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Developing Novel Integrin-Based Therapeutics

MARCH **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 15 months to date for clinical responders
- **Well tolerated in Ph1 Study**
- **Oral small molecule** showed **dose-dependent** plasma exposure
- Ph1b dose expansion will explore 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)

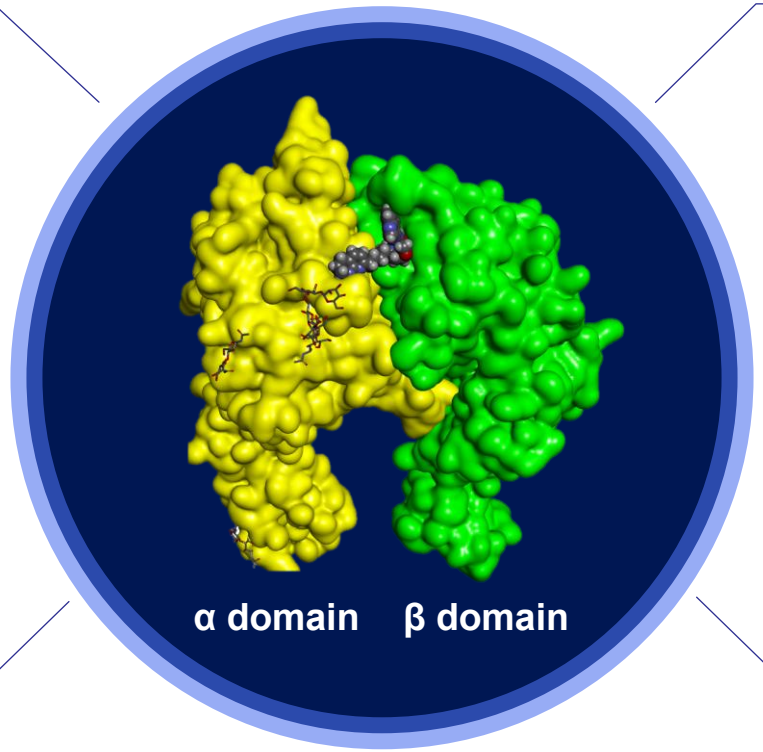
Pipeline

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					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

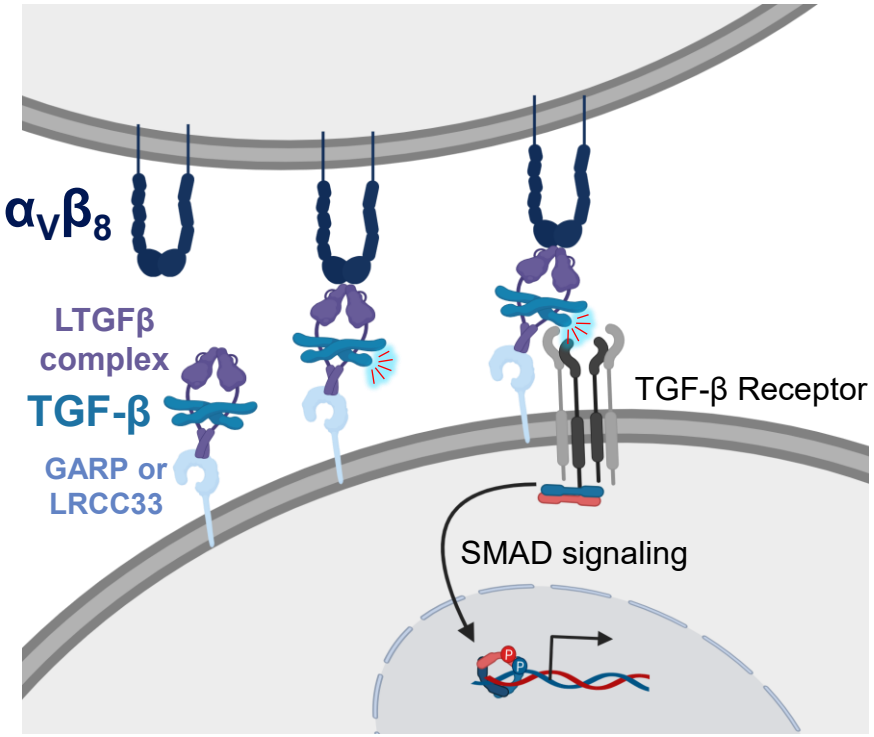
- Multiple approved drugs in I&I indications
- Clinically validated receptors for delivery of drug payloads into specific cell types

