42463

Safety, tolerability and antifibrotic activity of bexotegrast: Phase 2a INTEGRIS-IPF study (NCT04396756)

Wuyts WA, Valenzuela C, Jenkins G, Goldin JG, Kim GJ, Jurek M, Turner S, Decaris M, Barnes CN, Lefebvre É, Cosgrove G, Cottin V

SEPTEMBER 10, 2023

© 2023 PLIANT THERAPEUTICS

Conflict of interest disclosure

❑ I have no real or perceived conflicts of interest that relate to this presentation.

☑ I have the following real or perceived conflicts of interest that relate to this presentation:

Affiliation/Financial interest	Commercial company
Grants/research support:	Roche, Boehringer Ingelheim, Pliant Therapeutics, Inc., Galapagos, and Alentis Therapeutics
Honoraria or consultation fees:	Roche, Boehringer Ingelheim, Pliant Therapeutics, Inc., Galapagos, and Alentis Therapeutics
Participation in a company sponsored bureau:	
Stock shareholder:	
Spouse/partner:	
Other support/potential conflict of interest:	

This event is accredited for CME credits by EBAP and speakers are required to disclose their potential conflict of interest. The intent of this disclosure is not to prevent a speaker with a conflict of interest (any significant financial relationship a speaker has with manufacturers or providers of any commercial products or services relevant to the talk) from making a presentation, but rather to provide listeners with information on which they can make their own judgments. It remains for audience members to determine whether the speaker's interests, or relationships may influence the presentation. The ERS does not view the existence of these interests or commitments as necessarily implying bias or decreasing the value of the speaker's presentation. Drug or device advertisement is forbidden.

© 2023 PLIANT THERAPEUTICS

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; future availability of clinical trial data; the sufficiency of our cash, cash equivalents and short-term investments; the timing and outcome of regulatory decisions; 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's most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q on file with the Securities and Exchange Commission (the "SEC") and our other filings with the SEC.

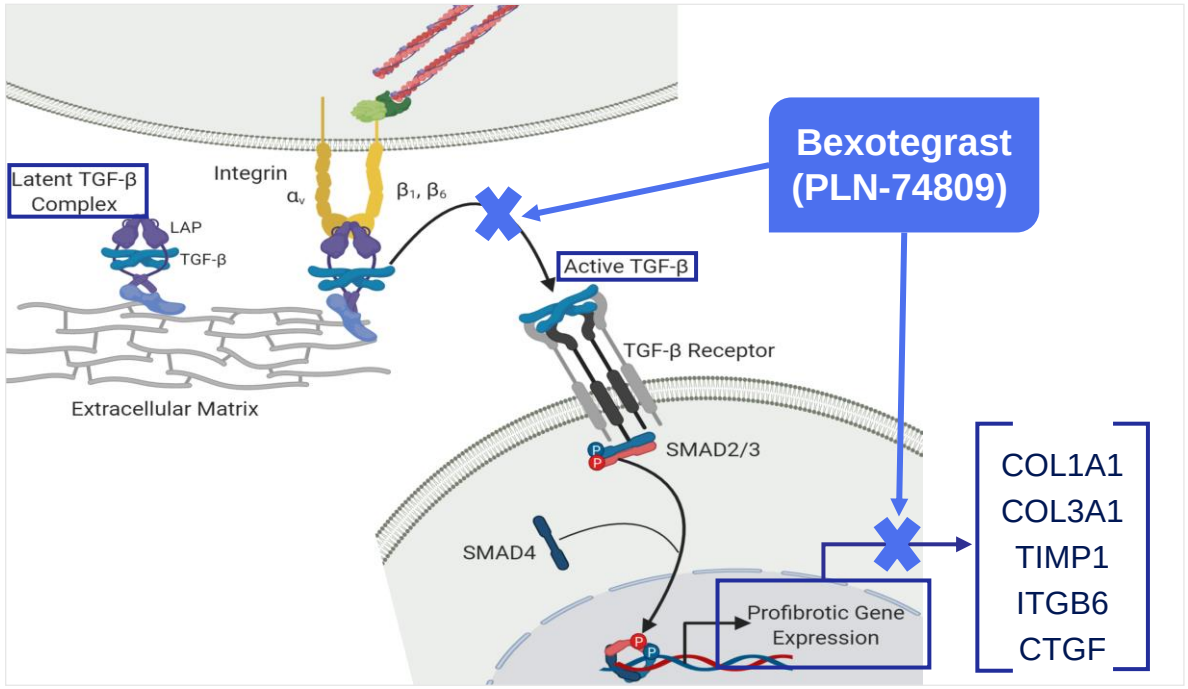
This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. 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.

