



Developing Novel Treatments for Fibrotic Diseases

OCTOBER 2023

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Pliant Development Pipeline

Program	Indication	Preclinical	Clinical			Anticipated Milestone	Global Rights
			Phase I	Phase II	Phase III		
Bexotegast (PLN-74809) Dual selective inhibitor of $\alpha_v\beta_6/\alpha_v\beta_1$	Idiopathic Pulmonary Fibrosis					BEACON-IPF Phase 2b trial underway	
	Primary Sclerosing Cholangitis					12-Week 320 mg data 1Q 2024	
PLN-101095 Inhibitor of $\alpha_v\beta_8/\alpha_v\beta_1$	Solid Tumors					Phase 1 trial underway	
PLN-101325 Anti-integrin mAb of $\alpha_7\beta_1$	DMD Other Muscular Dystrophies					IND Filing 1Q 2024	
PLN-1474 Selective inhibitor of $\alpha_v\beta_1$	NASH-Associated Liver Fibrosis					Phase 2 Ready	

Pliant's Integrin Focused Library

Core Platform for Novel Pipeline and Partner Programs

Integrins

- Cell surface receptors that facilitate cell-cell and cell-extracellular matrix adhesion and interaction
- A major path of communication between the extracellular matrix, inflammatory cells, fibroblasts
- Closely involved in signaling processes governing tissue fibrosis

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

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

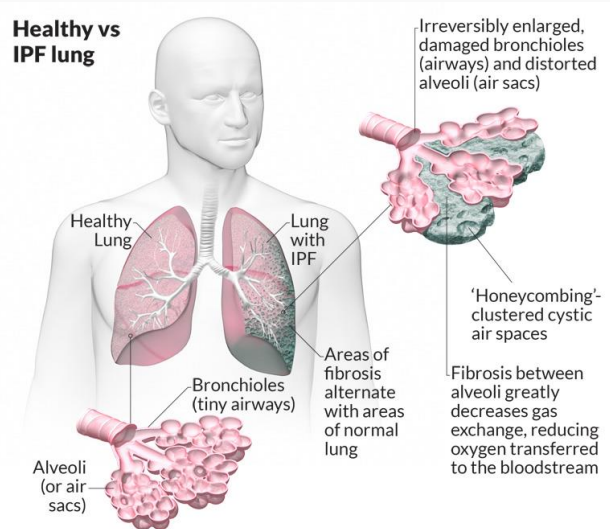


Fibrosis – A Silent Killer



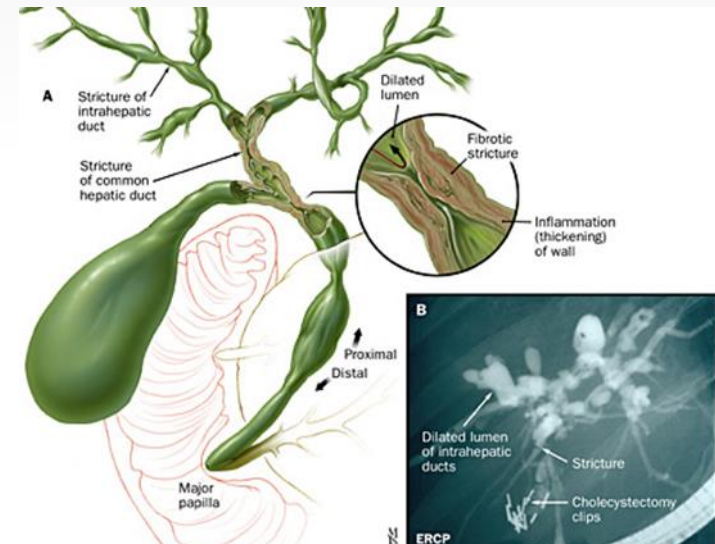
Idiopathic Pulmonary Fibrosis (IPF) is a lethal pathological process with limited therapeutic options

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



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

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



Bexotegrast

Understanding the IPF commercial opportunity



CURRENT COMMERCIAL LANDSCAPE IN IPF

- Two marketed agents – Esbriet® and Ofev® with **>\$4 billion total global revenues** in 2022
- Growing market with positive tailwinds
 - Increasing incidence of IPF with aging population
 - New therapies expanding treatable population



CHANGING TREATMENT LANDSCAPE

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



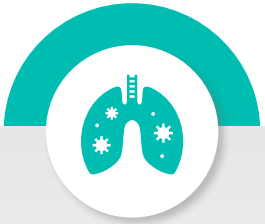
SIGNIFICANT NEED FOR NEW THERAPEUTIC OPTIONS

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

Bexotegrast

A Potential Preferred Treatment Option

ANTI-FIBROTIC MoA



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

MONO & COMBO TREATMENT



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

ORAL 1X DAILY DOSING



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

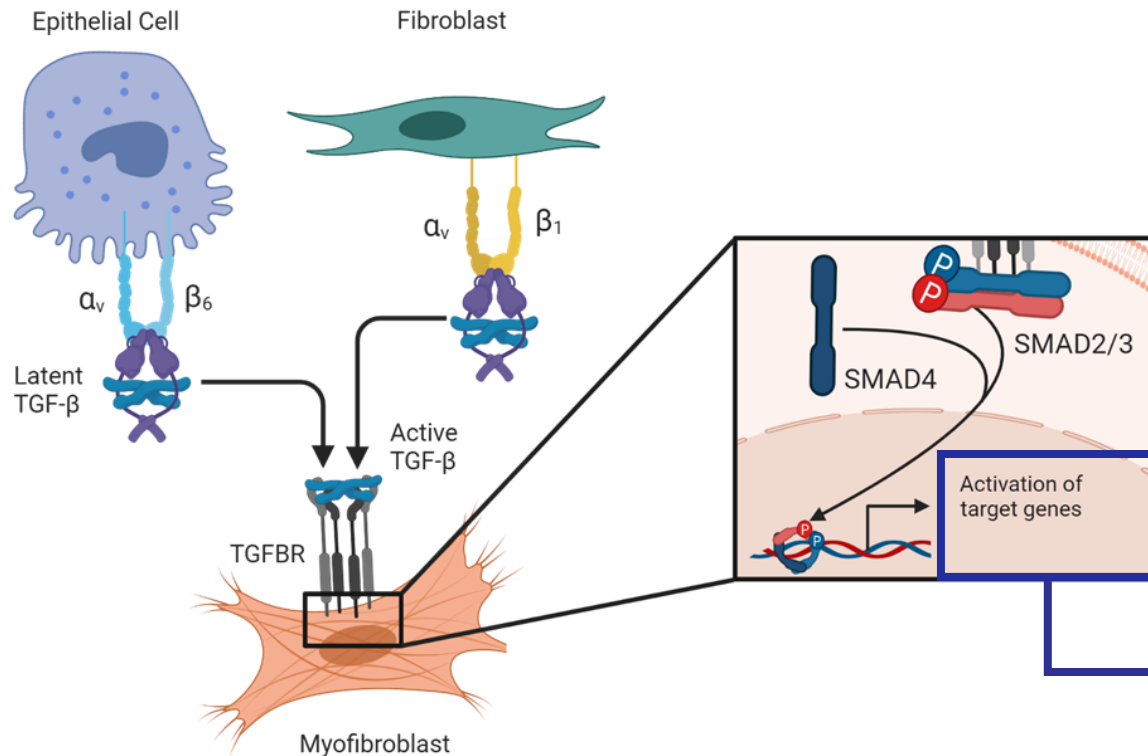
SAFETY / TOLERABILITY



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

$\alpha_v\beta_6$ / $\alpha_v\beta_1$ Integrins Drive TGF- β Activation in Lung Fibrosis

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

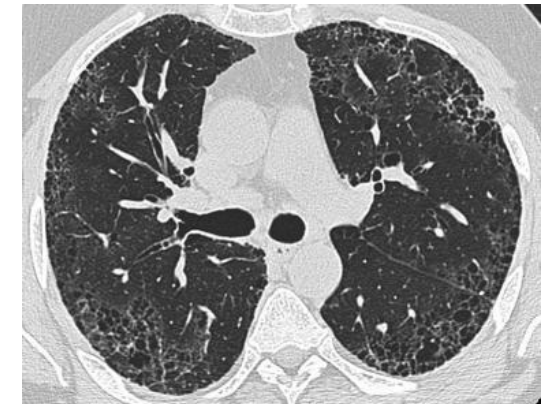


- TGF- β is a central mediator of fibrosis
- $\alpha_v\beta_6$ / $\alpha_v\beta_1$ integrins activate latent TGF- β in fibrotic tissue
- Systemic TGF- β blockade carries toxicity risks

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

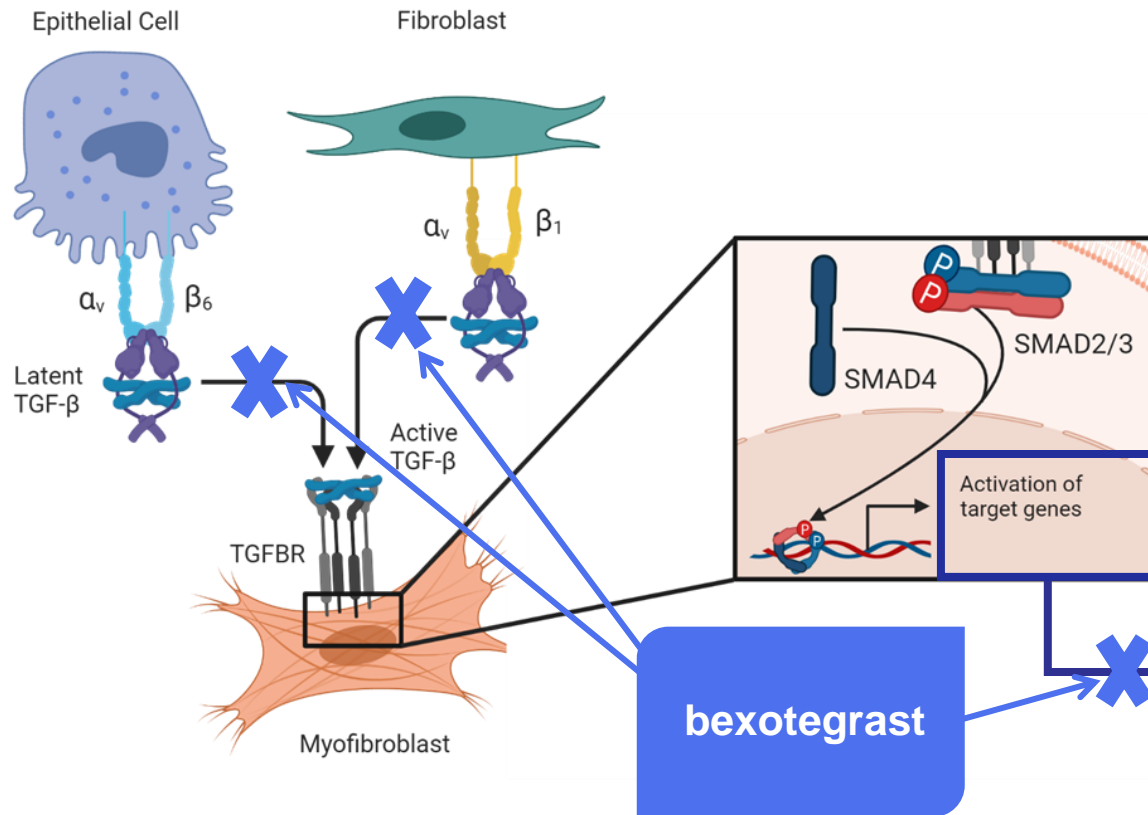
FIBROSIS

COL1A1
COL3A1
TIMP1
CCN2
ENPP2
...



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

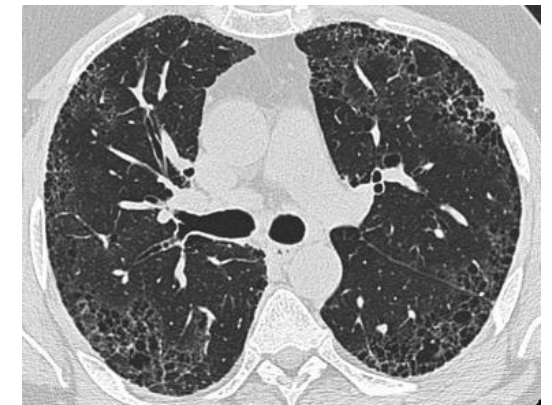
$\alpha_v\beta_6$ / $\alpha_v\beta_1$ integrins promote fibrosis by activating TGF- β



- 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

FIBROSIS



COL1A1
COL3A1
TIMP1
CCN2
ENPP2
...

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

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

Affected organ system	Systemic TGF-β blockade	Observed with Pliant compounds? ¹
Cardiovascular System	Cardiotoxicity	NO
Immune System	Autoimmunity/Inflammation	NO
GI System	Autoimmunity/Inflammation	NO
Skin	Keratoacanthomas/SCC	NO
Hematology	Thrombocytopenia/Anemia	NO

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

Bexotegrast - Nonclinical Toxicology Studies

No concerns for clinical advancement

GLP Study category	Studies completed	Findings with Bexotegrast (PLN-74809)
Repeat Dose Toxicology	<ul style="list-style-type: none"> 1-Month IND-enabling NHP and mouse 3-Month Sub-chronic NHP and mouse 9-Month Chronic NHP 6-Month Chronic Mouse 	<p>No findings limiting clinical advancement including</p> <ul style="list-style-type: none"> No pulmonary infiltrates No bladder cancer <p>NOAEL¹ in sub-chronic and chronic GLP tox studies at the highest dose tested in NHPs</p>
Safety Pharmacology	<ul style="list-style-type: none"> Standard cardiac ion channel panel Cardiovascular/respiratory in telemetered NHP 	<p>No findings:</p> <ul style="list-style-type: none"> No effect on respiratory or cardiovascular parameters
Genetic Toxicology	<ul style="list-style-type: none"> Ames <i>In vitro</i> micronucleus <i>In vivo</i> micronucleus 	<p>No genotoxic findings:</p> <ul style="list-style-type: none"> Ames negative Micronucleus negative
Reproductive Toxicology	<ul style="list-style-type: none"> Mouse Embryofetal Development Rabbit Embryofetal Development Mouse Fertility 	<p>No findings:</p> <ul style="list-style-type: none"> No embryofetal effects No effects on fertility

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

¹ – No observed adverse effect level.

INTEGRIS-IPF – Introduction

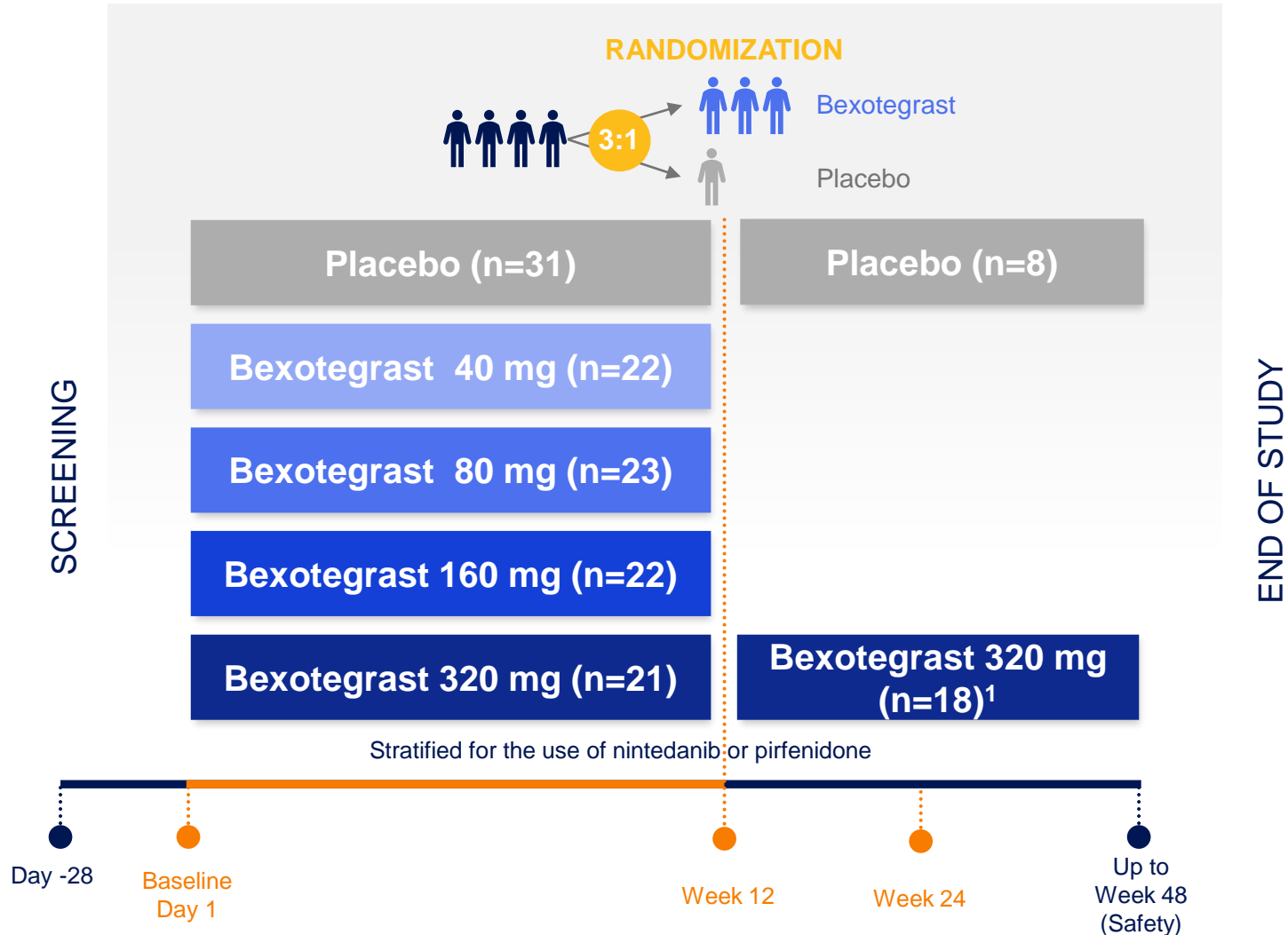
Purpose of Evaluating Long-Term Treatment with Bexotegrast 320 mg

- Evaluate long term safety of the top dose planned for late-stage development
- Evaluate durability of treatment effect (FVC) including symptomatic improvement (cough)
- Assess long-term effects on pulmonary fibrosis as measured through QLF imaging

Key Takeaways from the Trial

- Bexotegrast continues to demonstrate a favorable safety and tolerability profile
- Bexotegrast demonstrated durable improvements across physiologic (FVC), radiographic (QLF) and symptomatic (cough) assessments versus placebo
- Data provide strong support to advance bexotegrast into late-stage development

INTEGRIS-IPF 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

Key Takeaways from the INTEGRIS-IPF Trial



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



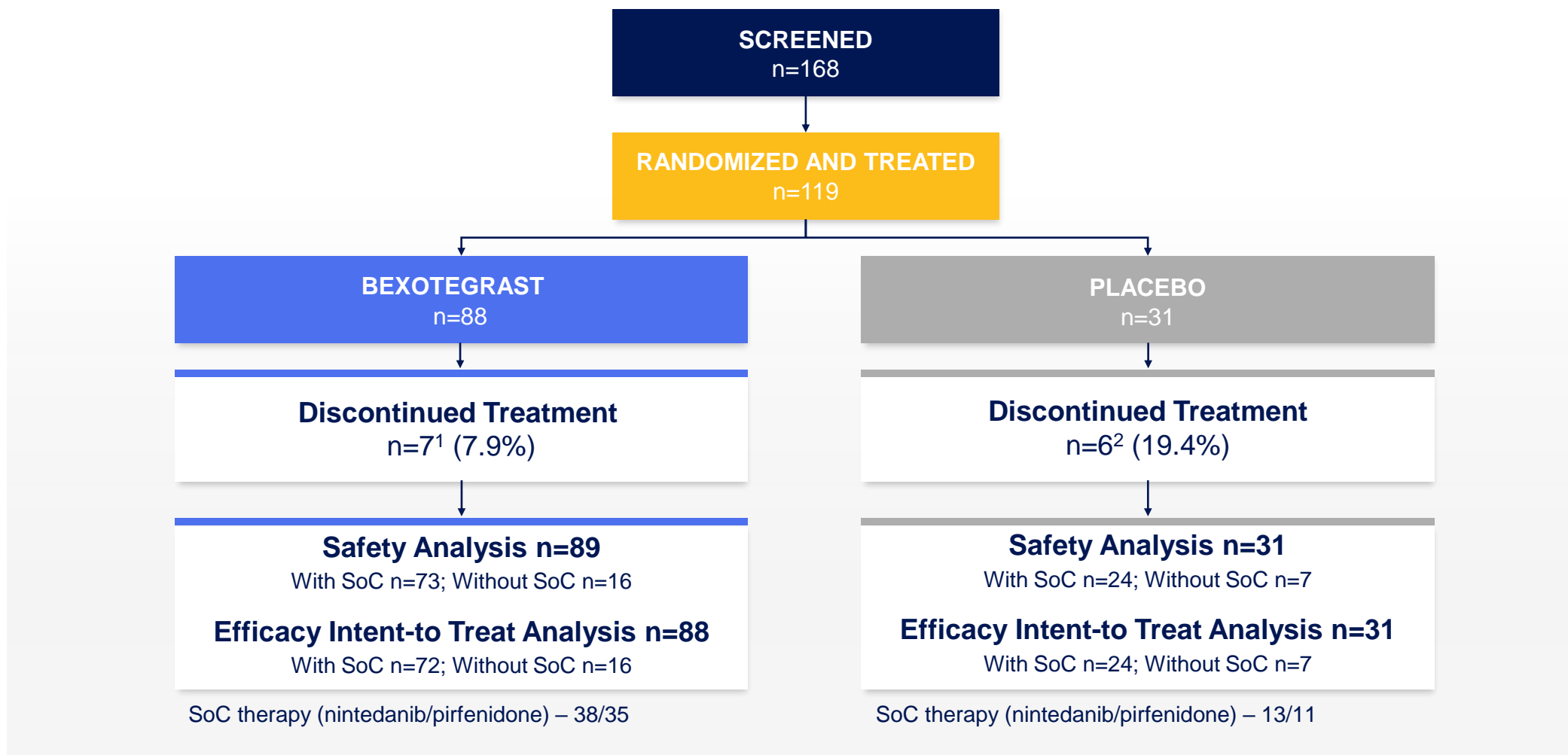
Bexotegrast Demonstrated a Dose-dependent Treatment Effect on Registrational Endpoint

- 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 to Advance Bexotegrast into Late-stage Development

INTEGRIS-IPF – Final Participant Disposition



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

Baseline Demographics

Characteristic	Bexotegrast 320mg (n=22)	Placebo (n=8)
Male sex, n (%)	21 (95.5)	5 (62.5)
Female sex, n (%)	1 (4.5)	3 (37.5)
Age (yr), mean (SD)	70.5 (7.14)	73.3 (7.98)
Race, n (%)		
White	21 (95.5)	8 (100)
Other / Not Reported / Unknown	1 (4.5)	0
Weight (kg), mean (SD)	88.5 (15.61)	80.6 (13.18)
Body-mass index (kg/m ²), mean (SD)	28.1 (4.08)	27.1 (2.95)

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

Baseline Disease Characteristics

Characteristic	Bexotegast 40 mg (n=22)	Bexotegast 80 mg (n=23)	Bexotegast 160 mg (n=22)	Bexotegast 320 mg (n=21)	Bexotegast 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)

Well Tolerated Through Twelve Weeks

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

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

4 – Diarrhea in participant with concomitant use of nintedanib

* One placebo participant received 1 week of treatment with Bexotegast 320 mg. The participant is not included in the 320 mg treatment group. 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.

