Pliant Therapeutics Announces Positive Data from the INTEGRIS-IPF Phase 2a Trial Demonstrating Bexotegrast 320 mg was Well Tolerated and Achieved Statistically Significant FVC Increase in Patients with Idiopathic Pulmonary Fibrosis

01-22-2023 at 2:00 PM EST

Bexotegrast demonstrated statistically significant increase in FVC at 4, 8 and 12 weeks of treatment, outperforming lower dose groups

No bexotegrast-treated patients experienced disease progression as defined by FVCpp decline of greater than or equal to 10%

Bexotegrast was well tolerated over 12 weeks of treatment with no drug-related severe or serious adverse events

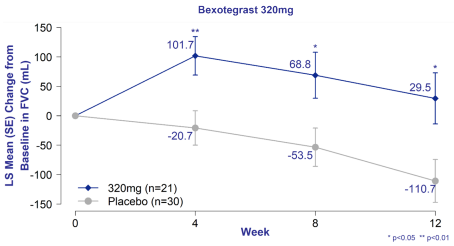
Company to host webcast and conference call tomorrow, Monday, January 23rd at 8:00 a.m. ET

SOUTH SAN FRANCISCO, Calif., Jan. 22, 2023 (GLOBE NEWSWIRE) -- Pliant Therapeutics, Inc. (Nasdaq: PLRX) today announced 12-week interim data from the 320 mg dose group of INTEGRIS-IPF, a multinational, randomized, double-blind, placebo-controlled Phase 2a clinical trial of bexotegrast (PLN-74809) in patients with idiopathic pulmonary fibrosis (IPF). The 320 mg group met its primary and secondary endpoints demonstrating that bexotegrast was well tolerated over a 12-week treatment period and displayed a favorable pharmacokinetic profile. The trial's exploratory efficacy endpoints assessed changes in forced vital capacity (FVC), Quantitative Lung Fibrosis (QLF) imaging and biomarkers. Bexotegrast at 320 mg demonstrated a statistically significant mean increase in FVC from baseline at all timepoints, surpassing all lower dose cohorts, and showed a strong treatment effect on FVC percent predicted (FVCpp), QLF and profibrotic biomarkers versus placebo at 12 weeks.

The INTEGRIS-IPF Phase 2a trial is evaluating bexotegrast at once-daily doses of 40 mg, 80 mg, 160 mg, 320 mg or placebo for 12 weeks in 119 patients with IPF.

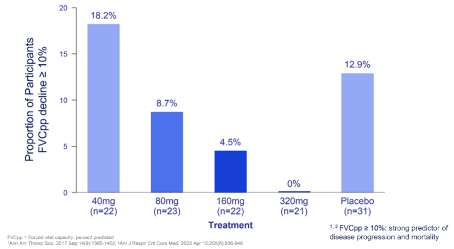
The 320 mg group enrolled 21 patients in the active arm and 8 patients in the placebo arm. Comparable to the lower dose groups, approximately 80% of all enrolled patients were on standard of care and were equally distributed between nintedanib and pirfenidone. The 320 mg group will continue until all patients have been treated for at least 24 weeks, with final data expected in the second quarter of 2023.

Figure 1.



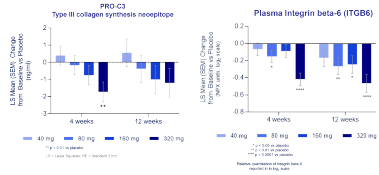
Change in FVC from Baseline of Bexotegrast 320 mg Over 12 Weeks in INTEGRIS-IPF; Mixed Model Repeat Measures Analysis – Modified Intent to Treat Population

Figure 2.



Proportion of Participants with FVCpp Decline ≥10% - Intent to Treat Population

Figure 3.



Circulating PRO-C3 and Integrin beta-6 Biomarker Levels– Change from Baseline at 4- and 12-Weeks vs Placebo

Bexotegrast 320 mg was Well Tolerated with No Drug-Related Severe or Serious Adverse Events

The primary endpoint of the INTEGRIS-IPF trial is the evaluation of the safety and tolerability of bexotegrast. The secondary endpoint is an assessment of its pharmacokinetics.