© 2023 PLIANT THERAPEUTICS

$\alpha_v\beta_6$ and $\alpha_v\beta_1$ integrins drive cell-matrix interactions in fibrosis

$\alpha_v\beta_6$ and $\alpha_v\beta_1$ integrins promote fibrosis through activation of TGF-β[1,2]



- TGF-β is a central mediator of fibrosis[1,2]
- Systemic TGF-β blockade carries toxicity risks[2]
- Activation of latent TGF-β by $\alpha_v\beta_6$ (lung epithelial cells) and $\alpha_v\beta_1$ (lung fibroblasts) is increased in fibrotic lung tissue[2–6]

Localized TGF-β inhibition in the fibrotic lung may provide a novel approach to treat IPF, without affecting TGF-β signaling systemically

COL1A1, collagen type I alpha 1; COL3A1, collagen type III alpha 1; CTGF, connective tissue growth factor; IPF, idiopathic pulmonary fibrosis; ITGB6, integrin beta-6; LAP, latency-associated peptide; SMAD, family of proteins similar to the gene products of the Drosophila gene 'mothers against decapentaplegic' (*Mad*) and the *C. elegans* gene *Sma*; TGF-β, transforming growth factor-beta; TIMP1, tissue inhibitor matrix metalloproteinase 1

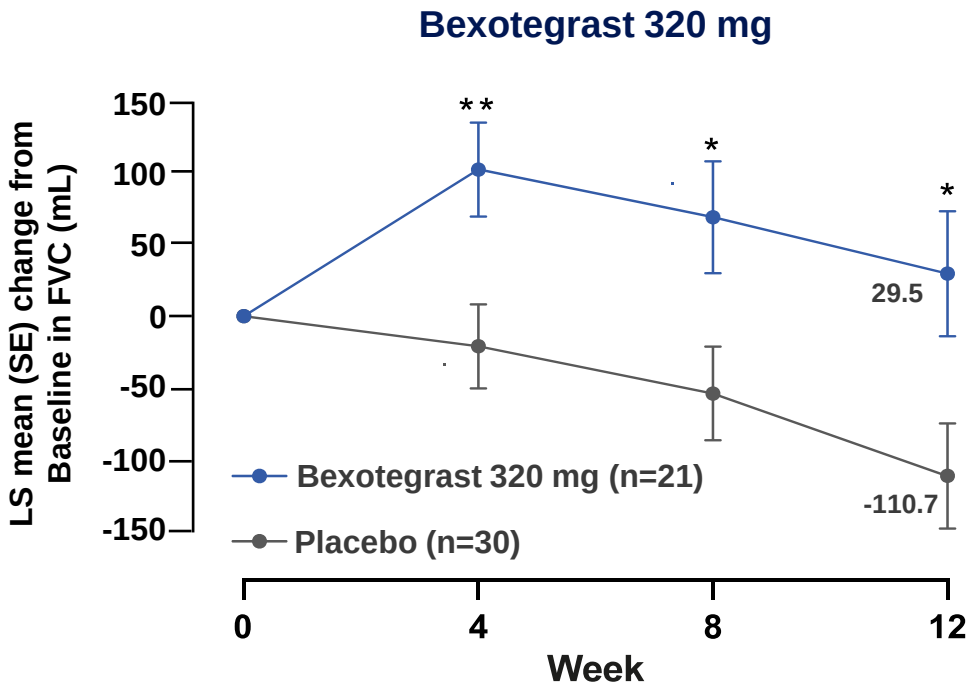
1. Saito A, et al. *Int J Mol Sci* 2018;19(8):2460; 2. Decaris ML, et al. *Respir Res* 2021;22(1):265; 3. Reed NI, et al. *Sci Transl Med* 2015;7(288):288ra79; 4. Munger JS, et al. *Cell* 1999;96(3):319–328; 5. Horan GS, et al. *Am J Respir Crit Care Med* 2008;177(1):56–65; 6. Saini G, et al. *Eur Respir J* 2015;46(2):486–494

© 2023 PLIANT THERAPEUTICS

Phase 2a INTEGRIS-IPF study – 12-week analyses

FVC change from Baseline to Week 12

(MMRM analysis) (efficacy mITT population[a])



- Bexotegrast was well tolerated across all dose groups over 12 weeks of treatment; most TEAEs were mild to moderate in severity, with no drug-related SAEs
- Bexotegrast-treated participants experienced a reduction in FVC decline over 12 weeks vs. placebo, with the treatment effect observed with and without the use of a background therapy
- There was a dose-dependent antifibrotic effect observed with QLF imaging, with no or limited progression at 160 mg and 320 mg
- A decrease in serum biomarkers of collagen synthesis (PRO-C3 and PRO-C6) and ITGB6 was observed relative to placebo

*p<0.05 vs. placebo; **p<0.01 vs. placebo

[a]One participant in the placebo group was identified as a statistical outlier across all treatment groups and excluded from the mITT analysis

FVC, forced vital capacity; ITGB6, integrin beta-6; LS, least squares; mITT, modified intent-to-treat; MMRM, mixed model with repeated measures; QLF, quantitative lung fibrosis; SAE, serious adverse event; SE, standard error; TEAE, treatment-emergent adverse event

