Pliant Therapeutics Announces Interim Data from PLN-101095 in Patients with Immune Checkpoint Inhibitor-Refractory Advanced Solid Tumors

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One complete response and three partial responses observed in heavily pretreated ICI-secondary refractory patients in high dose cohorts

Deep and durable ongoing responses with median time on treatment of 15 months

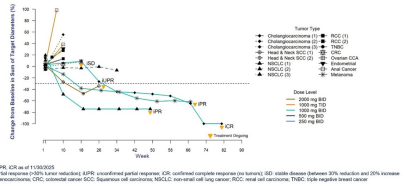
Company to accelerate development of PLN-101095 with initiation of a Phase 1b expansion trial in 2026

Strong cash position supports planned operations through 2028

SOUTH SAN FRANCISCO, Calif., Dec. 04, 2025 (GLOBE NEWSWIRE) -- Pliant Therapeutics, Inc. (Nasdaq: PLRX) today announced interim data from its Phase 1 dose escalation clinical trial evaluating PLN-101095, in combination with pembrolizumab, in patients with immune checkpoint inhibitor (ICI)-refractory advanced or metastatic solid tumors. PLN-101095 is an oral, small molecule, dual selective inhibitor of αvβ8 and αvβ1. It is the fourth clinical-stage drug candidate to be generated from Pliant's integrin-based drug development platform.

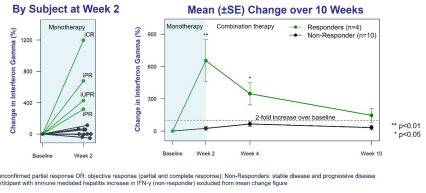
In a heavily pretreated patient population with advanced and/or metastatic solid tumors refractory to ICIs, PLN-101095 demonstrated anti-tumor activity in combination with pembrolizumab. Across the three highest dose cohorts, there were four responders consisting of one confirmed complete response (CR) and three partial responses (PR) (two confirmed, one unconfirmed) out of the 10 secondary ICI refractory patients. Clinical responses were observed in patients with cholangiocarcinoma, melanoma, head and neck squamous cell carcinoma and non-small cell lung cancer (NSCLC). The median time on treatment in these patients is 15 months, as of November 30th, 2025. Sixty percent of secondary refractory patients demonstrated stable disease or tumor reduction.