Integrins are a promising delivery modality

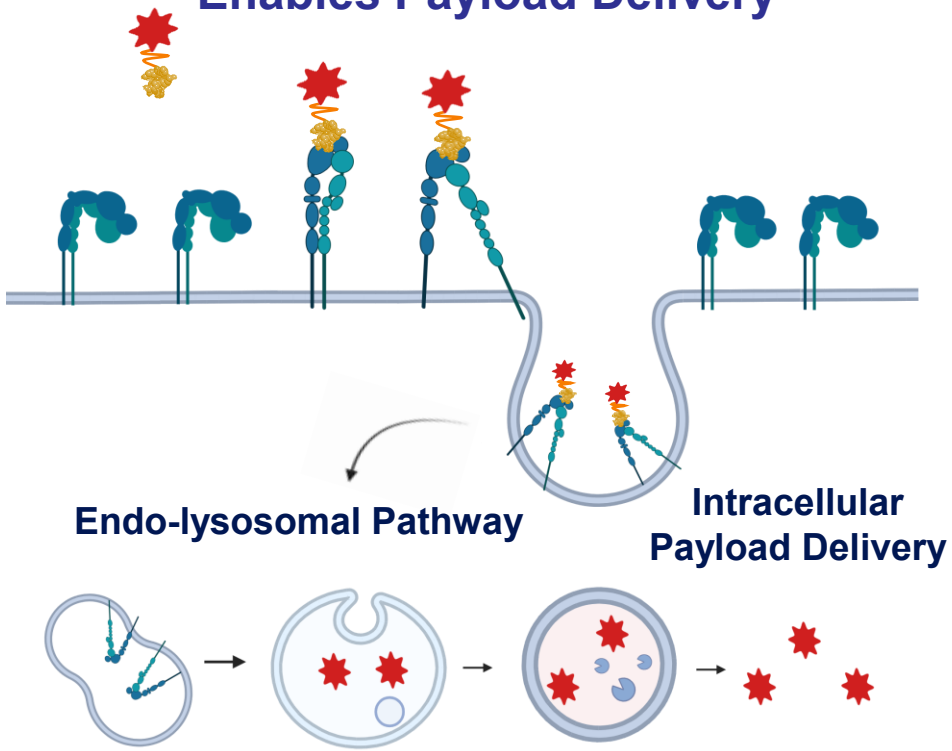
- Each integrin has a unique cell type-restricted expression profile
- Integrins readily internalize, enabling payload delivery

Integrins – Multifunctional Targets for Modulation and Delivery

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



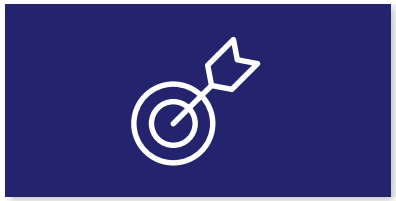
Integrin Internalization & Recycling Enables Payload Delivery



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 $\alpha_V\beta_1$

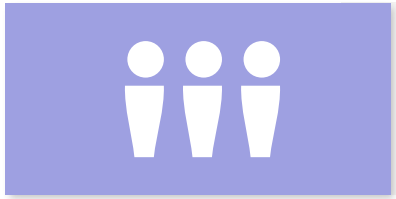
- Tumors that overexpress $\alpha_V\beta_8$ have a poor prognosis
- $\alpha_V\beta_1$ upregulated on cancer-associated fibroblasts

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



Initiating indication expansion cohorts

- Assessing NSCLC and other tumor types with strong mechanistic rationale for integrin inhibition

