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Developing Novel Treatments for Fibrotic Diseases

JANUARY 2025

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Pliant Therapeutics – Breaking New Ground in Fibrosis Treatment

Industry-Leading Integrin/Fibrosis Platform

- **Four approved INDs**
- Proprietary library of **10,000+ integrin binding molecules**
- **Bexotegrast in Ph2b/3 BEACON-IPF registrational program: Phase 2b data expected 2Q 2026**

Blockbuster Opportunities in Areas of High Unmet Need

- Pulmonary fibrosis is currently a **$4+ billion market -** expected to reach **$6-$10 billion** within 10 years
- High unmet need due to tolerability/efficacy issues with approved IPF agents
- Opportunity to **expand the market** to additional patients and indications (i.e. progressive pulmonary fibrosis)

Bexotegrast – Disease modifying Potential in IPF

- Bexotegrast has shown **improvement in FVC** vs. placebo as **monotherapy and in combo** with SOC
- Reduction in total lung collagen seen post 12-week treatment: **potentially disease modifying reversal of fibrosis**
- Clinically meaningful **reduction in cough severity**

Funded Through Phase 2b Data

- $406.5 million of cash[1] as of September 30, 2024
- **Operations are funded into 2027**

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1 – Includes cash, cash equivalents and short-term investments.

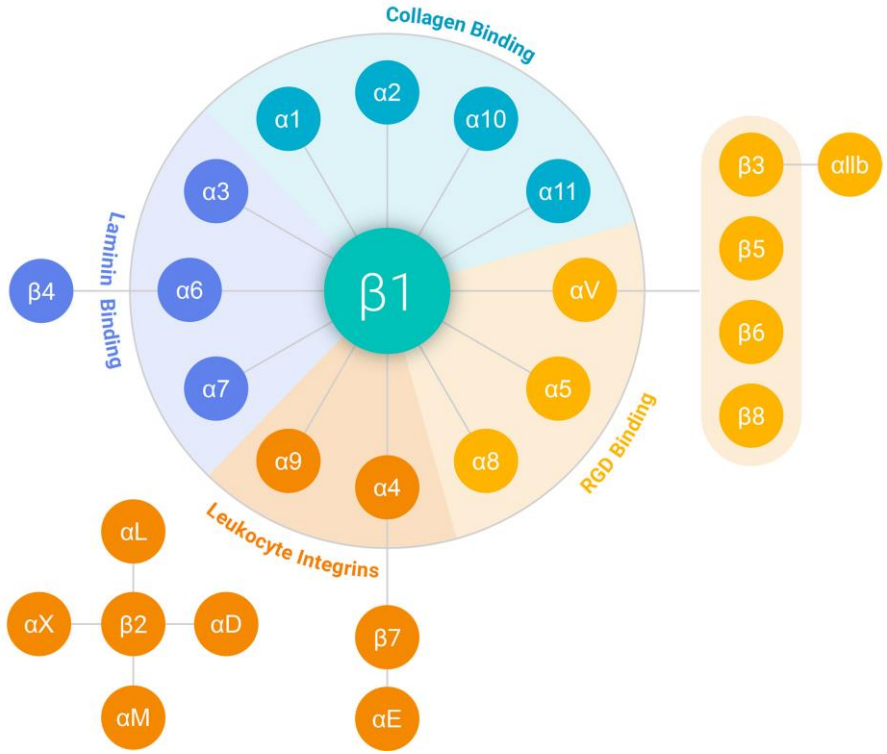
Pliant Development Pipeline

Program	Indication	Preclinical	Clinical			Anticipated Milestone	Timing
			Phase 1	Phase 2a	Phase 2b / 3		
Bexotegrast (PLN-74809) Dual selective inhibitor of $\alpha_v\beta_6$ /$\alpha_v\beta_1$	Idiopathic Pulmonary Fibrosis					**BEACON-IPF Phase 2b enrollment complete** **Phase 3 Start** **Phase 2b Data**	**1Q 2025** **1Q 2025** **2Q 2026**
	Progressive Pulmonary Fibrosis					**Initiate Phase 2b BEACON-PPF trial**	**2H 2025**
PLN-101095 Inhibitor of $\alpha_v\beta_8$ /$\alpha_v\beta_1$	Solid Tumors					**Phase 1 data**	**1Q 2025**
PLN-101325 Anti-integrin mAb of $\alpha_7\beta_1$	DMD & Other Muscular Dystrophies					**Phase 1 ready (CTA active)**	

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 and fibroblasts
- Closely involved in signaling processes that govern tissue fibrosis



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

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

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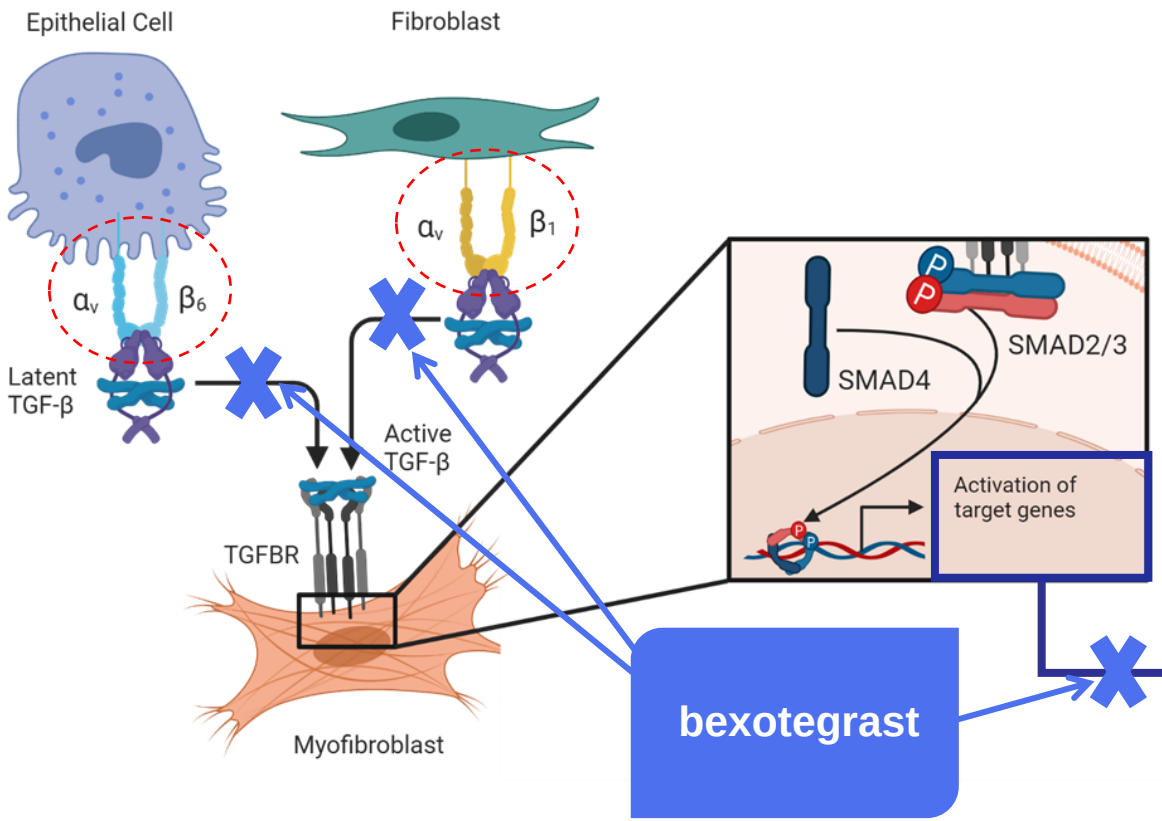
Bexotegrast Reduces TGF-β Signaling and Downstream Profibrotic Pathways Through Inhibition of Integrins $\alpha_v\beta_6$ / $\alpha_v\beta_1$

$\alpha_v\beta_6$ / $\alpha_v\beta_1$ integrins promote fibrosis by activating TGF-β

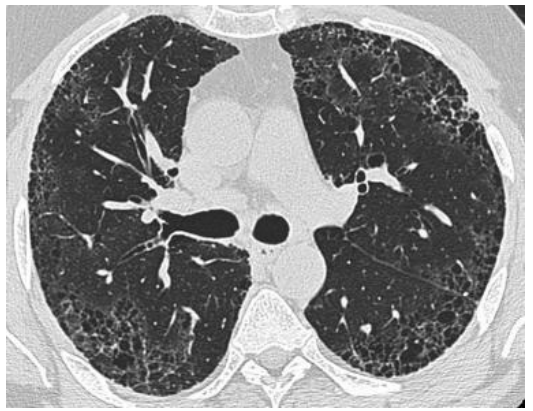


- TGF-β is a central mediator of fibrosis
- $\alpha_v\beta_6$ /$\alpha_v\beta_1$ Integrins activate latent TGF-β in fibrotic tissue
- Systemic TGF-β blockade carries toxicity risks

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

COL1A1
COL3A1
TIMP1
CCN2
ENPP2
…

FIBROSIS



Bexotegrast Has Outperformed at All Stages of Development

Bexotegrast Has Shown Blockbuster Potential in Early and Mid-Stage Trials

	Bexotegrast	
	PC/Phase 1	Phase 2
Improvement in Lung Function (FVC)		✓
Symptomatic Improvement (Cough)		✓
Reduction in Lung Fibrosis (HRCT and PET Imaging)		✓
Additive Effect on Top of SOC (80%)		✓
$\alpha_v\beta_6$ Target Saturation (PET Imaging)	✓	✓
Reduced TGF-β Signaling (pSMAD)	✓	✓
Reduced Pro-Fibrotic Gene Expression	✓	✓
Favorable Tolerability Profile	✓	✓
Oral, Once-Daily Dosing	✓	✓

Blockbuster Market Opportunity of $4+ Billion

- 2023 global pulmonary fibrosis (IPF and PPF) revenues of $4.1 billion
- **Increasing IPF incidence** expected with aging population
- **Significant portion of market unserved** due to tolerability/efficacy issues

Potential Backbone Therapy

- **Favorable tolerability profile** to date, as monotherapy, and in combination with SOC
- Bexotegrast + SOC **reduced FVC mL decline by 80%** over 24 weeks compared to SOC alone

Expanding Treatable Population

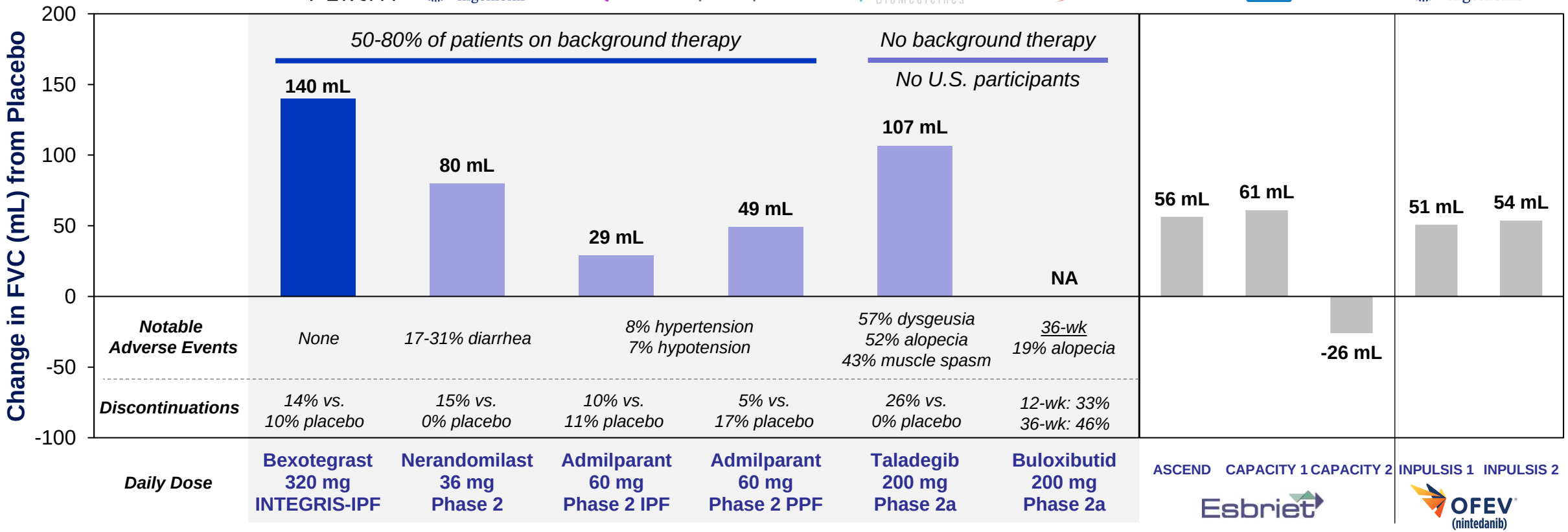
- **Impact on disease symptoms** – **clinically meaningful reduction in cough severity** seen in Phase 2a trials
- **Reduction in total lung collagen** seen in Phase 2 suggests reversal of fibrosis – **potential disease modifying therapy**

Absolute Change from Baseline vs. Placebo in FVC (mL) at 12 Weeks

Results of Approved and Select Investigational Agents in IPF / PPF

Agents in Development

Approved Agent Phase 3 Studies

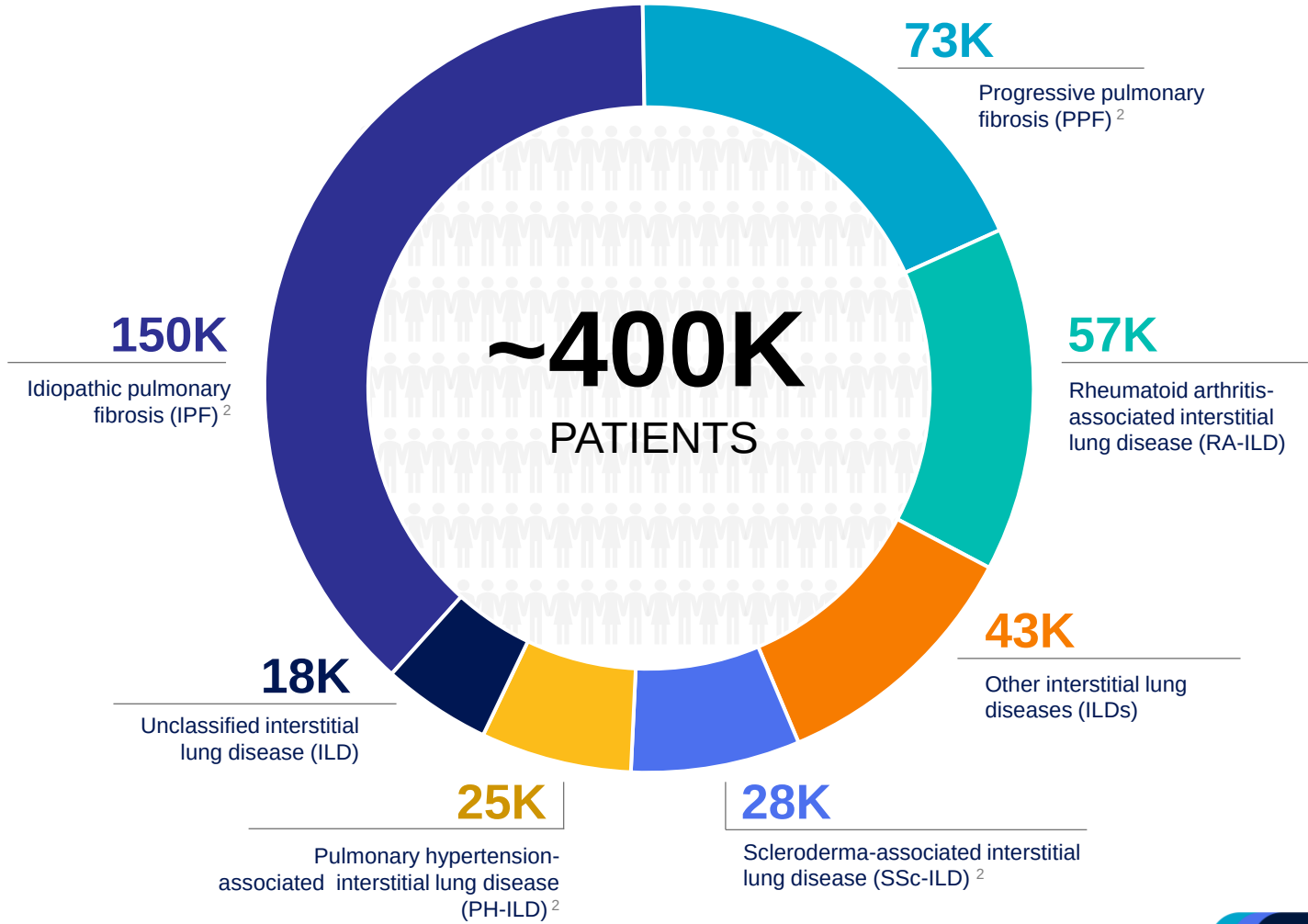


Bexotegrast, nerandomilast, admilparant, taladegib and buloxibutid values as reported in Phase 2 studies. 12-week values for Esbriet from CDER Medical Review 022535Orig1s00 table 14; for Ofev interpolated at 12 weeks with WebPlotDigitizer from CDER Medical Review 205832Orig1s000 fig. 6 & 7 and for admilparant interpolated at 12 weeks from Corte TJ et al., Am. J. Respir. Crit. Care Med. 2024. The data presented above are based on cross-study comparisons and are not based on any head-to-head clinical trials of bexotegrast against other drug products or candidates, based on our available data to date. Cross-study comparisons are inherently limited and may suggest misleading similarities and differences. The values shown in the cross-study comparisons are directional and may not be directly comparable due to different protocol designs, trial designs, patient selection and populations, number of patients, trial endpoints, trial objectives and other parameters that may not be the same across trials. Therefore, cross-study comparisons provide very limited information about the efficacy of safety of a drug. Bexotegrast INTEGRIS-IPF study consisted of n-22 subjects in the 320 mg arm, a significantly smaller number of patients than reflected in the other datasets represented on this slide. In larger trials of bexotegrast, the clinical activity suggested by our INTEGRIS-IPF trial may not be replicated.

