PLIANT

Developing Novel Treatments for Fibrotic Diseases

NOVEMBER 2024

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Pliant – Breaking New Ground in Fibrosis

Industry-Leading Integrin/Fibrosis Platform

- **Four approved INDs** utilizing small-molecule integrin inhibitors
  - Most in the industry
- Proprietary library of **10,000+ integrin binding molecules**

Bexotegrast – Disease modifying Potential in IPF

- Bexotegrast showed **improvement in FVC** vs. placebo at all doses tested
  - Effect seen as **monotherapy and in combo** with SOC
- Reduction in total lung collagen seen post 12-week treatment: **potential reversal of fibrosis**
- Clinically meaningful **reduction in cough severity**

Blockbuster Opportunities in Areas of High Unmet Need

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

Funded Through Phase 2b Data

- $406.5 million of cash[1] as of September 30, 2024
- Operations are funded through 2026 **– Runway well past Phase 2b data**

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

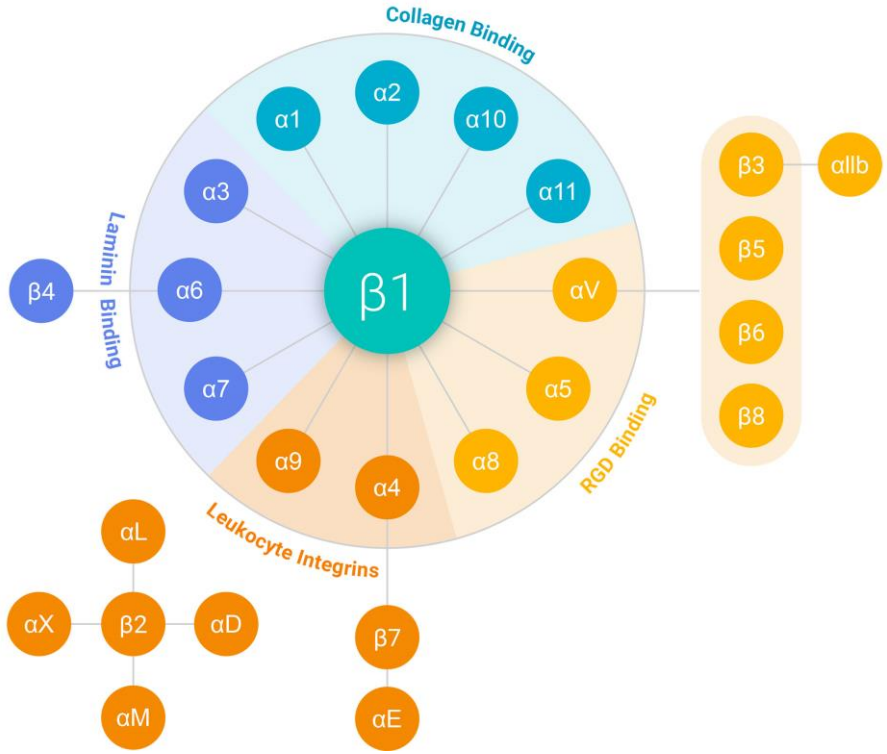
Pliant Development Pipeline

Program	Indication	Preclinical	Clinical			Anticipated Milestone	Global Rights
			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 1Q 2025; data mid-2026	PLIANT
	Primary Sclerosing Cholangitis					24-Week 320 mg data presented	PLIANT
PLN-101095 Inhibitor of $\alpha_v\beta_8$ /$\alpha_v\beta_1$	Solid Tumors					Initial data early 2025	PLIANT
PLN-101325 Anti-integrin mAb of $\alpha_7\beta_1$	DMD Other Muscular Dystrophies					Phase 1 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 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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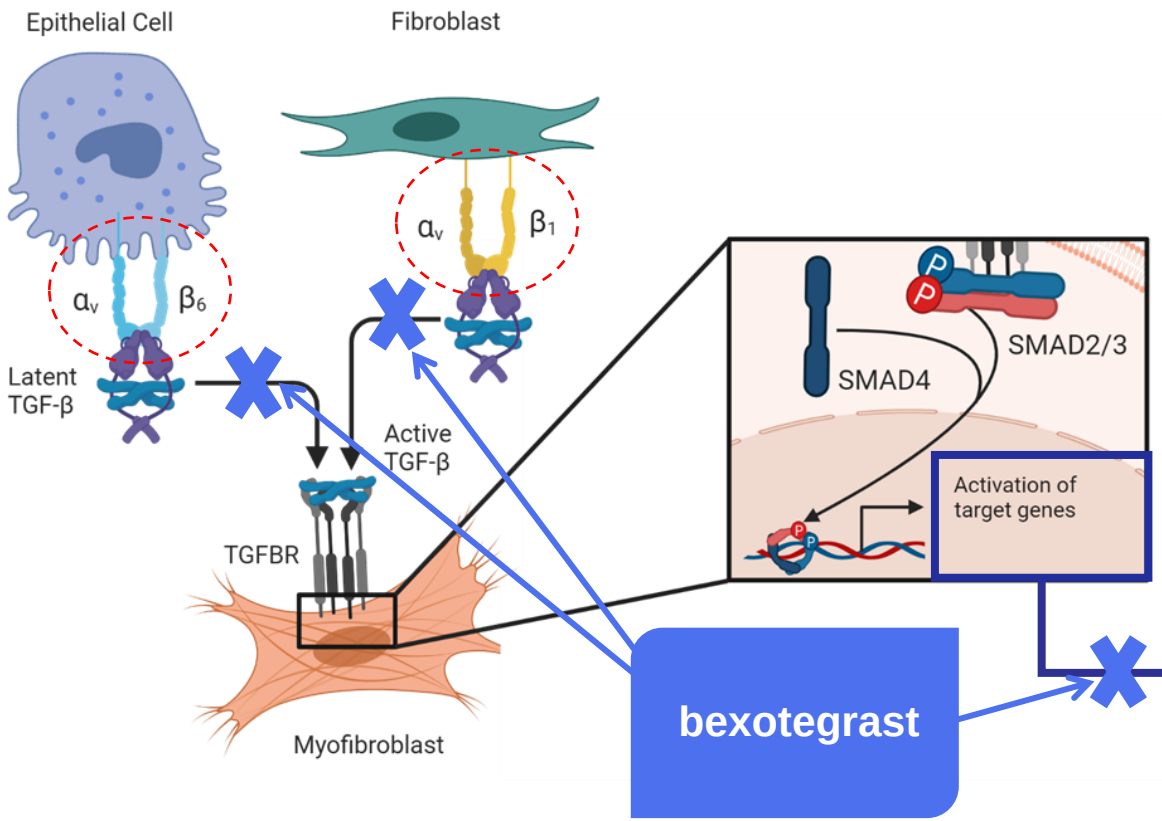
Bexotegrast Reduces TGF-β Signaling and Downstream Profibrotic Pathways Through Inhibition of Integrins $\alpha_v\beta_6$ / $\alpha_v\beta_1$

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

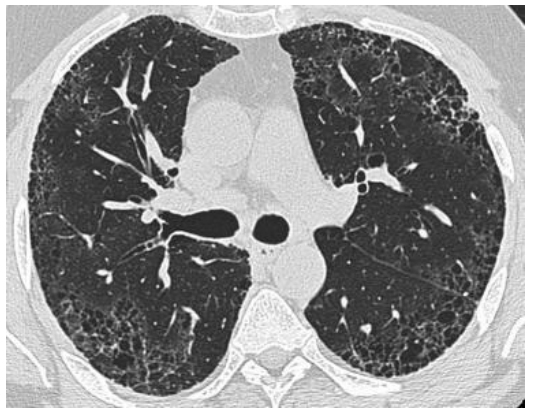


- TGF-β is a central mediator of fibrosis
- $\alpha_v\beta_6$ /$\alpha_v\beta_1$ Integrins activate latent TGF-β in fibrotic tissue
- Systemic TGF-β blockade carries toxicity risks

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		
	Preclinical	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

- Ofev 2023 revenues of **$3.9 billion**
- **Increasing IPF incidence** 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

- **Patients felt better** - Clinically meaningful **reduction in cough severity** seen in Phase 2a
- **Reduction in total lung collagen** seen in Phase 2 suggests reversal of fibrosis – **potential disease modifying therapy**

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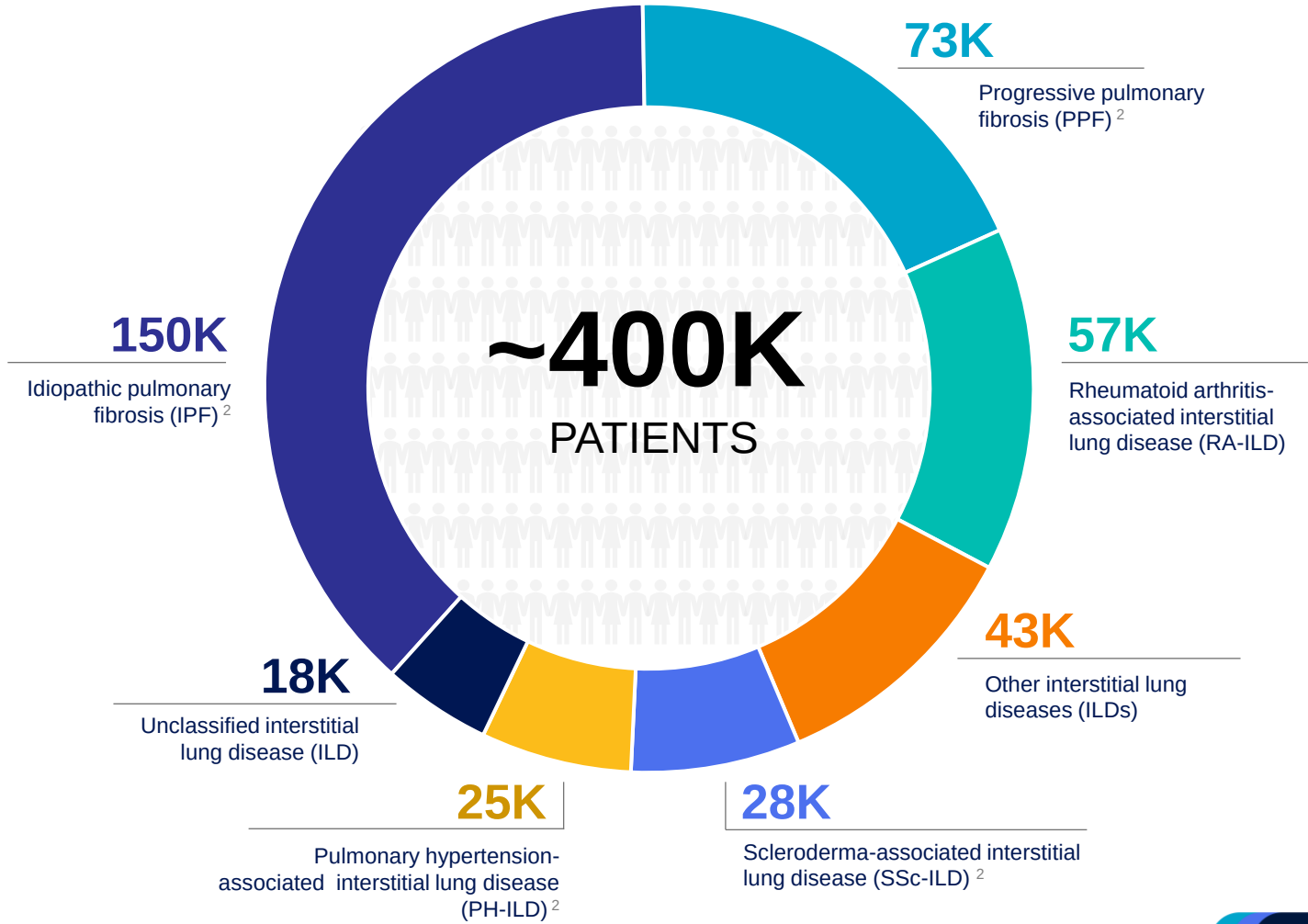
Bexotegrast Has Significant Respiratory Market Potential

- 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

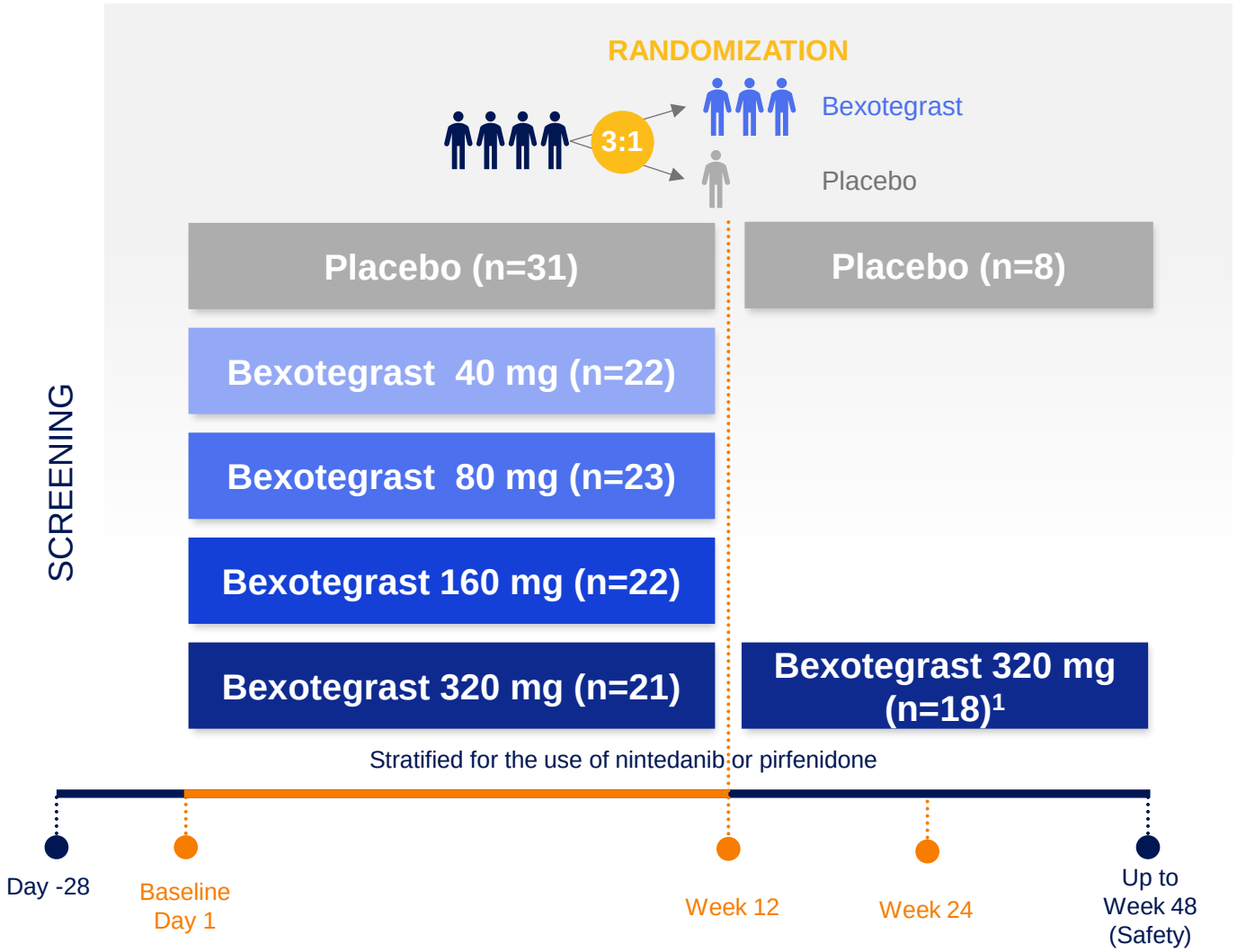
US PREVALENCE OF FIBROSING ILD INDICATIONS[1]



[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

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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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

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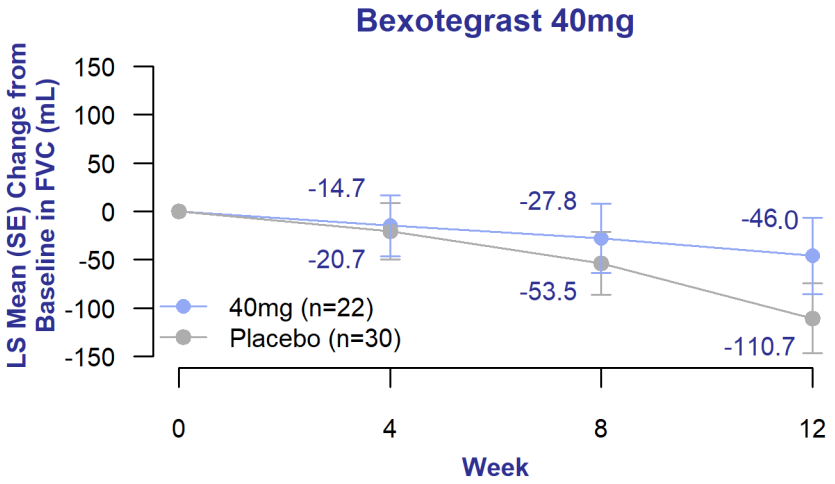
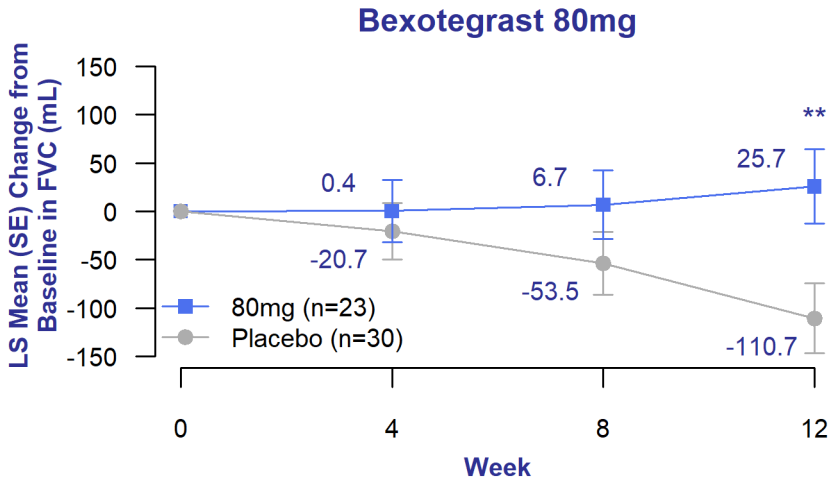
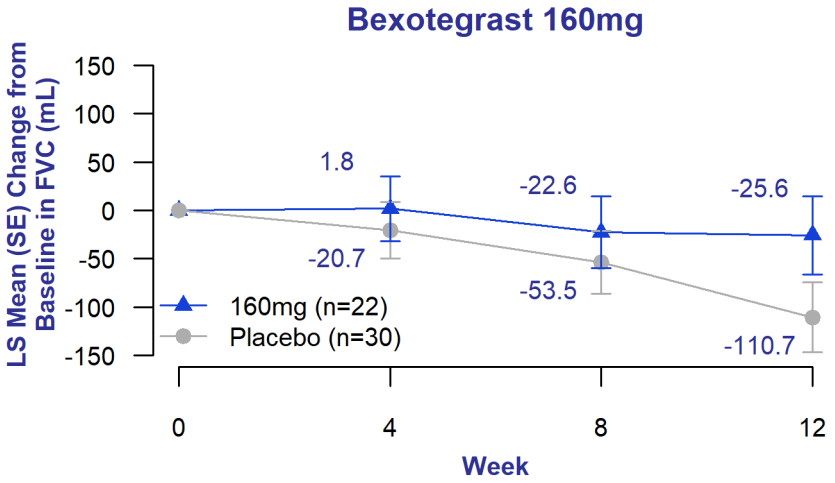
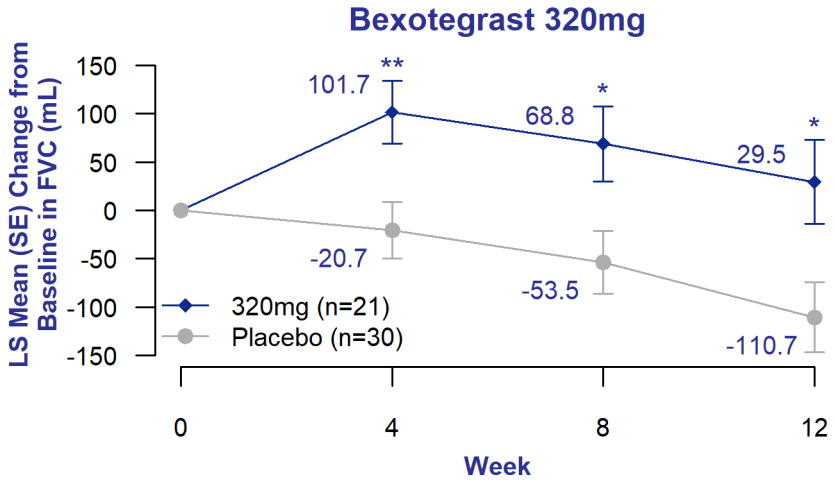
FVC Change from Baseline over 12 Weeks
mITT Population









* 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.

