UNITED STATES SECURITIES AND EXCHANGE COMMISSION WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 9, 2023

PLIANT THERAPEUTICS, INC.

(Exact name of Registrant as Specified in Its Charter)

Delaware (State or Other Jurisdiction of Incorporation)

001-39303 (Commission File Number)

47-4272481 (IRS Employer Identification No.)

260 Littlefield Avenue, South San Francisco, CA (Address of Principal Executive Offices)

94080 (Zip Code)

Registrant's Telephone Number, Including Area Code: (650) 481-6770

Not Applicable mer Address, if Changed Since Last Report) (Former Name or Forn

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

□ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12) П

D Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

D Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

	Trading	Name of each exchange
Title of each class	Symbol(s)	on which registered
Common Stock, par value \$0.0001 per share	PLRX	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company \Box

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. \Box

Item 7.01 Other Events.

Pliant Therapeutics, Inc. (the "Company") intends to conduct meetings with securities analysts, investors and others in connection with the 41st Annual J.P. Morgan Healthcare Conference beginning on January 9, 2023. As part of these meetings, the Company intends to utilize the corporate slide presentation furnished with this report as Exhibit 99.1.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Corporate Slide Presentation dated January 9, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

The information in this Item 7.01 is being furnished, not filed, pursuant to Regulation FD. Accordingly, the information in Item 7.01 of this report will not be incorporated by reference into any registration statement filed by the Company under the Securities Act of 1933, as amended, unless specifically identified therein as being incorporated therein by reference. The furnishing of the information in this report is not intended to, and does not, constitute a determination or admission by the Company that the information in this report is material or complete, or that investors should consider this information before making an investment decision with respect to any security of the Company.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

PLIANT THERAPEUTICS, INC.

Date: January 9, 2023

By: /s/ Keith Cummings Keith Cummings, M.D., MBA Chief Financial Officer



Developing Novel Treatments for Fibrotic Diseases

JANUARY 2023

Disclaimers

This presentation has been prepared by Pliant Therapeutics, Inc. ("we," "us," "our," "Pliant" or the "Company"). The information set forth herein does not purport to be complete or to contain all of the information you may desire. Statements contained herein are made as of the date of this presentation unless stated otherwise, and this presentation shall not under any circumstances create an implication that the information contained herein is correct as of any time after such date or that information will be updated or revised to reflect information that subsequently becomes available or changes occurring after the date hereof.

This presentation includes forward-looking statements regarding Pliant's proprietary drug candidates, the timing of the start and conclusion of ongoing or planned clinical trials, including the timing of, and our ability to achieve, anticipated milestones, the sufficiency of our cash, cash equivalents and short-term investments, the timing and outcome of regulatory decisions, future availability of clinical trial data, our collaborations for our product candidates and the maintenance of those collaborations; business and results from operations; and other matters. Actual results could differ materially from those contained in any forward-looking statements as a result of various factors, including without limitation: that Pliant's drug candidates do not advance in development or result in approved products on a timely or cost effective basis or at all; the cost, timing and results of clinical trials; our ability to manage and mitigate the impact of the ongoing COVID-19 pandemic; that many drug candidates that have completed early-stage trials do not become approved drugs on a timely or cost effective basis or at all; the ability to enroll patients in clinical trials; possible safety and efficacy concerns; regulatory developments; the ability of Pliant to protect its intellectual property rights, and unexpected costs, charges or expenses that reduce cash runway. Pliant's pipeline programs are in various stages of pre-clinical and clinical development, and the process by which such pre-clinical or clinical therapeutic candidates could potentially lead to an approved therapeutic is long and subject to significant risks and uncertainties. Pliant undertakes no obligation to update forward-looking statements as a result of new information or otherwise. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" and elsewhere in the Company'

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

This presentation concerns drugs that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration (the "FDA"). They are currently limited by Federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

PLIANT



Pliant – Company Highlights



Industry-Leading Fibrosis Platform

- Built on integrin-mediated inhibition of TGF-β pathway resulting in antifibrotic effect and shown to be safe
- Proprietary drug discovery platform based on novel in-house compound library of integrin binders
- Lead molecule bexotegrast (PLN-74809) is highly antifibrotic in lung and liver while well tolerated at highest doses tested



Strategic Partnership with Novartis Validates Platform

- Largest (\$80M) upfront for a preclinical NASH program
- Significant expense offset to pipeline programs
- Broad multi-target research collaboration
 - Next generation anti-fibrotic molecules targeting novel integrins