Bexotegrast Has Significant Respiratory Market Potential

- Fibrosing ILDs encompass over 200 indications with **common disease pathophysiology**
- Underdeveloped market with **limited treatment options** for non-IPF diseases including PPF, SSc-ILD, and PH-ILD
- Like in IPF, bexotegrast could provide the **only disease-modifying antifibrotic treatment** option across other fibrosing ILDs

US PREVALENCE OF FIBROSING ILD INDICATIONS[1]



[1] Estimated prevalence based on progressive fibrosing phenotype of various ILDs using Wijsenbeek M et al. *Curr Med Res Opin*. 2019;35(11):2015-2024.
[2] Indications with available therapies

Pulmonary Fibrosis Market Opportunity

	US	EU4 + UK	JP
IPF	150K	90K	34K
PPF	96K	90K	21K

~500,000

PEOPLE AFFECTED ACROSS 7 MAJOR MARKETS

35-65%

TREATED

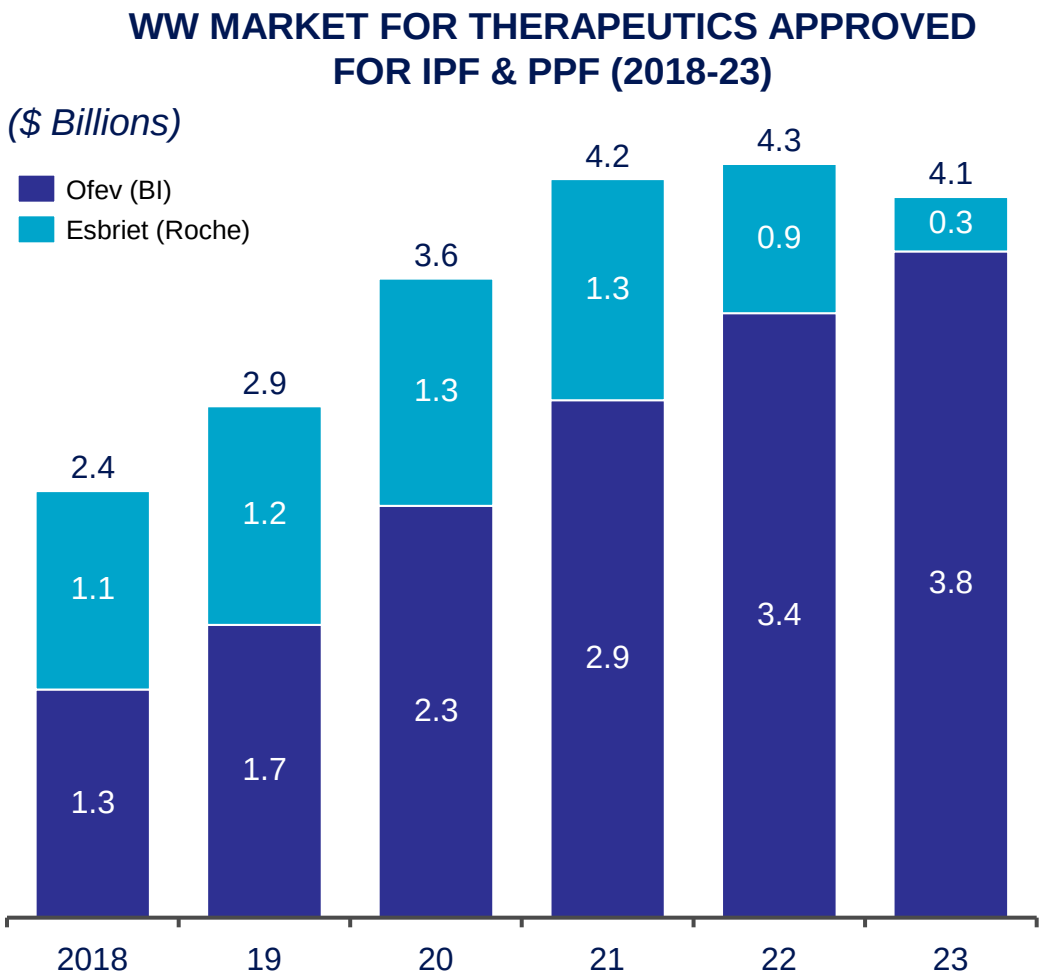
SIGNIFICANT UNADDRESSED MARKET OPPORTUNITY WITH ONLY:

2 APPROVED THERAPIES FOR IPF & **1** APPROVED THERAPY FOR PPF

IPF: Idiopathic Pulmonary Fibrosis; PPF: Progressive Pulmonary Fibrosis

1 - Maher TM. et al. Respir Res (2021) 22:197. 2- Olson A et al. Adv Ther 2021; 38(2): 854–867
3 - Kondoh Y et al. Respir Res (2022) 23:24

~ $4B+ Pulmonary Fibrosis Market is Underpenetrated

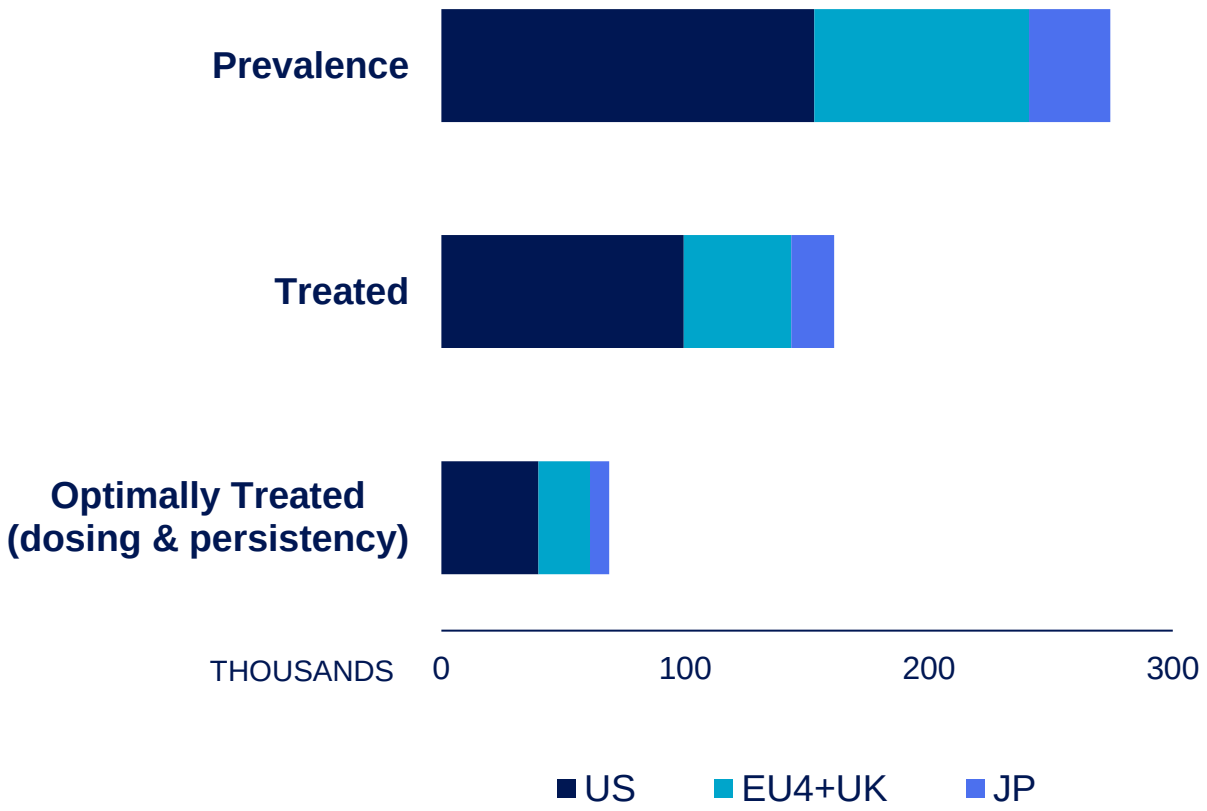


Drivers of Future Market Growth

- **Aging population** will increase treatment eligible patient population
- Earlier treatment initiation possible with **improved diagnosis**
- **Novel therapeutic entrants** expected to increase treatment rate and duration on treatment

Source: Boehringer Ingelheim and Roche Annual Reports 2018 – 2023

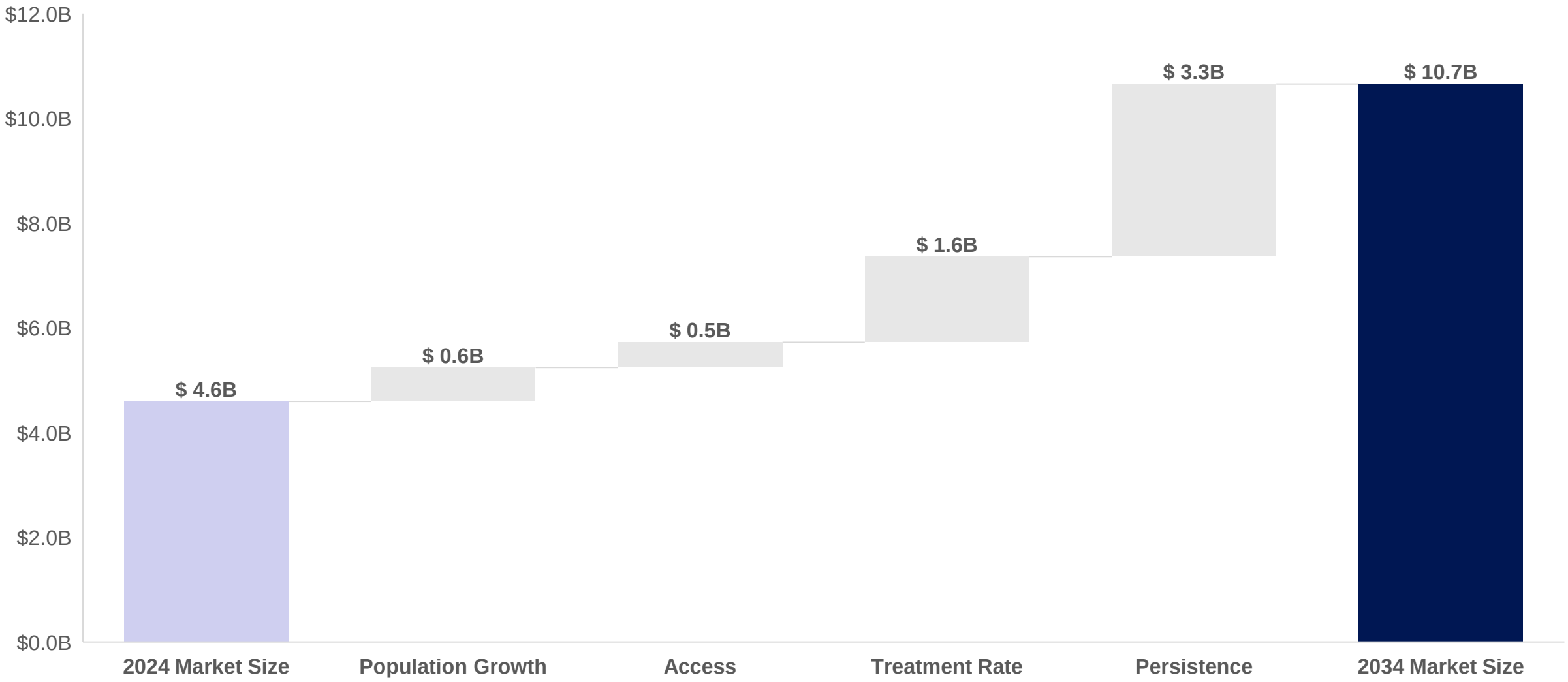
Over 75% of IPF Patients are NOT Optimally Treated



- Available therapies have no impact on progression of fibrosis, survival or quality of life
- Efficacy / safety tradeoffs of available therapies result in patient refusal to receive treatment
- Intolerability leads to suboptimal dosing, treatment disruption, and permanent discontinuation

Source: Data on file

Pulmonary Fibrosis Market Could More Than Double Within 10 Years



Source: Data on file

Bexotegrast Expected to Address Unmet Needs Across Key Patient Segments

Monotherapy Opportunity	**Active Switchers**	• Down dosing, poor adherence and low persistency impacts the real-world efficacy of current IPF treatments • Physicians' dissatisfaction with tolerability of existing agents and growing enthusiasm for novel agents that improve QoL in addition to FVC suggest demand for safer, effective options
	Untreated Naïve	• Improved safety/tolerability profile of novel agents shifts the risk-benefit of therapy for patients refusing existing antifibrotic options • As novel agents become available, physicians expect an increase in antifibrotic treatment initiations in diagnosed patients
	Untreated Discontinued	• Limited antifibrotic options result in premature discontinuation of treatment due to inadequate efficacy response and/or tolerability • Physicians anticipate new therapies to develop as more options become available that enable patients to remain on treatment
Combination Opportunity	**Add-On**	• Patients progressing on an existing treatment (efficacy failure) will have a novel therapy added

Source: Physician Research, Pliant analysis

Bexotegrast Positioned to Lead the Evolving IPF Treatment Landscape

Treatment Paradigm	First line monotherapy	→ Multiple lines of therapies & MOA-driven combinations Patient choice driven by efficacy, safety, & convenience	
Unique MOAs	2	3+	5+
ROAs	1	2	3
Generics	1	2	2

Bexotegrast is well positioned for the future treatment landscape

- Potential to become the **backbone antifibrotic therapy** used as either monotherapy or in combination
- Product profile most preferred by physicians and patients across 1L and 2L+

MOA: Mechanism of Action; ROA: Route of Administration

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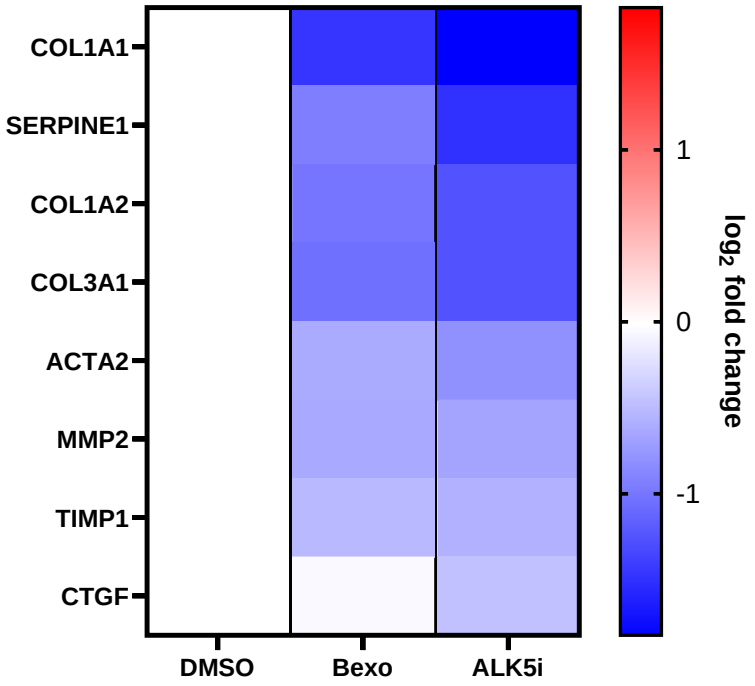
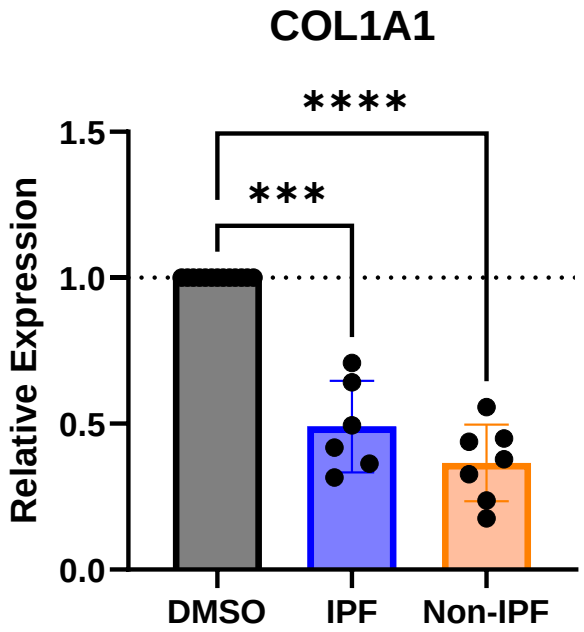
Bexotegrast for Treatment of Progressive Pulmonary Fibrosis

Bexotegrast Decreased Fibrotic Gene Expression in PPF Explant Tissue

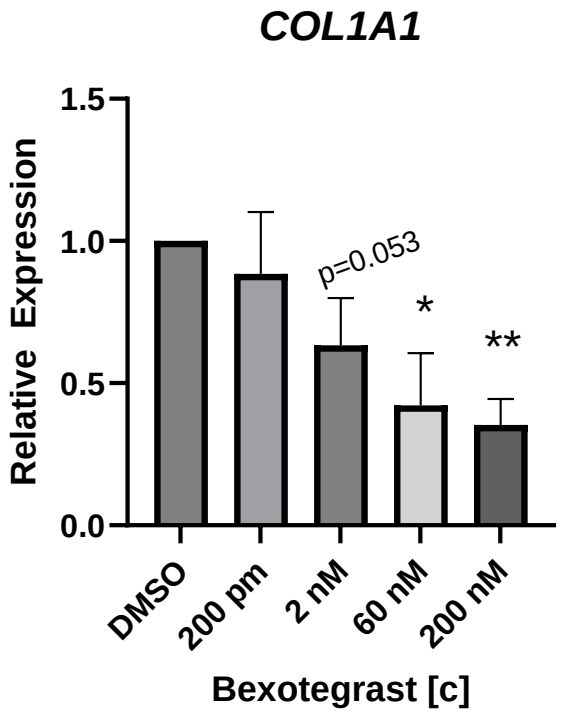


HP (3), RA-ILD (2), Scleroderma (2), NSIP (1)