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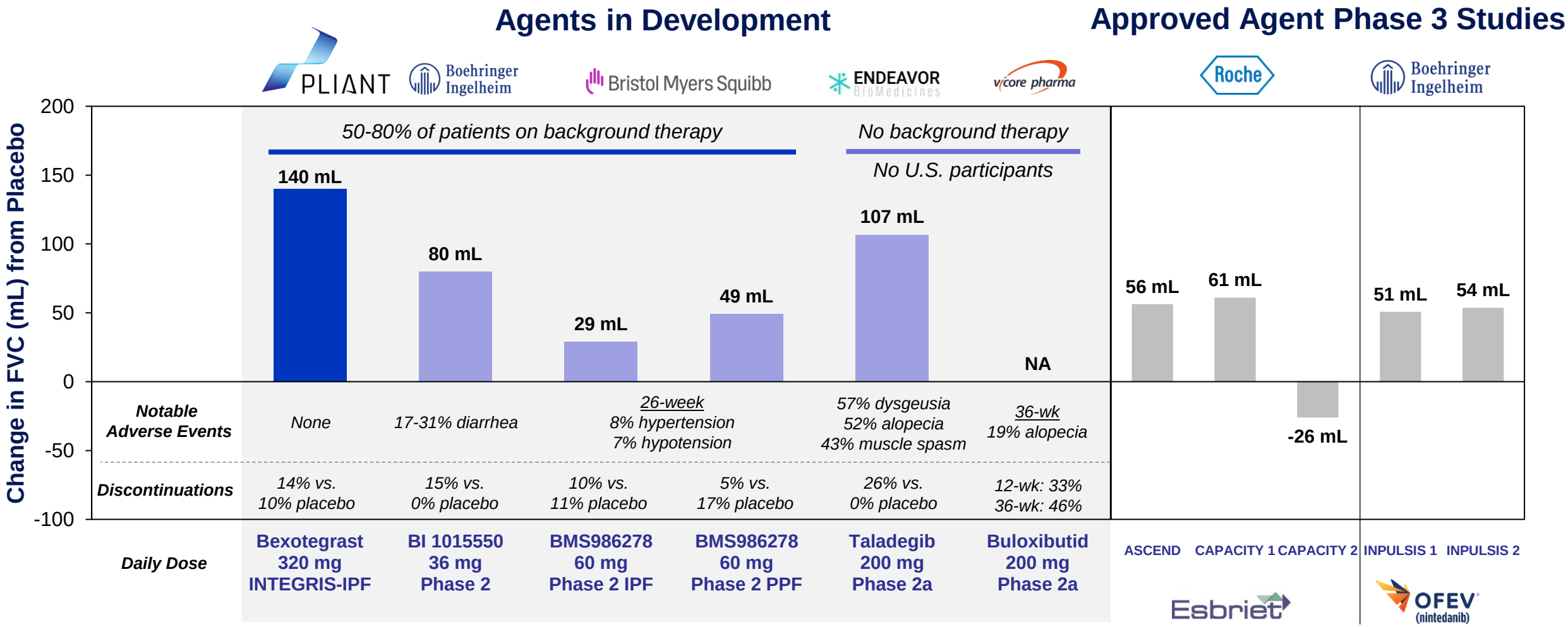
Comparison of Approved & Select Investigational Agents in IPF / PPF

Bexotegrast Shows Superior Effect on FVC with no Notable AEs



Bexotegrast, BI-1015550, BMS-986278, ENV-101 and C21 from Phase 2 trials. Graphic is not meant to represent a head-to-head study. Comparing the results from different trials may be unreliable 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

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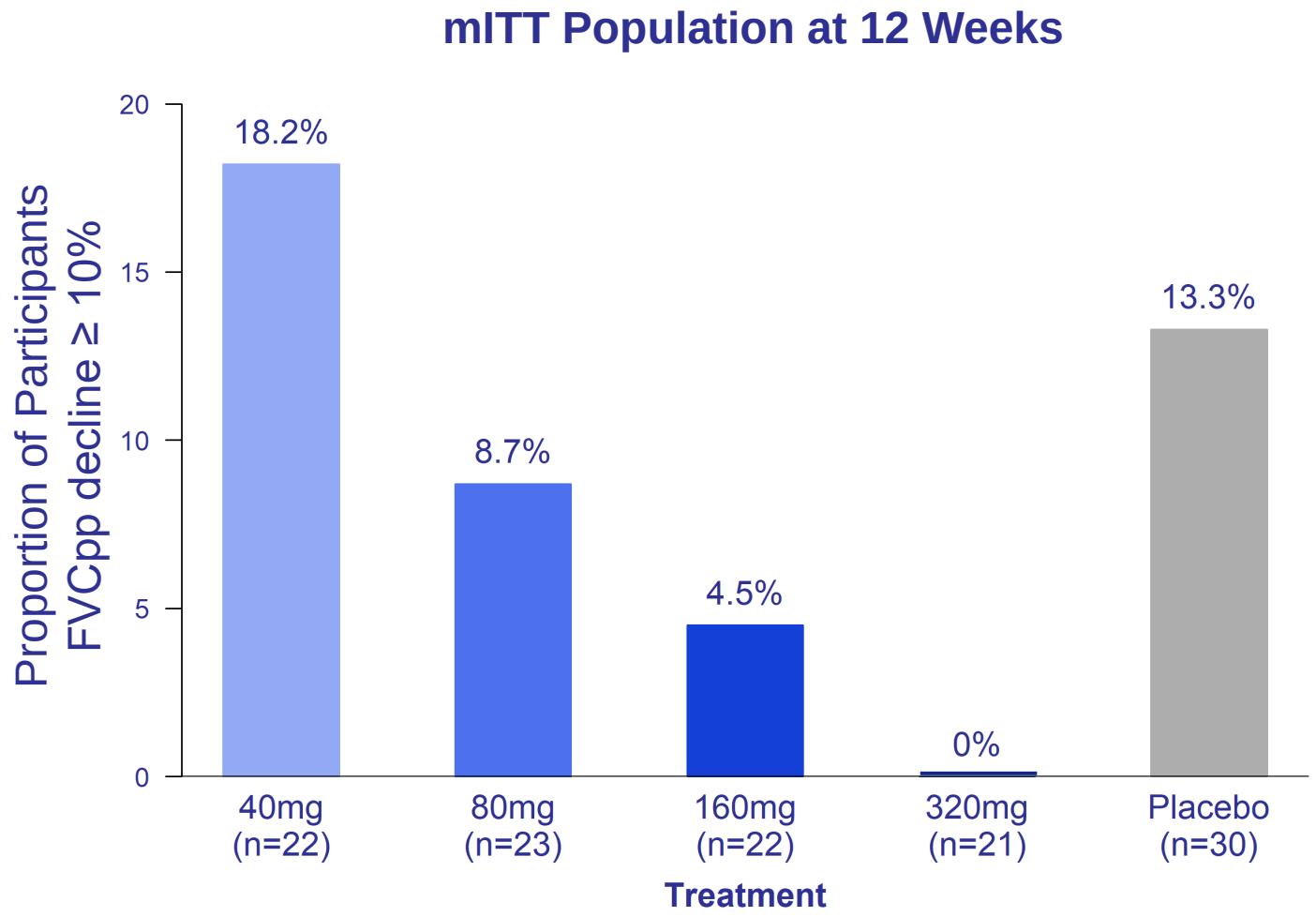
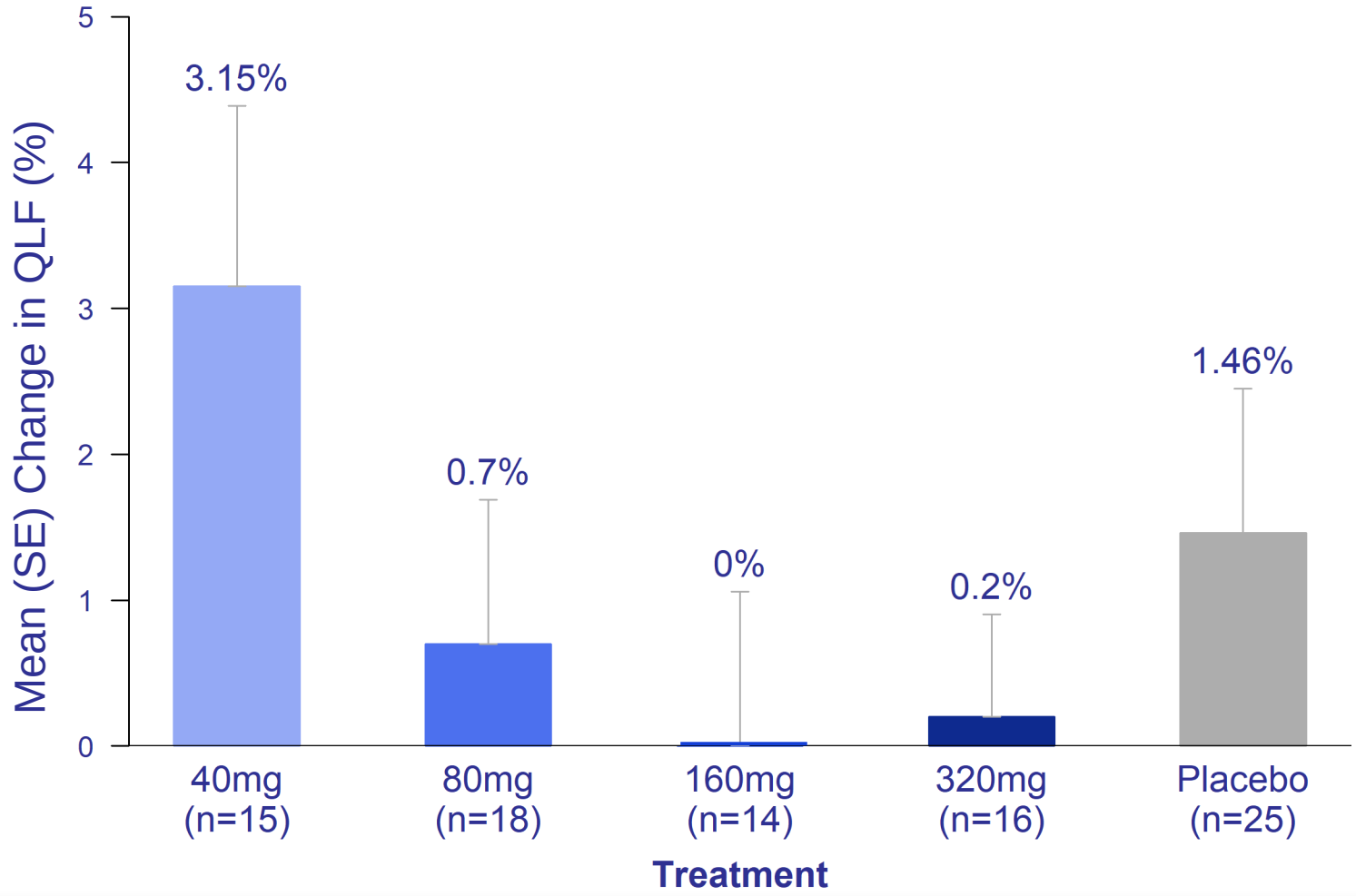
Proportion of Participants with Relative FVCpp Decline ≥ 10%
mITT Population



FVCpp = Forced vital capacity, percent predicted.

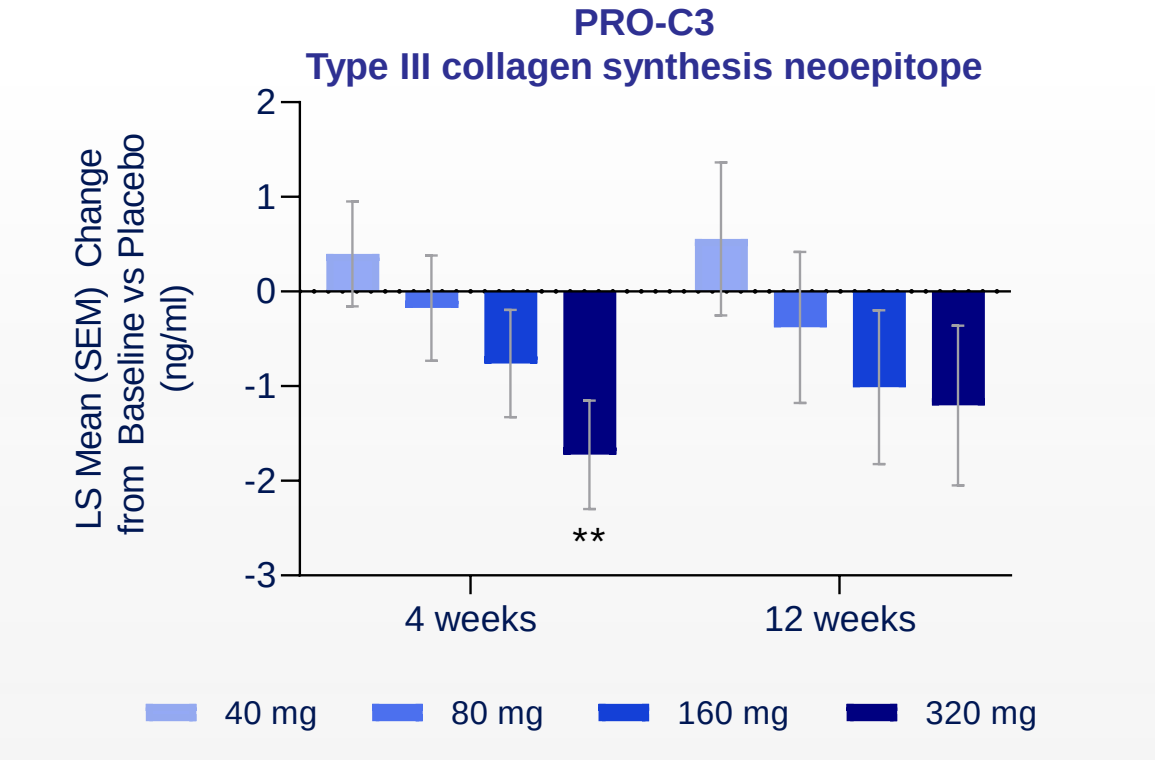
1- Ann Am Thorac Soc. 2017 Sep;14(9):1395-1402; 2- Am J Respir Crit Care Med. 2022 Apr 15;205(8):936-948.

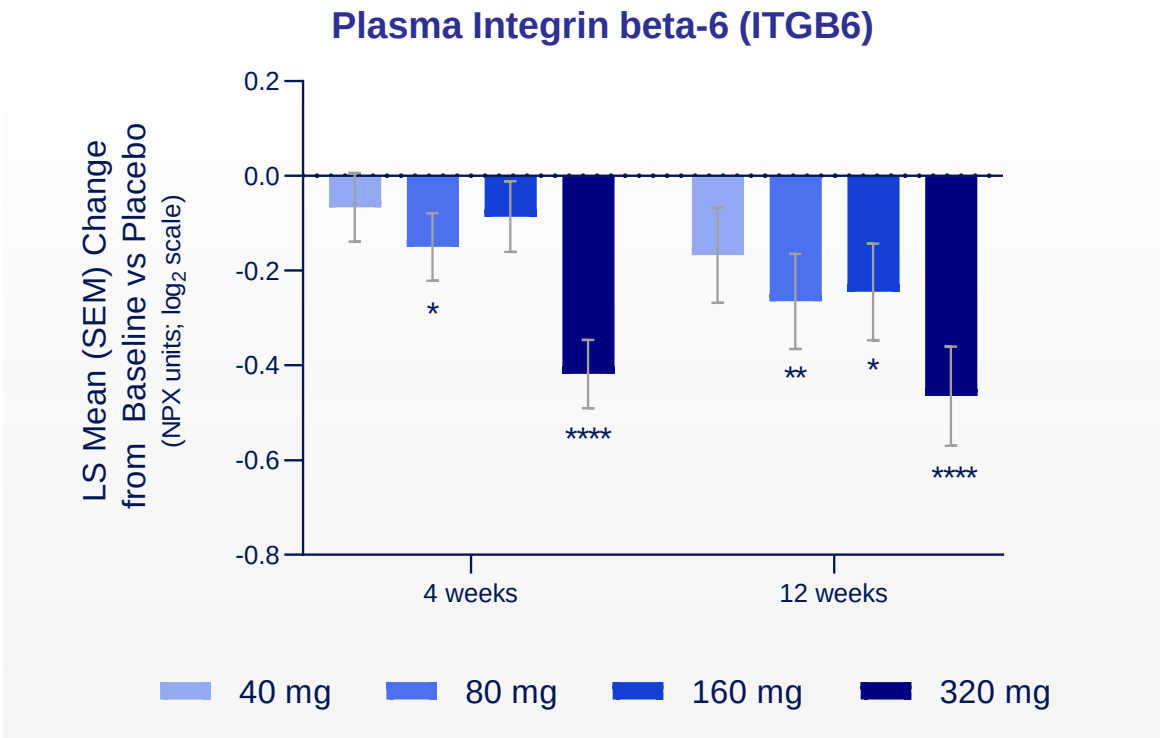
QLF Mean Percent Change from Baseline at Week 12
Per CT protocol population



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

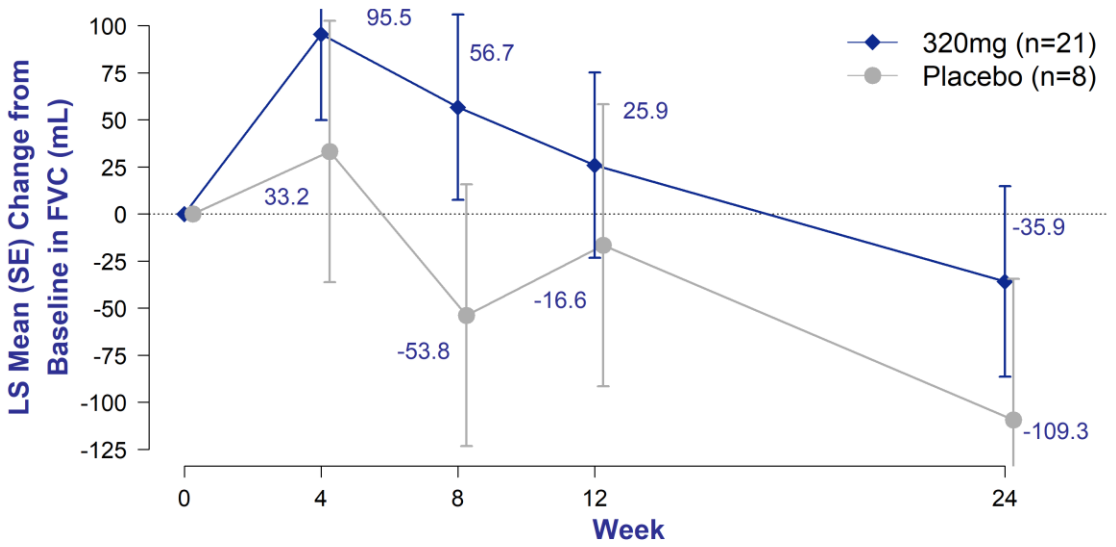
PRO-C3, a serum biomarker of type III collagen synthesis, was previously shown to be elevated in patients with IPF and associated with progressive disease[1]

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.

