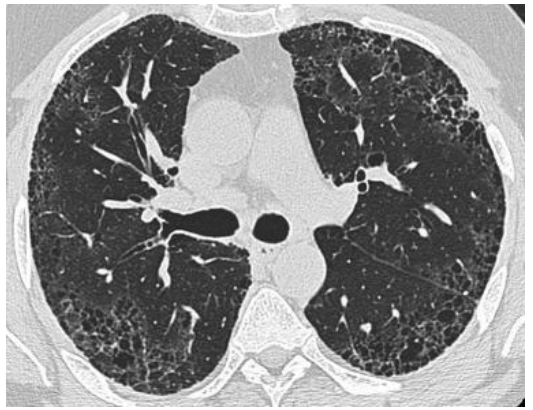


- TGF-β is central mediator of fibrosis
- $\alpha_v\beta_6$ /$\alpha_v\beta_1$ Integrins activate latent TGF-β only in fibrotic tissue
- Systemic TGF-β blockade carries toxicity risks

Bexotegrast selectively blocks TGF-β in fibrotic tissues may provide a low risk, effective antifibrotic approach

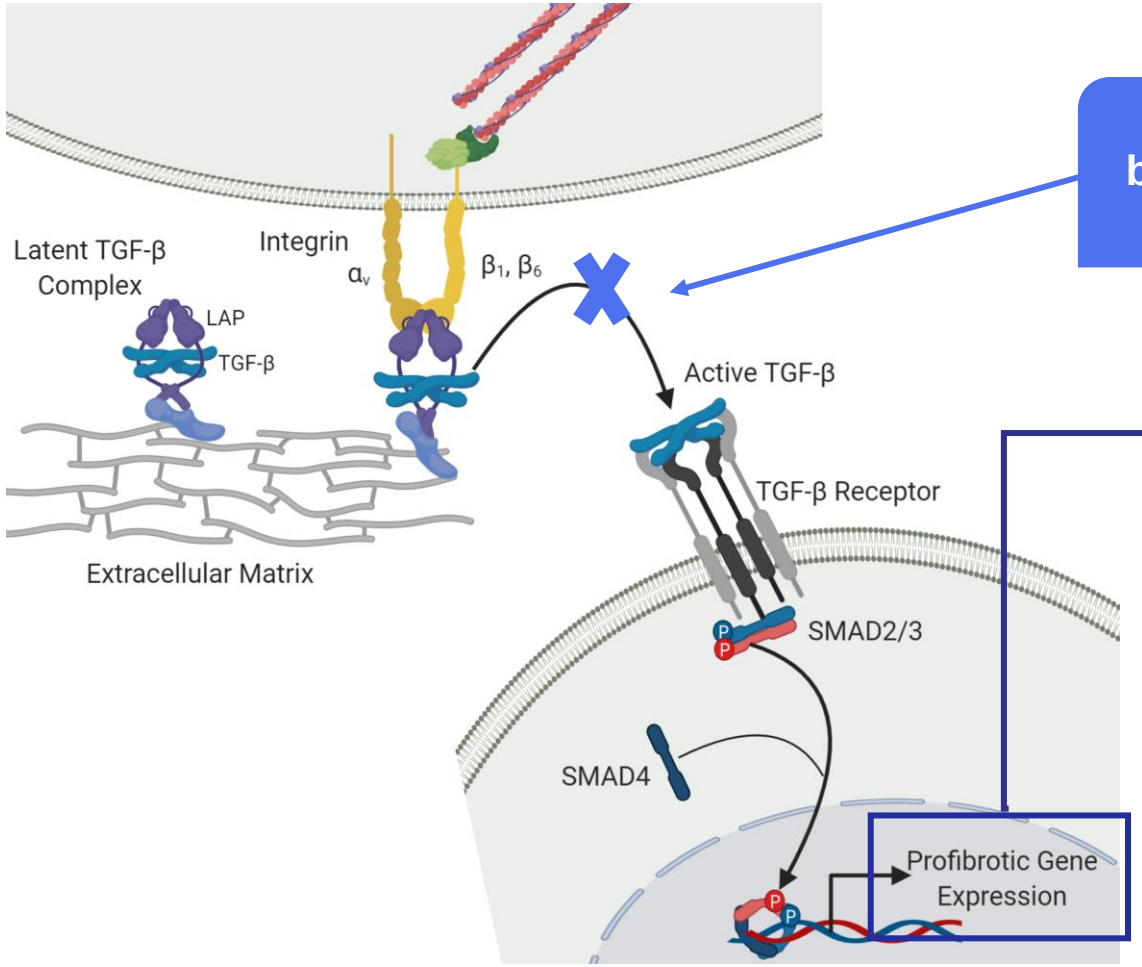
Col1a1
Col3a1
Timp1
CTGF
ATX
…

FIBROSIS



PLIANT

Bexotegrast Provides Profound Antifibrotic Activity Through Upstream Inhibition of TGF-β Activation

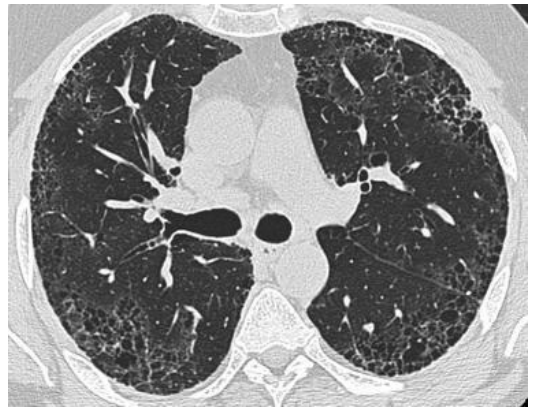


bexotegrast

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

Pliant Compounds Have Not Shown Adverse Effects Typical 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.

PLIANT

Bexotegrast - Nonclinical Toxicology Studies
No concerns for clinical advancement

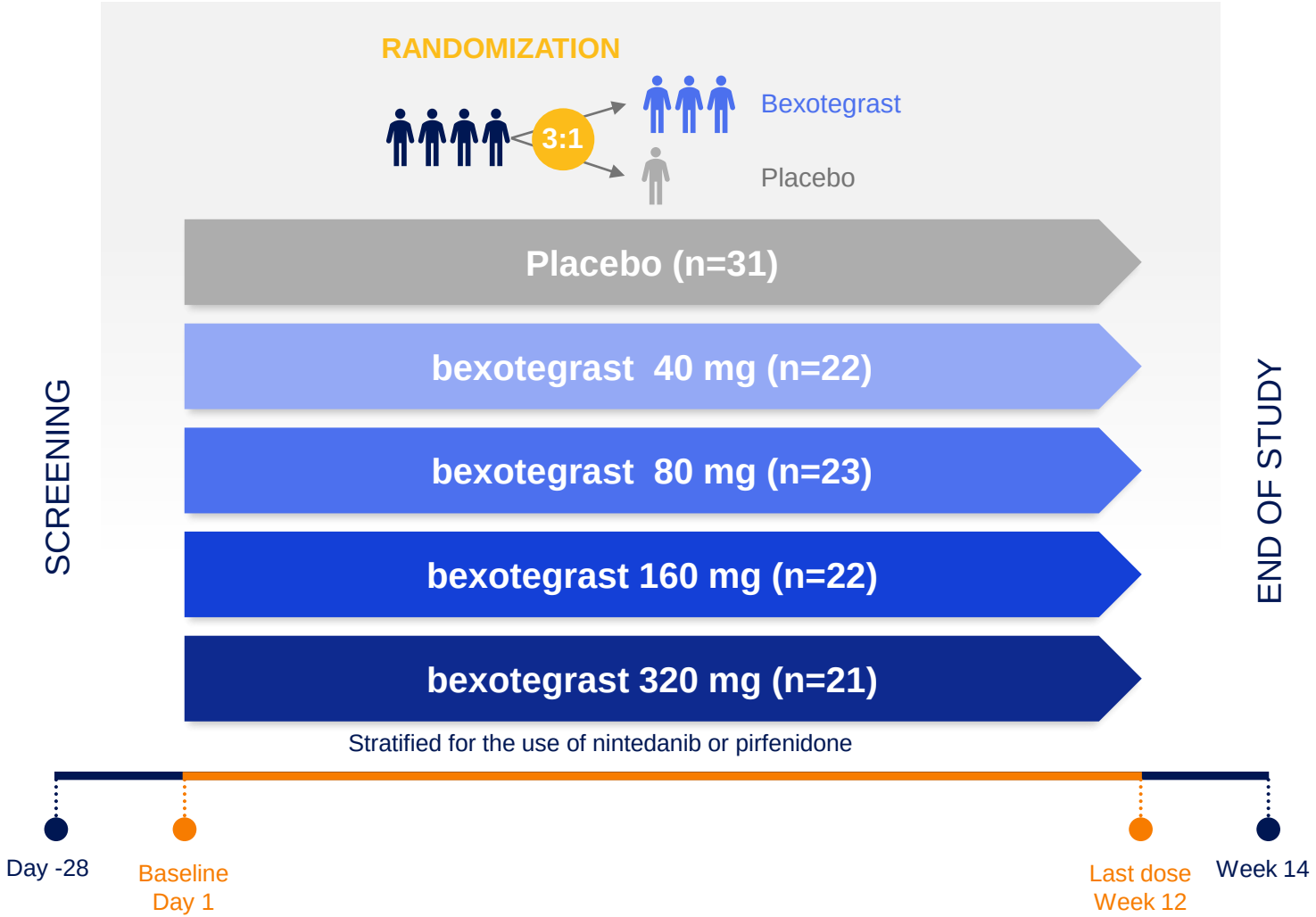
GLP Study category	Studies completed	Findings with Bexotegrast (PLN-74809)
Repeat Dose Toxicology	• 1-Month IND-enabling NHP and mouse • 3-Month Sub-chronic NHP and mouse • 9-Month Chronic NHP • 6-Month Chronic Mouse	**No findings limiting clinical advancement including** • No pulmonary infiltrates • No bladder cancer 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

600+ human subjects dosed to date with no safety concerns at doses up to 640 mg sd / 320 mg md

1 – No observed adverse effect level.

PLIANT

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
- Effect on selected biomarkers

PLIANT

Executive Summary

Bexotegrast 320 mg Well Tolerated Over 12 Weeks of Treatment

- All drug-related TEAEs were mild or moderate in severity
- Few discontinuations due to adverse events
- No drug-related SAEs

Bexotegrast 320 mg Demonstrated Statistically Significant Increase in FVC

- Statistically significant increase from baseline in mean FVC was observed at all timepoints with a mean difference from placebo of 140 mL at Week 12
- No participants experienced a decline of ≥10% in percent predicted FVC (FVCpp), a well-established predictor of death and disease progression in IPF [1,2]
- Bexotegrast treatment effect was observed with and without use of standard-of-care agents

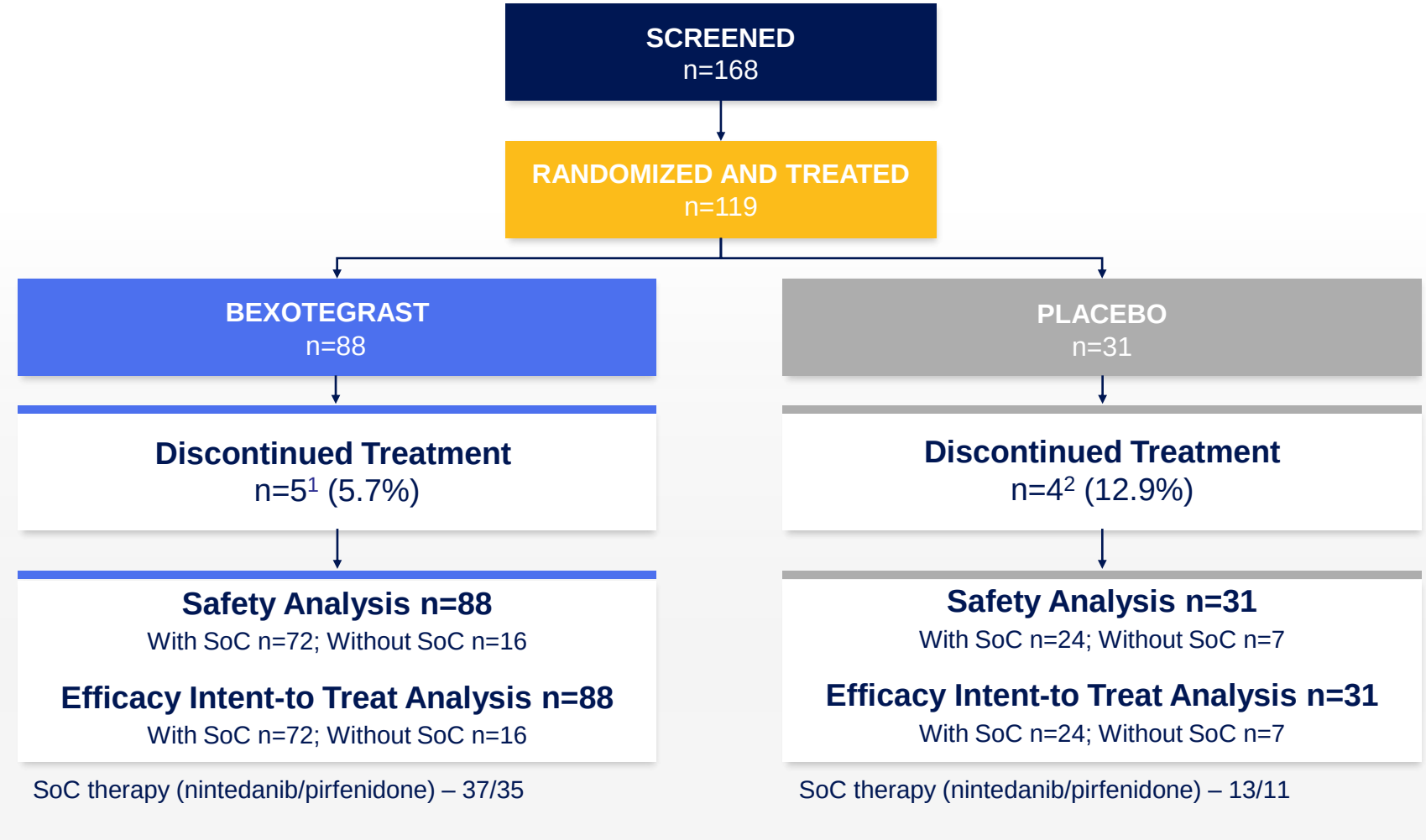
Biomarker Results Support Bexotegrast's Antifibrotic Mechanism

- Dose-dependent antifibrotic effect seen on QLF Imaging, with no or limited progression at 160 mg and 320 mg
- Bexotegrast reduced circulating PRO-C3 and integrin beta-6 levels with greatest effect observed at 320 mg

PLIANT

1 - Ann Am Thorac Soc. 2017 Sep;14(9):1395-1402; 2 - Am J Respir Crit Care Med. 2022 Apr 15;205(8):936-948;

Participant Disposition



1- Adverse event (n=3); withdrawal of consent (n=1); physician decision (n=1); 2- Adverse event (n=1); withdrawal of consent (n=2); physician decision (n=1).
SoC = Standard of Care

Baseline Demographics

Characteristic	Bexotegrast 40 mg (n=22)	Bexotegrast 80 mg (n=23)	Bexotegrast 160 mg (n=22)	Bexotegrast 320 mg (n=21)	Bexotegrast All (n=88)	Placebo (n=31)
Male sex, n (%)	18 (81.8)	19 (82.6)	16 (72.7)	20 (95.2)	73 (83.0)	27 (87.1)
Female sex, n (%)	4 (18.2)	4 (17.4)	6 (27.3)	1 (4.8)	15 (17.0)	4 (12.9)
Age (yr), mean (SD)	69.2 (7.11)	74.2 (4.70)	71.5 (6.63)	70.6 (7.31)	71.4 (6.64)	72.1 (6.20)
Race, n (%)						
White	22 (100.0)	21 (91.3)	22 (100.0)	20 (95.2)	85 (96.6)	30 (96.8)
Asian	0	1 (4.3)	0	0	1 (1.1)	1 (3.2)
Other / Not Reported / Unknown	0	1 (4.3)	0	1 (4.8)	2 (2.3)	0
Weight (kg), mean (SD)	86.1 (18.22)	85.9 (14.95)	85.4 (13.51)	88.6 (15.52)	86.46 (15.52)	84.0 (11.41)
Body-mass index (kg/m^2), mean (SD)	27.7 (4.21)	28.5 (5.79)	29.3 (4.66)	28.2 (4.18)	28.4 (4.73)	27.3 (2.57)

SD = Standard deviation; BMI = Body Mass Index; FVC = Forced Vital Capacity; DLCO = Diffusing capacity for carbon monoxide.