[c] = 200 nM

p = 0.053 vs DSMO
* p < 0.05 vs DSMO
** p < 0.01 vs DSMO
*** < 0.001 vs DSMO
**** < 0.0001 vs DSMO



N = 2 IPF, 1 HP, 1 NSIP

In precision-cut lung slices from 7 lungs exhibiting different forms of lung fibrosis, bexotegrast decreased pro-fibrotic gene expression strongly and in a dose-dependent manner after 7 days of culture

Progressive Pulmonary Fibrosis (PPF) Market Opportunity

PPF Has High Unmet Needs, Comparable to IPF

- 20 – 35% of Non-IPF ILDs can be classified as PPF. Patients follow a similar disease course to IPF with significant symptoms and mortality rates
- There is no difference in the approach to the treatment and management of PPF patients compared to IPF patients
- Majority of PPF patients remain untreated; one approved treatment option with safety and tolerability challenges

PPF Significantly Expands the Commercial Potential of Bexotegrast Beyond IPF

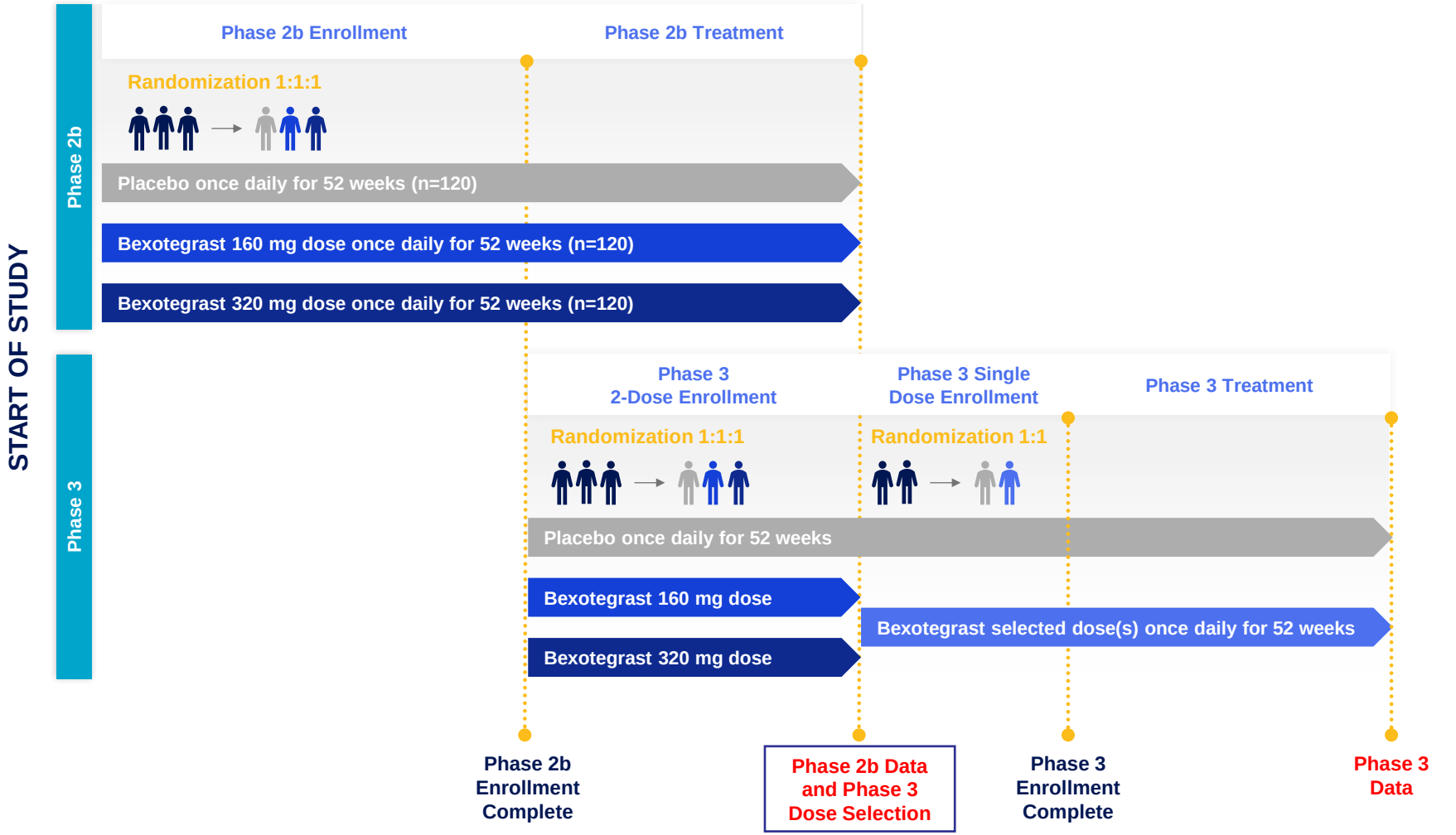
- PPF increases the addressable patient population by approximately 100 thousand in the U.S.
- Ofev net sales grew with PPF approval while Esbriet net sales remained flat with a single indication of IPF
- PPF lowers prescribing barrier by simplifying payer authorization process (progression criteria without definitive diagnosis)

Overall Pulmonary Fibrosis Opportunity

	IPF	PPF
Prevalence	• US: ~ 150K • Treatment eligible: 80 – 90%	• US: ~ 100K (excluding IPF) • Treatment eligible: 80 – 90%
Treatment	• Nintedanib and pirfenidone (branded and generic) for slowing of lung function loss	• Nintedanib for slowing of lung function loss • Pharmacologic treatment for underlying ILD (i.e. immunosuppressants)
Competition*	• P3: 4 • P2: >10	• P3: 3 • P2: < 3
Unmet Needs	• Disease modifying (feels, functions, survives) • Safety and Tolerability	• Disease modifying (feels, functions, survives) • Safety and Tolerability

* Estimated unique pipeline programs in development
Source: Informa, clintrials.gov 2024, Pliant analysis

BEACON-IPF Phase 2b/3 Study
On track for Enrollment Completion (1Q25) and Topline Data (2Q26)



BEACON-IPF

KEY PRIMARY ENDPOINT

- Change from baseline in absolute FVC (mL) at Week 52

KEY SECONDARY ENDPOINTS

- Time to disease progression (≥ 10% absolute decline from baseline in FVCpp, respiratory-related hospitalization, or all cause mortality through week 52)
- Change from baseline in absolute FVC (mL) at Week 52 in those ON and NOT on background therapy
- Change from baseline in Living with Pulmonary Fibrosis Dyspnea and Cough Domain scores at Week 52
- Safety and tolerability over 52 weeks

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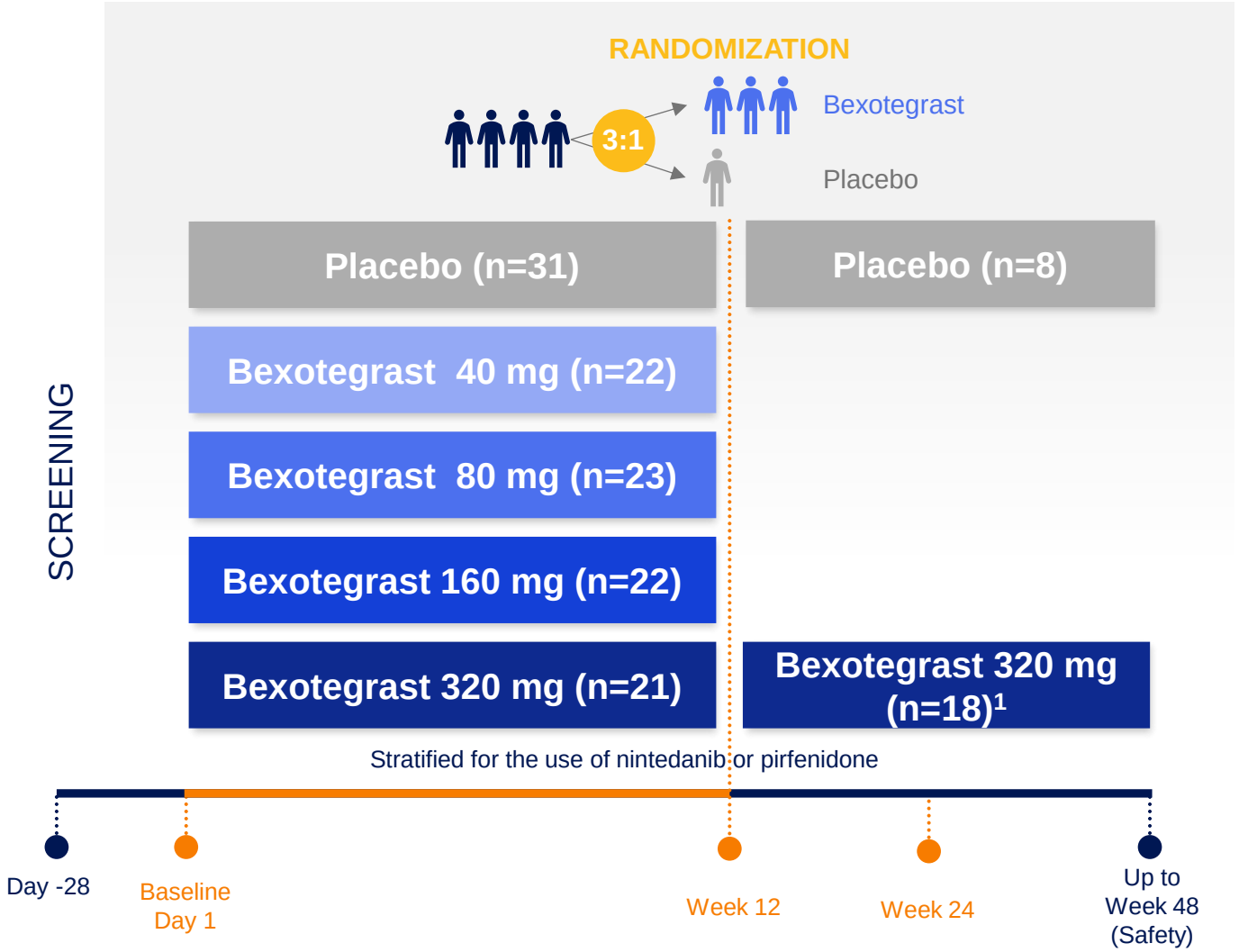
INTEGRIS-IPF – Phase 2a Study of Bexotegrast in IPF Patients

INTEGRIS-IPF Phase 2a Study Design and Objectives



PRIMARY AND SECONDARY ENDPOINTS

- Safety, tolerability, PK

EXPLORATORY ENDPOINTS

- Change in forced vital capacity (FVC) over 12 weeks and 24 weeks
- High resolution CT-based quantitative lung fibrosis (QLF) imaging
- Patient reported cough severity
- Effect on selected biomarkers

1 – Treatment duration per protocol: minimum of 24 weeks and a maximum of 48 weeks

Key Takeaways from the INTEGRIS-IPF Trial

Bexotegrast Demonstrated a Favorable Safety and Tolerability Profile up to 40 Weeks

Bexotegrast Demonstrated a Dose-dependent Treatment Effect on Registrational Endpoint

- Statistically significant increases from baseline in mean FVC at Week 12
- Treatment benefits were present at Week 24 across physiologic (FVC), radiographic (QLF) and symptomatic (cough) assessments versus placebo
- Bexotegrast treatment effect was observed with and without use of standard-of-care agents

Data Provide Strong Support of Bexotegrast's Antifibrotic Mechanism of Action

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Well Tolerated Up to 40 Weeks

AE, n (%) of Participants Reporting	Through 12 weeks						Up to 40 weeks	
	Bexotegrast 40 mg (n=22)	Bexotegrast 80 mg (n=23)	Bexotegrast 160 mg (n=22)	Bexotegrast 320 mg (n=22)*	Bexotegrast All (n=88)	Placebo (n=31)	Bexotegrast 320 mg (n=22)*	Placebo (n=8)
Any AEs	16 (72.7)	15 (65.2)	15 (68.2)	18 (81.8)	64 (72.7)	21 (67.7)	20 (90.9)	7 (87.5)
TEAE	16 (72.7)	15 (65.2)	14 (63.6)	17 (77.3)	62 (70.5)	21 (67.7)	20 (90.9)	7 (87.5)
Related to study drug	**4 (18.2)**	**7 (30.4)**	**4 (18.2)**	**4 (18.2)**	**19 (21.6)**	**10 (32.3)**	**5 (22.7)**	**2 (25.0)**
Serious TEAE	1 (4.5)	0	2 (9.1)	1 (4.5)	4 (4.5)	3 (9.7)	2 (9.1)	1 (12.5)
Related to study drug	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
TEAE of CTCAE Grade 3 or Higher	2 (9.1)	0	2 (9.1)	2 (9.1)	6 (6.8)	2 (6.5)	5 (22.7)	1 (12.5)
Related to study drug	**0**	**0**	**1 (4.5)**	**0**	**1 (1.1)**	**0**	**1 (4.5) [1]**	**0**
TEAE Leading to Interruption of Study Drug	0	0	1 (4.5) [1]	1 (4.5) [2]	2 (2.3)	0	4 (18.2) [2]	0
TEAE Leading to Withdrawal of Study Drug	0	0	0	3 (13.6) [2,3,4]	3 (3.4)	3 (9.7)	3 (13.6) [2,3,4]	1 (12.5)
TEAE Leading to Early Termination from Study	0	0	0	3 (13.6) [2,3,4]	3 (3.4)	2 (6.5)	3 (13.6) [2,3,4]	0
TEAE Leading to Death	0	0	0	1 (4.5) [3]	1 (1.1)	0	1 (4.5) [3]	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
* One placebo participant received 1 week of treatment with Bexotegrast 320 mg and is included in the 320 mg treatment groups. The participant did not have any AEs.

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.

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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.

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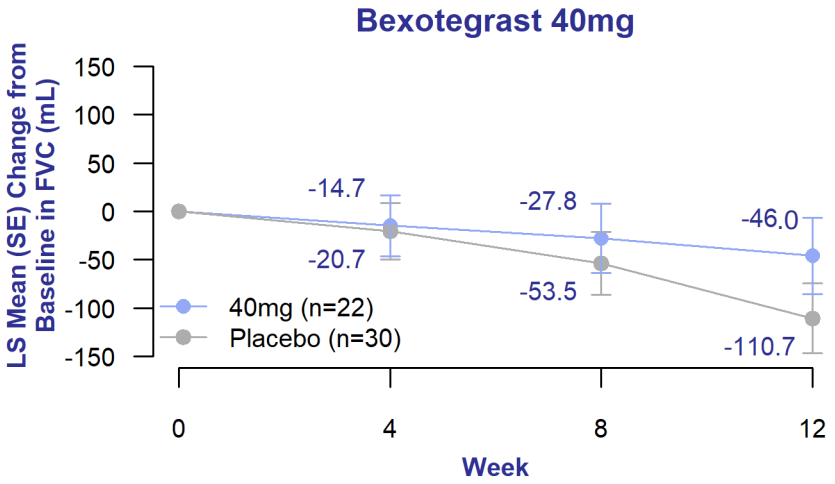
Most Frequent TEAEs – Idiopathic Pulmonary Fibrosis

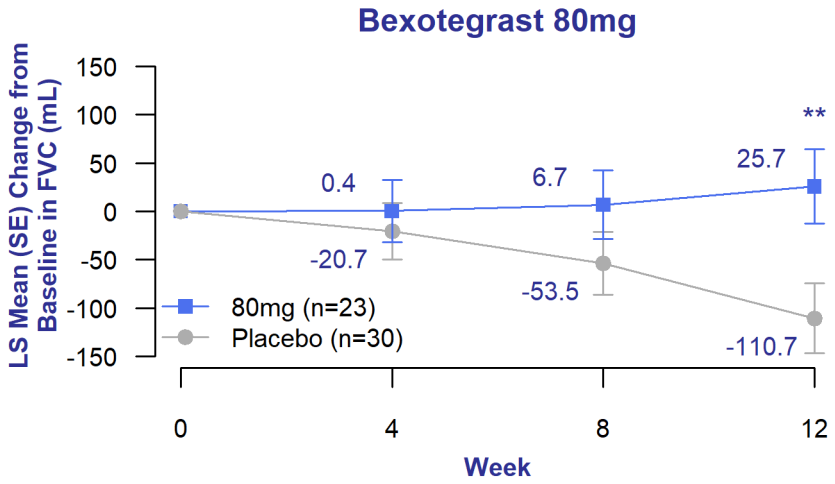
Participant	GAP Stage	Time to Occurrence	Description of Symptoms	Grade	Treatment Related
Bexotegrast 320 mg	GAP Stage II	Week 33	O2 Needed	Grade 2	Unrelated
Bexotegrast 320 mg	GAP Stage I	Week 21	IPF Progression	Grade 2	Unrelated
Bexotegrast 320 mg	GAP Stage II	Week 16	Worsening Disease, More Dyspnea, Under Study	Grade 3	Unrelated
Bexotegrast 320 mg	GAP Stage I	Week 42	Worsening of IPF	Grade 2	Unrelated

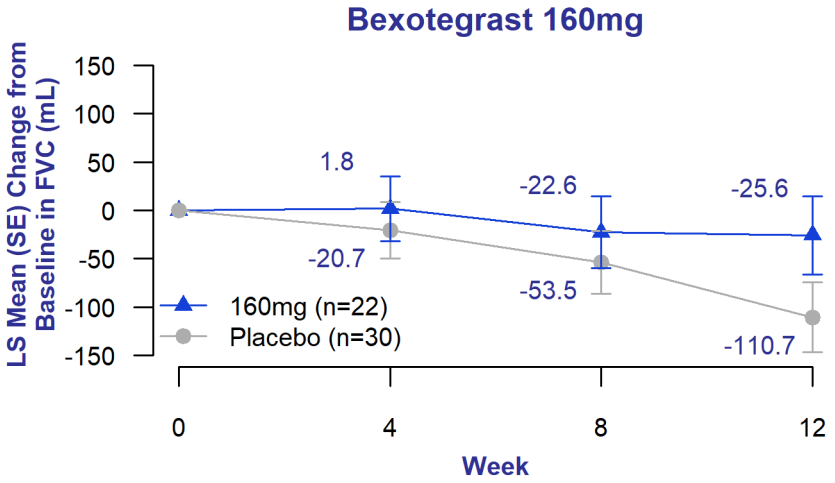
*No TEAE led to study drug interruption.
*No reported serious TEAEs or reported acute exacerbation of IPF by the PI