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

- Bexotegrast in Phase 2a development in IPF and PSC
 Phase 2a data in IPF showed bexotegrast was well tolerated with strong treatment effect on FVC and QLF
 - 320 mg: positive DSMB review (IPF/ PSC); interim 12-week IPF data early 1Q 2023
 - $\begin{array}{l} \quad \text{IND submitted for PLN-101095: a potential first in class small} \\ \text{molecule dual } \alpha_V\beta_8 \ / \ \alpha_V\beta_1 \ \text{inhibitor addressing ICI resistance} \end{array}$

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Strong Financial Position

- Over \$625 million raised to date including June 2020 IPO (Nasdaq: PLRX) and \$230 million follow on July 2022
- \$360.2M cash balance as of September 30, 2022
- \$100 million loan facility (\$10 million drawn)
- · Operations funded to mid-2025

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The Pliant Team Experienced in Fibrosis and Drug Development

Core Team		Founders	UCSF
Bernard Coulie, M.D., Ph.D., M.B.A. President, CEO, and Director	INTREXON' <u>ActoGeniX</u> Johnson-Johnson Mine Family of Comparises	Dean Sheppard, M.D. Professor of Medicine, Chie Pulmonary, Critical Care, Al	f of the Division of lergy and Sleep, and
Hans Hull, J.D. Chief Business Officer	A APRECIA Orthobond	Director of the Lung Biology	Center.
Éric Lefebvre, M.D. Chief Medical Officer	Allergan TOBIRA Johnson Johnson	William DeGrado, Ph.D. Professor of Pharmaceutica	I Chemistry
Keith Cummings, M.D., M.B.A. Chief Financial Officer	CITI LEHMAN BROTHERS	Rik Derynck, Ph.D. Professor, Cell and Tissue B the Eli and Edythe Broad C.	Biology, Co-Director of enter of Regeneration
Scott Turner, Ph.D. Senior Vice President, Head of Research	Kinemed	Medicine and Stem Cell Re	search
Greg Cosgrove, M.D., FCCP Vice President, Clinical Development (IPF)	Difference Viversity of Colorado Anschutz Medical Campus Chational Jewish Health	Harold Chapman, M.D. Professor of Medicine, Divis Critical Care, Allergy and SI	ion of Pulmonary, eep

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Pliant's Integrin Focused Library Core Platform for Novel Pipeline and Partner Programs

Integrins

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- 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 $\alpha_{\rm V}$ integrins, collagen and laminin binders



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Pliant Development Pipeline



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Fibrosis – A Silent Killer

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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



https://www.lungsandyou.com/ipf

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



www.jhmicall.org

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Bexotegrast Understanding the IPF Commercial Opportunity



Current Commercial Landscape in IPF

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

Changing Treatment Landscape

- Near-term patent expiry of current treatments
 - Esbriet: First generic sold May 2022
 - Ofev: Loss of US market exclusivity 2025 (2026 for sscILD)



Significant Need for New Therapeutic Options

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

Bexotegrast: A Potential Preferred Treatment Option

- Targeted inhibition of fibrotic process
 – tissue specific inhibition of TGF-β
- · Once daily oral administration
- · Well tolerated with anti-fibrotic effect
 - Dose-dependent FVC benefit across all doses, as monotherapy and in combination with current treatments
 - No discontinuations due to adverse events
- Bexotegrast will be evaluated as backbone therapy to be used as monotherapy, and with current treatments



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

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$\alpha_{\nu}\beta_{6}/\alpha_{\nu}\beta_{1}$ Integrins Drive Cell-Matrix Interactions in Fibrosis



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



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

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Bexotegrast Nonclinical Toxicology Studies No effects of concern for clinical advancement

GLP Study category	Studies completed	Findings with Bexotegrast (PLN-74809)
Repeat Dose Toxicology	 1-Month IND-enabling NHP and mouse 3-Month Sub-chronic NHP and mouse 9-Month Chronic NHP 6-Month Chronic Mouse 	 No findings limiting clinical advancement including No pulmonary infiltrates NOAEL¹ in sub-chronic and chronic GLP tox studies at the highest dose tested in NHPs
Safety Pharmacology	 Standard cardiac ion channel panel Cardiovascular/respiratory in telemetered NHP 	No findings:No effect on respiratory or cardiovascular parameters
Genetic Toxicology	 Ames In vitro micronucleus In vivo micronucleus 	No genotoxic findings: Ames negative Micronucleus negative
Reproductive Toxicology	 Mouse Embryofetal Development Rabbit Embryofetal Development Mouse Fertility 	No findings:No embryofetal effectsNo effects on fertility

600+ human subjects dosed to date with no safety concerns identified at doses up to 640 mg



1 - No observed adverse effect level.

