PLIANT

ADVANCING
NOVEL, TARGETED INTEGRIN-BASED THERAPIES

JUNE **2026**

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Near-term Oncology Opportunity with Long-Term Platform Potential

PLN-101095: Oral $\alpha_v\beta_8$ / $\alpha_v\beta_1$ Inhibitor for Treatment of ICI-resistant Tumors

- **4 clinical responders** (1 CR and 3 PRs [1 unconfirmed]) at 3 highest Ph1 doses, in heavily pre-treated patients with advanced and/or metastatic solid tumors, secondary refractory to ICIs
- **Durable** response with median time on treatment of 19 months to date for clinical responders
- **Well tolerated in Ph1 trial**
- **Oral small molecule** showed **dose-dependent** plasma exposure
- **Enrolling FORTIFY** a Ph1b indication expansion trial in NSCLC and other tumor types with strong mechanistic rationale for integrin inhibition

New Opportunity for Integrin Platform: Cell-selective Drug Delivery

- **Emerging cell-specific delivery platform for siRNA payloads**
- **Broad applicability** across multiple disease areas
- **Integrin-focused library** of 15k+ compounds built to interrogate all cell-specific integrin subtypes

Pliant's strong cash position funds operations through 2028

CR, complete response (100% tumor reduction); PR, partial response (≥30% tumor reduction)

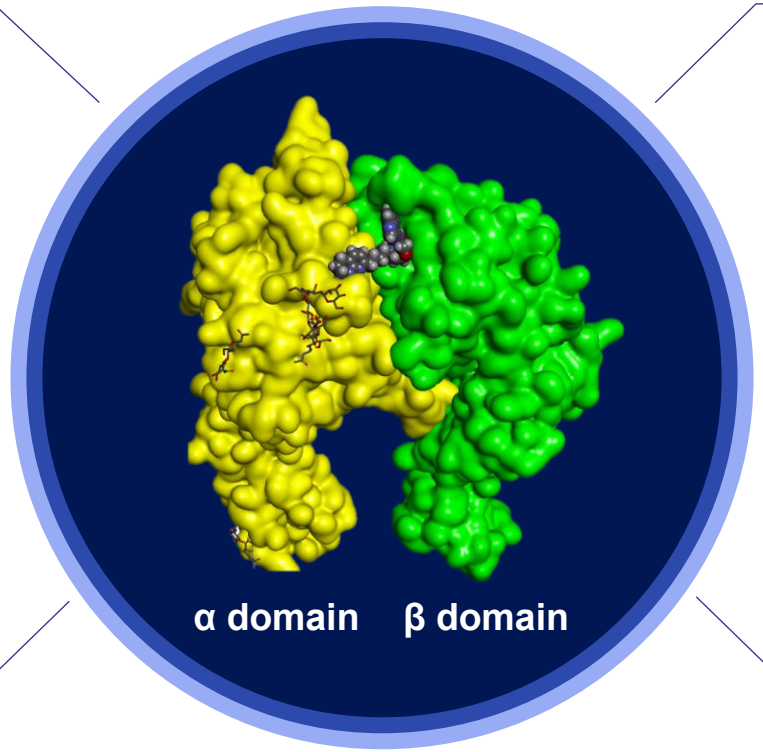
Pipeline

Program	Indication	Preclinical	Phase 1a/1b	Phase 2	Phase 3	Global Rights
PLN-101095 $\alpha_v\beta_8/\alpha_v\beta_1$ inhibitor	Solid Tumors			FORTIFY		PLIANT
INTEGRIN DRUG DELIVERY PLATFORM	Muscle					PLIANT
	Adipose Tissue					PLIANT
	Undisclosed					PLIANT

Integrins are an Attractive Target Class

Integrins are extracellular matrix receptors

- Cell surface receptors that facilitate cell-cell and cell-extracellular matrix adhesion and interaction
- A major path of communication between the inflammatory cells and fibroblasts
- Composed of 24 heterodimers across four classes



Pliant's integrin library

- Broad coverage of integrin heterodimers in 15,000+ compound library
- SAR understanding of binding motifs with desired biology
- Emphasis on optimal pharmacokinetic and potency/selectivity profiles

Integrins are a productive target class

- Multiple approved drugs in I&I indications
- Clinically validated receptors for delivery of drug payloads into specific cell types

Integrins are a promising delivery modality

- Each integrin has a unique cell type-restricted expression profile
- Integrins readily internalize, enabling payload delivery