320 mg Dose Well Tolerated Up To 40 Weeks

AE, n (%) of Participants Reporting	Bexotegrast 320 mg (n=22)	Placebo (n=8)
TEAE	20 (90.9)	7 (87.5)
Related to study drug	5 (22.7)	2 (25.0)
Serious TEAE	2 (9.1)	1 (12.5)
Related to study drug	0	0
TEAE of CTCAE Grade 3 or Higher	5 (22.7)	1 (12.5)
Related to study drug	1 (4.5) ¹	0
TEAE Leading to Interruption of Study Drug	4 (18.2) ²	0
TEAE Leading to Withdrawal of Study Drug	3 (13.6) ^{2,3,4}	1 (12.5)
TEAE Leading to Early Termination from Study	3 (13.6) ^{2,3,4}	0
TEAE Leading to Death	1 (4.5) ³	0

1 – Blood pressure increased; 2 – Abdominal pain/Diarrhea in participant with pre-existing ulcerative colitis;

3 – Acute respiratory failure in a GAP Stage III participant with pre-existing atrial fibrillation 8 days following elective atrioventricular node ablation; 4 – Diarrhea in participant with concomitant use of nintedanib

AE = Adverse Event; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Events. Adverse events coded using MedDRA v. 24.0.
TEAE is defined as any AE starting (or worsening) on or after the date of first dose.

Most Frequent TEAEs

AE, n (%) of Participants Reporting	Bexotegrast 320 mg (N=22)	Placebo (N=8)
Most frequent TEAEs (>10% in at least one arm and n >1 participant)		
Diarrhea	7 (31.8)	3 (37.5)
Related to study drug	4 (18.2)	0
Dyspnea	5 (22.7)	1 (12.5)
Related to study drug	0	0
Idiopathic Pulmonary Fibrosis/Pulmonary Fibrosis	4 (18.2)	2 (25.0)
Related to study drug	0	0
Cough	3 (13.6)	2 (25.0)
Related to study drug	0	0
Upper respiratory tract infection	2 (9.1)	1 (12.5)
Related to study drug	0	0

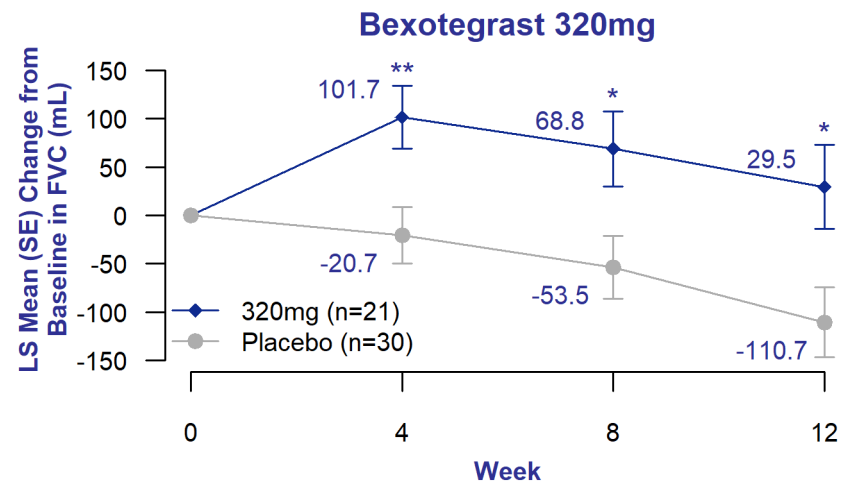
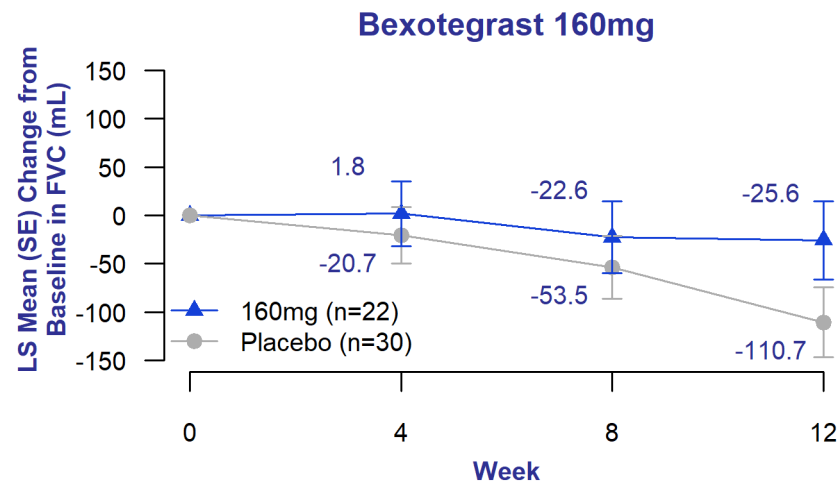
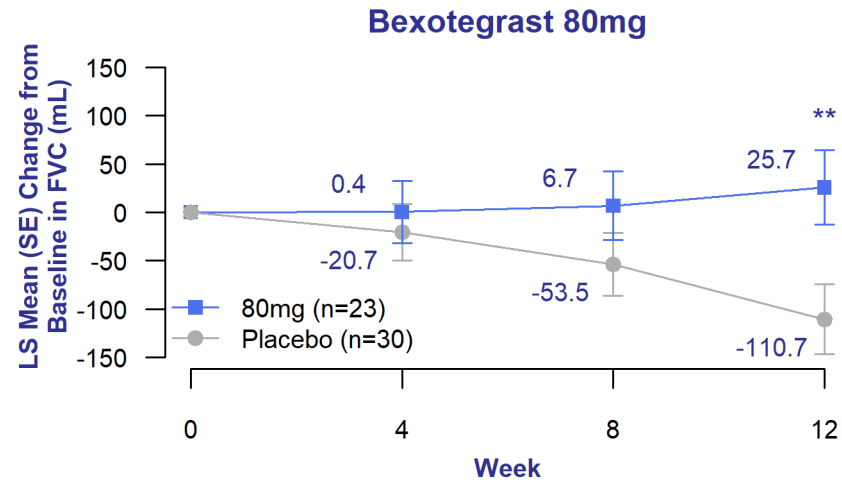
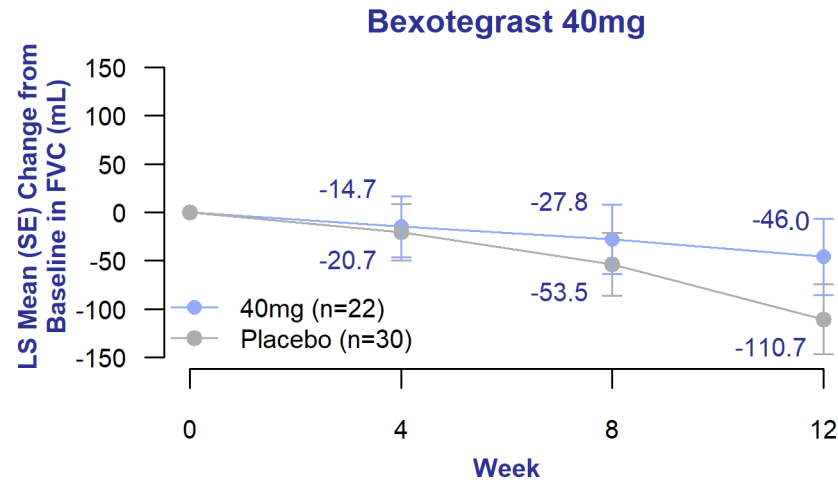
Adverse events coded using MedDRA version 24.0

TEAE is defined as any AE starting (or worsening) on or after the date of first dose

AE, adverse event; TEAE, treatment-emergent AE

FVC Change from Baseline over 12 Weeks

mITT Population

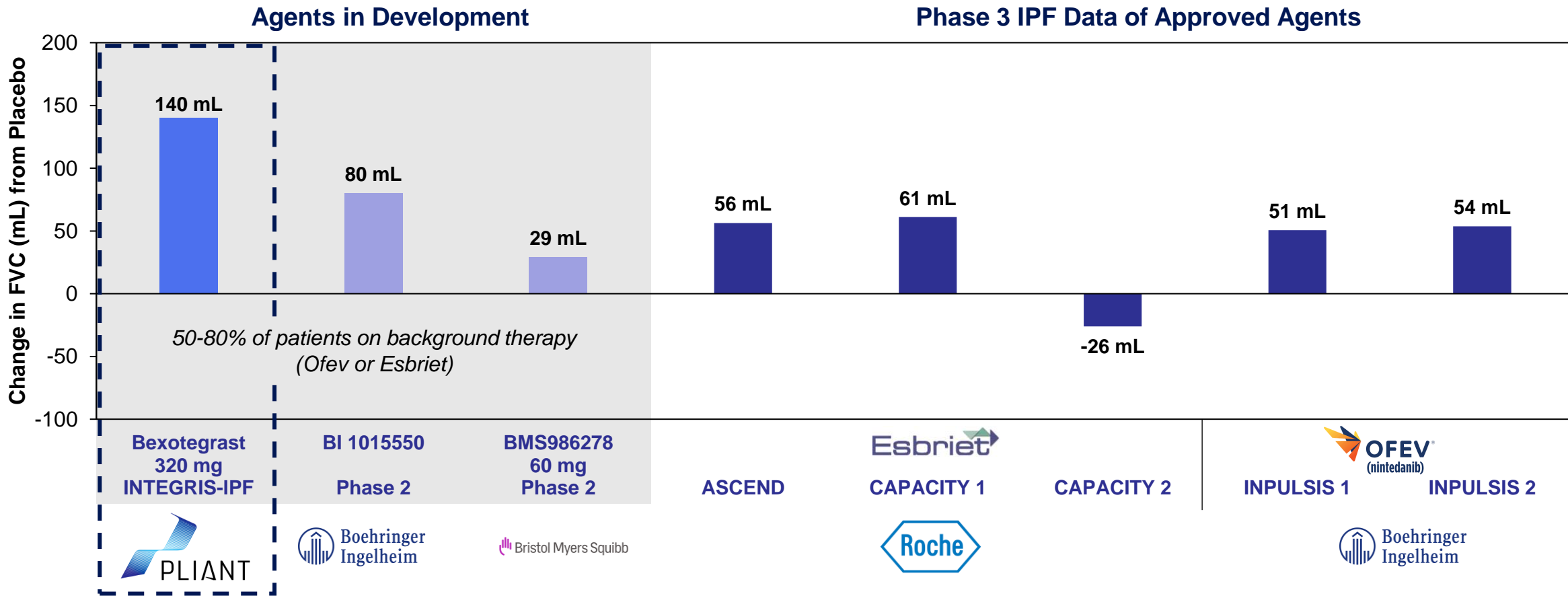


* p < 0.05 vs placebo
 ** p < 0.01 vs placebo

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.

Absolute Change from Baseline Versus Placebo at 12-Weeks for Approved and Select Investigational Agents

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

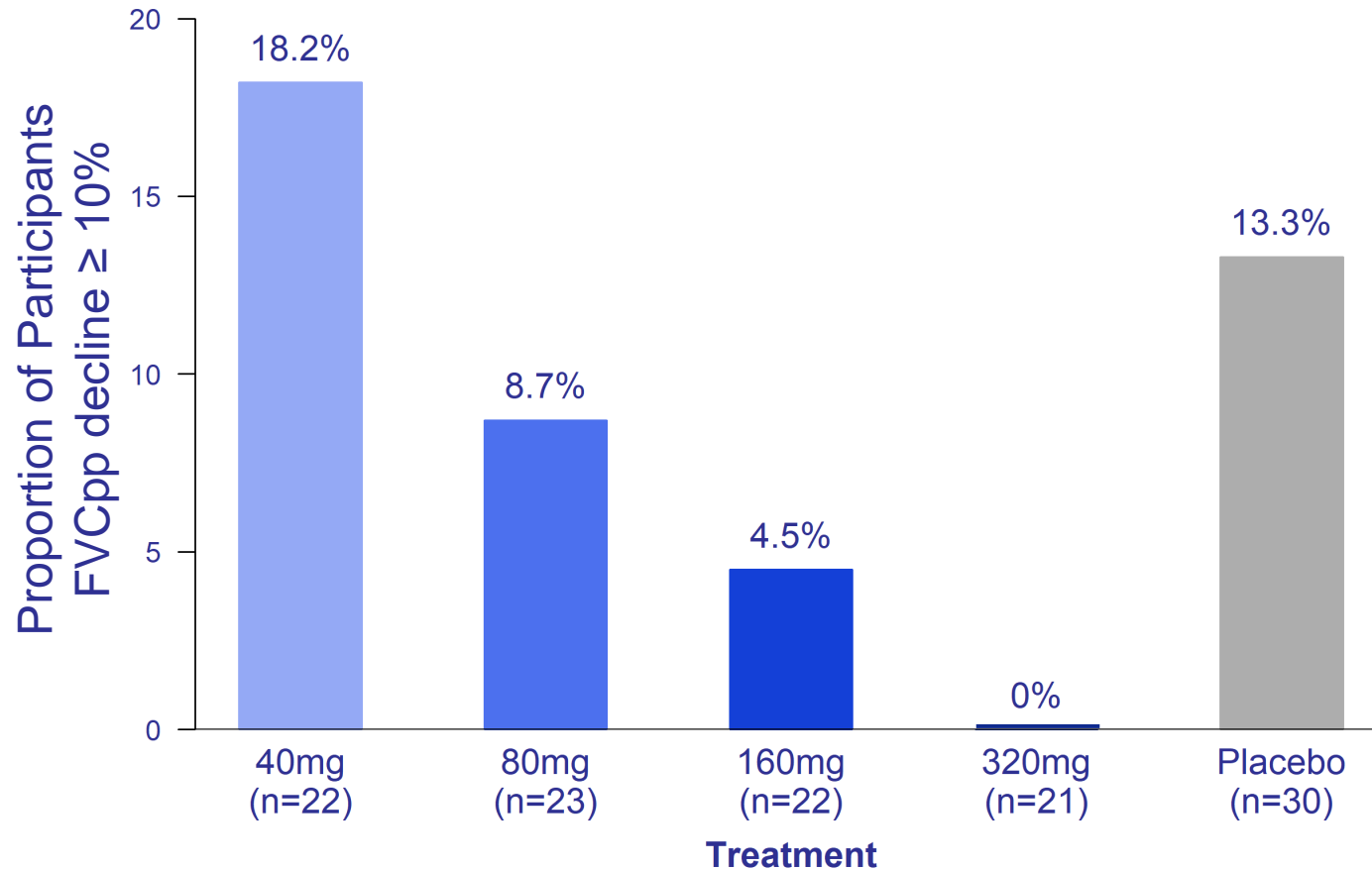


Bexotegrast, BI-1015550 and BMS-986278 from Phase 2 trials. Graphic is not meant to represent a head-to-head study. Comparing the results from different trials may be unreliable due to different protocol designs, trial designs, patient selection and populations, number of patients, trial endpoints, trial 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 $\geq 10\%$ mITT Population

mITT Population at 12 Weeks



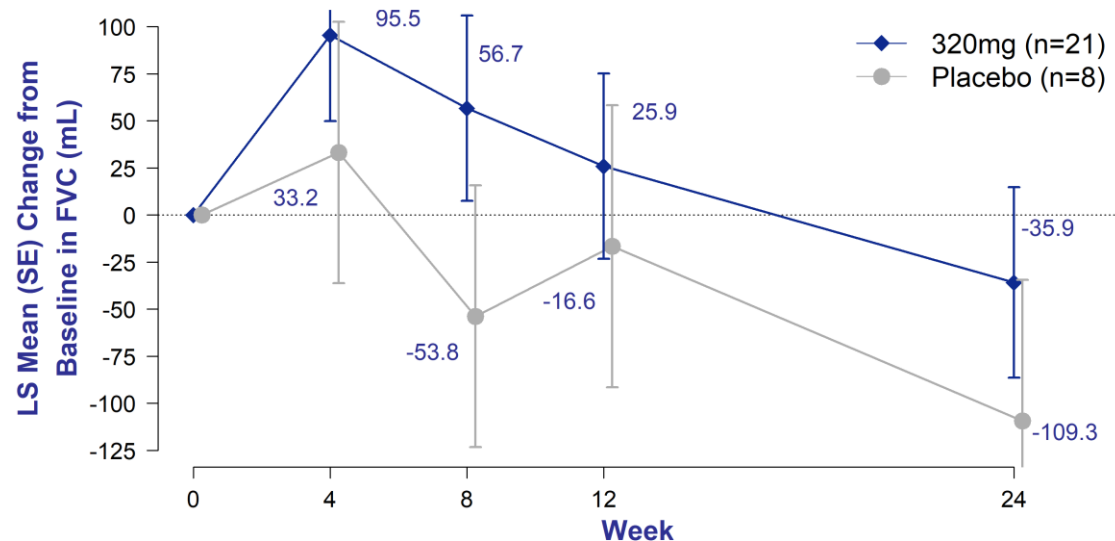
mITT Population at 24 Weeks

Bexotegrist reduced the decline in FVCpp by 68% relative to placebo from Baseline at Week 24

FVC Change from Baseline over 24 Weeks

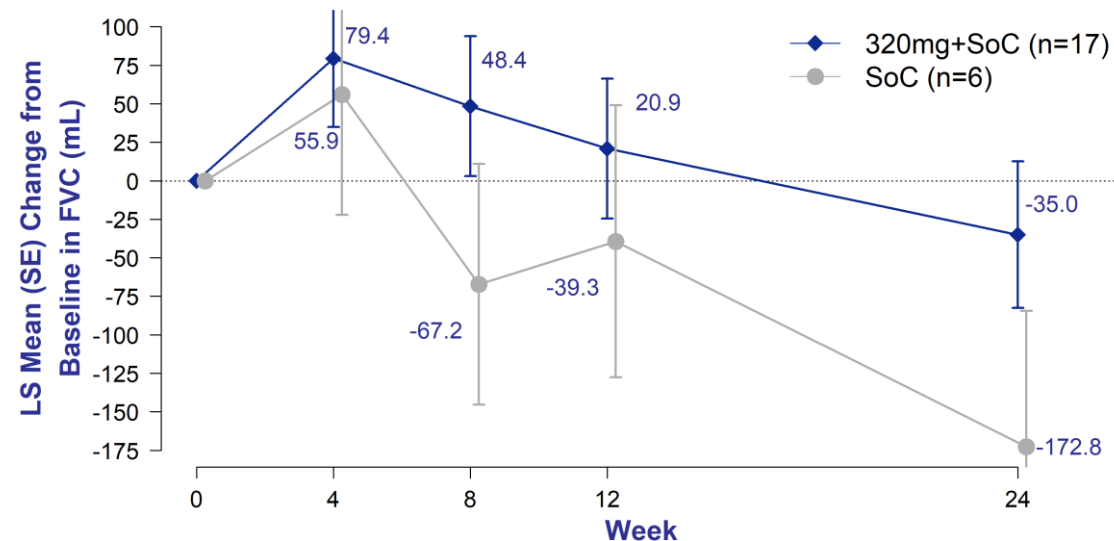
ITT Population vs. SoC Sub-Group

ITT Population



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

Standard-of-Care Sub-Group



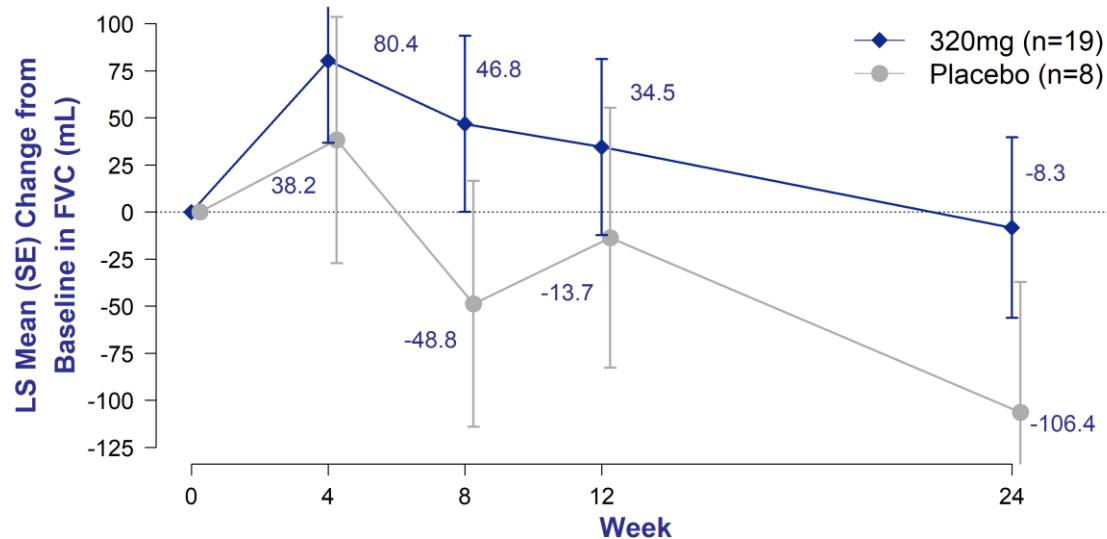
Bexotegrist + SOC reduced FVC decline by 80% relative to SOC alone at Week 24