PLIANT

Baseline Disease Characteristics

Characteristic	Bexotegrast 40 mg (n=22)	Bexotegrast 80 mg (n=23)	Bexotegrast 160 mg (n=22)	Bexotegrast 320 mg (n=21)	Bexotegrast All (n=88)	Placebo (n=31)
Time since diagnosis of IPF (mo), mean (SD)	22.2 (12.44)	28.6 (17.08)	27.8 (12.43)	35.6 (29.06)	28.5 (19.11)	34.0 (21.62)
Standard of Care Use, n (%)	17 (77.3)	19 (82.6)	19 (86.4)	17 (81.0)	72 (81.8)	24 (77.4)
None	5 (22.72)	4 (17.39)	3 (13.63)	4 (19.0)	16 (18.2)	7 (22.6)
Nintedanib	12 (54.5)	9 (39.1)	7 (31.8)	9 (42.9)	37 (42.0)	13 (41.9)
Pirfenidone	5 (22.7)	10 (43.5)	12 (54.5)	8 (38.1)	35 (39.8)	11 (35.5)
Duration of Standard of Care at Randomization (mo), mean (SD)	19.5 (11.53)	20.2 (11.52)	20.1 (11.63)	24.4 (21.88)	21.0 (14.48)	22.6 (17.85)
FVC (mL)						
Mean (SD)	2,976.5 (861.01)	3,128.7 (814.20)	2,863.0 (725.39)	3,193.7 (674.01)	3,039.7 (771.20)	3,073.9 (773.54)
Median	2937.0	2929.0	2702.5	3256.0	2898.5	3179.0
Percent of predicted value (%), mean (SD)	74.8 (14.70)	82.7 (13.47)	78.8 (16.36)	77.7 (15.41)	78.5 (15.01)	77.7 (16.44)
Percent of predicted DLCO, corrected for the hemoglobin level (%), mean (SD)	57.2 (14.74)	51.8 (14.67)	48.6 (15.11)	47.9 (13.18)	51.5 (14.69)	50.1 (15.23)
GAP Stage, n (%)						
GAP Stage I	11 (50.0)	8 (34.8)	7 (31.8)	7 (33.3)	33 (37.5)	10 (32.3)
GAP Stage II	10 (45.5)	15 (65.2)	13 (59.1)	12 (57.1)	50 (56.8)	18 (58.1)
GAP Stage III	1 (4.5)	0	2 (9.1)	2 (9.5)	5 (5.7)	3 (9.7)

BMI = Body Mass Index; mo = Month; SD = Standard Deviation;
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 Evaluation – Summary

Bexotegrast was well tolerated with no dose relationship for adverse events

No drug-related SAEs were observed

Most frequent TEAE was diarrhea (17.0% on active versus 9.7% on placebo)

- **14 of 15 participants receiving bexotegrast were on standard-of-care agents**

PLIANT

Safety Summary

AE, n (%) of Participants Reporting	Bexotegrast 40 mg (n=22)	Bexotegrast 80 mg (n=23)	Bexotegrast 160 mg (n=22)	Bexotegrast 320 mg (n=21)	Bexotegrast All (n=88)	Placebo (n=31)
Any AEs	16 (72.7)	15 (65.2)	15 (68.2)	18 (85.7)	64 (72.7)	21 (67.7)
TEAE	16 (72.7)	15 (65.2)	14 (63.6)	17 (81.0)	62 (70.5)	21 (67.7)
Related to study drug	**4 (18.2)**	**7 (30.4)**	**4 (18.2)**	**4 (19.0)**	**19 (21.6)**	**10 (32.3)**
Serious TEAE	1 (4.5)	0	2 (9.1)	1 (4.8)	4 (4.5)	3 (9.7)
Related to study drug	**0**	**0**	**0**	**0**	**0**	**0**
TEAE of CTCAE Grade 3 or Higher	2 (9.1)	0	2 (9.1)	2 (9.5)	6 (6.8)	2 (6.5)
Related to study drug	**0**	**0**	**1 (4.5)**	**0**	**1 (1.1)**	**0**
TEAE Leading to Interruption of Study Drug	0	0	1 (4.5) [1]	1 (4.8) [2]	2 (2.3)	0
TEAE Leading to Withdrawal of Study Drug	0	0	0	3 (14.3) [2,3,4]	3 (3.4)	3 (9.7)
TEAE Leading to Early Termination from Study	0	0	0	3 (14.3) [2,3,4]	3 (3.4)	2 (6.5)
TEAE Leading to Death	0	0	0	1 (4.8) [3]	1 (1.1)	0

1 – COVID-19; 2 – Abdominal pain/Diarrhea in participant with pre-existing ulcerative colitis; 3 – Acute respiratory failure in a GAP Stage III participant with pre-existing atrial fibrillation 8 days following elective atrioventricular node ablation; 4 – Diarrhea in participant with concomitant use of nintedanib

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.

PLIANT

Most Frequent TEAEs – Any Causality

TEAE, n (%) of Participants Reporting	Bexotegrast 40 mg (n=22)	Bexotegrast 80 mg (n=23)	Bexotegrast 160 mg (n=22)	Bexotegrast 320 mg (n=21)	Bexotegrast All (n=88)	Placebo (n=31)
Most frequent TEAEs (≥ 10% in at least one arm)						
Diarrhea	2 (9.1)	5 (21.7)	5 (22.7)	3 (14.3)	15 (17.0)	3 (9.7)
Related to study drug	1 (4.5)	3 (13.0)	4 (18.2)	2 (9.5)	10 (11.4)	1 (3.2)

- 14 of 15 participants receiving bexotegrast with TEAEs of diarrhea were on standard of care
  - One participant with diarrhea not receiving standard of care had pre-existing ulcerative colitis
- All but one event were mild to moderate in severity; 2 participants discontinued bexotegrast due to mild diarrhea
- Diarrhea infrequently reported in bexotegrast 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.

PLIANT

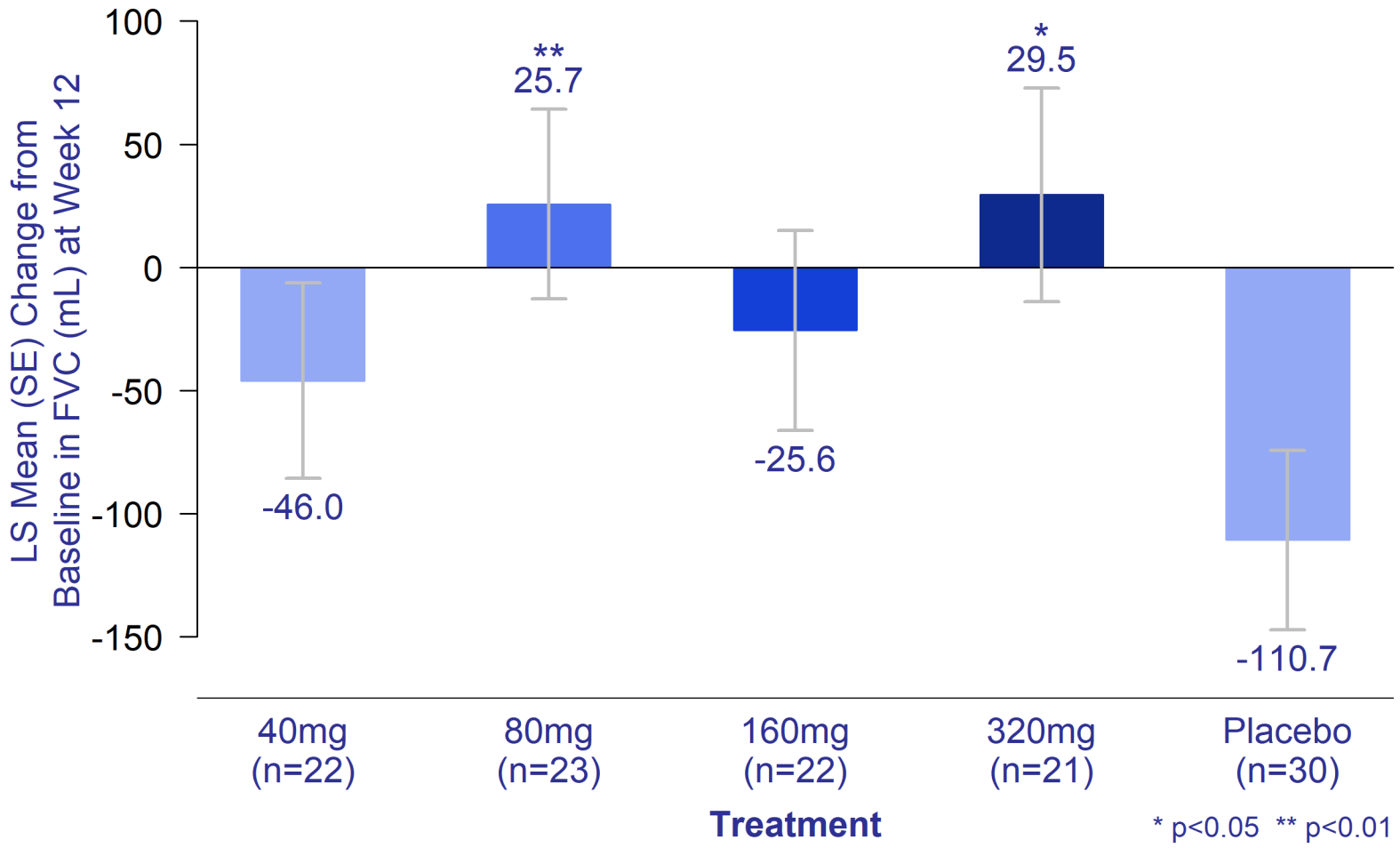
No SAEs were Related to Study Drug

Patient Treatment Group	SAE Preferred Term	Standard Toxicity Grade	Drug Related	Any alternative cause or confounding factors?	Action Taken	Outcome
Bexotegrast 40mg	Acute respiratory failure	Grade 3 (Severe)	No	Removed carpet from home without a mask	Dose not changed	Recovered / resolved
	Pneumonia	Grade 2 (Moderate)	No		Dose not changed	Recovered / resolved
Bexotegrast 160mg	Idiopathic pulmonary fibrosis [1]	Grade 3 (Severe)	No	Underlying disease and atrial fibrillation	Not applicable - hospitalization	Not recovered / not resolved
Bexotegrast 160 mg	Atrial flutter	Grade 3 (Severe)	No	Underlying disease	Not applicable - hospitalization	Recovered / resolved
Bexotegrast 320mg	Acute respiratory failure [2]	Grade 5 (Fatal)	No	Underlying disease [2]	Drug withdrawn	Fatal
Placebo	Bladder dilatation	Grade 2 (Moderate)	No	No	Dose not changed - Foley catheter placed	Recovered / resolved with sequelae
Placebo	Respiratory failure	Grade 3 (Severe)	No	Coronary artery disease with triple vessel disease	Not applicable - early termination from the study	Recovered / resolved with sequelae
Placebo	Pulmonary fibrosis [3]	Grade 3 (Severe)	No	No	Drug withdrawn - hospitalization	Recovered / resolved with sequelae

1 - Acute exacerbation of IPF occurring ≈2 weeks after 12-week treatment was completed; 2- A GAP Stage III participant with preexisting atrial fibrillation, following elective atrioventricular node ablation; 3- Progression of fibrosis.

PLIANT

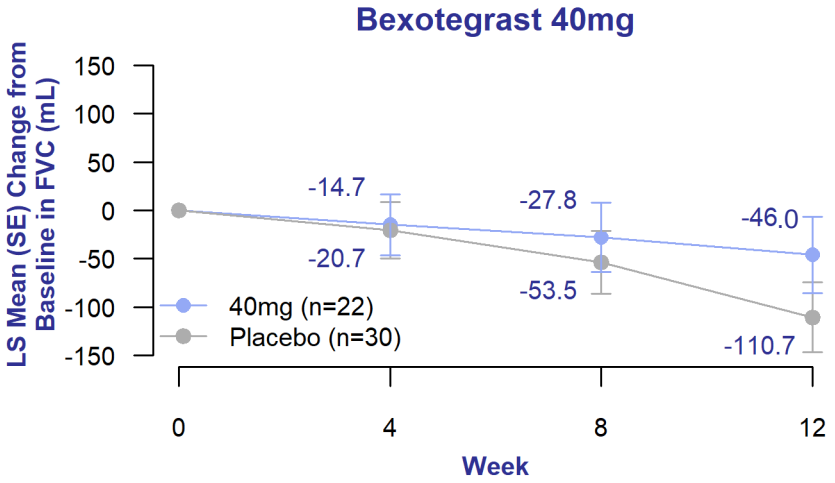
FVC Change from Baseline at Week 12
mITT Population