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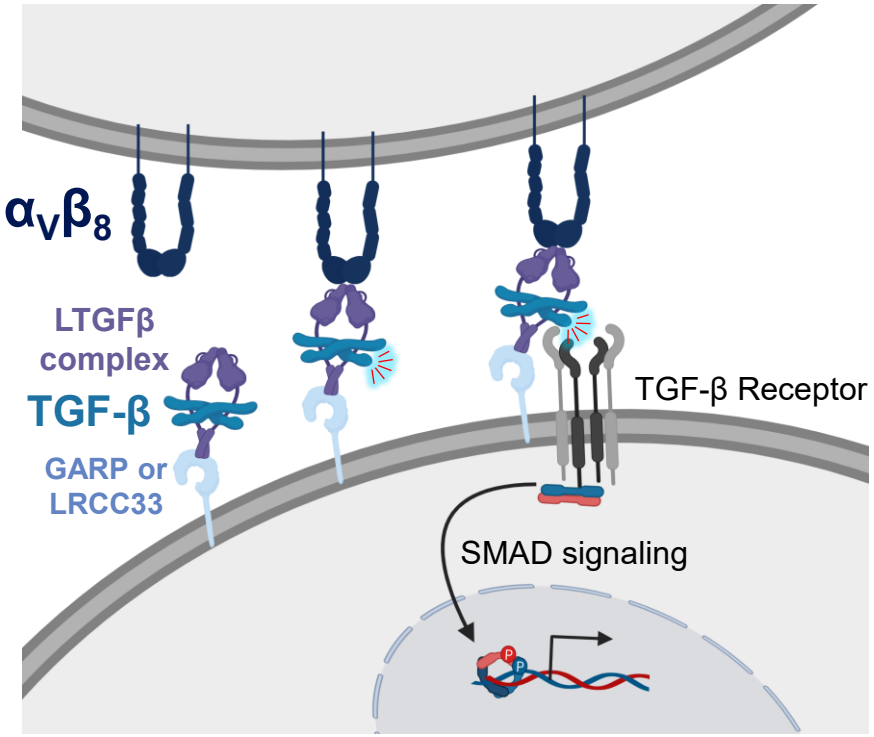
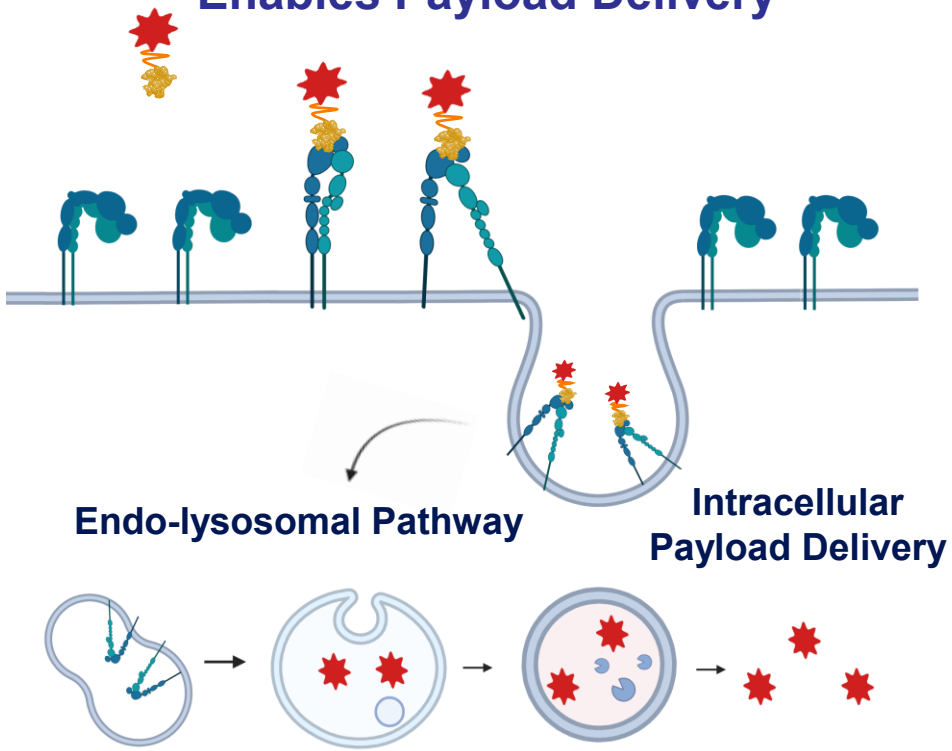
Integrins – Multifunctional Targets for Modulation and Delivery

$\alpha_v\beta_8$ Integrin Activation of TGF-β



Integrin Internalization & Recycling Enables Payload Delivery

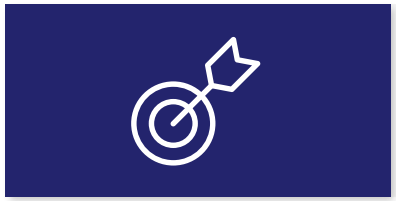


Pliant's programs are designed to modulate conserved biological features of integrins

PLN-101095 – $\alpha_V\beta_8$ / $\alpha_V\beta_1$ Dual Integrin Inhibitor

Clinical Stage Solid Tumor Program

Potential First-in-Class Oral $\alpha_V\beta_8/\alpha_V\beta_1$ Inhibitor



Potent dual inhibitor of $\alpha_V\beta_8$ and $\alpha_V\beta_1$

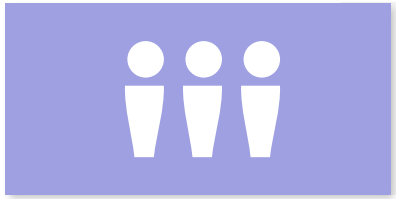
- Tumors that overexpress $\alpha_V\beta_8$ have a poor prognosis
- $\alpha_V\beta_1$ upregulated on cancer-associated fibroblasts

Small molecule - Oral administration

- High tissue penetration (vs. biologics) improves target coverage to maximize the therapeutic index

Dose escalation demonstrated encouraging efficacy in ICI secondary refractory tumors

- 4 out of 10 clinical responders (1 CR and 3 PR [1 unconfirmed]) in 3 highest doses
- Large increases in circulating IFN-γ observed in clinical responders only



Enrolling Phase 1b indication expansion trial

- Assessing NSCLC, tumors with high tumor mutational burden or clear cell renal cell carcinoma

CR, confirmed complete response (100% tumor reduction); PR, confirmed partial response (≥30% tumor reduction)

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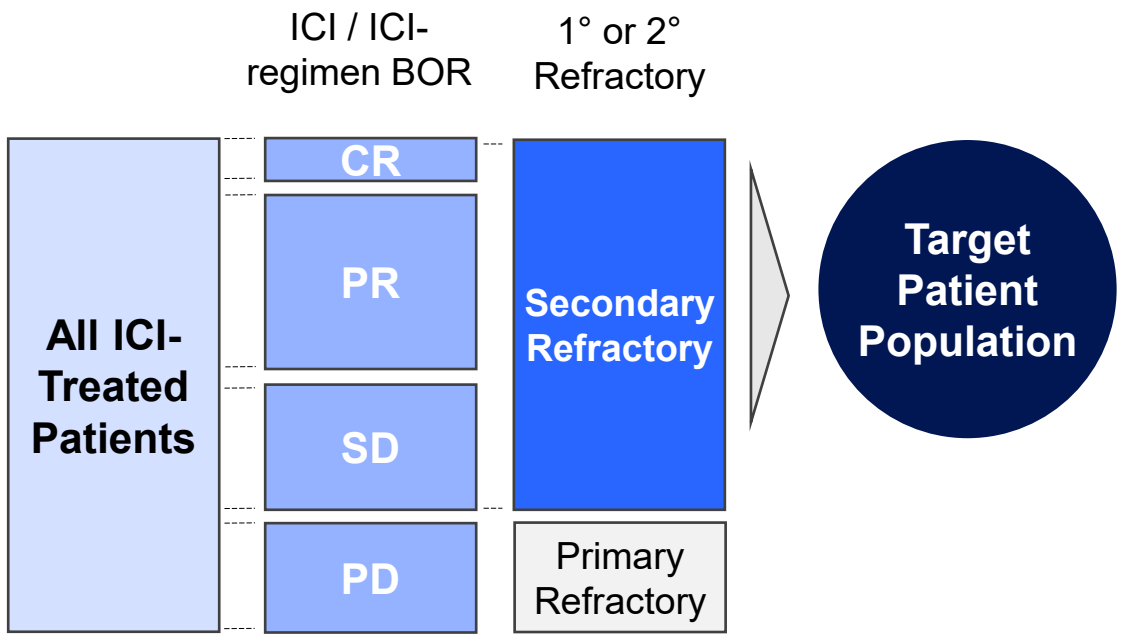
PLN-101095 Positioned as Preferred Agent in ICI Refractory Patients

