PLIANT

Developing Novel Treatments for Fibrotic Diseases

41st Annual J.P. Morgan Healthcare Conference

JANUARY 10, 2023

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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.

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Pliant – Company Highlights

Industry-Leading Fibrosis Platform

- Inhibition of integrin-mediated TGF-β activation resulting in antifibrotic effect and shown to be safe
- 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 submitted 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 $625 million raised to date including 2020 IPO (Nasdaq: PLRX) and $230 million follow on (July 2022)
- $360 million cash balance as of September 30, 2022 - Operations funded to mid-2025

Pliant - Development Pipeline

	Program	Indication	Preclinical	Clinical			Anticipated Milestone	Global Rights
				Phase I	Phase II	Phase III		
WHOLLY OWNED	Bexotegrast Dual selective inhibitor of $\alpha_v\beta_6$ /$\alpha_v\beta_1$	Idiopathic Pulmonary Fibrosis					Phase 2a 320 mg 12-Week Data Expected Early 1Q 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					IND Filed; Phase 1 initiation 2Q 2023	PLIANT
	PLN-101325 Anti-$\alpha_7\beta_1$ mAb	DMD Other Muscular Dystrophies					IND Filing Expected 2023	PLIANT
PARTNERED	PLN-1474 Selective inhibitor of $\alpha_v\beta_1$	NASH-Associated Liver Fibrosis					Phase 2 Initiation	NOVARTIS

Anticipated 2023 Milestones

Bexotegrast INTEGRIS-IPF – 320 mg

- 1Q 2023: 12 week interim data
- 2Q 2023: 24+ week final data

Bexotegrast INTEGRIS-PSC – 40, 80, 160 mg

- 3Q 2023: 12 week data

Bexotegrast IPF Phase 2b

- Start mid-2023

PLN-101095

- 2Q 2023: start Phase 1

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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 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

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
- 0% GI-related AEs in monotherapy setting

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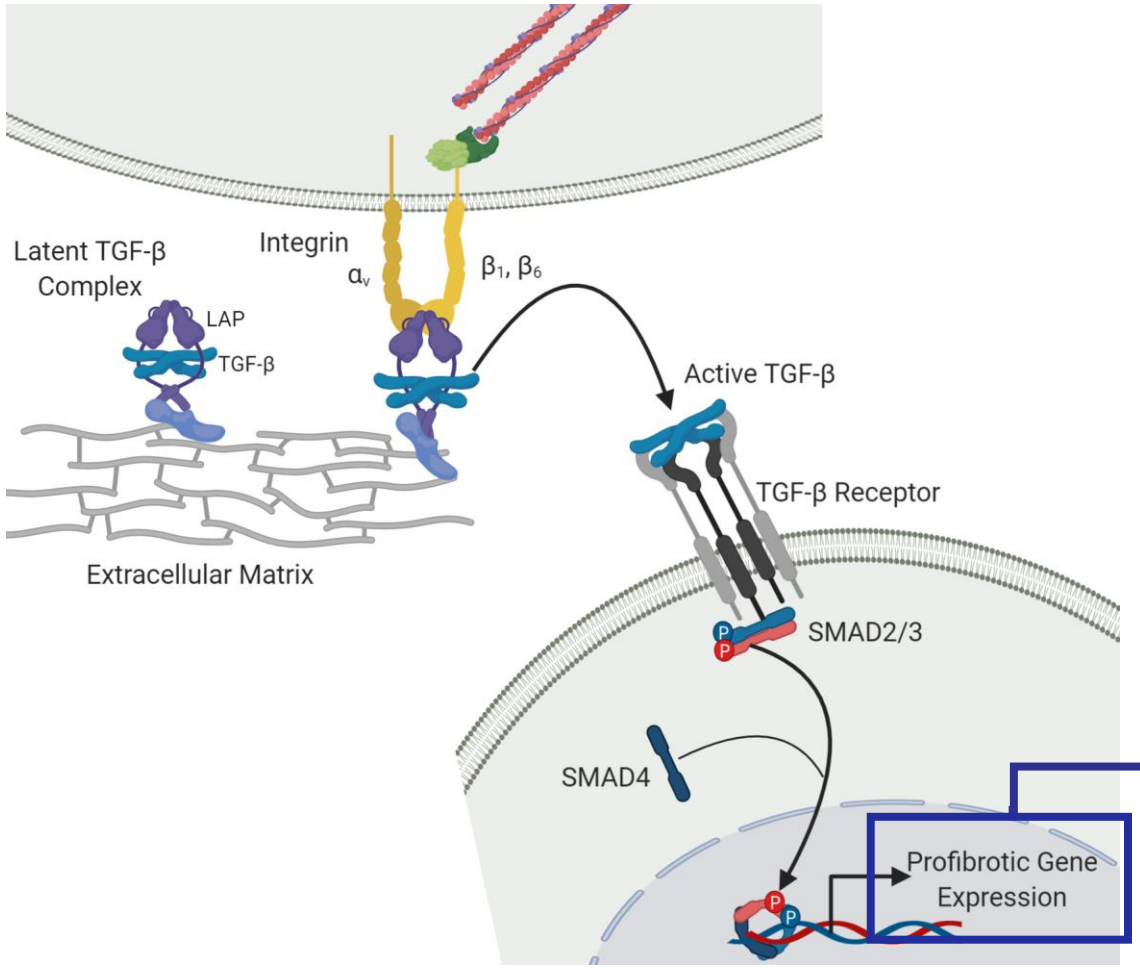
$\alpha_V\beta_6$ / $\alpha_V\beta_1$ Integrins Drive Cell-Matrix Interactions in Fibrosis

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

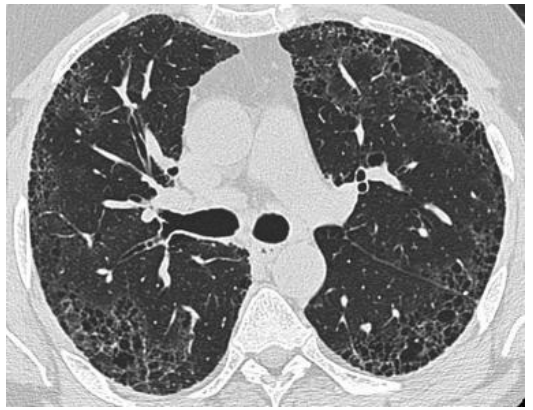


- **TGF-β is central mediator of fibrosis**
- **$\alpha_V\beta_6$ /$\alpha_V\beta_1$ Integrins activate latent TGF-β only in fibrotic tissue**
- **Systemic TGF-β blockade carries toxicity risks**

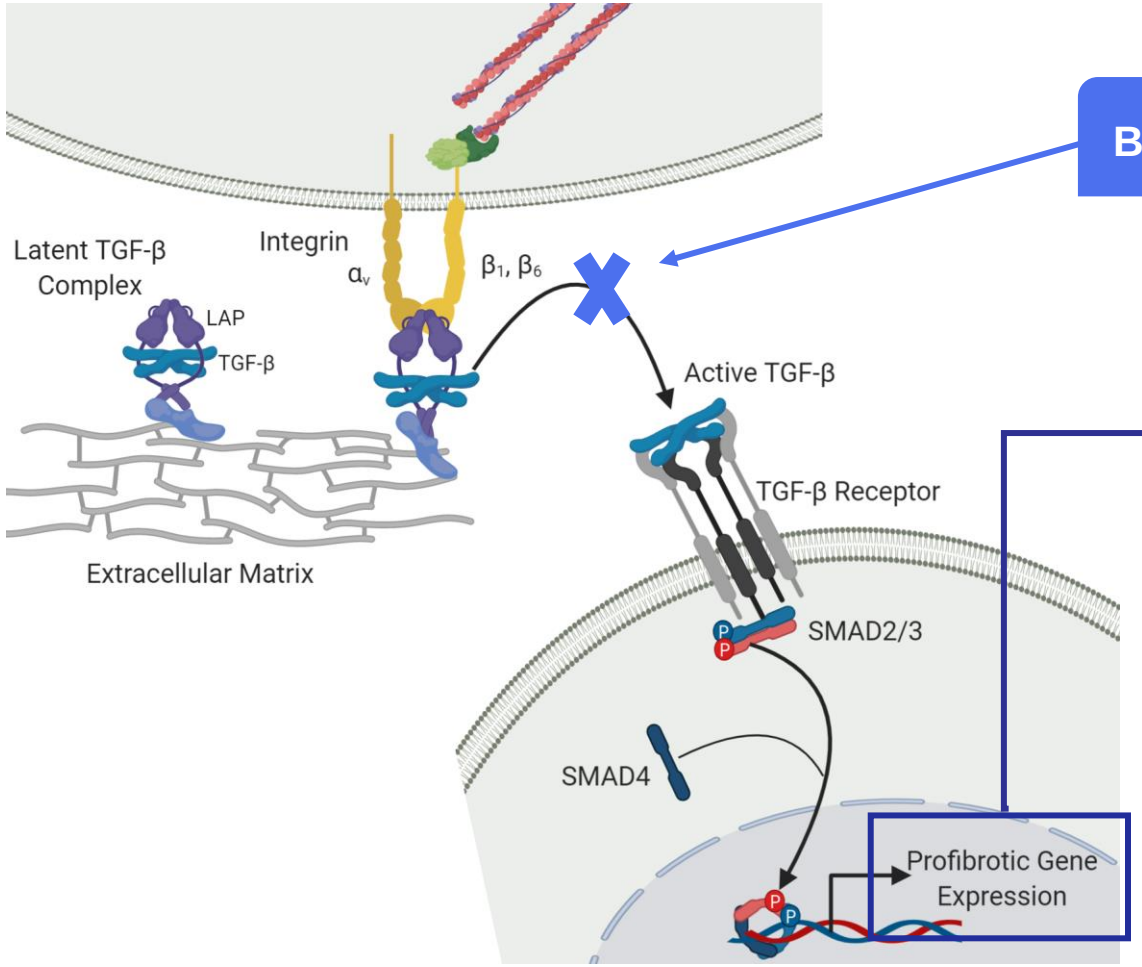
Selectively blocking TGF-β in fibrotic tissues may provide a low risk, effective antifibrotic approach