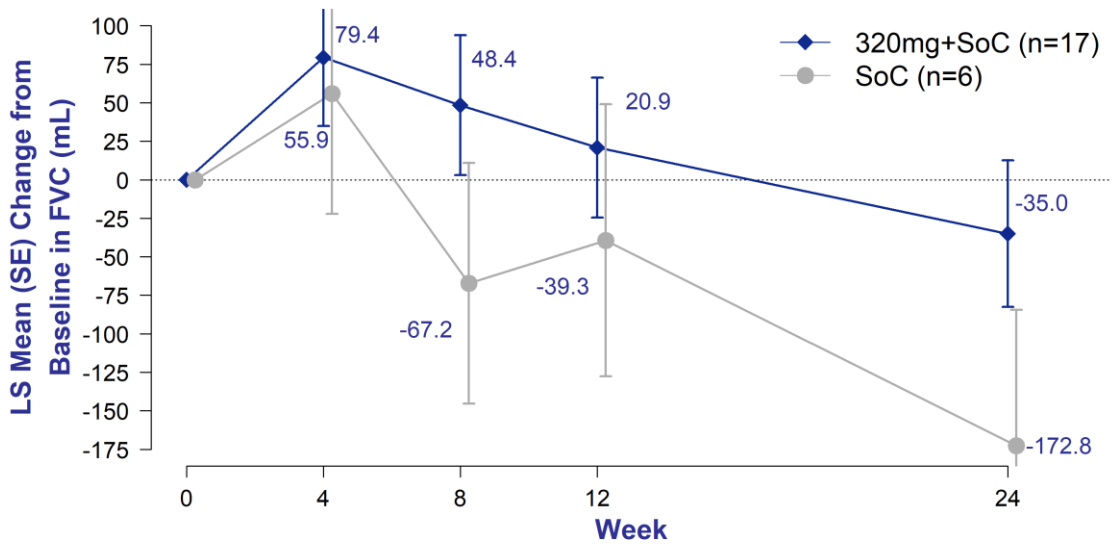
FVC Change from Baseline over 24 Weeks
ITT Population vs. SoC Sub-Group

ITT Population



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

Standard-of-Care Sub-Group



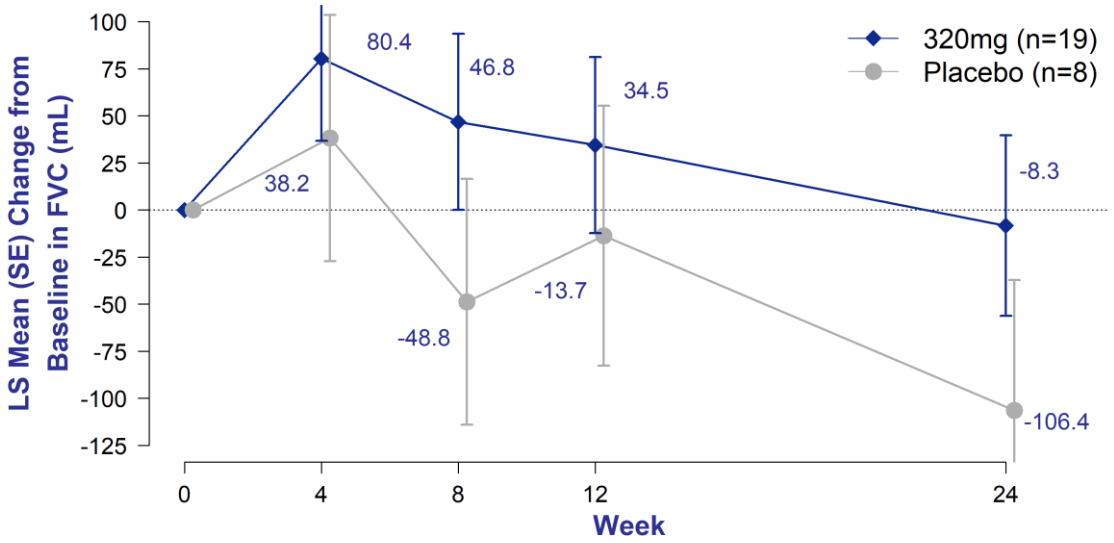
Bexotegrast + SOC reduced FVC decline by 80% relative to SOC alone at Week 24

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)

FVC Change from Baseline over 24 Weeks – Sensitivity Analysis

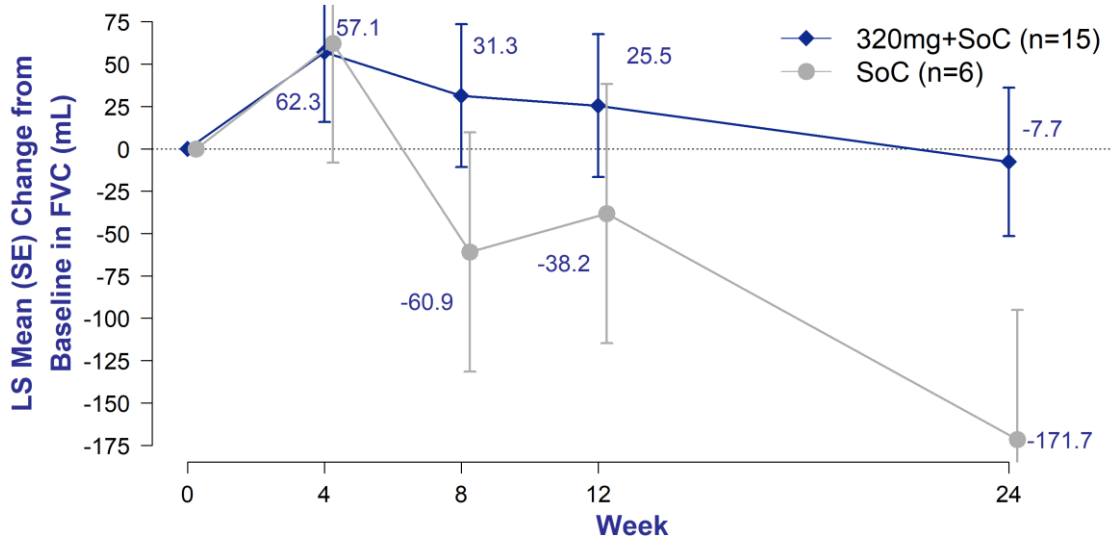
Trimmed Mean Sensitivity Analysis[1]

ITT Population



Bexotegrast reduced FVC decline by 92% relative to placebo at Week 24

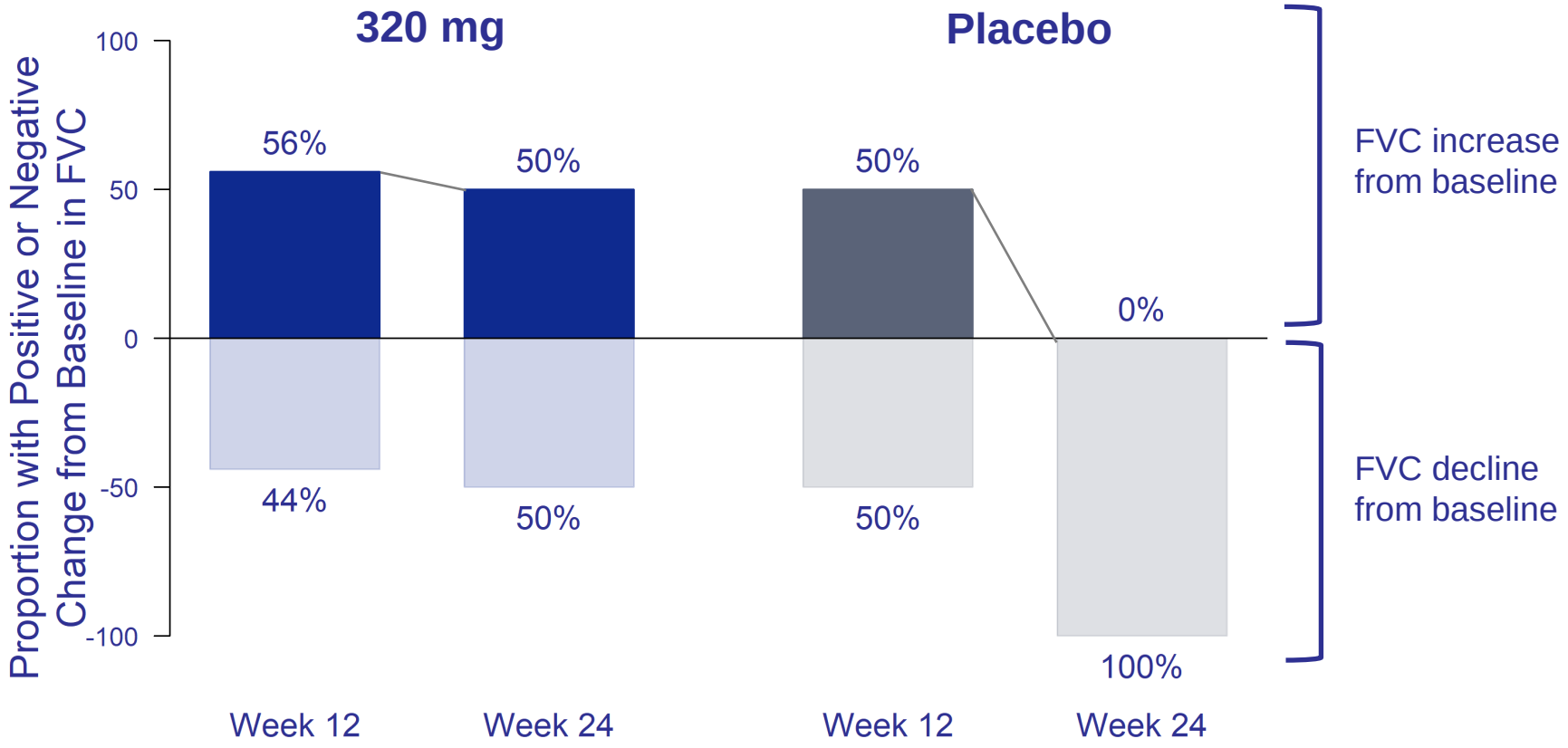
Standard-of-Care Sub-Group



Bexotegrast + SOC reduced FVC decline by 96% relative to SOC alone at Week 24

1 – Trimmed Mean Sensitivity Analysis excludes the two bexotegrast-treated participants with the highest and lowest FVC values 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)

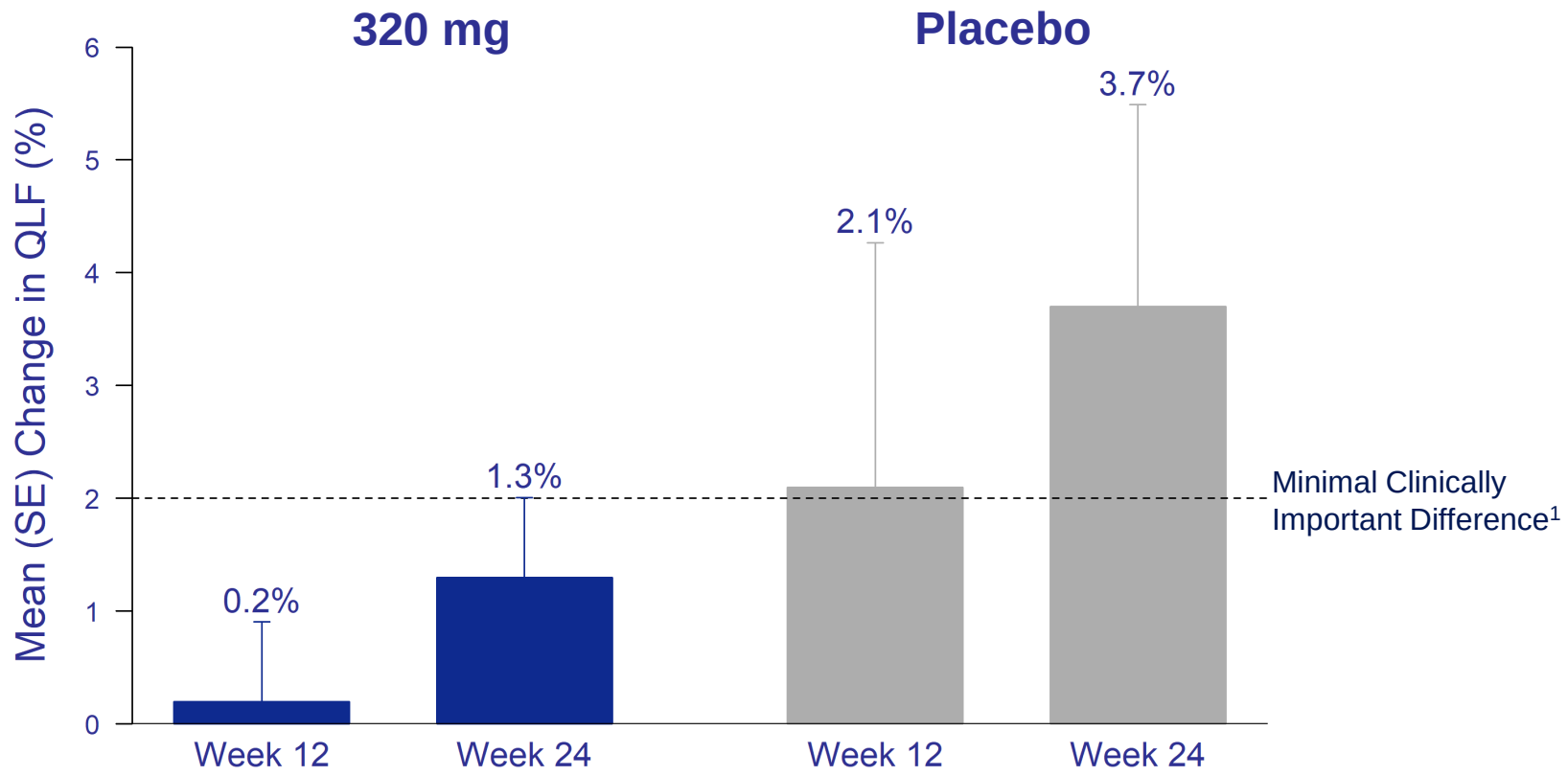
Bexotegrast Demonstrated Durable Increase in FVC at Week 24
ITT Population



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

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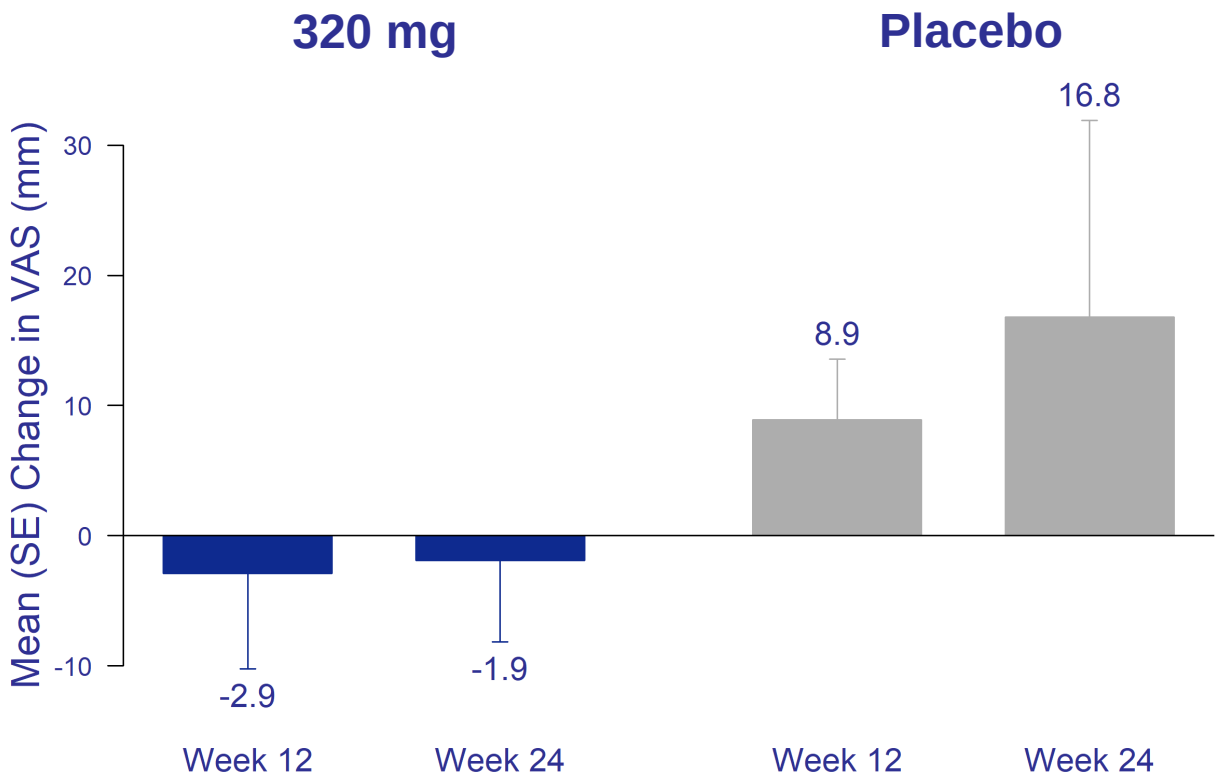
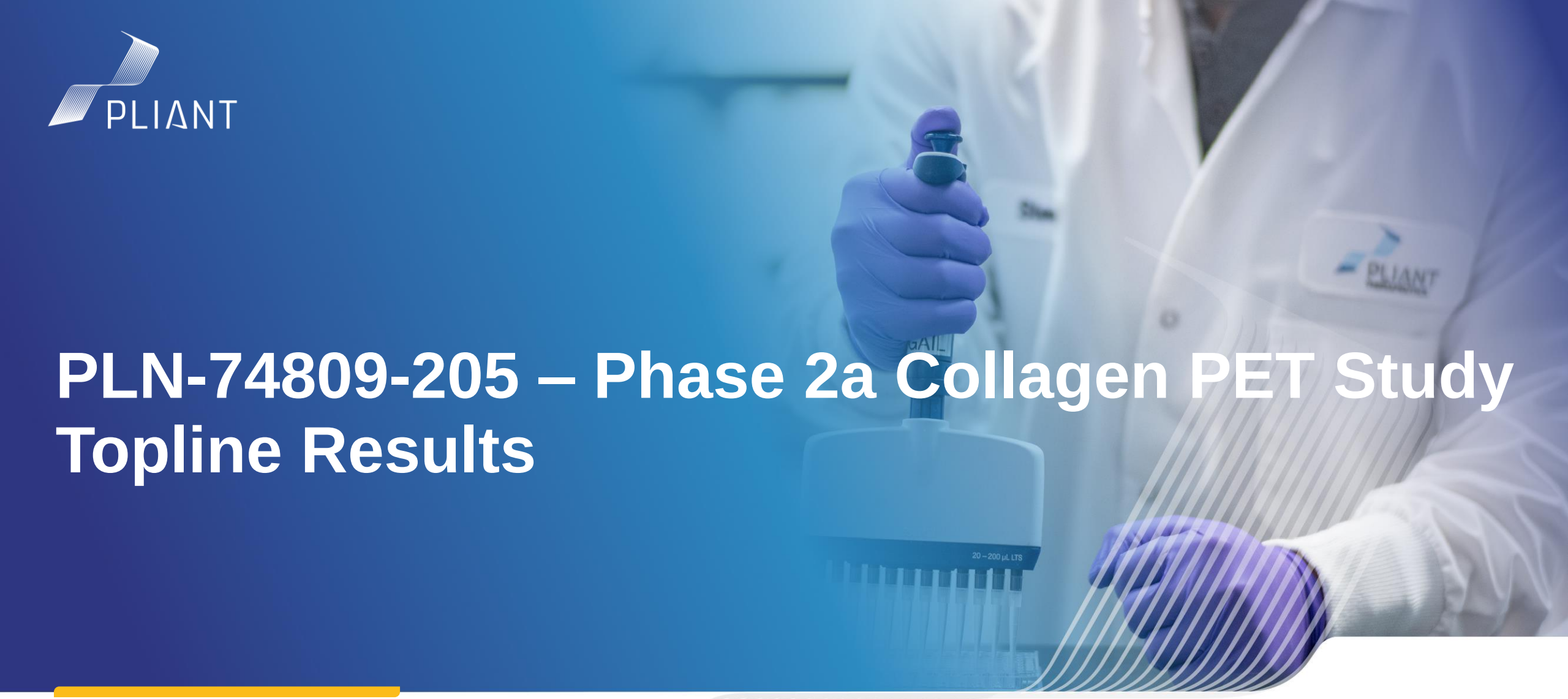
Cough Severity Visual Analog Scale (VAS) Change from Baseline
ITT Population