ICI Refractory Opportunity



Broad Opportunity in Secondary Refractory Tumors

- High unmet needs across the post-I/O setting
- Post-PD-(L)1 treatment choices offer limited efficacy
- Padcev (urothelial Ca) and Welireg (clear cell RCC) both launched in this setting with strong initial uptake

Post-ICI Progression in NSCLC

- Frequent utilization of ICI regimens in 1L
- Up to 50% of ICI-treated patients may be secondary refractory, depending on specific line of therapy
- Chemotherapy is the only post 2L treatment available
  - Median PFS in ICI refractory patients is 3-5 months

Target positioning for PLN-101095 as the preferred 2L agent

CR, confirmed complete response; PR, confirmed partial response; SD, stable diseases; PD, progressive diseases; BOR, best overall response; PFS: progression free survival.
Rates of PRs and acquired resistance estimated from US PI for approved PD-1 regimens.

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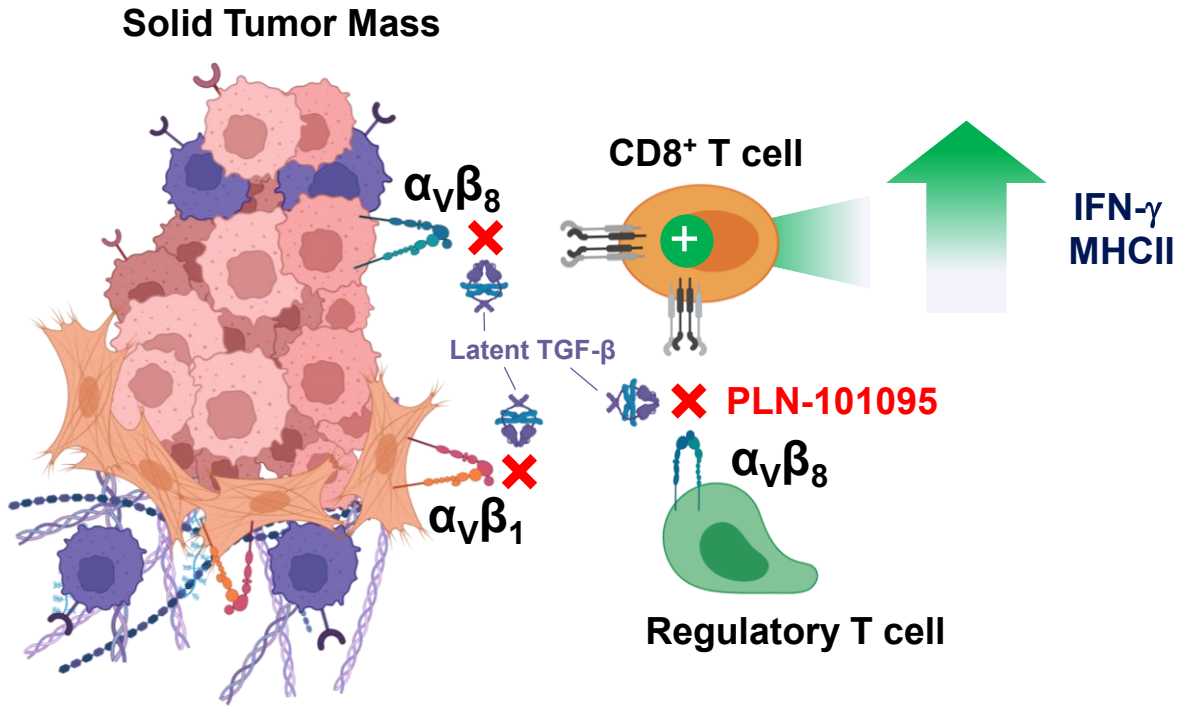
Differentiated Mechanism with Potential to Unlock the Promise of TGF-β Inhibition Across Solid Tumors

In response to sustained immune activity, solid tumors utilize $\alpha_V\beta_8$ and $\alpha_V\beta_1$ activation of TGF-β to suppress and escape immune control

PLN-101095 designed to:

- Selectively block $\alpha_V\beta_8$ and $\alpha_V\beta_1$ activation of TGF-β
- Modulate tumor microenvironment
- Selectively enhance T cell IFN-γ effector function
- Combine with orthogonal IO approaches like anti-PD-1
- Address TGF-β-related resistance to immune checkpoint blockade



Integrin inhibition of $\alpha_V\beta_8$ and $\alpha_V\beta_1$ blocks activation of TGF-β to reduce immunosuppression leading to a new or reinvigorated cancer immune response

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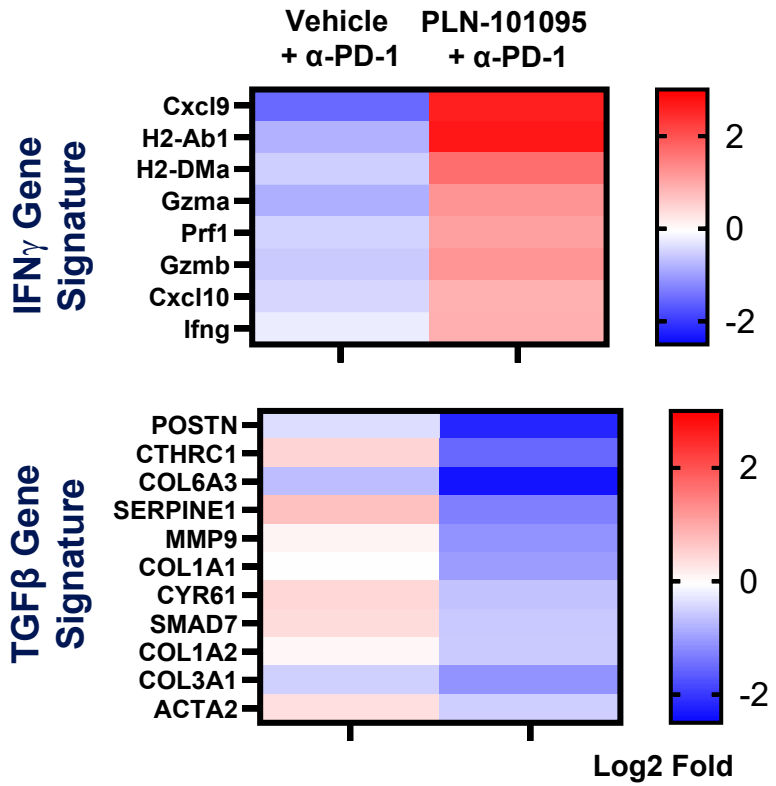
Mechanism of Action in Solid Tumors