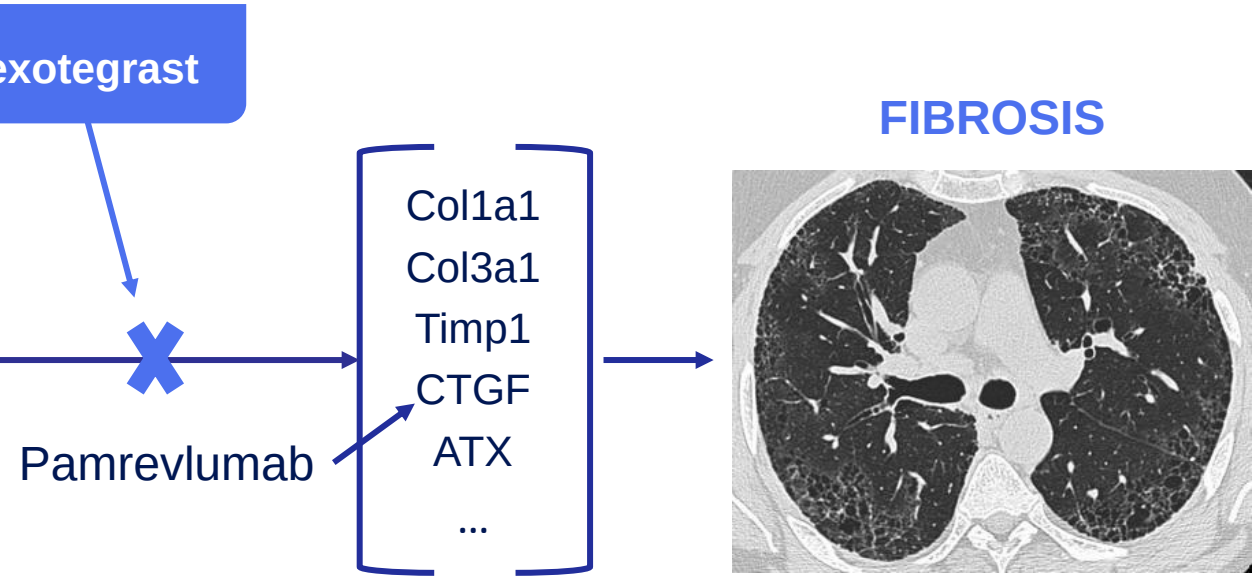
Col1a1
Col3a1
Timp1
CTGF
ATX
…

FIBROSIS



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





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

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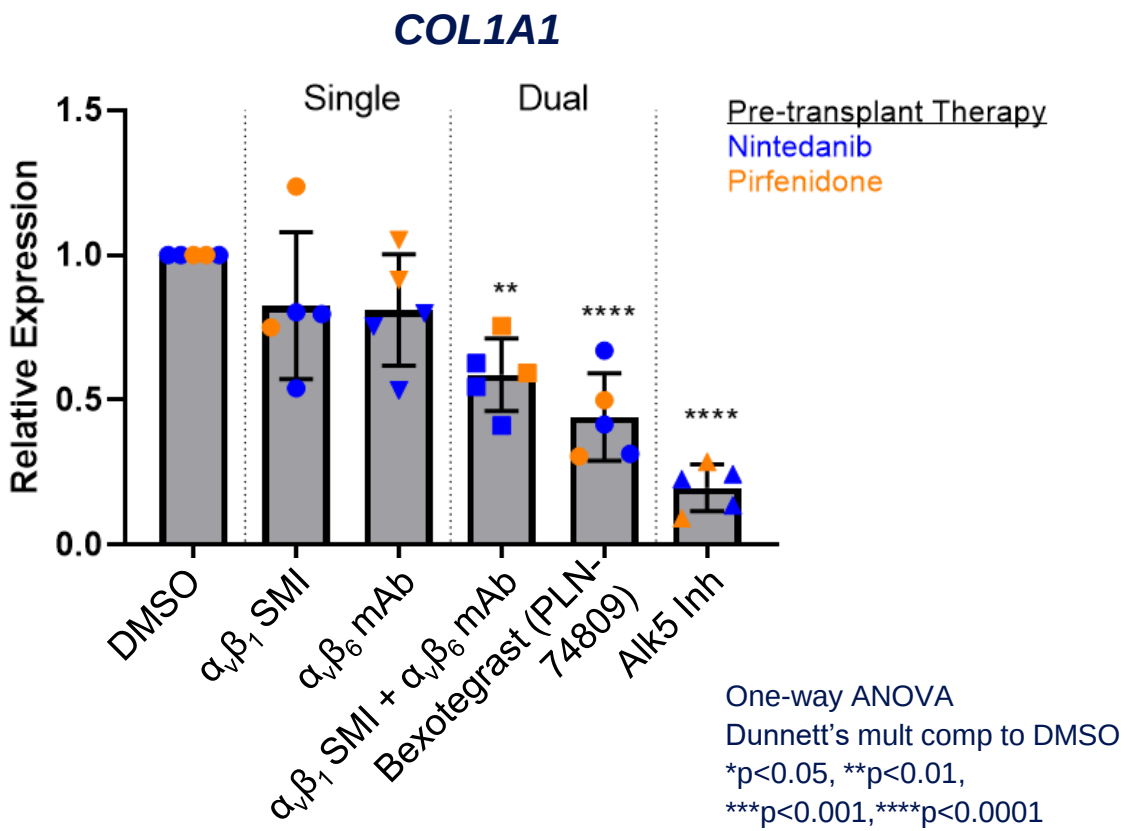
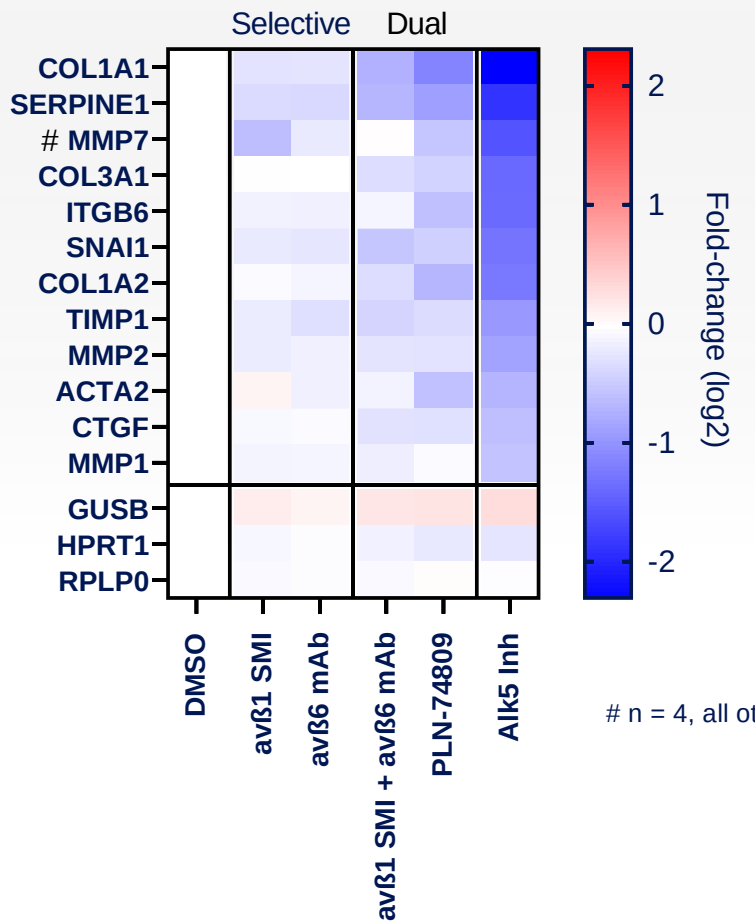
Dual $\alpha_v\beta_6/\alpha_v\beta_1$ Inhibition Blocks Expression of All Profibrotic Genes in Human IPF Tissue

- **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



n = 4, all others n = 5

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.

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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.

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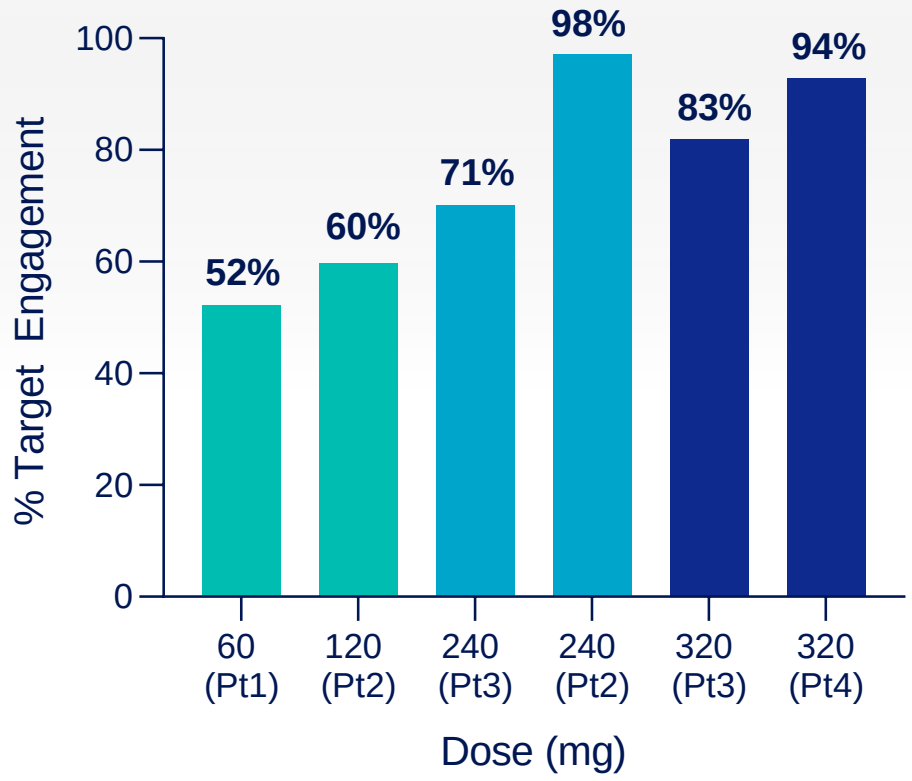
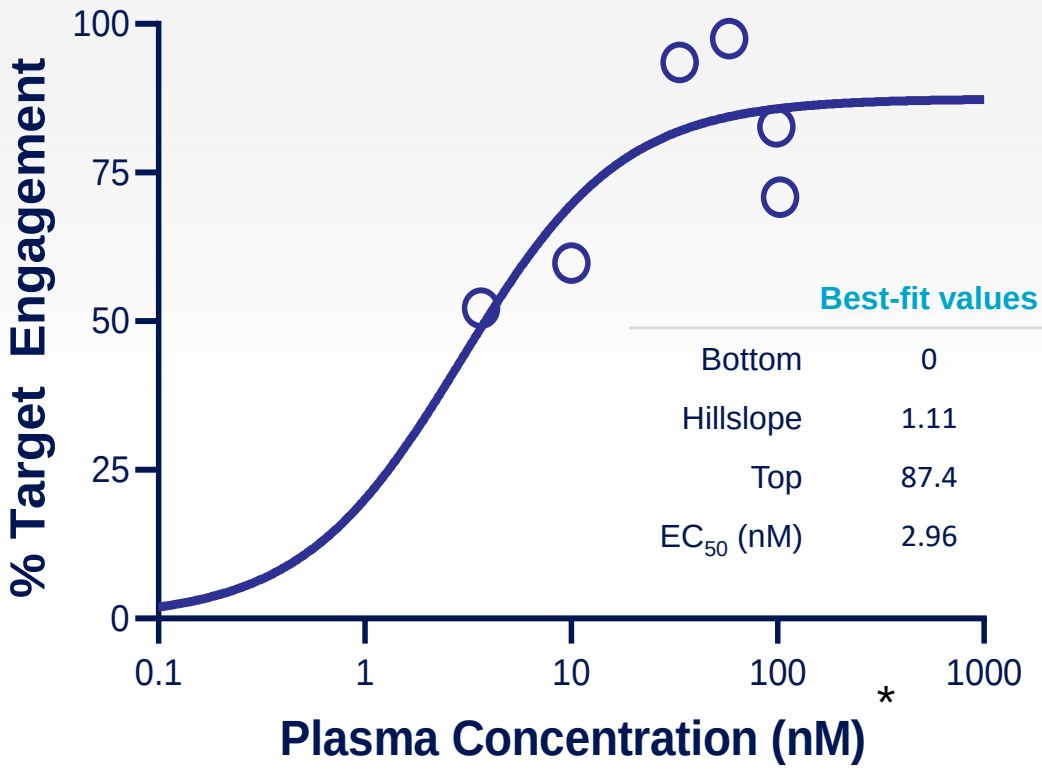
Dose- and Plasma Concentration-Dependent Target Engagement in IPF Patients
(phase 2a PET study)