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Dual $\alpha_v \beta_6 / \alpha_v \beta_1$ Inhibition Blocks COL1A1 Gene Expression More than Single Inhibition in Human IPF Tissue



Bexotegrast Phase 1a Data Summary Pharmacokinetics

Pharmacokinetics

- · Well absorbed, orally bio-available
- Long T_{1/2}: ~50 hrs QD dosing

Summary PK Curves by Cohort at Steady State





Data presented as box plots (max to min) with line at median and + at mean

PK sampling up to 144h; only 0-24hr plotted. Doses 10mg to 40mg from Study Bexotegrast (PLN-74809)-P1-01, Day 14. Doses 80mg, 160mg and 320mg from Study Bexotegrast (PLN-74809)-104, Day 7.





Bexotegrast Phase 1a Data Summary Safety - Well tolerated in healthy participants

Drug-Related Treatment-Emergent Adverse Events Reported in ≥2 Bexotegrast -Treated Healthy Participants from Seven Phase 1 Studies with Available Safety Data

	Participants, n (%)				
TEAE Preferred Term	Bexotegrast, All doses (n=283)	Placebo (n=52)			
	Drug-related	Drug-related			
Headache	4 (1.4)	2 (3.8)			
Constipation	4 (1.4)	0 (0.0)			
Nausea	3 (1.1)	0 (0.0)			
Dizziness	2 (0.7)	0 (0.0)			
Abdominal pain	2 (0.7)	0 (0.0)			
Palpitations	2 (0.7)	0 (0.0)			

Most Bexotegrast-related AEs were mild (82%) and none were severe



Am J Respir Crit Care Med 2022;205:A2437



Bexotegrast Phase 1b Proof of Biological Mechanism



Phase 1b Expansion Trial Investigating Higher Doses Data Presented February 2022

- Randomized, double-blind, placebo-controlled
- Treatment duration: 7 days
- BAL samples taken at 6 hours and 24 hours after last dose on day 7





* = p < 0.05 vs placebo and Cmax < 700 ng/mL group

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Bexotegrast Demonstrated Significant pSmad2 Suppression Relative to Baseline at 24 Hours

Alveolar pSmad2/Smad2 Percentage Change from Baseline at 24 Hours (Part 1: 80 mg and 160 mg)



Percent change pSmad2/Smad2 was statistically significant at both doses of Bexotegrast (PLN-74809) vs. placebo (p<0.0001)

Mean PK/PD Response



Durable reduction in pSmad2/Smad2 for 24 hours at 80 and 160 mg







eolar lavage; pSmad2/Smad2 - ratio of phosphorylated Smad2 to total Smad2; QD - once daily BAI

Bexotegrast Demonstrated Durable pSmad2 Suppression Relative to Placebo at 6 Hours and 24 Hours at All Dose Levels

pSmad2/Smad2 percentage change from baseline, delta versus placebo in Part 1 and Part 2



The difference in pSmad2/Smad2 % change was calculated for each treatment value vs. the mean placebo value at each timepoint

Placebo (n=8/4) Bexotegrast (PLN-74809) • 80 mg QD (n=7) • 160 mg QD (n=8 at 6hrs and n=5 at 24hrs) • 320 mg QD (n=4 at 6hrs and n=5 at 24hrs)



pSmad2/Smad2 – ratio of phosphorylated Smad2 to total Smad2

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Tissue pSmad Levels are Highly Significantly Correlated with Extractable Collagen Levels in normal and fibrotic lungs

Reduction in Pulmonary pSmad Appears to Be a Marker for Reduction of Fibrosis





 Diagnostic open lung biopsies from 10 patients with ILD and suspected IPF

- · 2-3 distinct lung regions sampled from each patient
- 5 controls (non-transplanted lungs)
- Total pSmad3 had a strong correlation vs. extractable Collagen I (Western Blot)