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

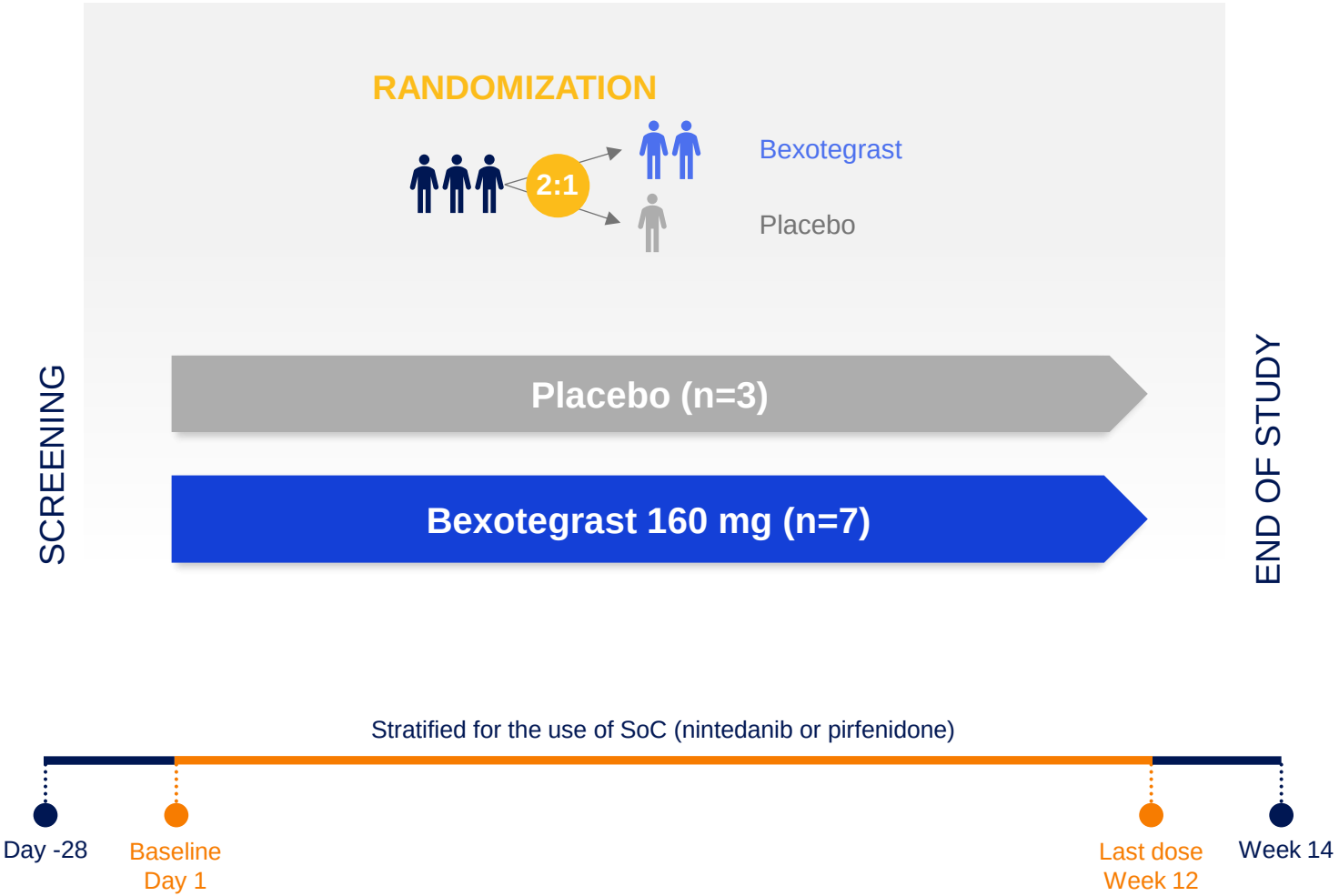
1 - *Respirology* 2011; 16: 969–975.
Cough VAS measures patient reported cough severity over last 2 weeks on scale of 0-100 mm



PLN-74809-205 – Phase 2a Collagen PET Study Topline Results

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

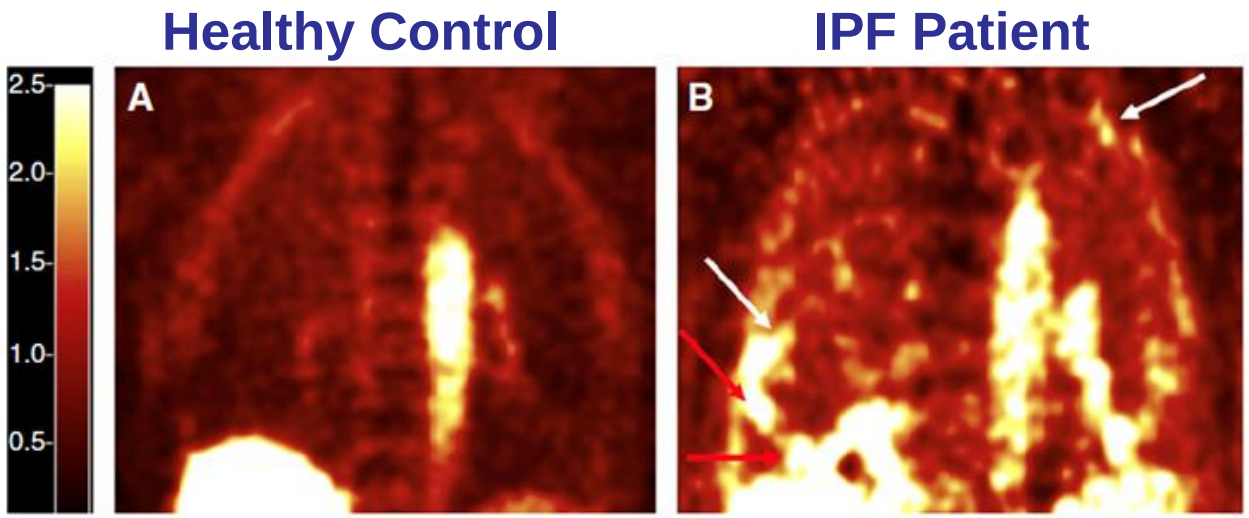
- Diagnosis of IPF (within 8 years)
- FVC percent predicted ≥ 45%
- DLCO ≥ 30%
- Estimated glomerular filtration rate ≥ 50mL/min

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

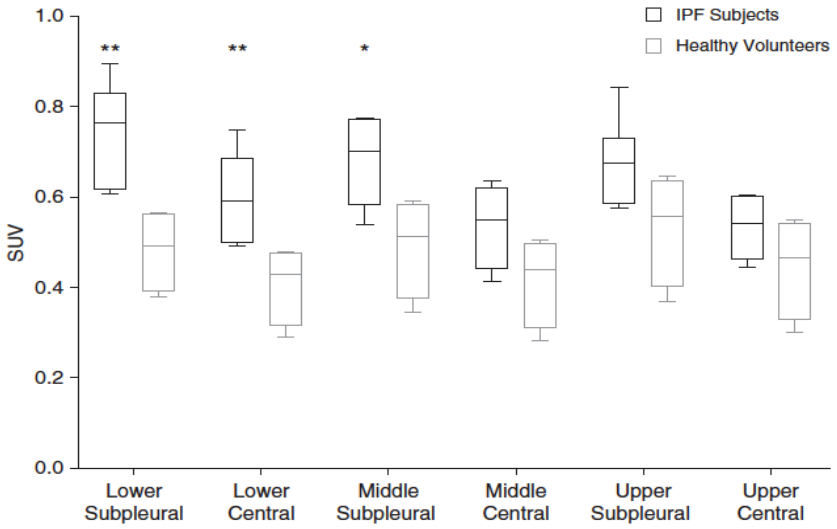
PLIANT

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

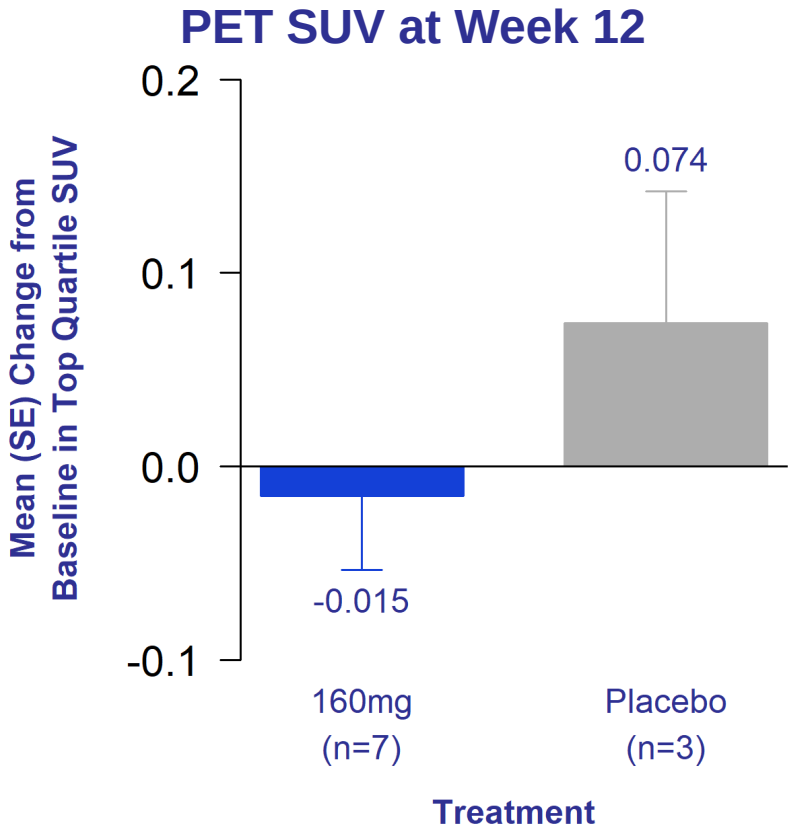
Biomarker results further support bexotegrast's antifibrotic mechanism

- 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

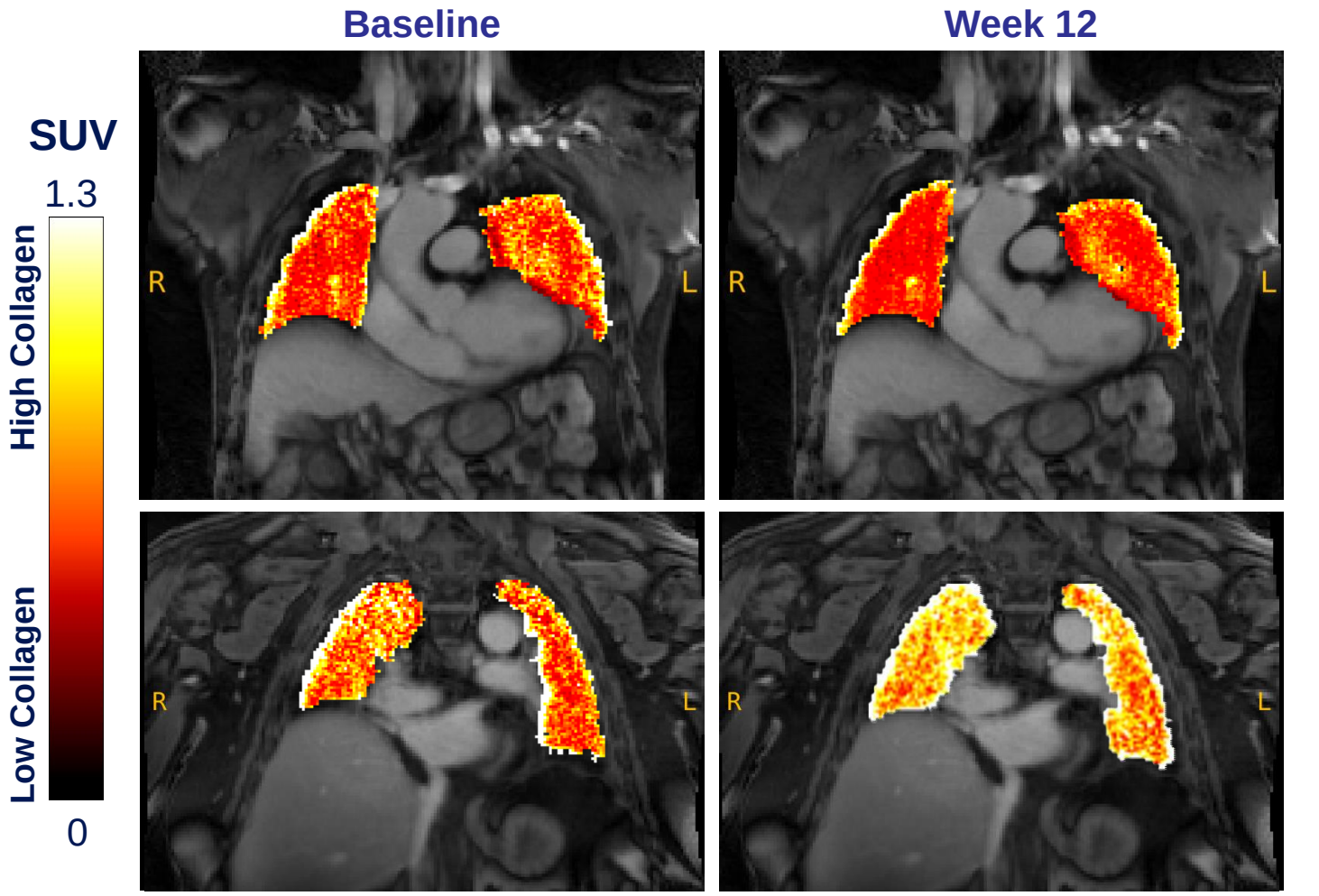
Reduced post-treatment total lung collagen suggests potential reversal of fibrosis

[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

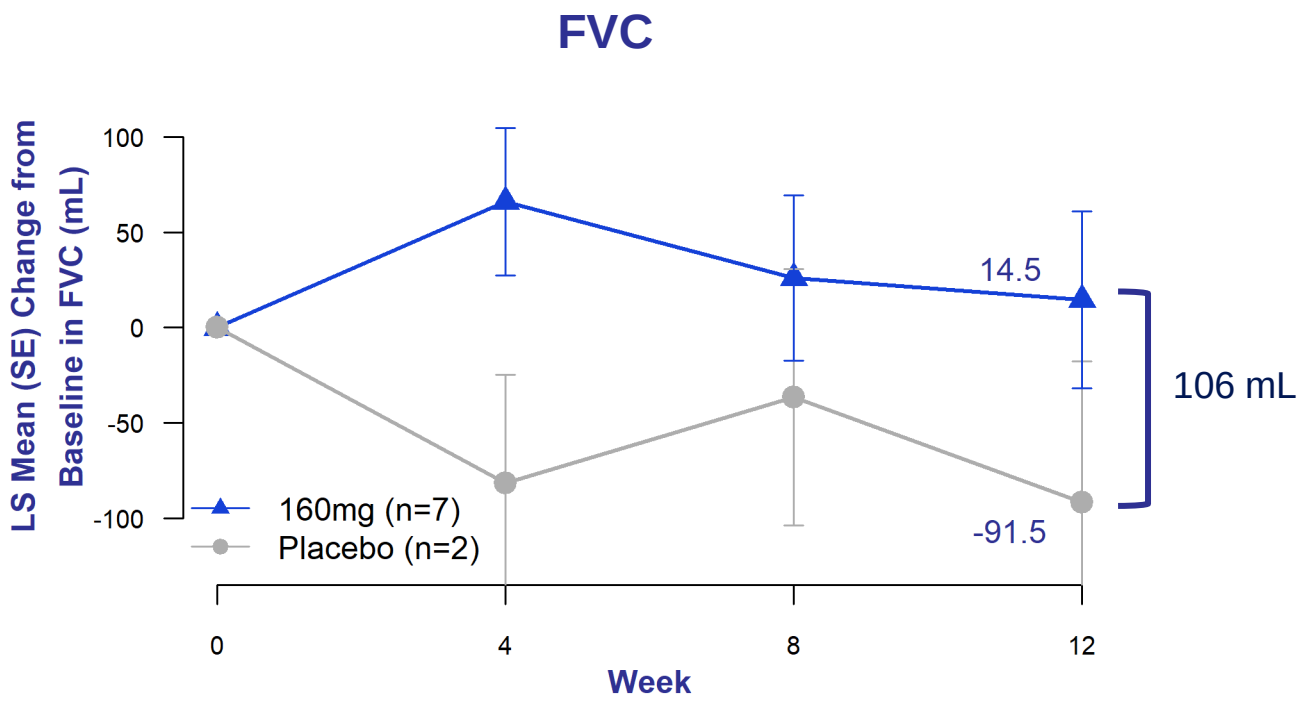
Participant B

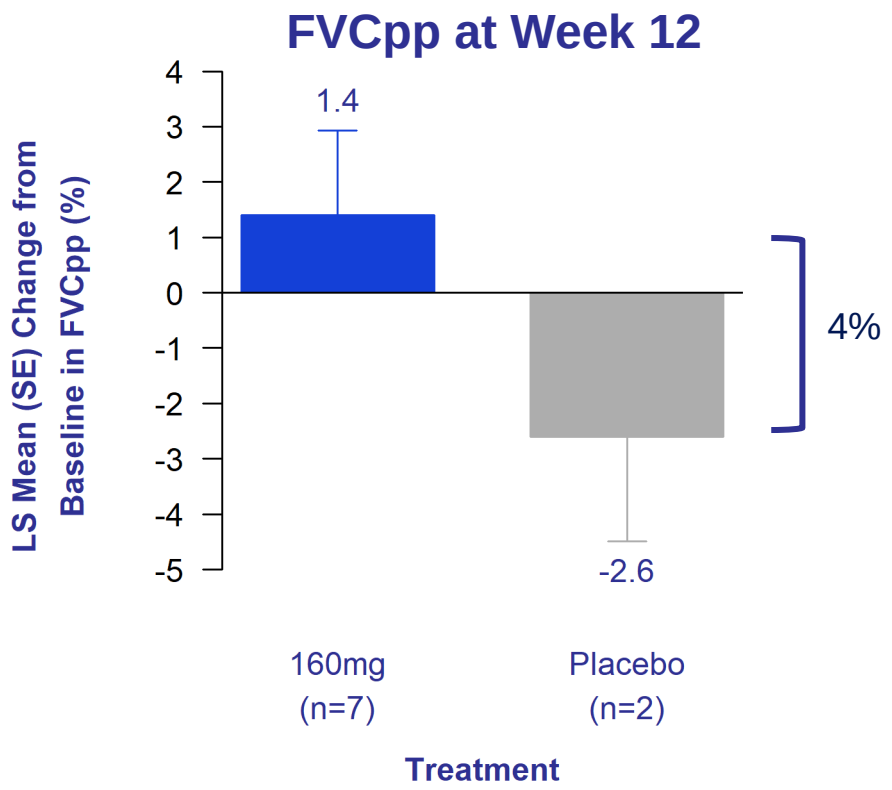
- Placebo for 12 weeks
- Increase in SUV_{Q4}, 0.21 (18.4%)
- Decline in FVC, -180 mL

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





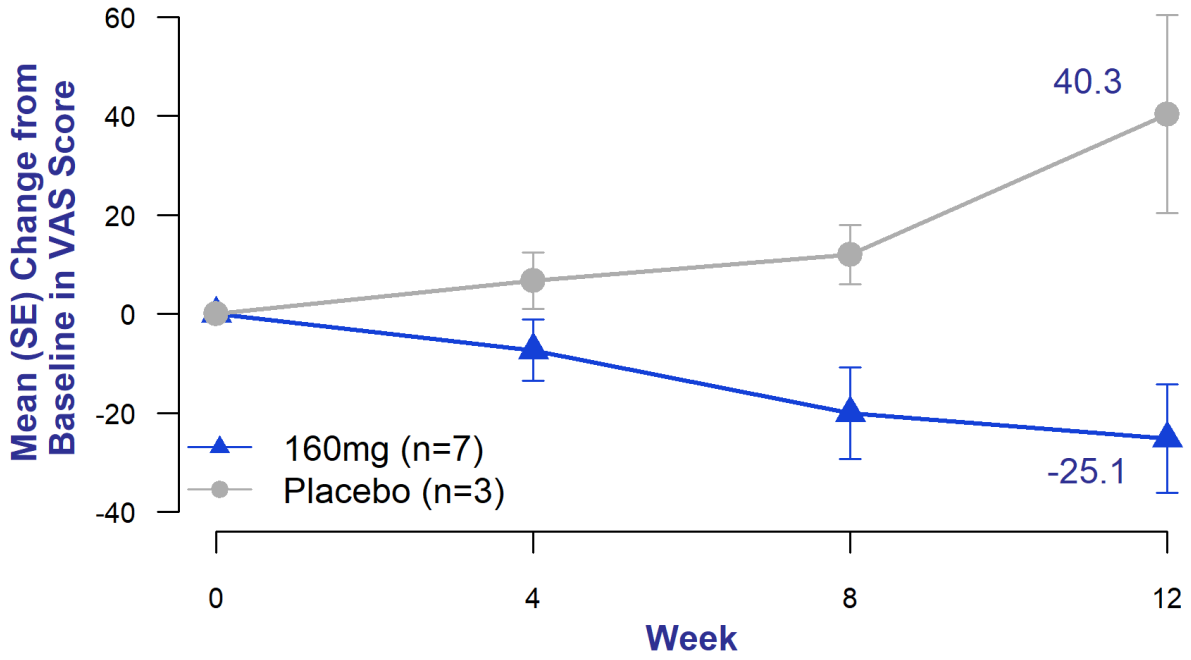
Bexotegrast cohort maintained a clear separation from placebo at all time points