Dose-Dependent Target Engagement

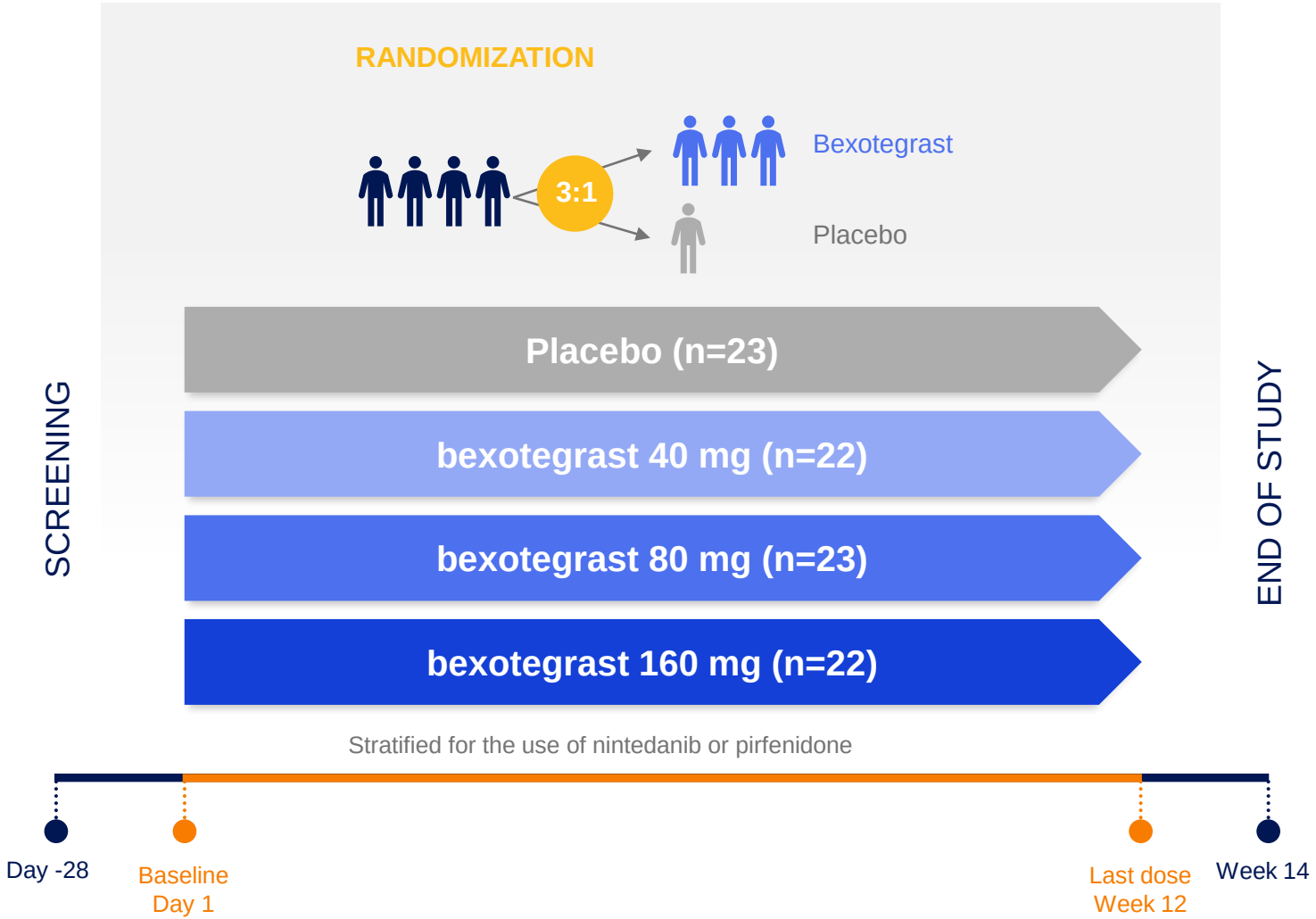


Plasma Conc-Dependent Target Engagement



* Free plasma concentration

INTEGRIS-IPF Study Design and Objectives



PRIMARY AND SECONDARY ENDPOINTS

- Safety, tolerability, PK

EXPLORATORY ENDPOINTS

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

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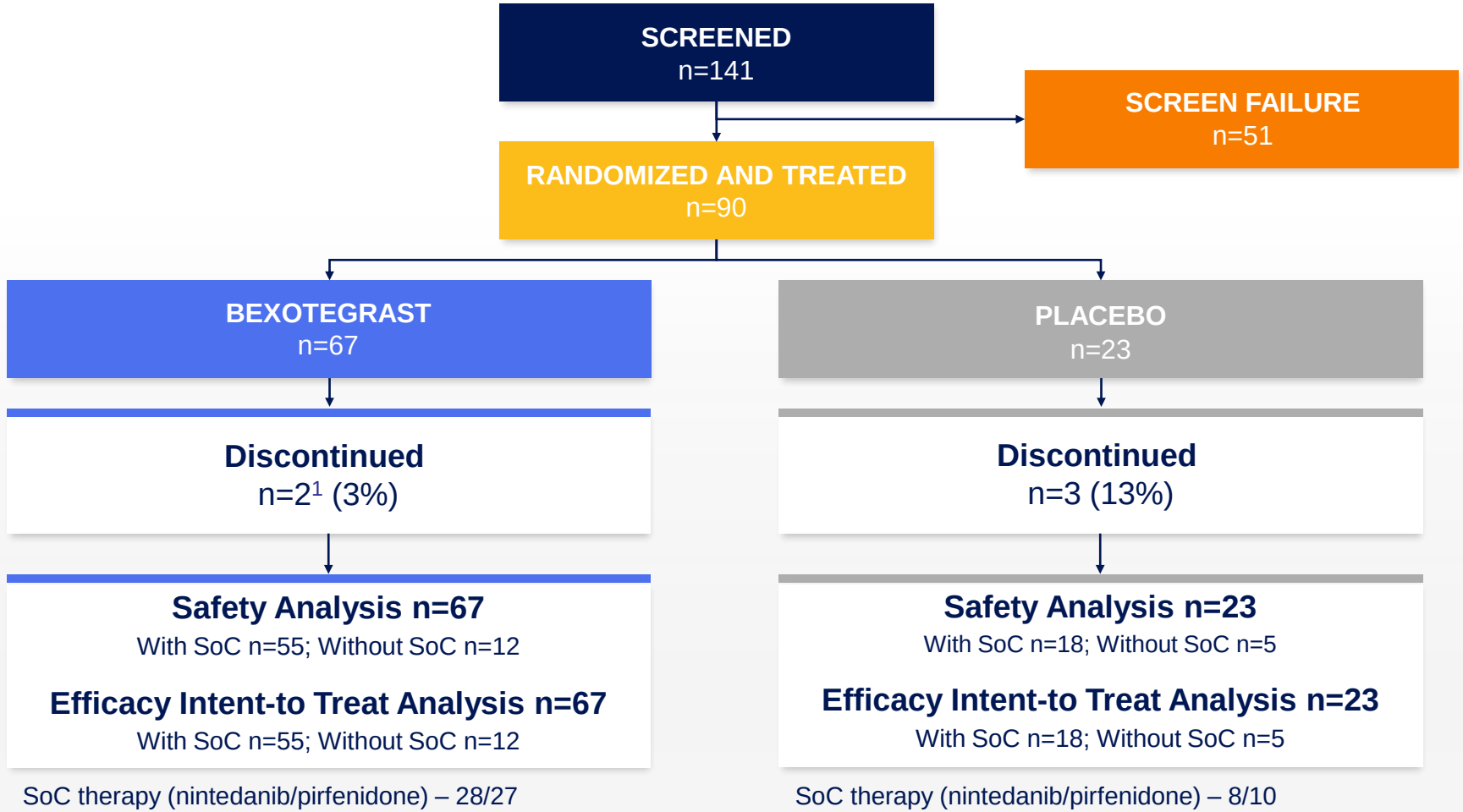
Participant Disposition



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

SoC = Standard of Care

INTEGRIS-IPF - Executive Data Summary

Bexotegrast well tolerated over 12 weeks of treatment

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

Bexotegrast treatment resulted in 80% reduction in FVC decline over 12 weeks

- **-15.1 mL (pooled active groups) vs -74.1 mL (placebo)**
- Effect was evident with and without use of standard-of-care agents
- An actual improvement in FVC (+24.6 mL) was observed in 80 mg dose cohort
- Dose-dependent reduction in proportion of patients with FVCpp decline of ≥10%

Similar treatment effect on exploratory fibrosis endpoints

- Dose-dependent antifibrotic effect seen on QLF Imaging, with no progression in 160 mg group at Week 12
- Bexotegrast decreased serum biomarkers of collagen synthesis (PRO-C3 and PRO-C6) relative to placebo