Adapted from Chapman HA et al. March 12, 2020; 382:1068-1070

The NEW ENGLAND JOURNAL of MEDICINE

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Putting the Phase 1b pSmad2 Data into Perspective

Durable pSmad2 suppression at all dose levels relative to placebo at 6 hours and 24 hours

Dose- and plasma concentration-dependent response with up to 92% and 76% suppression of pSmad2 from baseline at 6 and 24 hours, respectively

Bexotegrast well tolerated with no serious or severe adverse events

- Bexotegrast inhibits activation of TGF-β, a key molecular driver of fibrosis in the lung, as measured by pSmad2
- · Bexotegrast may disrupt the fibrosis pathway and affect disease progression in IPF patients
- De-risks the ongoing Phase 2a INTEGRIS-IPF trial, and future development programs



Bexotegrast Phase 2a PET Trial – $\alpha_v \beta_6$ Receptor Occupancy Measured by an $\alpha_v \beta_6$ PET Ligand

TRIAL DESIGN

- Single-site open-label trial at Stanford University
- Adults with IPF diagnosis (n=12) and FVC ≥ 45% of predicted
- Patients receive single oral dose of Bexotegrast with PET scans prior to dosing and at T_{max} post dose
- Dose cohorts being evaluated: 60 mg, 120 mg, 240 mg, and 320 mg

ENDPOINTS

- Primary: Evaluation of α_vβ₆ target engagement by bexotegrast assessed by change in PET tracer uptake following a single oral dose
- Secondary: Assessment of safety and tolerability of bexotegrast in IPF patients
- Exploratory: Relationship between bexotegrast systemic exposure and positron emission tomography (PET) imaging and biomarkers in IPF participants



PET Ligand Uptake Confined to IPF Lung in Unilateral Lung Transplant Patient



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Phase 2a PET Trial in IPF – Interim Analysis Methodology

- PET scan acquisitions at baseline (no drug) and after drug administration (4 hours post-dose)
 1 week interval between baseline and post-dose PET scan acquisition
- Administration of a single dose of bexotegrast: 60 mg 120 mg 240 mg 320 mg
- · Interim PK and target engagement data from 6 dose administrations in 4 patients
 - 2 out of 4 patients received one single dose
 - 2 out of 4 patients received two single doses with at least a 2-week washout interval between doses

	60 mg	120 mg	240 mg	320 mg
Patient 1	x			
Patient 2		x	x	
Patient 3			x	x
Patient 4				x

- · All patients on standard of care therapy (nintedanib)
- · Image analysis for target engagement in highly fibrotic regions of the lungs



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Dose- and Plasma Concentration-Dependent Target Engagement

100.

75.

50

25

0-

0.1

% Target Engagement



Plasma Conc-Dependent Target Engagement

1



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С

10

Plasma Concentration (nM)

* Free plasma concentration

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Bottom

Hillslope

EC₅₀ (nM)

Тор

100

Best-fit values

0

1.11

87.4

2.96

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1000

Putting the Interim Phase 2a PET Data into Perspective

Target engagement above the threshold for predicted anti-fibrotic activity across all doses (>50% target engagement)

Dose- and plasma concentration-dependent response approaching target saturation at the two highest doses

- · Bexotegrast penetrates highly fibrotic areas of the lung
- Potential anti-fibrotic activity of bexotegrast at clinical doses
- · Informs dose selection in Phase 2b trials and beyond
- · Provides robust PK/PD model to predict exposure-response relationship



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NORMAL LUNG

IPF LUNG

INTEGRIS-IPF Study Design and Objectives



PRIMARY AND SECONDARY ENDPOINTS

Safety, tolerability, PK

EXPLORATORY ENDPOINTS

- Change in Forced Vital Capacity (FVC) over 12 weeks
- High Resolution CT-based Quantitative Lung Fibrosis (QLF) imaging
- Patient-reported outcome (PRO): VAS-cough severity
- · Effect on selected biomarkers

Executive Summary

Bexotegrast Well Tolerated Over 12 Weeks of Treatment

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

Bexotegrast-Treated Patients Experienced an 80% Reduction in FVC Decline Over 12 Weeks (-15.1 mL, Pooled Active Groups) Compared to Placebo (-74.1 mL)

- · Bexotegrast treatment effect was evident with and without use of standard-of-care agents
- An improvement in FVC (+24.6 mL) was observed in bexotegrast 80 mg dose cohort
- Dose-dependent reduction in proportion of patients with percent predicted FVC (FVCpp) decline of ≥10%, a well-established predictor of death and disease progression in IPF