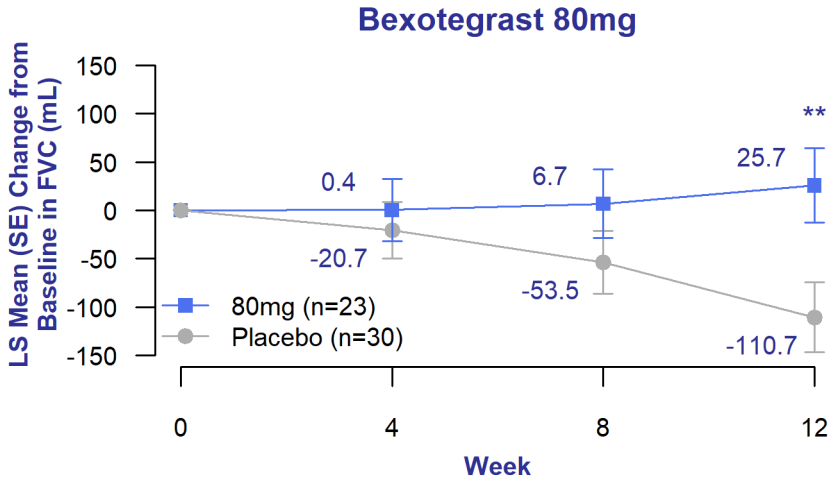


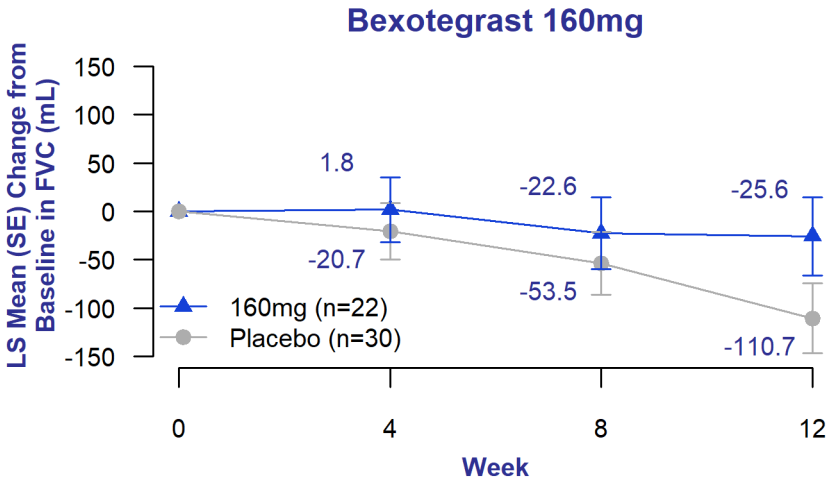
FVC = Forced Vital Capacity; mITT= Modified Intent to Treat; 1 participant in the placebo group was identified as a statistical outlier across all treatment groups and excluded from the mITT analysis

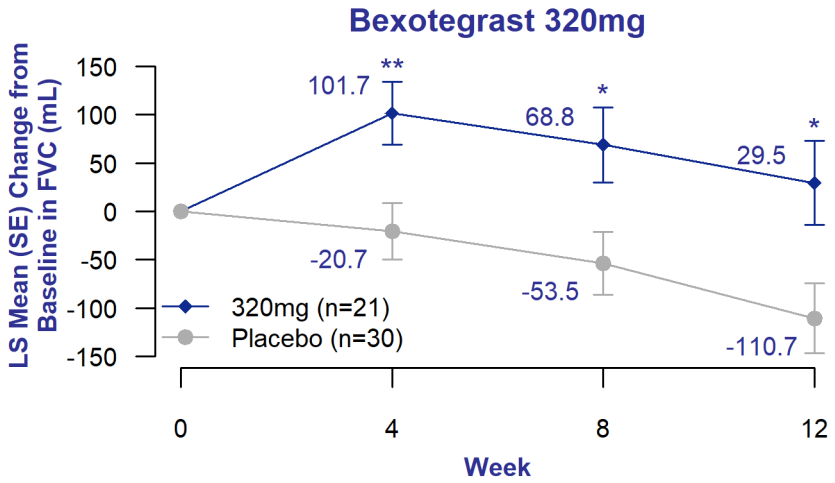
PLIANT

FVC Change from Baseline over 12 Weeks
mITT Population





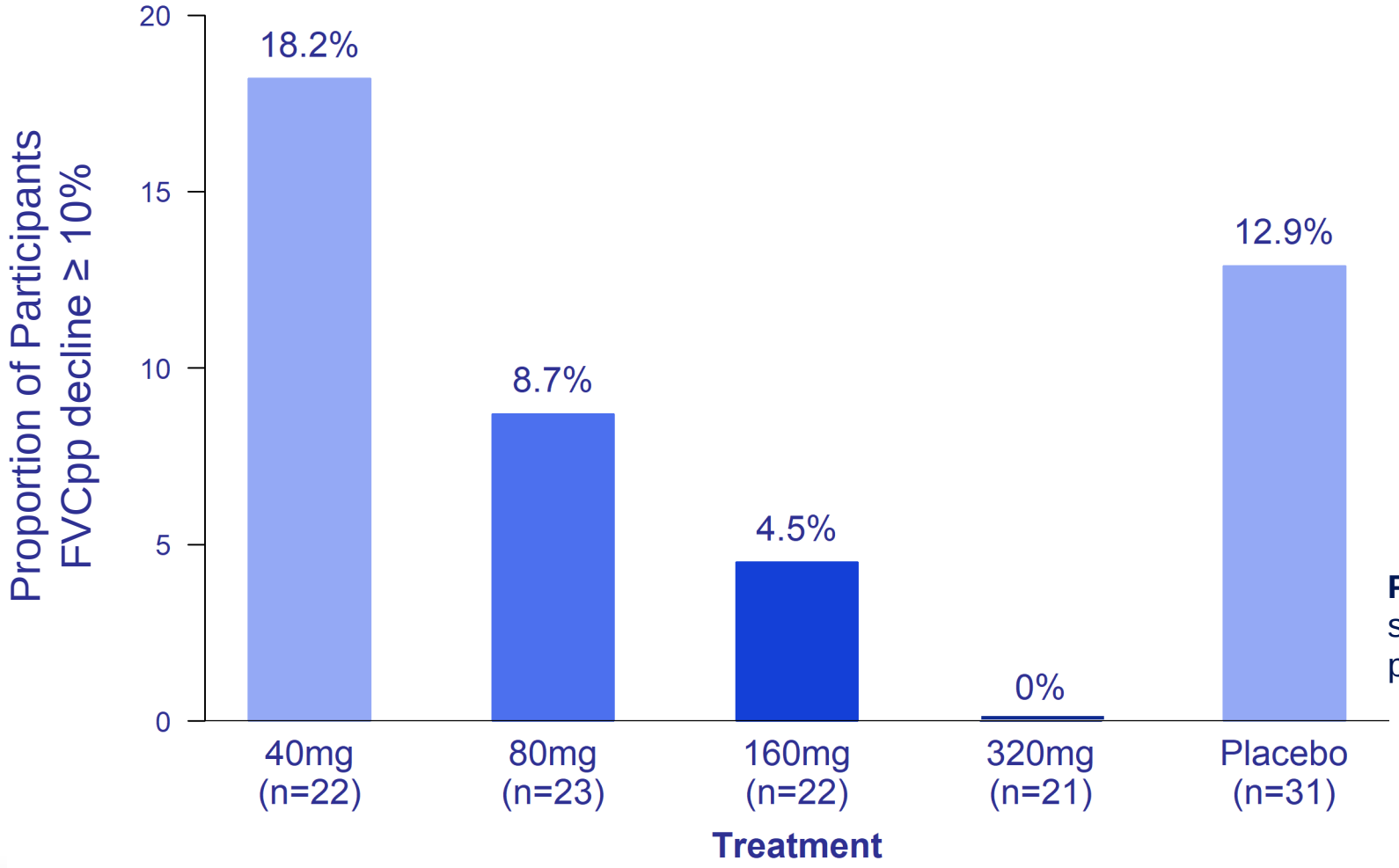




* p < 0.05 vs placebo
** p < 0.01 vs placebo

FVC = forced vital capacity; mITT= modified intent to treat; 1 participant in the placebo group was identified as a statistical outlier across all treatment groups and excluded from the mITT analysis.

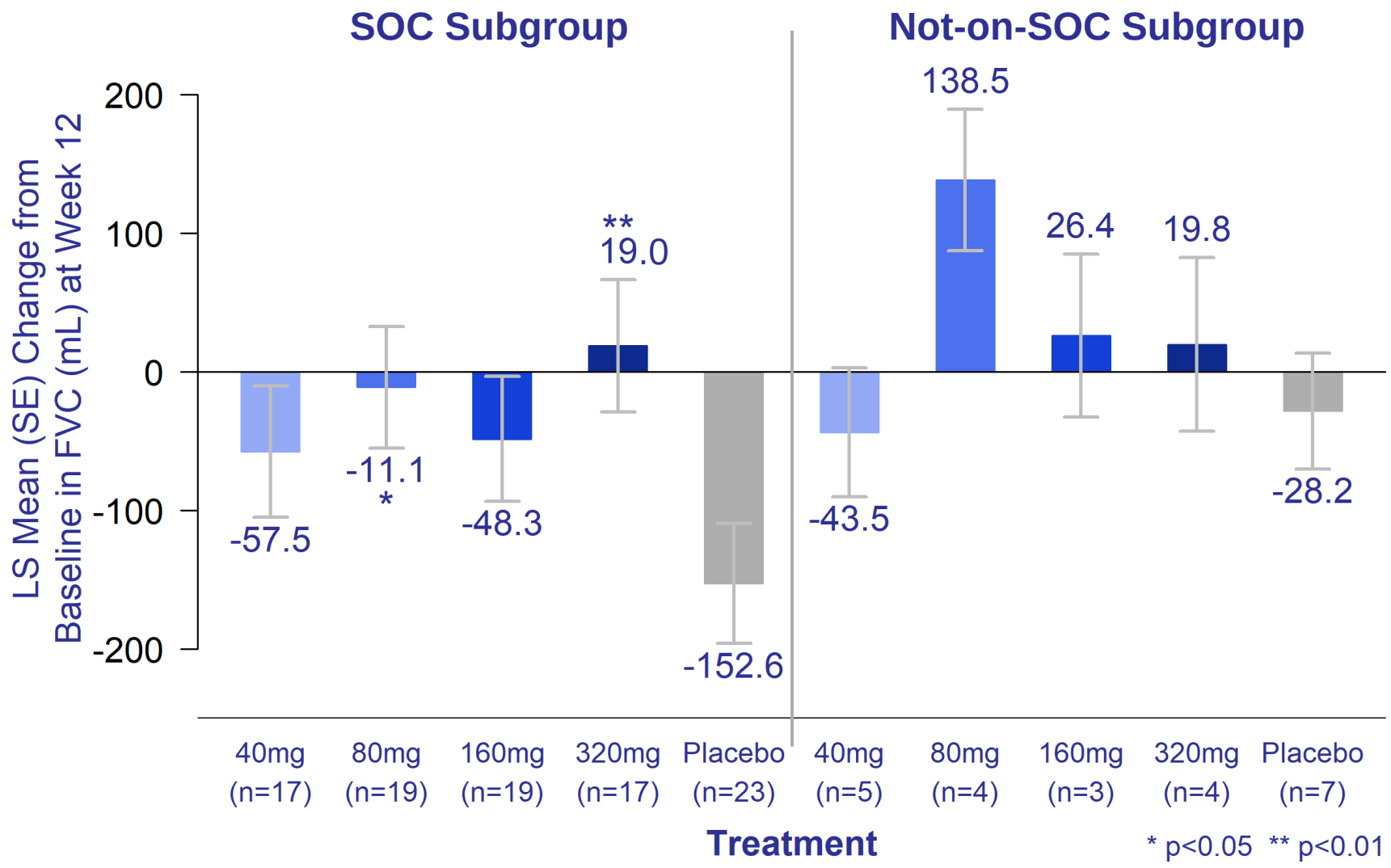
Proportion of Participants with Relative FVCpp Decline ≥ 10%
ITT Population



FVCpp ≥ 10%:
strong predictor of disease progression and mortality[1, 2]

FVCpp = Forced vital capacity, percent predicted.
1- Ann Am Thorac Soc. 2017 Sep 14(9):1395-1402; 2- Am J Respir Crit Care Med. 2022 Apr 15;205(8):936-948.

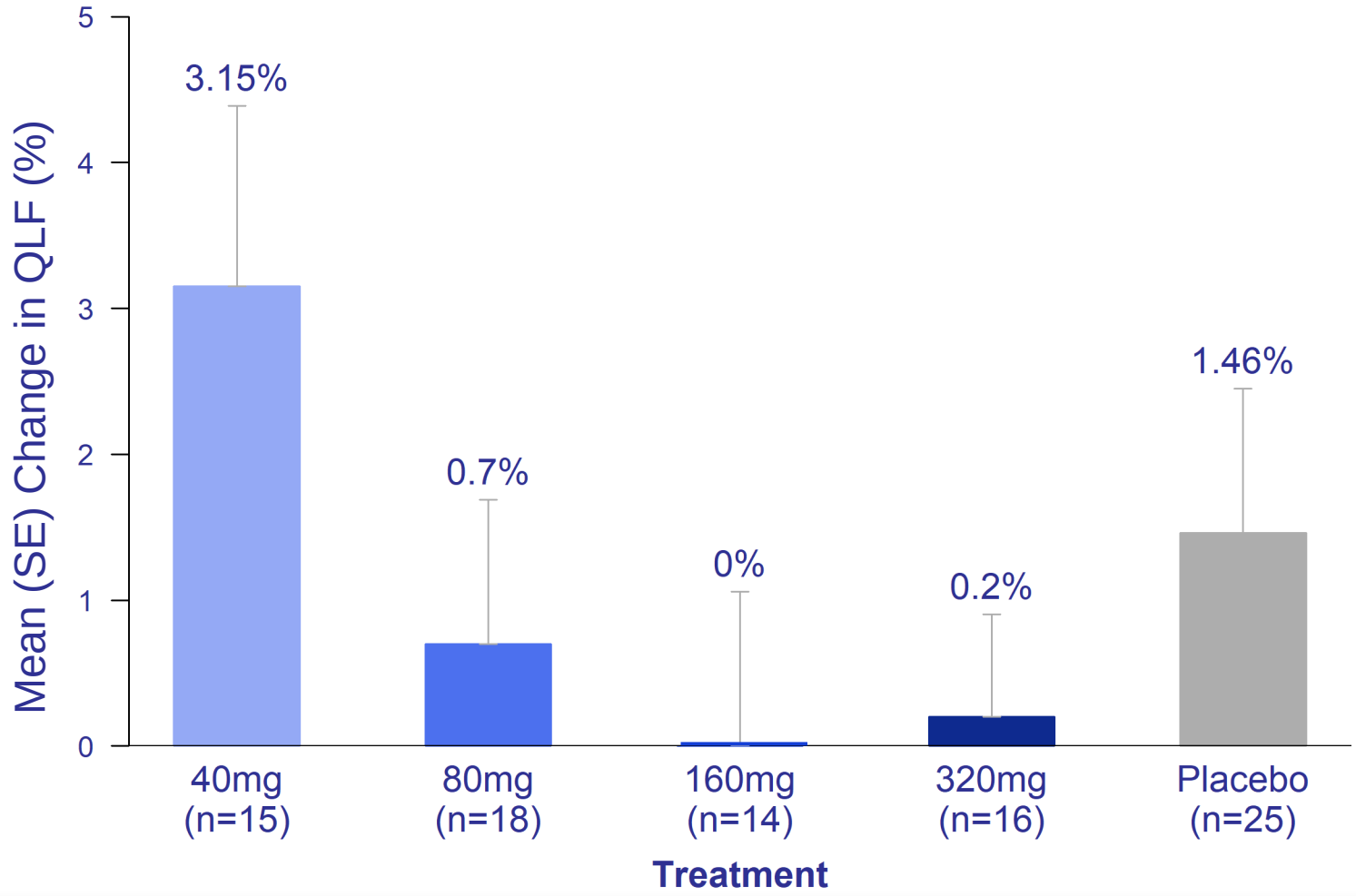
FVC Change from Baseline at Week 12 by SOC Subgroup
mITT Population



FVC = Forced Vital Capacity; mITT = modified intent to treat; 1 participant in the placebo group was identified as a statistical outlier across all treatment groups and excluded from the mITT analysis.