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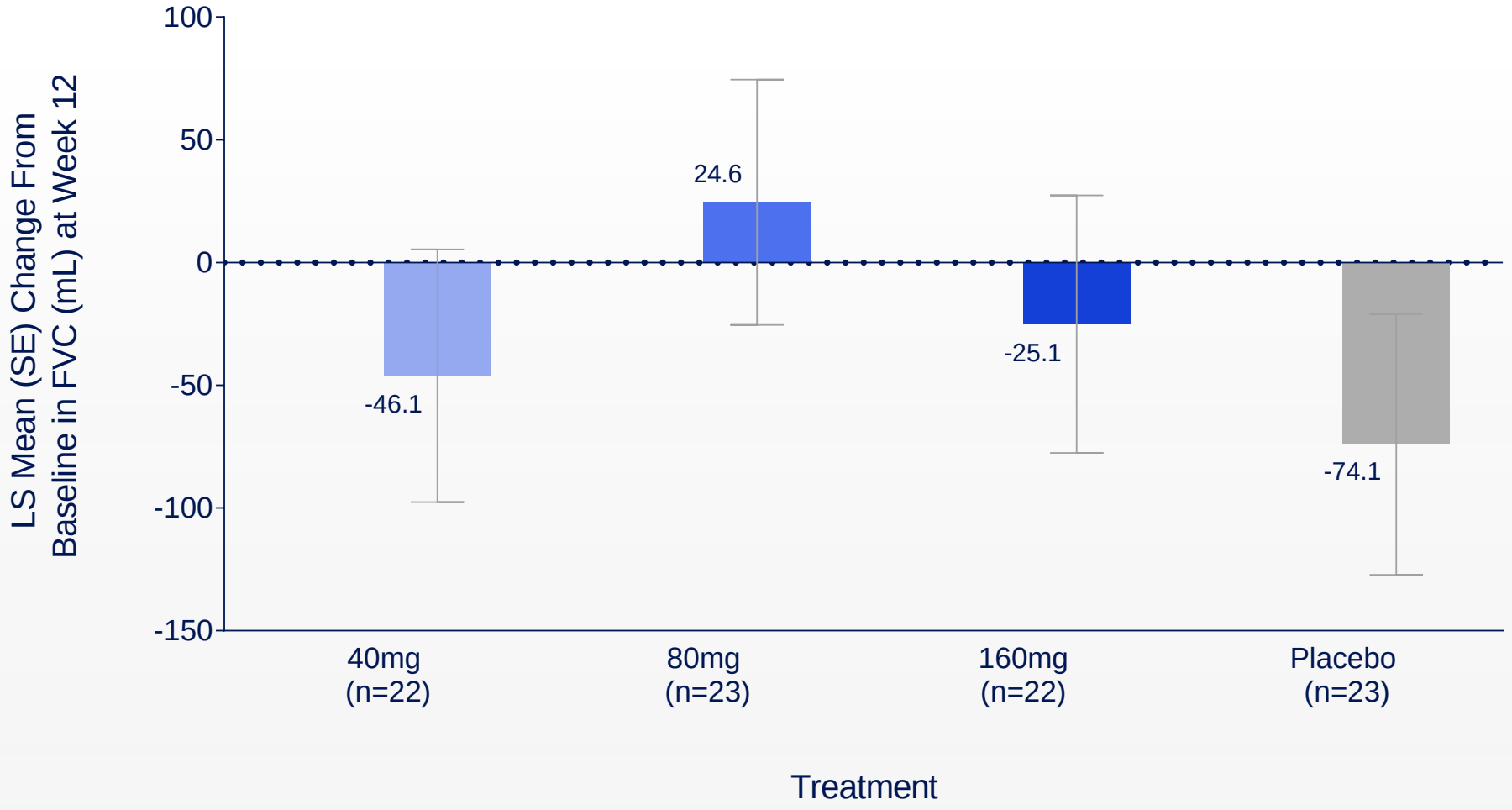
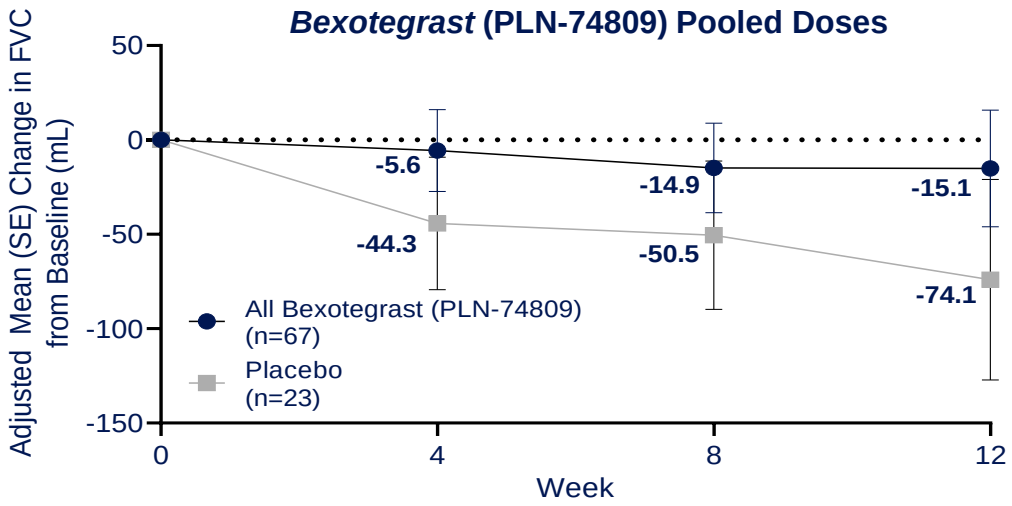
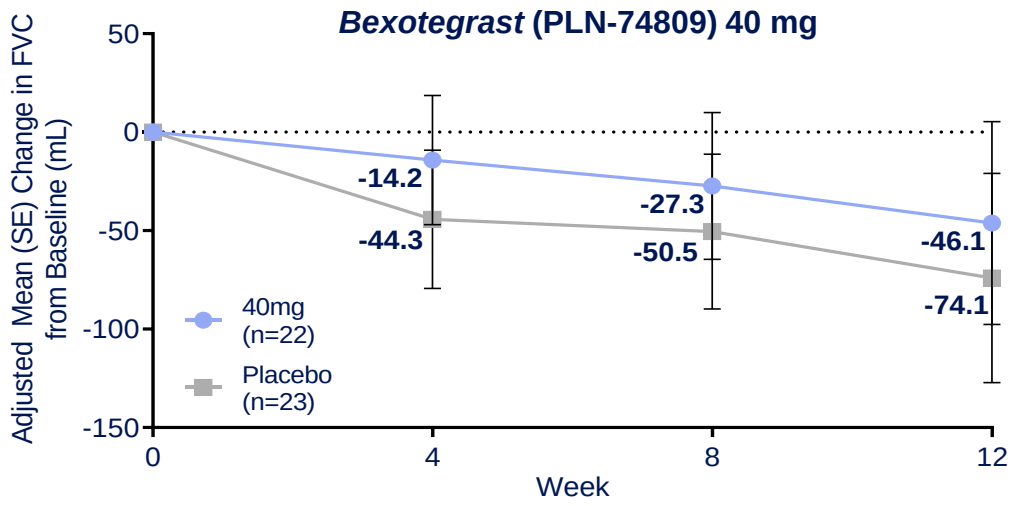
Change in FVC from Baseline to Week 12
MMRM analysis - ITT population

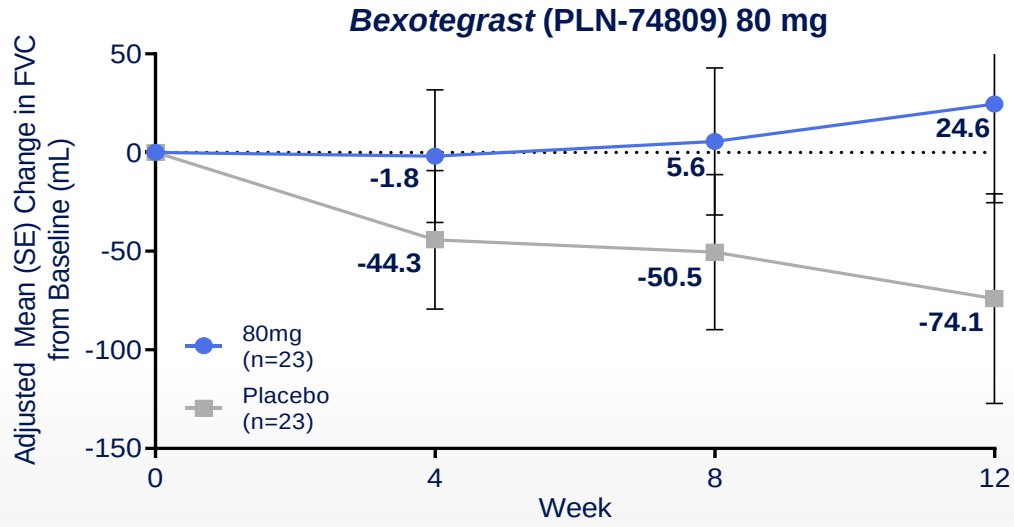


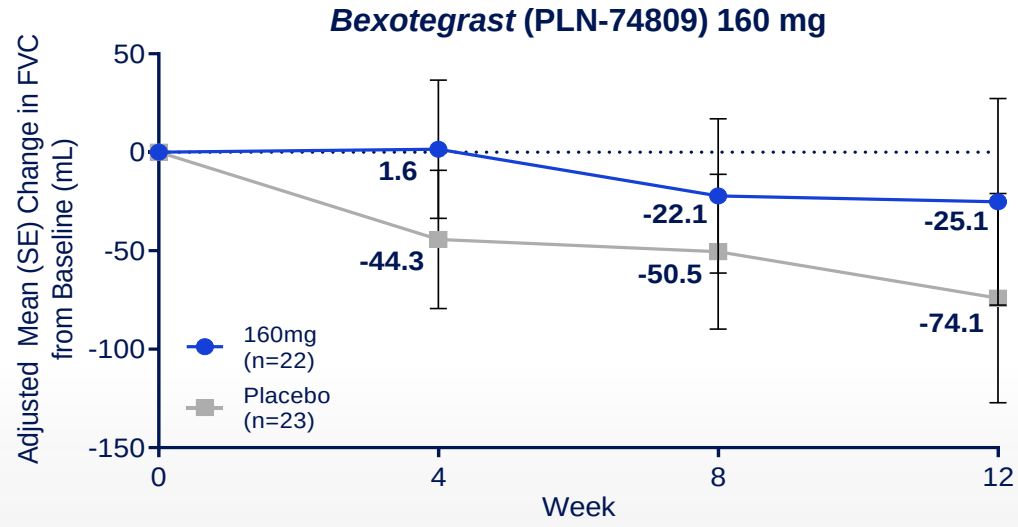
Change from baseline analyzed using a mixed model for repeated measures with terms for treatment group, SOC (Y/N), visit, baseline value, and treatment-by-visit interaction. An unstructured covariance (UN) structure was used.