Lancaster LH, et al. Oral presentation at the American Thoracic Society (ATS) International Conference, May 17–22, 2023, Washington, DC, USA. A11463

© 2023 PLIANT THERAPEUTICS

Aims and objectives

To present Week 24 results from INTEGRIS-IPF (NCT04396756) for the safety, tolerability, and durability of effects on FVC and QLF of bexotegrast 320 mg in participants with IPF

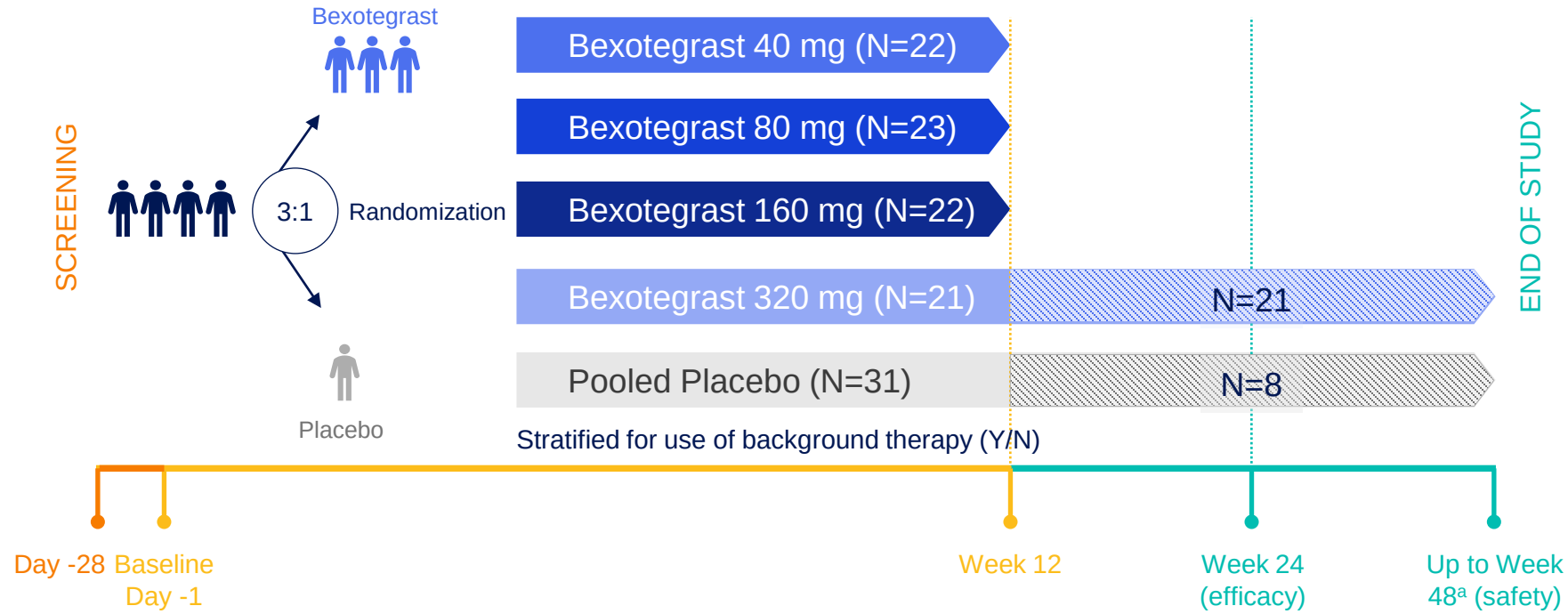
Purpose of evaluating longer term treatment with bexotegrast 320 mg

- Safety and tolerability of the highest dose planned for late-stage development
  - Participants were evaluated for at least 24 weeks and up to 48 weeks, with the longest duration of evaluation at Week 40
- Treatment effect at Week 24 (FVC, QLF imaging)

FVC, forced vital capacity; IPF, idiopathic pulmonary fibrosis; QLF, quantitative lung fibrosis

© 2023 PLIANT THERAPEUTICS

INTEGRIS-IPF study design and endpoints



PRIMARY AND SECONDARY ENDPOINTS

- Safety and tolerability, including TEAEs

EXPLORATORY ENDPOINTS

- Change in FVC over 12 and 24 weeks[b]
- Change in high-resolution CT-based QLF score at 12 and 24 weeks[b]

This study design figure represents all participants in the intent-to-treat population
[a]Once the last participant in the bexotegrast 320 mg dose cohort reached Week 24, all participants still on study continued to the next scheduled visit and then discontinued the study;
[b]protocol-specified assessment timepoints
CT, computed tomography; FVC, forced vital capacity; QLF, quantitative lung fibrosis; TEAEs, treatment emergent adverse events; Y/N, yes/no