Other Exploratory Endpoints

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

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Baseline Demographics

Characteristic	bexotegrast 40 mg (n=22)	bexotegrast 80 mg (n=23)	bexotegrast 160 mg (n=22)	bexotegrast All (n=67)	Placebo (n=23)
Male sex—no. (%)	18 (81.8)	19 (82.6)	16 (72.7)	53 (79.1)	22 (95.7)
Female sex-no. (%)	4 (18.2)	4 (17.4)	6 (27.3)	14 (20.9)	1 (4.3)
Age—yr (SD)	69.2 (7.11)	74.2 (4.70)	71.5 (6.63)	71.7 (6.45)	71.7 (5.61)
Race—no. (%)					
White	22 (100.0)	21 (91.3)	22 (100.0)	65 (97.0)	22 (95.7)
Asian	0	1 (4.3)	0	1 (1.5)	1 (4.3)
Not Reported / Unknown	0	1 (4.3)	0	1 (1.5)	0
Weight—kg, Mean (SD)	86.09 (18.223)	85.89 (14.949)	85.37 (13.507)	85.79 (15.437)	85.23 (10.743)
Body-mass index (kg/m²), Mean (SD)	27.67 (4.205)	28.54 (5.790)	29.28 (4.663)	28.50 (4.915)	27.43 (2.488)



SD = Standard deviation; BMI = Body Mass Index; FVC = Forced Vital Capacity; DLCO = Diffusing capacity for carbon monoxide; Duration since diagnosis at screening is calculated from the first reported date for preferred terms of Idopathic Pulmonary Fibrosis, Pulmonary Fibrosis or Intersbital Lung Disease. Percentages are based on the number of participants in the Safety Population by treatment group.

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Baseline Disease Characteristics

Characteristic	bexotegrast 40 mg (n=22)	bexotegrast 80 mg (n=23)	bexotegrast 160 mg (n=22)	bexotegrast All (n=67)	Placebo (n=23)
Time since diagnosis of IPF—yr, Mean (SD)	1.78 (0.925)	2.39 (1.422)	2.13 (1.083)	2.10 (1.176)	2.62 (1.378)
Standard of Care Use	17 (77.3)	19 (82.6)	19 (86.4)	55 (82.1)	18 (78.3)
None	5 (22.72)	4 (17.39)	3 (13.63)	12 (17.91)	5 (21.74)
Nintedanib	12 (54.5)	9 (39.1)	7 (31.8)	28 (41.8)	8 (34.8)
Pirfenidone	5 (22.7)	10 (43.5)	12 (54.5)	27 (40.3)	10 (43.5)
Duration of Standard of Care at Randomization (months), Mean, (SD)	19.47 (11.527)	20.21 (11.523)	20.07 (11.632)	19.93 (11.350)	24.12 (17.295)
FVC					
Mean—mL (SD)	2976.5 (861.01)	3128.7 (814.20)	2863.0 (725.39)	2991.5 (797.76)	3211.7 (792.68)
Median-mL	2937.0	2929.0	2702.5	2806.0	3282.0
Percent of predicted value, Mean (SD)	74.81 (14.698)	82.67 (13.471)	78.75 (16.356)	78.80 (14.995)	78.30 (15.859)
Percent of predicted DLCO, corrected for the hemoglobin level, Mean (SD)	57.200 (14.7434)	51.782 (14.6690)	48.615 (15.1082)	52.521 (15.0362)	50.335 (16.2161)
GAP Stage					
GAP Stage I, n (%)	11 (50.0)	8 (34.8)	7 (31.8)	26 (38.8)	7 (30.4)
GAP Stage II, n (%)	10 (45.5)	15 (65.2)	13 (59.1)	38 (56.7)	13 (56.5)
GAP Stage III, n (%)	1 (4.5)	0	2 (9.1)	3 (4.5)	3 (13.0)

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Standard deviation; BMI = Body Mass Index; n since diagnosis at screening is calculated from the first reported date for preferred terms tages are based on the number of patricipants in the Safety Population by treatment group. tage i = GAP Index 0-3; GAP Stage II = GAP Index 4-3; GAP Stage III = GAP Index 6-8; dex score (1-6) derived from Gender Age, FVC; Shredited and DECO, % Predicted.