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

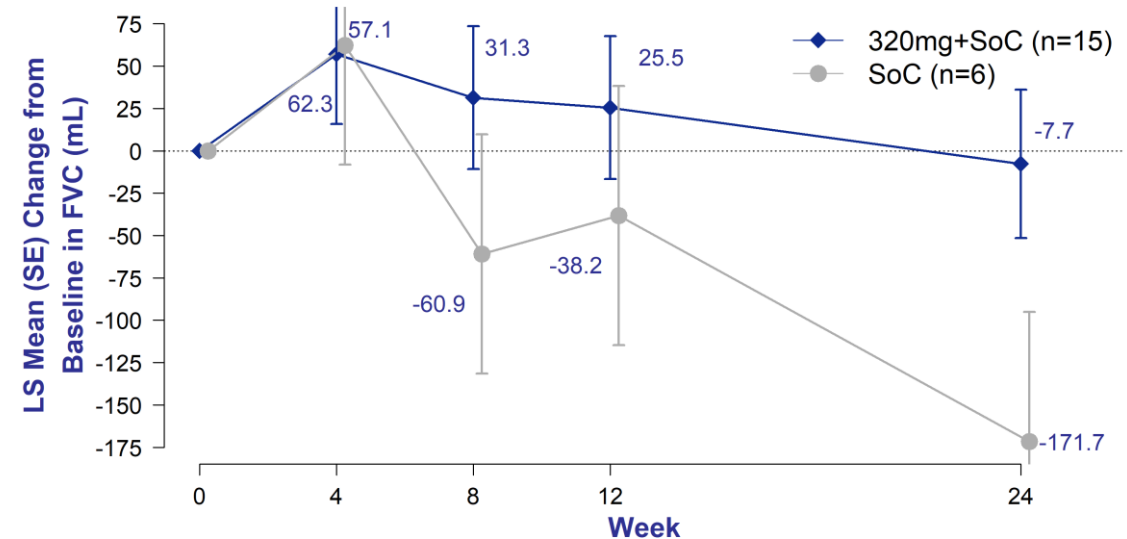
Trimmed Mean Sensitivity Analysis¹

ITT Population



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

Standard-of-Care Sub-Group

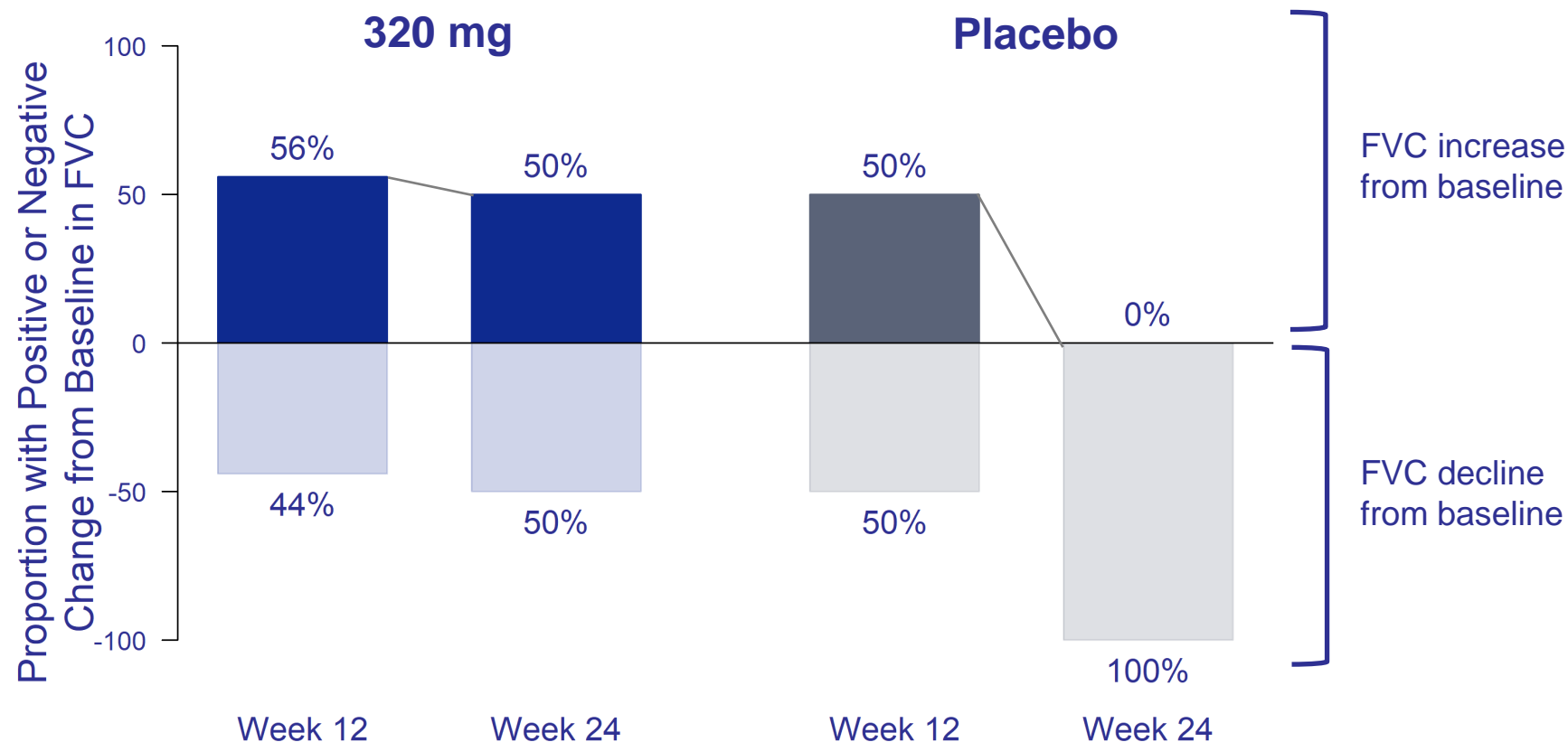


Bexotegast + SOC reduced FVC decline by 96% relative to SOC alone at Week 24

¹ – Trimmed Mean Sensitivity Analysis excludes the two bexotegast-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)

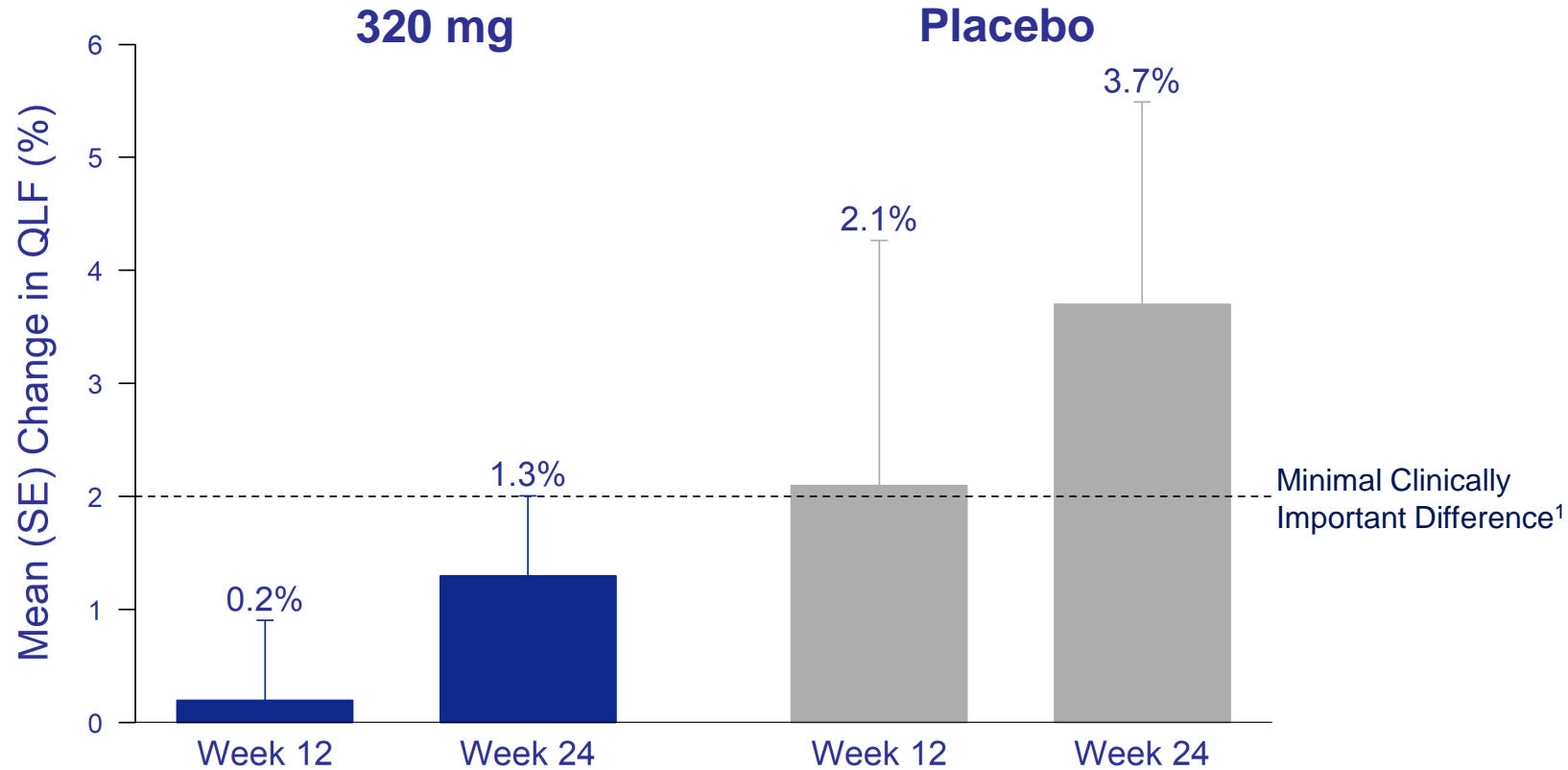
Bexotegraft Demonstrated Durable Increase in FVC at Week 24

ITT Population



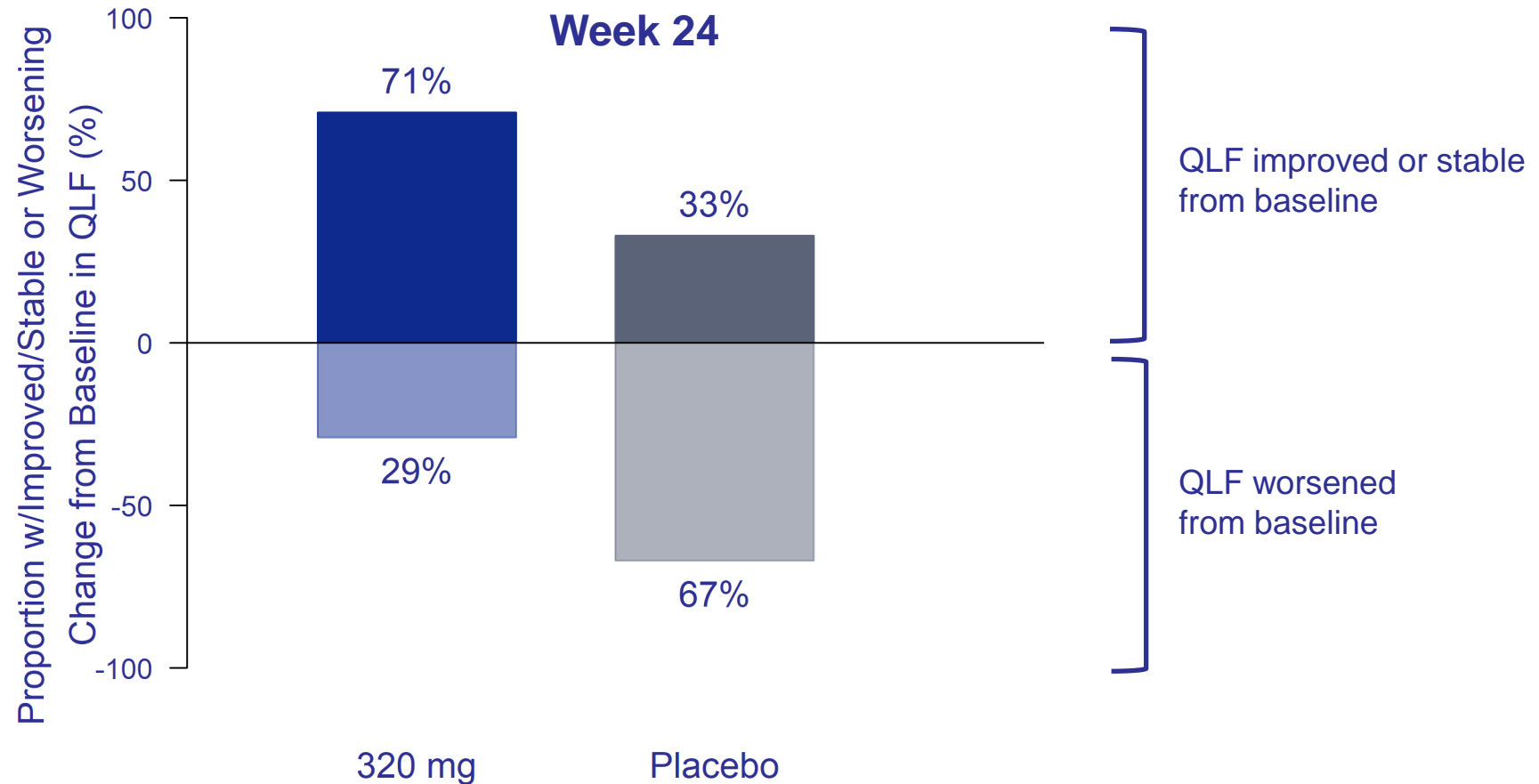
89% of bexotegraft-treated participants with FVC increase at Week 12 maintained an increase at Week 24

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



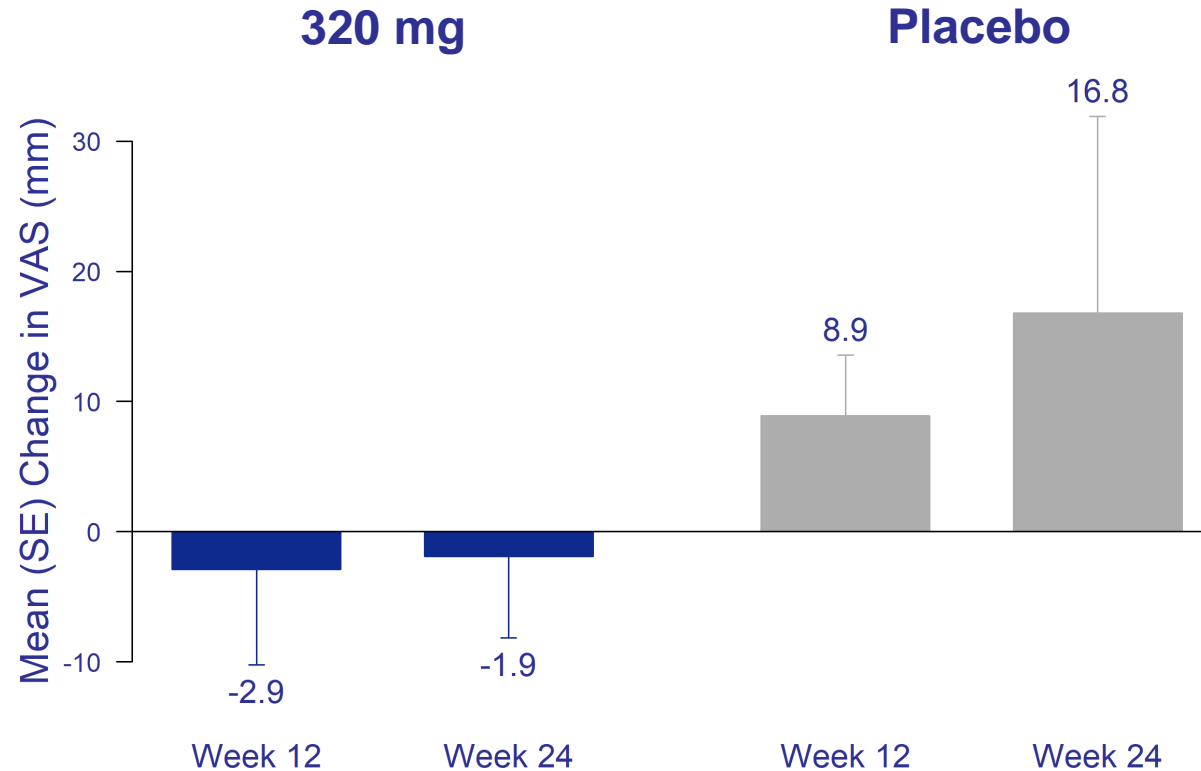
Bexotegrast group demonstrated stabilization of fibrosis, in contrast to placebo group which showed clinically meaningful progression at Weeks 12 and 24

More Patients on Bexotegrist Showed Stabilization of Fibrosis at Week 24 Per CT Protocol Population



At Week 24, bexotegrist-treated participants were more than twice as likely to show stabilization or improvement of fibrosis relative to placebo

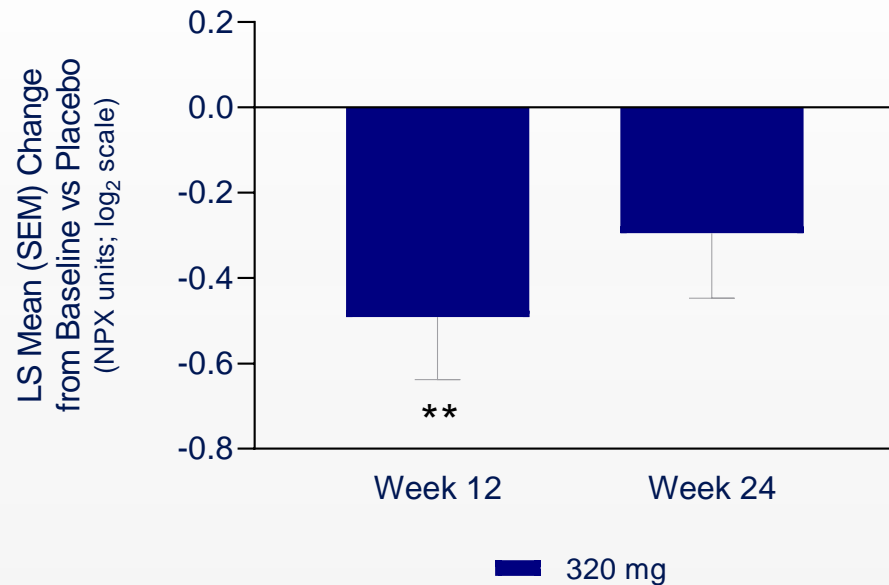
Cough Severity Visual Analog Scale (VAS) Change from Baseline ITT Population



Chronic cough in IPF is an independent predictor of disease progression and mortality¹