PLIANT

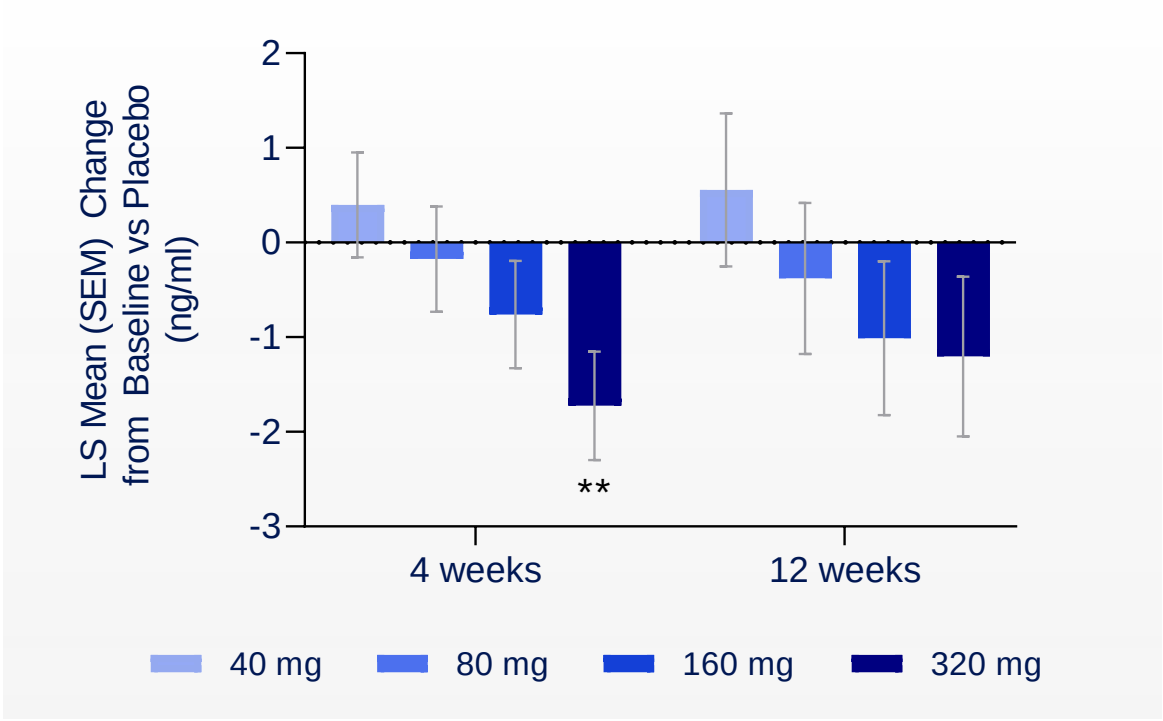
QLF Mean Percent Change from Baseline at Week 12
Per CT protocol population



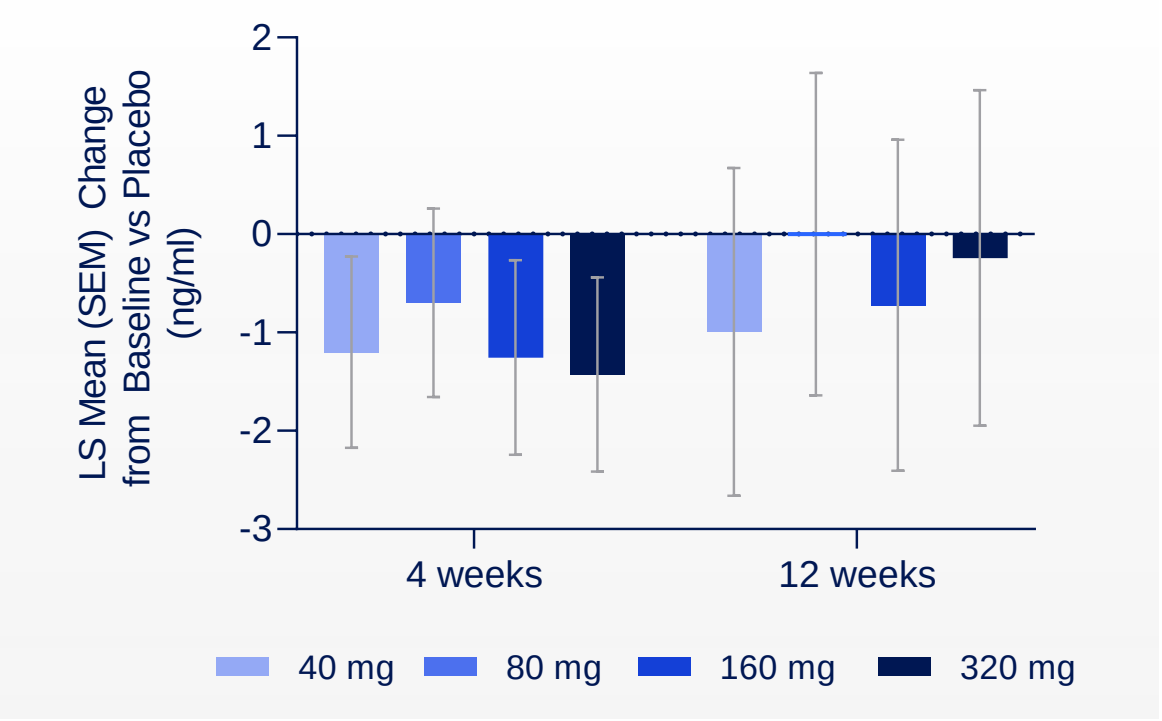
QLF = quantitative lung fibrosis

Bexotegrast Reduced Serum Biomarkers of Collagen Synthesis
Change from Baseline at 4 and 12 Weeks vs. Placebo

PRO-C3
Type III collagen synthesis neoepitope



PRO-C6
Type VI collagen synthesis neoepitope



** $p < 0.01$ vs placebo

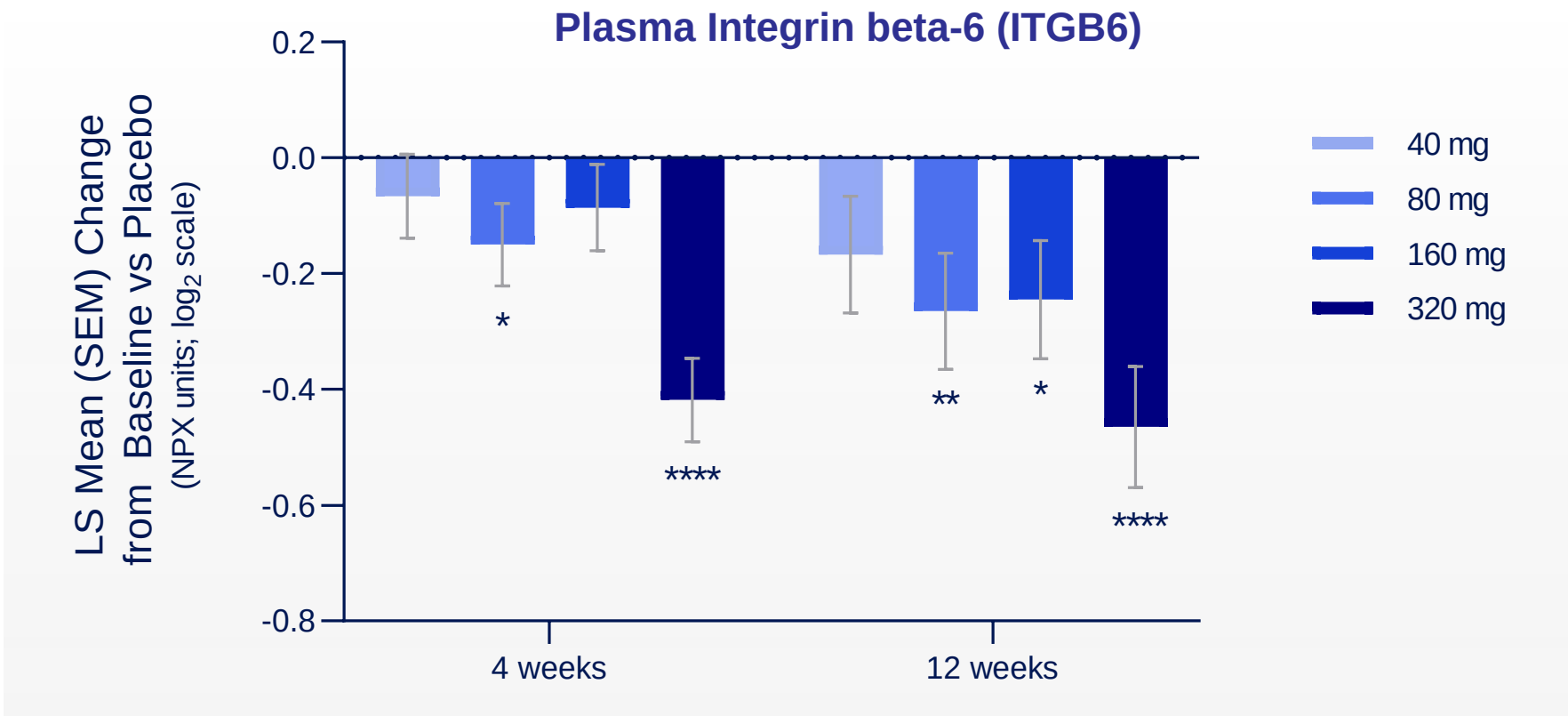
LS = Least Squares; SE = Standard Error

PRO-C3 and PRO-C6, serum biomarkers of type III and VI collagen synthesis, were previously shown to be elevated in patients with IPF and associated with progressive disease[1]

1- Respir Res. 2019 Jul 12;20(1):148.

PLIANT

Bexotegrast Reduced Integrin beta-6 Plasma Levels
Change from Baseline at 4 and 12 Weeks vs. Placebo



* p < 0.05 vs placebo
** p < 0.01 vs placebo
**** p < 0.0001 vs placebo

Relative quantitation of integrin beta-6 reported in in log_2 scale

Elevated integrin beta-6 plasma levels previously shown to be associated with ILD progression, as defined by mortality, transplant, or ≥ 10% relative reduction in FVC (mL) over 12 months[1]

1- Lancet Respir Med. 2022 Jun;10(6):593-602.
LS = Least Squares; SE = Standard Error

PLIANT

Conclusion and Next Steps

- Bexotegrast 320 mg dose demonstrated favorable safety and tolerability profile, and outperformed lower dose groups in overall treatment effects
- Observed treatment effect on top of standard-of-care therapy supports bexotegrast's potential to advance the treatment of IPF
- The 320 mg group will continue until all participants have been treated for at least 24 weeks, with final data expected in the second quarter of 2023
- Pliant plans to initiate Phase 2b clinical trial of bexotegrast in mid-2023

PLIANT

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

Enrollment Complete; 24-Week Data Expected in Second Quarter 2023

Randomization 3:1
(bexotegrast : placebo)

Placebo (n=7)

bexotegrast 320 mg (n=21)

KEY INCLUSION/EXCLUSION CRITERIA

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

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

Bexotegrast INTEGRIS-PSC – Phase 2a Global Safety-PK-Fibrosis and Cholestasis Biomarker Trial in PSC

Enrollment Complete; 12-Week Data Expected in Third Quarter 2023

KEY INCLUSION/EXCLUSION CRITERIA

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

Randomization 3:1 (bexotegrast : placebo)

- Placebo (n=21)
- bexotegrast 40 mg (n=21)
- bexotegrast 80 mg (n=21)
- bexotegrast 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

PLIANT

Bexotegrast Phase 2a 320 mg Dose Global Safety-PK-Exploratory Efficacy Trial in PSC

Enrollment Open

Randomization 3:1
(bexotegrast : placebo)

Placebo (n=7)

bexotegrast 320 mg (n=21)

KEY INCLUSION/EXCLUSION CRITERIA

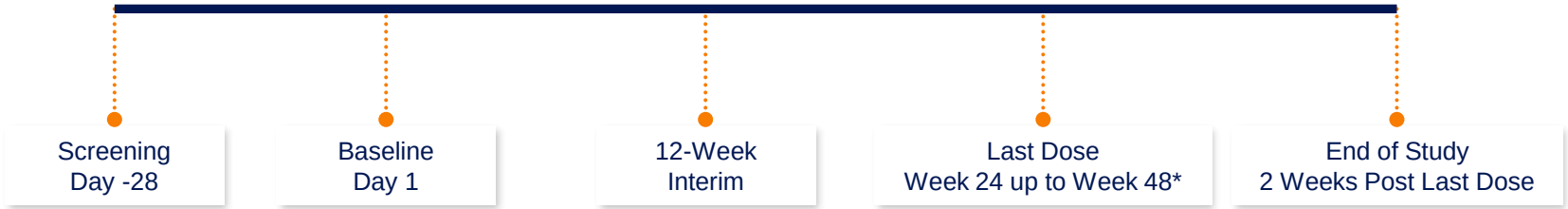
- Adults with large duct PSC
- Pre-cirrhotic
- Stable IBD, if present
- Stratified for UDCA use

PRIMARY AND SECONDARY ENDPOINTS

- Safety, tolerability, PK

EXPLORATORY ENDPOINTS

- Effect on fibrosis biomarkers (e.g., Pro-C3, ELF) at Wk 12 and 24
- Change in ALP at Wk 12 and 24



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

PLIANT

PLN-101095

Dual Selective $\alpha_V\beta_8$ / $\alpha_V\beta_1$ Integrin Inhibitor

Reprograming the Immunosuppressive Tumor Micro-Environment of Solid Tumors

Potential First-in-Class Small Molecule Dual $\alpha_V\beta_8$ / $\alpha_V\beta_1$ Inhibitor

$\alpha_V\beta_8$ Biology	Pharmacology	Differentiation	Development Status
$\alpha_V\beta_8$ regulates **TGFβ** activation with a central role in immune suppression in cancer	Highly selective inhibitor of **$\alpha_V\beta_8$** & **$\alpha_V\beta_1$** Supports human dose projections and **high target coverage** Compelling rationale for **$\alpha_V\beta_8$** combination therapy with **PD-(L)1**	**Dual mode of action targeting** T cells **$\alpha_V\beta_8$** & Fibroblasts **$\alpha_V\beta_1$** **PO Dosing**	No major findings in 28D GLP rat & dog toxicology studies IND submitted Q4 2022 FIH study to start 2Q 2023

Substantial opportunity for an oral medicine **targeting TGFβ activation** in ICI resistance **via $\alpha_V\beta_8$**

PLIANT

Pliant's Approach to Addressing Immune Checkpoint Inhibitor Resistance

Common Mechanisms of I-O Resistance	Pliant's Approach
Tumor-specific IFNγ levels at baseline predict pembrolizumab responses [4,5]	Potently inhibit general immunosuppressive immune checkpoint to restore CD8 T cell IFNy secretion
Immunosuppressive stroma / myeloid compartment associated with active TGFβ signaling predicts atezolizumab responses [3]	Prevent both free and latent-TGFβ signaling from major integrin sources found in solid tumors
Tumor infiltrating lymphocytes highly sensitive to TGFβ immunosuppression [e.g.1,2]	Dual mechanism significantly increases quantity of TILs and increase resistance to exhaustion

Dual inhibition of $\alpha_V\beta_8$ & PD-1 exploit unexpected synergistic pathways leading to enhanced tumor killing[6]

1- Thomas DA, et al. Cancer Cell. 2005 Nov;8(5):369-80. 2- Yang, ZZ. et al. Leukemia. 2014 28, 1872–1884. 3- Mariathasan, S. et al. 2018 Nature 554, 544–548.
4- Ayers, M et al. J Clin Invest. 2017 127(8):2930-2940. 5- Cindy Yang, S.Y. et al. Nat Commun. 2021 12, 5137. 6- Larrick J et al., DOI: https://doi.org/10.21203/rs.3.rs-1778271/v1