as of Idiopathic Pulmonary Fibrosis, Pulmonary Fibrosis or Interstitial Lung Disease

Safety summary

AE, n (%) of Participants Reporting	bexotegrast 40 mg (n=22)	bexotegrast 80 mg (n=23)	bexotegrast 160 mg (n=22)	bexotegrast All (n=67)	Placebo (n=23)
Any AEs	16 (72.7)	15 (65.2)	15 (68.1)	46 (68.7)	14 (60.9)
TEAE	16 (72.7)	15 (65.2)	14 (63.6)	45 (67.2)	14 (60.9)
Related to study drug	4 (18.2)	7 (30.4)	4 (18.2)	15 (22.4)	8 (34.8)
Serious TEAE	1 (4.5)	0	2 (9.1)	3 (4.5)	2 (8.7)
Related to study drug	0	0	0	0	0
TEAE of CTCAE Grade 3 or Higher	2 (9.1)	0	2 (9.1)	4 (6.0)	1 (4.3)
Related to study drug	0	0	1 (4.5)	1 (1.5)	0
TEAE Leading to Interruption of Study Drug	0	0	1 (4.5) ¹	1 (1.5) ¹	0
TEAE Leading to Withdrawal of Study Drug	0	0	0	0	2 (8.7)
TEAE Leading to Early Termination from Study	0	0	0	0	1 (4.3)
TEAE Leading to Death	0	0	0	0	0



1 – COVID-19 AE = Adverse Event; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Events. Adverse events coded using MedDRA v. 24.0. TEAE is defined as any AE starting (or worsening) on or after the date of first dose.

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Safety Summary by SOC use in Pooled Bexotegrast Groups

	Without Background SOC (N=17)		With Background SOC (N=73)		
AE, n (%) of Participants Reporting	bexotegrast (n=12)	Placebo (n=5)	bexotegrast (n=55)	Placebo (n=18)	
Any AEs	8 (66.7)	3 (60.0)	38 (69.1)	11 (61.1)	
TEAE	8 (66.7)	3 (60.0)	37 (67.3)	11 (61.1)	
Related to study drug	2 (16.7)	2 (40.0)	13 (23.6)	6 (33.3)	
Serious TEAE	0	0	3 (5.5)	2 (11.1)	
Related to study drug	0	0	0	0	
TEAE of CTCAE Grade 3 or Higher	0	0	4 (7.3)	1 (5.6)	
Related to study drug	0	0	1 (1.8)	0	
TEAE Leading to Interruption of Study Drug	1 (8.3)	0	0	0	
TEAE Leading to Withdrawal of Study Drug	0	1 (20.0)	0	1 (5.6)	
TEAE Leading to Early Termination from Study	0	1 (20.0)	0	0	
TEAE Leading to death	0	0	0	0	



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

Most Frequent TEAEs – Any Causality

AE, n (%) of Participants Reporting	bexotegrast 40 mg (n=22)	bexotegrast 80 mg (n=23)	bexotegrast 160 mg (n=22)	bexotegrast All (n=67)	Placebo (n=23)
Most frequent TEAEs (≥ 10% in at least one arm)					
Diarrhea	2 (9.1)	5 (21.7)	5 (22.7)	12 (17.9)	1 (4.3)
 Related to study drug 	1 (4.5)	3 (13.0)	4 (18.2)	8 (11.9)	1 (4.3)

All TEAEs of Diarrhea Occurred in Patients on Standard of Care

- 12 of 13 participants with diarrhea were taking nintedanib
- · All but one event were mild to moderate in severity
- Diarrhea infrequently reported in bexotegrast Phase 1 trials



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

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Incidence of Diarrhea in IPF Randomized Clinical Trials


No Treatment-Emergent SAEs were Related to Study Drug

Treatment Group	Preferred term	Standard toxicity grade	Any alternative cause or confounding factors?	Action taken	Outcome
bexotegrast 40 mg	Acute respiratory failure	Grade 3 (Severe)	No	Dose not changed	Recovered / Resolved
	Pneumonia	Grade 2 (Moderate)	Removed carpet from home without a mask	Dose not changed	Recovered / Resolved
bexotegrast 160 mg	Idiopathic pulmonary fibrosis	Grade 3 (Severe)	Underlying disease and atrial fibrillation	Not applicable - hospitalization	Not Recovered / Not Resolved
bexotegrast 160 mg	Atrial flutter	Grade 3 (Severe)	Underlying disease	Not applicable - hospitalization	Recovered / Resolved
Placebo	Bladder dilatation	Grade 2 (Moderate)	No	Dose not changed - Foley catheter placed	Recovered / Resolved with Sequelae
Placebo	Respiratory failure	Grade 3 (Severe)	Coronary artery disease with triple vessel disease	Not applicable - early termination from the study	Recovered / Resolved with sequelae