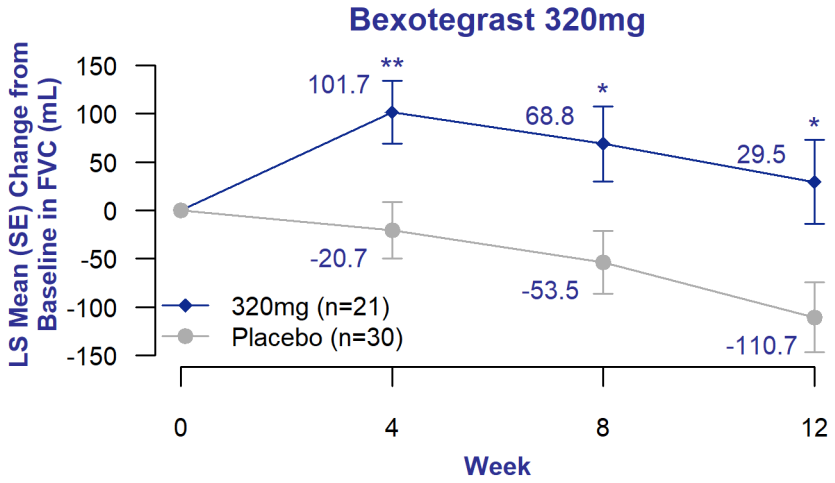
PLIANT

FVC Change from Baseline over 12 Weeks
mITT Population







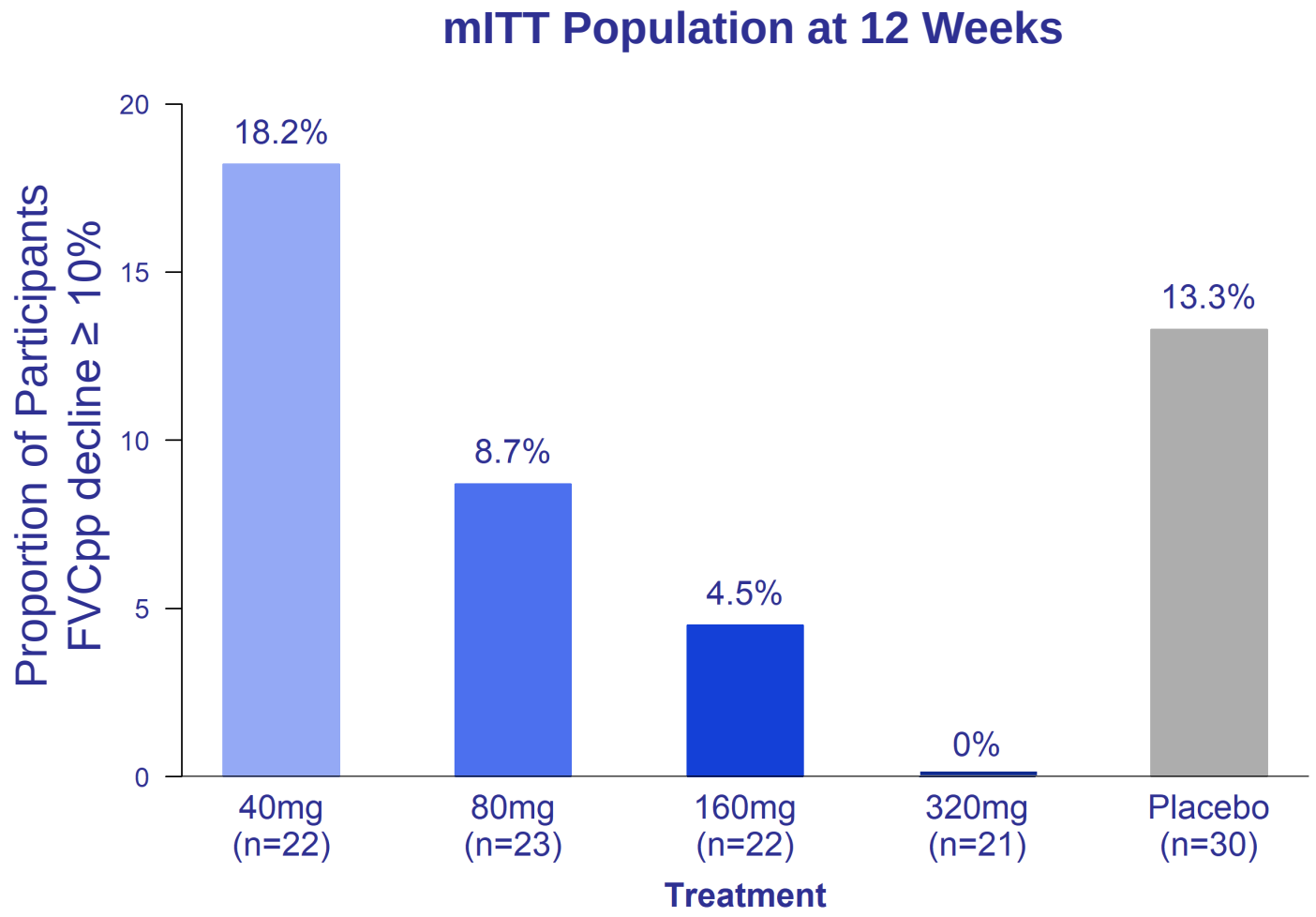


* p < 0.05 vs placebo
** p < 0.01 vs placebo

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.

PLIANT

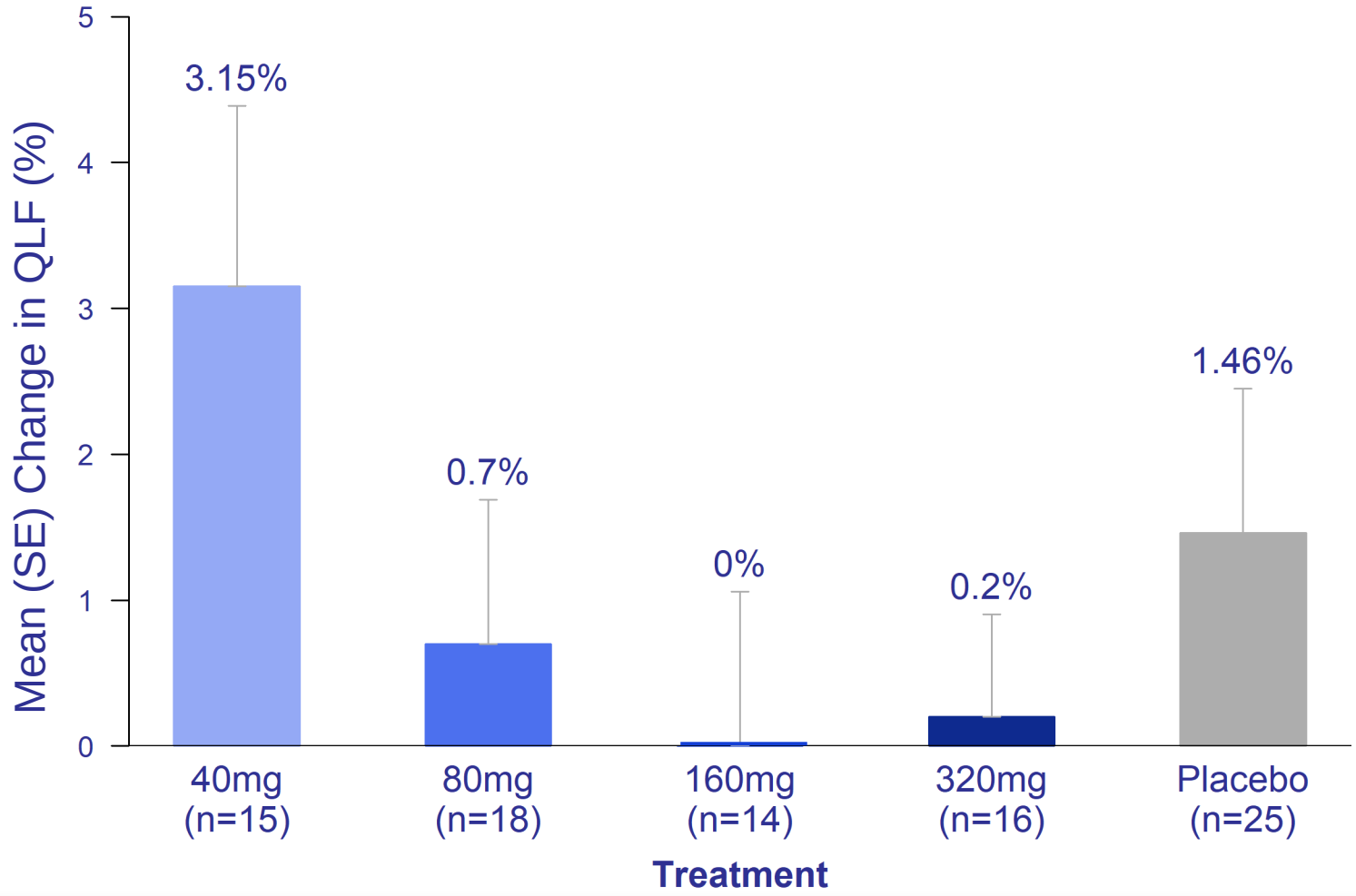
Proportion of Participants with Relative FVCpp Decline ≥ 10%
mITT Population



FVCpp = Forced vital capacity, percent predicted.

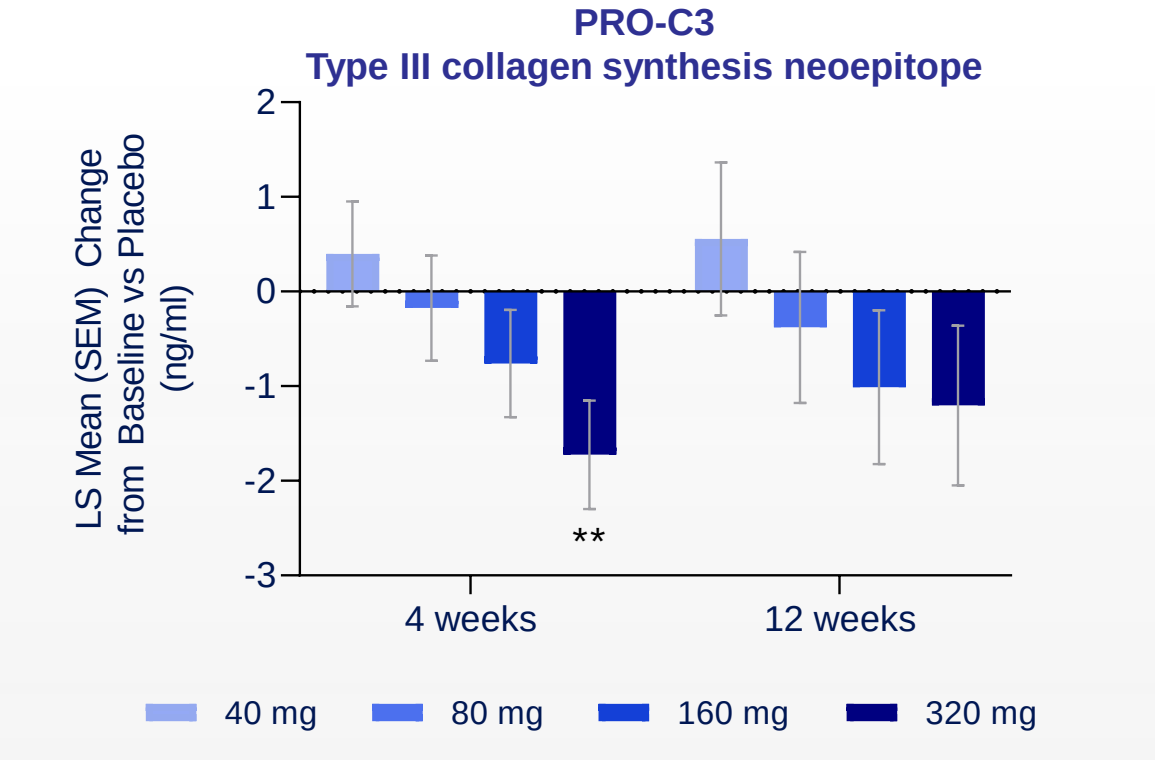
1- Ann Am Thorac Soc. 2017 Sep;14(9):1395-1402; 2- Am J Respir Crit Care Med. 2022 Apr 15;205(8):936-948.

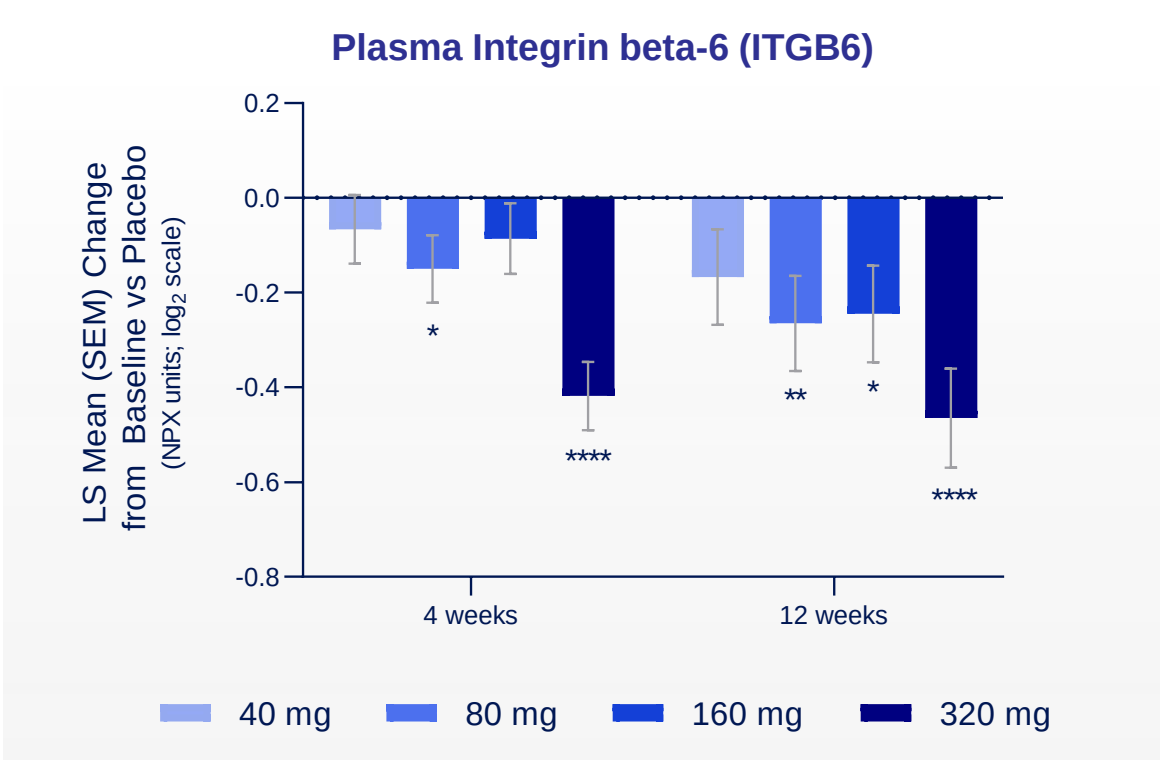
QLF Mean Percent Change from Baseline at Week 12
Per CT protocol population



QLF = quantitative lung fibrosis

Bexotegrast Reduced Serum Fibrosis Biomarkers
Change from Baseline at 4 and 12 Weeks vs. Placebo





LS = Least Squares; SE = Standard Error

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

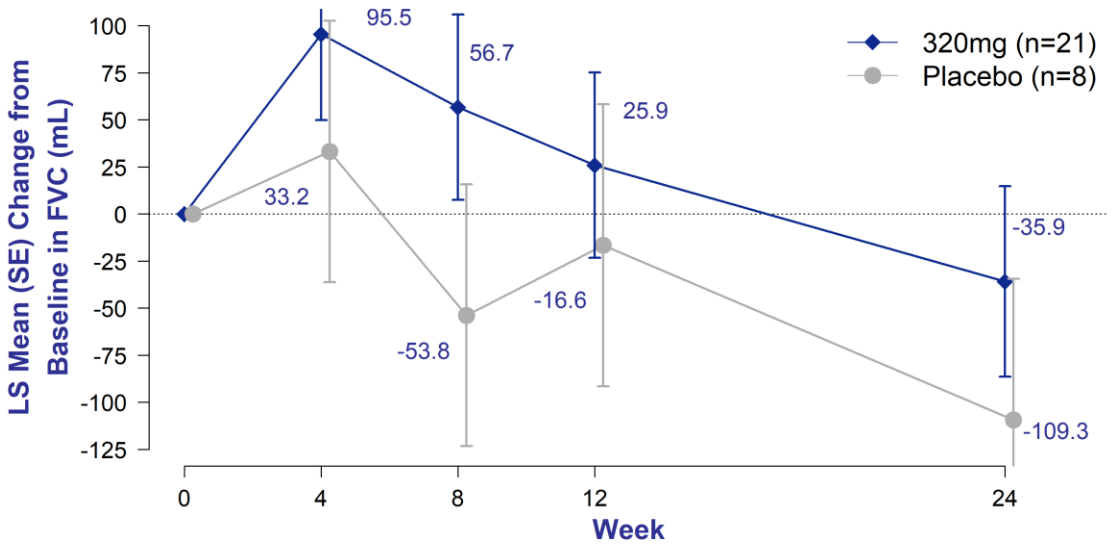
PRO-C3, a serum biomarker of type III collagen synthesis, was previously shown to be elevated in patients with IPF and associated with progressive disease[1]

Elevated ITGB6 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[2]

1- Respir Res. 2019 Jul 12;20(1):148.
2- Lancet Respir Med. 2022 Jun;10(6):593-602.