Promotes ICI Responsiveness by Inhibiting TGF-β & Increasing IFN-γ Expression

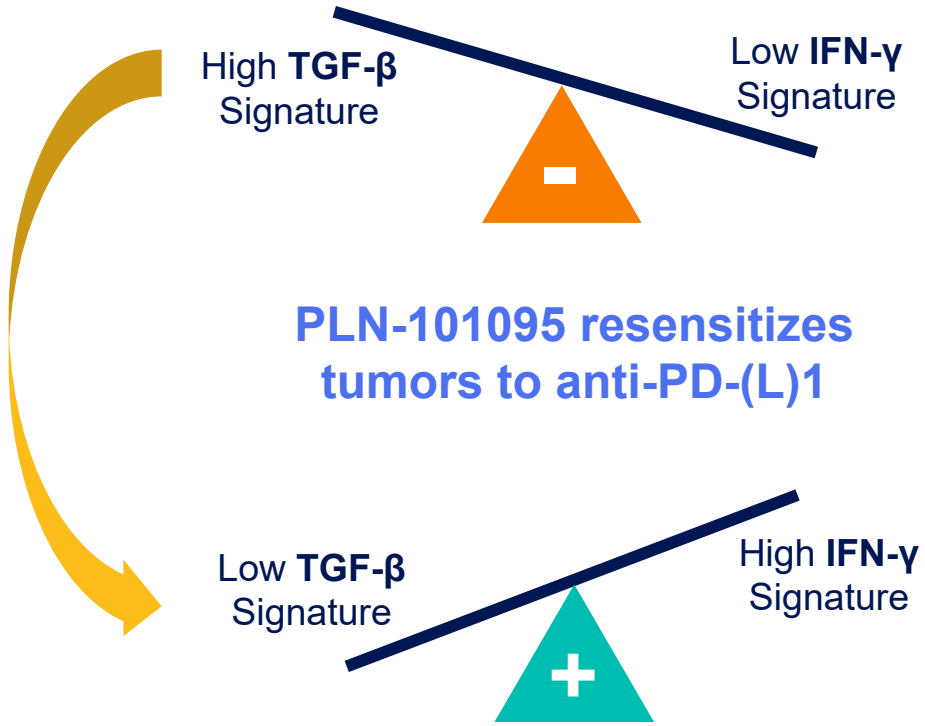
By inhibiting TGF-β, PLN-101095 shifts solid tumors to a high IFN-γ signature, ICI-responsive state

Tumor Gene Expression Change After Treatment



EMT6 tumor model, day 28, 300 mg/kg PLN-101095 dosed by minipump.

Anti-PD-(L)1 non-responsive baseline gene signature



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PLN-101095 Updated Phase 1a Data

Summary – Phase 1 Interim Analysis in ICI Refractory Solid Tumors

PLN-101095 showed antitumoral activity with pembrolizumab in ICI secondary refractory participants

- 4 clinical responders (1 CR and 3 PRs [1 unconfirmed]) in ICI secondary refractory population[1] at doses ≥1000 mg BID
- Durable response with median time on treatment of 19 months, to date, in cholangiocarcinoma (CR), non-small cell lung cancer (PR), melanoma (PR) and head and neck SCC (uPR) with an 89% average tumor reduction

PLN-101095 dosed in combination with pembrolizumab was generally well tolerated

- Rash was the most common adverse event (all mild or moderate)

Circulating biomarker IFN-γ was identified as a potential early predictor of treatment response

- Significant increases in plasma IFN-γ observed at Day 14 (monotherapy), comparing clinical responders to non-responders ($p<0.01$)
- IFN-γ increases maintained through 8 weeks (combination therapy)

[1] ICI secondary refractory defined as stable disease, partial or complete response while on prior ICI therapy with at least 6 months of prior ICI therapy
CR, confirmed complete responses (100% tumor reduction); PR, confirmed partial response (≥30% tumor reduction); uPR, unconfirmed partial response (≥30% tumor reduction)

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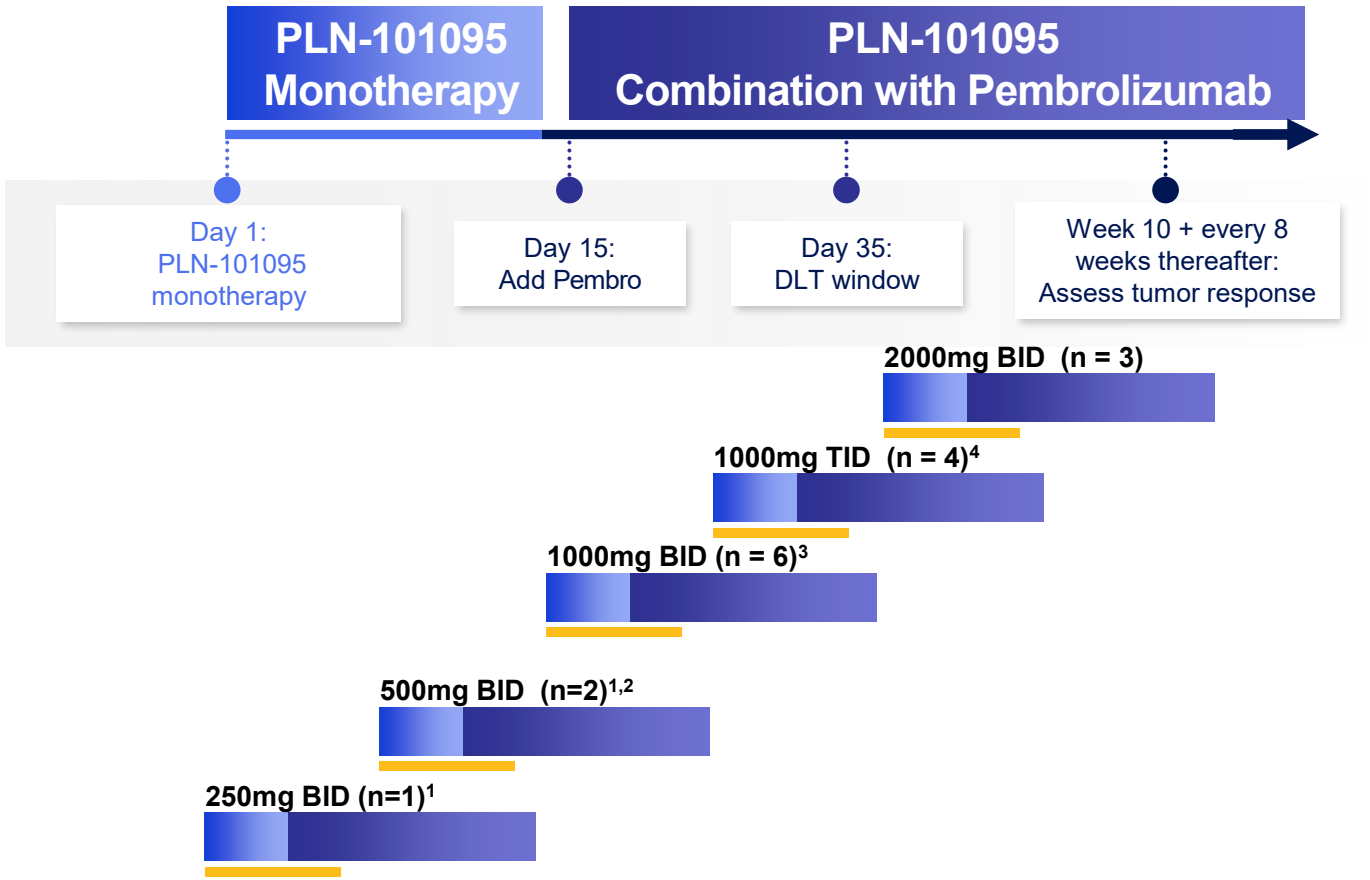
Phase 1 Trial in Patients Refractory to ICIs