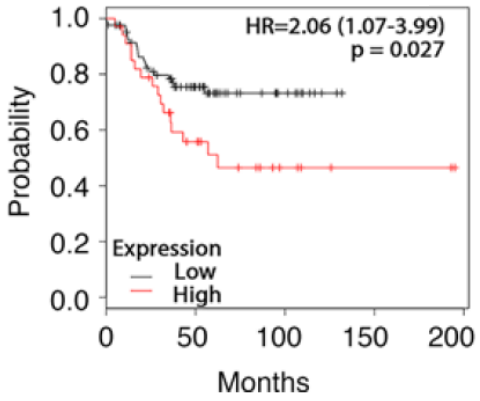
PLIANT

High ITGB8 on Tumor or T cells Has Poor Prognosis

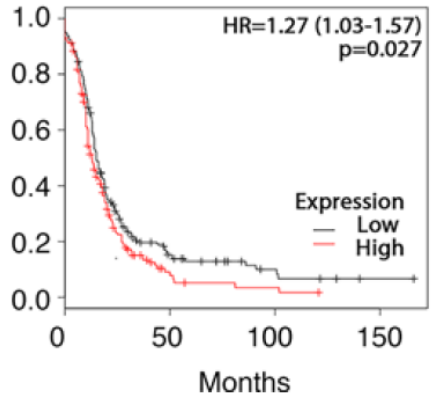
High ITGB8 expression on tumor cells has a worse clinical prognosis

Takasaka N. et al. *JCI Insight 2018;3*
doi 10.1172/jci.insight.122591

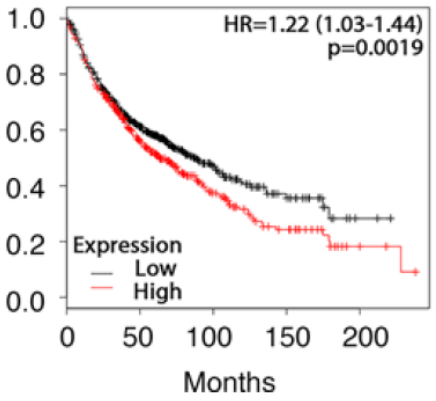
Breast Cancer



Ovarian Cancer



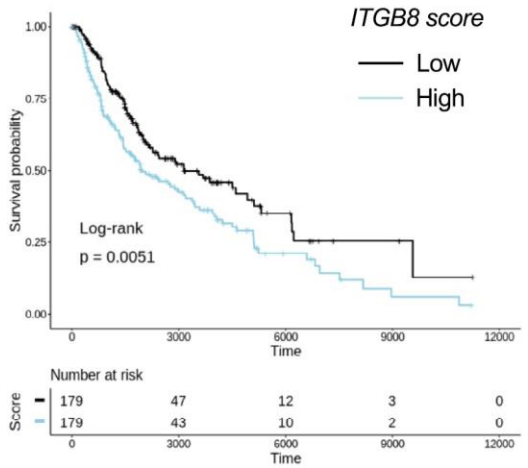
Lung Cancer



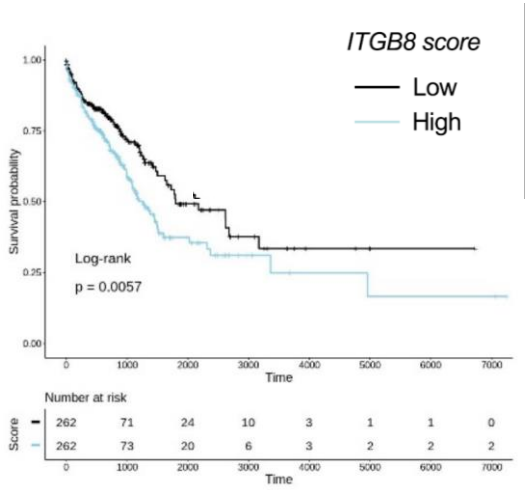
High ITGB8 score on infiltrating T cells correlates with worse prognosis

Lainé A., *Nat Commun* **12**, 6228 (2021)
doi: 10.1038/s41467-021-26352-2

Melanoma



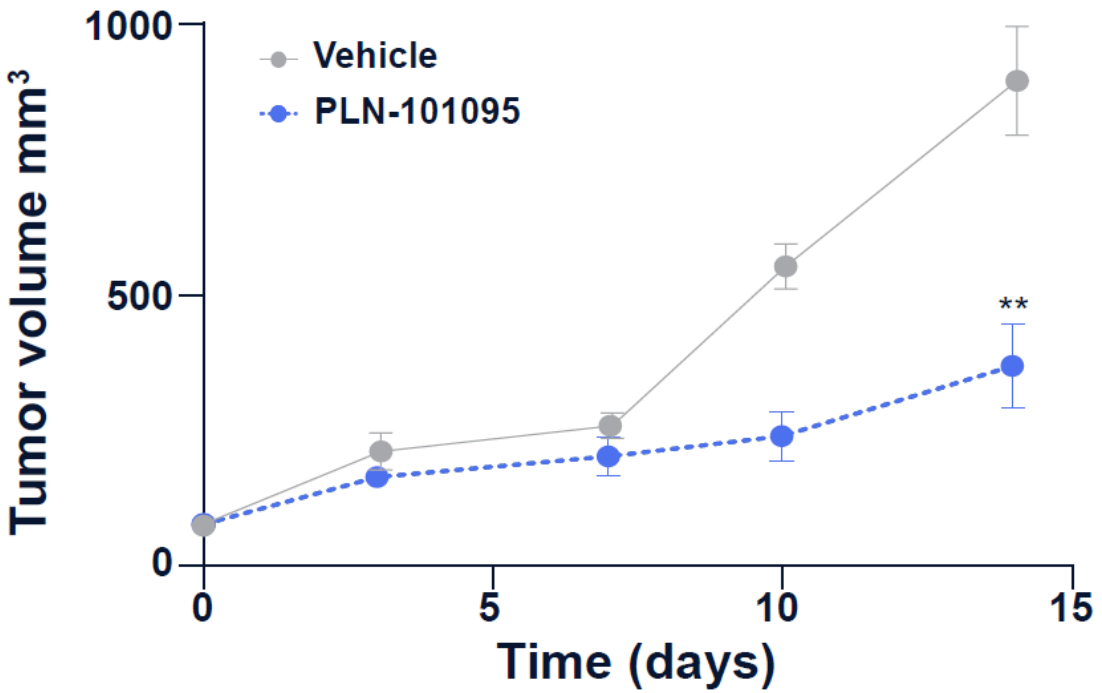
Non-Small Cell Lung Cancer



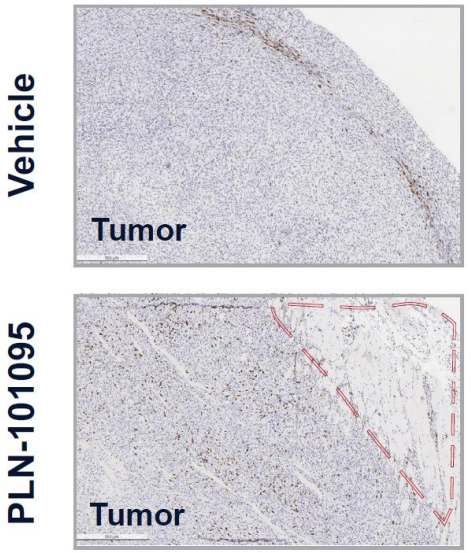
PLIANT

PLN-101095 Inhibited Tumor Growth and Promoted T cell Infiltration in the EMT6 Model

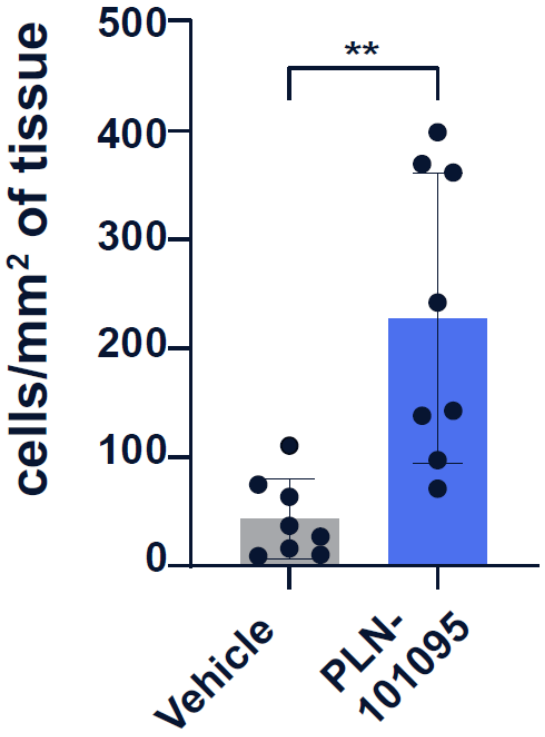
Tumor Growth Inhibition in EMT6 Tumors



CD8⁺ T Cells



CD8⁺ T Cells

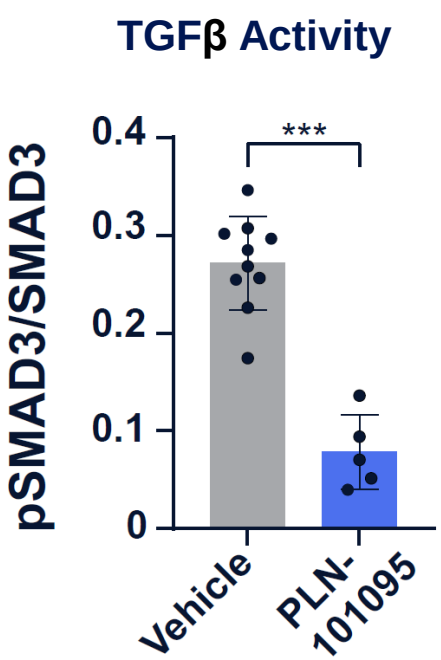


SITC 2022 Poster #1352

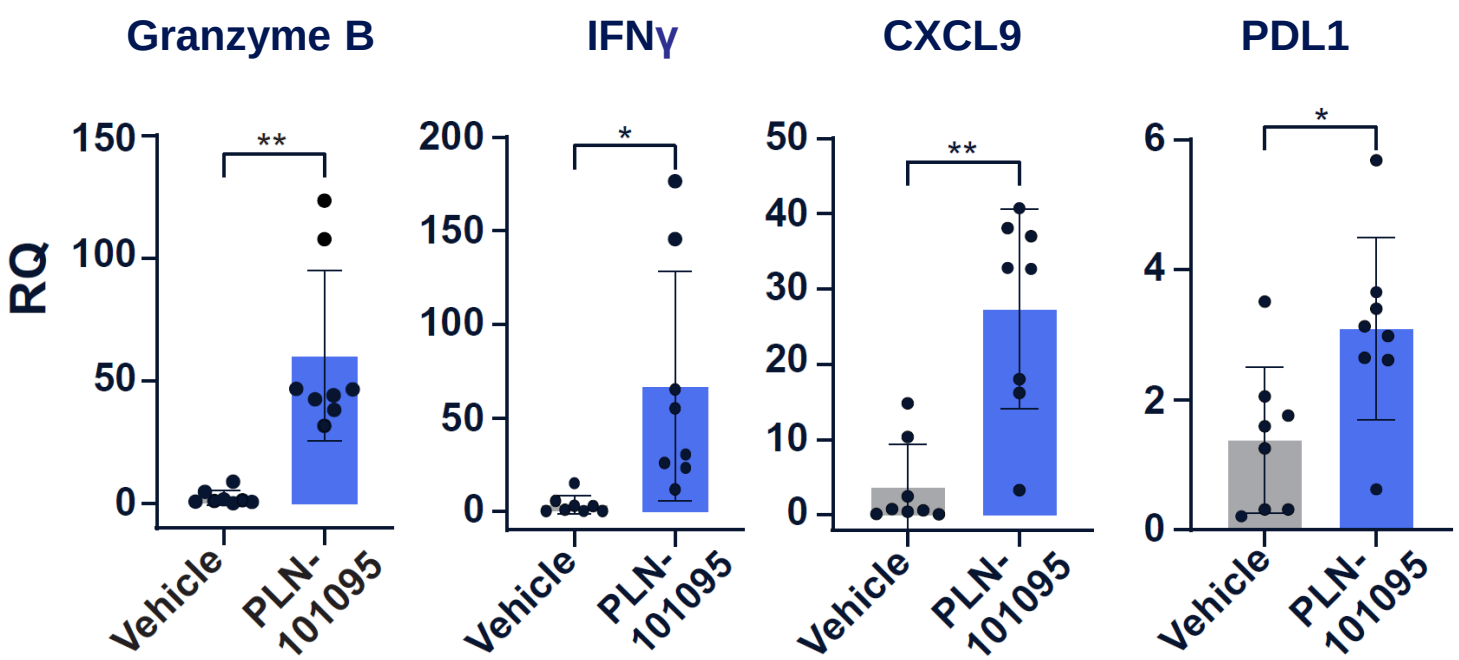
PLIANT

Single Agent PLN-101095 Promoted T Cell Infiltration

Reduced TGF-β Signaling



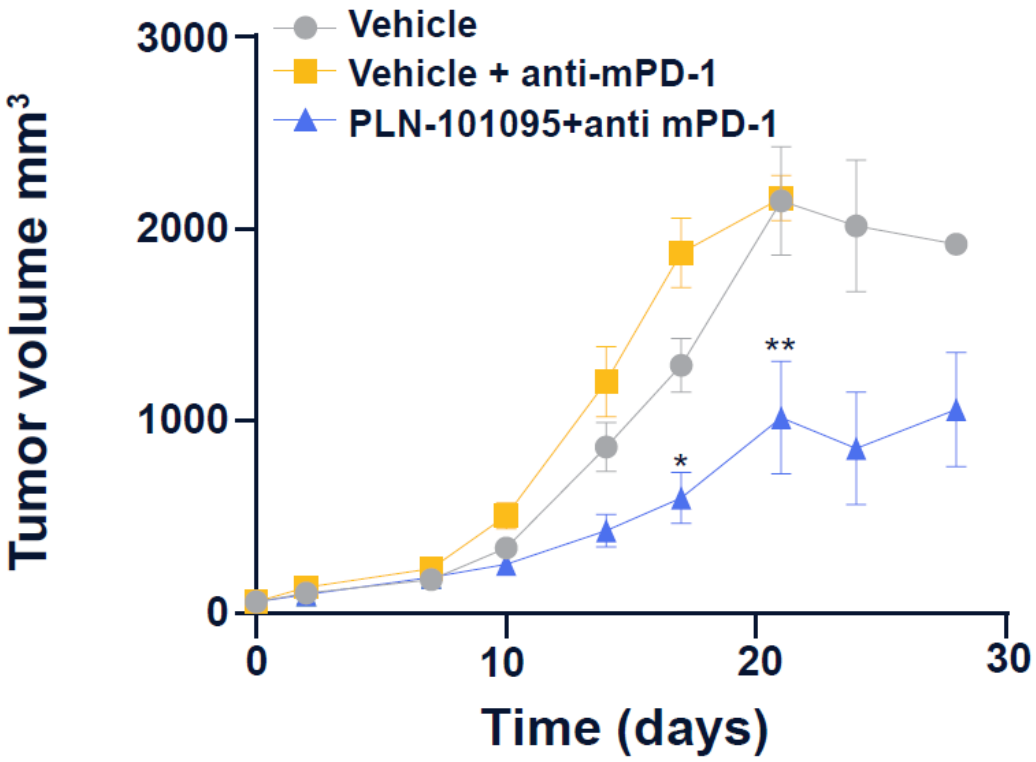
Increased Expression of IFNγ-Regulated Genes