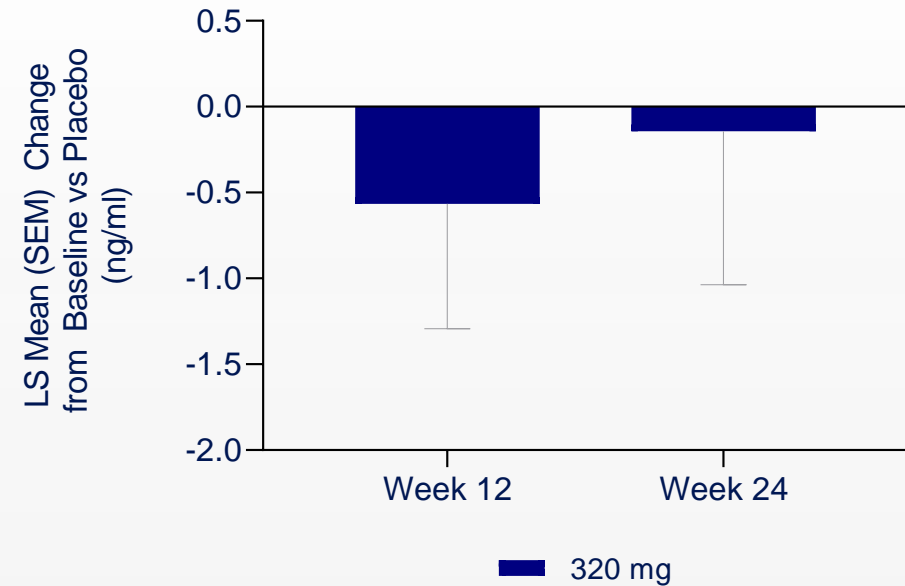
Bexotegrast Reduced Circulating Biomarkers ITGB6 and PRO-C3 Relative to Placebo

Plasma Integrin beta-6 (ITGB6)



** p < 0.01 vs placebo

Serum PRO-C3 Type III collagen synthesis neopeptide



Elevated integrin beta-6 plasma levels shown to be associated with ILD progression over 12 months¹

PRO-C3 shown to be elevated in patients with IPF and associated with progressive disease²

BEACON-IPF Phase 2b Study Design

Trial Initiated Mid-Year 2023

Randomization 1:1:1

Placebo (n=89)

bexotegrast 160 mg (n=89)

bexotegrast 320 mg (n=89)

Stratified for (a) the use of nintedanib or pirfenidone and
(b) GAP index 1 or GAP index 2/3 at study entry

SCREENING

END OF STUDY

Day -28

Baseline
Day 1

Last dose
Week 52

Week 54

PRIMARY ENDPOINT

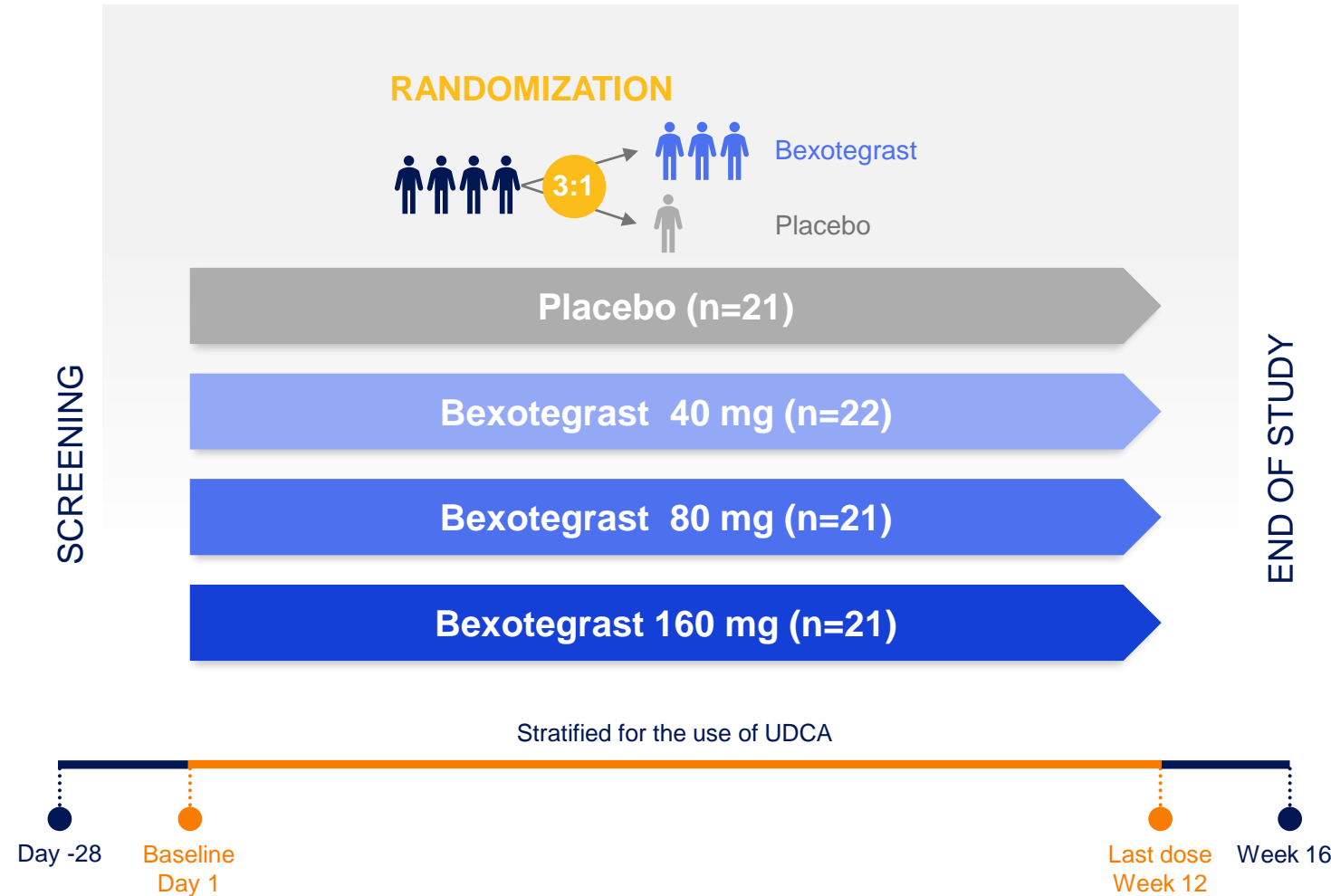
- Change from baseline in absolute FVC (mL) at Week 52

SECONDARY ENDPOINTS

- Time to disease progression ($\geq 10\%$ absolute decline from baseline in FVCpp, respiratory-related hospitalization, or all-cause mortality)
- Change from baseline in absolute FVC (mL) in participants on and off background therapy
- Change from baseline in Living with Pulmonary Fibrosis total score at Week 52
- Safety and Tolerability

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:
 - $\text{ELF} \geq 7.7$
 - $\text{TE} \geq 8$ but ≤ 14.4 kPa
 - $\text{MRE} \geq 2.4$ but ≤ 4.9 kPa
 - Historical biopsy

INTEGRIS-PSC – Key Findings

Bexotegrast was Well Tolerated Over 12 Weeks of Treatment in Participants with PSC

- Adverse events rates were comparable to placebo with all drug-related TEAEs mild or moderate in severity
- Low rate of discontinuation due to AEs and no treatment-related severe or serious AEs
- Patients with IBD experienced no clinically-relevant changes in IBD symptoms
- Bexotegrast total and unbound plasma concentrations increased with dose

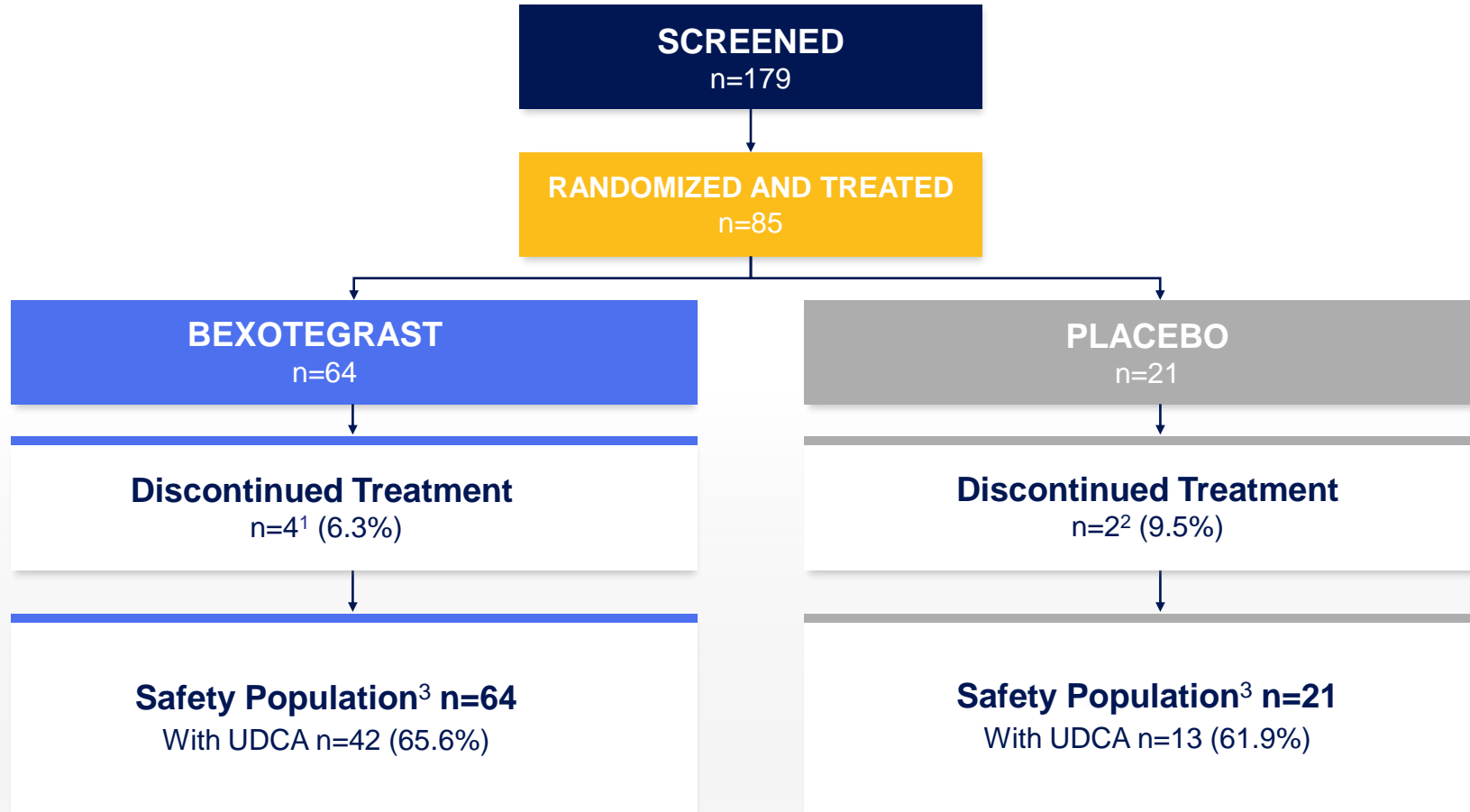
Bexotegrast Demonstrated Antifibrotic Activity in a PSC Population with Suspected Moderate to Severe Liver Fibrosis

- All doses reduced ELF scores relative to placebo with a statistically significant difference for 160 mg
 - 160 mg achieved statistical significance at Week 12 across all components of the ELF score (TIMP-1, PIIINP, HA)
- All doses reduced collagen synthesis (PRO-C3) relative to placebo with statistical significance for the 160 mg dose

Additional Key Supportive Findings

- MRI imaging analysis suggests improved hepatocyte function and bile flow relative to placebo at Week 12
- Liver biochemistry markers, including ALP, were improved relative to placebo at Week 12
- Dose dependent reduction in itch, with statistical significance at the 160 mg dose relative to placebo at Week 12

INTEGRIS-PSC – Participant Disposition



INTEGRIS-PSC – Baseline Demographics

Characteristic	Bexotegraft 40mg (n=24)*	Bexotegraft 80mg (n=20)*	Bexotegraft 160mg (n=20)*	Bexotegraft All (n=64)	Placebo (n=21)
Male sex, n (%)	17 (70.8)	16 (80.0)	14 (70.0)	47 (73.4)	17 (81.0)
Age (yr), mean (SD)	46.9 (15.06)	40.5 (15.32)	45.1 (12.65)	44.3 (14.46)	45.6 (12.48)
Race, n (%)					
White	20 (83.3)	16 (80.0)	18 (90.0)	54 (84.4)	18 (85.7)
Black	2 (8.3)	2 (10.0)	1 (5.0)	5 (7.8)	1 (4.8)
Asian	2 (8.3)	1 (5.0)	1 (5.0)	4 (6.3)	1 (4.8)
Other / Not Reported / Unknown	0	1 (5.0)	0	1 (1.6)	1 (4.8)
Time since diagnosis of PSC (yr), mean (SD)	11.1 (8.15)	8.3 (7.97)	7.8 (6.78)	9.2 (7.72)	10.0 (7.95)
Concomitant UDCA use, n (%)	14 (58.3)	15 (75.0)	13 (65.0)	42 (65.6)	13 (61.9)
IBD, n (%)	18 (75.0)	12 (60.0)	11 (55.0)	41 (64.0)	12 (57.1)
Ulcerative colitis	11 (45.8)	6 (30.0)	7 (35.0)	24 (37.5)	7 (33.3)
Crohn's disease	6 (25.0)	4 (20.0)	2 (10.0)	12 (18.8)	4 (19.0)
IBD Other	3 (12.5)	2 (10.0)	2 (10.0)	7 (10.9)	1 (4.8)
Partial Mayo Score, mean (SD)	0.7 (1.08)	1.6 (2.54)	1.1 (1.27)	1.1 (1.70)	0.7 (1.56)
Itch NRS, mean (SD)	1.8 (2.54)	2.1 (2.63)	1.4 (1.50)	1.7 (2.27)	1.1 (1.58)

Duration since diagnosis at screening is calculated from the first reported date for preferred terms of PSC.
 Partial Mayo score only reported for those with active IBD at Baseline
 BMI = Body Mass Index; IBD= inflammatory bowel diseases; NRS= numerical Rating scale;
 SD = Standard deviation

* Two participants (80 mg and 160mg) were dispensed incorrect number of tablets and provided incorrect dosing instructions for the full treatment period due to an error at a single site. The participants' daily dose corresponded to a ≤40 mg dose. These 2 participants are grouped in the 40 mg dose group for all summaries.

INTEGRIS-PSC – Baseline Disease Activity Markers

	Bexotegrast 40mg (n=24)	Bexotegrast 80mg (n=20)	Bexotegrast 160mg (n=20)	Bexotegrast All (n=64)	Placebo (n=21)
Serum Liver tests, mean (SD)					
Alkaline phosphatase (U/L)	315.1 (140.26)	199.2 (81.03)	273.8 (165.63)	266.0 (140.68)	259.7 (185.76)
Alanine aminotransferase (U/L)	91.5 (62.08)	67.6 (63.15)	98.4 (73.11)	86.2 (66.25)	67.5 (49.19)
Aspartate aminotransferase (U/L)	67.2 (49.34)	46.4 (30.12)	69.0 (39.62)	61.3 (41.70)	48.8 (30.57)
Total Bilirubin (mg/dL)	0.66 (0.307)	0.79 (0.493)	0.88 (0.396)	0.77 (0.405)	0.84 (0.357)
Direct bilirubin (mg/dL)	0.27 (0.164)	0.26 (0.188)	0.31 (0.166)	0.28 (0.171)	0.30 (0.189)
Markers of Fibrosis, mean (SD)					
ELF Score	9.6 (0.77)	9.2 (1.01)	9.4 (0.79)	9.4 (0.86)	9.2 (1.08)
PRO-C3 (ng/mL)	49.96 (13.844)	48.84 (42.790)	46.12 (11.670)	48.39 (25.904)	43.24 (10.828)
Transient Elastography (kPa), mean (SD)	10.1 (2.62)	9.1 (2.99)	8.2 (3.16)	9.2 (2.98)	8.5 (2.86)

INTEGRIS-PSC – Safety Summary

AE, n (%) of Participants Reporting	Bexotegast 40mg (n=24)	Bexotegast 80mg (n=20)	Bexotegast 160mg (n=20)	Bexotegast All (n=64)	Placebo (n=21)
TEAE	10 (41.7)	16 (80.0)	15 (75.0)	41 (64.1)	16 (76.2)
Related to study drug	1 (4.2)	6 (30.0)	4 (20.0)	11 (17.2)	7 (33.3)
Serious TEAE	1 (4.2)	1 (5.0)	0	2 (3.1)	0
Related to study drug	0	0	0	0	0
TEAE of CTCAE Grade 3 or Higher	1 (4.2)	2 (10.0)	1 (5.0)	4 (6.3)	3 (14.3)
Related to study drug	0	0	0	0	2 (9.5)
TEAE Leading to Interruption of Study Drug	1 (4.2) ¹	0	0	1 (1.6) ¹	0
TEAE Leading to Withdrawal of Study Drug	1 (4.2) ²	1 (5.0) ³	1 (5.0) ⁴	3 (4.7) ^{2,3,4}	2 (9.5) ^{5,6}
TEAE Leading to Early Termination from Study	0	0	1 (5.0) ⁴	1 (1.6) ⁴	0
TEAE Leading to Death	0	0	0	0	0

1 – chills/fatigue/nausea/pyrexia/vomiting; 2 – COVID-19; 3 –Hepatic enzyme increase/Pruritus ; 4 – Fatigue; 5- cardiomegaly/dyspnoea/malaise; 6 - headache

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.

INTEGRIS-PSC – Most Frequent TEAEs

TEAE, n (%) of Participants Reporting	Bexotegrast 40mg (n=24)	Bexotegrast 80mg (n=20)	Bexotegrast 160mg (n=20)	Bexotegrast All (n=64)	Placebo (n=21)
Most frequent TEAEs (n ≥ 3 in at least one arm)					
Pruritus ¹	2 (8.3)	4 (20.0)	3 (15.0)	9 (14.1)	5 (23.8)
Fatigue	3 (12.5)	2 (10.0)	4 (20.0)	9 (14.1)	2 (9.5)
Headache	1 (4.2)	2 (10.0)	3 (15.0)	6 (9.4)	4 (19.0)
Nausea	1 (4.2)	2 (10.0)	3 (15.0)	6 (9.4)	0
COVID-19	2 (8.3)	1 (5.0)	0	3 (4.7)	3 (14.3)
Frequent bowel movements	0	3 (15.0)	0	3 (4.7)	3 (14.3)
Cholangitis	0	1 (5.0)	1 (5.0)	2 (3.1)	3 (14.3)

1- Pruritus includes preferred terms for pruritus and cholestatic pruritus

TEAE = Treatment Emergent Adverse Event; Adverse events coded using MedDRA version 24.0.
TEAE is defined as any AE starting (or worsening) on or after the date of first dose

INTEGRIS-PSC – Serious Adverse Events

No SAEs were Related to Study Drug

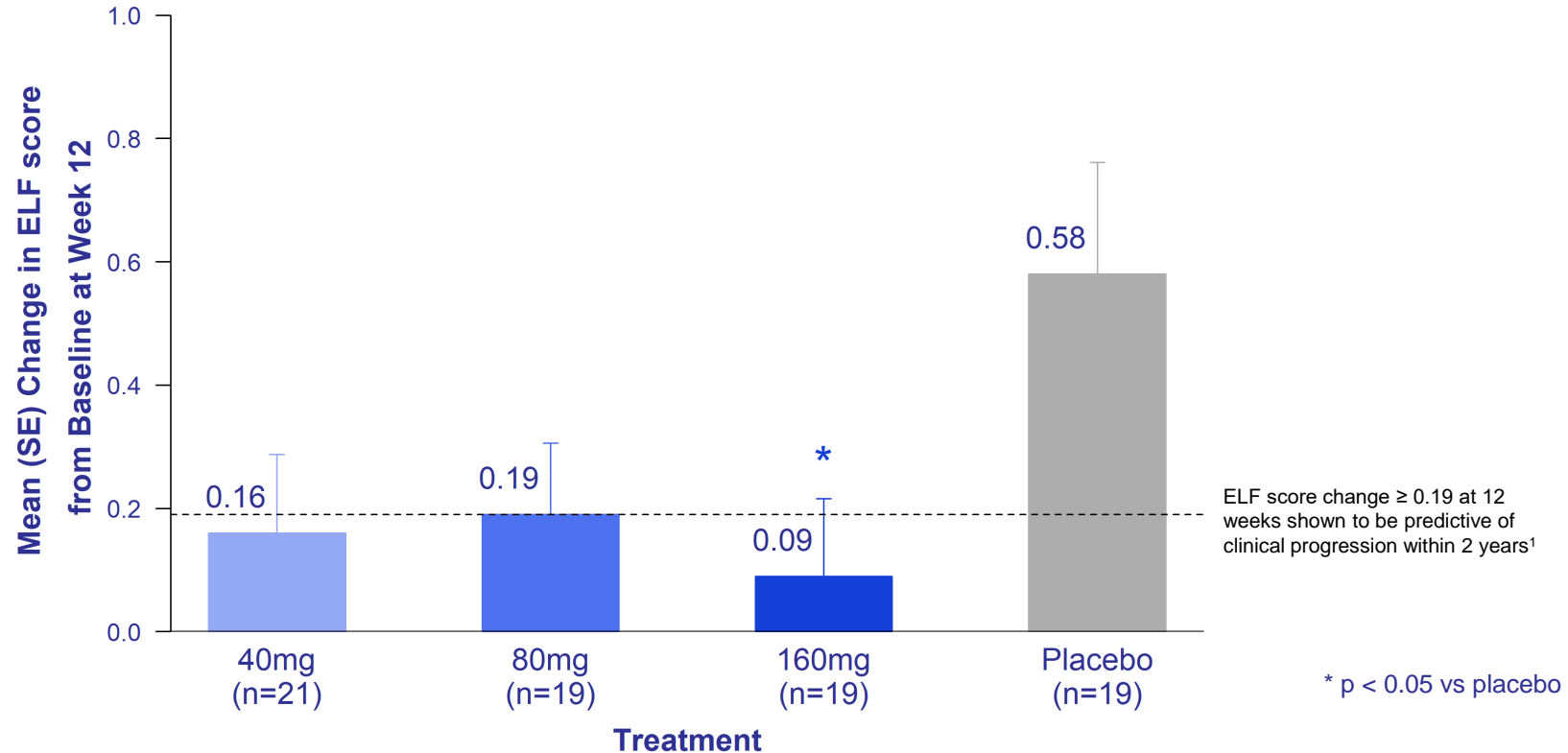
Treatment Group	SAE Preferred Term	Standard Toxicity Grade	Treatment Related	Any alternative cause or confounding factors?	Action Taken	Outcome
40 mg	Cholecystitis / Abdominal pain / Pancreatitis	Grade 3 (all) (Severe)	No	ERCP (post-procedure)	Hospitalization; Event in follow-up Period (3-4 weeks post last dose)	Recovered / Resolved
80 mg	Cholangitis	Grade 3 (Severe)	No	No ¹	Hospitalization; Dose not changed	Recovered / Resolved