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

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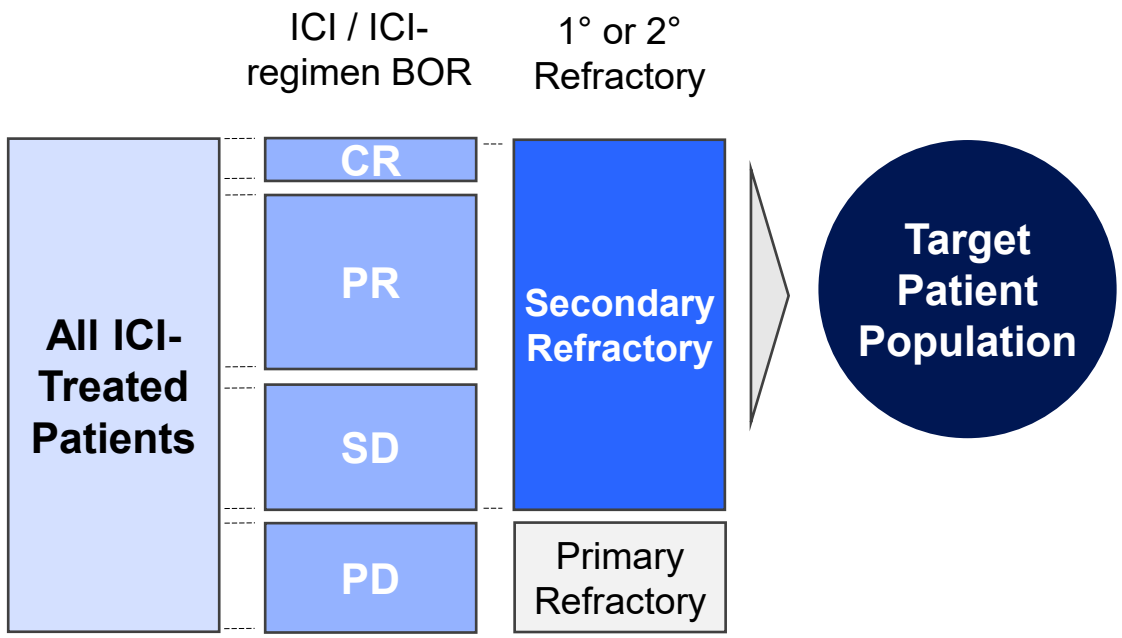
PLN-101095 Positioned as Preferred Agent in ICI Refractory Patients

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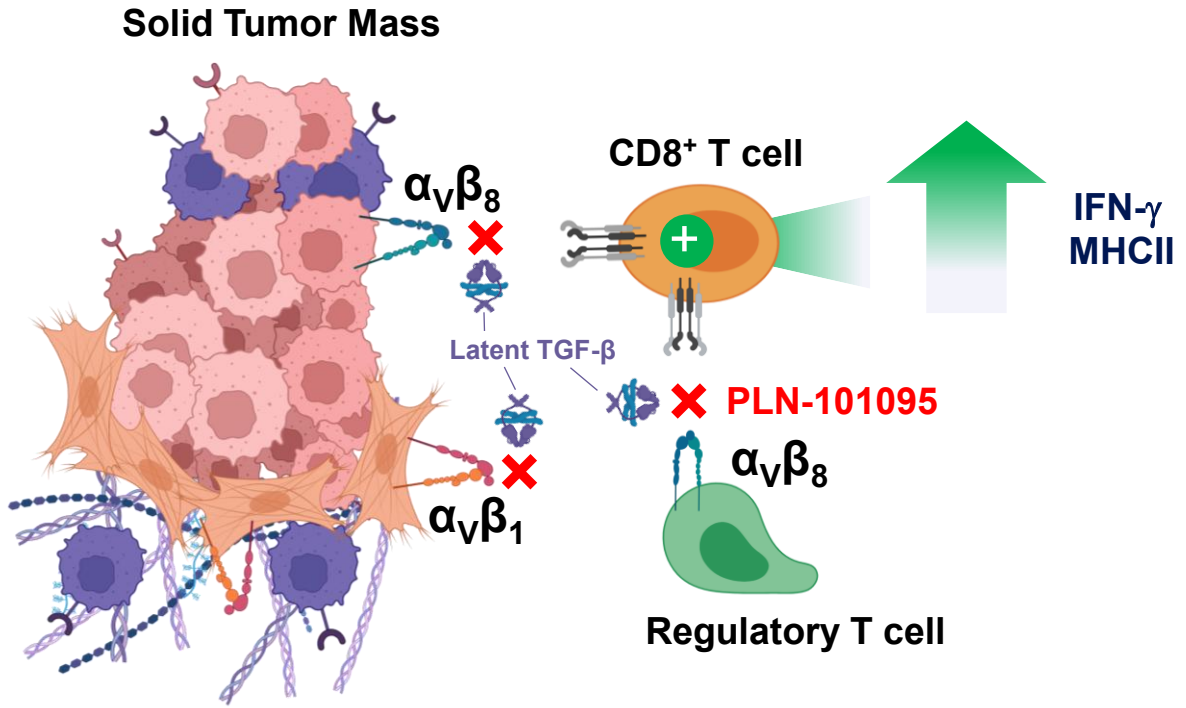
Differentiated Mechanism with Potential to Unlock the Promise of TGF-β Inhibition Across Solid Tumors