Enrollment Complete with All Doses Cleared



PRIMARY AND SECONDARY ENDPOINTS

- TEAEs, serious TEAEs, and DLT events
- PK parameters in monotherapy and combination therapy with pembrolizumab

EXPLORATORY ENDPOINTS

- Antitumor activity: ORR, DCR and mDOR
- Changes in blood-based biomarkers
- PK/PD relationships

POPULATION

- Primary or secondary ICI-refractory tumors for which pembrolizumab is approved with documented disease progression ≥ 75 days from start of prior ICI
- At least 1 measurable lesion

1 Cohorts 1 and 2 used accelerated titration
2 One participant discontinued at Day 14 due to disease progression (non-evaluable)
3 Cohort expanded due to single dose limiting toxicity (DLT)
4 One participant added as part of backfill

DCR: Disease Control Rate (stable disease, partial and complete responses)
mDOR: median Duration of Response
ICI: Immune Checkpoint Inhibitor
ORR: Objective Response Rate (partial and complete responses)

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Demographics and Baseline Characteristics

- Predominantly white (75%), mixed gender (50% male) population
- Average [range] age of 60 [34,72] years

- Heterogenous group of tumor types enrolled
  - Cohorts 1-2 (doses < 1000 mg BID): NSCLC, HNSCC and RCC
  - Cohorts 3-5 (doses ≥ 1000 mg BID): NSCLC (n=2), Cholangiocarcinoma (n=3), RCC, melanoma, CRC, endometrial cancer, TNBC, ovarian CCA, HNSCC, and anal cancer

- Population was 75% ICI secondary refractory with median prior ICI exposure of therapy 12 months
- Prior failed ICI regimens: pembrolizumab (n=9), {pembrolizumab, nivolumab} (n=4), durvalumab (n=2), {pembrolizumab, avelumab} (n=1)

- Median of 3 prior lines of therapy before trial entry with the last line including a chemotherapy agent in 88% of participants

CCA: clear cell adenocarcinoma; CRC; colorectal cancer HNSCC: Head and neck squamous cell carcinoma; NSCLC: non-small cell lung cancer; RCC: renal cell carcinoma; TNBC: triple negative breast cancer

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PLN-101095 Was Generally Well Tolerated

n (%)	Cohort 1 250 mg BID (n=1)	Cohort 2 500 mg BID (n=2)	Cohort 3 1000 mg BID (n=6)	Cohort 4 1000 mg TID (n=4)	Cohort 5 2000 mg BID (n=3)	Total (n=16)
Any TRAE	**1 (100)**	**1 (50)**	**4 (67)**	**4 (100)**	**2 (67)**	**12 (75)**
Grade 3/4[a]	0	0	1 (17)[c]	0	0	1 (6)
Serious	1 (100)[b]	0	1 (17)[c]	0	0	2 (13)
Led to discontinuation	0	0	1 (17)[c]	1 (25)[d]	0	2 (13)
Most common TRAEs (in >1 participant)						
Rash	0	1 (50)	2 (33)	2 (50)	1 (33)	6 (38)
Fatigue	0	0	2 (33)	0	0	2 (13)
Hypomagnesemia	0	0	0	1 (25)	1 (33)	2 (13)

The most common TRAE was rash[e]

- All rashes were grade 1 or 2
- One treatment-related rash was reported during the monotherapy period, but otherwise these were primarily observed within 2 days of starting combination treatment

[a]No Grade 5 TRAEs occurred. [b]Keratoacanthoma (Grade 2). [c]Immune-mediated hepatitis (Grade 3), considered a DLT. [d]Dermatitis bullous (Grade 2).
[e]Includes rash, rash erythematous, rash maculo-papular, dermatitis acneiform and dermatitis bullous. TRAE, treatment-related adverse event.