INTEGRIS-PSC – TEAEs Leading to Withdrawal of Study Drug

Treatment Group	AE Preferred Term (s)	Standard Toxicity Grade	Treatment Related	Any alternative cause or confounding factors?	Action Taken	Outcome
40 mg	COVID-19 / Nasal congestion / Dyspnoea	Grade 1 (Mild)	No	COVID-19	Drug withdrawn	Recovered / Resolved
80 mg	Hepatic enzyme increased / Pruritus	Grade 1 (Mild)	Yes	Variation in PSC / Aggravation of PSC	Drug withdrawn	Recovered / Resolved
160 mg	Fatigue	Grade 2 (Moderate)	Yes	No	Drug withdrawn	Recovered / Resolved
Placebo	Dyspnoea / Malaise / Cardiomegaly	Grade 2 (Moderate) / Grade 3 (Severe) / Grade 1 (Mild)	Yes	No	Drug withdrawn	Recovered / Resolved
Placebo	Headache	Grade 1 (Mild)	Yes	Fasting before drug administration	Drug withdrawn	Recovered / Resolved

ELF Score – Change from Baseline at Week 12

Safety Population

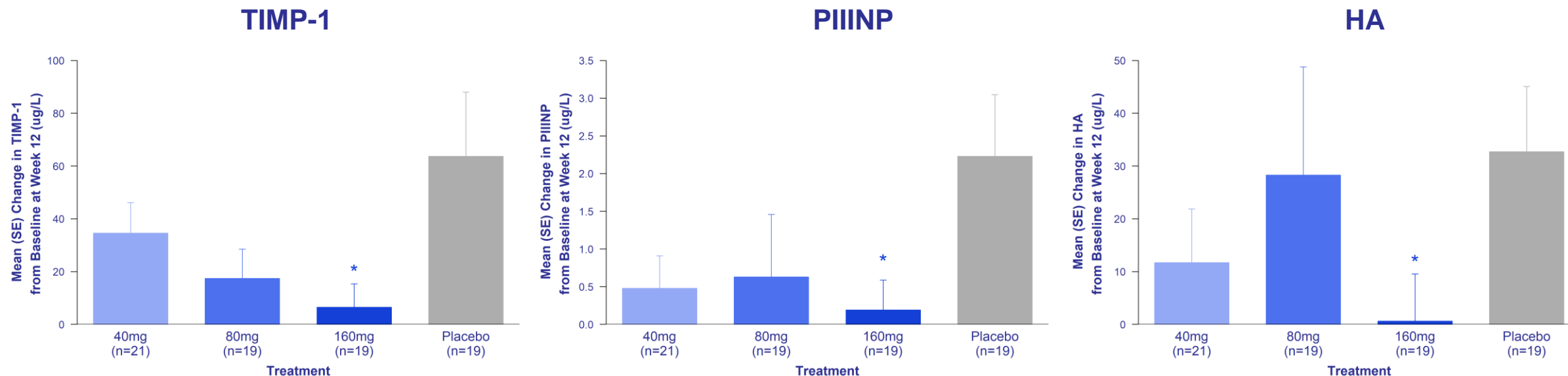


**Bexotegrast reduced ELF relative to placebo at all doses
with statistical significance at the 160 mg dose**

160 mg dose demonstrated an 84% reduction relative to placebo

ELF Score Components - Change from Baseline at Week 12

Safety Population

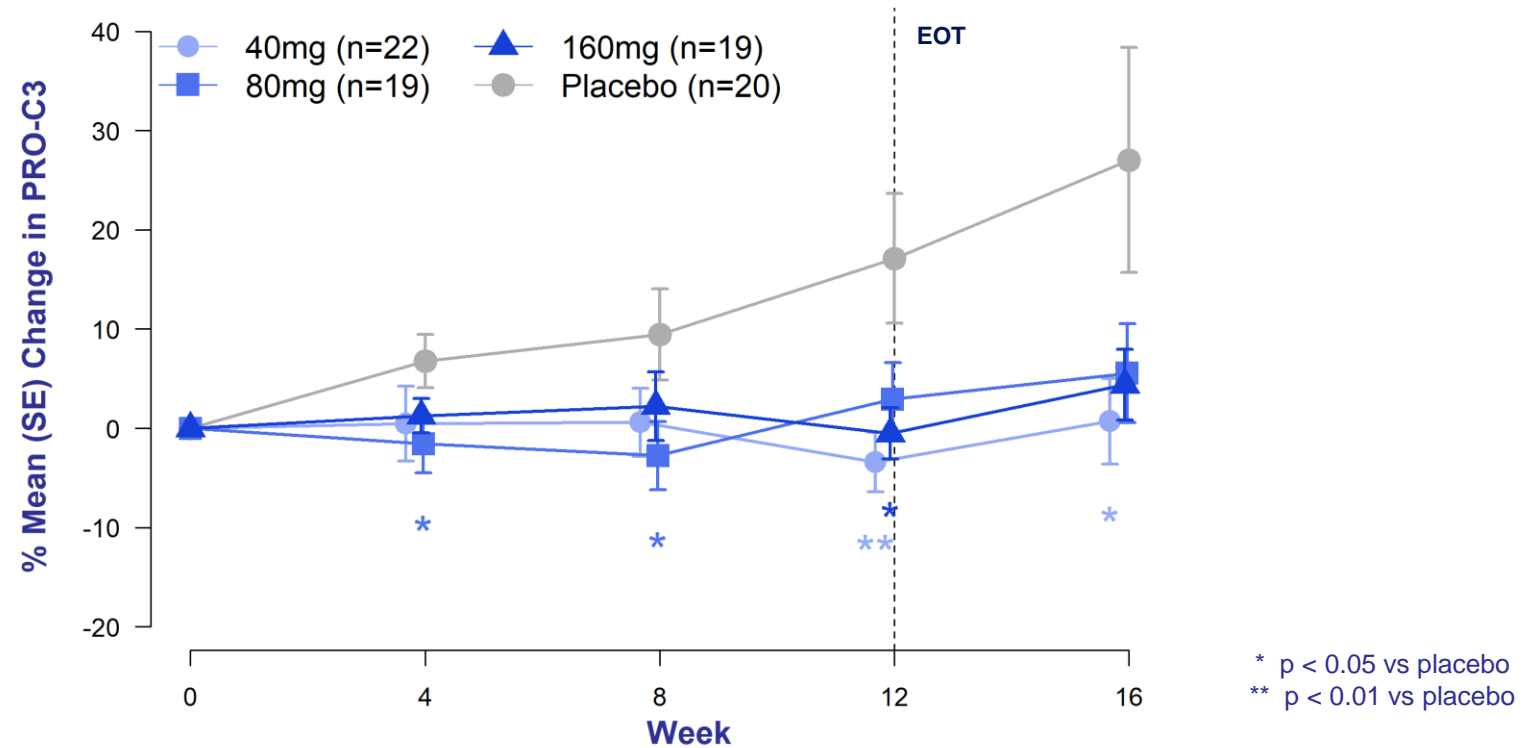


* p < 0.05 vs placebo

Bexotegast 160 mg demonstrated statistically significant reductions of all three ELF score components relative to placebo

PRO-C3 - Percent Change from Baseline

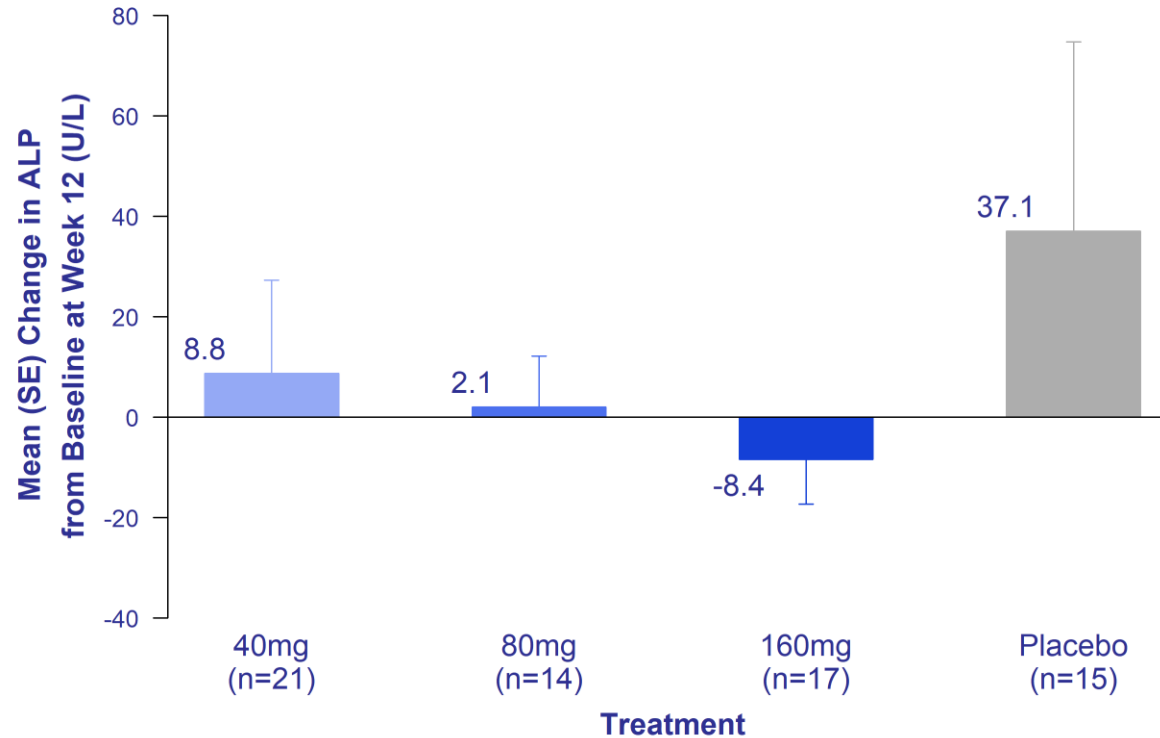
Safety Population



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

ALP – Change from Baseline at Week 12

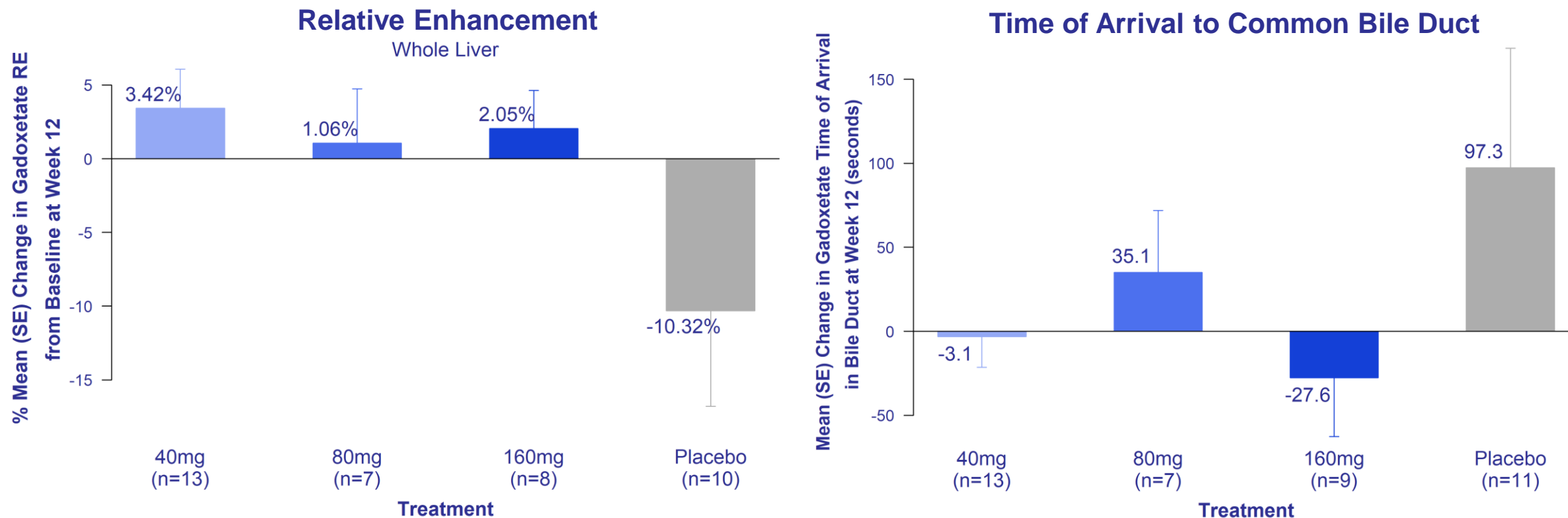
Safety Population – Participants with ALP > ULN at Baseline



Bexotegrist showed a dose-dependent trend of reduction in ALP relative to placebo

MRI Parameters – Change from Baseline at Week 12

Sub Study Safety Population

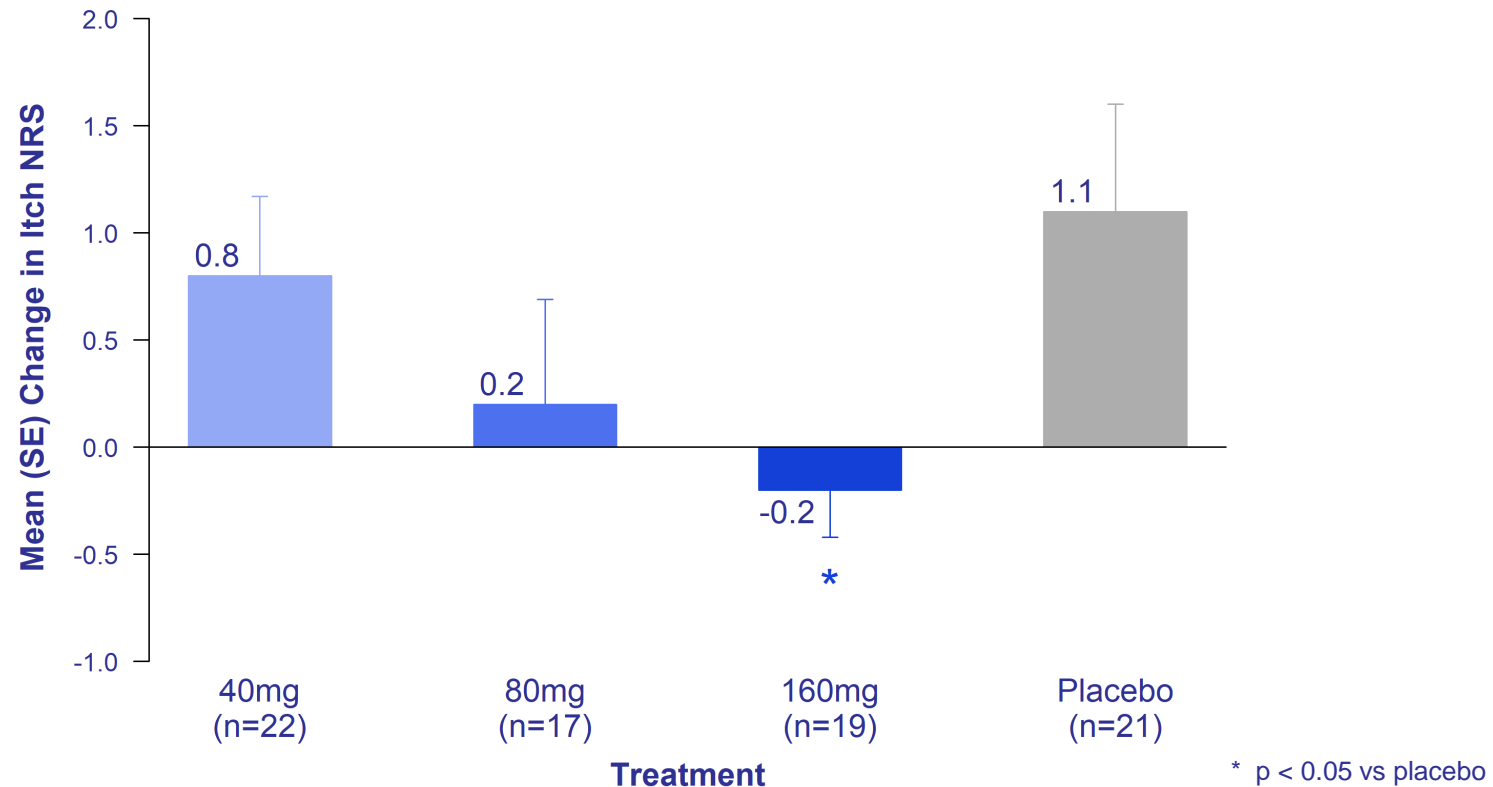


All doses showed an increase in relative enhancement compared to a reduction in placebo, suggesting improved hepatocyte function

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

Itch Numerical Rating Scale – Change from Baseline at Week 12

Safety Population



Bexotegast showed dose-dependent reductions in itch relative to placebo with statistical significance for the 160 mg dose

INTEGRIS-PSC – Summary and Next Steps



Bexotegrast demonstrated a favorable safety and tolerability profile in a PSC patient population with suspected moderate to severe liver fibrosis



Bexotegrast showed antifibrotic activity (ELF and PRO-C3) with statistically significant differences relative to placebo observed at Week 12 for the 160 mg dose



Liver biochemistry and imaging parameters were improved relative to placebo at Week 12



Dose dependent changes in Itch Numerical Rating Scale at Week 12 with statistical significance for the 160 mg dose



320 mg 12-week data expected in Q1 2024 with 24-week 320 mg data mid 2024

Bexotegrast – A Potentially Broadly Applicable Antifibrotic



Growing Evidence that Localized TGF- β Inhibition has Potential as Backbone Antifibrotic

- TGF- β inhibition is a potent antifibrotic pathway, but systemic toxicity has challenged drug development
- Tissue-specific TGF- β inhibition avoids systemic toxicity while maintaining the antifibrotic effect



Bexotegrast Continues to Demonstrate a Favorable Safety and Tolerability Profile

- Well tolerated in over 600 participants across multiple different patient populations
- No drug-related serious adverse events observed to date across all trials

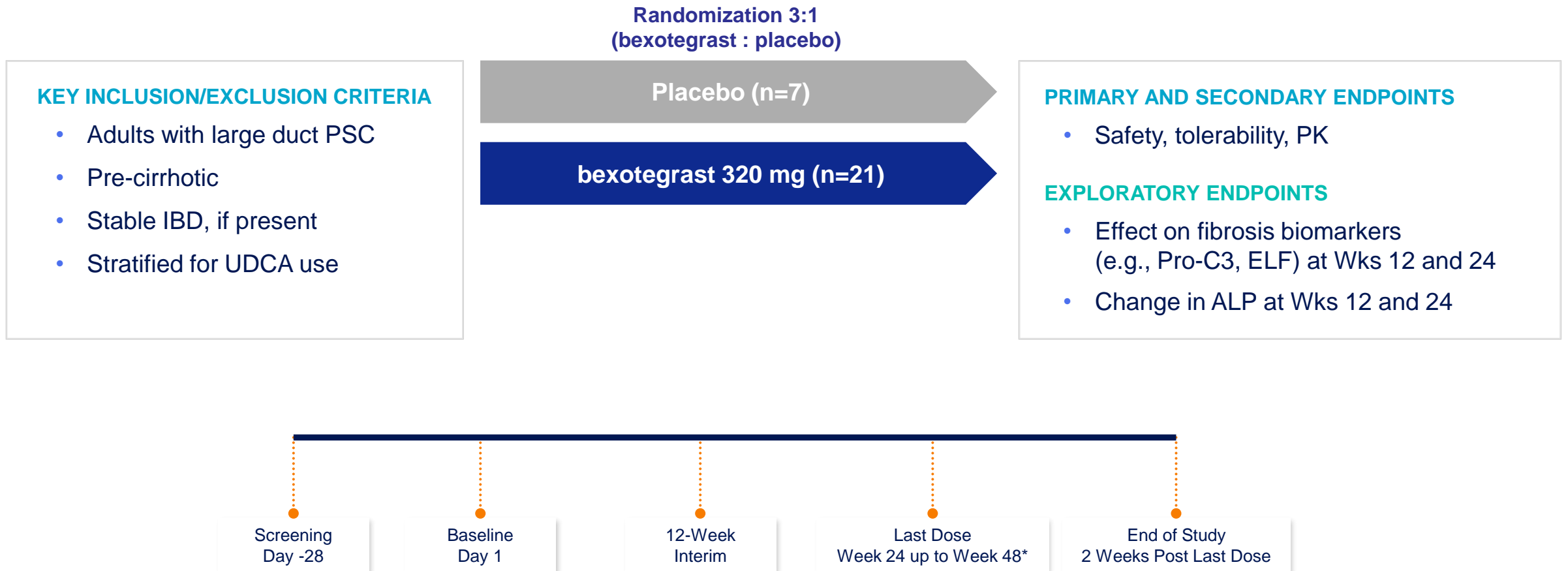


Bexotegrast Shows Potential to Treat Fibrotic Diseases Across Multiple Organ Systems