© 2023 PLIANT THERAPEUTICS

Baseline demographics and disease characteristics – bexotegrast 320 mg cohort

	Participants, n (%)	
Demographics	**Bexotegrast 320 mg (N=22)[a]**	**Placebo (N=8)[a]**
Male sex, n (%)	21 (95.5)	5 (62.5)
Mean age, years (SD)	70.5 (7.14)	73.3 (7.98)
Mean time since IPF diagnosis, months (SD)	34.4 (28.97)	41.6 (32.56)
Background therapy use, n (%)	**18 (81.8)**	**6 (75.0)**
None	4 (18.2)	2 (25.0)
Pirfenidone	8 (36.4)	1 (12.5)
Nintedanib	10 (45.5)	5 (62.5)
Mean duration of background therapy use at Randomization, months (SD)	**23.29 (21.76)**	**17.82 (20.30)**
Mean FVC, mL (SD)	3192.0 (678.39)	2658.4 (587.10)
FVCpp, mean (SD)	77.5 (15.83)	75.5 (18.90)
DLco percent predicted, corrected for hemoglobin level, mean (SD)	47.6 (12.97)[b]	49.4 (12.91)

[a]One participant, randomized to placebo, received both placebo and bexotegrast 320 mg for approximately 1 week due to incorrect study-drug dispensation, which was identified after the Week 12 interim analysis. Here, they are included in the denominator of both groups; [b]data available for 21 participants
DLco, diffusing capacity of the lungs for carbon monoxide; FVC, forced vital capacity; FVCpp, FVC percent predicted; IPF, idiopathic pulmonary fibrosis; SD, standard deviation

© 2023 PLIANT THERAPEUTICS

Safety summary—bexotegrast 320 mg cohort

	Participants, n (%)	
Participants with any:	**Bexotegrast 320 mg (N=22)[a]**	**Placebo (N=8)[a]**
TEAE	20 (90.9)	7 (87.5)
TEAE related to study drug	**5 (22.7)**	**2 (25.0)**
Grade ≥3 TEAE[b]	5 (22.7)	1 (12.5)
Grade ≥3 TEAE related to study drug	**1 (4.5)[c]**	**0 (0.0)**
SAE	2 (9.1)	1 (12.5)
SAE related to study drug	**0 (0.0)**	**0 (0.0)**
TEAE leading to interruption of study drug	4 (18.2)[d,e,f,g]	0 (0.0)
TEAE leading to withdrawal of study drug	3 (13.6)[d,h,i]	1 (12.5)
TEAE leading to death	1 (4.5)[h]	0 (0.0)

[a]One participant, randomized to placebo, received both placebo and bexotegrast 320 mg for approximately 1 week due to incorrect study-drug dispensation, which was identified after the Week 12 interim analysis. Here, they are included in the denominator of both groups; [b]graded using Common Terminology Criteria For Adverse Events; [c]blood pressure increase; [d]abdominal pain/diarrhea in 1 participant with pre-existing ulcerative colitis; [e]acute kidney injury, constipation, gastritis, hyperlactacidemia, and ileus in 1 participant; [f]IPF; [g]diarrhea in 1 participant with concomitant use of nintedanib; [h]acute respiratory failure in 1 participant with GAP Stage III and pre-existing atrial fibrillation following elective atrioventricular node ablation; [i]diarrhea in 1 participant with concomitant use of nintedanib

AE, adverse event; GAP, gender-age-physiology; IPF, idiopathic pulmonary fibrosis; SAE, serious AE; TEAE, treatment-emergent AE

© 2023 PLIANT THERAPEUTICS

Most frequently reported TEAEs were not related to study drug – bexotegrast 320 mg cohort

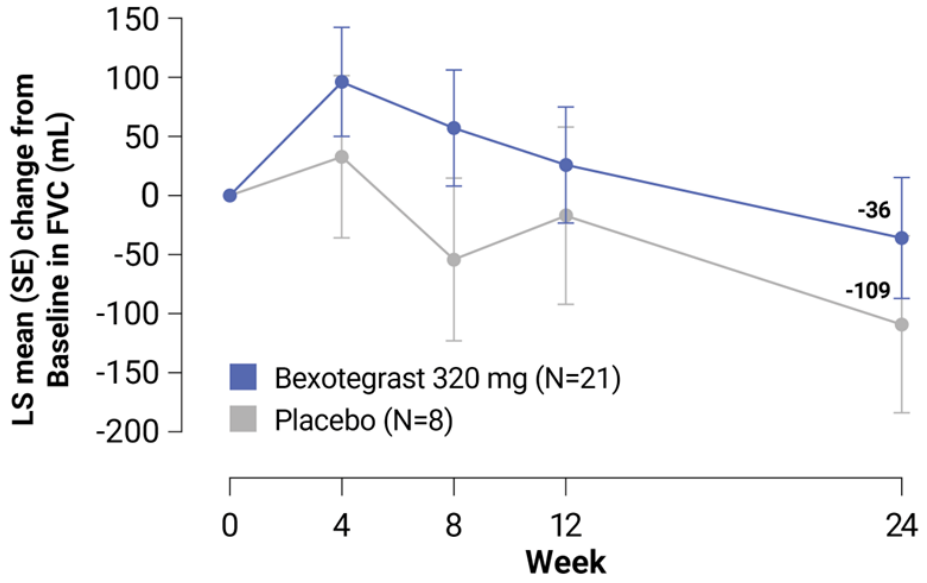
AE, n (%) of Participants Reporting	Bexotegrast 320 mg (N=22)	Placebo (N=8)
Most frequent TEAEs (>10% in at least one arm and n >1 participant)		
Diarrhea	7 (31.8)	3 (37.5)
Related to study drug	4 (18.2)	0
Dyspnea	5 (22.7)	1 (12.5)
Related to study drug	0	0
Idiopathic Pulmonary Fibrosis/Pulmonary Fibrosis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