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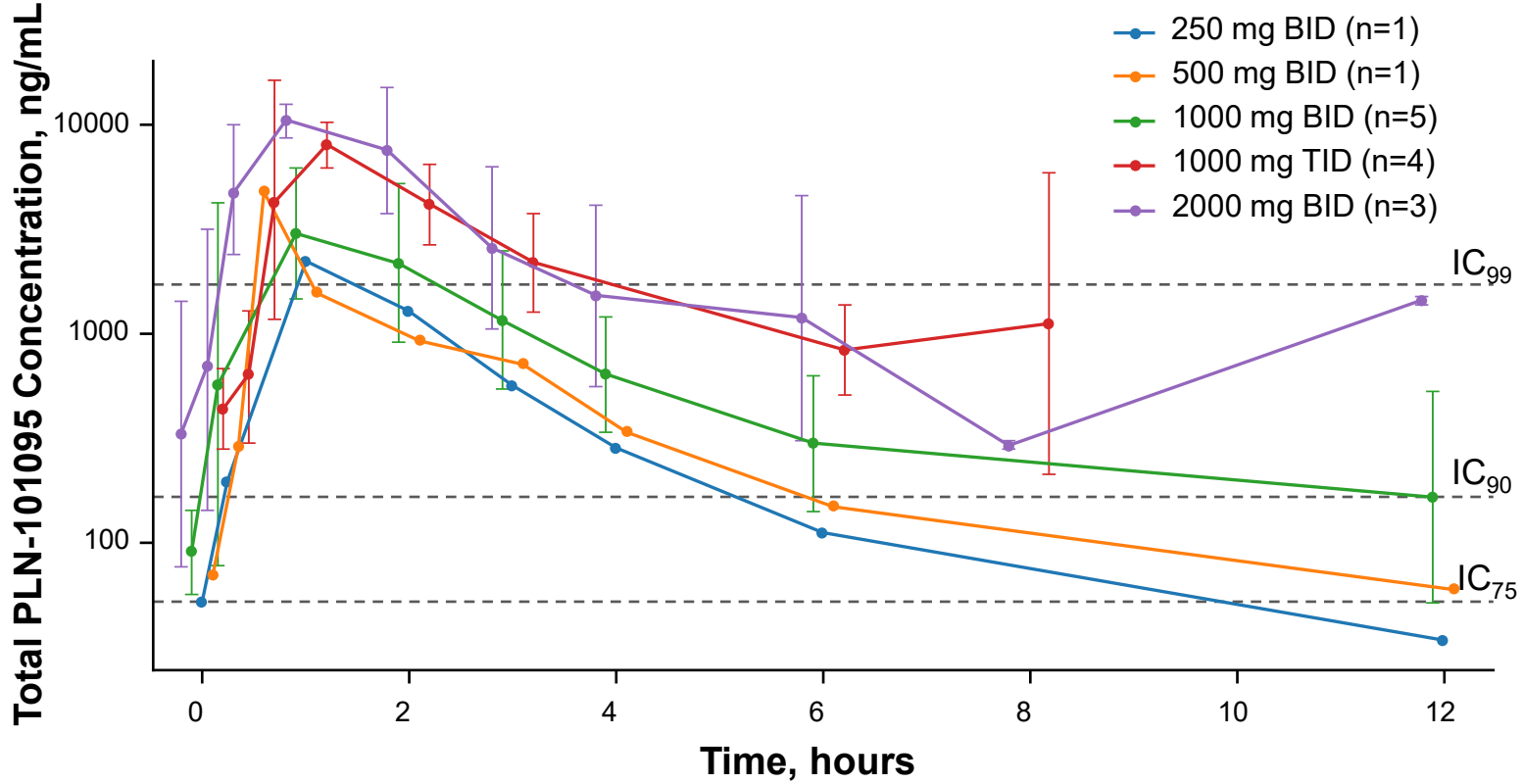
PLN-101095 Monotherapy Demonstrated Dose-Ordered Exposure at Day 14

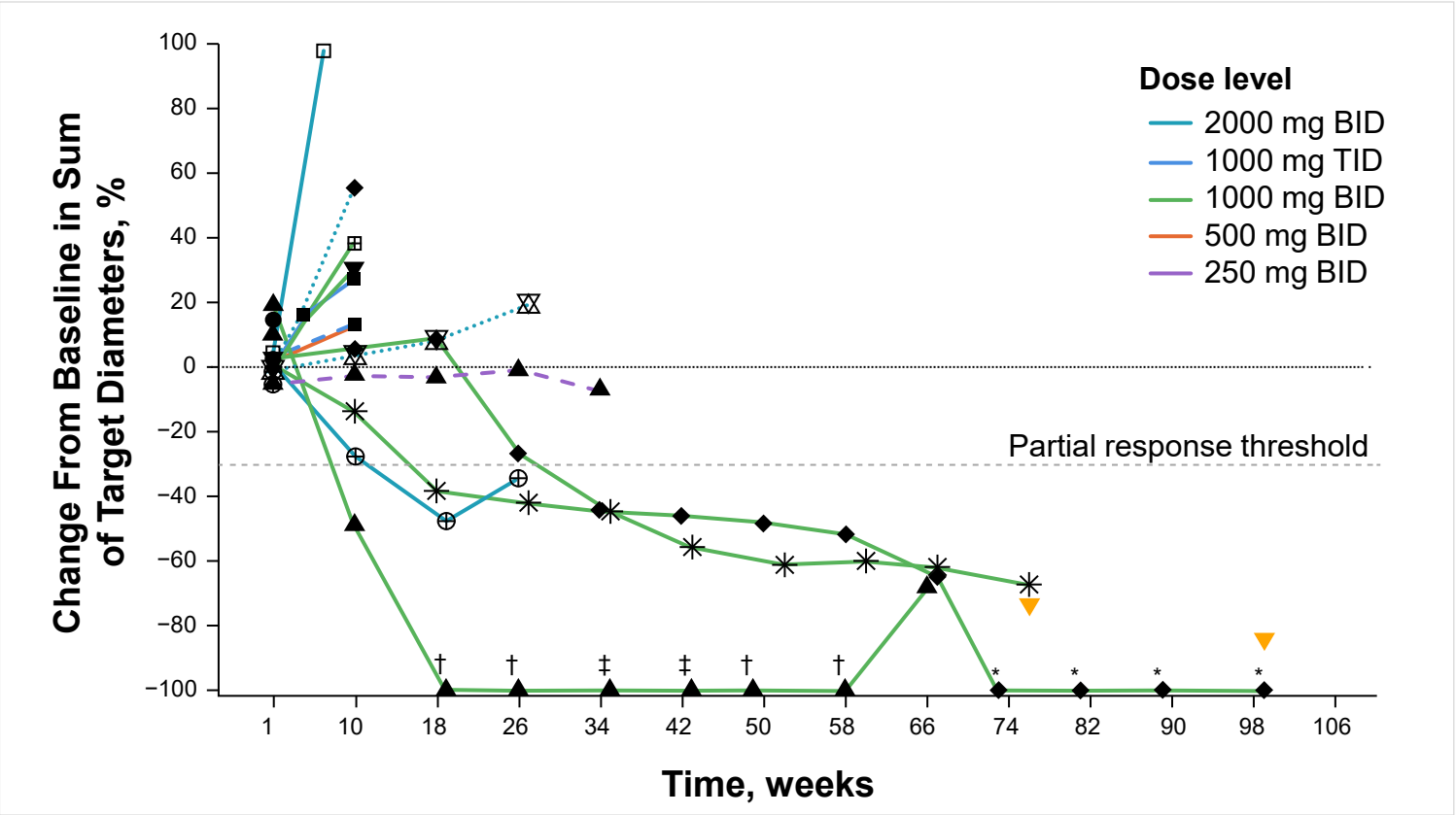


- All participants receiving ≥1000 mg BID maintained IC_{75} coverage over 24 hours, supporting consistent target engagement
- PK profile supports continuous pharmacologic inhibition with BID dosing at steady state

All participants treated with ≥1000 mg BID maintained IC75 coverage over 24 hours, supporting consistent target engagement

IC_{75}, 75% maximal inhibitory concentration; IC_{90}, 90% maximal inhibitory concentration; IC99, 99% maximal inhibitory concentration; PK, pharmacokinetics.