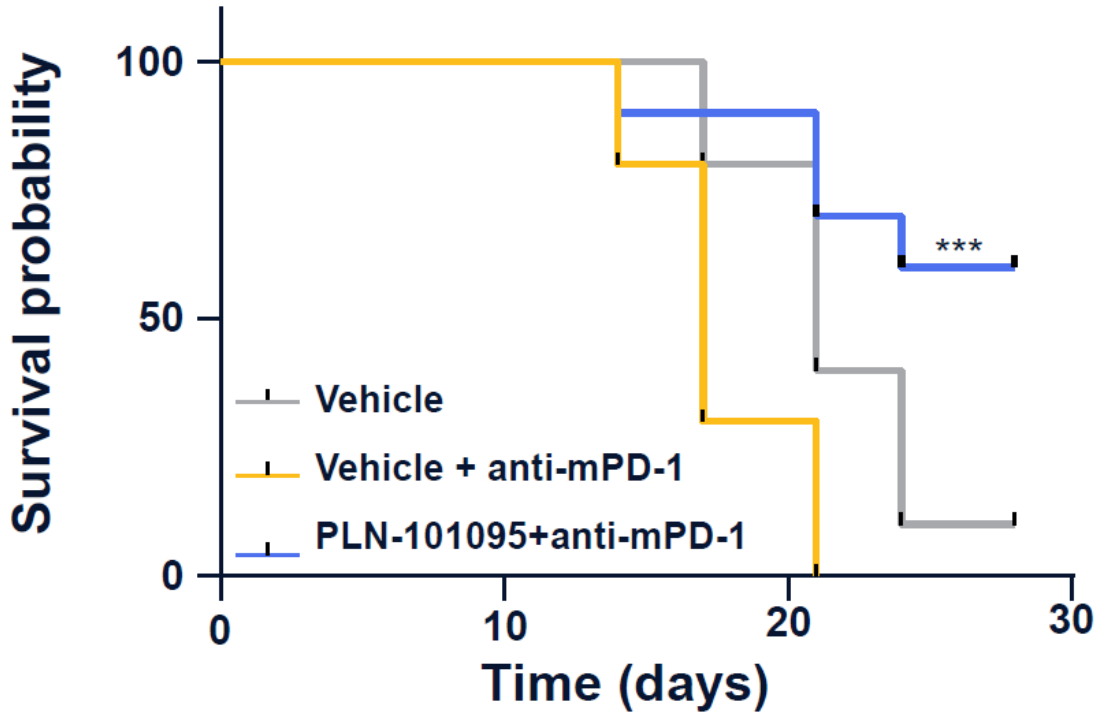
SITC 2022 Poster #1352

PLN-101095 Plus αPD-1 Demonstrated High Tumor Growth Inhibition in EMT6 Syngeneic Mouse Model

Tumor Growth Inhibition in EMT6 Tumors



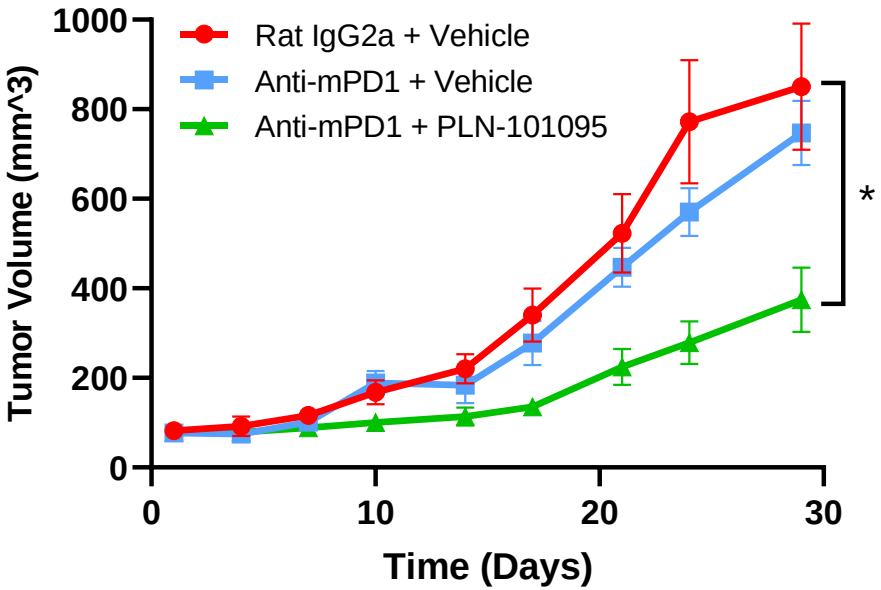
Survival



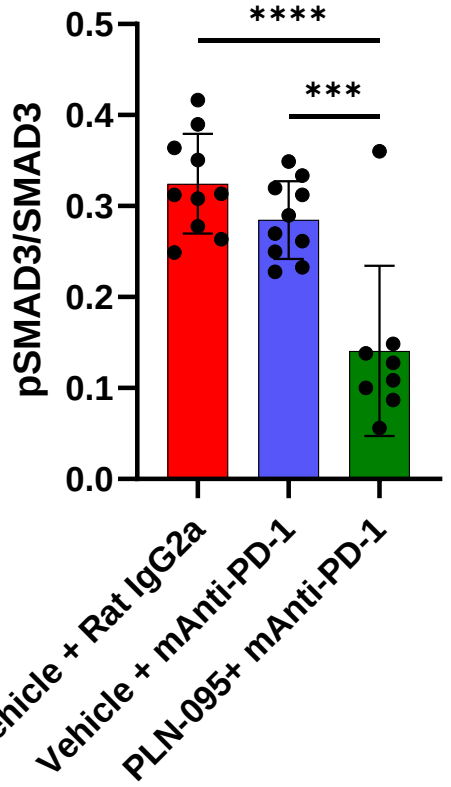
SITC 2022 Poster #1352

PLN-101095 Inhibited Pan02 Tumor Growth & Increases T cell Infiltration

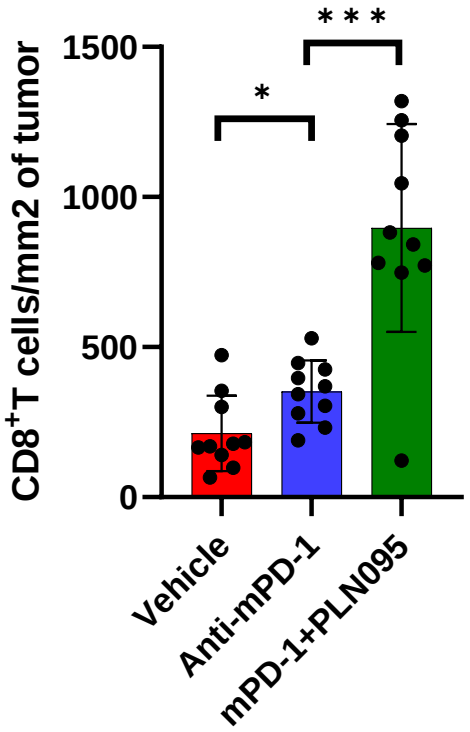
Tumor Growth Inhibition in Pan02 Tumors



TGFβ Signaling

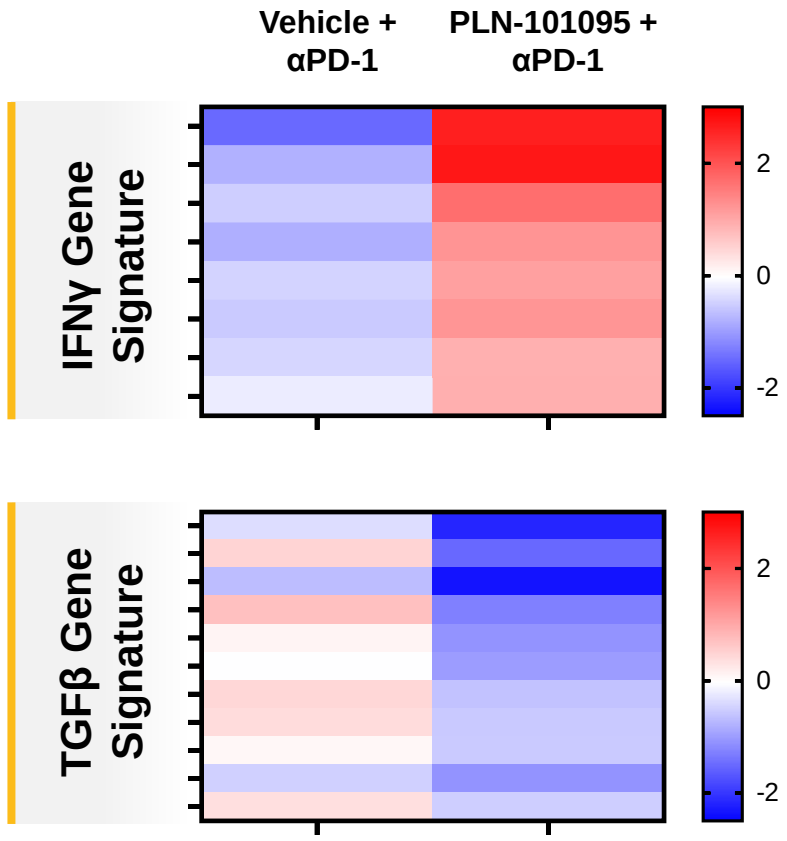


CD8⁺ T Cells



SITC 2022 Poster #1352

PLN-101095 Potently Increased IFNγ Signature & Reduces TGFβ Gene Signatures



Anti-PD-(L)1 Non-Responsive Baseline Gene Signature

High **TGFβ** Signature

Low **IFNγ** Signature

PLN-101095 Promotes ICI Responsiveness

Sensitized to Anti-PD-(L)1

High **IFNγ** Signature

Low **TGFβ** Signature

PLIANT

PLN-101095 Nonclinical Safety Studies
No Effects of Concern for Clinical Advancement

Study Category	Studies Completed	Findings with PLN-101095
Repeat Dose Toxicology	• 14-day DRF in rat • 7-day DRF in dog • GLP 1-Month IND-enabling rat • GLP 1-Month IND-enabling dog	• **No adverse findings** in rat or dog DRF • All doses tolerated • **NOAEL[1] set at highest dose**
Safety Pharmacology	• GLP hERG • Safety44	• **No findings**
Genetic Toxicology	• GLP Ames • GLP In vitro micronucleus	• **No findings**

1 – No observed adverse effect level.

Key Program Highlights

- **Oral route** of administration of small molecule $\alpha_V\beta_8$ inhibitor
- **Highly potent** dual inhibitor of $\alpha_V\beta_8$ / $\alpha_V\beta_1$ inhibitor
- **Activity** demonstrated in multiple **PD-1 resistant** tumor models
- **Greater reduction** in **TGF-β signaling** than either $\alpha_V\beta_8$ or TGF-$\beta_{1,2}$ mAb
- **Significant reduction** in tumor **fibrogenesis**
- **Phase 1 study initiation for** PLN-101095 in **second quarter 2023**

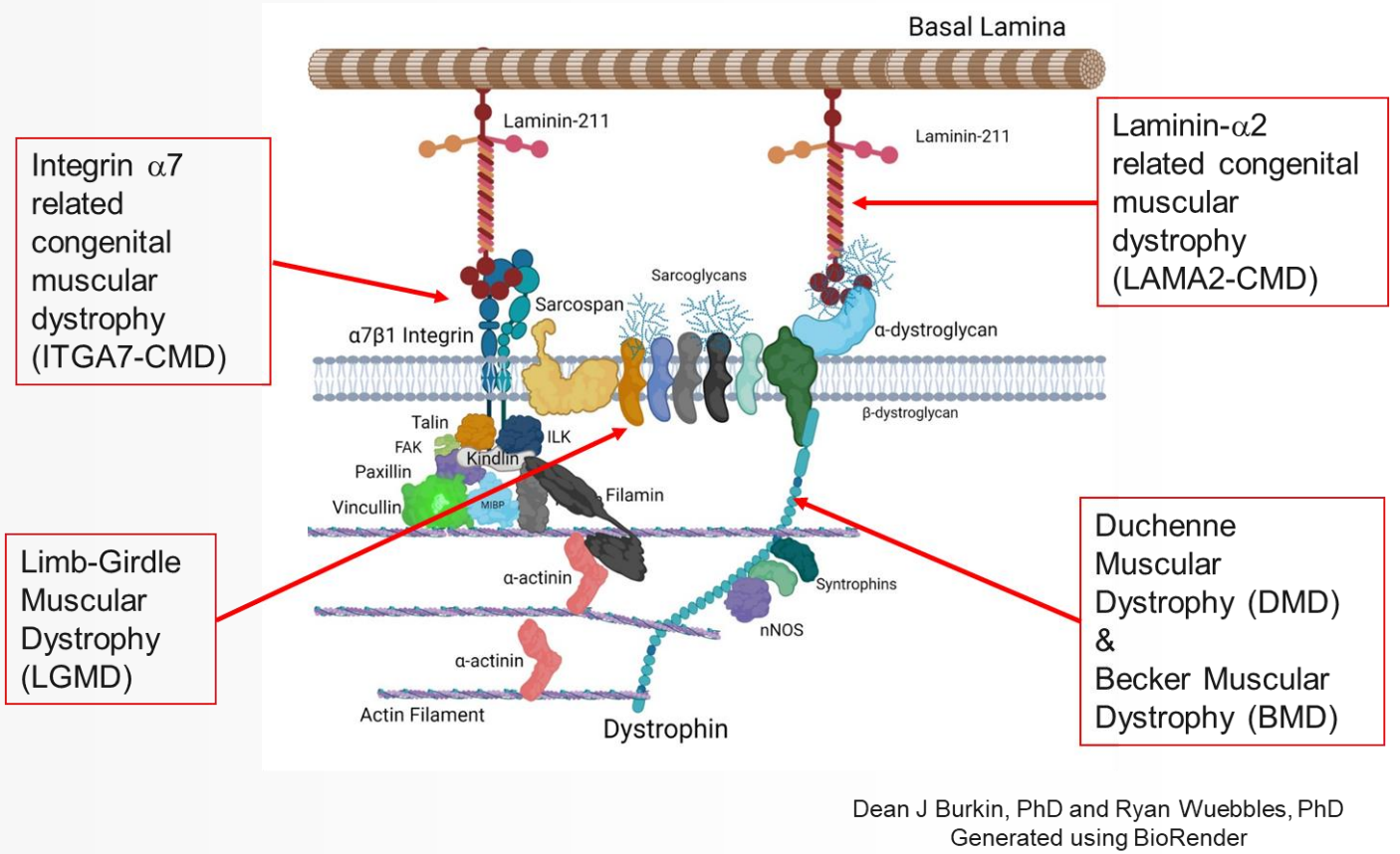
PLIANT

PLIANT

Selective Muscle Cell Integrin Agonism for the Treatment of Muscular Dystrophies

$\alpha_7\beta_1$: A Drug Target in Muscular Dystrophies

- Predominantly expressed in skeletal, heart and smooth muscle
- $\alpha_7\beta_1$ strong genetic modifier in MDX mice
  - Lack of $\alpha_7\beta_1$ worsens disease phenotype
  - Over expression increases survival and improves function
    - Pharmacological agents that increase expression show similar effects
- Human mutations in $\alpha_7\beta_1$ result in congenital MD
- ITGA7 frameshift (heterozygous, nonfunctional mutation is associated with lean muscle volume reduction (UK Biobank)