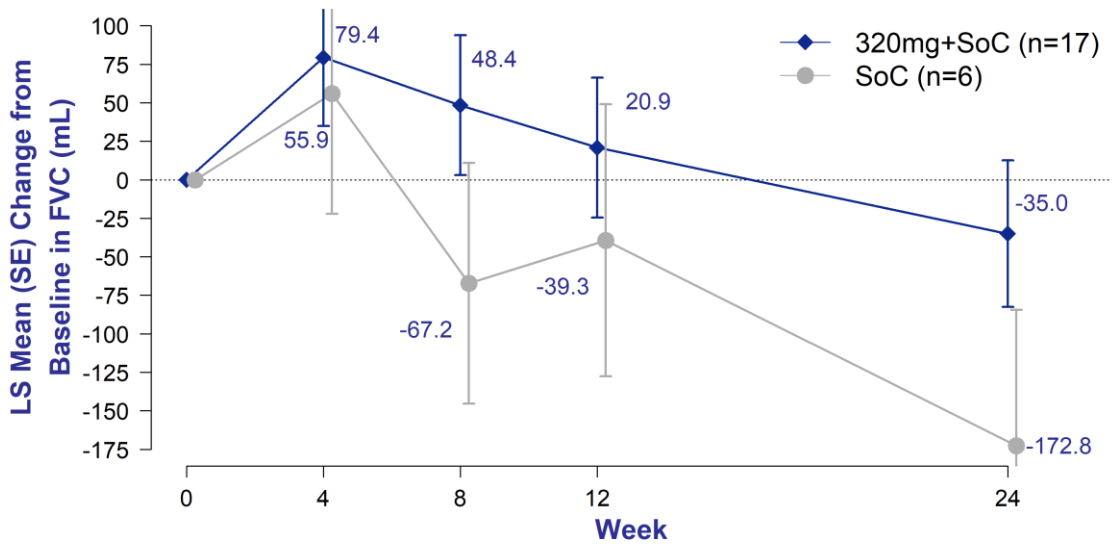
FVC Change from Baseline over 24 Weeks
ITT Population vs. SoC Sub-Group

ITT Population



Bexotegrast reduced FVC decline by 67% relative to placebo at Week 24

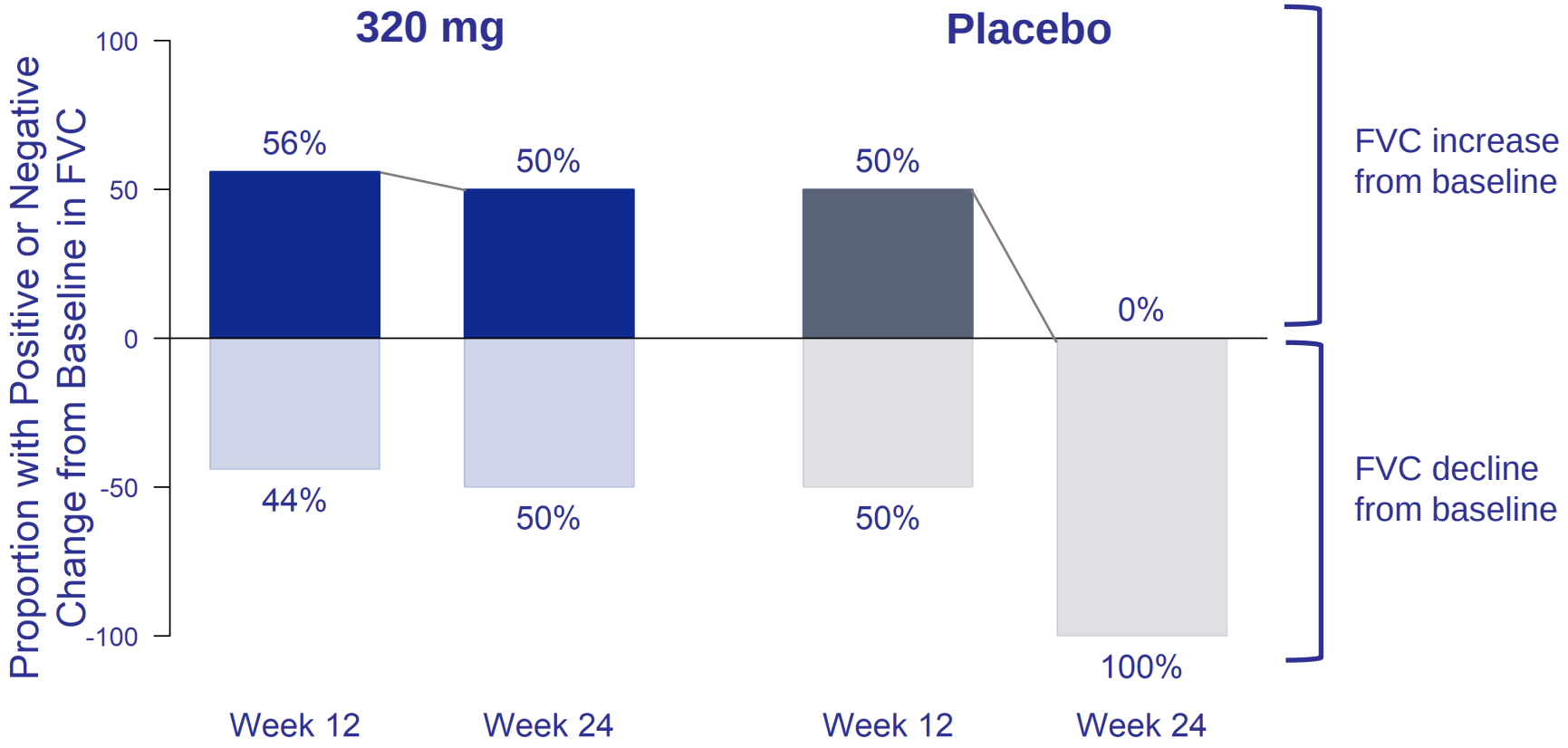
Standard-of-Care Sub-Group



Bexotegrast + SOC reduced FVC decline by 80% relative to SOC alone at Week 24

Participants not on SoC not shown due to small sample size, n=4 (320 mg) and n=2 (placebo)
FVC = forced vital capacity; ITT=intent to treat; SoC = standard of care (nintedanib or pirfenidone)

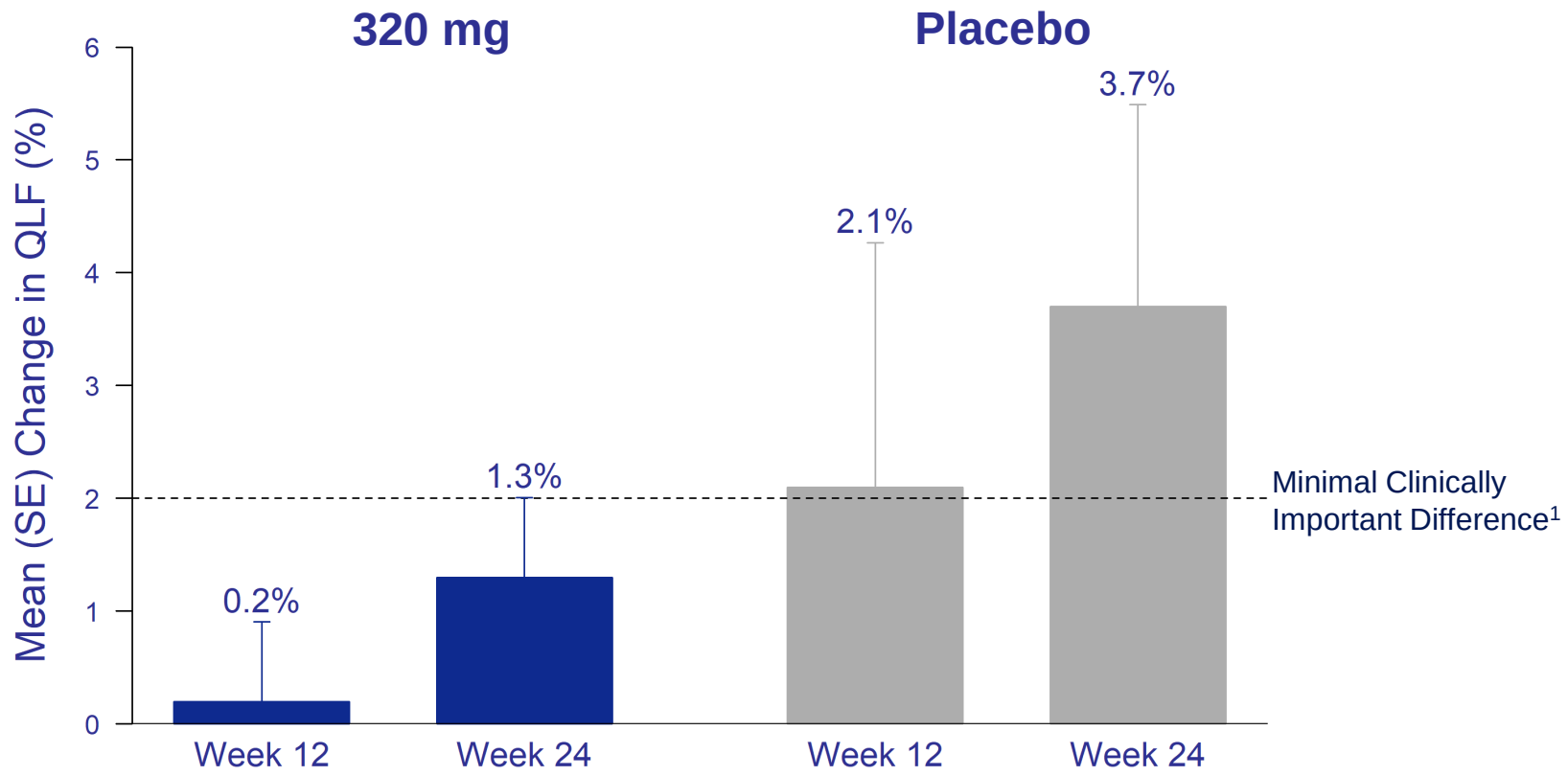
Bexotegrast Demonstrated Durable Increase in FVC at Week 24
ITT Population



89% of bexotegrast-treated participants with FVC increase at Week 12 maintained an increase at Week 24

FVC = forced vital capacity; ITT = intent to treat.
Participants with missing data not included

QLF Mean Percent Change from Baseline at Weeks 12 and 24
Per CT Protocol Population

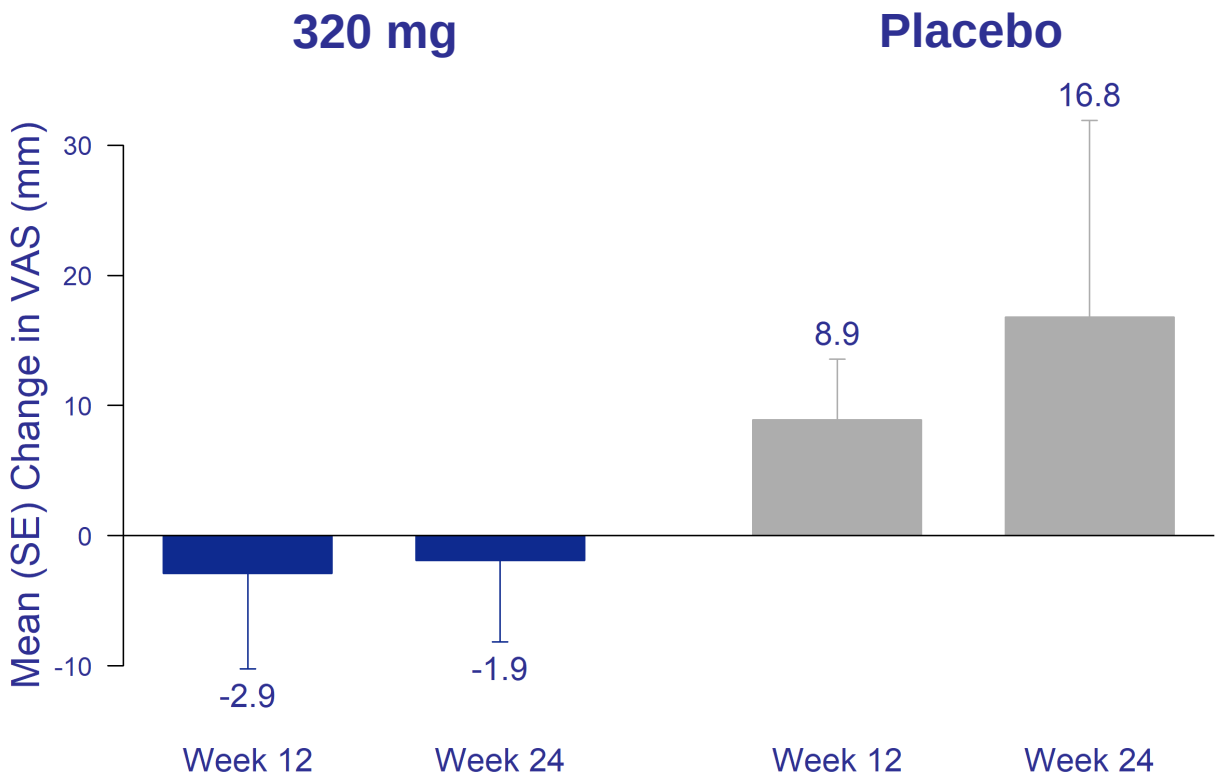


Bexotegrast group demonstrated stabilization of fibrosis, in contrast to placebo group which showed clinically meaningful progression at Weeks 12 and 24

QLF = quantitative lung fibrosis; QLF Minimal Clinically Important Difference for whole lung: 2%; stable disease (-2%, 2%)
Per CT protocol population: Participants with both baseline and post baseline high resolution computed tomography (HRCT) scans meeting evaluability criteria per Imaging Charter
1 EU Radiology 2020 30:726-734

PLIANT

Cough Severity Visual Analog Scale (VAS) Change from Baseline
ITT Population



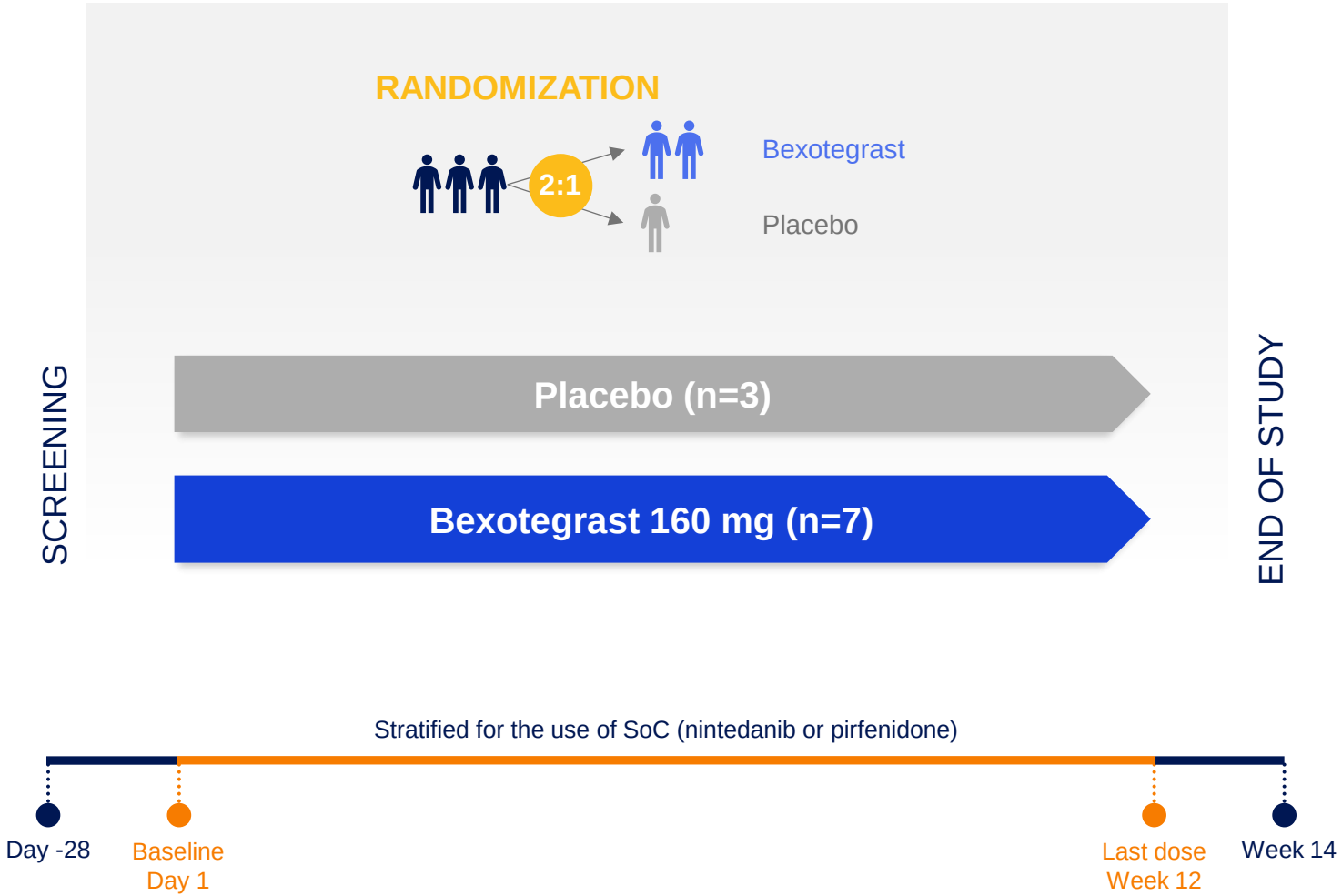
Chronic cough in IPF is an independent predictor of disease progression and mortality[1]

1 - *Respirology* 2011; 16: 969–975.
Cough VAS measures patient reported cough severity over last 2 weeks on scale of 0-100 mm