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

Bexotegrast Showed Decreased Cough Severity Compared to Placebo

ITT Population

Cough Severity Over 12 Weeks of Treatment

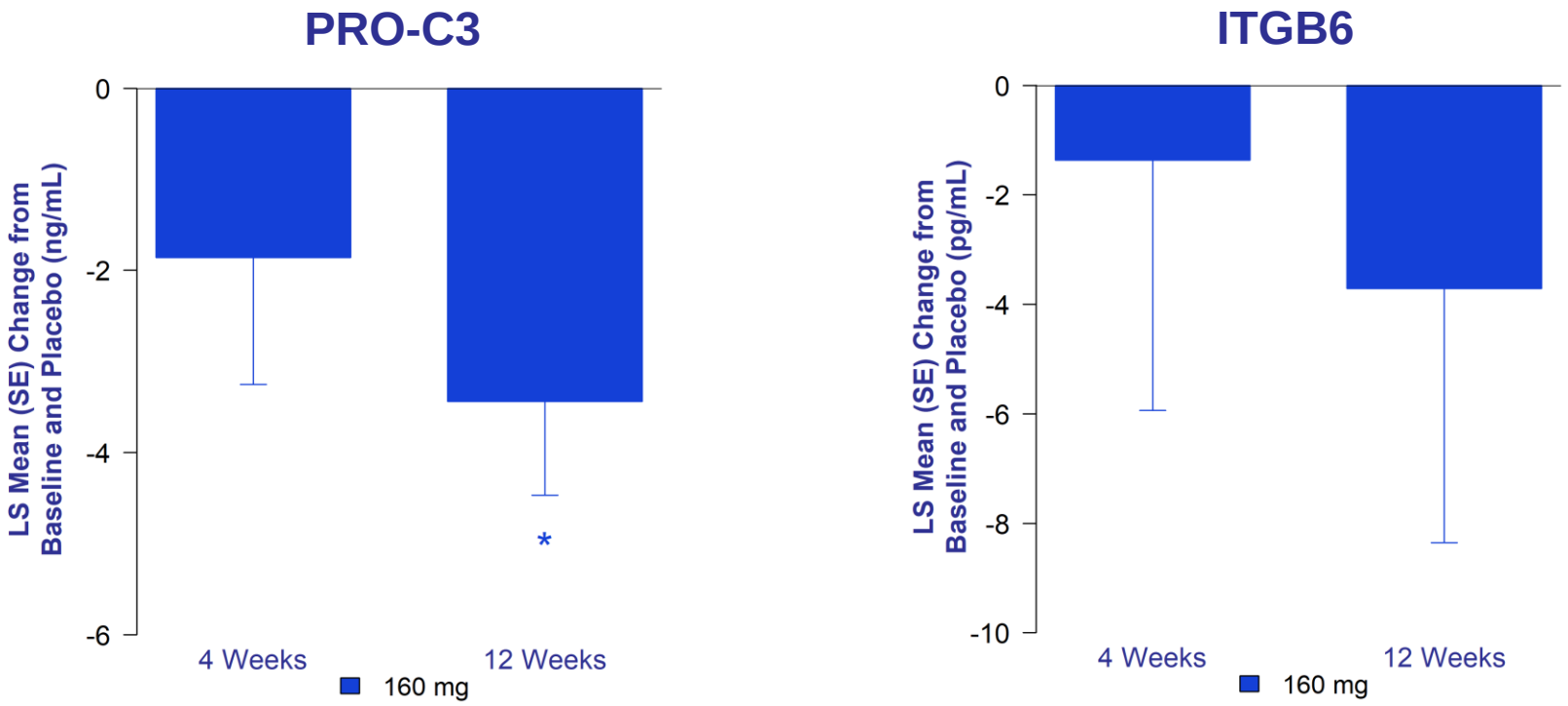


Bexotegrast cohort experienced decreased cough severity across all timepoints compared to increased severity on placebo

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]

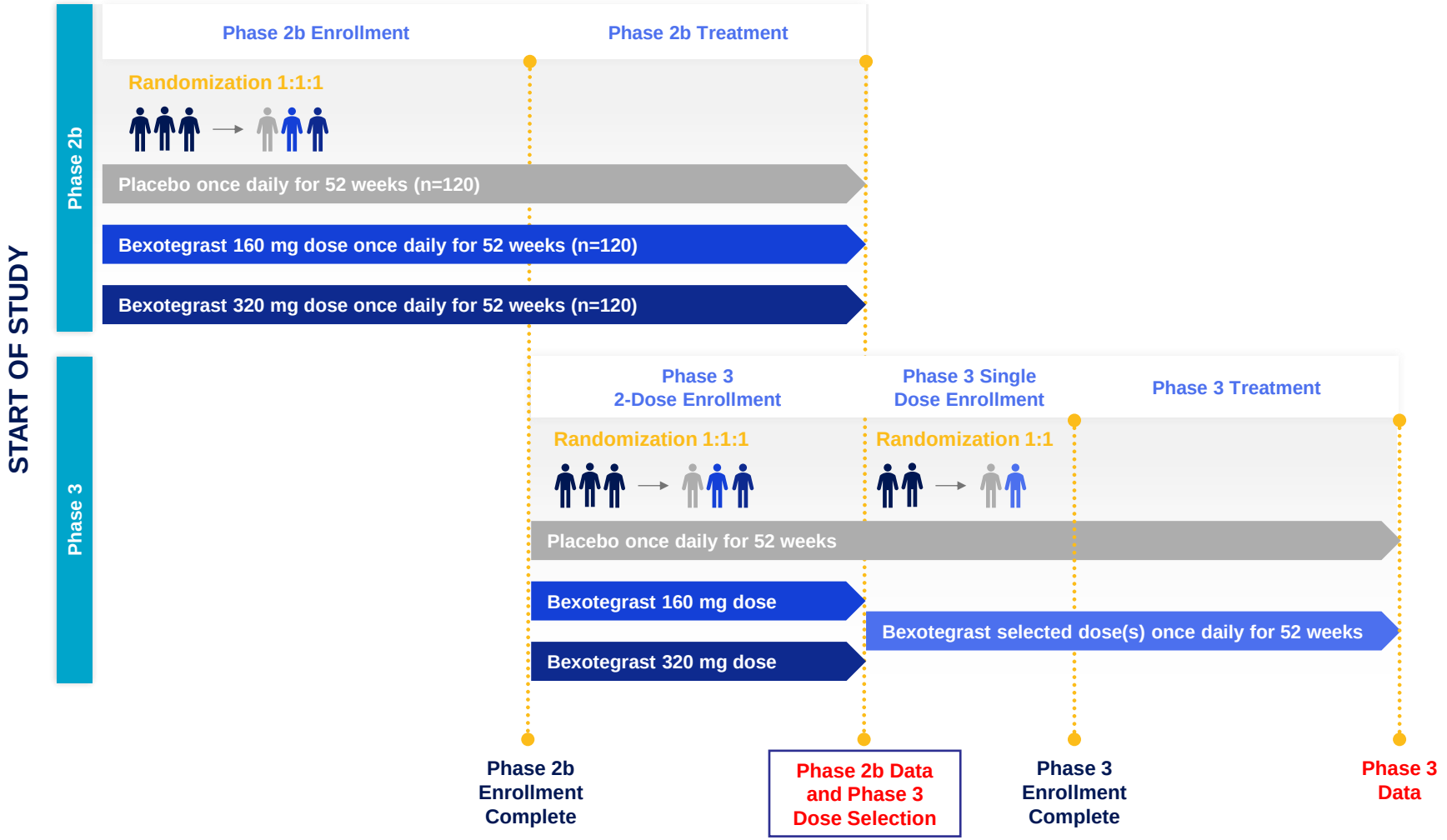
[3]Respir Res. 2019 Jul 12;20(1):148. doi: 10.1186/s12931-019-1118-7; [4]Lancet Respir Med. 2022 Jun;10(6):593-602. doi: 10.1016/S2213-2600(21)00503-8. Epub 2022 Jan 18

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

PLIANT

BEACON-IPF – Seamless Adaptive Phase 2b/3 Trial of Bexotegrast in IPF

BEACON-IPF Phase 2b/3 Study Design – Currently Enrolling



BEACON-IPF

KEY PRIMARY ENDPOINT

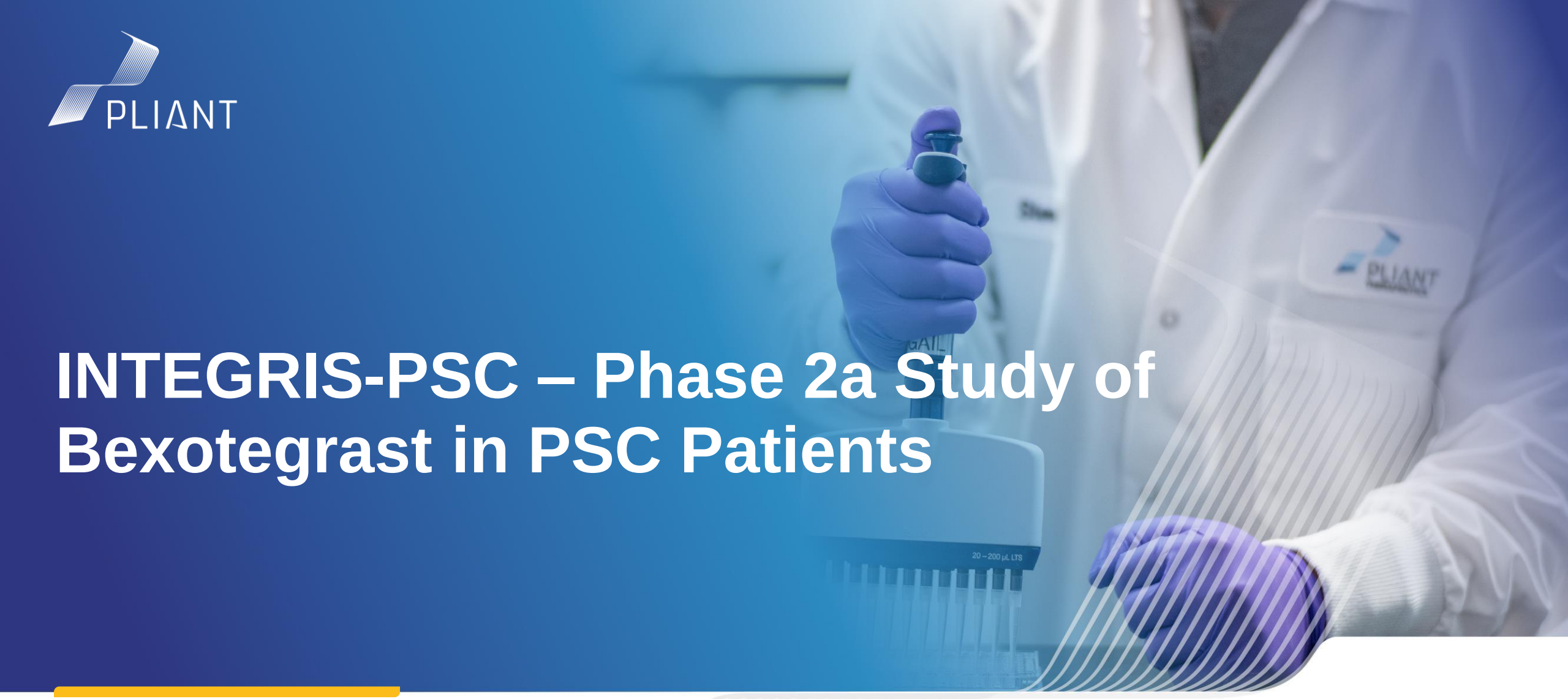
- Change from baseline in absolute FVC (mL) at Week 52

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

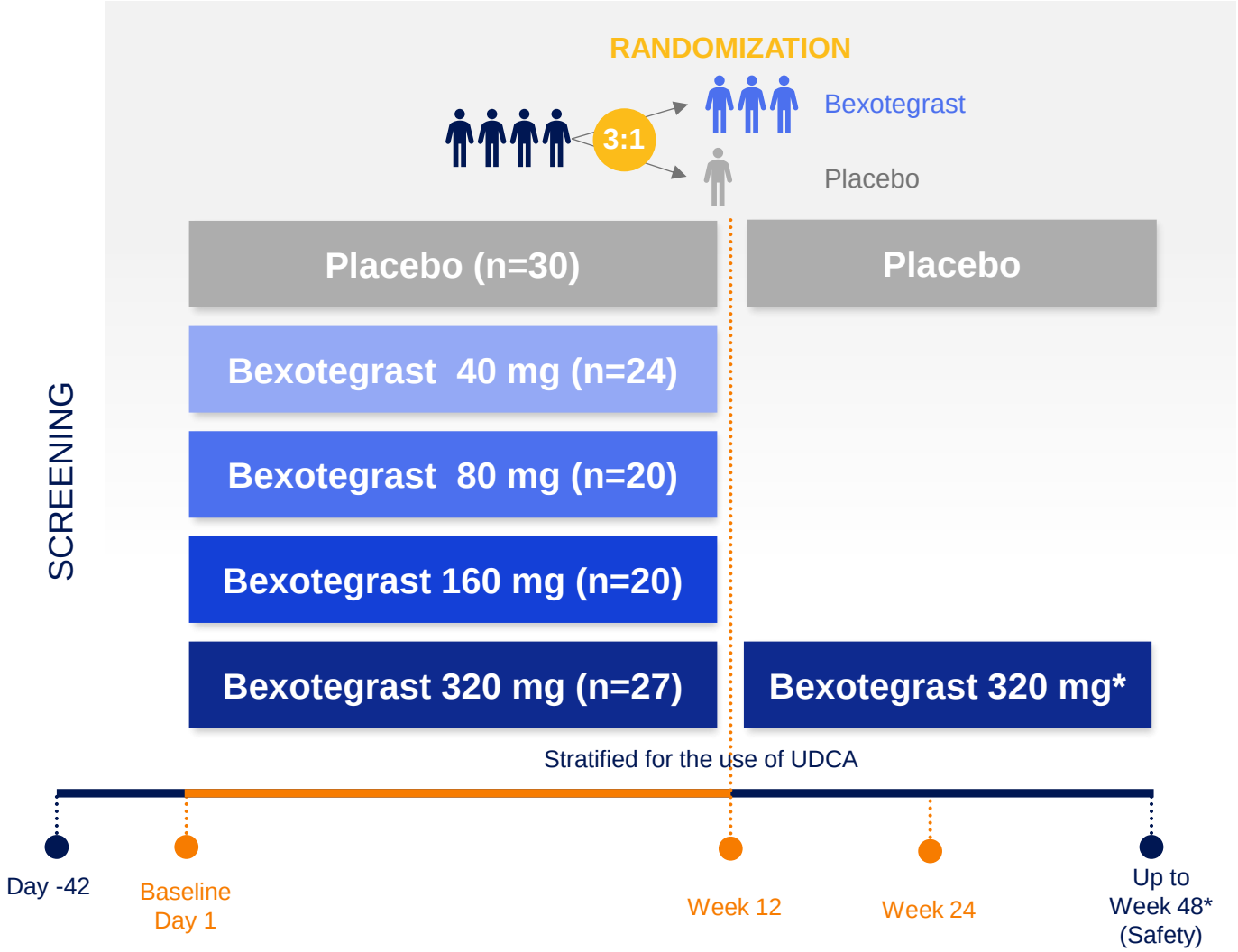
PLIANT

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



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

INTEGRIS-PSC – Key Findings at Week 12

Bexotegrast was Well Tolerated in Participants with PSC

- No safety concerns identified across all dose groups, including the 320 mg dose group
- The most common AEs were observed at lower rates in bexotegrast-treated patients vs. placebo
- No treatment-related SAEs on bexotegrast

Bexotegrast Demonstrated Antifibrotic Activity in a PSC Population with Suspected Liver Fibrosis

- Reduced liver fibrosis markers ELF and PRO-C3 at all doses relative to placebo over short-term treatment
- Contrast MRI suggested improved hepatocyte function and bile flow at all doses relative to placebo

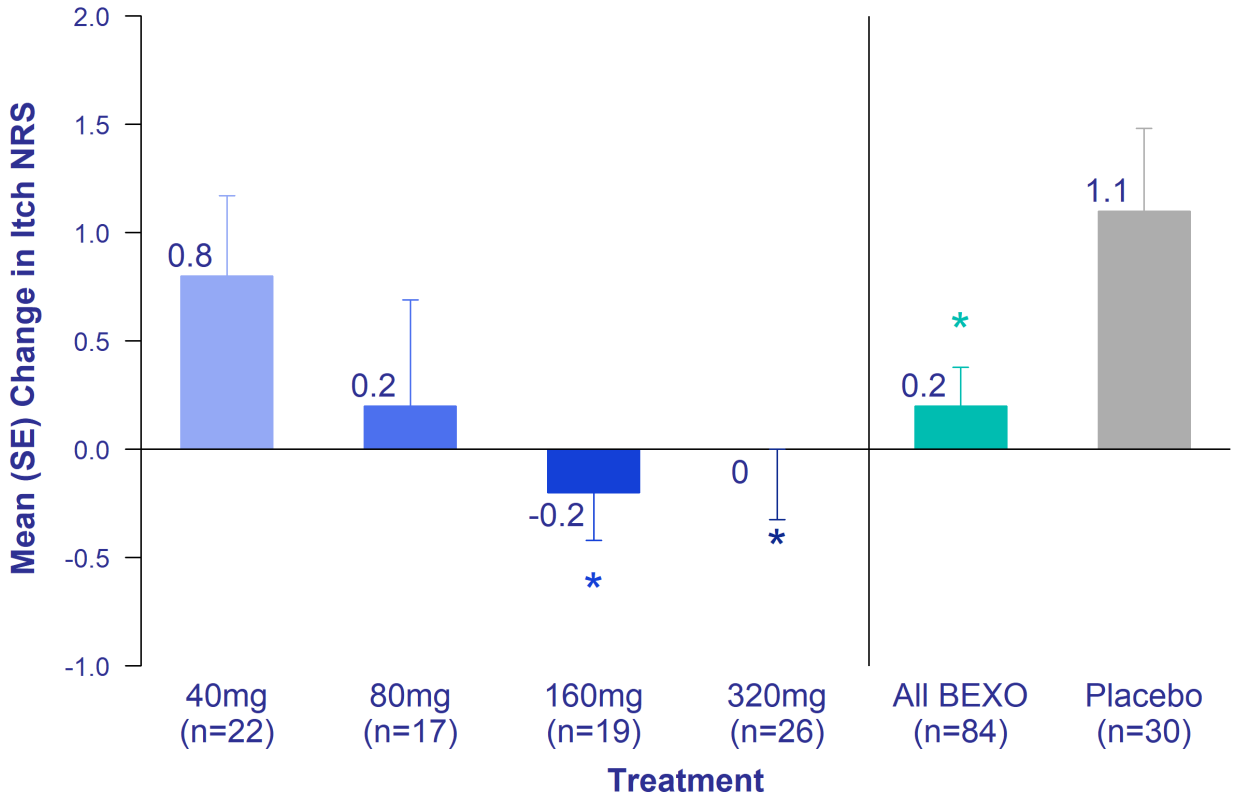
Additional Findings

- Statistically significant reductions in itch relative to placebo for the 160 mg and 320 mg doses
- ALP remained stable at all doses relative to increases on placebo

PLIANT

Itch Numerical Rating Scale – Change from Baseline at Week 12

Safety Population



* p < 0.05 vs placebo

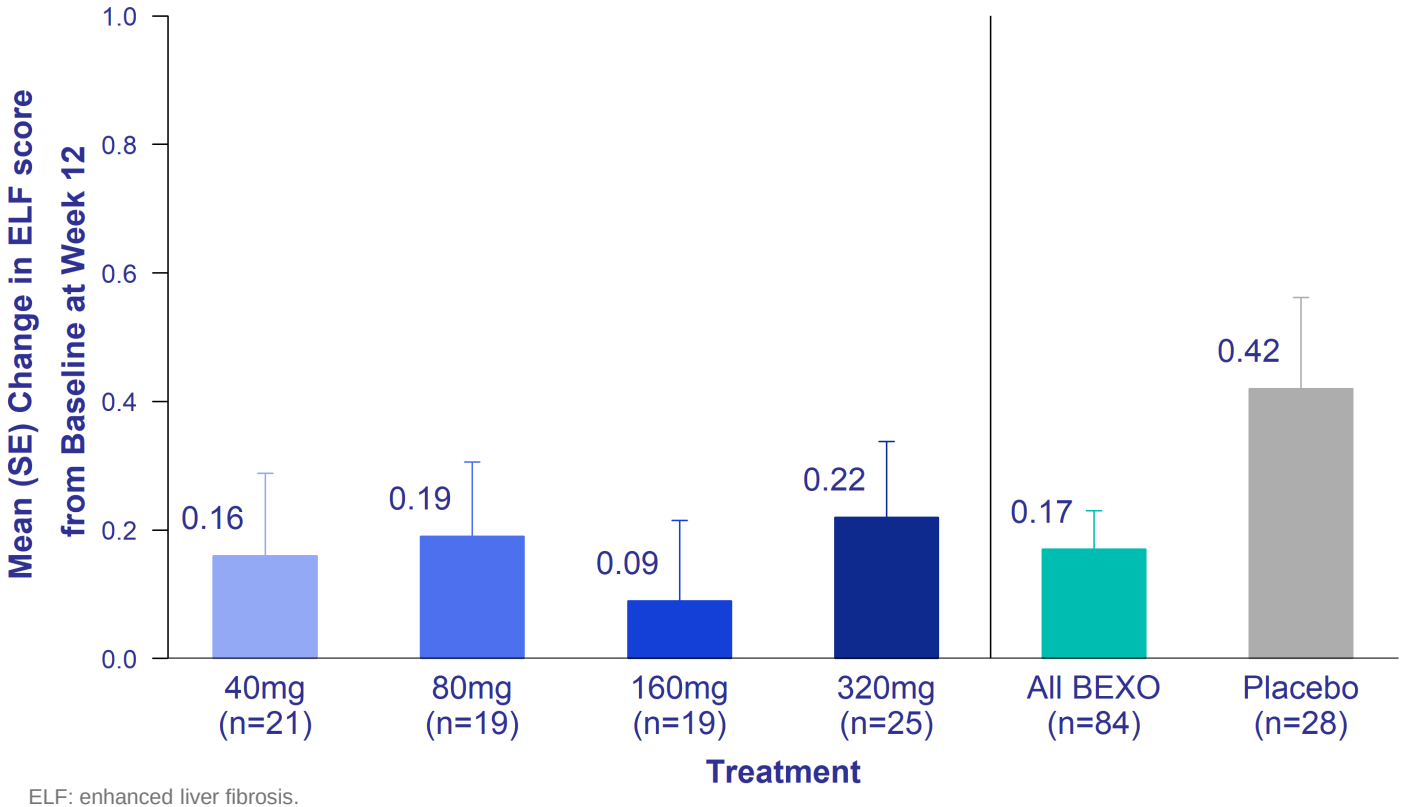
Bexotegrast showed statistically significant reductions in itch relative to placebo for the 160 mg and 320 doses

NRS: Numerical Rating scale; Itch NRS is a patient reported outcome which assesses severity of itch, over the last 24 hours, on a scale of 0 (no itch) to 10 (Worst imaginable itching).