Change in FVC over 12 Weeks in INTEGRIS-IPF
MMRM analysis - ITT population





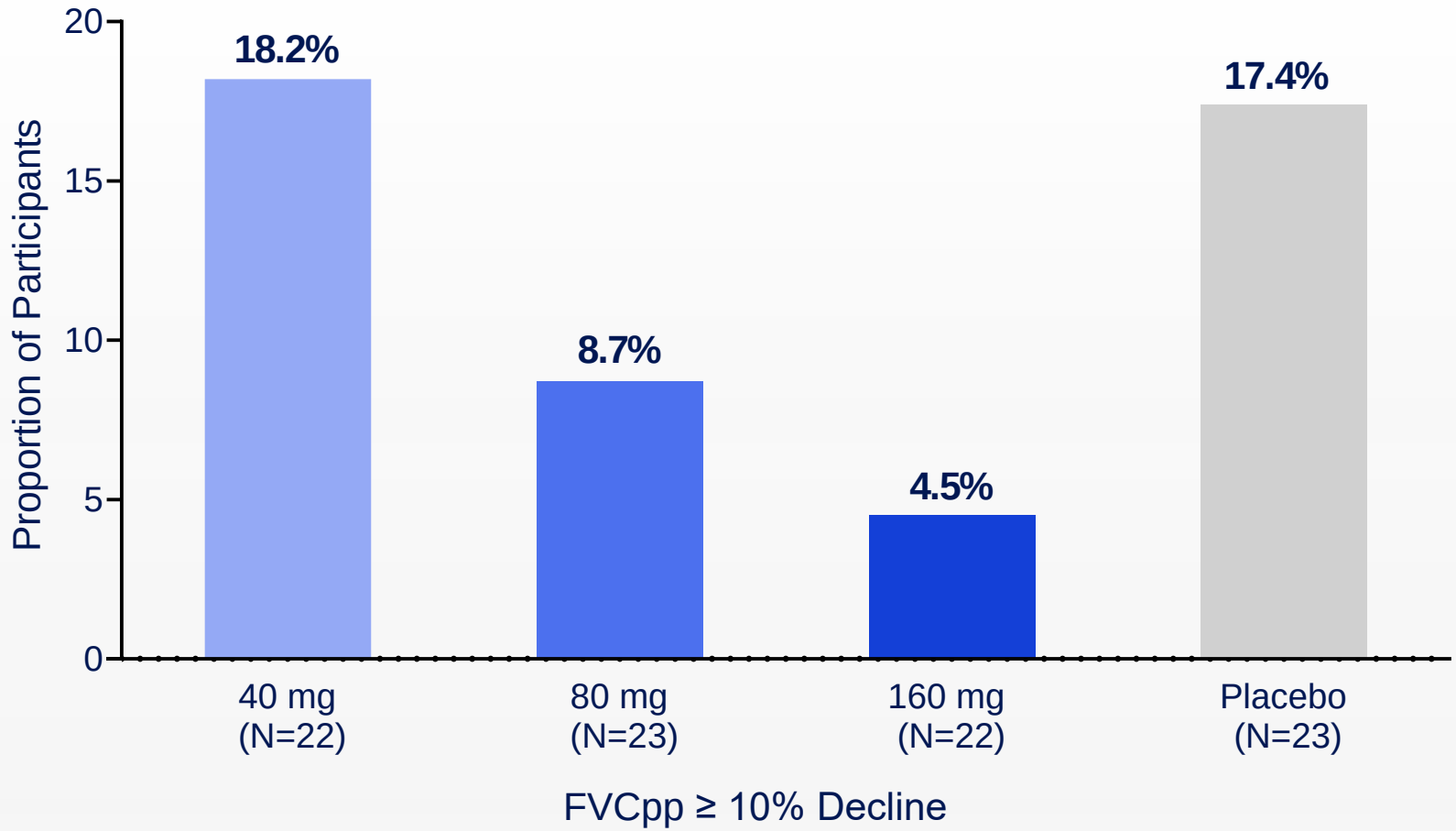




FVC = Forced Vital Capacity
MMRM = Mixed Model Repeat Measures.

Proportion of Participants with FVCpp Decline ≥ 10%

ITT population

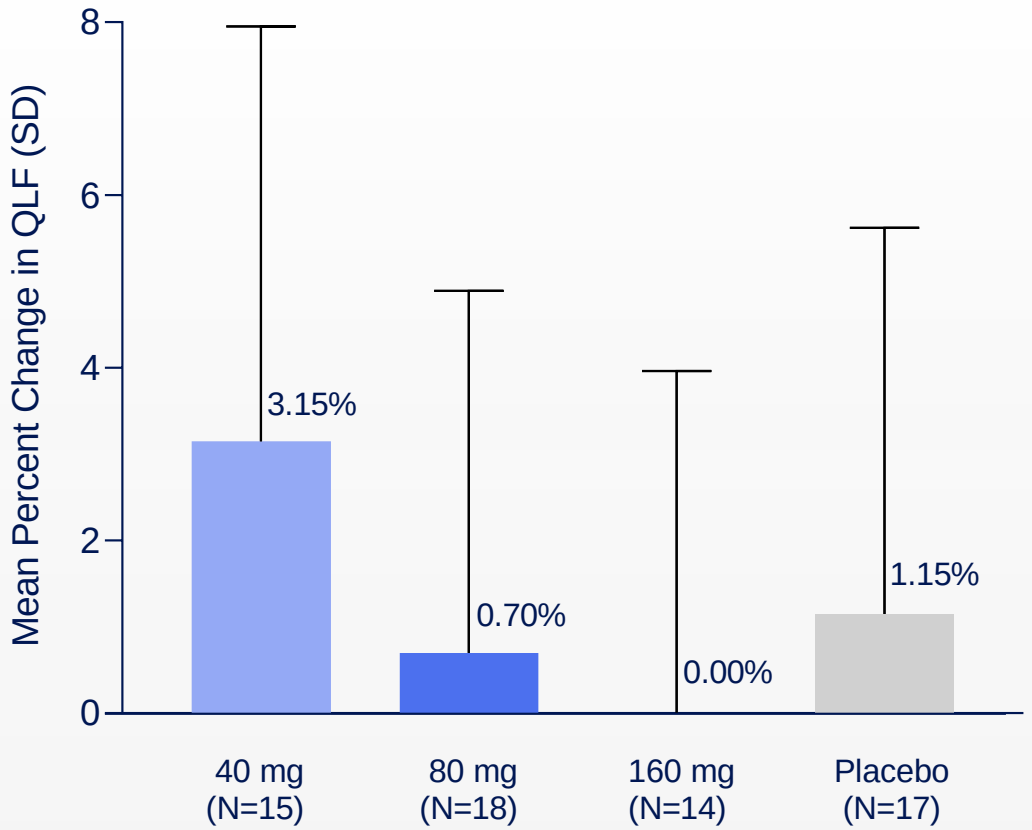


FVCpp ≥ 10%: strong predictor of disease progression and mortality[1]

FVCpp = Forced vital capacity, percent predicted

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

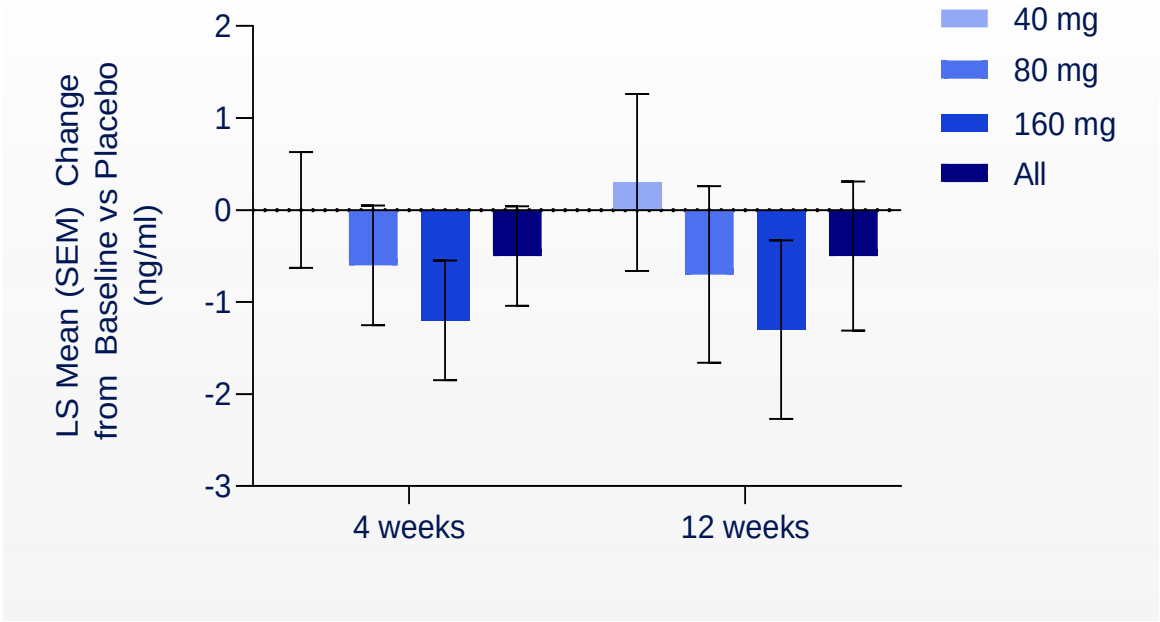
Mean Percent Change in QLF Extent from Baseline to Week 12