- Clear antifibrotic effect across multiple organ systems and indications
- Effect has been observed across multiple exploratory endpoints and biomarkers
- Bexotegrast is positioned to expand into multiple indications across pulmonary and liver fibrosis

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

Enrollment Complete; 12-Week Data Expected in First Quarter 2024; 24-Week Data in Mid-2024



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



PLN-101095

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

Reprogramming the Immunosuppressive Tumor Micro-Environment of Solid Tumors

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

$\alpha_v\beta_8$ Biology

$\alpha_v\beta_8$ regulates **TGF β** activation with a central role in immune suppression in cancer

Pharmacology

Highly selective inhibitor of $\alpha_v\beta_8$ & $\alpha_v\beta_1$

Supports human dose projections and **high target coverage**

Compelling rationale for $\alpha_v\beta_8$ combination therapy with **PD-(L)1**

Differentiation

Dual mode of action targeting T cells $\alpha_v\beta_8$ & Fibroblasts $\alpha_v\beta_1$

PO Dosing

Development Status

No major findings in 28D GLP rat & dog toxicology studies

IND submitted Q4 2022

FIH study initiated 2Q 2023

Substantial opportunity for an oral medicine **targeting TGF β activation** in ICI resistance **via $\alpha_v\beta_8$**

Pliant's Approach to Addressing Immune Checkpoint Inhibitor Resistance

Common Mechanisms of I-O Resistance

Tumor-specific IFN γ 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]

Pliant's Approach

Potently inhibit general immunosuppressive immune checkpoint to restore CD8 T cell IFN γ 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 increase resistance to exhaustion

Dual inhibition of $\alpha_v\beta_8$ & PD-1 exploit unexpected synergistic pathways leading to enhanced tumor killing⁶

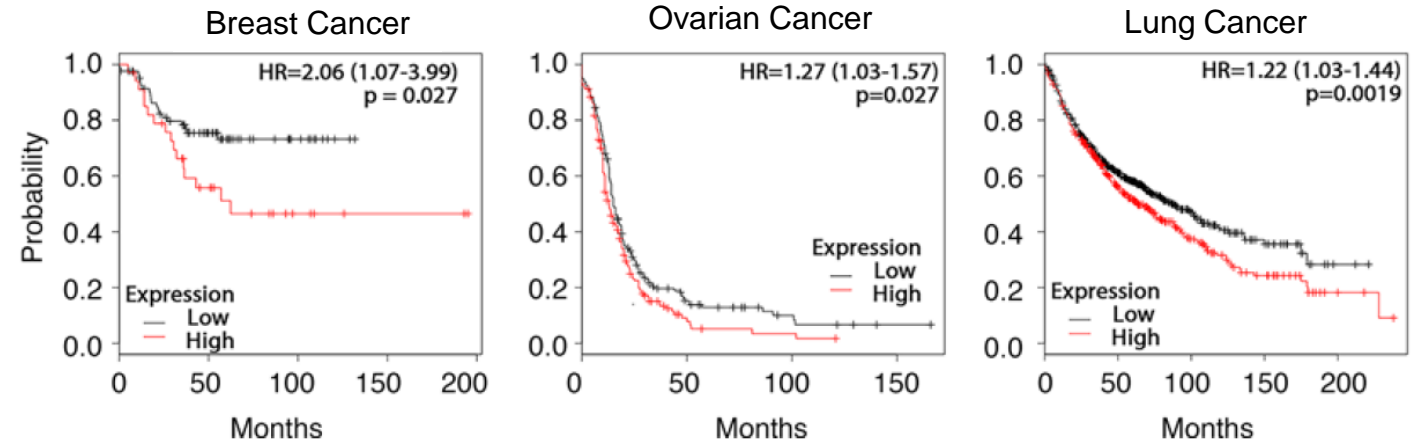
1- Thomas DA, et al. *Cancer Cell*. 2005 Nov;8(5):369-80. 2- Yang, ZZ. et al. *Leukemia*. 2014 28, 1872–1884. 3- Mariathasan, S. et al. 2018 *Nature* 554, 544–548.

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>

High ITGB8 on Tumor or T cells Has Poor Prognosis

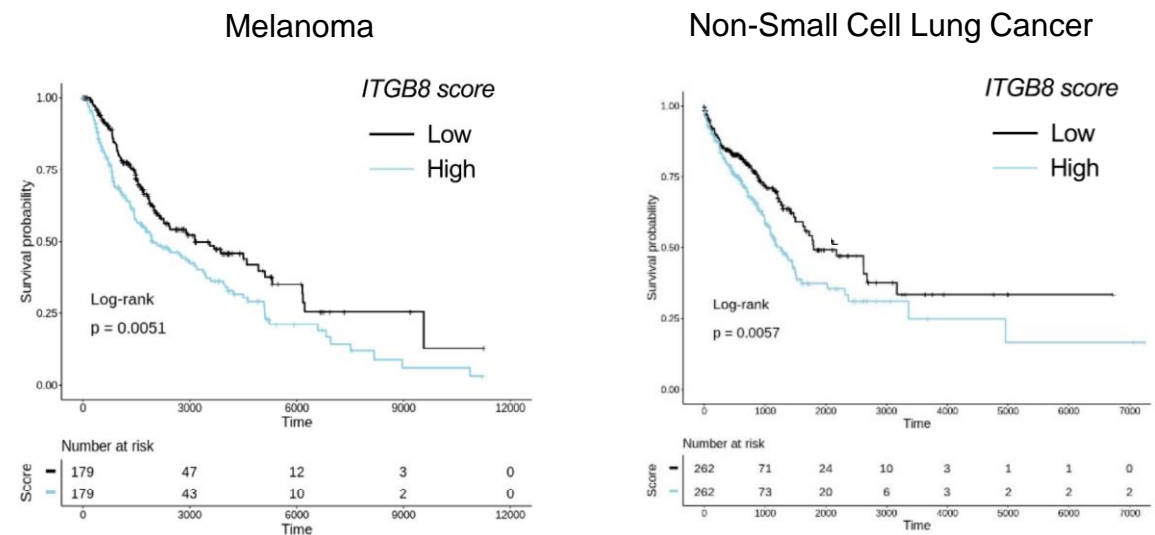
High ITGB8 expression on tumor cells has a worse clinical prognosis

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



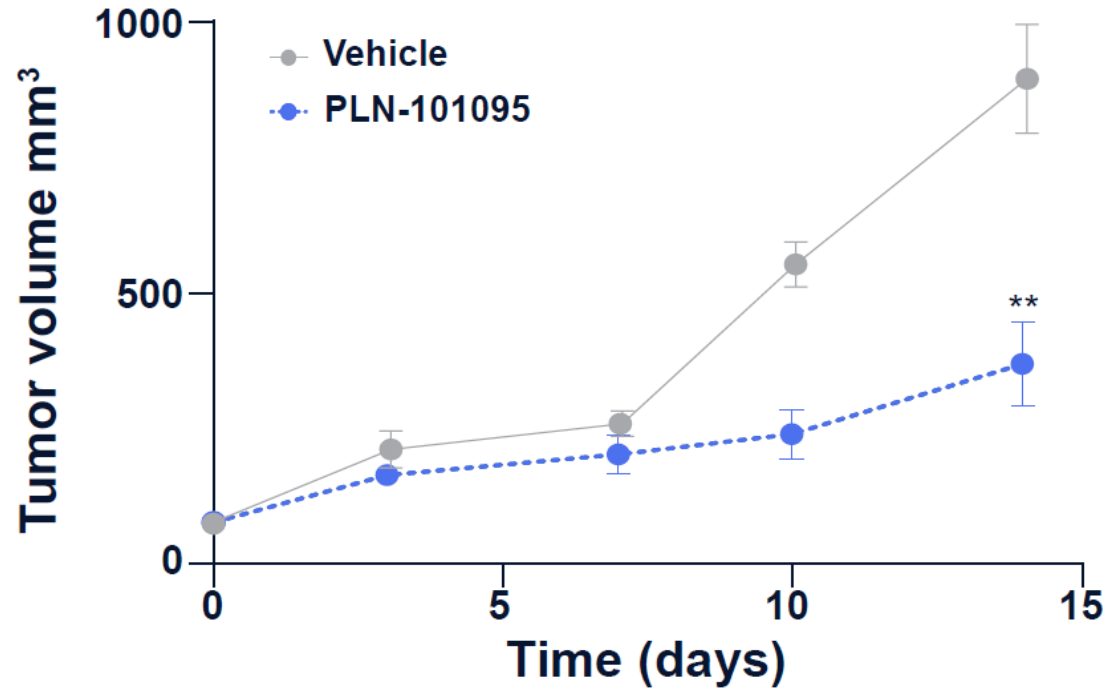
High ITGB8 score on infiltrating T cells correlates with worse prognosis

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

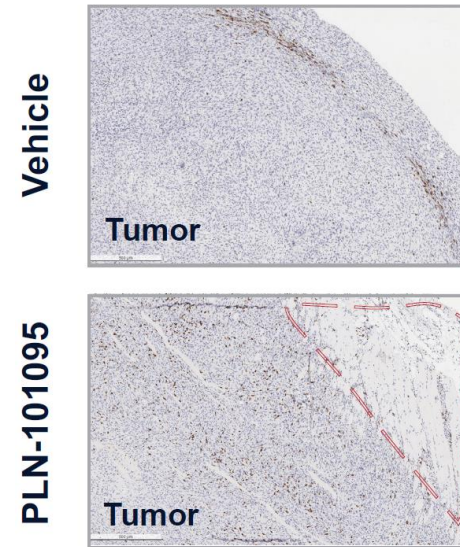


PLN-101095 Inhibited Tumor Growth and Promoted T cell Infiltration in the EMT6 Model

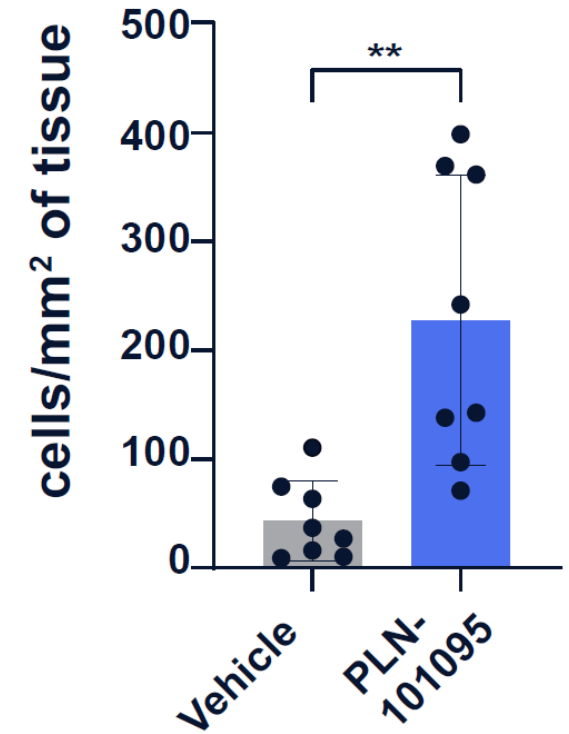
Tumor Growth Inhibition in EMT6 Tumors



CD8⁺ T Cells

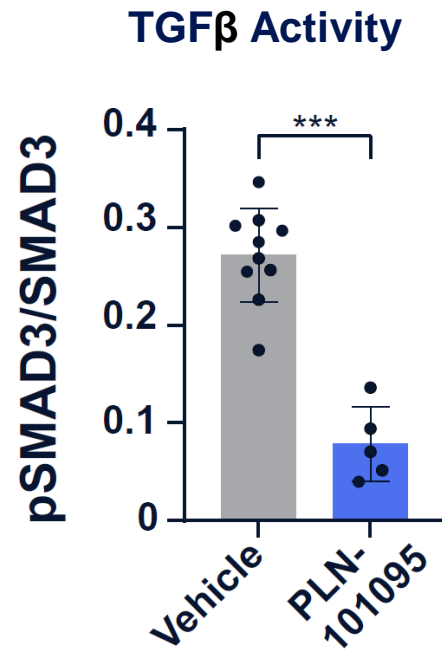


CD8⁺ T Cells

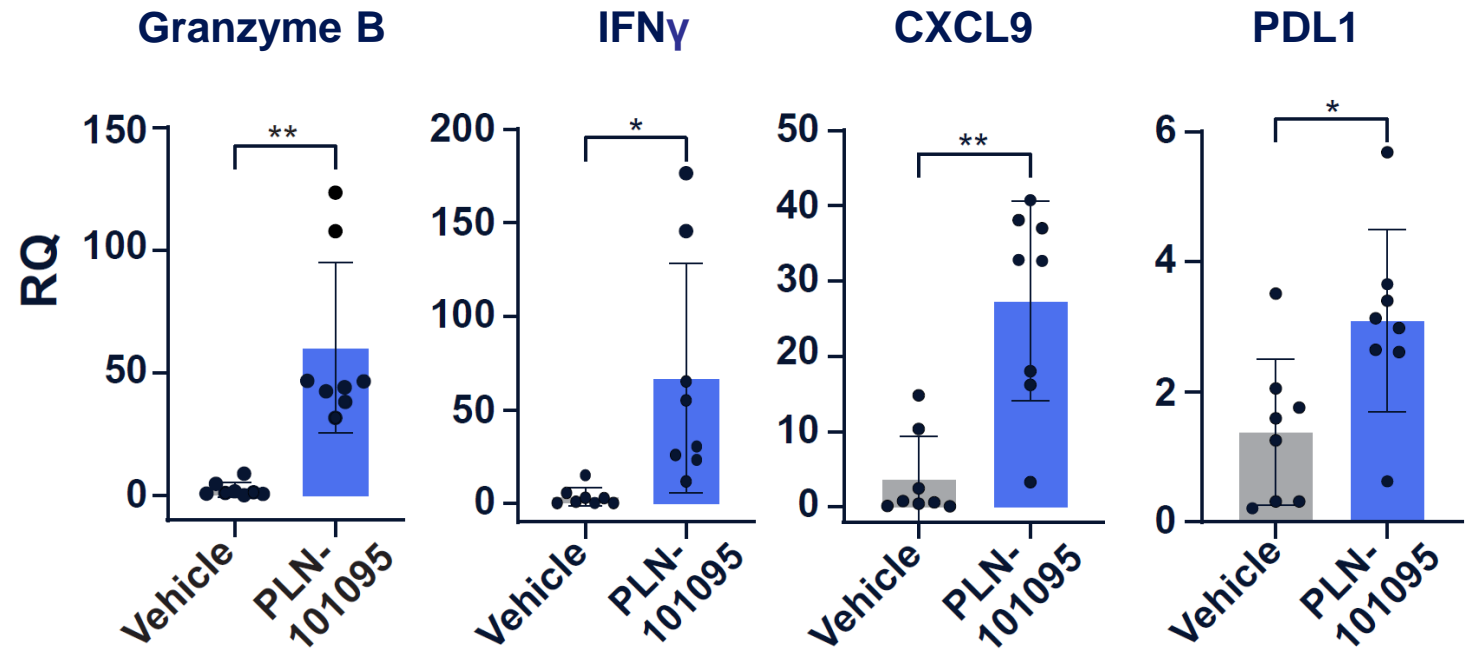


Single Agent PLN-101095 Promoted T Cell Infiltration

Reduced TGF- β Signaling



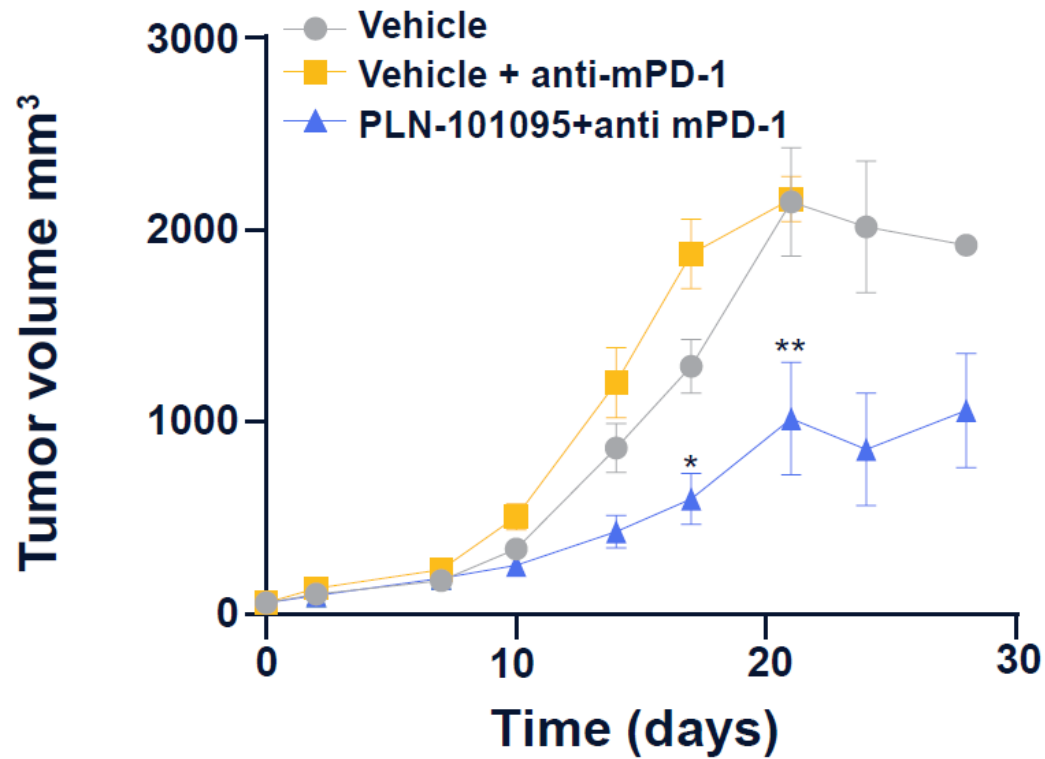
Increased Expression of IFN γ -Regulated Genes