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



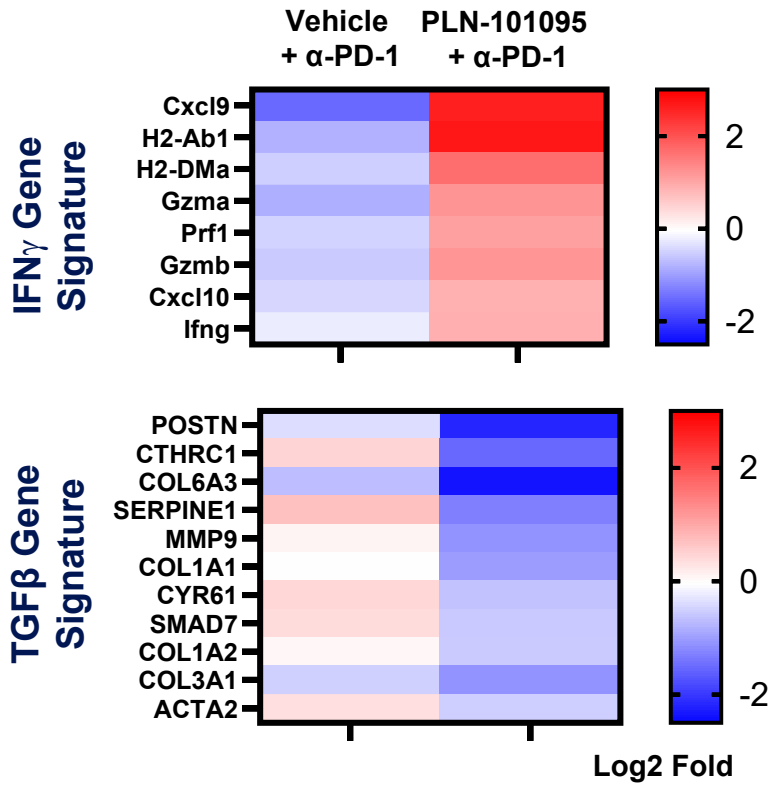
Integrin inhibition of $\alpha_V\beta_8$ and $\alpha_V\beta_1$ blocks activation of TGF-β to reduce immunosuppression leading to a new or reinvigorated cancer immune response

Mechanism of Action in Solid Tumors

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

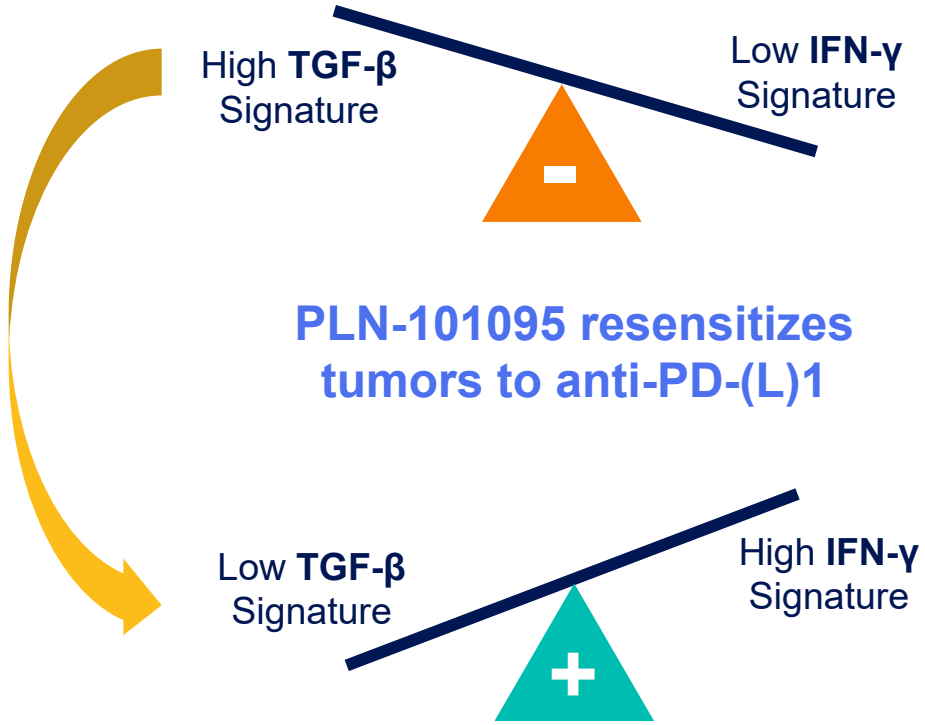
By inhibiting TGF-β, PLN-101095 shifts solid tumors to a high IFN-γ signature, ICI-responsive state