Phase 2a Collagen PET Study

Phase 2a Collagen PET Study – Design and Objectives

Quantification of Type 1 Collagen in the Lung using PET Imaging



PRIMARY AND SECONDARY ENDPOINTS

- Change in whole lung standardized uptake value (SUV) of ^{68}GA-CBP8 (type-1 collagen probe)
- Safety and tolerability

EXPLORATORY ENDPOINTS

- Changes in FVC and FVCpp
- Change in VAS for cough severity
- Changes in fibrosis biomarkers

INCLUSION CRITERIA

- Diagnosis of IPF (within 8 years)
- FVC percent predicted ≥ 45%
- DLCO ≥ 30%
- Estimated glomerular filtration rate ≥ 50mL/min

FVC: forced vital capacity, FVCpp: forced vital capacity percent predicted; SoC = Standard of care; VAS: visual analog scale
^{68}GA-CBP8: peptide-based collagen binding probe 8 tagged with Gallium-68 radioisotope

PLIANT

Baseline Demographics

Characteristic	Bexotegrast 160mg (n=7)	Placebo (n=3)
Male sex, n (%)	6 (85.7)	3 (100)
Age (yr), median (IQR)	70 (64 – 72)	74 (72 – 76)
Weight (kg), median (IQR)	81.2 (79.0 – 88.5)	78.0 (77.6 – 85.3)
BMI (kg/m^2), median (IQR)	25.7 (23.7 – 30.4)	26.4 (24.0 – 30.3)
Race, n (%)		
White	6 (85.7)	3 (100)
Black	0	0
Asian	1 (14.3)	0
Other / Not Reported / Unknown	0	0

IQR = Interquartile range (Q1, Q3); BMI = Body Mass Index

Baseline Disease Characteristics

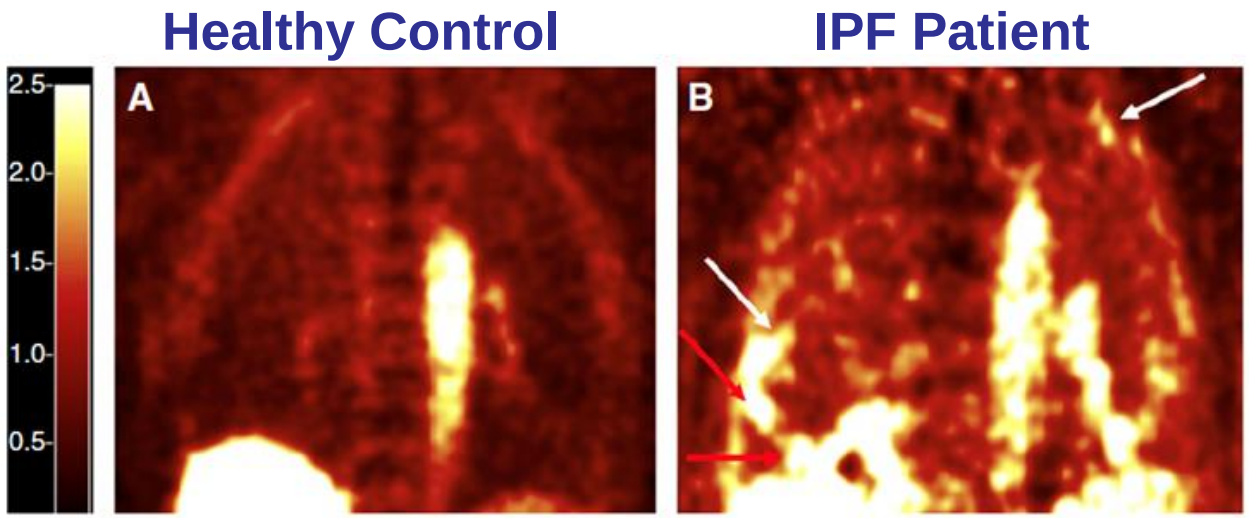
Characteristic	Bexotegrast 160mg (n=7)	Placebo (n=3)
Time since diagnosis of IPF (mo), median (IQR)	50 (22 – 70)	9 (7 – 72)
Standard of Care Use, n (%)		
Nintedanib	5 (71.4)	1 (33.3)
Pirfenidone	1 (14.3)	1 (33.3)
Duration of Standard of Care at Randomization (mo), median (IQR)	34.5 (17 – 55)	40.0 (6 – 74)
FVC		
Absolute (mL), median (IQR)	2,750 (2,400 – 3,080)	2,250 (1,700 – 2,640)
Percent of predicted value (%), median (IQR)	66.0 (56.0 - 92.0)	58.0 (49.0 - 69.0)
Percent of predicted DLCO, corrected for the hemoglobin level (%), median (IQR)	49 (40.0 – 58.0)	43 (36.5 – 45.0)
GAP Stage, n (%)		
GAP Stage I	4 (57.1)	0
GAP Stage II	2 (28.6)	2 (66.7)
GAP Stage III	1 (14.3)	1 (33.3)

GAP Index score derived from Gender, Age, FVC, % Predicted and DLCO, % Predicted.
IQR = Interquartile range (Q1, Q3); DLCO= Diffusing Capacity for Carbon Monoxide; FVC = Forced Vital Capacity

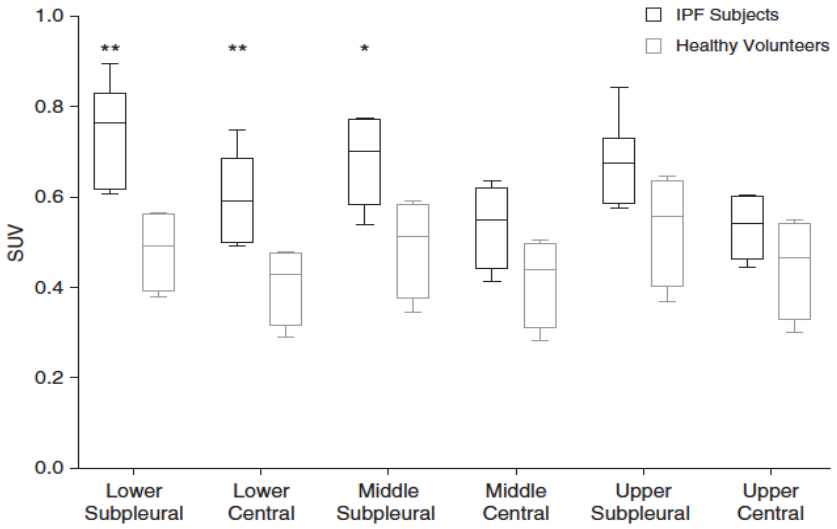
PLIANT

Quantification of Collagen in the Lung using PET Imaging

- ^{68}Ga-CBP8 is a PET probe that binds type I collagen with high specificity[1]
- The probe binds to both freshly synthesized and mature collagen
- IPF patients have higher standardized uptake values (SUV) compared to healthy volunteers[2], indicating higher amounts of total lung collagen
- ^{68}Ga-CBP8 previously detected treatment response to anti-fibrotic therapy in a mouse model of pulmonary fibrosis[1]



Note: Uptake in the heart and vasculature as well as in the liver is to be expected based on the probe's half-life and biodistribution



^{68}GA-CBP8: peptide-based collagen binding probe 8 tagged with Gallium-68 radioisotope
SUV: standardized uptake value; SUV measures the ratio of the uptake of a radiotracer in tissue
[1]Désogere et al, Sci Trans Med. 2017; [2]Montessi Am J Respir Crit Care Med 200:2 2019

PLIANT

Key Findings

Bexotegrast cohort showed reduced PET ligand standardized uptake values (SUV) compared to placebo

- Reduction in SUV post-treatment indicates less total lung collagen, suggesting potential reversal of fibrosis
- Additional support of bexotegrast's antifibrotic mechanism of action

No safety concerns identified over 12 weeks of treatment

- Most adverse events were mild with no study discontinuations observed
- No SAEs observed

Bexotegrast cohort showed improved lung function and decreased cough severity across all timepoints

- Positive FVC change compared to decline in placebo across all time points
- Decrease in cough severity observed at all time points compared to worsening seen on placebo

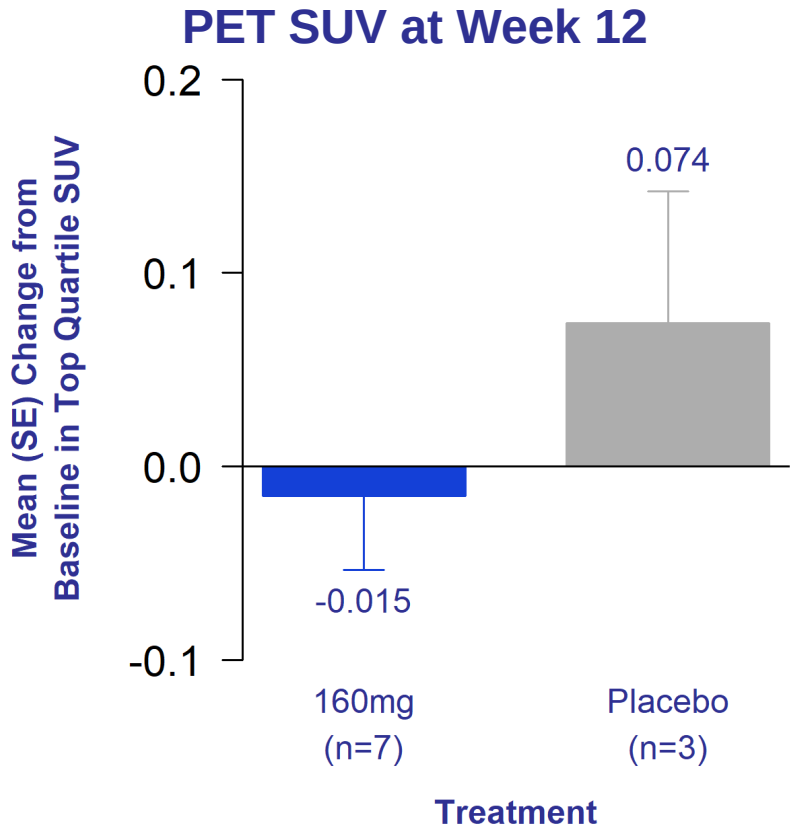
Biomarker results further support bexotegrast's antifibrotic mechanism

- Bexotegrast cohort showed reduced circulating PRO-C3 and Integrin Beta-6 levels at Weeks 4 and 12 compared to placebo

PLIANT

Bexotegrast Showed Reduced PET Tracer SUV Compared to Placebo

ITT Population



Reduction in post-treatment SUV indicates a reduction in total lung collagen

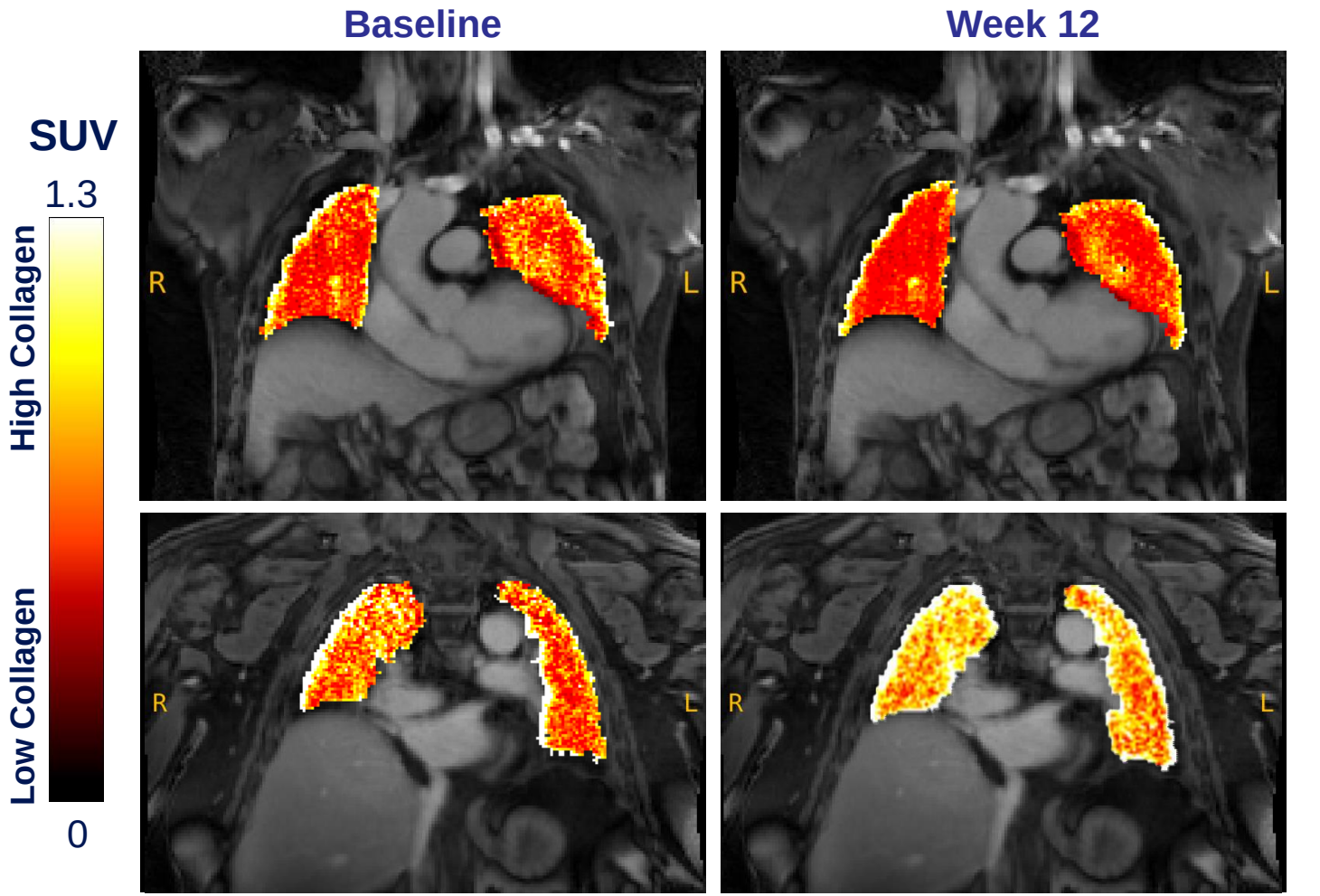
Reduced post-treatment total lung collagen suggests potential reversal of fibrosis

[2] Montessi AJRCCM 200:2 2019

SUV = Standardized Uptake Value; SE = Standard Error; ^{68}GA-CBP8: peptide-based collagen binding probe 8 tagged with Gallium-68 radioisotope
SUV measures the ratio of the uptake of a radiotracer in tissue; Top quartile SUV is the mean of SUVs within the top quartile for each lung section; Whole lung is the average of the left and right lungs

PLIANT

PET Imaging Study – Clearly Visible Reduction of Total Lung Collagen



Participant A

- Bexotegrast 160 mg for 12 weeks
- Decrease in SUV_{Q4}, -0.17 (-15.5%)
- Improvement in FVC, 130 mL

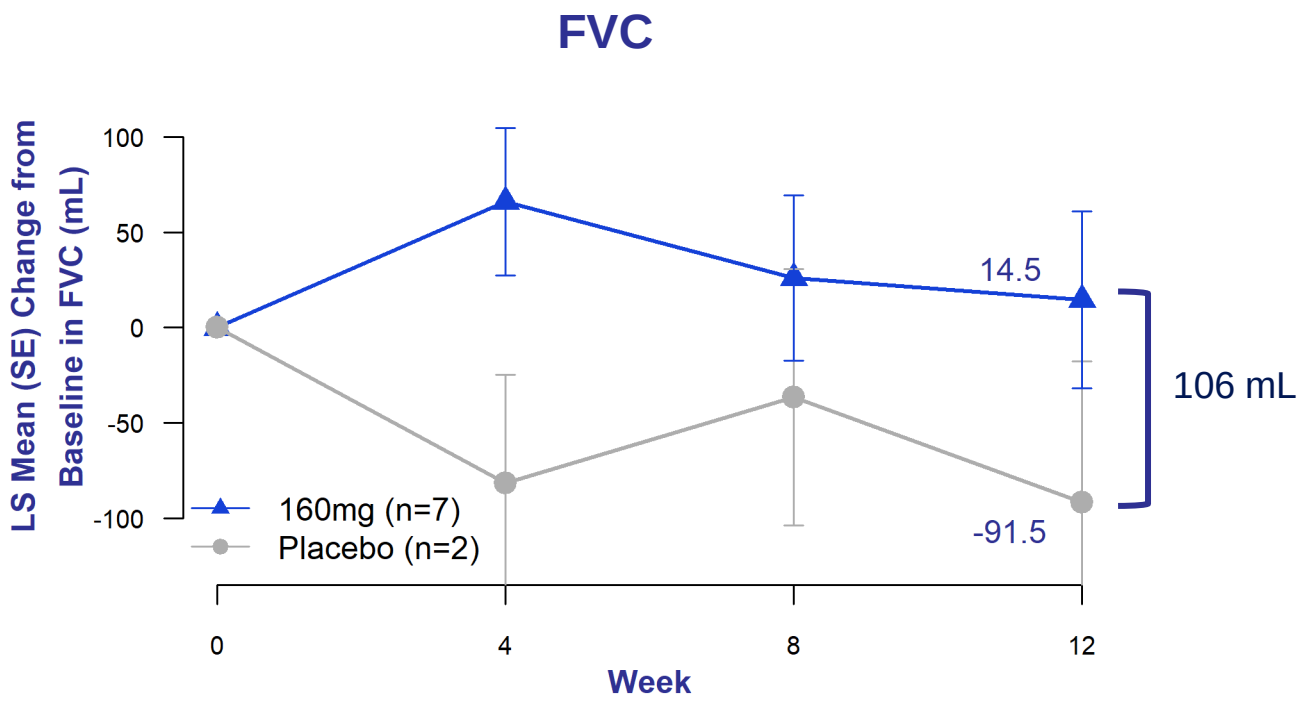
Participant B

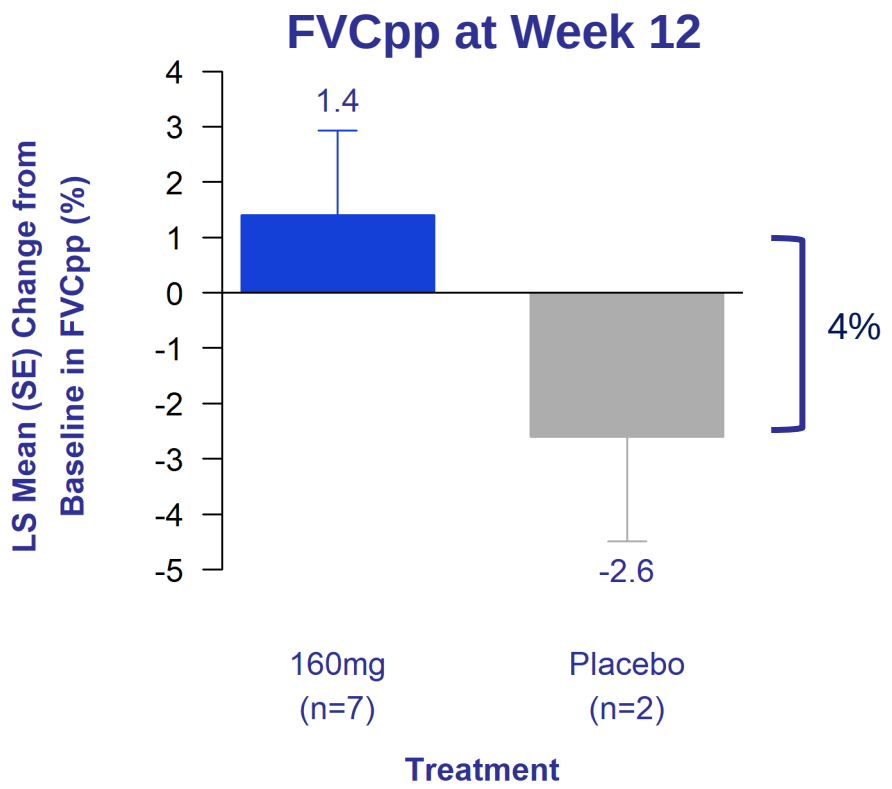
- Placebo for 12 weeks
- Increase in SUV_{Q4}, 0.21 (18.4%)
- Decline in FVC, -180 mL