© 2023 PLIANT THERAPEUTICS

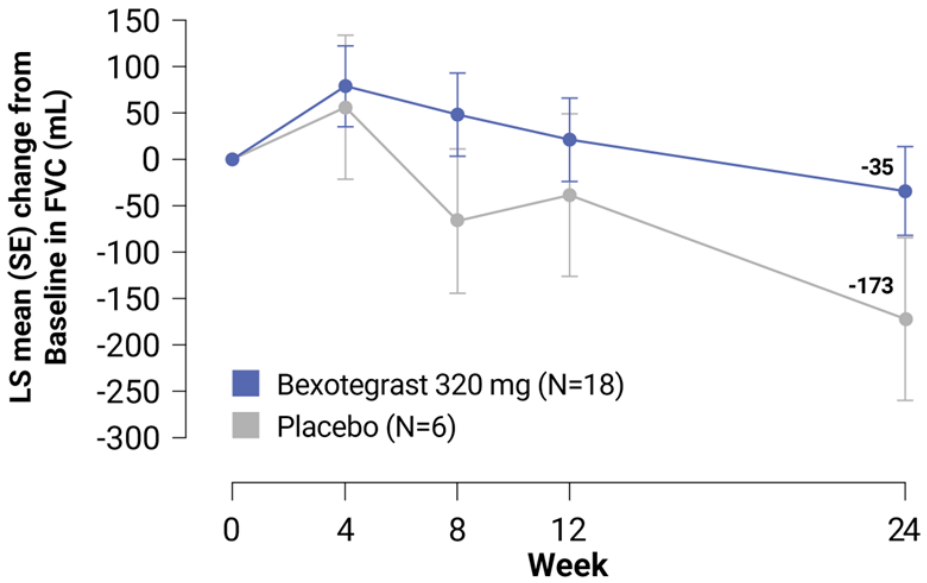
FVC change from Baseline to Week 24
ITT population and background therapy subgroup