Figure 1



Percent Change from Baseline in Tumor Size by Week

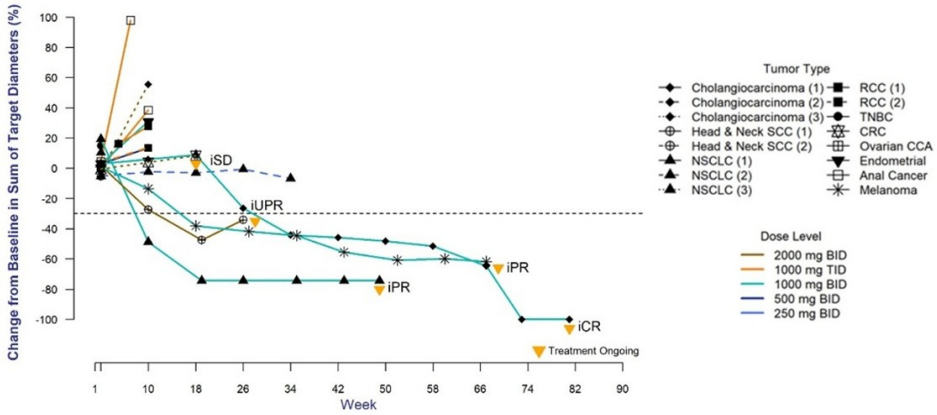
Figure 2



Percentage Change (+, -) from Baseline in Plasma IFN- γ

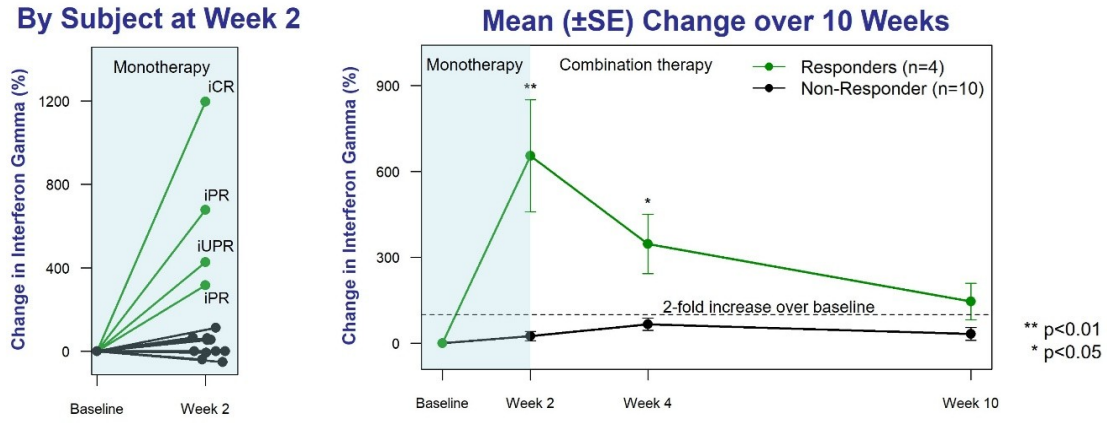
All responding patients showed large increases (4- to 13-fold vs. baseline) in plasma interferon gamma (IFN-γ) after a 14-day run-in period of monotherapy with PLN-101095. No non-responders showed meaningful increases in IFN- γ. PLN-101095 was generally well tolerated across all doses tested with few discontinuations (n=2) due to adverse events. PLN-101095 demonstrated a dose-dependent pharmacokinetic profile.

Sixteen patients with nine different tumor types were enrolled in five cohorts. Patients were treated for 14 days with PLN-101095 monotherapy administered orally at doses of 250 mg twice a day (BID) (n=1), 500 mg BID (n=2), 1000 mg BID (n=6), 1000 mg three times a day (TID) (n=4) or 2000 mg BID (n=3), followed by the addition of pembrolizumab at 200 mg administered intravenously every three weeks. Scans were conducted at baseline, Day 14, Week 10, and every 8 weeks thereafter.



[1] including iUPR, iPR, iCR as of 11/30/2025
iPR: confirmed partial response (>30% tumor reduction); iUPR: unconfirmed partial response; iCR: confirmed complete response (no tumors); iSD: stable disease (between 30% reduction and 20% increase
CCA: clear cell adenocarcinoma; CRC; colorectal cancer SCC: Squamous cell carcinoma; NSCLC: non-small cell lung cancer; RCC: renal cell carcinoma; TNBC: triple negative breast cancer

Figure 1. Percent Change from Baseline in Tumor Size by Week



iUPR: unconfirmed partial response OR: objective response (partial and complete response); Non-Responders: stable disease and progressive disease
One participant with immune mediated hepatitis increase in IFN-γ (non-responder) excluded from mean change figure

Figure 2. Percentage Change (+, -) from Baseline in Plasma IFN- γ

Based on the response data, coupled with the supportive IFN- γ biomarker data, Pliant plans to accelerate the development of PLN-101095 with the initiation of a Phase 1b indication expansion trial assessing NSCLC and other tumor types with strong mechanistic rationale for integrin inhibition in 2026.

"These data surpassed our expectations given the number of clinical responses observed with PLN-101095 in difficult-to-treat ICI refractory tumors in similar Phase 1 trials," said Bernard Coulie, M.D., PhD., Chief Executive Officer of Pliant. "The growing validation of PLN-101095's mechanism of action, including the supportive IFN-γ biomarker correlation, gives us confidence in PLN-101095's development. We believe PLN-101095 has the potential to create new treatment options for patients in need and deliver significant value for investors."