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



PLN-101095 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 15 months, to date, in cholangiocarcinoma (CR), non-small cell lung cancer (PR), melanoma (PR) and head and neck SCC (uPR) with a 71% 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 Day 28 (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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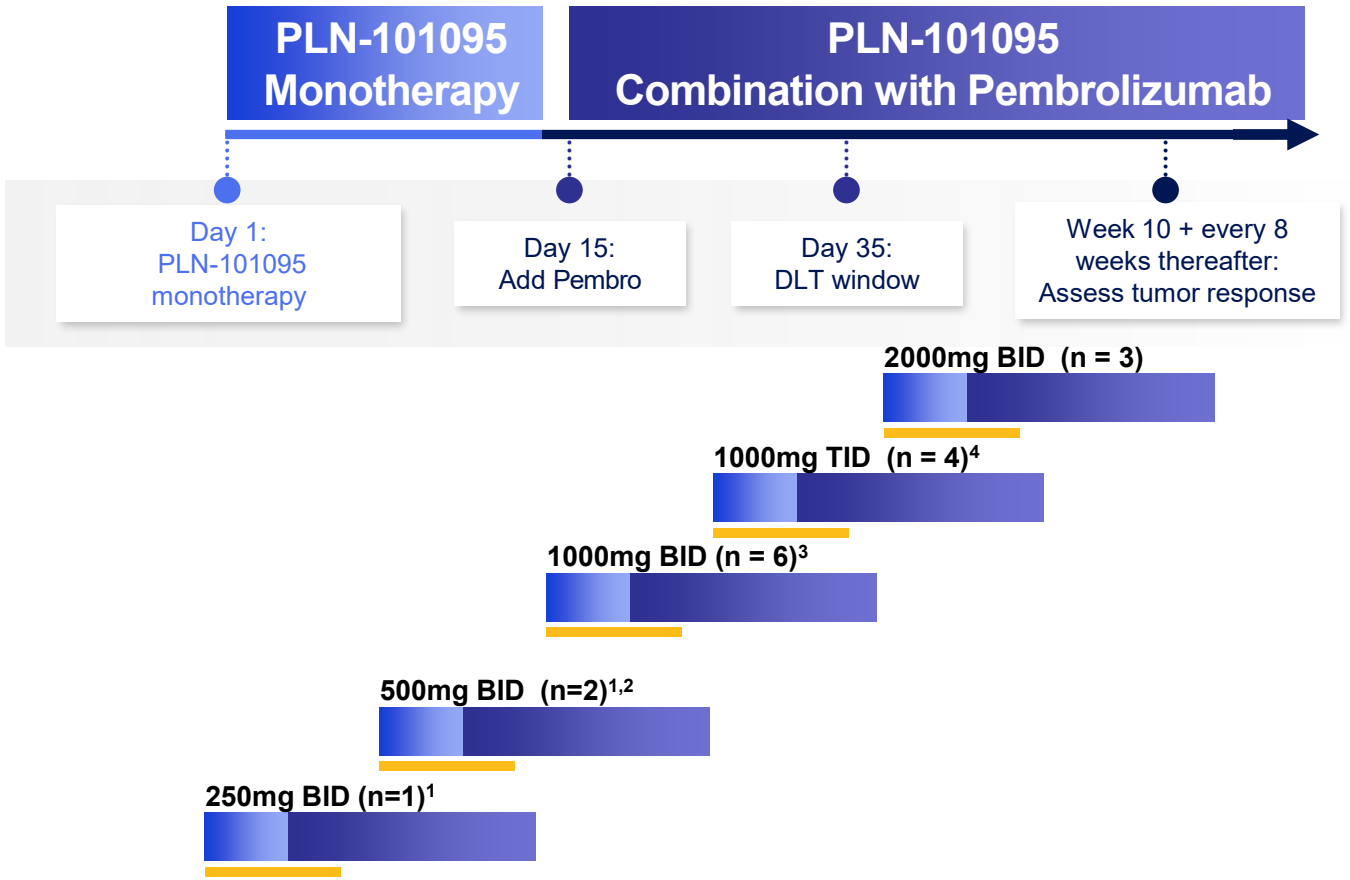
Phase 1 Study in Patients Refractory to ICIs

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 Exhibiting Dose-dependent PK