Bexotegrast was well tolerated at 320 mg over 12 weeks of treatment with no drug-related severe or serious adverse events (SAEs) reported. All drug-related adverse events were mild or moderate in severity.

Bexotegrast exhibited dose-proportional increases in plasma concentrations, consistent with prior studies.

Bexotegrast 320 mg Group Demonstrated Strong Treatment Effects on FVC, QLF and Profibrotic Biomarkers Versus Placebo over 12 Weeks

The exploratory efficacy endpoints of the INTEGRIS-IPF trial measured changes in FVC, high-resolution CT (HRCT)-based QLF, and profibrotic biomarkers over 12 weeks of treatment.

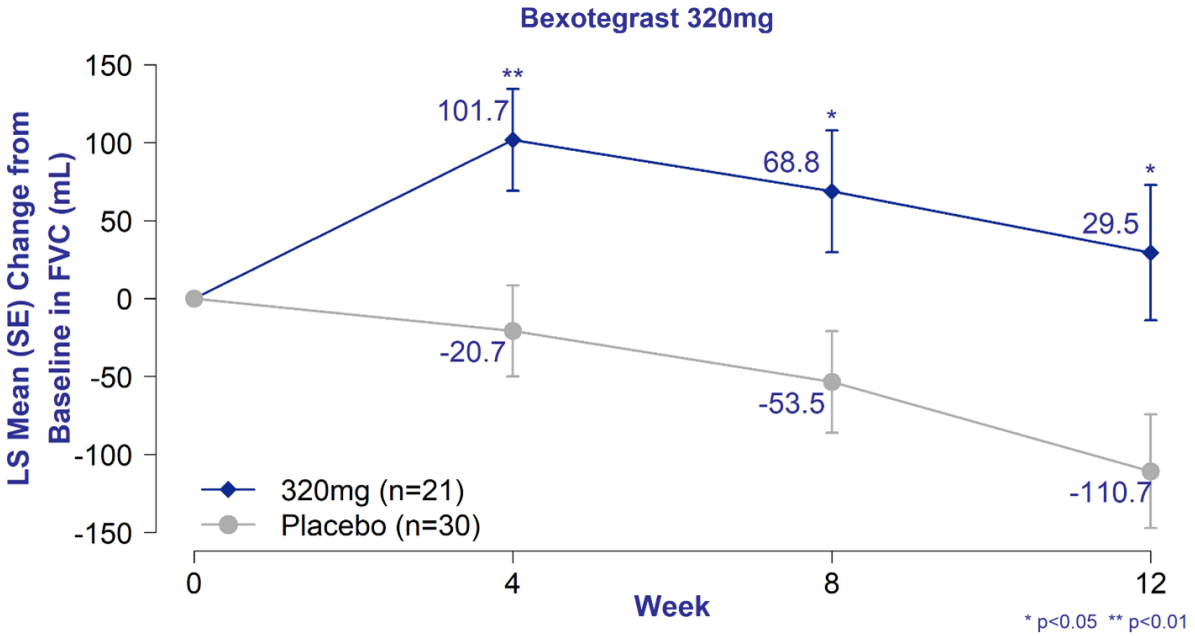


Figure 1. Change in FVC from Baseline of Bexotegrast 320 mg Over 12 Weeks in INTEGRIS-IPF; Mixed Model Repeat Measures Analysis – Modified Intent to Treat Population

A strong dose-dependent treatment effect was observed in the bexotegrast 320 mg dose group, with and without standard of care therapy. The bexotegrast 320 mg group demonstrated mean FVC increase of +29.5 mL relative to baseline at 12 weeks, versus a decline of 110.7 mL in the placebo group resulting in a 140 mL increase compared to placebo. Mean increases in FVC versus placebo reached statistical significance at all timepoints.