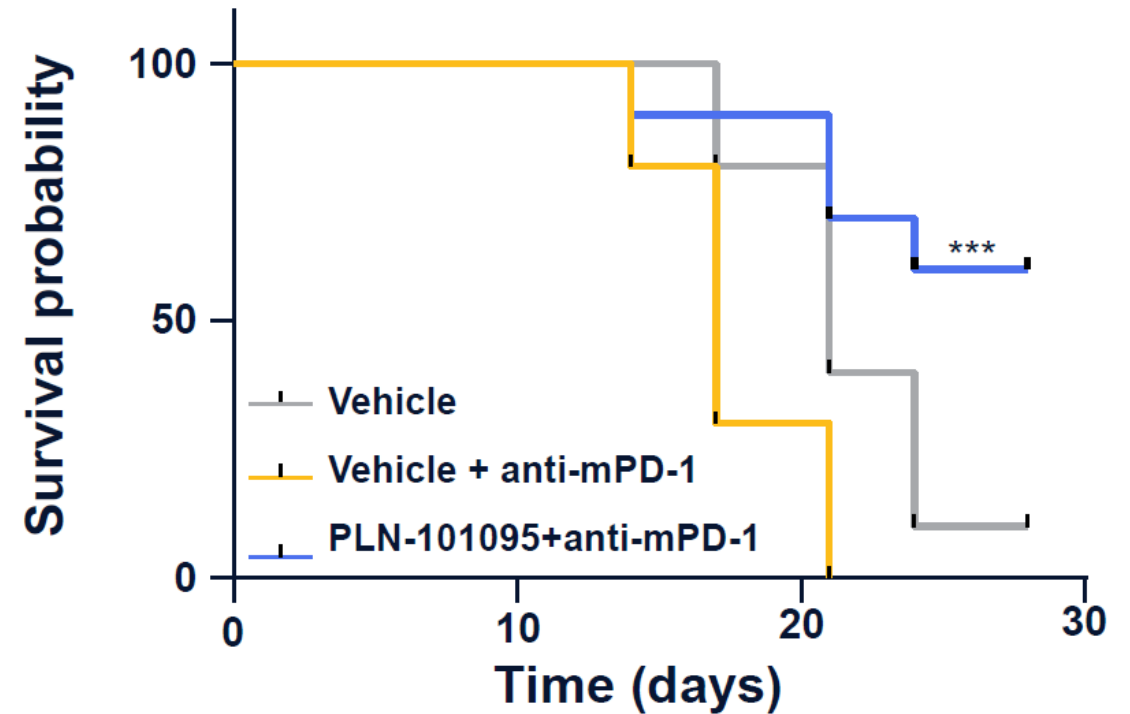
SITC 2022 Poster #1352

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

Tumor Growth Inhibition in EMT6 Tumors



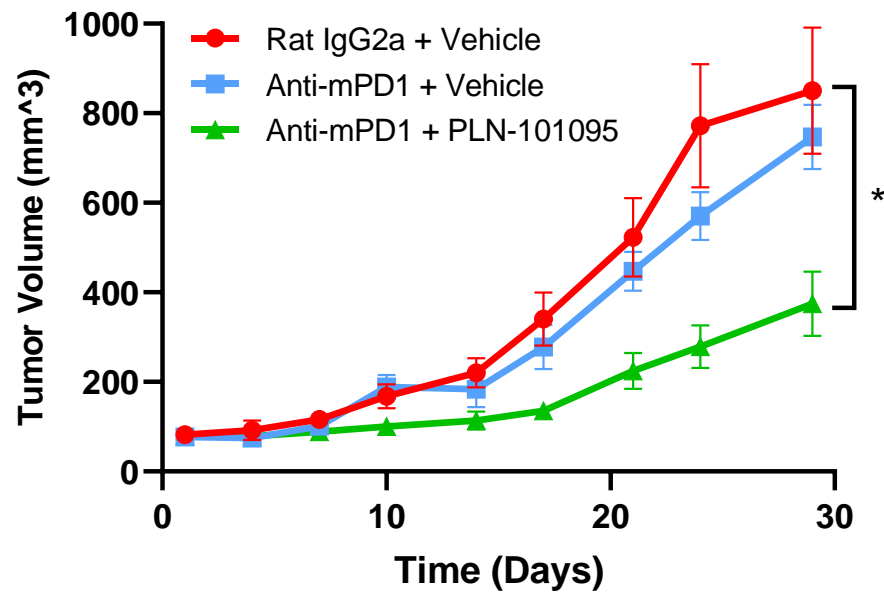
Survival



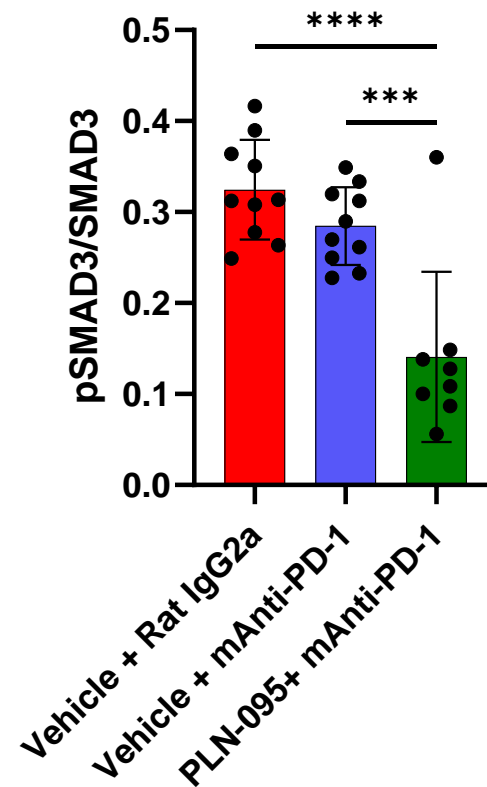
SITC 2022 Poster #1352

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

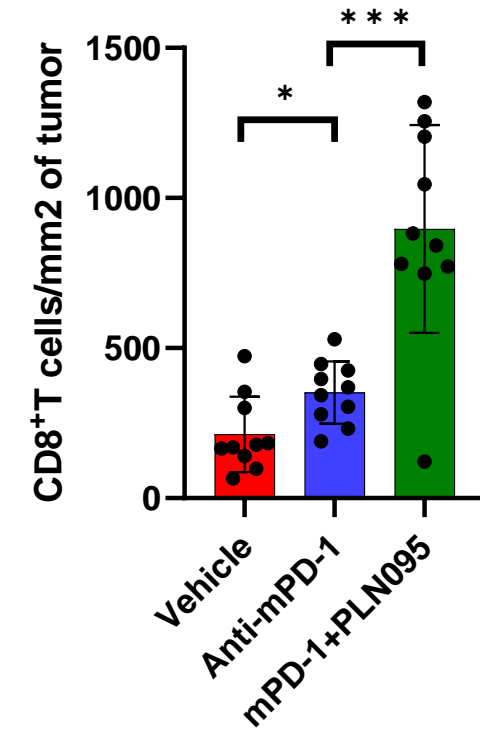
Tumor Growth Inhibition in Pan02 Tumors



TGFβ Signaling

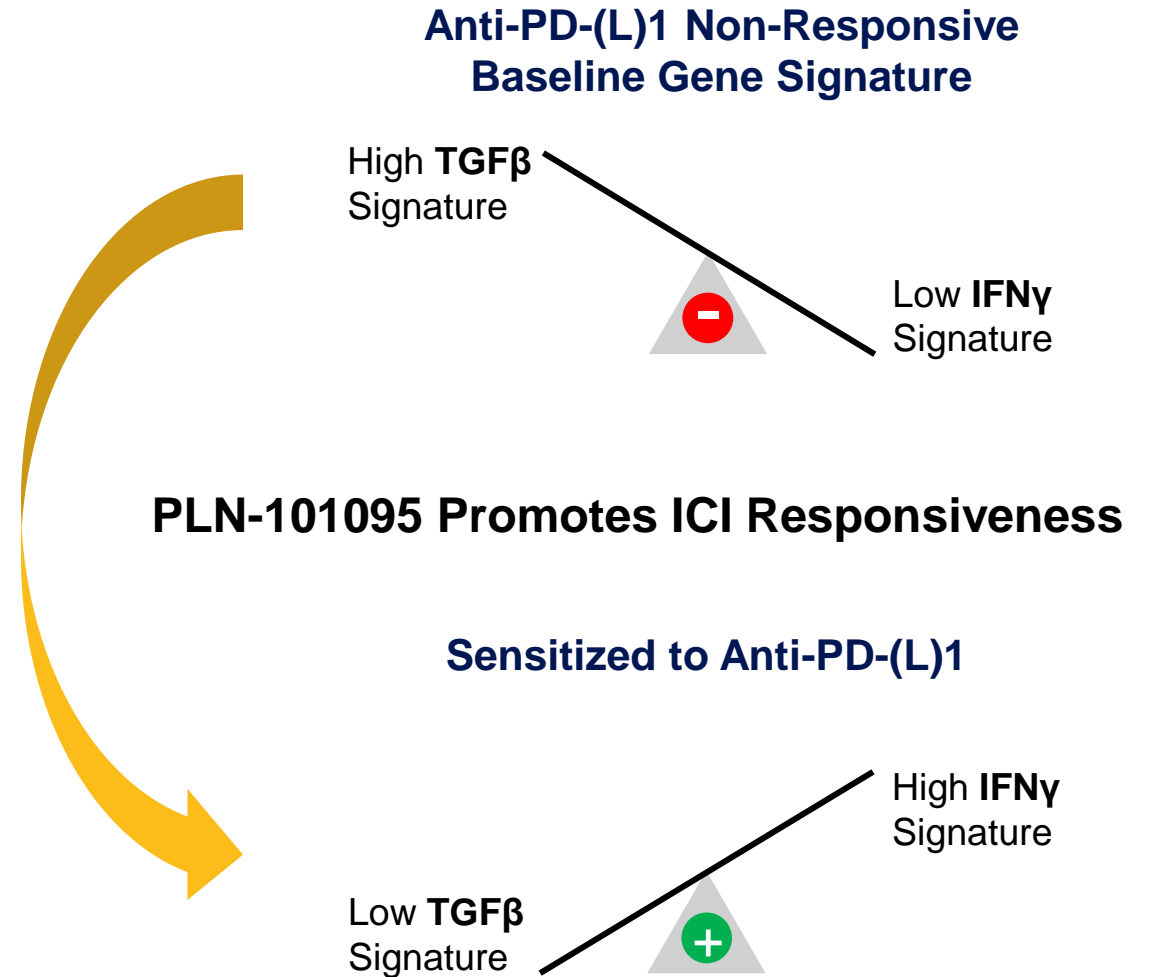
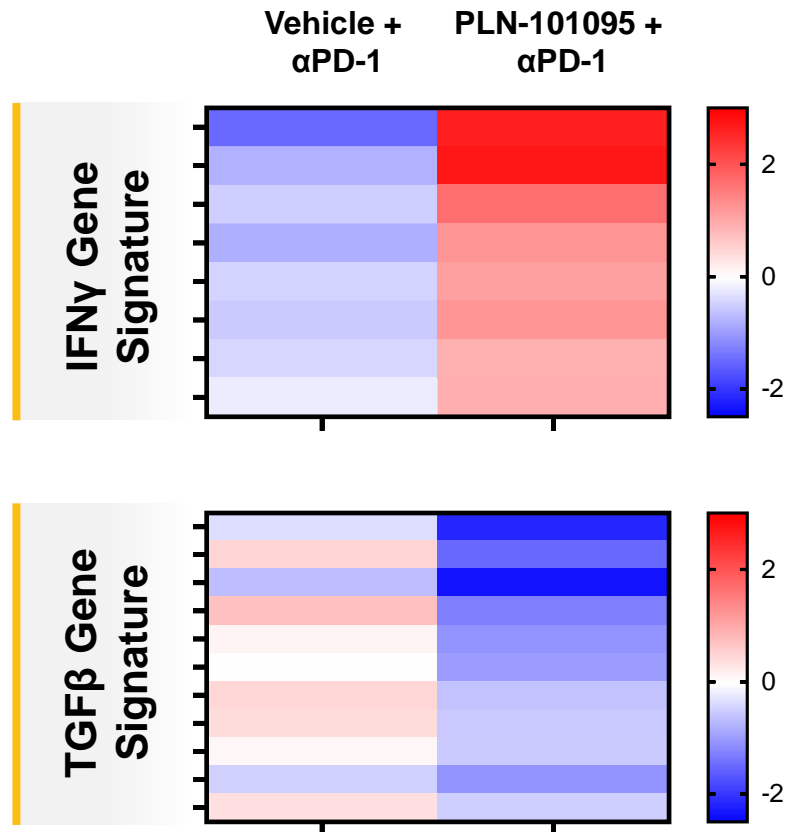


CD8⁺ T Cells



SITC 2022 Poster #1352

PLN-101095 Potently Increased IFN γ Signature & Reduces TGF β Gene Signatures



PLN-101095 Nonclinical Safety Studies

No Effects of Concern for Clinical Advancement

Study Category	Studies Completed	Findings with PLN-101095
Repeat Dose Toxicology	<ul style="list-style-type: none">• 14-day DRF in rat• 7-day DRF in dog• GLP 1-Month IND-enabling rat• GLP 1-Month IND-enabling dog	<ul style="list-style-type: none">• No adverse findings in rat or dog DRF• All doses tolerated• NOAEL¹ set at highest dose
Safety Pharmacology	<ul style="list-style-type: none">• GLP hERG• Safety44	<ul style="list-style-type: none">• No findings
Genetic Toxicology	<ul style="list-style-type: none">• GLP Ames• GLP In vitro micronucleus	<ul style="list-style-type: none">• No findings

¹ – No observed adverse effect level.

Key Program Highlights



Oral route of administration of small molecule $\alpha_v\beta_8$ inhibitor



Highly potent dual inhibitor of $\alpha_v\beta_8$ / $\alpha_v\beta_1$ inhibitor



Activity demonstrated in multiple **PD-1 resistant** tumor models



Greater reduction in **TGF- β signaling** than either $\alpha_v\beta_8$ or TGF- $\beta_{1,2}$ mAb



Significant reduction in tumor **fibrogenesis**



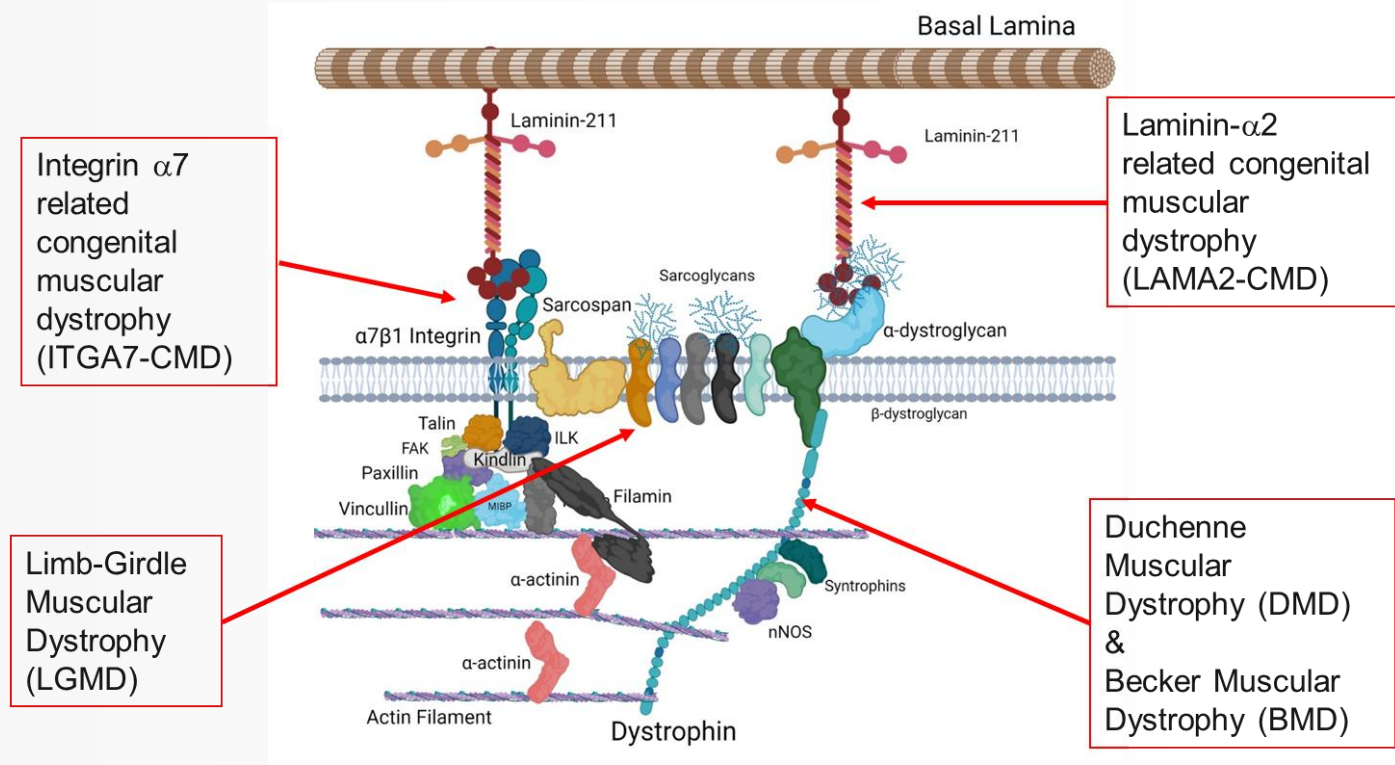
Phase 1 study initiated for PLN-101095 in **second quarter 2023**



Selective Muscle Cell Integrin Agonism for the Treatment of Muscular Dystrophies

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

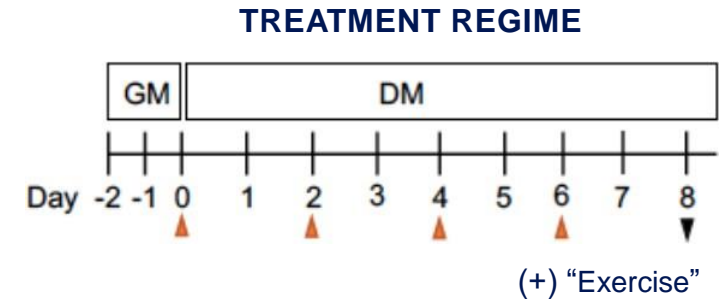
- Predominantly expressed in skeletal, heart and smooth muscle
- $\alpha_7\beta_1$ strong genetic modifier in MDX mice
 - Lack of $\alpha_7\beta_1$ worsens disease phenotype
 - Over expression increases survival and improves function
 - Pharmacological agents that increase expression show similar effects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



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

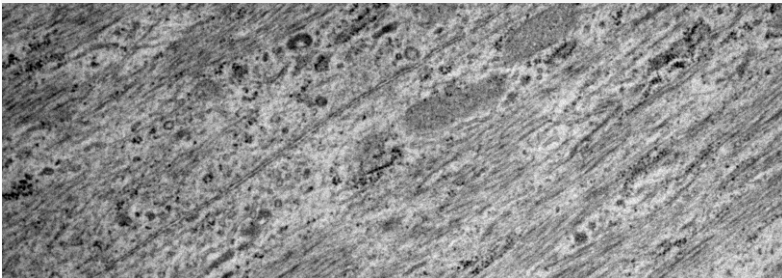
Integrin $\alpha_7\beta_1$ Agonist Antibody Promoted Muscle Maturation

AB1071 hMMTs treated with 1 $\mu\text{g/ml}$ or 10 $\mu\text{g/ml}$ Pliant antibody contain myotubes with substantially improved sarcomere organization that can withstand tetanic stimulation compared to IgG4 control

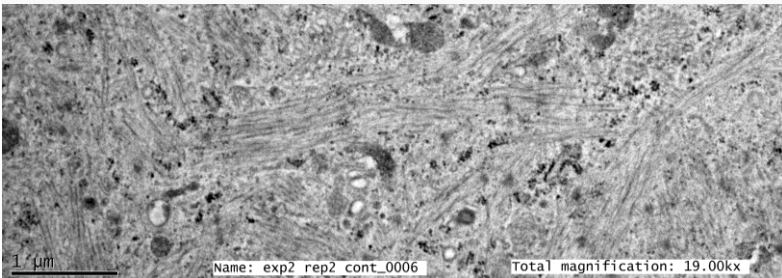


IgG4

1 $\mu\text{g/ml}$

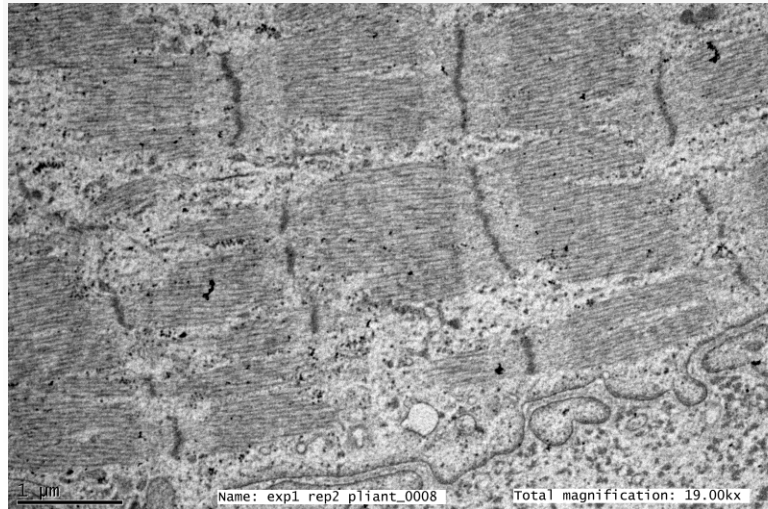


10 $\mu\text{g/ml}$

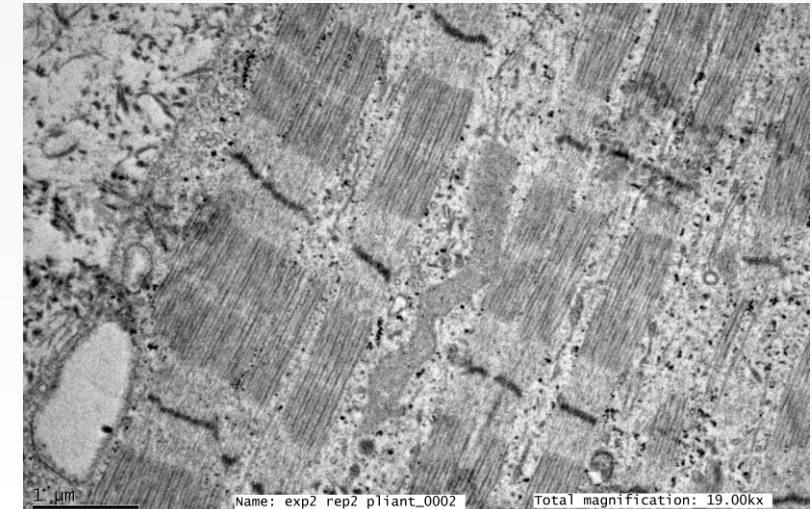


$\alpha_7\beta_1$ agonist

1 $\mu\text{g/ml}$

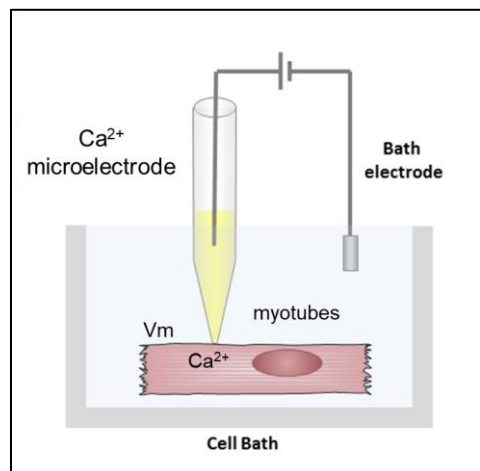


10 $\mu\text{g/ml}$

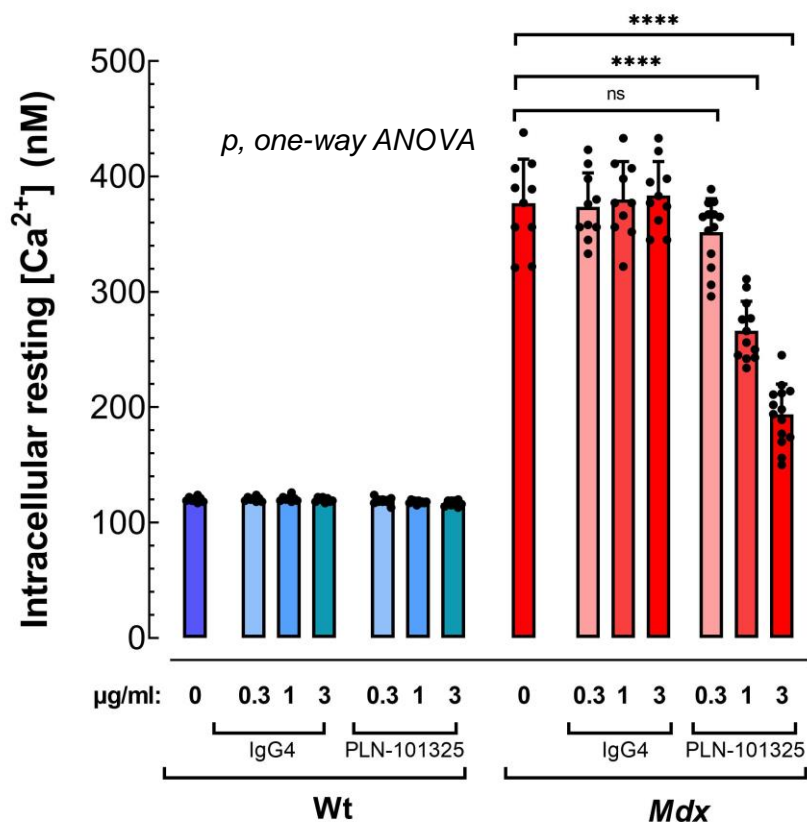


Effect of PLN-101325 in Ca²⁺ Homeostasis and Resting Membrane Potential of B10-mdx Myotubes