	Cohort 1 & 2 <1000 mg BID (n=3)	Cohort 3 1000 mg BID (n=6)	Cohort 4 1000 mg TID (n=4)	Cohort 5 2000 mg BID (n=3)	Total (n=16)
Most Common TEAEs					
Rash[1]	1 (33)	3 (50.0)	3 (75)	1 (33)	8 (50)
Anemia	0	1 (17)	2 (50)	0	3 (19)
Diarrhea	0	2 (33)	0	1 (33)	3 (19)
Serious TEAE	1 (33)	3 (50)[2]	1 (25)[2]	0	5 (31)

Safety

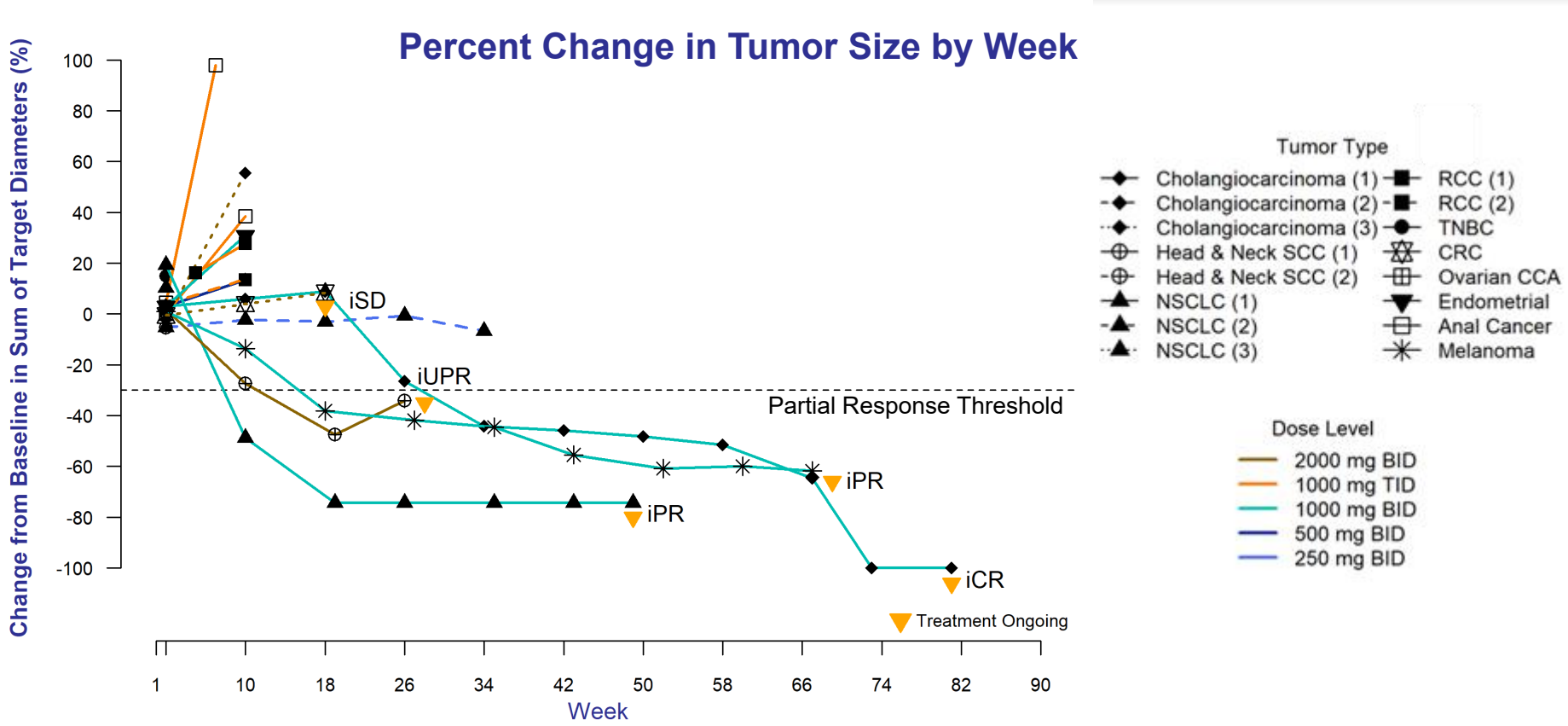
- Rash was the most common TEAE with all events mild or moderate in severity
- Two participants discontinued PLN-101095 due to TEAEs
  - Immune-mediated hepatitis (DLT, Cohort 3)
  - Grade 2 dermatitis bullous (Cohort 4)