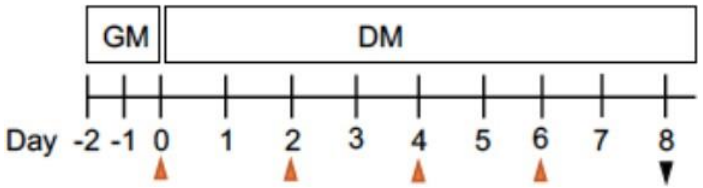
Dean J Burkin, PhD and Ryan Wuebbles, PhD
Generated using BioRender

J Cell Bio 2001, *Human Gen Ther* 2015, *Molecular Therapy* 2017

Integrin $\alpha_7\beta_1$ Agonist Antibody Promoted Muscle Maturation

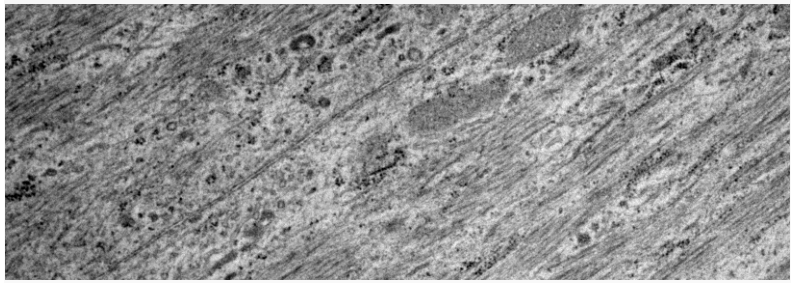
AB1071 hMMTs treated with 1 ug/ml or 10 ug/ml
Pliant antibody contain myotubes with substantially improved sarcomere organization that can withstand tetanic stimulation compared to IgG4 control

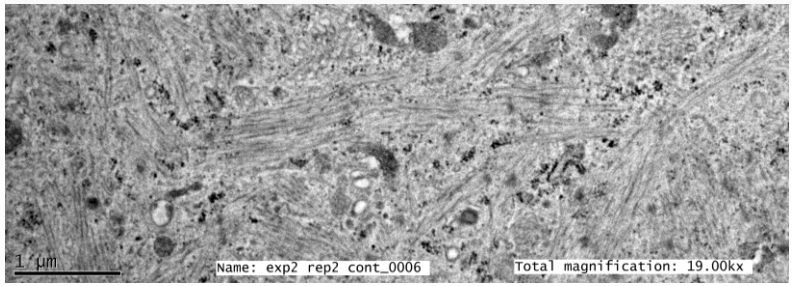
TREATMENT REGIME



(+) “Exercise”

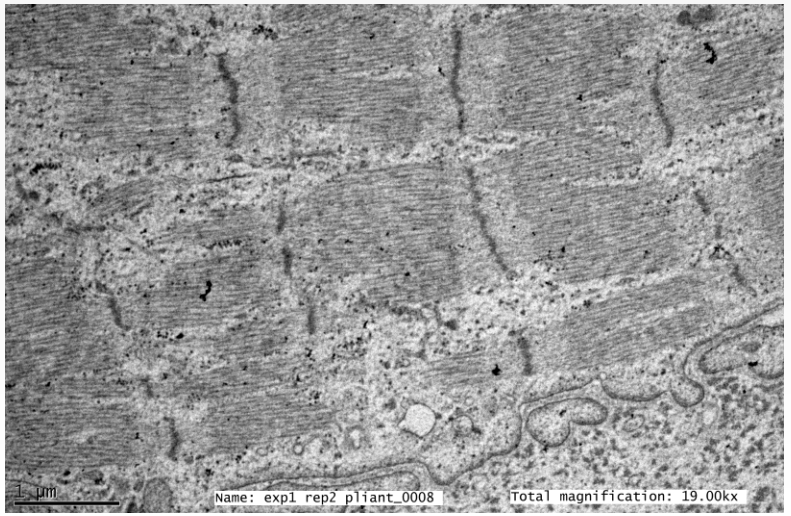
IgG4



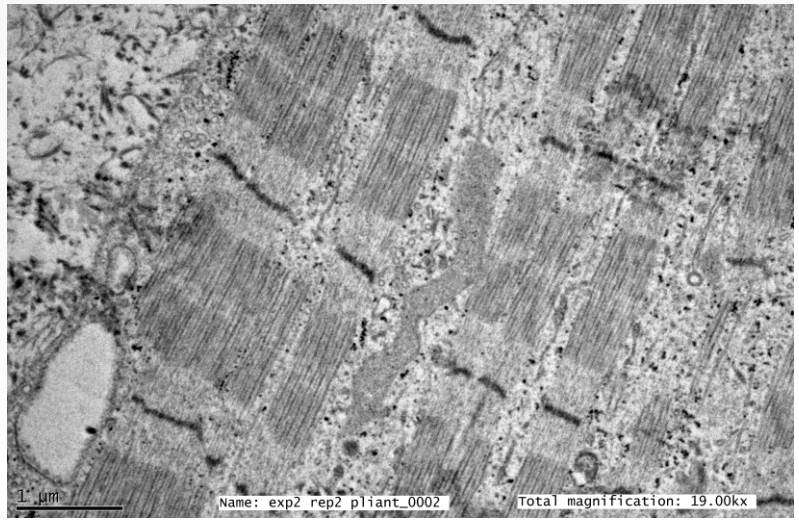


α7β1 agonist

1 µg/ml



10 µg/ml

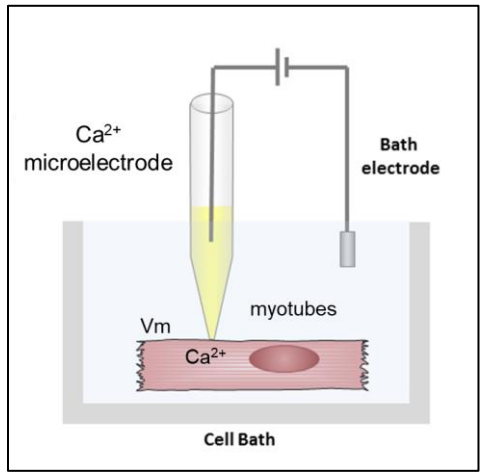


PLIANT

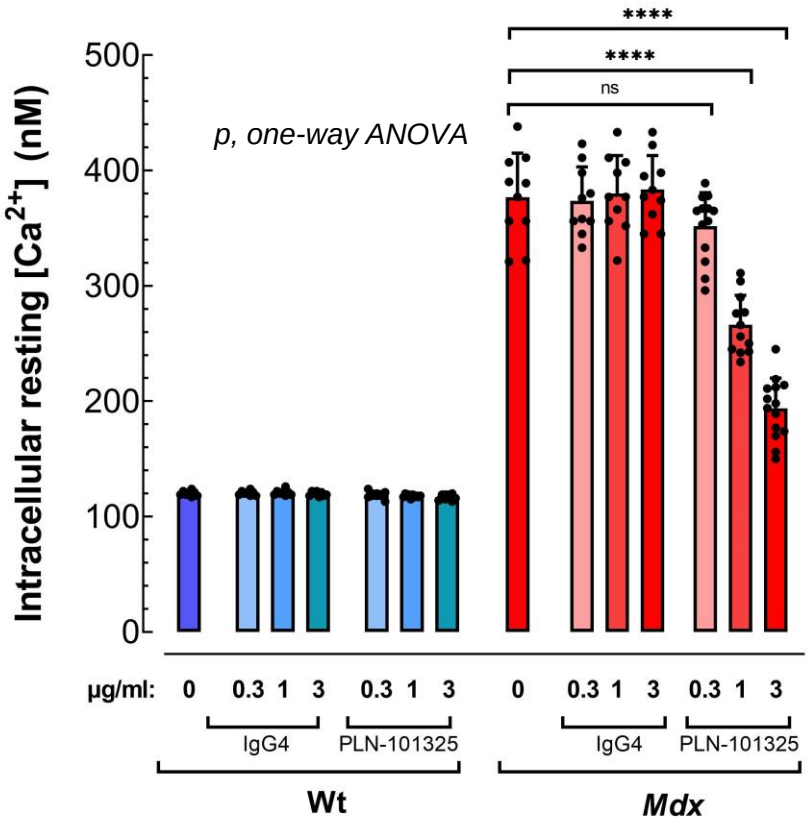
Institute of Biomedical Engineering
UNIVERSITY OF TORONTO

Effect of PLN-101325 in Ca2+ Homeostasis and Resting Membrane Potential of B10-mdx Myotubes

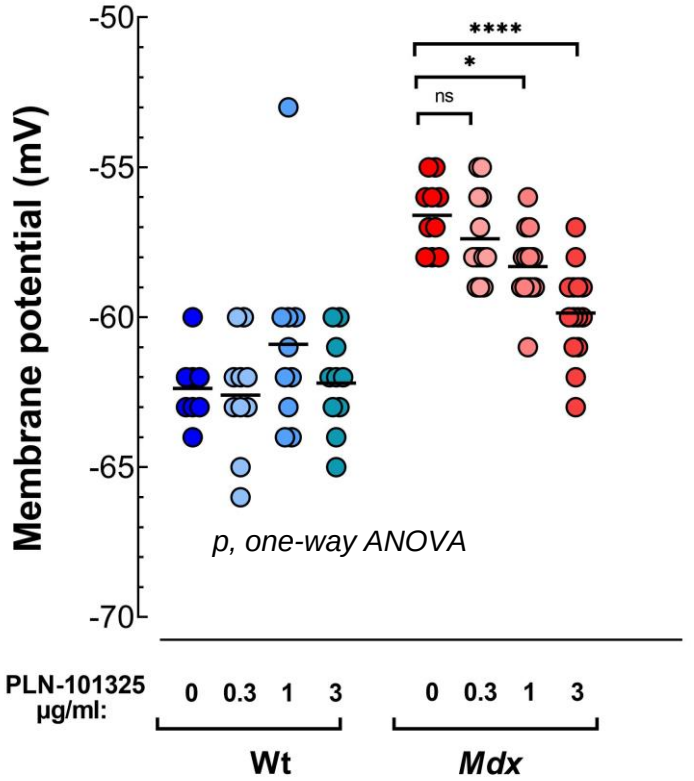
Reduced intracellular resting calcium and hyperpolarization of the membrane potentially support improved plasmalemmal integrity by PLN-101325