Clinically Significant, Durable Responses Observed in 3 of 4 iRECIST Responders at Doses ≥1000 mg BID



Tumor type

- Cholangiocarcinoma (1)
- Cholangiocarcinoma (2)
- Cholangiocarcinoma (3)
- HNSCC (1)
- HNSCC (2)
- NSCLC (1)
- NSCLC (2)
- NSCLC (3)
- RCC (1)
- RCC (2)
- TNBC
- CRC
- Ovarian CCA
- Endometrial
- Anal SCC
- Melanoma

† Target lesions nonmeasurable with nontarget lesions present (BOR=iPR)

‡ Target lesions disappeared with nontarget lesions present (BOR=iPR)

* Complete resolution of target and nontarget lesions

▼ Treatment ongoing

Median time on treatment is 19 months for the 3 confirmed objective responders, who had an average maximum tumor reduction of 89%

Data as of Feb 27, 2026. Confirmed objective responders had BOR of iPR or iCR.
iCR, complete response per iRECIST; iPR, partial response per iRECIST.

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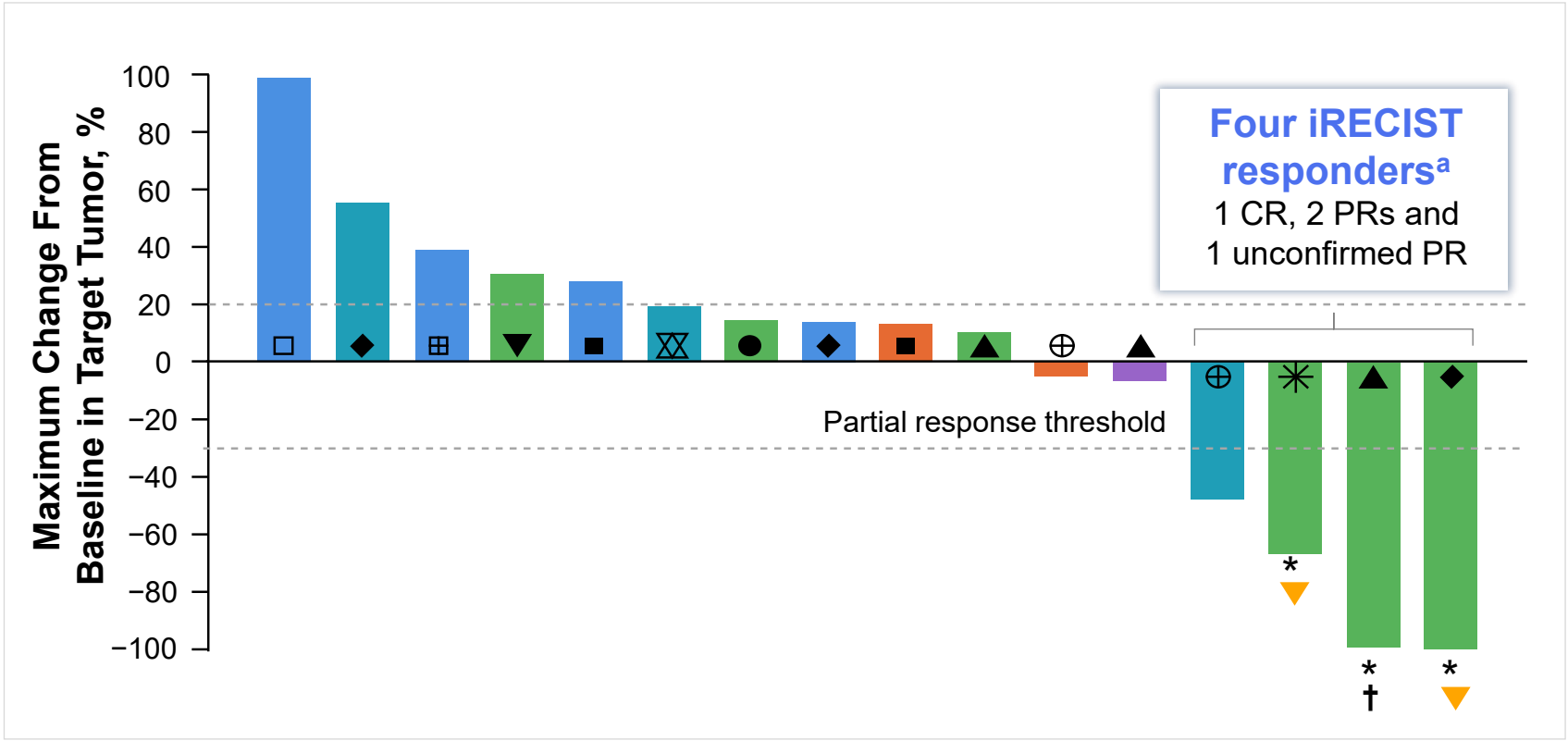
Responses Were Observed in Patients With Secondary ICI Resistance



Dose level

- 2000 mg BID
- 1000 mg TID
- 1000 mg BID
- 500 mg BID
- 250 mg BID

Tumor type

- Cholangiocarcinoma
- HNSCC
- NSCLC
- RCC
- TNBC
- CRC
- Ovarian CCA
- Endometrial
- Anal SCC
- Melanoma

† Nontarget lesions present (BOR=iPR)

* Confirmed response

▼ Treatment ongoing

Overall study population: 19% ORR | 56% DCR

ICI secondary resistance: 30% ORR | 60% DCR

[a]As of Feb 27, 2026.