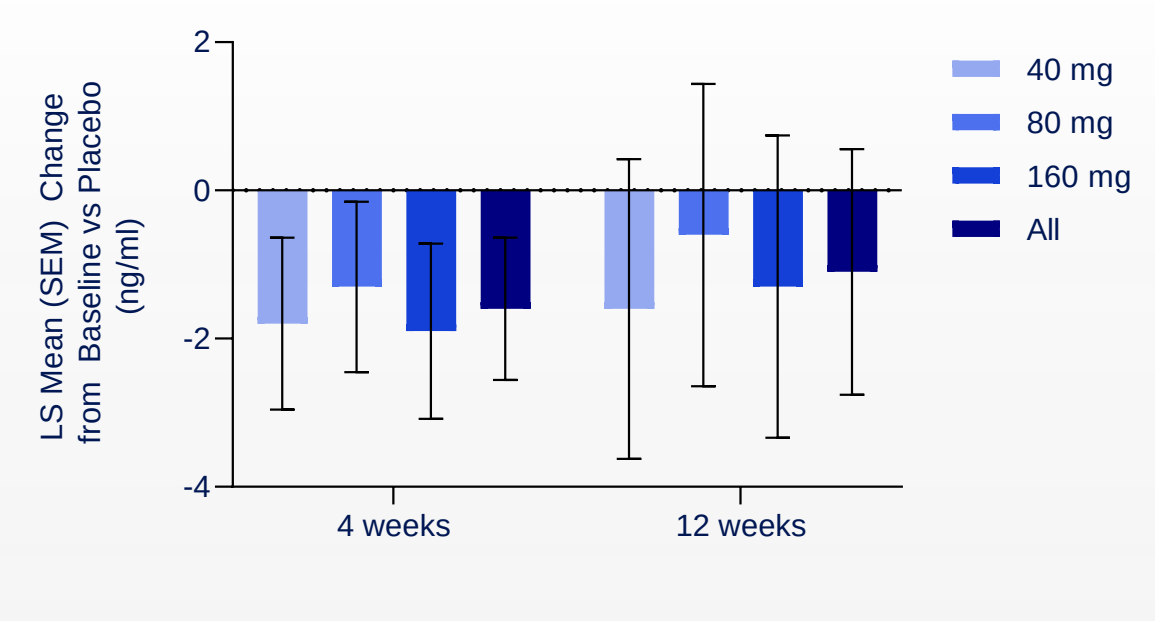
QLF = quantitative lung fibrosis

Serum Biomarkers of Collagen Synthesis were Reduced in Participants Receiving Bexotegrast (Change from Baseline after 4- and 12-weeks vs Placebo)

PRO-C3
Type III collagen synthesis neoepitope



PRO-C6
Type VI collagen synthesis neoepitope



PRO-C3 and PRO-C6, serum biomarkers of type III and VI collagen synthesis, respectively, have previously been shown to be elevated in patients with IPF and associated with progressive disease (Organ et al Respir Res 2019)

Change from baseline analyzed using a mixed model for repeated measures with terms for treatment group, visit, baseline value, and treatment-by-visit interaction.
LS = Least Squares; SE = Standard Error

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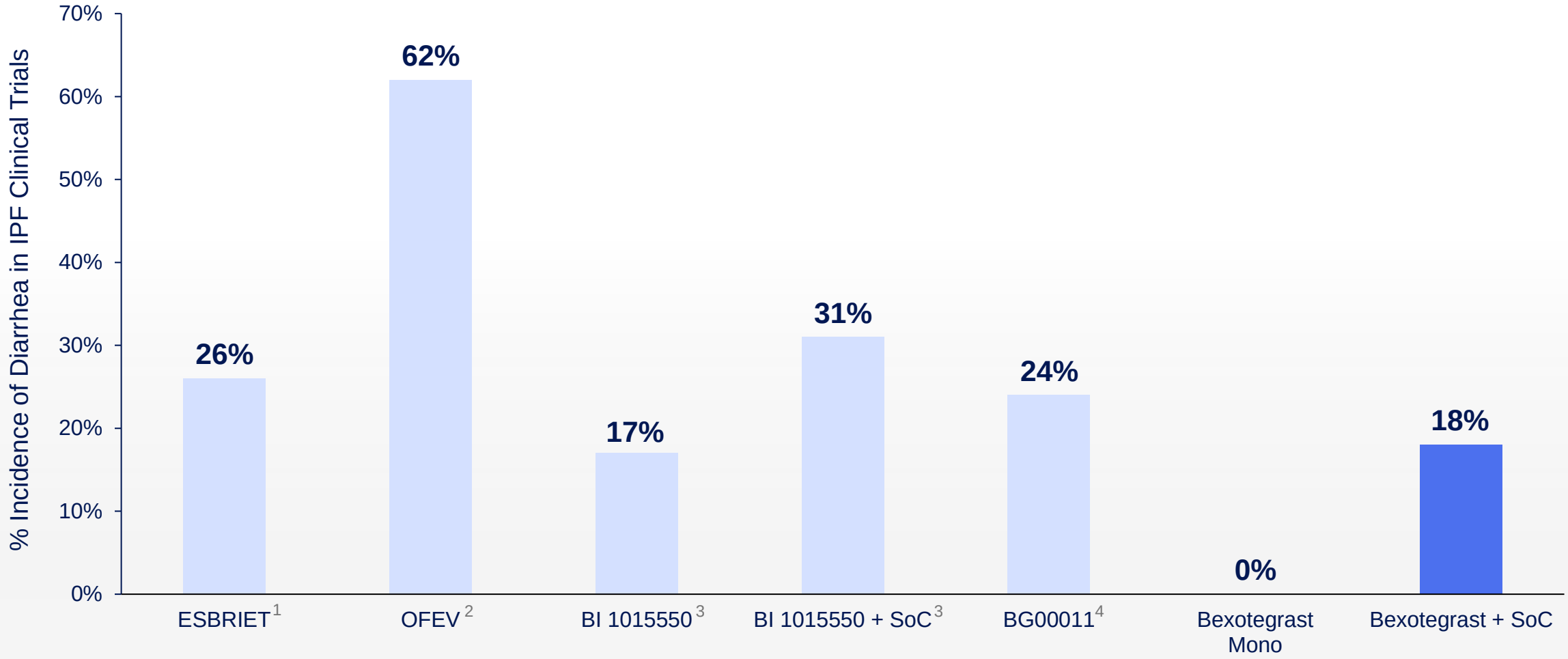
Incidence of Diarrhea in IPF Randomized Clinical Trials



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

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

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

Randomization 3:1
(bexotegrast :placebo)

KEY INCLUSION/EXCLUSION CRITERIA

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

Placebo (n=7)

bexotegrast 320 mg (n=21)

PRIMARY AND SECONDARY ENDPOINTS

- Safety, tolerability, PK

EXPLORATORY ENDPOINTS

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

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

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

Data Expected in the Third Quarter of 2023

Randomization 3:1 (bexotegrast :placebo)

KEY INCLUSION/EXCLUSION CRITERIA

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

- 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

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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
$\alpha_V\beta_8$ drives **TGFβ** activation with a central role in immune suppression in cancer	Highly selective inhibitor of $\alpha_V\beta_8$ & $\alpha_V\beta_1$ 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 2Q2023

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

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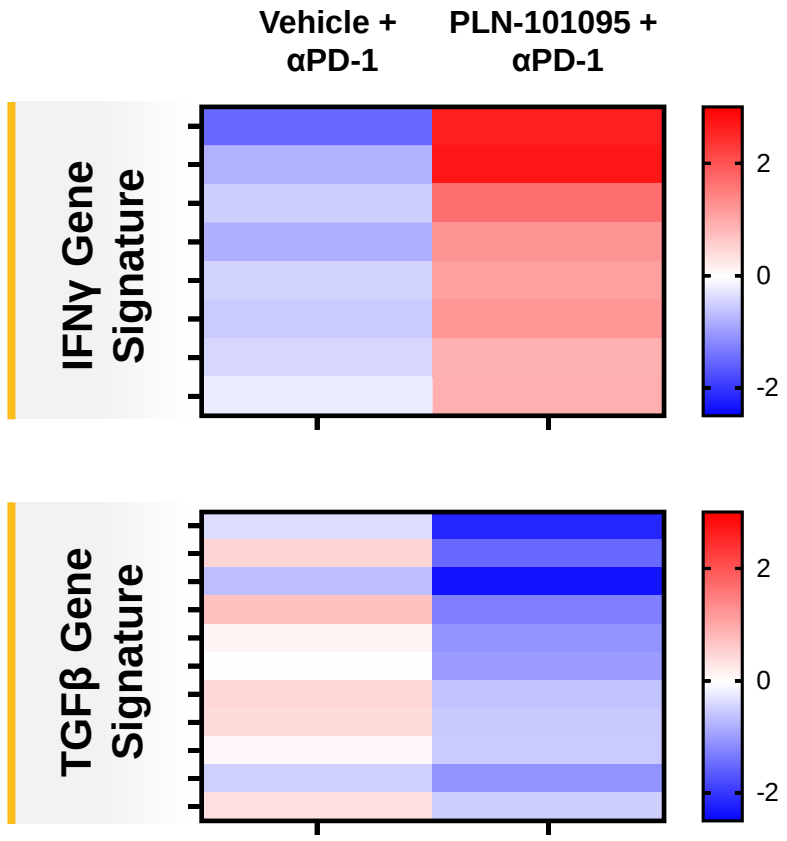
PLN-101095 Potently Increases IFNγ Signature & Reduces TGFβ Gene Signatures



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

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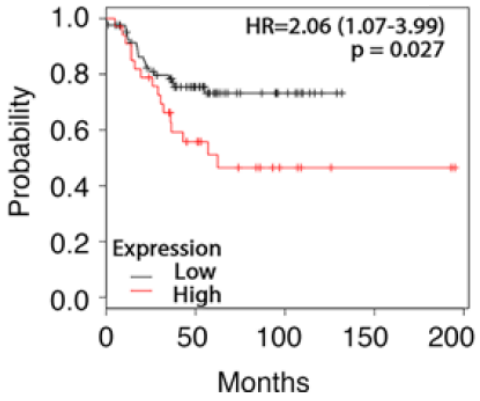
High ITGB8 on Tumor or T cells Has Poor Prognosis

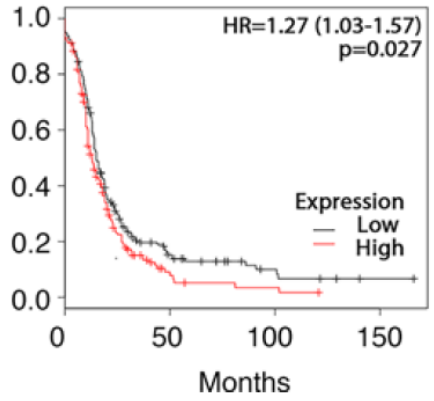
High ITGB8 expression on tumor cells has a worse clinical prognosis