ITT population



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

Background therapy subgroup

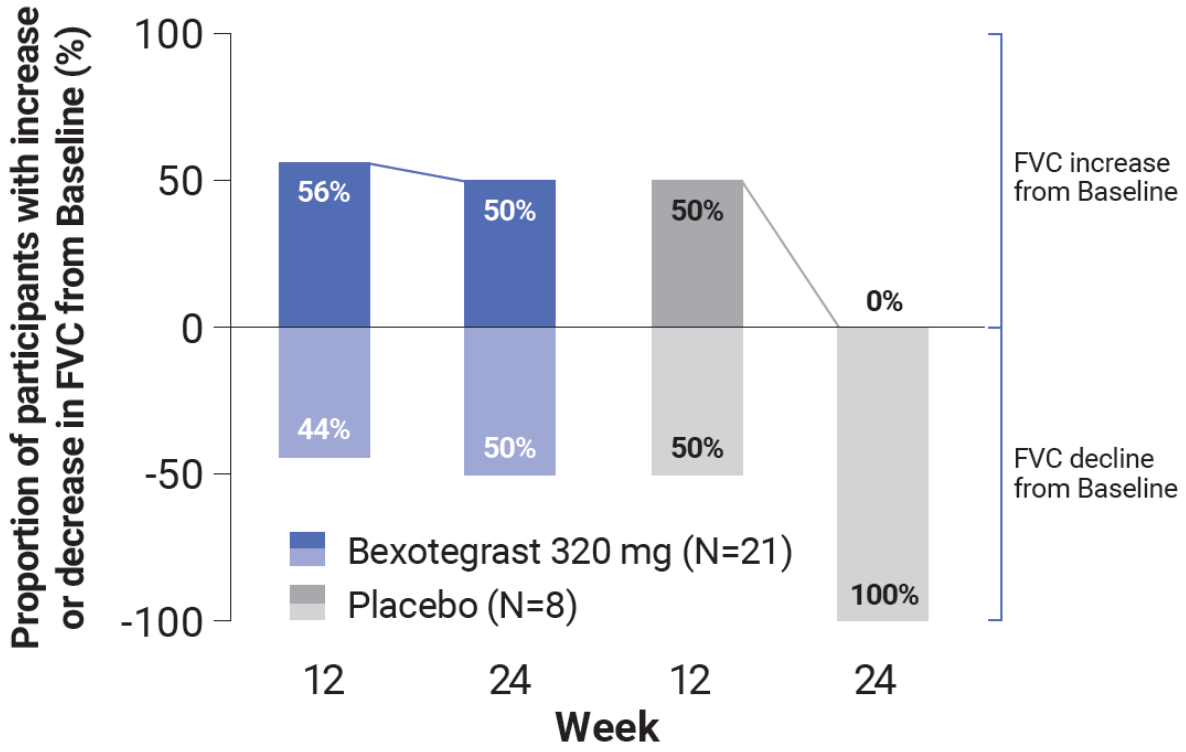


Bexotegrast + a background therapy reduced FVC decline by 80% relative to a background therapy alone at Week 24

Participants not receiving a background therapy (nintedanib or pirfenidone) are not shown due to small sample size: n=4 (bexotegrast 320 mg) and n=2 (placebo)
FVC, forced vital capacity; ITT, intent-to-treat; LS, least squares; SE, standard error

© 2023 PLIANT THERAPEUTICS

FVC change at Week 24
ITT population



FVC change data suggest a persistent treatment effect from 12 to 24 weeks with bexotegrast 320 mg

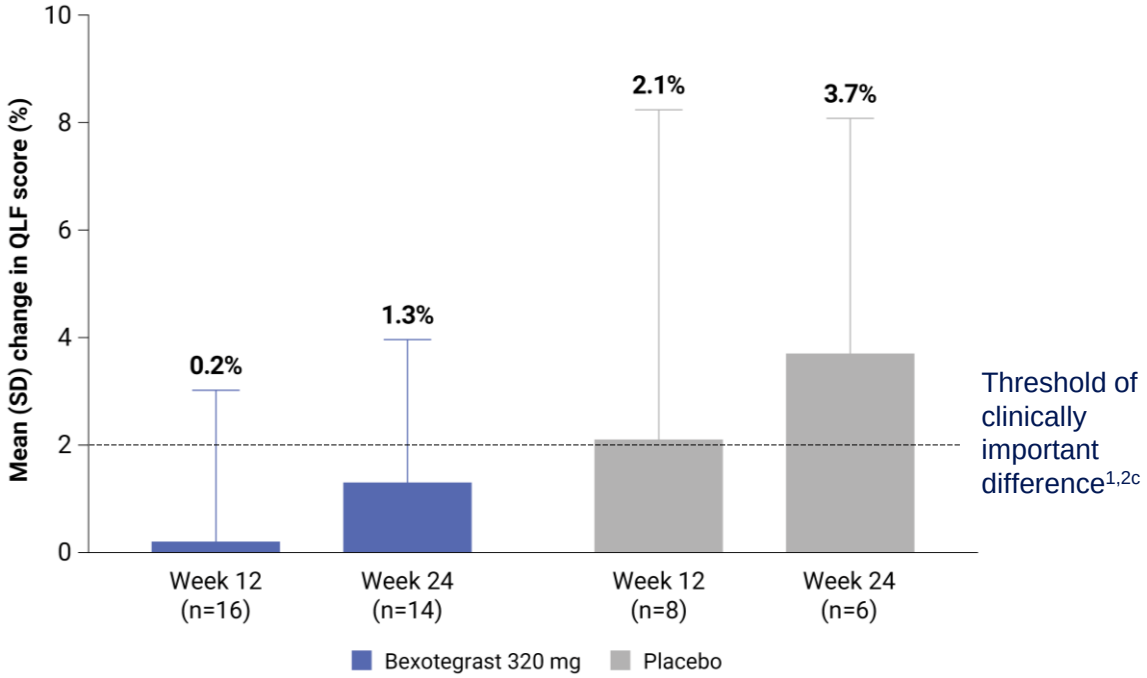
Participants with missing data are not included here
FVC, forced vital capacity; ITT, intent-to-treat