Adverse events coded using MedDRA version 24.0

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Incidence of Acute Exacerbations in Recent Phase 2 IPF Randomized Clinical Trials

Investigational agent	Trial phase	Trial duration	Proportion of participants with acute exacerbation of IPF
Bexotegrast	2a	12 weeks	Active, 1.5% (n=1/67) Placebo, 0% (n=0/23)
BG00011	2b 1	52 weeks (prematurely terminated)	Active, 17% (n=9/54) Placebo, 0% (n=0/52)
BG00011	2a ²	8 weeks	Active, 16% (n=5/31) Placebo, 0% (n=0/10)
Pamrevlumab	2b ³	48 weeks	Active, 10%* (n= 5/50) Placebo, 13%* (n=7/53)
Pentraxin 2	2b ⁴	24 weeks	Active, 1.3% (n=1/77) Placebo, 2.6% (n=1/39)
BI 1015550	2b ⁵	12 weeks	Active, 1% (n=1/97) Placebo, 0% (n=0/50)
GLPG1690	2a ⁶	12 weeks	Active, 0% (n=0/17) Placebo, 0% (n=0/6)



* Acute exacerbations for pamrevlumab not specifically described; includes all adverse event related to IPF or respiratory in nature 1 Raghu et al, 2022; 2 Raghu et al, 2022; 3 Richeldi et al, 2019; 4 Raghu et al, 2018; 5 Richeldi et al, 2022; 6 Maher et al, 2018

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Safety Evaluation – Conclusions

Bexotegrast was well tolerated with no dose relationship for adverse events

No deaths or treatment related SAEs

No participants discontinued bexotegrast due to TEAE

Most frequent TEAE seen was diarrhea, but only seen in patients on standard of care





Pharmacokinetic Evaluation



Based on sparse sampling, overall, bexotegrast pharmacokinetics and % unbound in IPF consistent with that of previous studies

Concentrations in IPF participants increased approximately proportionally with dose

Overall % unbound was ~0.3 to 0.5%

Full PK curve will be predicted using population PK model to project AUC_{0_24} and C_{max}





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



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

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



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



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

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Change in FVC from Baseline to Week 12 in not on SoC Subgroup MMRM analysis - ITT population



Proportion of Participants with FVCpp Decline ≥ 10% ITT population



Forced Vital Capacity (FVC) Evaluation – Conclusions

Bexotegrast -treated participants experienced a benefit in FVC change from Baseline to Week 12 (-15.1 mL for pooled bexotegrast group) compared to those on placebo (-74.1 mL)¹

Bexotegrast treatment effect was evident with and without use of standard of care

Bexotegrast 80 mg dose demonstrated an improvement in FVC (+24.6 mL)

Dose-dependent reduction in proportion of participants with FVCpp decline of ≥ 10%



¹ MMRM analysis ITT population



Mean Percent Change in QLF Extent from Baseline to Week 12 CT protocol population within screening window





QLF = quantitative lung fibrosis



Mean Percent Change in QLF Extent from Baseline to Week 12 CT protocol population

Proportion of Participants with "Improved", "Stable" or "Worse" QLF Score at 12 Weeks



Drop Line Plot of Change in Individual QLF Scores at Week 12 for Bexotegrast and Placebo Groups



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QLF = quantitative lung fibrosis

Quantitative Lung Fibrosis Evaluation – Conclusions

Dose-dependent antifibrotic effect as evidenced by QLF Imaging

No progression in 160 mg group at Week 12 based on mean change from baseline

Higher proportion of participants remained stable or improved in the 80 mg and 160 mg groups versus placebo





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

PRO-C3 Type III collagen synthesis neoepitope



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

Change from baseline analyzed using a mixed model for repeated measures with terms for treatment group, visit, baseline value, and treatment-by-visit interaction. LS = Least Squares; SE = Standard Error © 2023 PLIANT THERAPEUTICS