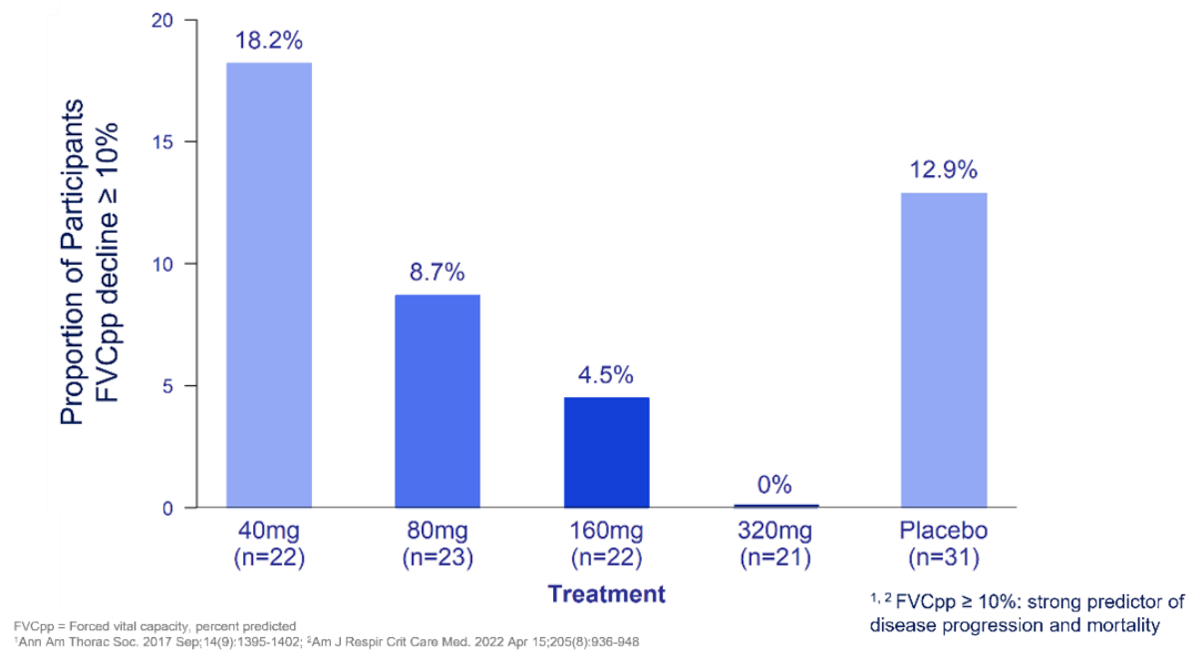
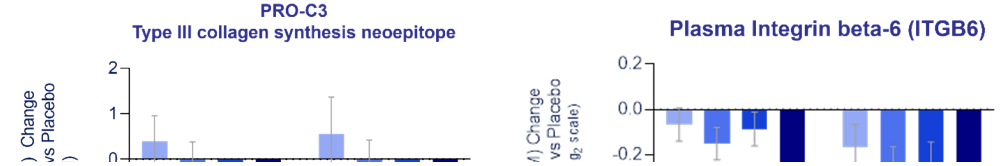


Figure 2. Proportion of Participants with FVCpp Decline ≥10% - Intent to Treat Population

A decline of ≥10% in FVCpp at 12 weeks has been associated with increased mortality in IPF patients over a two-year period.[1,2] Over 12 weeks of treatment, no patients in the 320 mg group experienced ≥10% decline in FVCpp.

An increase in QLF score has been associated with worsening of pulmonary fibrosis.[3] The mean percentage change in QLF at 12 weeks was 0.20% in the 320 mg group versus 1.46% in the placebo group.



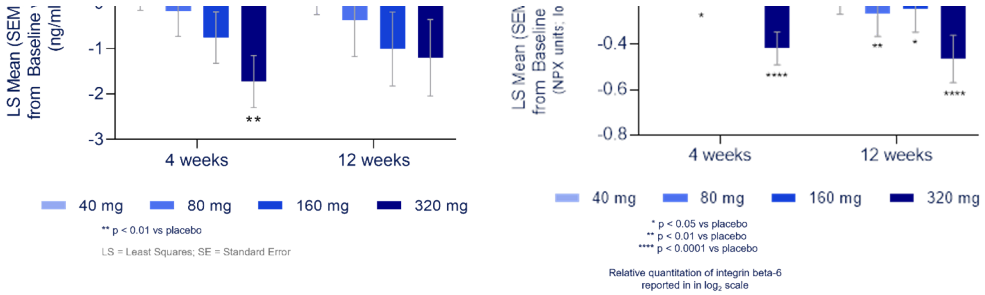


Figure 3. Circulating PRO-C3 and Integrin beta-6 Biomarker Levels–Change from Baseline at 4- and 12-Weeks vs Placebo