"These first-in-human data suggest that this novel approach of selectively targeting αvβ8 and αvβ1 may hold promise for treating patients with advanced solid tumors resistant to checkpoint inhibitors," Manish Sharma, M.D. Co-Director of Clinical Research, START Midwest in Grand Rapids, Michigan. "These data support the further clinical investigation of this novel mechanism of action to meet the high unmet medical needs in anti-PD-1 resistant tumors."

Final data from this trial will be presented at an upcoming scientific conference.

Slides accompanying these data can be found here and under the Investors & Media page of the Pliant website at www.PliantRx.com.

Investigating full potential of integrin-based drug delivery

Utilizing tissue-specific integrin receptors, Pliant has developed a platform to deliver drug payloads including siRNAs to selective cell types. Current programs are focused on delivering siRNAs to skeletal muscle cells, adipocytes, and renal cells. We believe this platform potentially has broad applicability across multiple disease areas utilizing a variety of drug payloads.

PLN-101095 for the Treatment of Checkpoint Resistant Tumors

PLN-101095 is an oral small molecule inhibitor of integrins αvβ8 and αvβ1. It is currently being evaluated in an ongoing first-in human Phase 1 dose-escalation trial. The open-label trial (NCT06270706) is designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary antitumor activity of PLN-101095 alone and in combination with the immunotherapy pembrolizumab. Activated transforming growth factor-β (TGF-β) has been shown to foster an immuno-suppressive tumor microenvironment (TME) that contributes to immune-checkpoint inhibitor (ICI) resistance and treatment failure in cancer.[1] Blocking integrins αvβ8 and αvβ1 has been shown to prevent the activation of TGF-β and is expected to stimulate immune activation by increasing immune cell infiltration into the tumor microenvironment.[2,3] In preclinical studies, PLN-101095 demonstrated monotherapy activity in reduction of tumor volume and increased cluster of differentiation (CD)8+ T cell infiltration. In addition, PLN-101095 in combination with an anti-PD-1 monoclonal antibody (mAb) elicited a dose-dependent reduction in tumor volume and increased CD8+ T cell tumor infiltration in the tumor microenvironment compared with anti-PD-1 mAb therapy alone.[4]

About Pliant Therapeutics, Inc.

Pliant Therapeutics is a clinical-stage biopharmaceutical company focused on the discovery and development of integrin-based therapeutics. The Company's lead program is PLN-101095, a small molecule, dual-selective inhibitor of $\alpha_v\beta_8$ and $\alpha_v\beta_1$ integrins, that is being developed for the treatment of solid tumors. In addition, Pliant has received regulatory clearance for the conduct of a Phase 1 study of PLN-101325, a monoclonal antibody agonist of integrin $\alpha_7\beta_1$ targeting muscular dystrophies. Pliant's early-stage platform includes preclinical research focused on tissue-specific delivery and internalization of drug payloads utilizing integrin receptor-binding molecules. For additional information, please visit: www.PliantRx.com. Follow us on social media X, LinkedIn and Facebook.

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 our cash position and anticipated cash runway through 2028; the potential benefits of PLN-101095; and our plans for the continued development of PLN-10195 and our integrin-based drug delivery platform. 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 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 current macroeconomic, geopolitical and marketplace conditions on our business, operations, clinical supply and plans, our reliance on single-source third parties located in foreign jurisdictions, including China, 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 sufficiency of our cash to support our planned operations, 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 Quarterly Report on Form 10-Q for the period ended September 30, 2025, are 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] Pickup M. et al. *Nat Rev Cancer*. 2013 Nov;13(11):788-99.

[2] Takasaka N. et al. *JCI Insight*. 2018 Oct 18;3(20).

[3] Reed NI. et al. *Sci Transl Med*. 2015 May 20;7(288):288ra79.

[4] Kothari V, et al. *J Immunother Cancer*. 2022;10(Suppl 2): A1403 abstract 1352 (SITC 2022)