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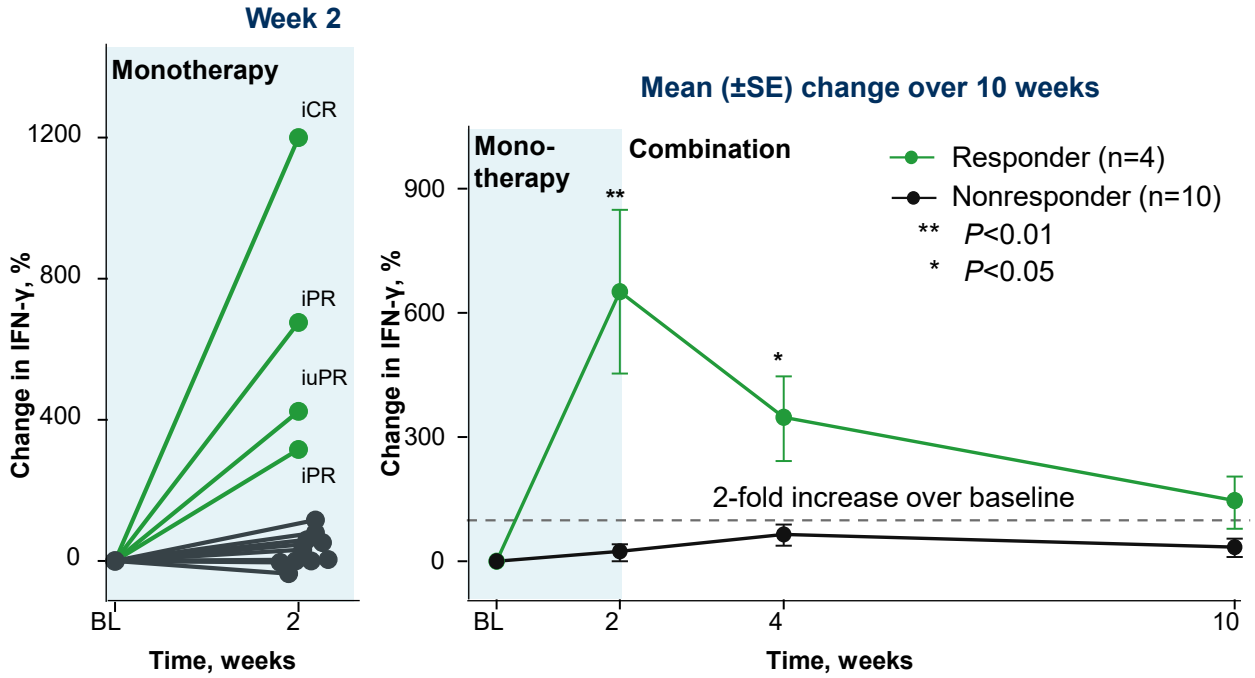
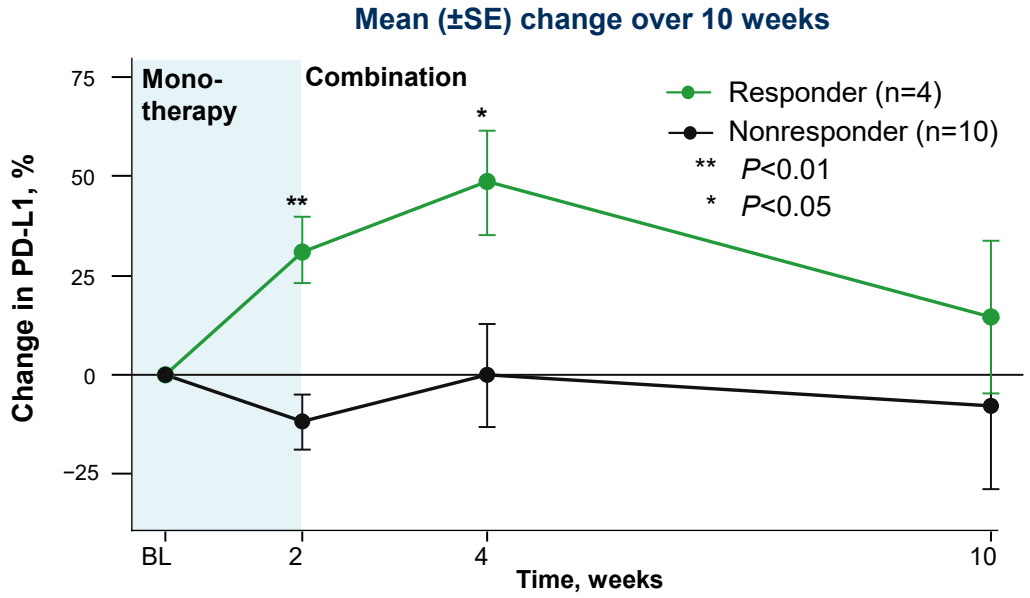
Clinical Response to PLN-101095 Is Associated With Elevated Plasma IFN-γ and PD-L1 Levels After 14 Days' Monotherapy

Change in Plasma IFN-γ



- Elevated plasma IFN-γ was observed in responders

Change in PD-L1



- Elevated plasma PD-L1 was observed in responders
  - Known to be induced by IFN-γ; higher tumor PD-L1 expression predicts improved response to ICIs[1]

Increase in IFN-γ during monotherapy may act as a potential biomarker of TGF-β inhibition; this will be studied further in dose-expansion cohorts

1. Incorvaia I, et al. Adv Ther. 2019;36:2600-2617. Responders: PR and CR. Nonresponders: SD and PD. One patient with immune-mediated hepatitis and resultant increase in IFN-γ (nonresponder) was excluded from the mean change analyses. iuPR, unconfirmed partial response per iRECIST.

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Key Findings and Next Steps

PLN-101095 produced anti-tumor activity in multiple tumor types in ICI secondary refractory patients

PLN-101095 was well tolerated with a low discontinuation rate across all dose cohorts

IFN-γ biomarker data has potential to serve as response predictor

Enrolling FORTIFY, a Phase 1b indication expansion trial in patients with NSCLC, tumors with high tumor mutational burden or clear cell renal cell carcinoma

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A Phase 1b Trial of PLN-101095

FORTIFY

Part 2 Dose Expansion and Indication Selection

Trial of Acquired Resistance to Prior Immune Checkpoint Blockade

FORTIFY

Testing Single PLN-101095 Dose Level

1000 mg BID

Evaluating Three Cohorts

(n = up to 34 per cohort)

NSCLC	ccRCC	TMB-H[a]

STUDY POPULATION

- Advanced or metastatic tumors
- Prior exposure to PD-1 therapy with documented disease progression
- Secondary resistance by SITC definition
- TMB-H[a] cohort composed of melanoma, CRC, endometrial, and BTC
  - n ≥5 in each tumor type

PRIMARY AND SECONDARY ENDPOINTS

- Antitumor activity: ORR and DCR
- Safety: TEAEs, serious TEAEs, and DLT events

EXPLORATORY ENDPOINTS

- Durability of antitumor activity
- Changes in blood-based biomarkers
- Pharmacokinetics and PK/PD relationships

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[a]TMB-H based on historical data showing ≥10 mutations per megabase.
[b]Per cohort.