PRO-C3, a serum biomarker of type III collagen synthesis, is elevated in patients with IPF and associated with progressive disease.[4] The 320 mg group demonstrated a reduction in PRO-C3 at both 4 ($p < 0.01$) and 12 weeks versus placebo.

Elevated integrin beta-6 plasma levels have been associated with ILD progression as defined by mortality, transplant or ≥ 10% relative reduction in FVC (mL) over 12 months.[5] The 320 mg group demonstrated a reduction in integrin beta-6 at both 4 and 12 weeks ($p < 0.0001$ at both timepoints) versus placebo.

These findings support a potential dose-dependent antifibrotic effect of bexotegrast, consistent with its mechanism of action and preclinical findings.

“Data from the INTEGRIS-IPF trial have far exceeded our expectations, supporting bexotegrast’s favorable safety profile and demonstrating a statistically significant treatment response on FVC at 320 mg,” said Éric Lefebvre, M.D., Chief Medical Officer at Pliant Therapeutics. “Additionally, we are extremely encouraged to see a consistent dose response on FVC, QLF and profibrotic biomarkers. We look forward to advancing bexotegrast into Phase 2b clinical development.”

“The statistically significant increase in mean FVC versus placebo seen throughout the 12-week treatment period of the INTEGRIS-IPF trial at 320 mg is unprecedented in clinical trials observed to date,” said Lisa H. Lancaster, M.D., Professor of Medicine, Vanderbilt School of Medicine and INTEGRIS-IPF Principal Investigator. “Additionally, the dose-dependent changes in the beta-6 integrin biomarker data aligned with changes in FVC and the antifibrotic mechanism of action of bexotegrast.”

Bexotegrast Clinical Development Next Steps

Data from the 320 mg group of the INTEGRIS-IPF trial in patients treated for at least 24 weeks are expected in the second quarter of 2023. Pliant is planning to initiate a Phase 2b clinical trial of bexotegrast in mid-2023. Trial details will be shared closer to initiation.

INTEGRIS-IPF Multinational Phase 2 Trial of PLN-74809 (NCT04396756)

INTEGRIS-IPF is a Phase 2a, randomized, dose-ranging, double-blind, placebo-controlled trial evaluating the safety, tolerability, and pharmacokinetics of PLN-74809 administered in patients with IPF. Patients were enrolled in doses of 40 mg, 80 mg, 160 mg or 320 mg with a 3:1 randomization ratio (active:placebo) and stratification based on use of standard of care therapy. The primary endpoint is the evaluation of PLN-74809 safety and tolerability and the secondary endpoint is the assessment of pharmacokinetics across a dose range. Exploratory endpoints will measure change in Forced Vital Capacity (FVC), HRCT-based Quantitative Lung Fibrosis (QLF) score and selected biomarkers**.**

Background on Idiopathic Pulmonary Fibrosis

IPF is a chronic, progressive, fibrosing lung disease of unknown cause with few treatment options and a poor prognosis. Patients experience debilitating symptoms, including shortness of breath and difficulty performing daily activities, such as walking and talking. Currently, there is no pharmacological cure for IPF, with neither of the approved two therapies demonstrating an ability to stop the progression of IPF. Therefore, there is a high unmet need for new therapeutic options to address the symptoms and modify the disease progression of this grievous illness.

Conference Call and Webcast Information

The Company will host a conference call and webcast with a slide presentation tomorrow, Monday, January 23 at 8:00 a.m. ET to discuss this update. Interested parties may access the webcast live via Pliant’s website at https://edge.media-server.com/mmc/p/fjeazzr9. The live audio of the conference call can be accessed by telephone by registering in advance at the following link: Pliant Therapeutics INTEGRIS-IPF Conference Call. Upon registration, all telephone participants will receive the dial-in number along with a unique passcode to access the call. An archived replay of the webcast via Pliant’s website for 30 days following completion of the event.