© 2023 PLIANT THERAPEUTICS

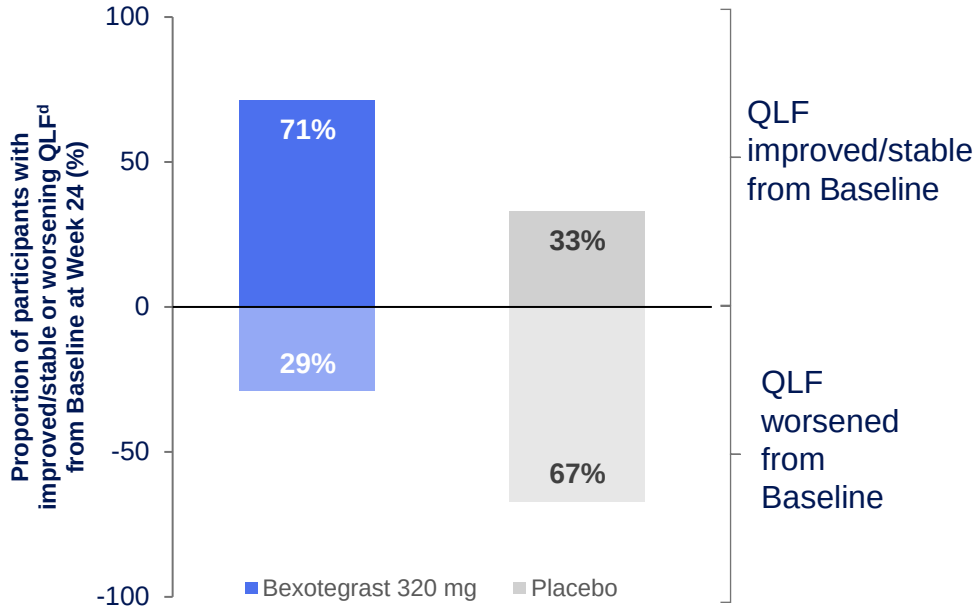
Change in QLF score[a] change from Baseline and stabilization/improvement in fibrosis

Per CT protocol population[b]

Change in QLF score



Stabilization/improvement in fibrosis



[a]QLF assessed on whole lung; [b]the per CT protocol population is a subset of the intent-to-treat population, with imaging data that meets quality standards and scans conducted within the specified time intervals; [c]a threshold of 2% change in QLF has been proposed as a potential minimal clinically important difference for the whole lung[1,2]; [d]changes in QLF score between -2% and 2% were considered stable fibrosis; a reduction from Baseline >2% was considered improved fibrosis; an increase from Baseline >2% was considered worsening fibrosis
CT, computed tomography; QLF; quantitative lung fibrosis; SD, standard deviation

1. Kim GHJ, et al. *Eur Radiol* 2020;30(2):726–734; 2. Kim GHJ, et al. *Ther Adv Respir Dis* 2021;15:17534666211004238

© 2023 PLIANT THERAPEUTICS

Conclusions and future research

Bexotegrast 320 mg was well tolerated in participants with IPF for up to 40 weeks of treatment

- Most TEAEs were mild or moderate in severity
- No discontinuations due to TEAEs occurred from Week 12 to Week 40
- No drug-related SAEs were reported

There was evidence of a durable treatment effect on FVC over 24 weeks

QLF evaluation supports the antifibrotic mechanism of bexotegrast

- QLF imaging showed stabilization of fibrosis in bexotegrast 320 mg-treated participants, while those receiving placebo were more likely to have clinically meaningful progression
- At Week 24, the proportion of bexotegrast 320 mg-treated participants with stabilization or improvement of fibrosis was twice as high as those in the placebo group

Limitations

- The current study was designed to assess safety and tolerability and was not powered to adequately assess efficacy with relatively small patient populations and limited treatment duration

Future research

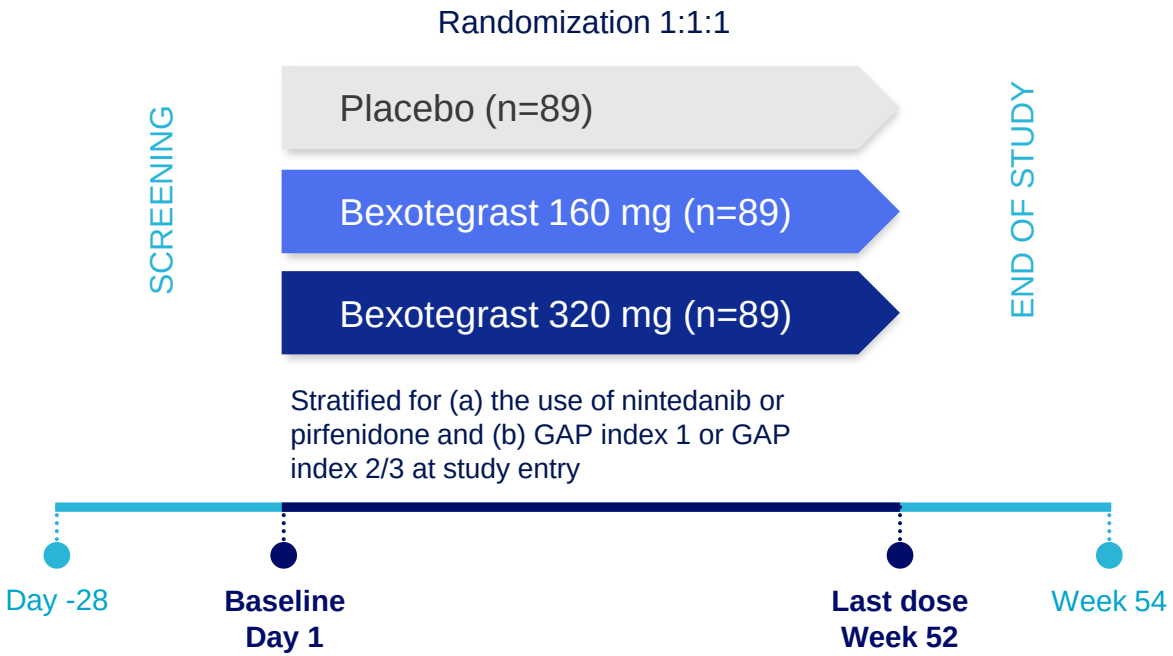
- Late-stage evaluation of bexotegrast was initiated in mid-2023 in the BEACON-IPF study