SUV = Standardized Uptake Value; SUV_{Q4}: top quartile SUV; 68GA-CBP8: peptide-based collagen binding probe 8 tagged with Gallium-68 radioisotope
FVC: forced vital capacity; VAS; visual assessment scale for cough severity (0-100)
SUV measures the ratio of the uptake of a radiotracer in tissue and quantifies the amount of type I collagen detected

Bexotegrast Showed Improved Lung Function Compared to Placebo

ITT Population





Bexotegrast cohort maintained a clear separation from placebo at all time points

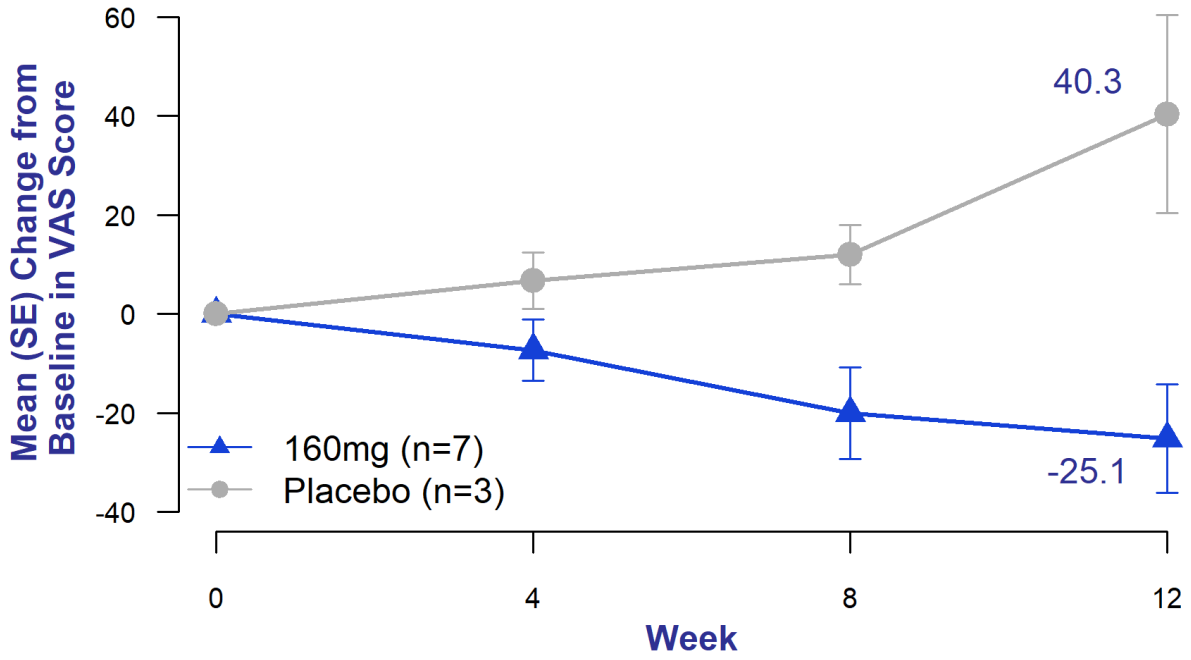
Note: One placebo subject did not have FVC that meet quality standards per ATS guidelines at Weeks 4, 8 and 12
LS = Least Squares; SE = Standard Error; FVC = Forced Vital Capacity; FVCpp = Forced Vital Capacity Percent Predicted

PLIANT

Bexotegrast Showed Decreased Cough Severity Compared to Placebo

ITT Population

Cough Severity Over 12 Weeks of Treatment

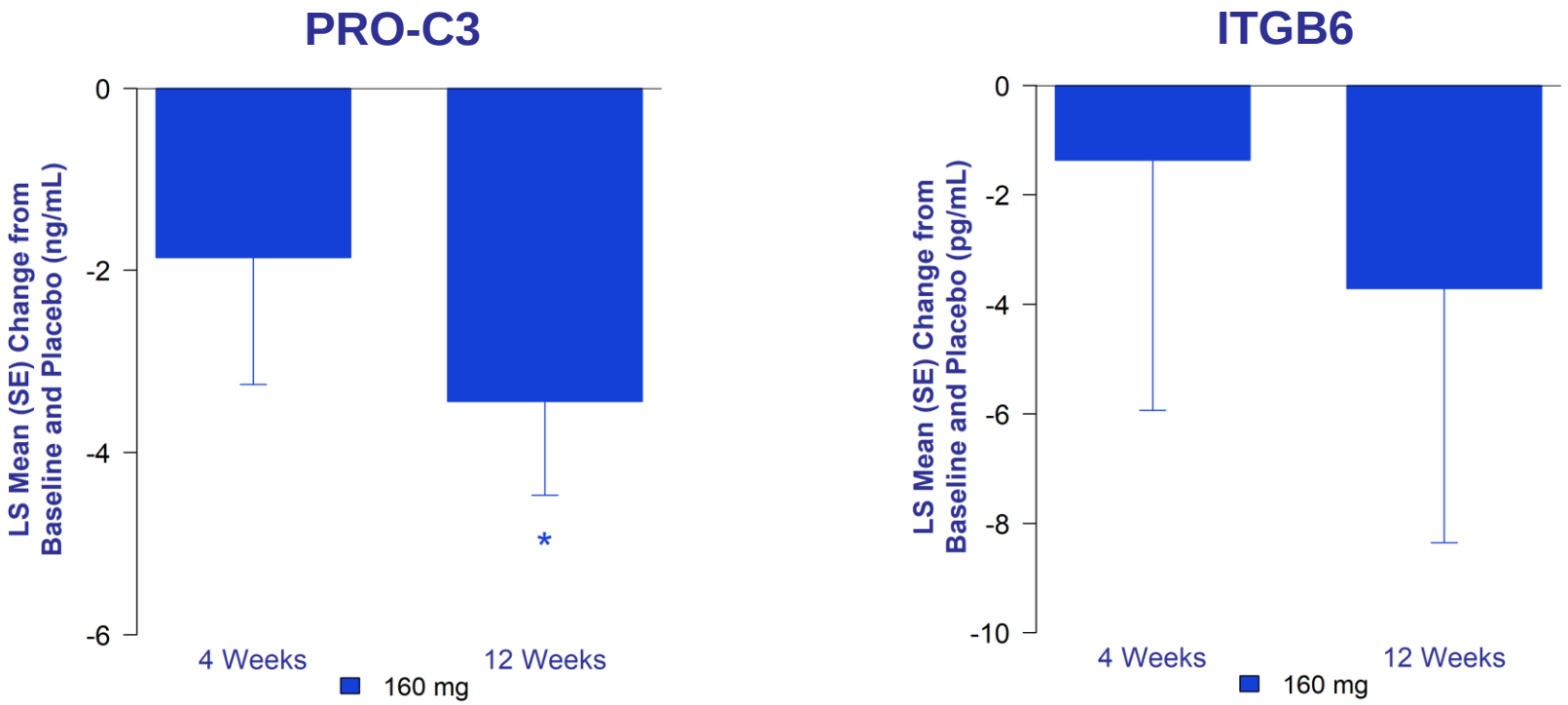


Bexotegrast cohort experienced decreased cough severity across all timepoints compared to increased severity on placebo

EOT: end of treatment; SE: standard error; VAS = Visual Analog Scale
Cough VAS measures patient reported cough severity over last 2 weeks on scale of 0-100 mm

Bexotegrast Showed Reduced Fibrosis Biomarkers Compared to Placebo

ITT Population



* $p < 0.05$ vs placebo

PRO-C3 has been shown to be elevated in patients with IPF and associated with progressive disease[3]

Elevated ITGB6 plasma levels have been shown to be associated with ILD progression[4]

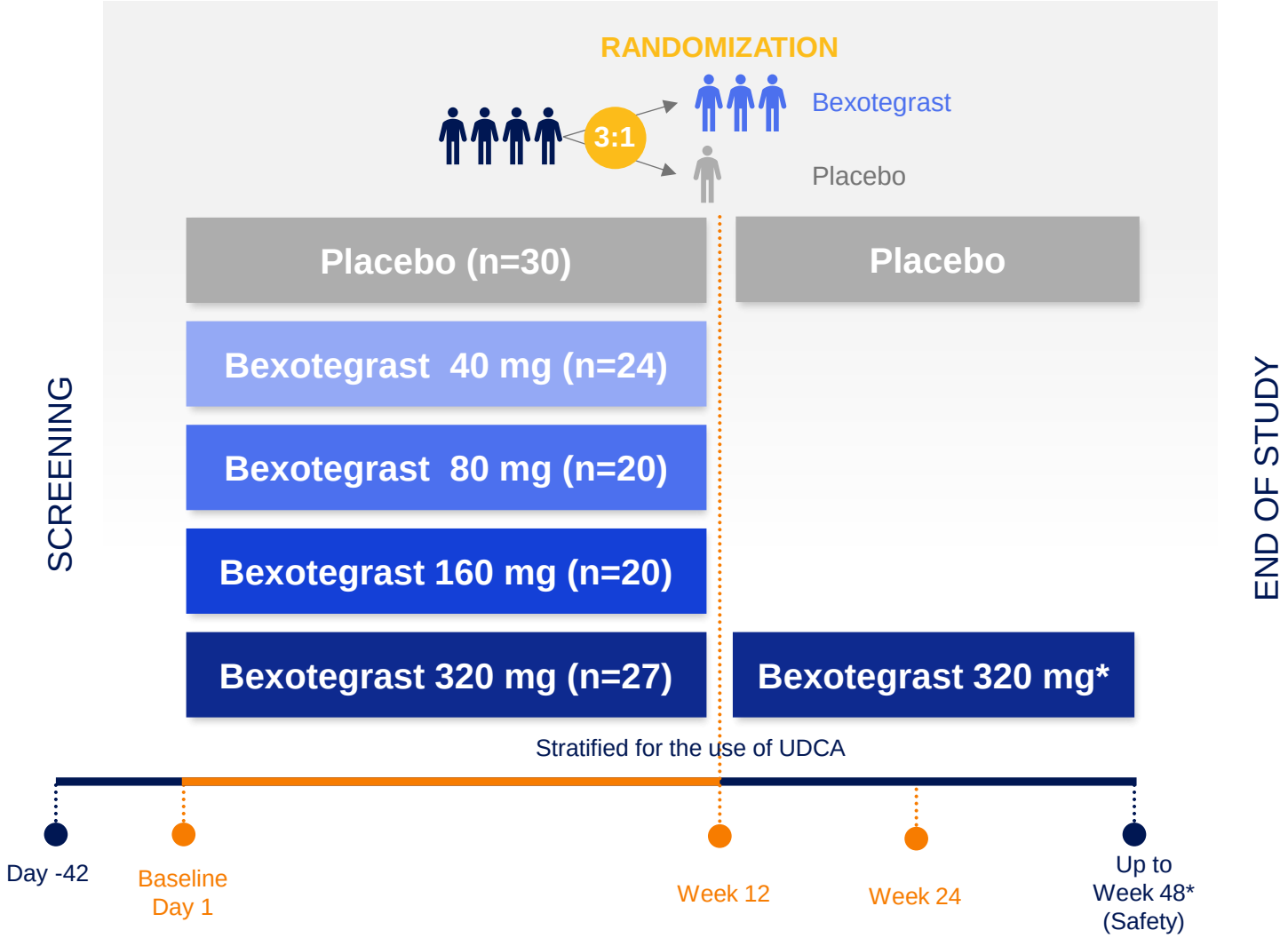
[3]Respir Res. 2019 Jul 12;20(1):148. doi: 10.1186/s12931-019-1118-7; [4]Lancet Respir Med. 2022 Jun;10(6):593-602. doi: 10.1016/S2213-2600(21)00503-8. Epub 2022 Jan 18

ITGB6: Integrin Beta 6; LS = Least Squares; PRO-C3 = Type III Collagen Synthesis Neoepitope; SE = Standard Error

PLIANT

INTEGRIS-PSC Study Design and Objectives

First PSC Trial Enriched with Participants with Suspected Liver Fibrosis



PRIMARY AND SECONDARY ENDPOINTS

- Safety, tolerability, PK

EXPLORATORY ENDPOINTS

- Changes in liver fibrosis markers, ELF score and PRO-C3
- Changes in liver biochemistry
- Changes in liver imaging

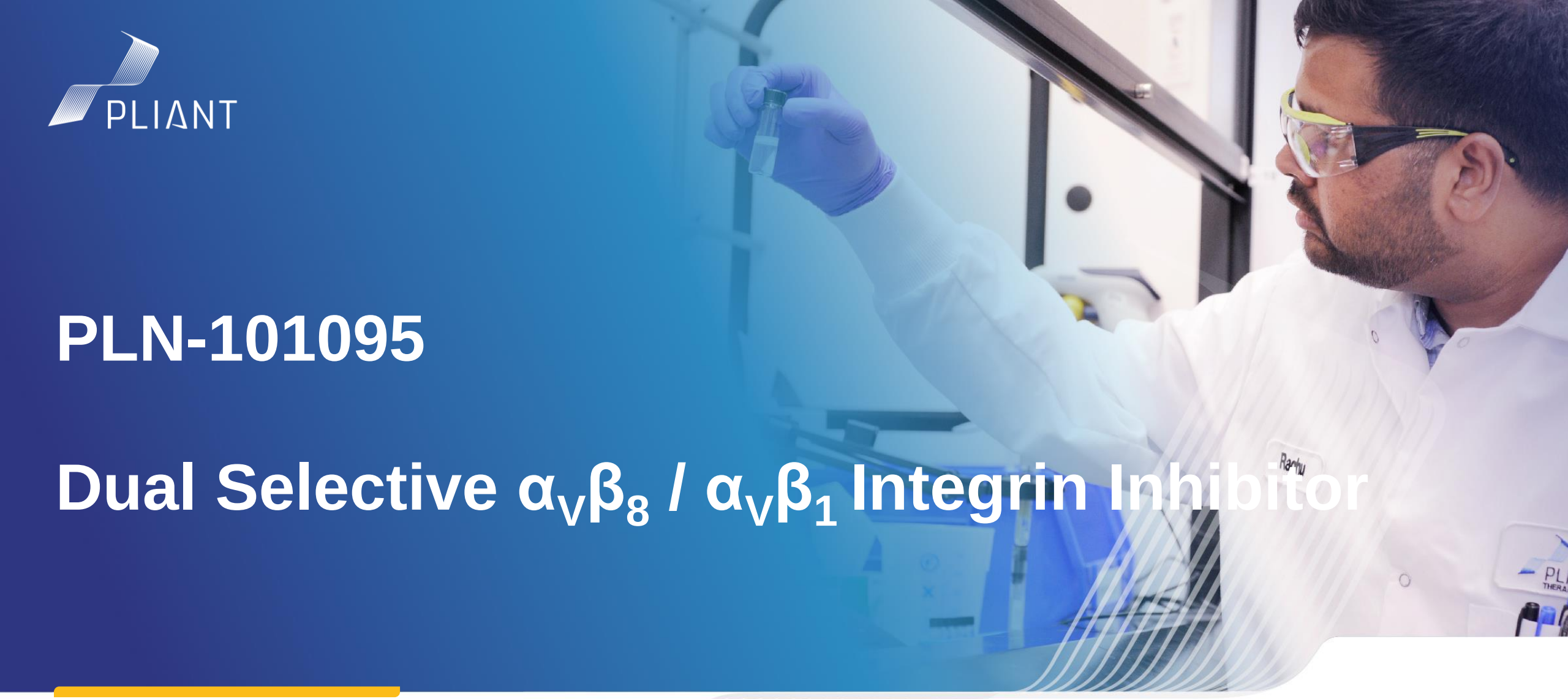
INCLUSION CRITERIA

- Suspected moderate/severe fibrosis defined by at least one criterion:
  - ELF ≥ 7.7
  - TE ≥ 8 but ≤ 14.4 kPa
  - MRE ≥ 2.4 but ≤ 4.9 kPa
  - Historical biopsy