Pharmacokinetics

- Dose dependent increases in exposures observed
- Doses ≥ 1000 mg BID achieved sustained 24-hour IC_{90} coverage

[1] Rash grouping includes Preferred Terms of rash, rash erythematous, rash maculo-papular, dermatitis acneiform and dermatitis bullous; [2] One participant with outcome of death in cohort (Not related to PLN-101095, due to disease progression)

Deep, Durable Responses in Majority of Clinical Responders at Doses of ≥1000 mg BID



Median time on treatment for clinical responders is 15 months

Average maximum tumor lesion reduction of 71% observed in clinical responders[1]

[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

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60% of ICI Secondary Refractory Participants Experienced Disease Stabilization or Tumor Reduction with a Median Duration of treatment of 10 months[2]

	<1000 mg BID (n=3)	1000 mg BID (n=6)	1000 mg TID (n=4)	2000 mg BID (n=3)	All (n=16)	Secondary Refractory ≥1000 mg BID (n=10)
Clinical Responders, n (%)	0	3 (50)	0	1 (33)	4 (25)	**4 (40)**
Time on treatment[1], median, mo	0	16	0	6	15	**15**
Responders + Stable disease, n (%)	2 (67)	3 (50)	2 (50)	2 (67)	9 (56)	**6 (60)**
Time on treatment[2], median, mo	5	16	3	6	6	**10**
iCR, n (%)	0	1 (17)	0	0	1 (6)	**1 (10)**
iPR, n (%)	0	2 (33)	0	0	2 (13)	**2 (20)**
iUPR, n (%)	0	0	0	1 (33)	1 (6)	**1 (10)**
iSD, n (%)	2 (67)	0	2 (50)	1 (33)	5 (31)	**2 (20)**
iPD, n (%)	1 (33)	3 (50)	2 (50)	1 (33)	7 (44)	**4 (40)**

[1] As of November 30,2025
[2] As of November30, 2025 for those still on treatment and as of first scan with progression for those with best overall response of stable disease
iCR, confirmed complete response by IRECISIT; iPR, confirmed partial response by iRECIST; iUPR, unconfirmed partial response by iRECIST; iSD, Stable disease by IRECIST; iPD, progressive disease by iRECIST
DCR: disease control rate (iSD, iPR, iCR); mDOR: median duration of response

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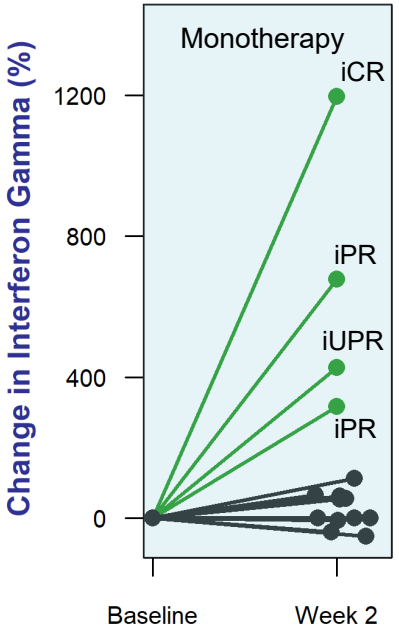
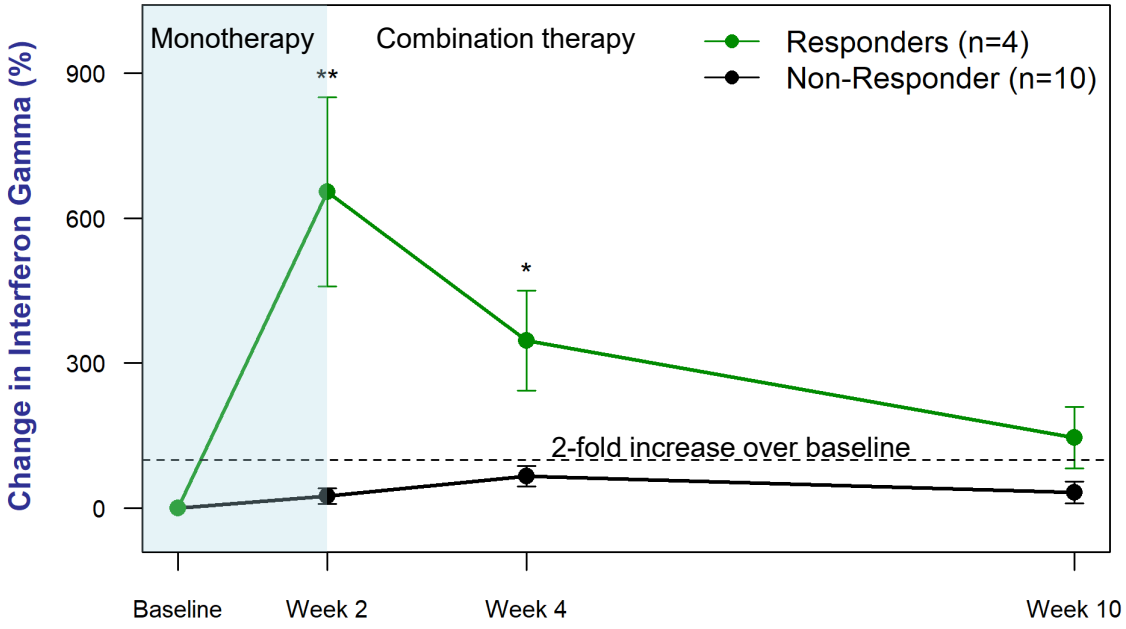
Clinical Response to PLN-101095 is Associated with Elevated Plasma IFN-γ Levels Following 14-day PLN-101095 Monotherapy