PLIANT

ELF Score – Change from Baseline at Week 12

Safety Population

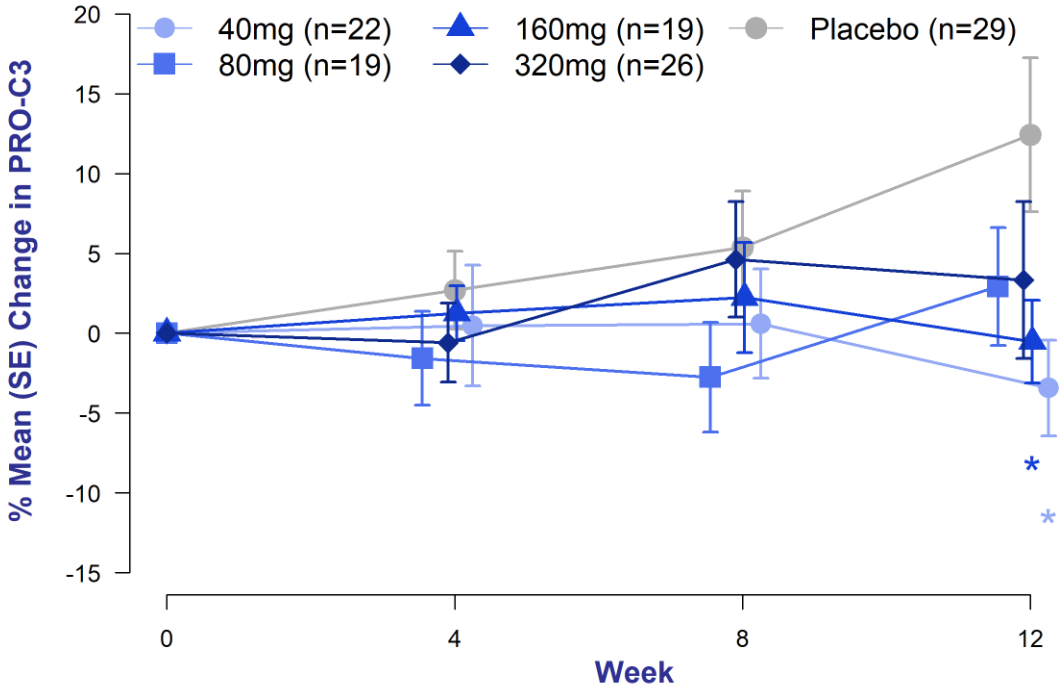


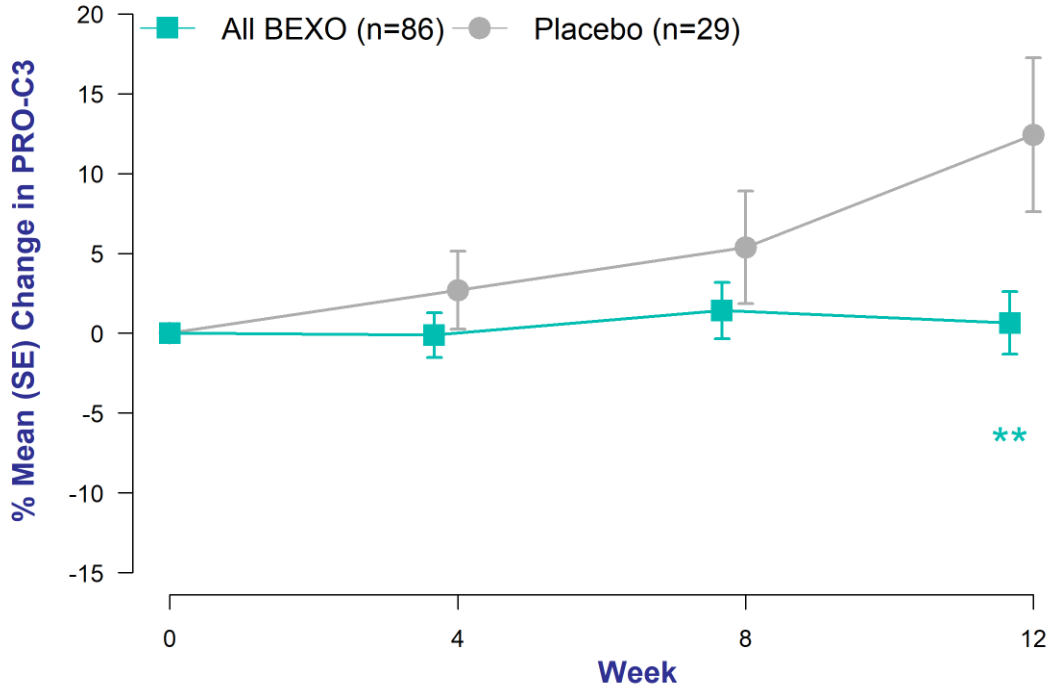
ELF: enhanced liver fibrosis.

Bexotegrast reduced ELF score relative to placebo at all doses

PRO-C3 – Percent Change from Baseline

Safety Population





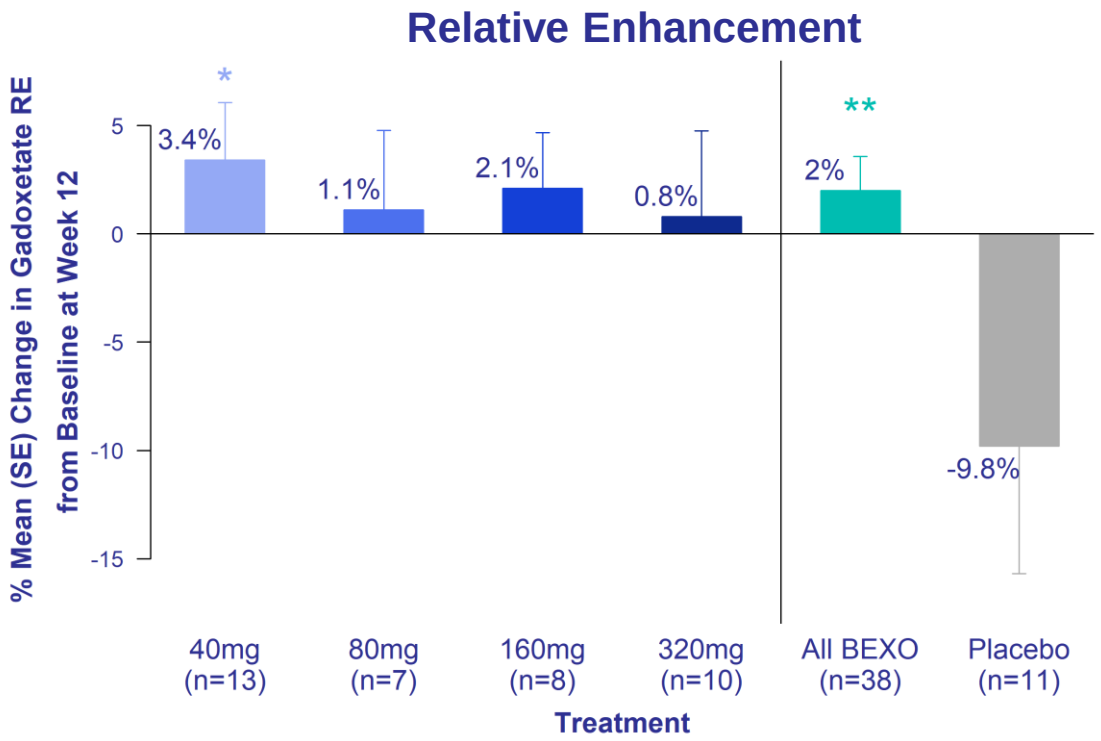
* p < 0.05 vs placebo
** p < 0.01 vs placebo

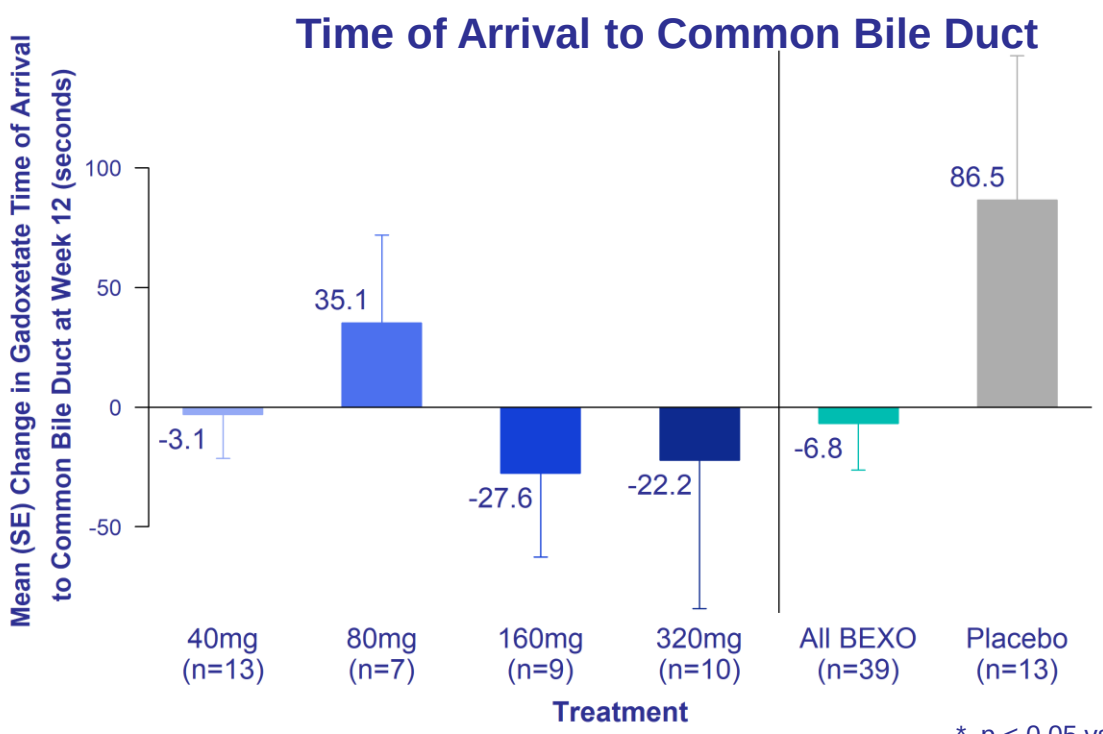
All doses reduced collagen synthesis (PRO-C3) relative to placebo with statistical significance at Week 12 for 40 mg and 160 mg doses

PROC-C3: neo-epitope pro-peptide of type III collagen formation.
Only participates with both a baseline and post baseline are summarized.

MRI Parameters – Change from Baseline at Week 12

Sub-Study Safety Population





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

All doses showed increased relative enhancement compared to placebo, suggesting improved hepatocyte function

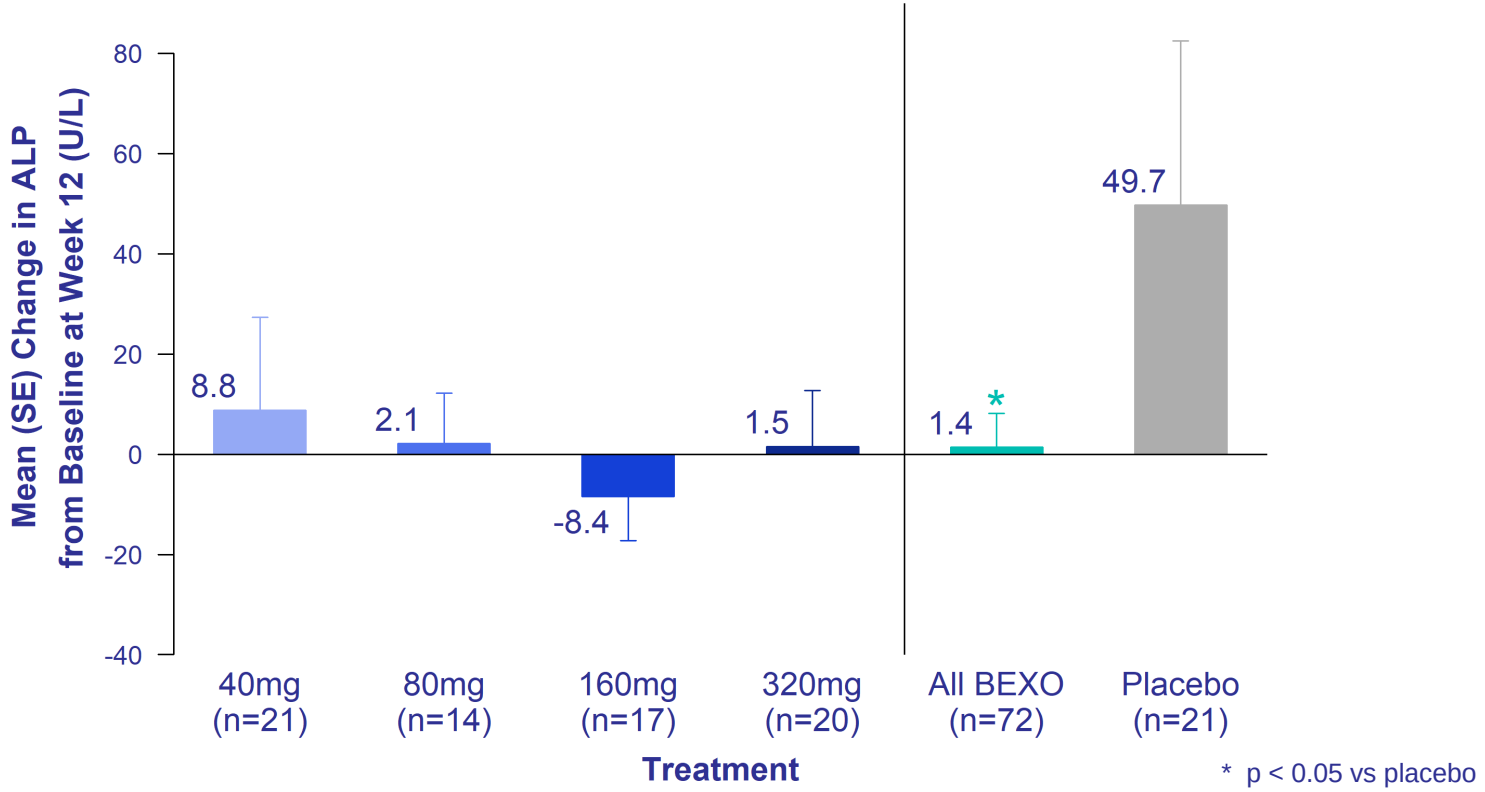
All doses reduced time of arrival to the common bile duct compared to placebo, suggesting improved bile flow

Relative enhancement (RE), using the contrast agent gadoxetate, is a measure of hepatocyte function. Time of arrival of gadoxetate to bile duct is a measure of excretory function.
MRI was an optional sub study to main study.

PLIANT

ALP – Change from Baseline at Week 12

Safety Population – Participants with ALP > ULN at Baseline

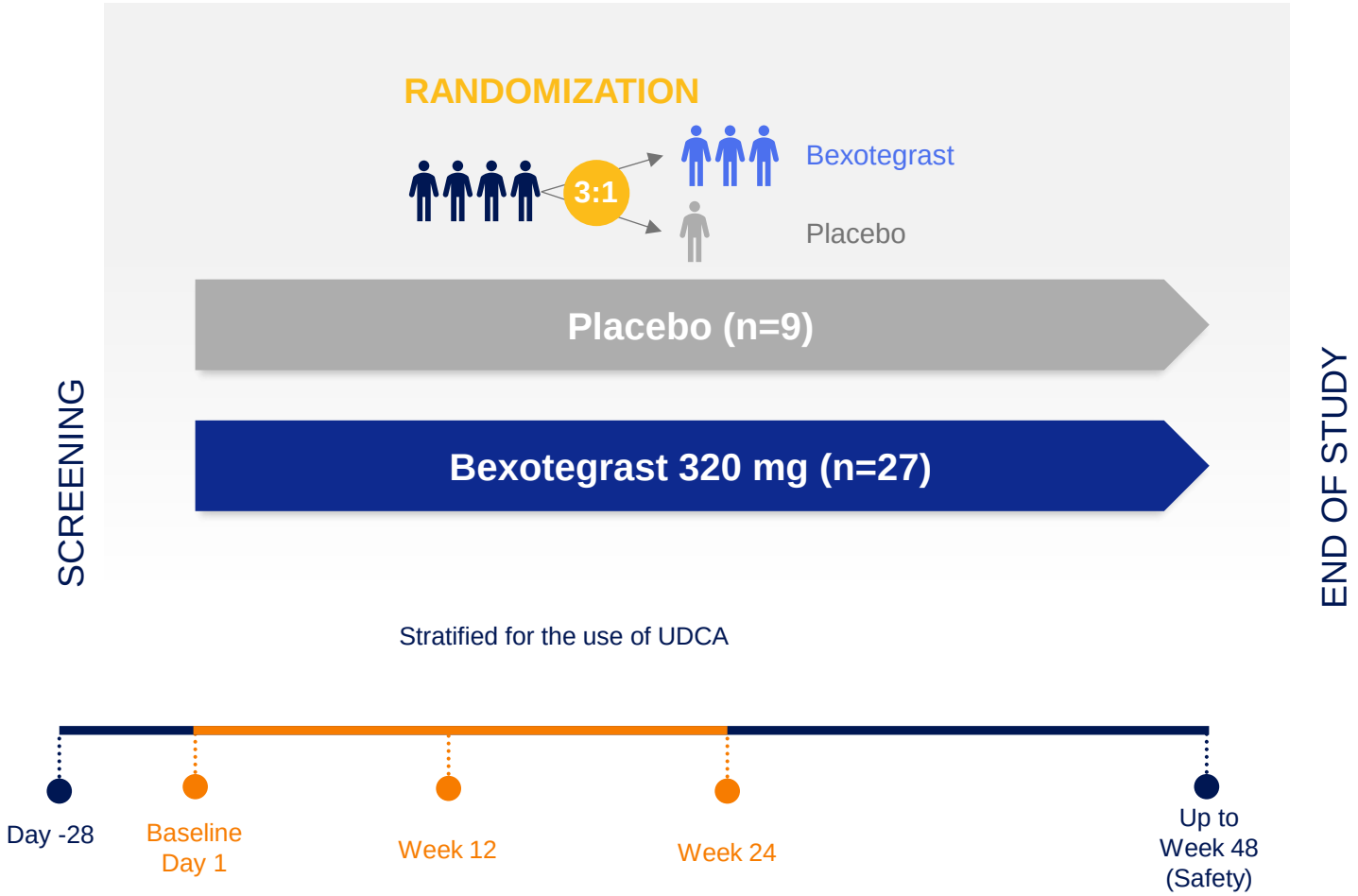


Bexotegrast improved ALP relative to placebo at all doses in subgroup with elevated ALP at baseline

ALP -Alkaline phosphatase.