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

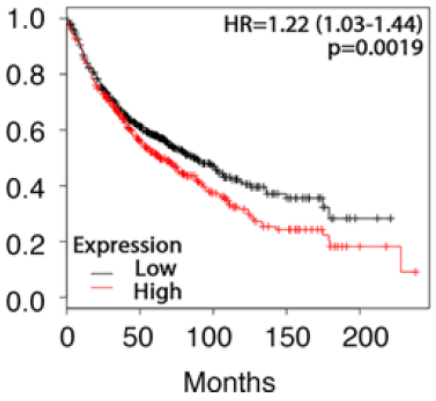
Breast Cancer



Ovarian Cancer



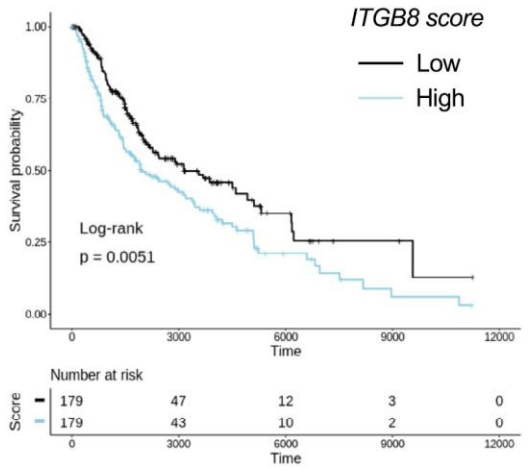
Lung Cancer



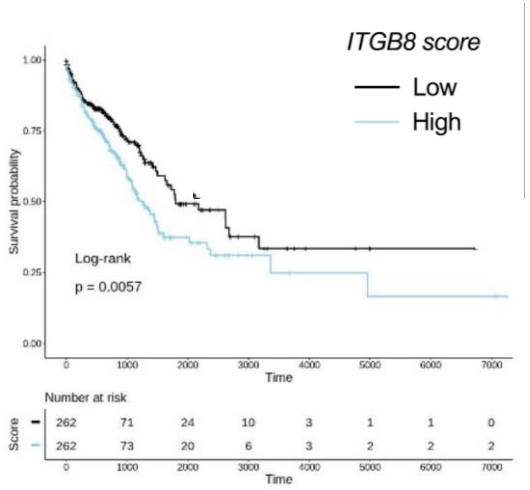
High ITGB8 score on infiltrating T cells correlates with worse prognosis

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

Melanoma



Non-Small Cell Lung Cancer



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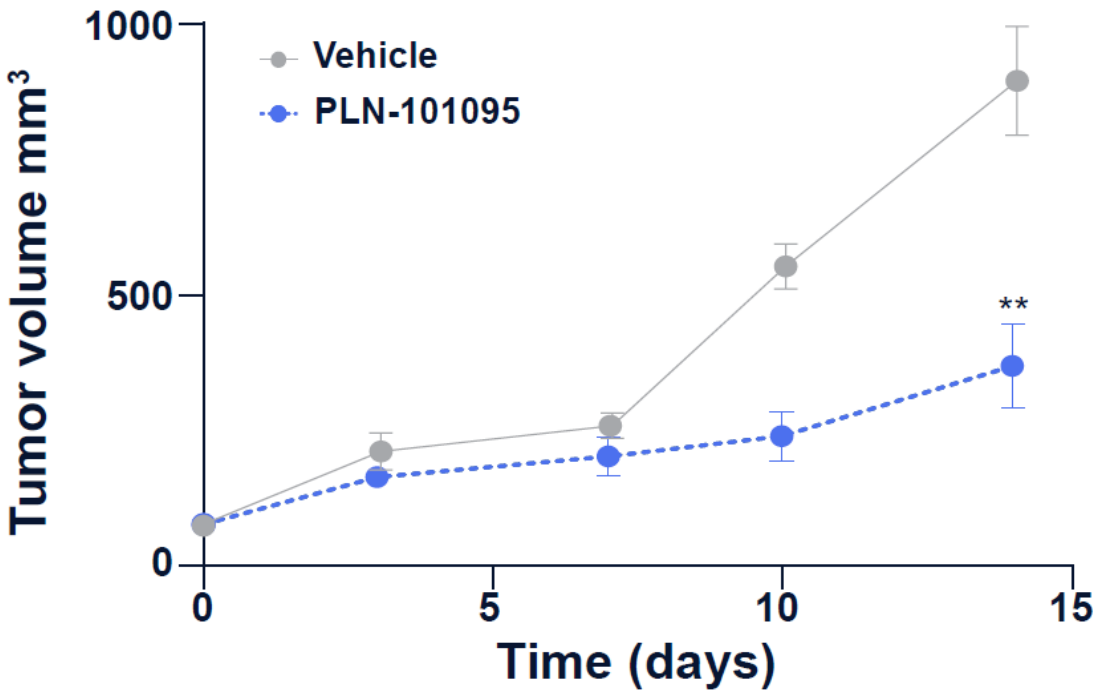
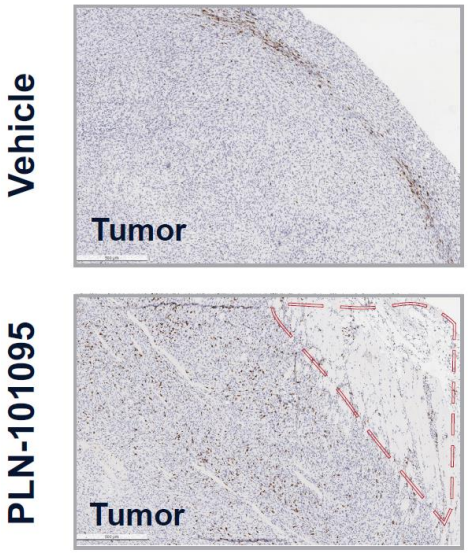
PLN-101095 Inhibited Tumor Growth & Promotes T cell Infiltration in the EMT6 Model

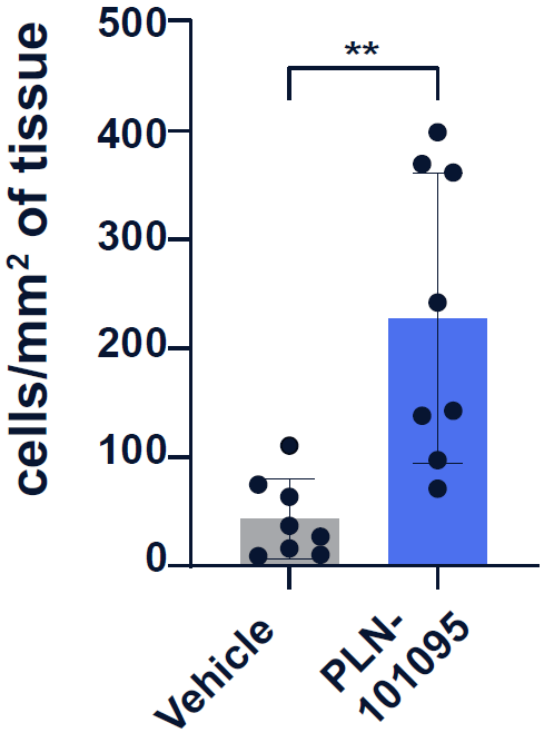
Tumor Growth Inhibition in EMT6 Tumors



CD8⁺ T Cells



CD8⁺ T Cells



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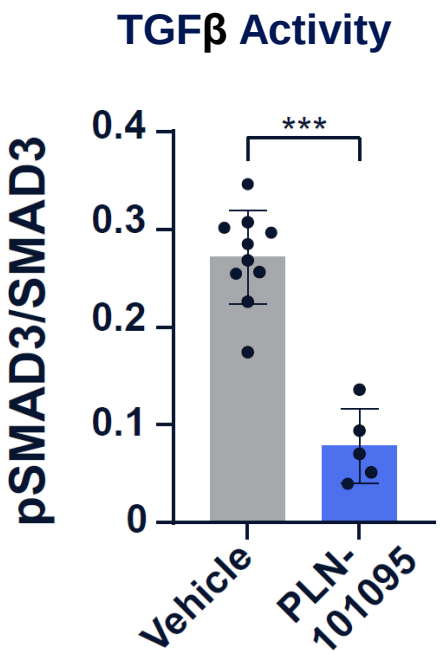
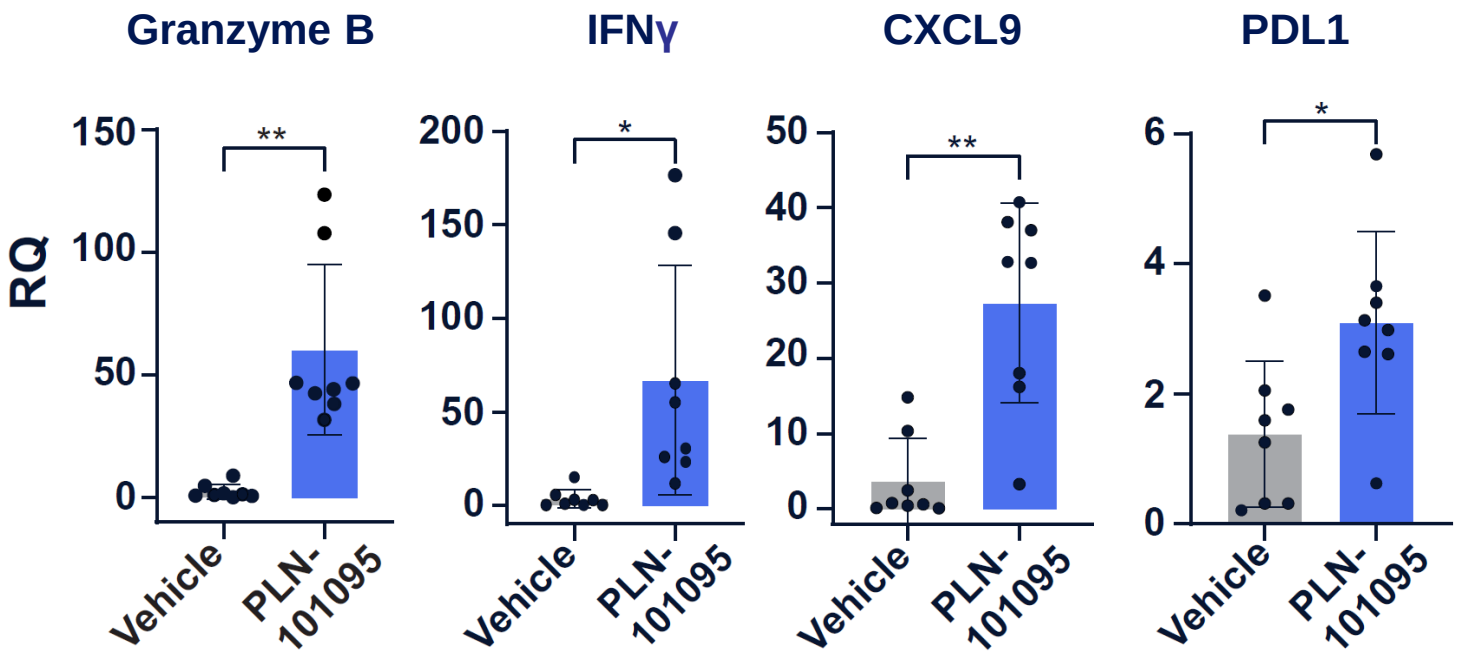
Single Agent PLN-101095 Promoted T Cell Infiltration