Percentage Change from Baseline in Plasma IFN-γ

By Subject at Week 2



Mean (±SE) Change over 10 Weeks



** p<0.01
* p<0.05

Change in circulating IFN-γ may provide a potential early predictor of treatment response

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

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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

Initiating Phase 1b cohorts in NSCLC and other tumor types in 2026

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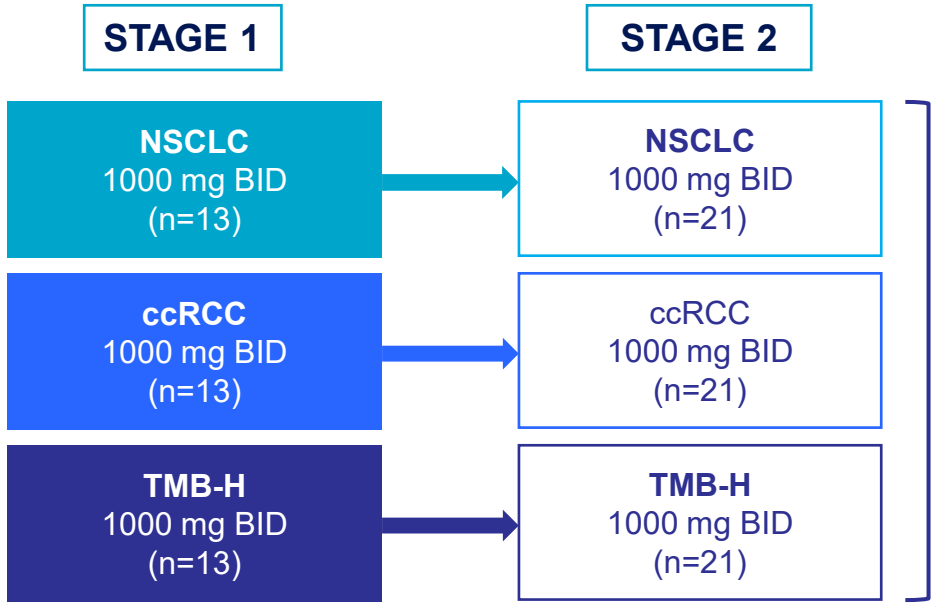
PLN-101095 Phase 1b Trial

Phase 1b: 3 Cohorts Grouped By Indication Using a Staged Approach

2-Stage Cohort Design



Dosing Schedule

PRIMARY ENDPOINTS

- ORR and DCR per iRECIST
- Safety and tolerability

SECONDARY ENDPOINTS

- PK parameters

KEY EXPLORATORY BIOMARKER ENDPOINTS

- Change in plasma interferon gamma (IFN-γ) and PD-L1
- Change in tumor tissue-based biomarkers

POPULATION

- Advanced or metastatic tumor types: NSCLC, ccRCC or TMB-H - melanoma, CRC, BTC, endometrial, and urothelial
- ≥12 weeks of continuous anti–PD(L)-1 therapy and ICI secondary refractory
- Life expectancy of at least 3 months

NSCLC: non small cell lung cancer, ccRCC: clear cell renal cell carcinoma; TMB-H: tumor mutational burden high; CRC: colorectal cancer; BTC: biliary tract cancer

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