



Developing Novel Integrin-Based Therapeutics

DECEMBER 2025

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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

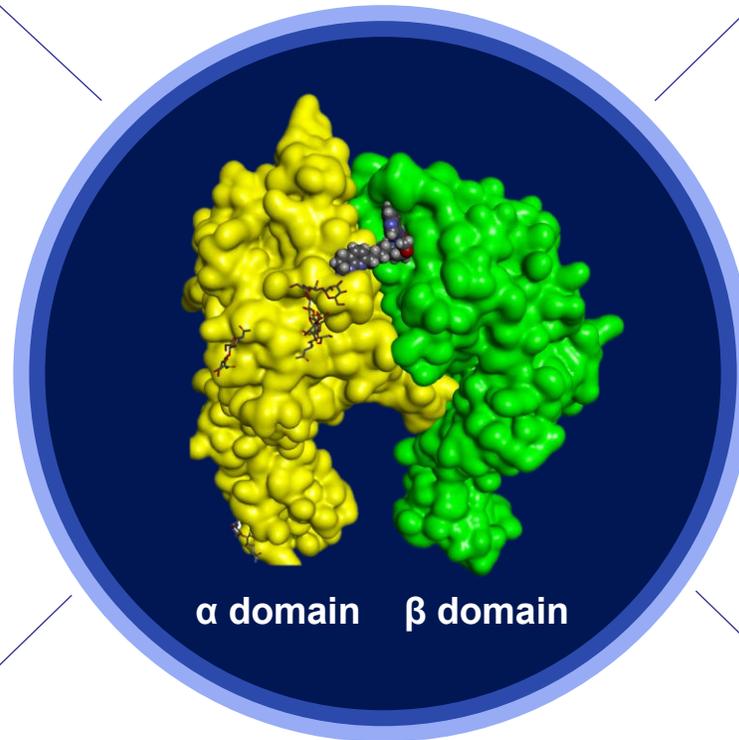
Integrins are an Attractive Target Class

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

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



Pliant's integrin library

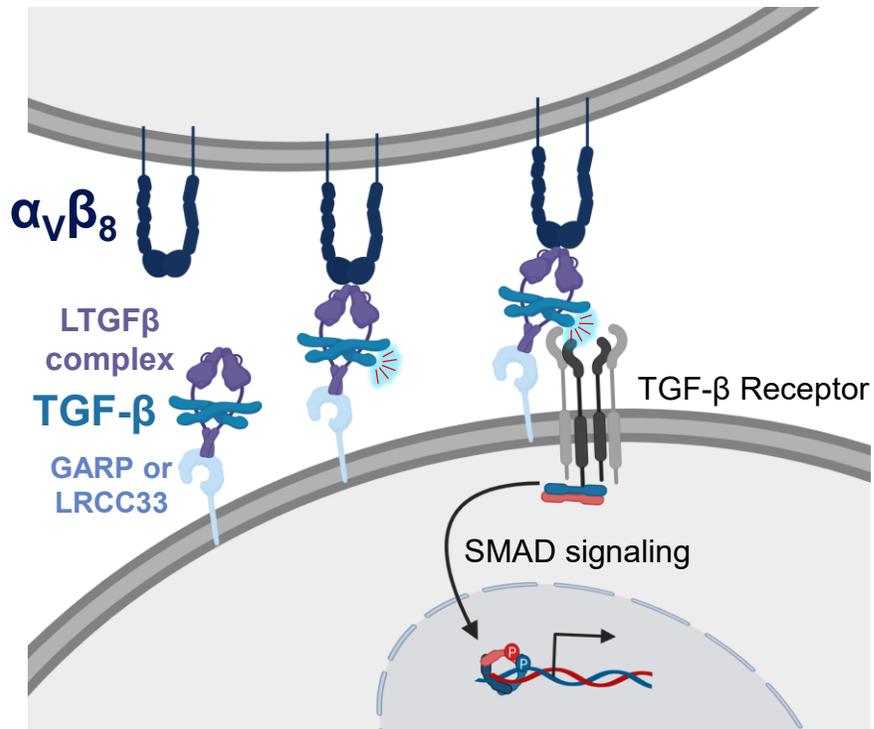
- Broad coverage of integrin heterodimers in 15,000+ compound library
- SAR understanding of binding motifs with desired biology
- Emphasis on optimal pharmacokinetic and potency/selectivity profiles