About Pliant Therapeutics, Inc.

Pliant Therapeutics is a clinical stage biopharmaceutical company focused on discovering and developing novel therapies for the treatment of fibrosis. Pliant's lead product candidate, bexotegrast (PLN-74809), is an oral small molecule dual selective inhibitor of αvß6 and αvß1 integrins that is in development in the lead indications for the treatment of idiopathic pulmonary fibrosis, or IPF, and primary sclerosing cholangitis, or PSC. Bexotegrast has received Fast Track Designation and Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) in IPF and PSC and Orphan Drug Designation from the European Medicines Agency in IPF and PSC. Pliant is currently conducting Phase 2a trials of bexotegrast in the lead indications of IPF and PSC. Pliant has also developed PLN-1474, a small molecule selective inhibitor of αvß1 for the treatment of nonalcoholic steatohepatitis, or NASH with liver fibrosis, which Pliant has transferred to Novartis pursuant to our development partnership. In December 2022, Pliant submitted an IND for its third clinical program, PLN-101095, a small molecule dual-selective inhibitor of αvß8 and αvß1 integrins, that is being developed for the treatment of solid tumors. In addition to clinical stage programs, Pliant currently has a preclinical program targeting muscular dystrophies. For additional information about Pliant Therapeutics, visit www.PliantRx.com and follow us on Twitter, LinkedIn, Facebook and YouTube.

Forward-Looking Statements

Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "may," "will," "expect," "anticipate," "estimate," "intend," and similar expressions (as well as other words or expressions referencing future events, conditions, or circumstances) are intended to identify forward-looking statements. These statements include those regarding the safety, tolerability, pharmacodynamics and therapeutic potential of PLN-74809; our plans for the future development of bexotegrast and PLN-101095; bexotegrast's potential to become a treatment for IPF; the anticipated timing of data from the 320 mg group of the INTEGRIS-IPF Phase 2a trial in patients treated for at least 24 weeks; the timing and design of Pliant's Phase 2b clinical trial of bexotegrast; discussions with regulatory authorities; and the efficacy and safety profile and potential of our product candidates. Because such statements deal with future events and are based on our current expectations, they are subject to various risks and uncertainties and actual results, performance or achievements of Pliant Therapeutics could differ materially from those described in or implied by the statements in this press release. These forward-looking statements are subject to risks and uncertainties, including those related to the development and commercialization of our product candidates, including any delays in our ongoing or planned preclinical or clinical trials, the impact of the ongoing COVID-19 pandemic on our business, operations, clinical supply and plans, our reliance on third parties for critical aspects of our development operations, the risks inherent in the drug development process, the risks regarding the accuracy of our estimates of expenses and timing of development, our capital requirements and the need for additional financing, and our ability to obtain and maintain intellectual property protection for our product candidates. These and additional risks are discussed in the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K filed for the year ended December 31, 2021 with the SEC on September 30, 2022, as updated by our Quarterly Report on Form 10-Q filed for the quarter ended November 8, 2022 with the SEC on May 9, 2022, each available on the SEC's website at www.sec.gov. Unless otherwise noted, Pliant is providing this information as of the date of this news release and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

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[1] Paterniti MO et al. *Ann Am Thorac Soc*. 2017 Sep 14(9):1395-1402.

[2] Khan FA et al. Am J Respir Crit Care Med. 2022 Apr 15;205(8):936-948.

[3] Kim GHJ et al. *Ther Adv Respir Dis*. 2021 Jan (15): 1–11.

[4] Organ LA et al. *Respir Res*. 2019 Jul 12;20(1):148.

[5] Bowman WS et al. Lancet Respir Med. 2022 Jun;10(6):593-602.

Photos accompanying this announcement are available at:

https://www.globenewswire.com/NewsRoom/AttachmentNg/792e83b2-2e65-4312-a1a3-91a17bc67977

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