Conclusion and Next Steps

Results from the INTEGRIS-IPF trial exceeded our expectations showing a favorable safety and tolerability profile and a treatment effect on FVC and QLF

Importantly, the fact the treatment effect was also observed on top of standard of care therapy gives us confidence that bexotegrast has the potential to advance the treatment of IPF

Pliant completed enrollment of the 320 mg cohort of the INTEGRIS-IPF Phase 2a trial in 2Q 2022. Interim data (12 weeks) from this trial is anticipated in early 2023. Final data (24+ weeks) is anticipated in 2Q 2023

Pliant plans to initiate a Phase 2b trial in patients with IPF in mid-2023

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



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





PLN-101095

Dual Selective α_Vβ₈ / α_Vβ₁ Integrin Inhibitor

Reprograming the Immunosuppressive Tumor Micro-Environment of Solid Tumors

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

$\alpha_V \beta_8$ Biology	Pharmacology	Differentiation	Development Status
α _v β ₈ regulates TGF β activation with a central role in immune suppression in cancer	 Highly selective inhibitor of α_Vβ₈ & α_Vβ₁ Supports human dose projections and high target coverage Compelling rationale for α_Vβ₈ combination therapy with PD-(L)1 	Dual mode of action targeting T cells α _v β ₈ & Fibroblasts α _v β ₁ PO Dosing	No major findings in 28D GLP rat & dog toxicology studies IND submitted Q4 2022 FIH study to start 2Q 2023

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



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Pliant's Approach to Addressing Immune Checkpoint Inhibitor Resistance

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

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

[1] TGFb directly targets cytotoxic T cells in cancer, DOI 10.1016/j.ccr.2005.10.012; [2] TGFb induces exhaustion in memory T cells, doi:10.1038/leu.2014.84; [3] TGFb attenuates PDL1 responses, doi:10.1038/nature25501 [4] IFN-y-related mRNA profile predicts clinical response to PD-1 blockade, https://doi.org/10.1172/JCI91190; [5] Pancancer analysis reveals associations with pembrolizumab sensitivity, https://doi.org/10.1016/j.ccr.2005.10.012; [2] TGFb induces exhaustion in memory T cells, doi:10.1038/nature25501 [4] IFN-y-related mRNA profile predicts clinical response to PD-1 blockade, https://doi.org/10.1172/JCI91190; [5] Pancancer analysis reveals associations with pembrolizumab sensitivity, https://doi.org/10.1172/JCI91190; [5] Pancancer analysis reveals associations with pembrolizumab sensitivity.

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High ITGB8 on Tumor or T cells Has Poor Prognosis

High ITGB8 expression on tumor cells has a worse clinical prognosis

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

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



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



Single Agent PLN-101095 Promoted T Cell Infiltration

Reduced TGF-β Signaling







PLIANT SITC 2022 Poster #1352



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



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







PLIANT SITC 2022 Poster #1352

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





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

Study Category	Studies Completed	Findings with PLN-101095
Repeat Dose Toxicology	 14-day DRF in rat 7-day DRF in dog GLP 1-Month IND-enabling rat GLP 1-Month IND-enabling dog 	 No adverse findings in rat or dog DRF All doses tolerated NOAEL¹ set at highest dose
Safety Pharmacology	GLP hERGSafety44	No findings
Genetic Toxicology	GLP AmesGLP In vitro micronucleus	No findings



PLIANT 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

IND submitted for PLN-101095 at year-end 2022

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Selective Muscle Cell Integrin Agonism for the Treatment of Muscular Dystrophies PLIANT

α₇β₁: A Drug Target in Muscular Dystrophies

- Predominantly expressed in skeletal, heart and smooth muscle
- α₇β₁ 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

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Integrin α₇β₁ Agonist Antibody Promoted Muscle Maturation



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



Body Weight Improvement at 4 and 12 Weeks of Treatment



5-6 wk old D2-MDX mice



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

Plantar flexion test

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



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

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MYOLOGICA

Post-eccentric injury, 12 week Force Force (Normalized to initial contraction) DBA-IgG Control Mdx-IgG Control Mdx-3mg/K Mdx-15mg/K 5 10 25 15 20 ò Stimulation Frequency (Hz) Post-injury Force, 12w 1.2 . Forque, (Fpost/Fpre) Π

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Diaphragm Force Significantly Improved at 4 Weeks of Treatment



MYOLOGICA

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



 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

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Pliant Development Pipeline



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