UDCA = Ursodeoxycholic acid; ELF = enhanced liver fibrosis

*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

PLN-101095 – Potential First-in-Class SMI Dual $\alpha_V\beta_8/\alpha_V\beta_1$ Inhibitor

Highly potent dual inhibitor of $\alpha_V\beta_8$ and $\alpha_V\beta_1$

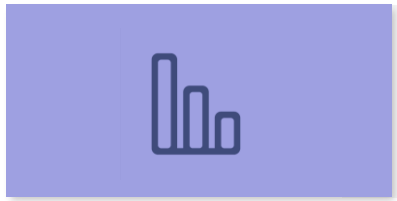
- Tumors that overexpress $\alpha_V\beta_8$ have a poor prognosis

Small molecule with oral administration

- Ease of administration compared to mAb programs

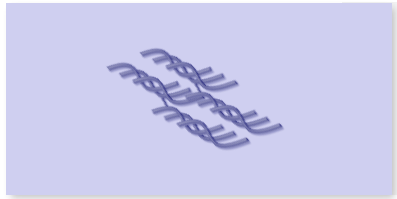
Activity demonstrated in multiple PD-1 resistant tumor models

- Increased T-cell infiltration and high tumor growth inhibition



Greater reduction in TGF-β signaling than either $\alpha_V\beta_8$ or TGF-β1,2 mAb

- TGF-β is a central mediator of immune suppression in the tumor microenvironment



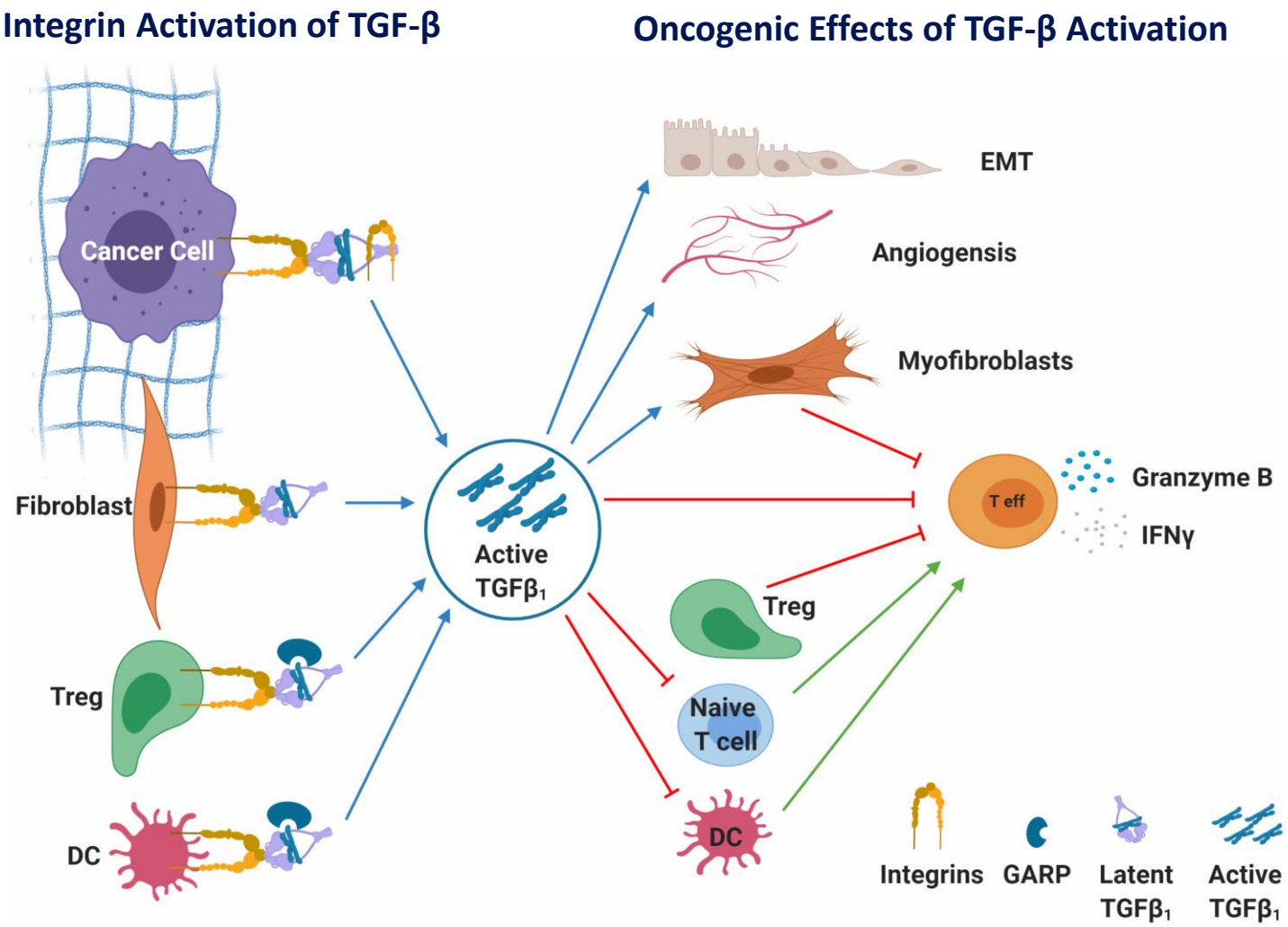
Significant reduction in tumor fibrogenesis

- Inhibition of $\alpha_V\beta_1$ on fibroblasts may aid immune infiltration of fibrotic tumors

PLIANT

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



PLN-101095 – Approach to Immune Checkpoint Inhibitor Resistance

Common Mechanisms of I-O Resistance

- Tumor-specific IFNγ levels at baseline predict pembrolizumab responses [4,5]
- Immunosuppressive stroma / myeloid compartment associated with active TGF-β signaling predicts atezolizumab responses [3]
- Tumor infiltrating lymphocytes highly sensitive to TGF-β immunosuppression [e.g.1,2]

PLN-101095 Approach

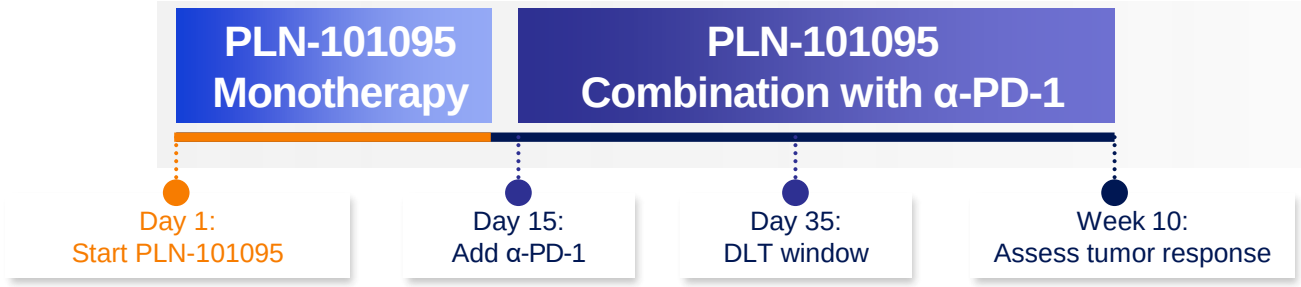
- Potently inhibit general immunosuppressive immune checkpoint to restore CD8 T cell IFNγ secretion
- Prevent both free and latent TGF-β signaling from major integrin sources found in solid tumors
- Dual mechanism significantly increases quantity of TILs and increases resistance to exhaustion

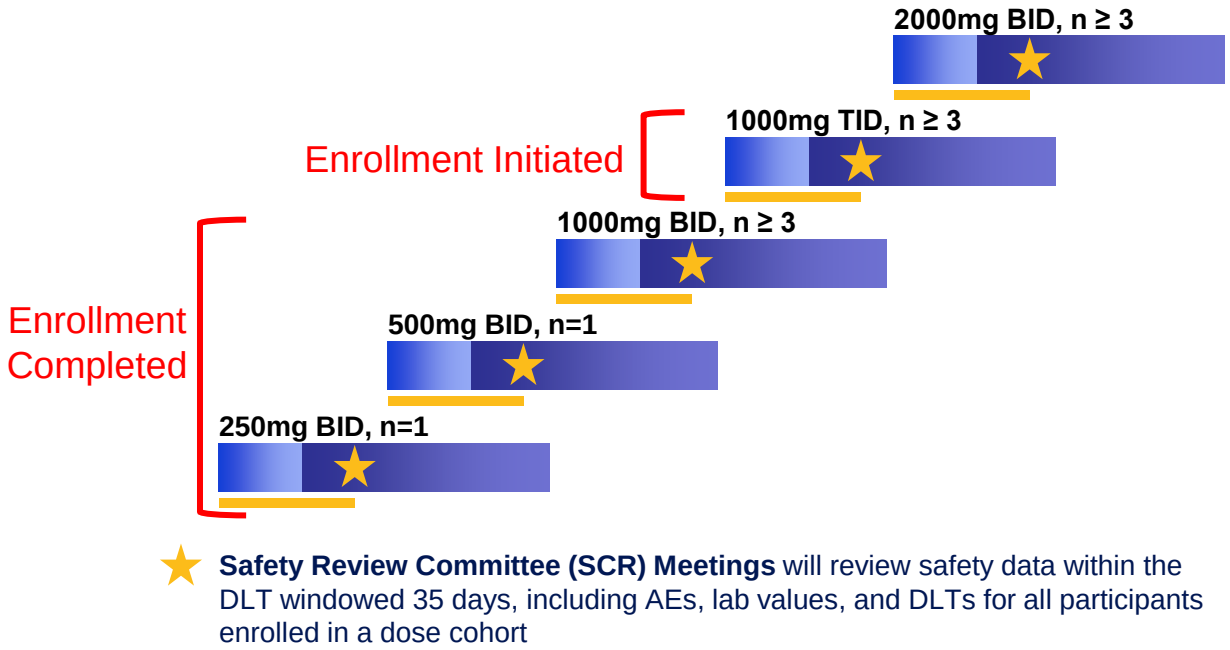
Dual inhibition of $\alpha_V\beta_8$ & PD-1 exploit unexpected synergistic pathways leading to enhanced tumor killing[6]

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

PLN-101095 – Ongoing Phase 1 Study in Patients Resistant to ICIs





★ **Safety Review Committee (SCR) Meetings** will review safety data within the DLT windowed 35 days, including AEs, lab values, and DLTs for all participants enrolled in a dose cohort

STUDY POPULATION

- Advanced or metastatic solid tumors for which pembrolizumab is indicated & have received at least 2 doses pembrolizumab
- Pembrolizumab relapsed or refractory

ENDPOINTS

- Primary: safety & tolerability
- Secondary: mono- and combination therapy PK
- Exploratory:
  - PK & PD
  - Antitumor activity: ORR, TTR, DOR, PFS & OS

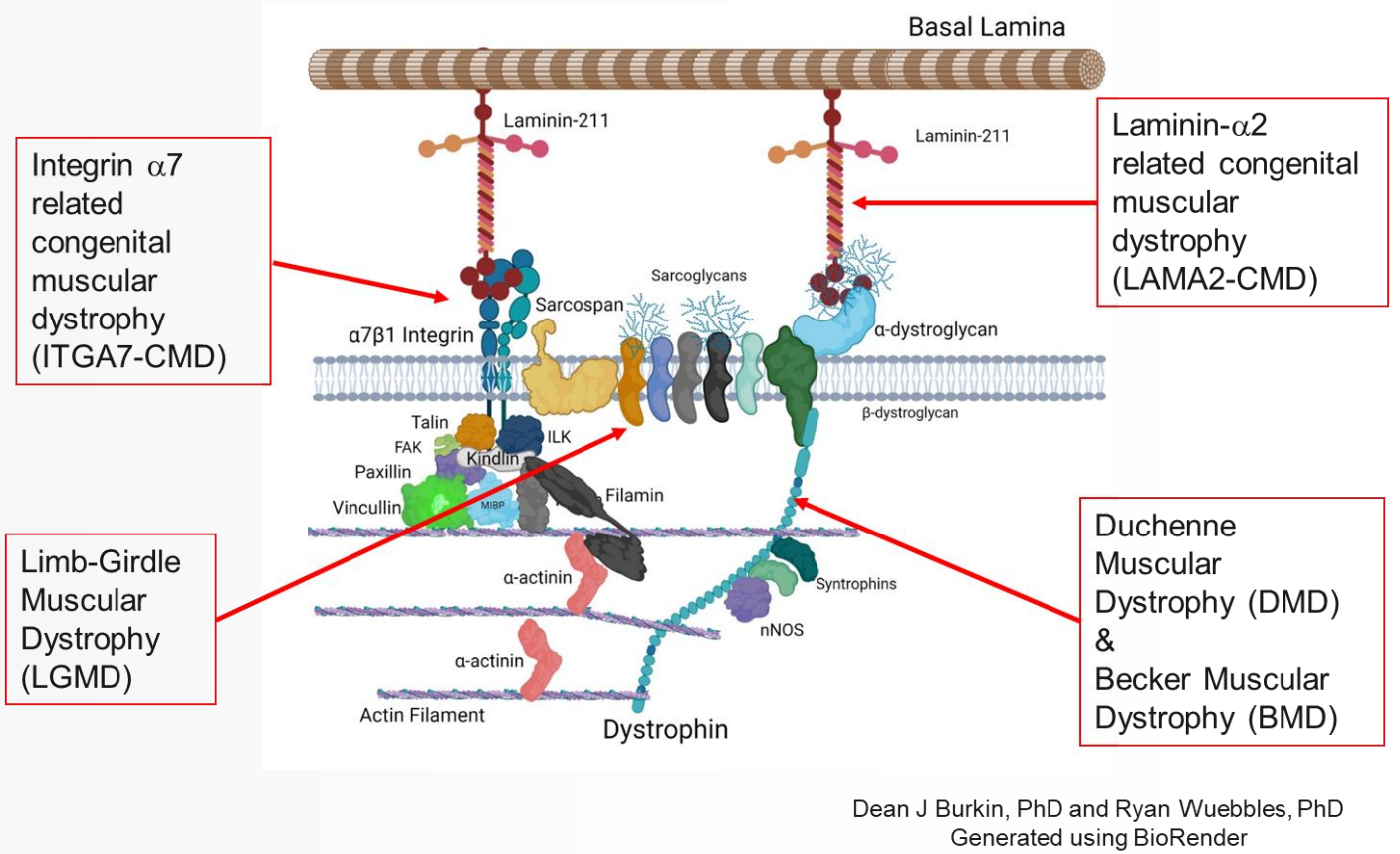
PLIANT

PLIANT

PLN-101325 – Selective Muscle Cell Integrin Agonist 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

PLN-101325 – Pliant's Muscular Dystrophy Program – Overview

Targeting $\alpha_7\beta_1$,an integrin receptor on the muscle cell surface

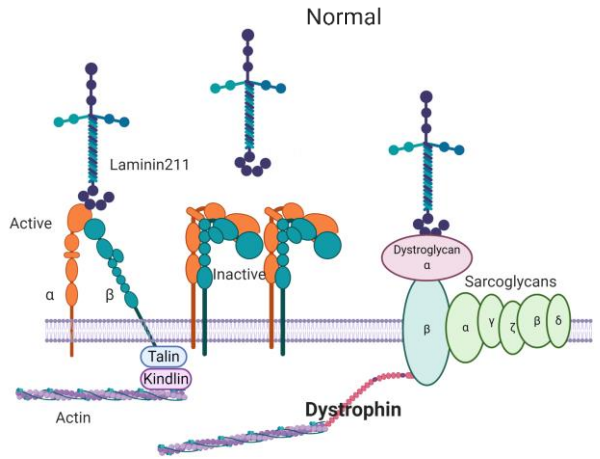
- α7β1 is upregulated as a **compensatory mechanism** in **different types of muscular dystrophy**
- Acts as a **substitute for dystrophin**, helping to stabilize the muscle membrane, decreasing muscle damage
- **Mutations in the target result in human congenital myopathy**

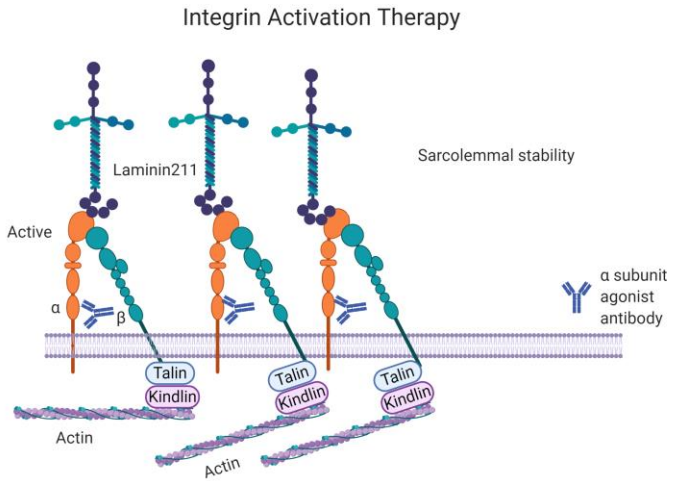
Allosteric agonistic monoclonal antibody

- 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,…)





PLN-101325 – Data from MDX Knockout Suggest High Potential in DMD

Improved Muscle Cell Membrane Integrity

- Reduced intracellular resting calcium
- Reduced hyperpolarization of muscle cell membrane

Increased Diaphragm Force

- Dose dependent increase in both diaphragm weight and force
- Highest dose of PLN-101325 approaches wild-type diaphragm force

Increased Body Weight

- Dose-dependent increase in body weight over 12 weeks of treatment
- 9% total increase in body weight at 12 weeks of treatment at high dose

Improved Response to Muscle Injury

- Dose-dependent improvement in contractile force over 12 weeks of treatment post-injury compared to placebo

PLIANT