INTEGRIS-PSC Part 3 Study Design and Objectives

First PSC Trial Enriched for Participants with Suspected Liver Fibrosis



Due to trial design and enrollment trajectory, longest treatment duration was 40 weeks

PRIMARY AND SECONDARY ENDPOINTS

- Safety, tolerability, PK

EXPLORATORY ENDPOINTS

- Changes in transient elastography at Week 24
- Changes in liver fibrosis markers, ELF score and PRO-C3
- Changes in liver imaging
- Changes in liver biochemistry

INCLUSION CRITERIA

- At-risk for 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

PLIANT

UDCA = Ursodeoxycholic acid ; TE = Transient elastography; ELF = enhanced liver fibrosis

INTEGRIS-PSC – Key Findings at Week 24 for 320 mg Cohort

Bexotegrast 320 mg was well tolerated in participants with PSC over longer term dosing

- Favorable safety and tolerability profile maintained up to 40 weeks
- No treatment-related severe or serious adverse events on bexotegrast

Bexotegrast continued to demonstrate antifibrotic activity

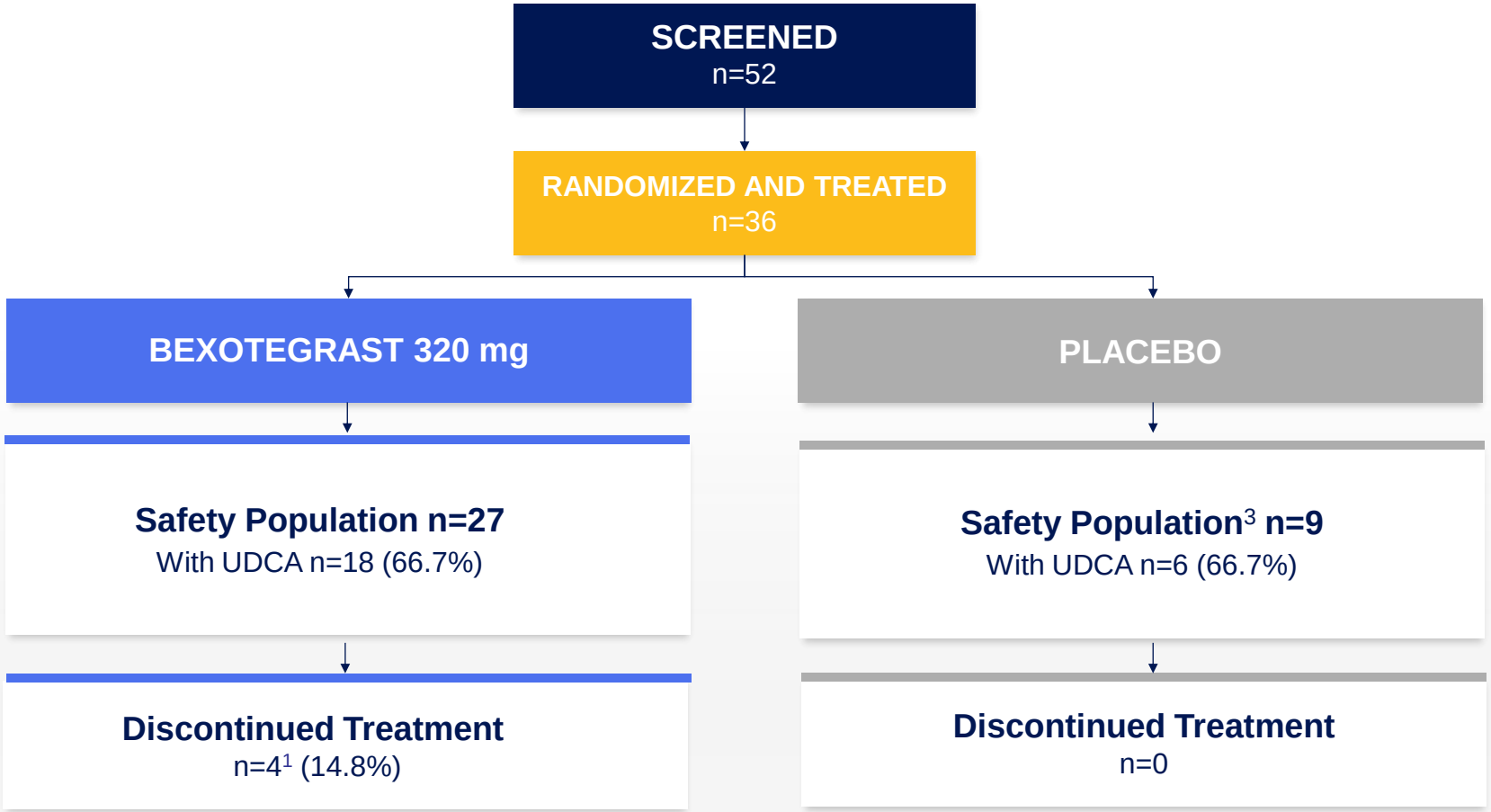
- Improvement in liver stiffness compared to placebo by transient elastography at Week 24
- Reduction in ELF score at Week 24 observed relative to an increase on placebo in high-risk subpopulation
- Stable ELF score observed from Week 12 to 24 in the overall bexotegrast-treated population

Bexotegrast improved markers and symptoms of cholestasis

- Statistically significant improvement in ALP levels at Week 24 compared to placebo
- Contrast MRI suggests continued improvement in hepatocyte function and bile flow from Week 12 to 24
- Stable score on the Itch NRS compared to an increase on placebo over 24 weeks
- Pruritis and cholangitis AEs reported in lower proportions of bexotegrast treated patients than placebo

PLIANT

INTEGRIS-PSC – Participant Disposition – 320 mg Cohort



1 – Adverse Event (n=1), Withdrawal by subject (n=2) other (n=1); One discontinuation occurred post Week 12.

UDCA = Ursodeoxycholic acid

Baseline Disease Activity Markers – 320 mg Cohort Participants

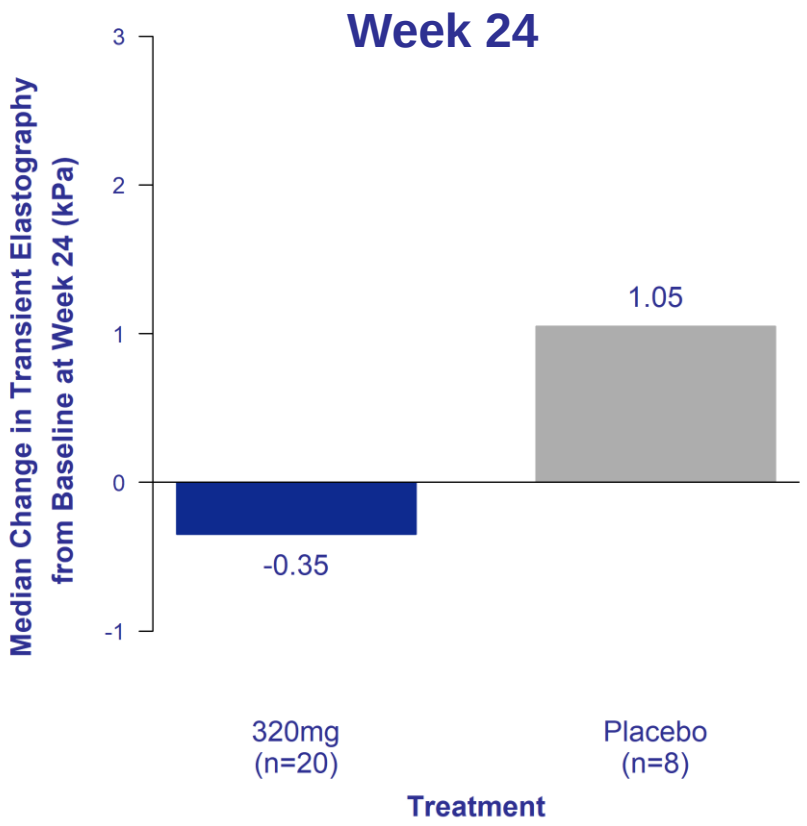
	Bexotegrast 320mg (n=27)	Placebo (n=9)
Liver Biochemistry, mean (SD)		
Alkaline phosphatase (ALP) (U/L)	190.6 (91.29)	318.6 (282.73)
> ULN, n (%)	22 (81.5)	6 (66.7)
Alanine aminotransferase (ALT) (U/L)	60.4 (37.76)	85.8 (70.79)
Aspartate aminotransferase (AST) (U/L)	44.6 (24.69)	58.2 (50.91)
Total Bilirubin (mg/dL)	0.53 (0.208)	0.76 (0.424)
Direct bilirubin (mg/dL)	0.16 (0.062)	0.33 (0.341)
Markers of Fibrosis, mean (SD)		
ELF Score	9.0 (0.84)	9.5 (0.93)
PRO-C3 (ng/mL)	46.48 (19.536)	60.18 (39.630)
Transient Elastography (kPa)	8.7 (3.14)	8.6 (2.85)

ELF: Enhanced Liver Fibrosis; PROC-C3: neo-epitope pro-peptide of type III collagen formation.
PRO-C3 quantified using Roche COBAS platform (assay reports approximately 2x higher concentrations than previous generation PRO-C3 ELISA)

PLIANT

Improvement in Liver Stiffness with Bexotegrast Compared to Placebo

Safety Population – 320 mg Cohort

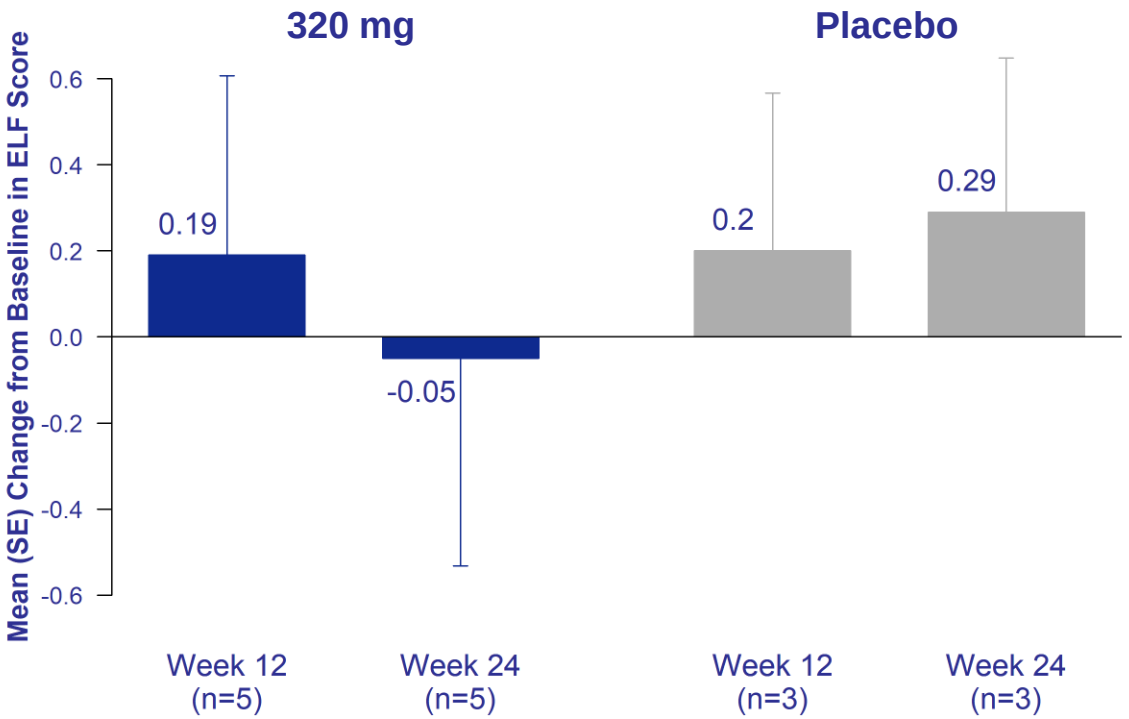


Reduced liver stiffness by transient elastography suggests stabilization of liver fibrosis

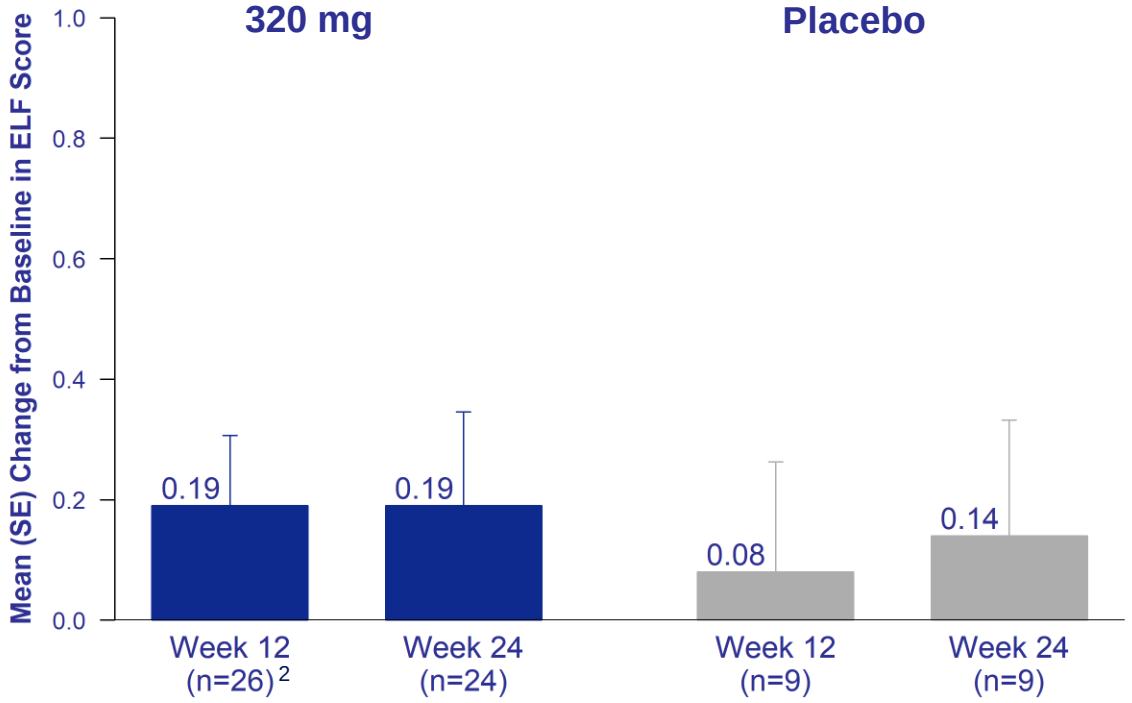
Reduction in ELF Observed with Bexotegrast in High-Risk Patients

Safety Population – 320 mg Cohort

Participants at High Risk of Progression[1]
(Baseline ELF > 9.8)



All Participants



Reduction in ELF score at Week 24 observed, compared to an increase on placebo in patients at high risk for disease progression

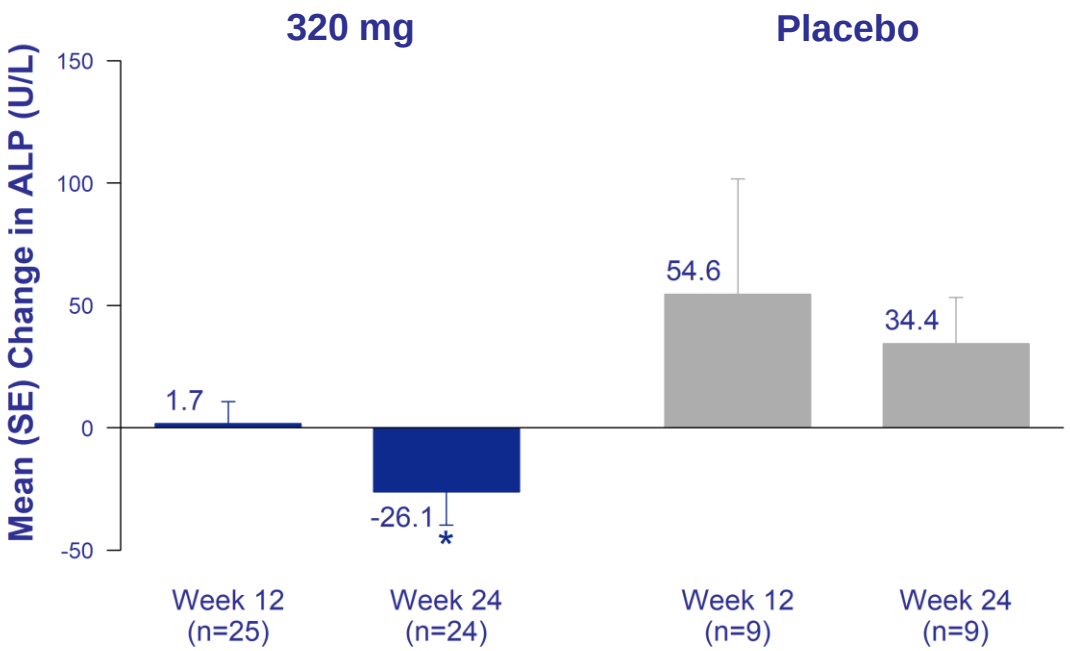
ELF: enhanced liver fibrosis.
1 – ELF score >9.8 is associated with increased risk for advanced liver fibrosis and disease progression.
2 – Includes one patient who was not included in 12-week interim analysis due to sample unavailability at the time of interim analysis.

PLIANT

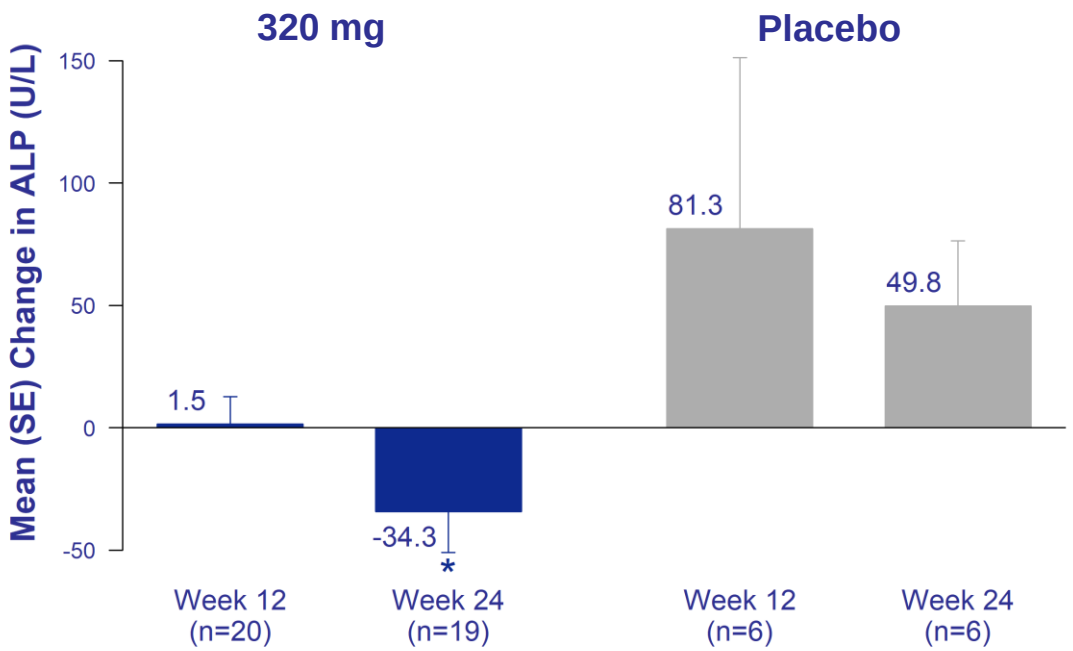
Bexotegrast Reduced ALP over 24 Weeks

Safety Population – 320 mg Cohort

All Participants



Elevated ALP at Baseline



Statistically significant ALP reductions observed in bexotegrast participants compared to increased ALP on placebo