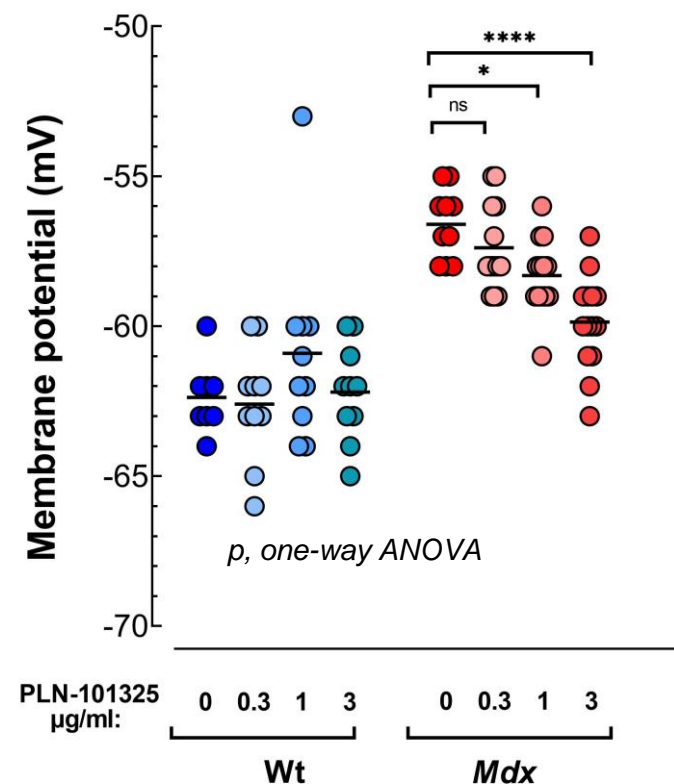
Reduced intracellular resting calcium and hyperpolarization of the membrane potentially support improved plasmalemmal integrity by PLN-101325



Intracellular resting Ca²⁺



Resting membrane potential



Dr. Jose R. Lopez

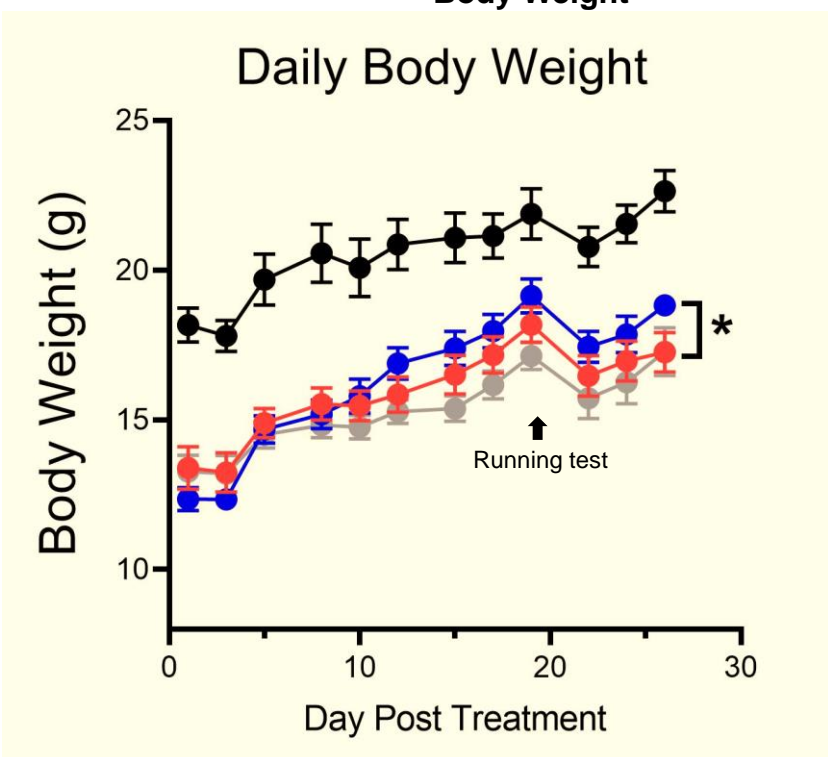
Mount Sinai
MEDICAL CENTER

Body Weight Improvement at 4 and 12 Weeks of Treatment

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

4-week

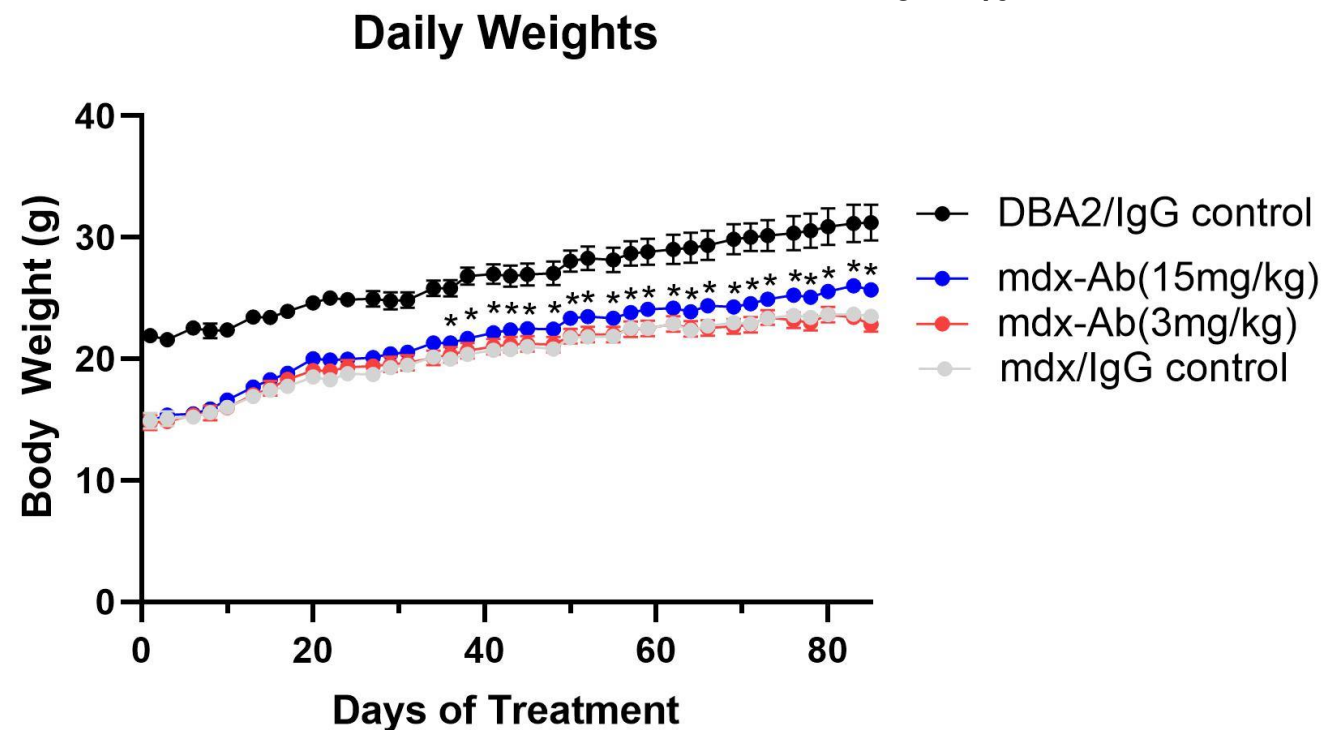
$8 \pm 3\%$ Increase in
Body Weight



12-week

$9 \pm 1\%$ Increase in
Body Weight

Weight Increase
 $9 \pm 1\%$



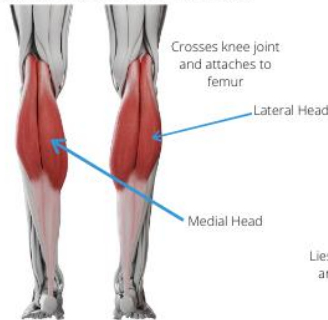
Improved Response to Post Eccentric Injury at 4 and 12 Weeks of Treatment

Plantar flexion test

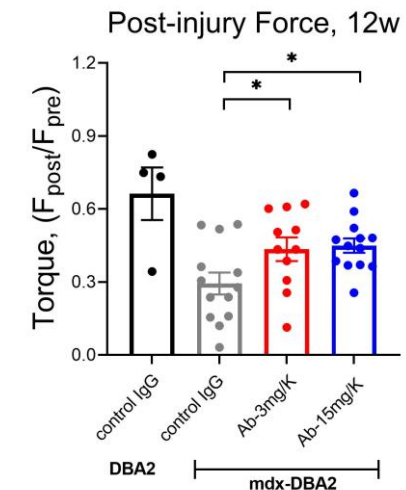
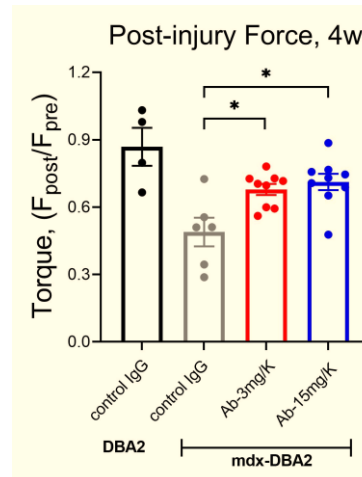
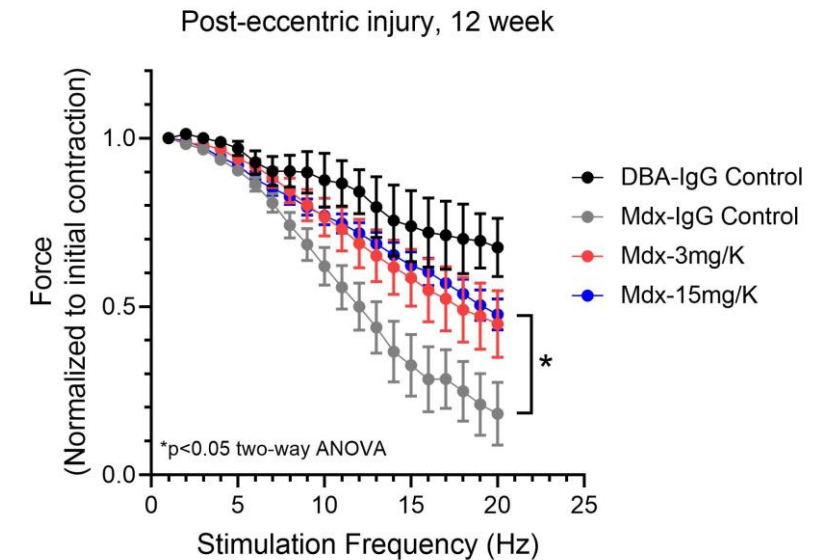
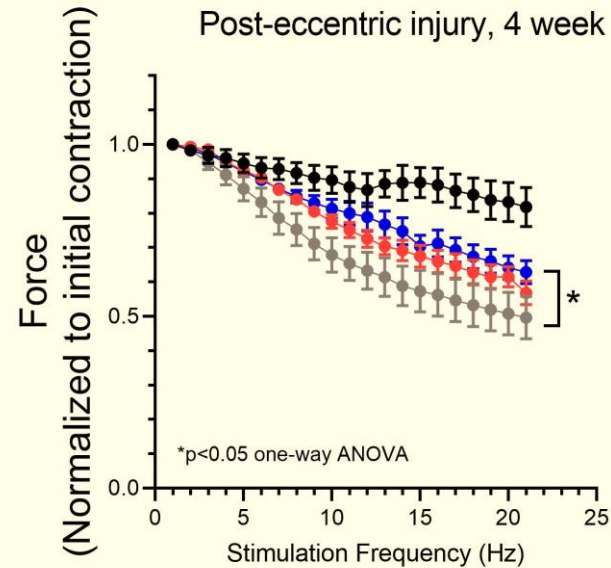
- Gastrocnemius (GC): Premier mover muscle for plantar flexion.
- GC only muscle to join both ankle and knee.



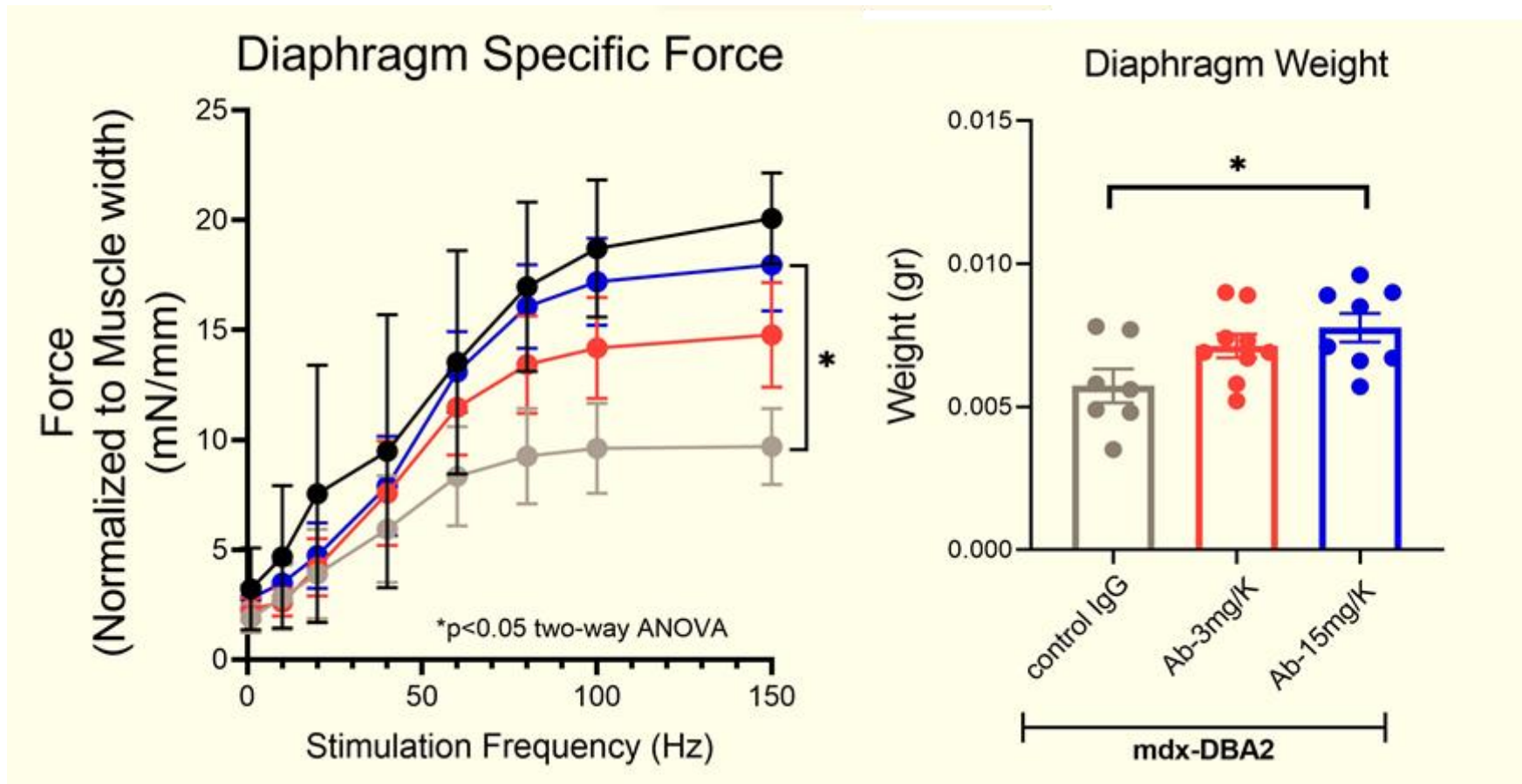
Gastrocnemius



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



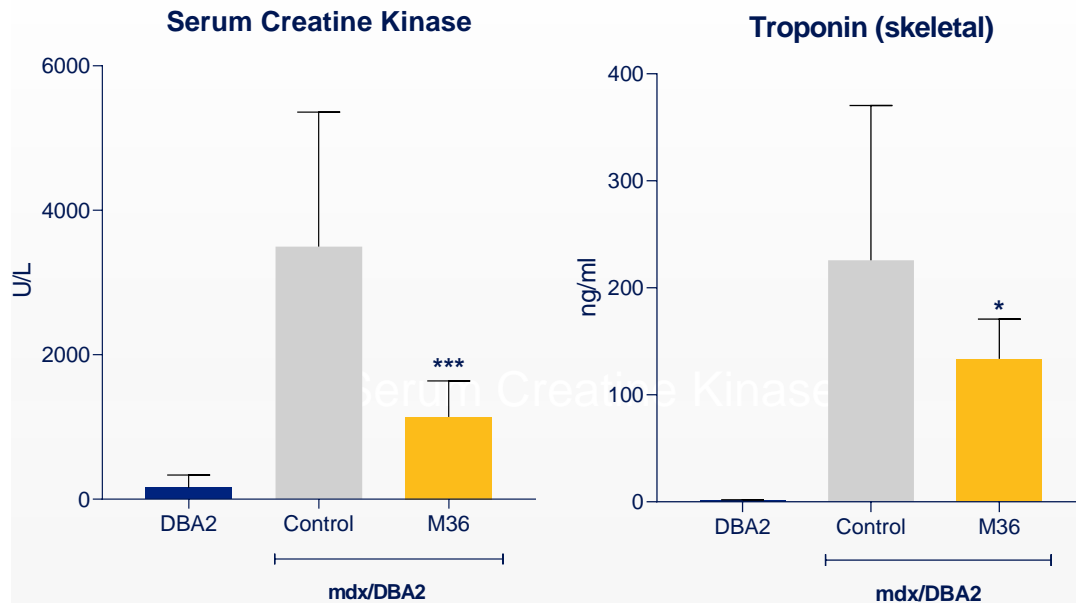
Diaphragm Force Significantly Improved at 4 Weeks of Treatment



MYOLOGICA

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

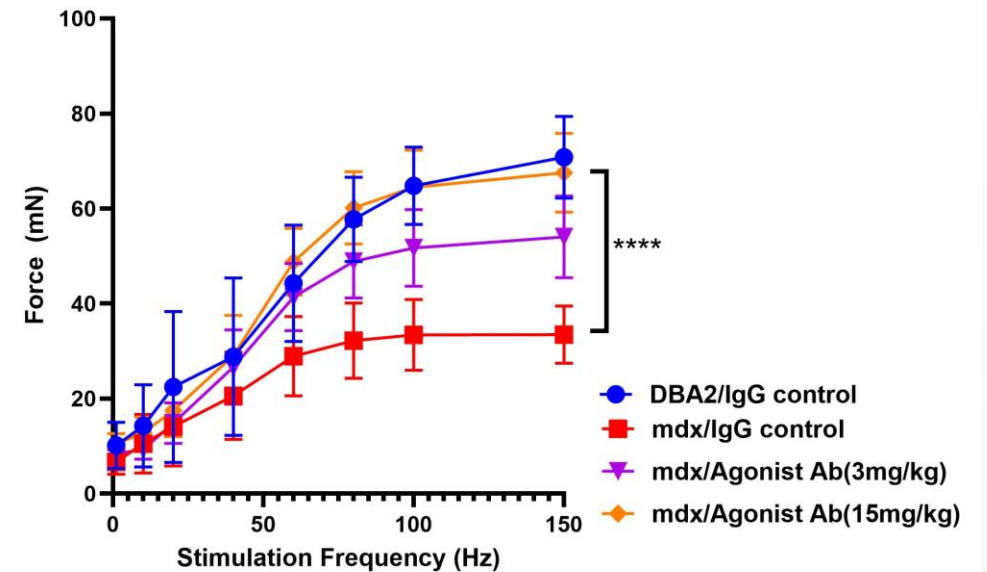
Antibody treatment protected against muscle damage



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

***p 0.001, *p<0.05, one-way ANOVA
Mean +/- SD n=10/group

Duchenne muscular dystrophy (DMD) causes progressive wasting of cardiac and respiratory muscles (main cause of death)



- Improvement in diaphragm function is expected to significantly improve patient pulmonary function

****p 0.0001, two-way ANOVA