Reduced TGF-β Signaling



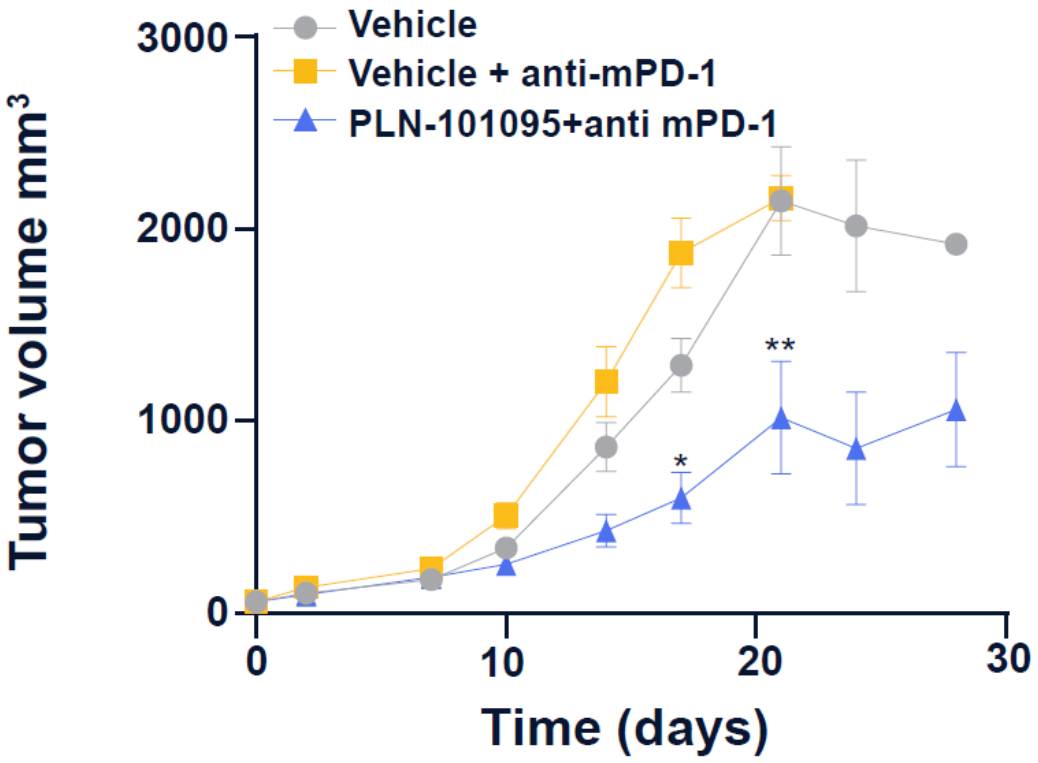
Increased Expression of IFNγ-Regulated Genes



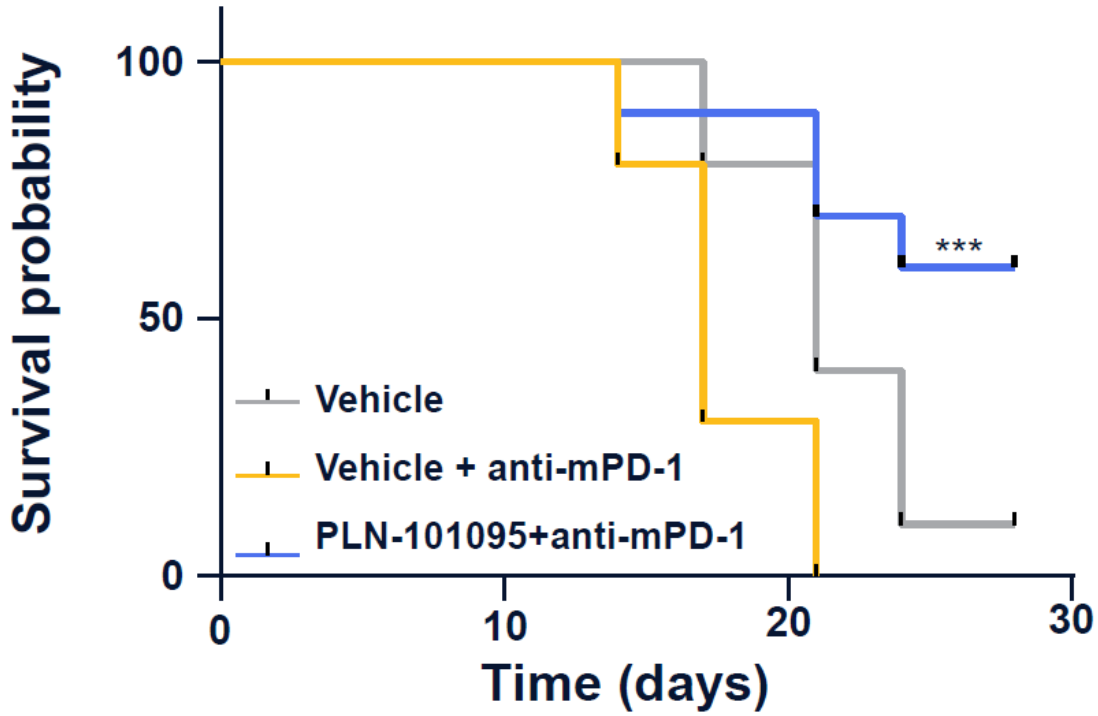
SITC 2022 Poster #1352

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

Tumor Growth Inhibition in EMT6 Tumors



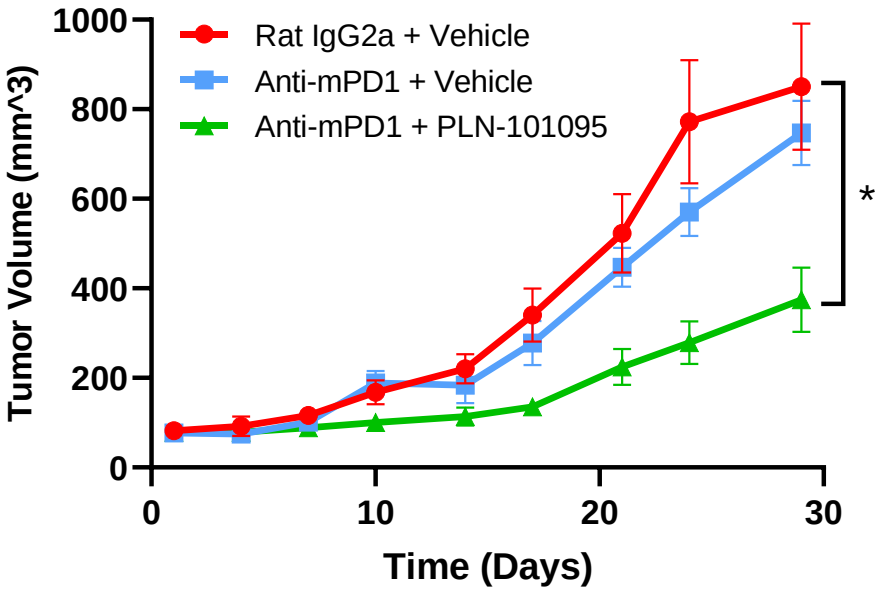
Survival



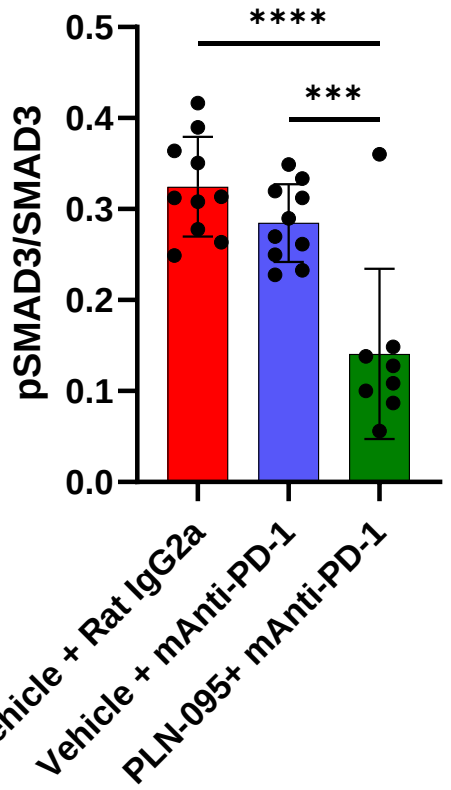
SITC 2022 Poster #1352

PLN-101095 Plus αPD-1 Inhibited Pan02 Tumor Growth & Increases T cell Infiltration

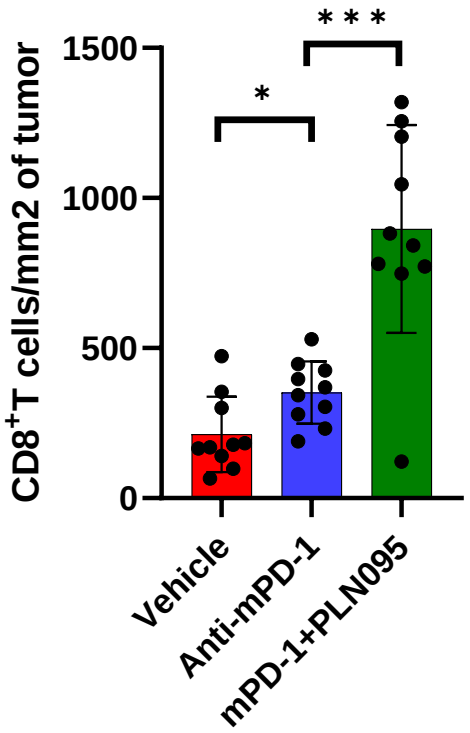
Tumor Growth Inhibition in Pan02 Tumors



TGFβ Signaling



CD8⁺ T Cells



SITC 2022 Poster #1352

PLIANT

PLN-101095 - Key Program Highlights

- **Oral route** of administration
- **Highly potent** dual inhibitor of $\alpha_V\beta_8$ / $\alpha_V\beta_1$ inhibitor
- **Activity** 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**
- First in Human study to start **in 2Q 2023**

PLIANT

Pliant - Development pipeline

	Program	Indication	Preclinical	Clinical			Anticipated Milestone	Global Rights
				Phase I	Phase II	Phase III		
WHOLLY OWNED	Bexotegrast Dual selective inhibitor of $\alpha_v\beta_6$ /$\alpha_v\beta_1$	Idiopathic Pulmonary Fibrosis					Phase 2a 320 mg 12-Week Data Expected Early 1Q 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					IND Filed; Phase 1 initiation 2Q 2023	PLIANT
	PLN-101325 Anti-$\alpha_7\beta_1$ mAb	DMD Other Muscular Dystrophies					IND Filing Expected 2023	PLIANT
PARTNERED	PLN-1474 Selective inhibitor of $\alpha_v\beta_1$	NASH-Associated Liver Fibrosis					Phase 2 Initiation	NOVARTIS