Intracellular resting Ca^{2+}



Resting membrane potential



Dr. Jose R. Lopez

Mount Sinai MEDICAL CENTER

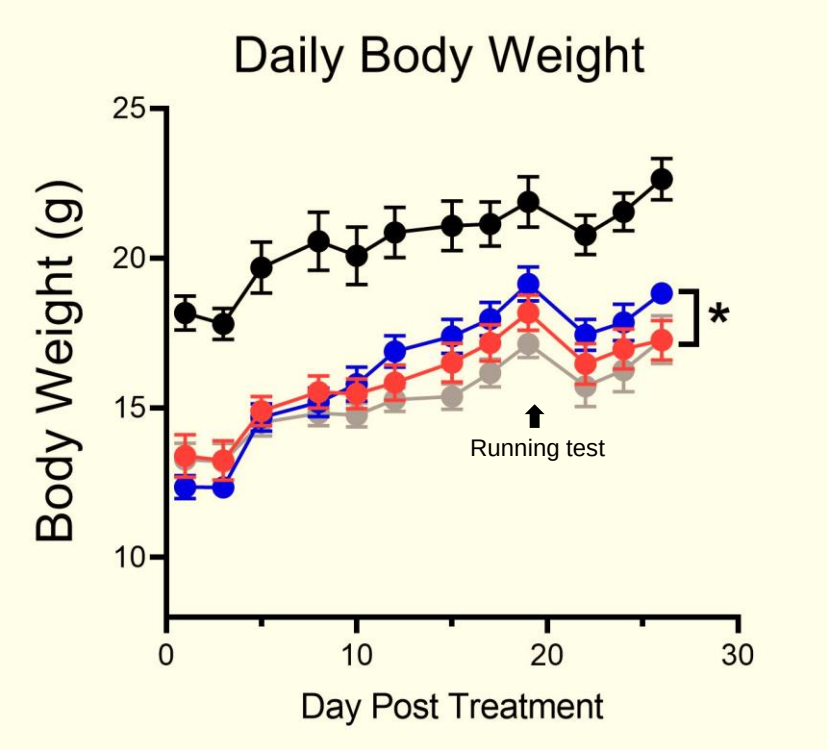
PLIANT

Body Weight Improvement at 4 and 12 Weeks of Treatment

- PLN-101325 3x/ wk IP
- 5-6 wk old D2-MDX mice

4-week

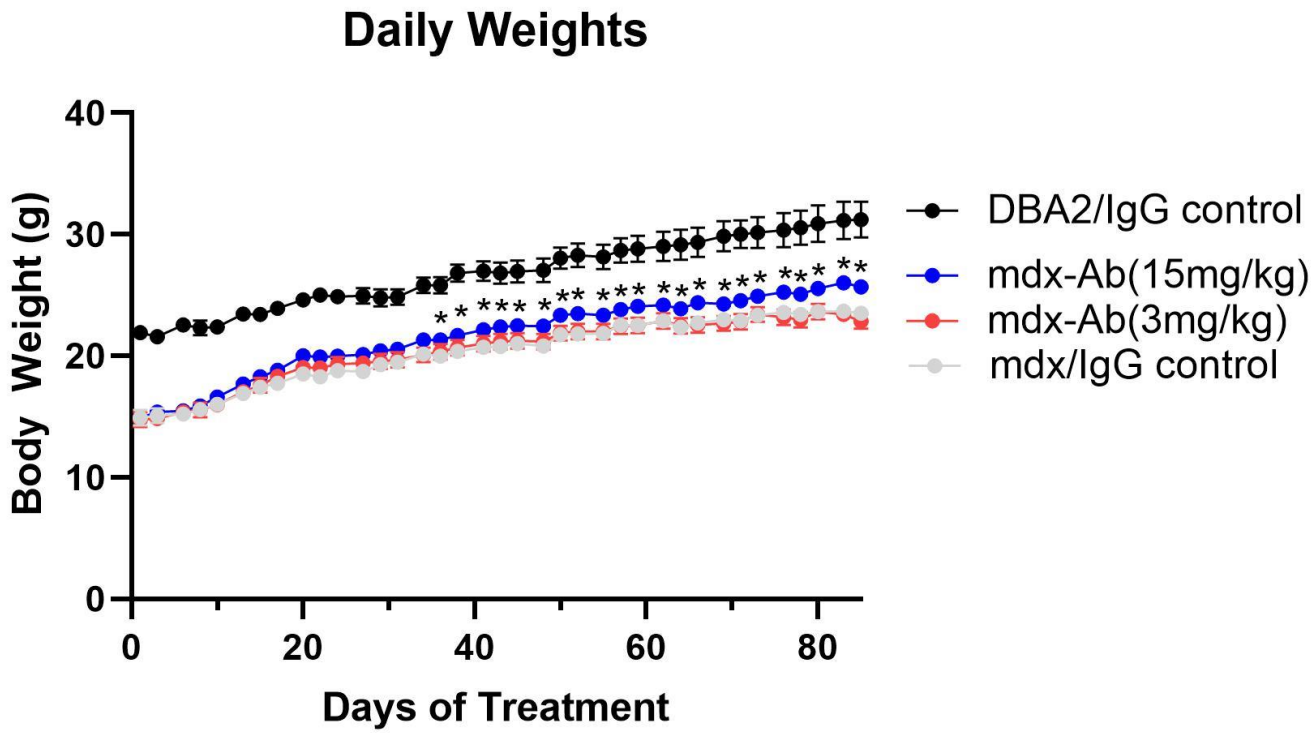
8 ± 3% Increase in Body Weight



12-week

9 ± 1% Increase in Body Weight

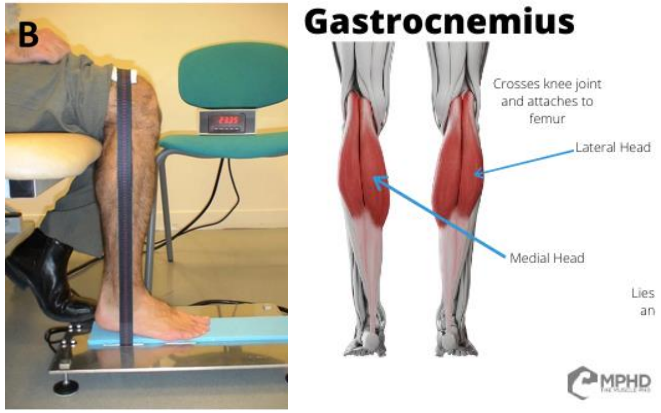
Weight Increase 9 ± 1%



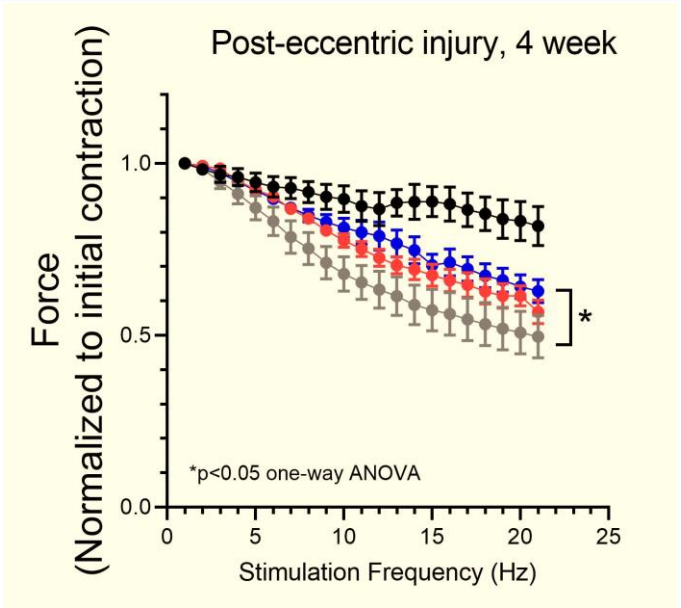
Improved Response to Post Eccentric Injury at 4 and 12 Weeks of Treatment

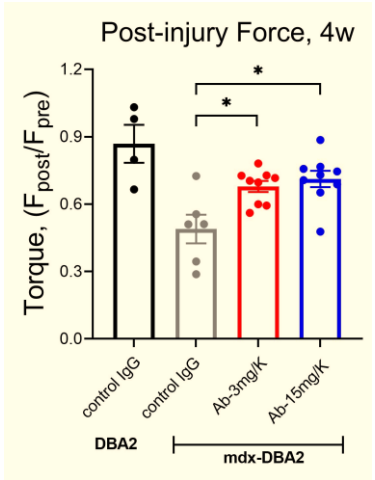
Plantar flexion test

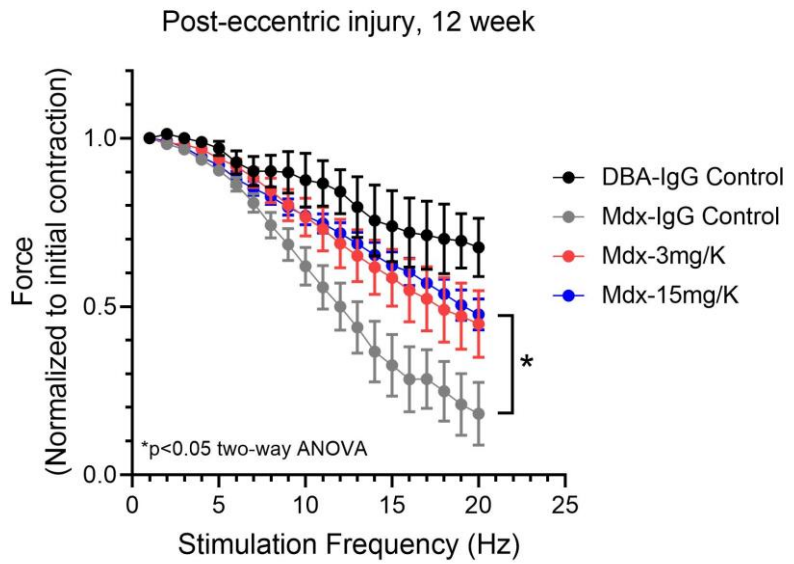
- Gastrocnemius (GC): Premier mover muscle for plantar flexion.
- GC only muscle to join both ankle and knee.

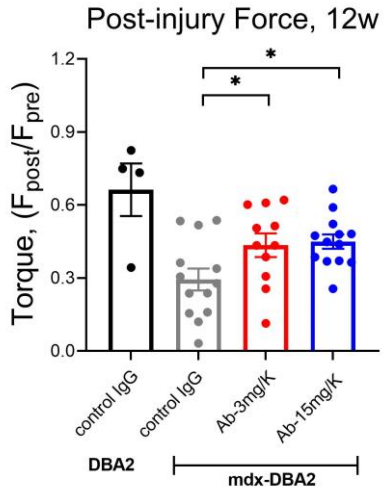


Eccentric muscle injury protocol: A series of 20 tetanic stimulations (80Hz, 0.2ms pulse, 500ms duration) are delivered at 0.1Hz frequency. The foot is rotated against the direction of contraction by 10° over 250ms, resulting in an eccentric contraction

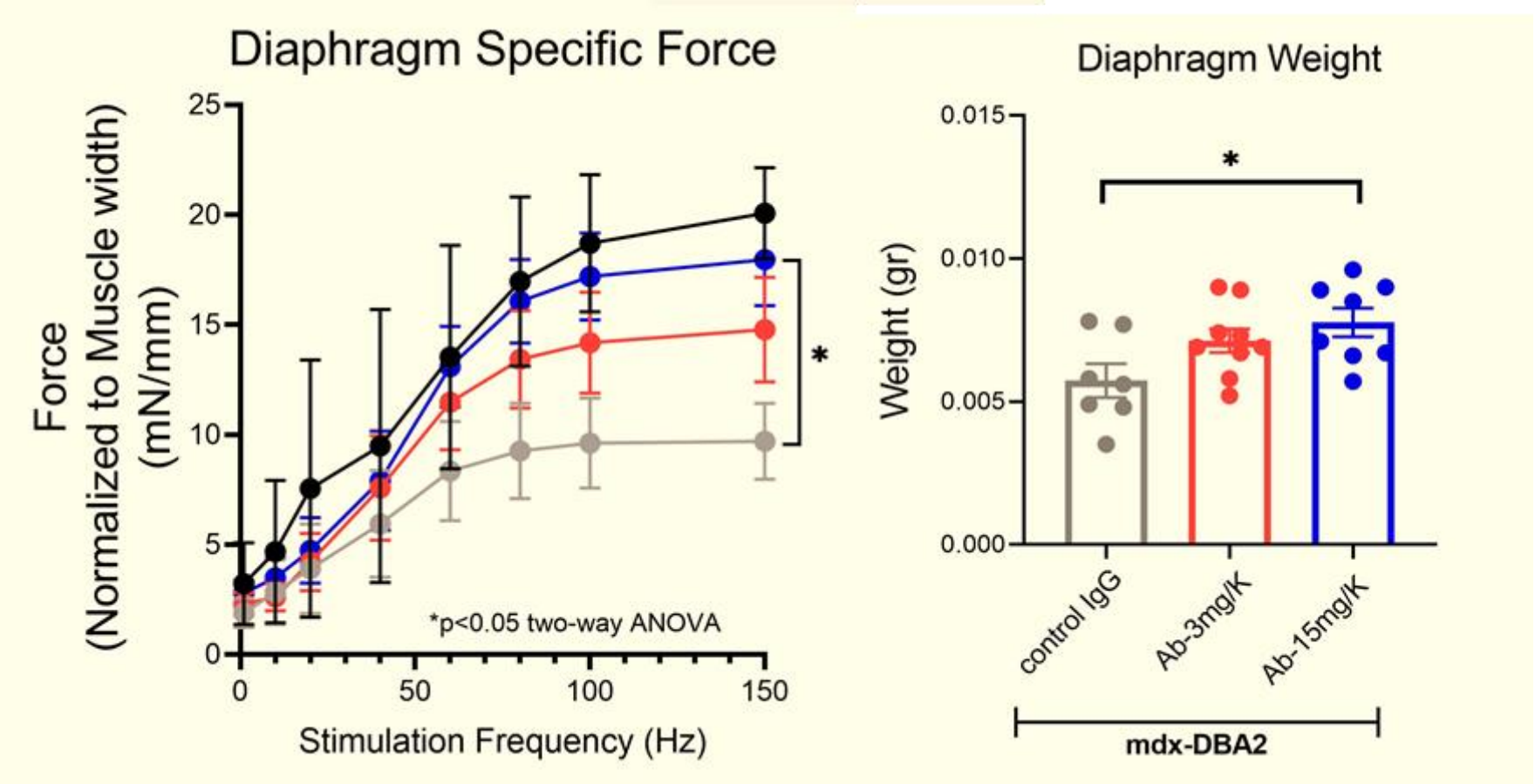








Diaphragm Force Significantly Improved at 4 Weeks of Treatment

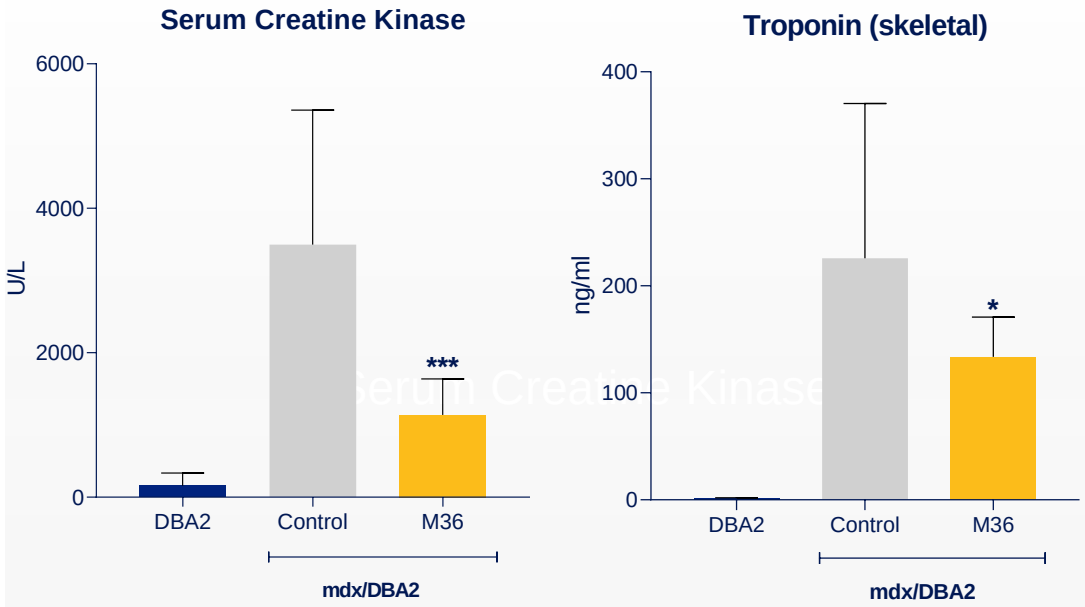


MYOLOGICA

PLIANT

Pliant's $\alpha_7\beta_1$ mAb Demonstrated Improved Muscle Membrane Integrity and Diaphragm Function in Mouse DMD Model

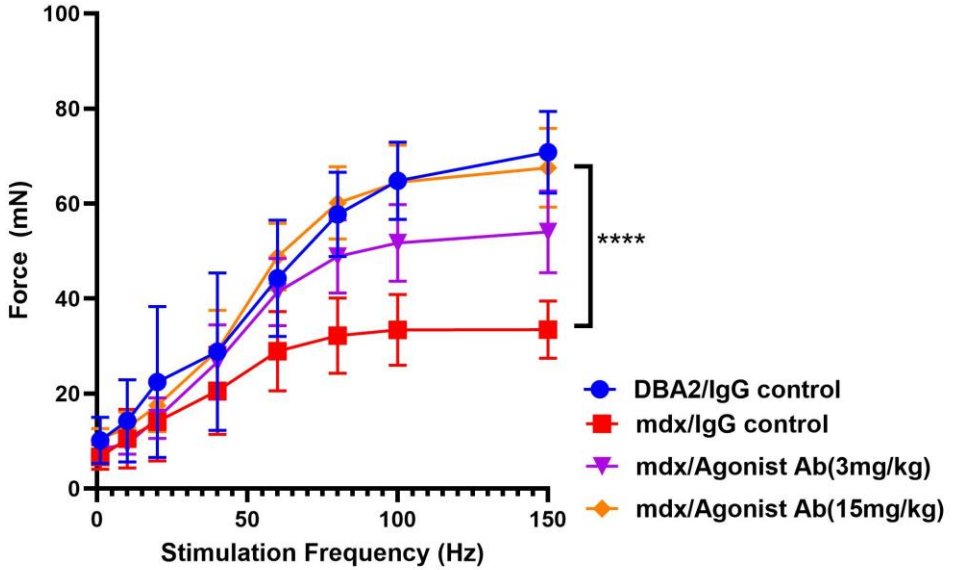
Antibody treatment protected against muscle damage



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

***p 0.001, *p<0.05, one-way ANOVA
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

****p 0.0001, two-way ANOVA

PLIANT

Pliant Development Pipeline

Program	Indication	Preclinical	Clinical			Anticipated Milestone	Global Rights
			Phase I	Phase II	Phase III		
Bexotegrast (PLN-74809) Dual selective inhibitor of $\alpha_v\beta_6$ /$\alpha_v\beta_1$	Idiopathic Pulmonary Fibrosis					Phase 2a 320 mg 24-Week Data Expected 2Q 2023	PLIANT
	Primary Sclerosing Cholangitis					Phase 2a Data Expected 3Q 2023	PLIANT
PLN-101095 Inhibitor of $\alpha_v\beta_8$ /$\alpha_v\beta_1$	Solid Tumors					Phase 1 Initiation 2Q 2023	PLIANT
PLN-101325 Anti-integrin mAb of $\alpha_7\beta_1$	DMD Other Muscular Dystrophies					IND Filing Expected 2023	PLIANT
PLN-1474 Selective inhibitor of $\alpha_v\beta_1$	NASH-Associated Liver Fibrosis					Phase 2 Ready	PLIANT