FVC, forced vital capacity; IPF, idiopathic pulmonary fibrosis; QLF, quantitative lung fibrosis; SAE, serious adverse event; TEAE, treatment-emergent adverse event

1. Pliant Therapeutics, Inc. [Press release]. April 30, 2023. https://www.globenewswire.com/news-release/2023/04/30/2658013/0/en/Pliant-Therapeutics-Announces-Positive-Long-Term-Data-from-the-INTEGRIS-IPF-Phase-2a-Trial-Demonstrating-Bexotegrast-was-Well-Tolerated-at-320-mg-with-Durable-Improvement-Shown-in-. Accessed August 4, 2023

© 2023 PLIANT THERAPEUTICS

BEACON-IPF study design



PRIMARY ENDPOINT

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

SECONDARY ENDPOINTS

- Time to disease progression (≥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

FVC, forced vital capacity; FVCpp, FVC percent predicted; GAP, gender-age-physiology

© 2023 PLIANT THERAPEUTICS

Acknowledgements

- Thank you to the clinical site staff and the patients who participated in this study
- The INTEGRIS-IPF study was sponsored by Pliant Therapeutics, Inc.
- Thank you to Hardean E Achneck, MD (Senior Vice President, Head of Clinical Development at Pliant Therapeutics, Inc.) and Annie Clark, PharmD PhD (Senior Director, Clinical Pharmacology at Pliant Therapeutics, Inc.) for their contributions
- Editorial assistance was provided by Aimee Sherlock, MSc of Alpharmaxim Healthcare Communications and funded by Pliant Therapeutics, Inc.

© 2023 PLIANT THERAPEUTICS

References

- Decaris ML, Schaub JR, Chen C, et al. Dual inhibition of $\alpha_v\beta_6$ and $\alpha_v\beta_1$ reduces fibrogenesis in lung tissue explants from patients with IPF. *Respir Res* 2021;22(1):265
- Horan GS, Wood S, Ona V, et al. Partial inhibition of integrin alpha($_v$)beta$_6$ prevents pulmonary fibrosis without exacerbating inflammation. *Am J Respir Crit Care Med* 2008;177(1):56–65
- Kim GHJ, Weight SS, Belpiro JA, et al. Prediction of idiopathic pulmonary fibrosis progression using early quantitative changes on CT imaging for a short term of clinical 18-24-month follow-ups. *Eur Radiol* 2020;30(2):726–734
- Munger JS, Huang X, Kawakatsu H, et al. The integrin alpha $_v$ beta $_6$ binds and activates latent TGF beta 1: a mechanism for regulating pulmonary inflammation and fibrosis. *Cell* 1999;96(3):319–328
- Pliant Therapeutics, Inc. [Press release]. April 30, 2023. https://www.globenewswire.com/news-release/2023/04/30/2658013/0/en/Pliant-Therapeutics-Announces-Positive-Long-Term-Data-from-the-INTEGRIS-IPF-Phase-2a-Trial-Demonstrating-Bexotegrast-was-Well-Tolerated-at-320-mg-with-Durable-Improvement-Shown-in-. Accessed August 4, 2023
- Reed NI, Jo H, Chen C, et al. The $\alpha_v\beta_1$ integrin plays a critical in vivo role in tissue fibrosis. *Sci Transl Med* 2015;7(288):288ra79
- Saini G, Porte J, Weinreb PH, et al. $\alpha_v\beta_6$ integrin may be a potential prognostic biomarker in interstitial lung disease. *Eur Respir J* 2015;46(2):486–494
- Saito A, Horie M, Nagase T. TGF-β signaling in lung health and disease. *Int J Mol Sci* 2018;19(8):2460

© 2023 PLIANT THERAPEUTICS

Please use the QR codes shown to download a copy of the ePoster (OA1423)

pliantrx.com

live.ersnet.org

The ERS is not responsible for and does not endorse the data and information presented on external sites

© 2023 PLIANT THERAPEUTICS