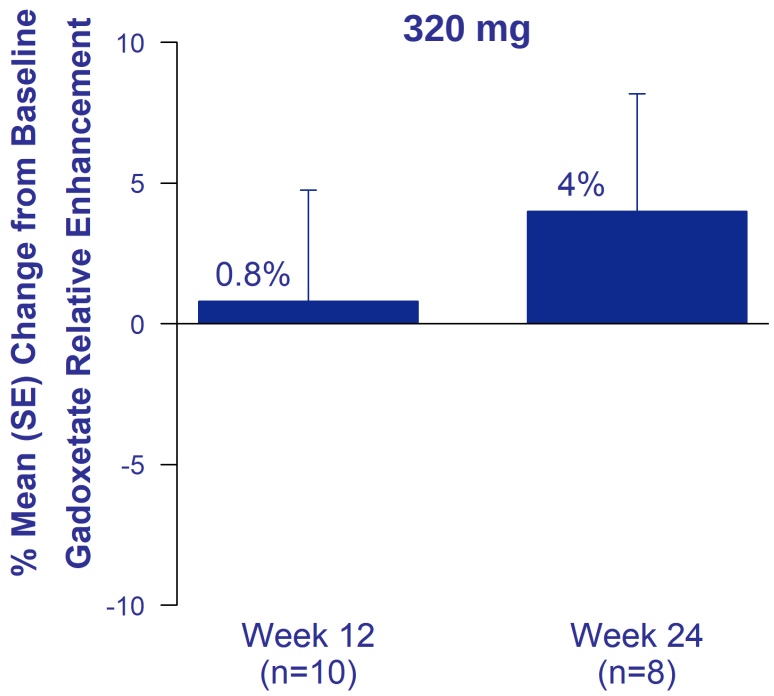
ALP - alkaline phosphatase

* $p < 0.05$ vs placebo

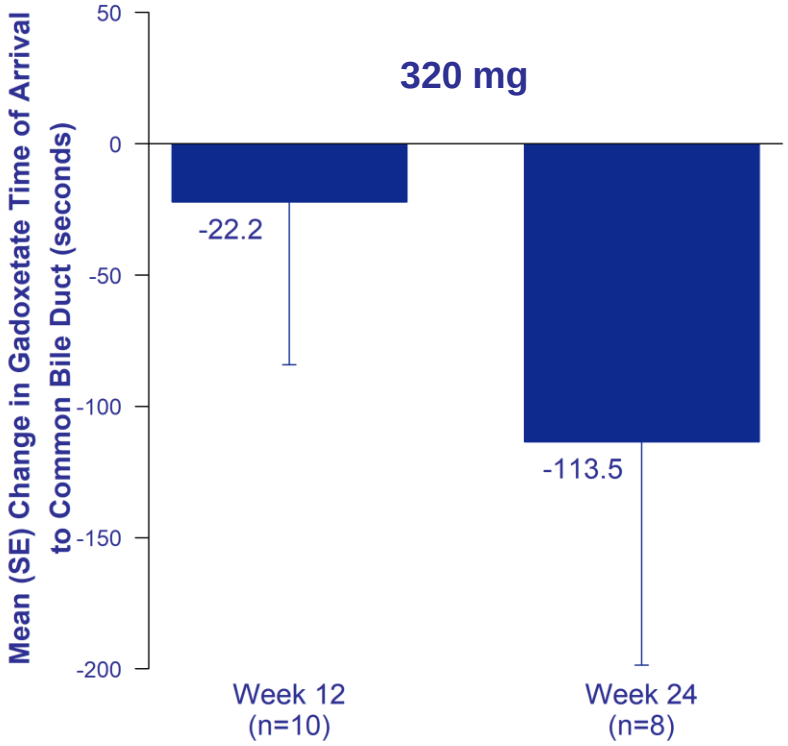
Continued Improvement in MRI Parameters Observed from Week 12 to 24

Safety Population – Sub Study - 320 mg Cohort

Relative Enhancement



Time to Arrival to Common Bile Duct



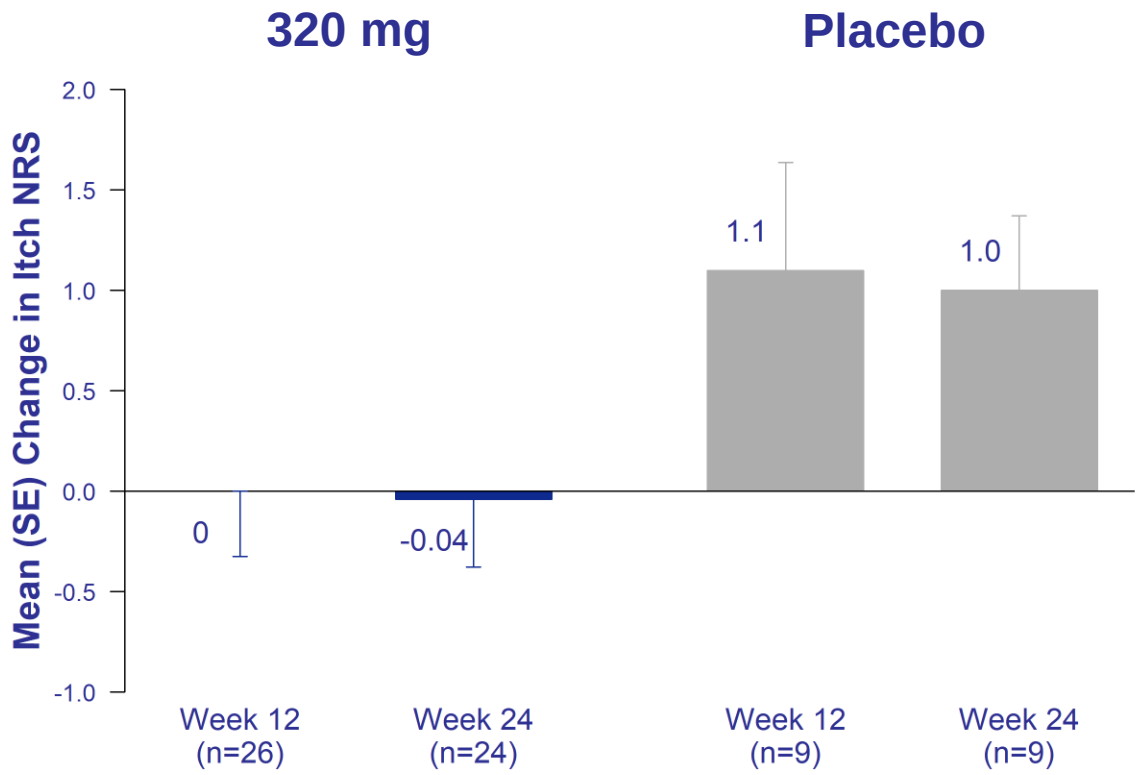
Relative Enhancement and time to arrival continued to improve at Week 24 suggesting further improvement in hepatocyte function and bile flow

Placebo not shown due to small n. n=1 placebo for relative enhancement; n=2 placebo for time to arrival to common bile duct.
Relative enhancement (RE), using the contrast agent gadoxetate, is a measure of hepatocyte function. Time of arrival of gadoxetate to bile duct is a measure of bile flow/excretory function.
MRI was an optional sub study to main study.

PLIANT

Stable Itch NRS Observed with Bexotegrast Compared to Increase on Placebo

Safety Population – 320 mg Cohort



Mean Itch NRS score did not increase over 24 weeks of treatment with bexotegrast compared to an increase on placebo

NRS: Numerical Rating scale; Itch NRS is a patient reported outcome which assesses severity of itch, over the last 24 hours, on a scale of 0 (no itch) to 10 (Worst imaginable itching)

PLIANT

Bexotegrast – Conclusions and Next Steps

Bexotegrast continues to be well tolerated across multiple patient populations

- Well tolerated in over 700 trial participants treated with bexotegrast to date
- No treatment-related SAEs observed in patient studies to date

Bexotegrast continues to demonstrate broad antifibrotic activity across multiple indications

- Strong evidence for antifibrotic activity across pulmonary and hepatic fibrosis indications
- Evidence to date suggests potential disease modification in both IPF and PSC
- Totality of evidence provide strong confidence in ongoing BEACON-IPF Phase 2b/3 trial

Path forward for bexotegrast

- Pliant remains focused on execution of the ongoing BEACON-IPF
- Pliant will continue to evaluate the best path forward in PSC

PLIANT

PLIANT

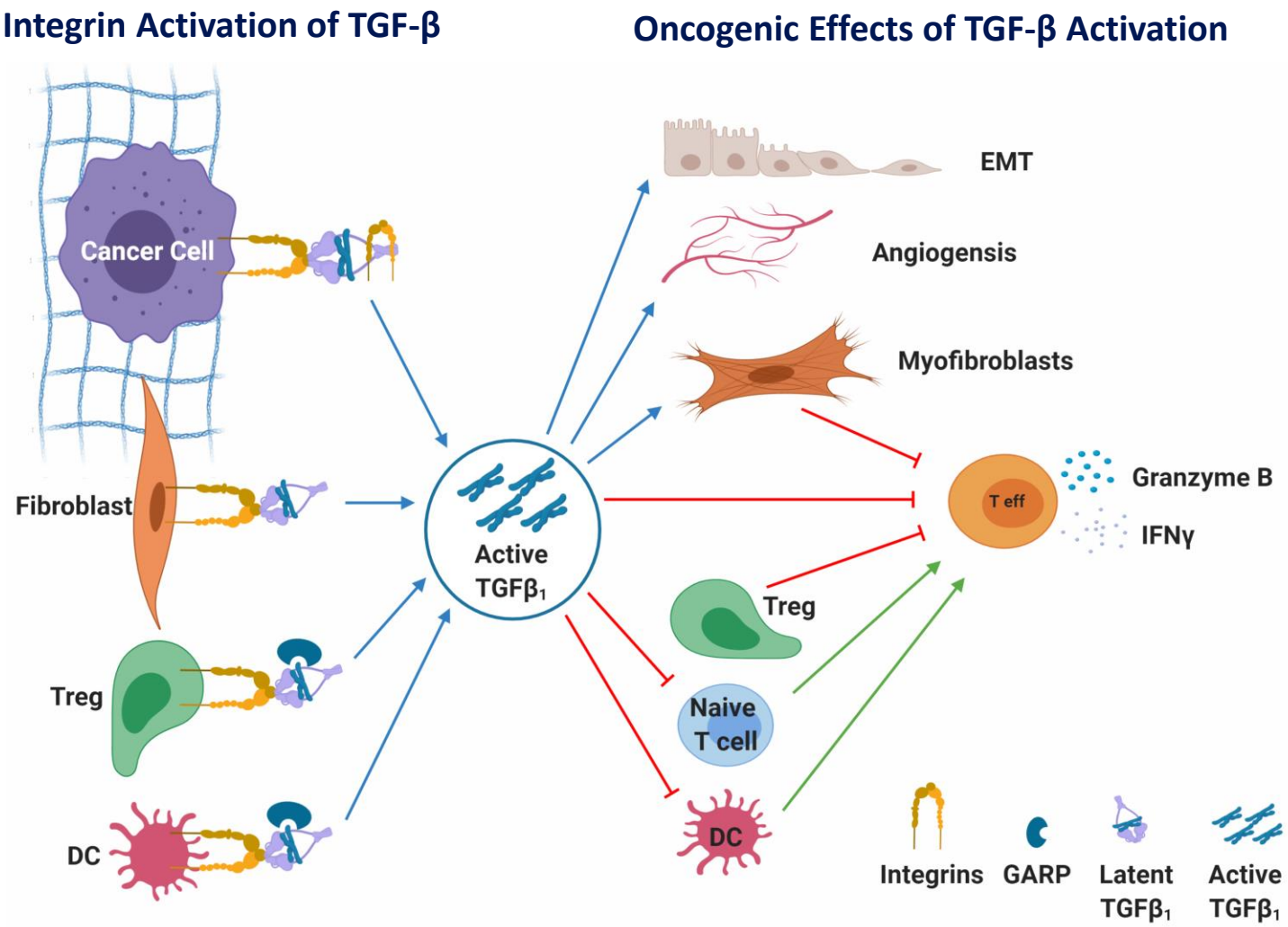
PLN-101095

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

Reprograming the Immunosuppressive Tumor Micro-Environment of Solid Tumors

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 – 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 $\alpha_V\beta_1$

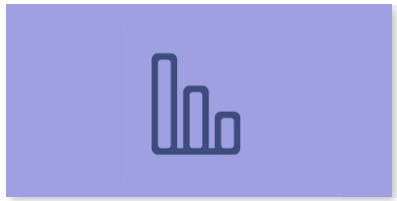
- Tumors that overexpress $\alpha_V\beta_8$ have a poor prognosis

Small molecule with oral administration

- Ease of administration compared to mAb programs

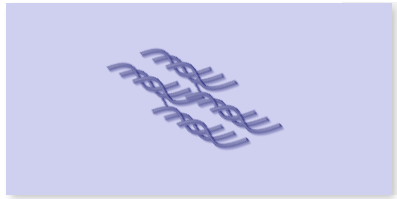
Activity demonstrated in multiple PD-1 resistant tumor models

- 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

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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

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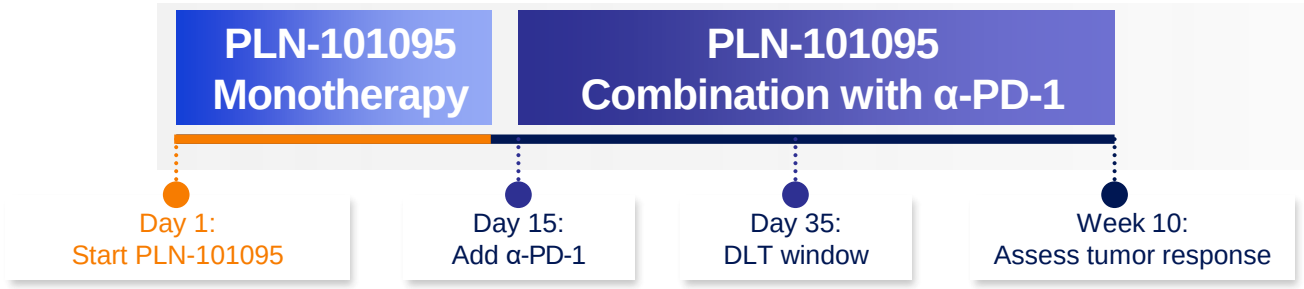
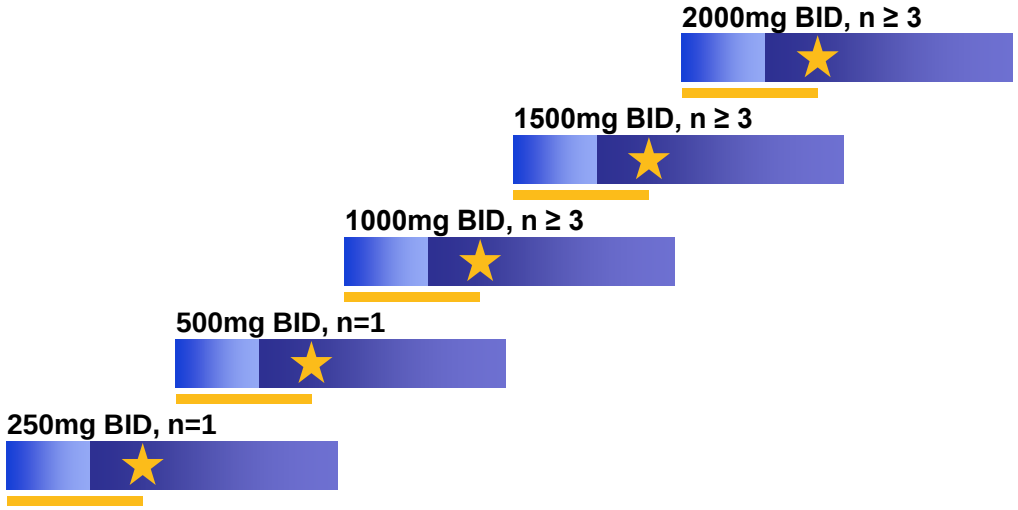
PLN-101095 – Ongoing Phase 1 Study in Patients Resistant to ICIs





★ **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

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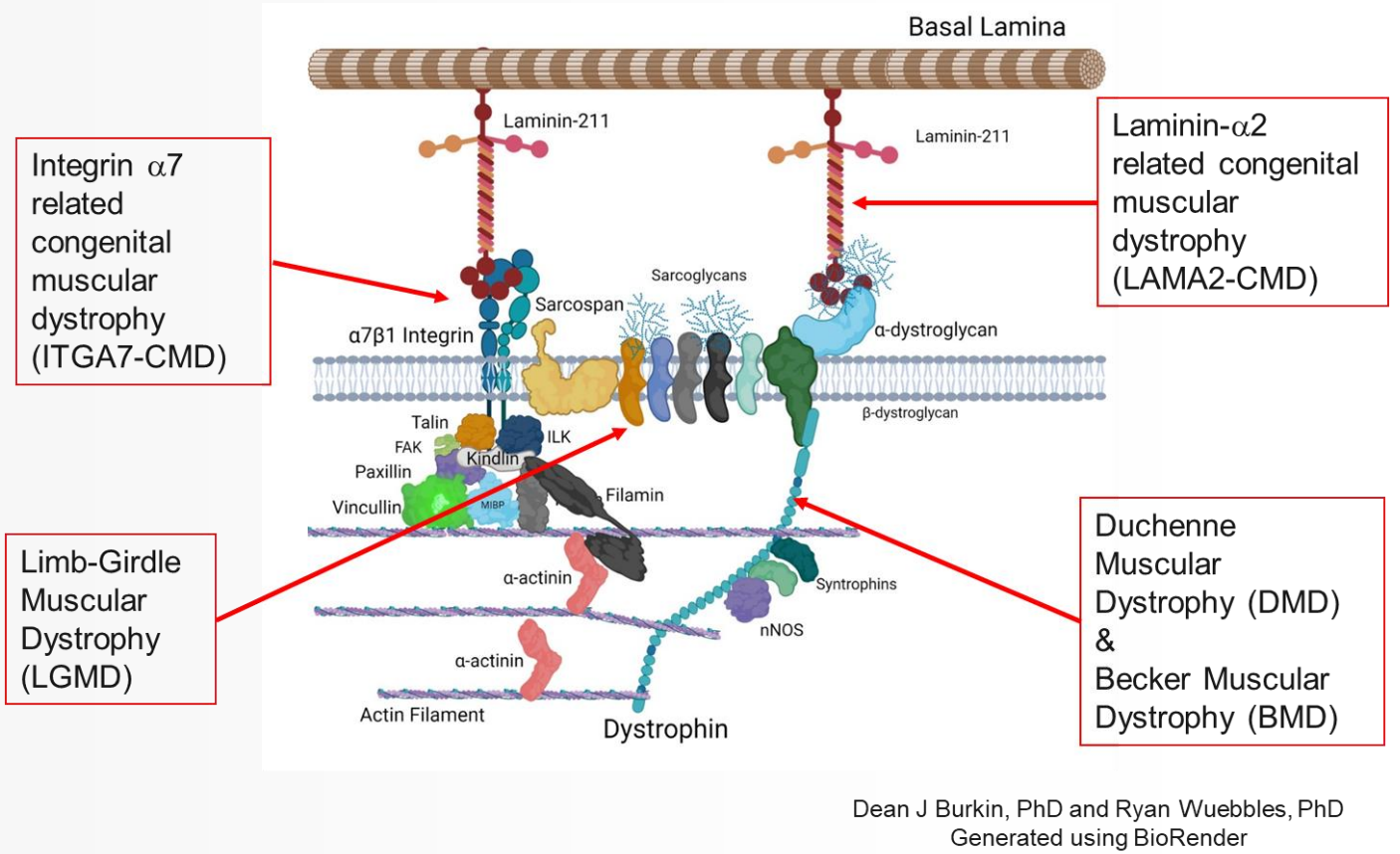
PLN-101325 – Selective Muscle Cell Integrin Agonist for the Treatment of Muscular Dystrophies

$\alpha_7\beta_1$: 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

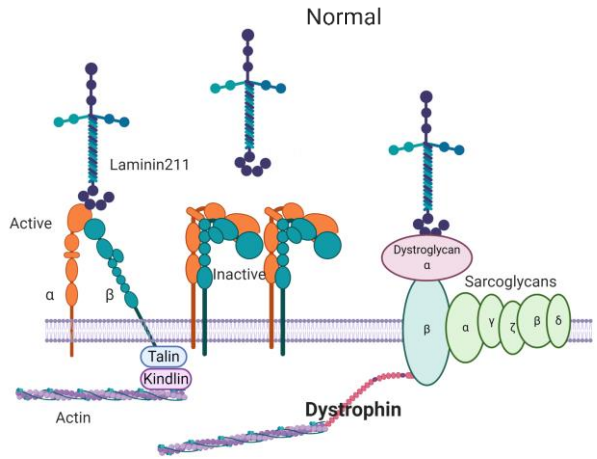
- α7β1 is upregulated as a **compensatory mechanism** in **different types of muscular dystrophy**
- Acts as a **substitute for dystrophin**, helping to stabilize the muscle membrane, decreasing muscle damage
- **Mutations in the target result in human congenital myopathy**

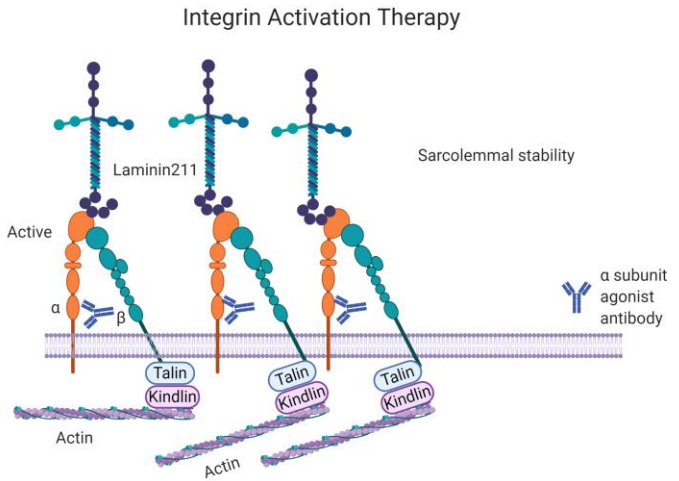
Allosteric agonistic monoclonal antibody

- 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