Integrins are a promising delivery modality

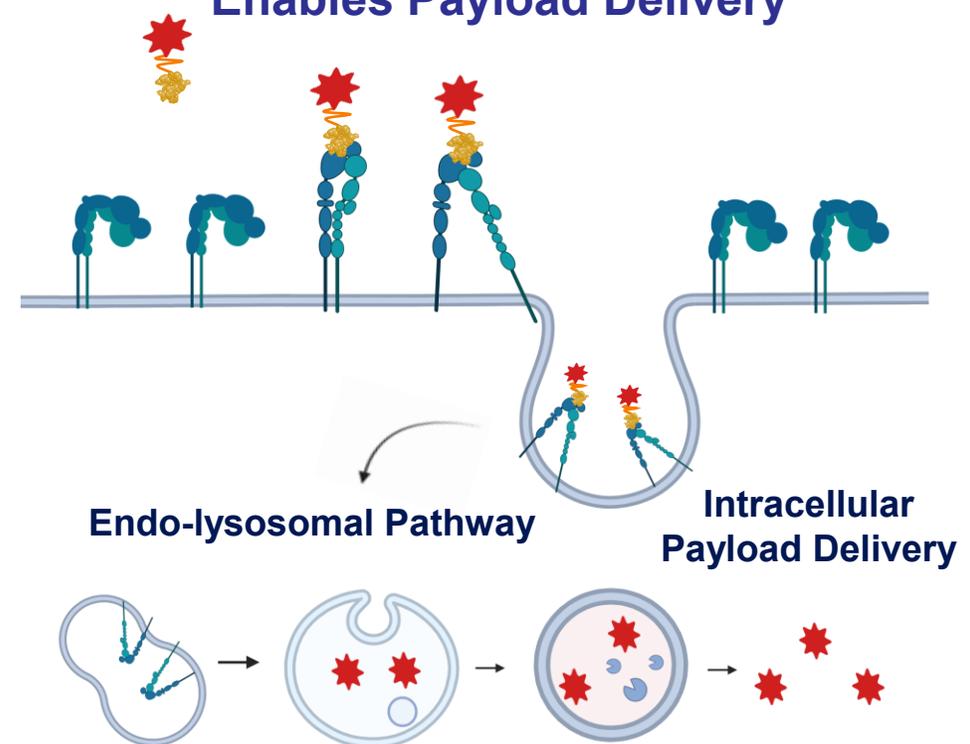
- Each integrin has a unique cell type-restricted expression profile
- Integrins readily internalize, enabling payload delivery

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



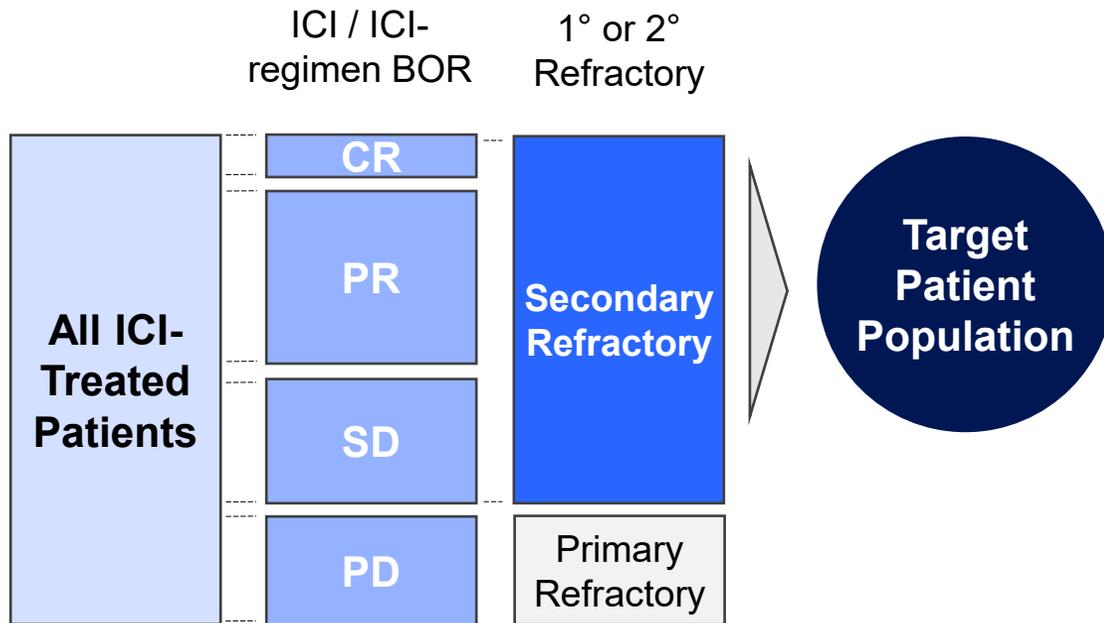
Initiating indication expansion cohorts

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

CR, confirmed complete response (100% tumor reduction); PR, confirmed partial response ($\geq 30\%$ tumor reduction)

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

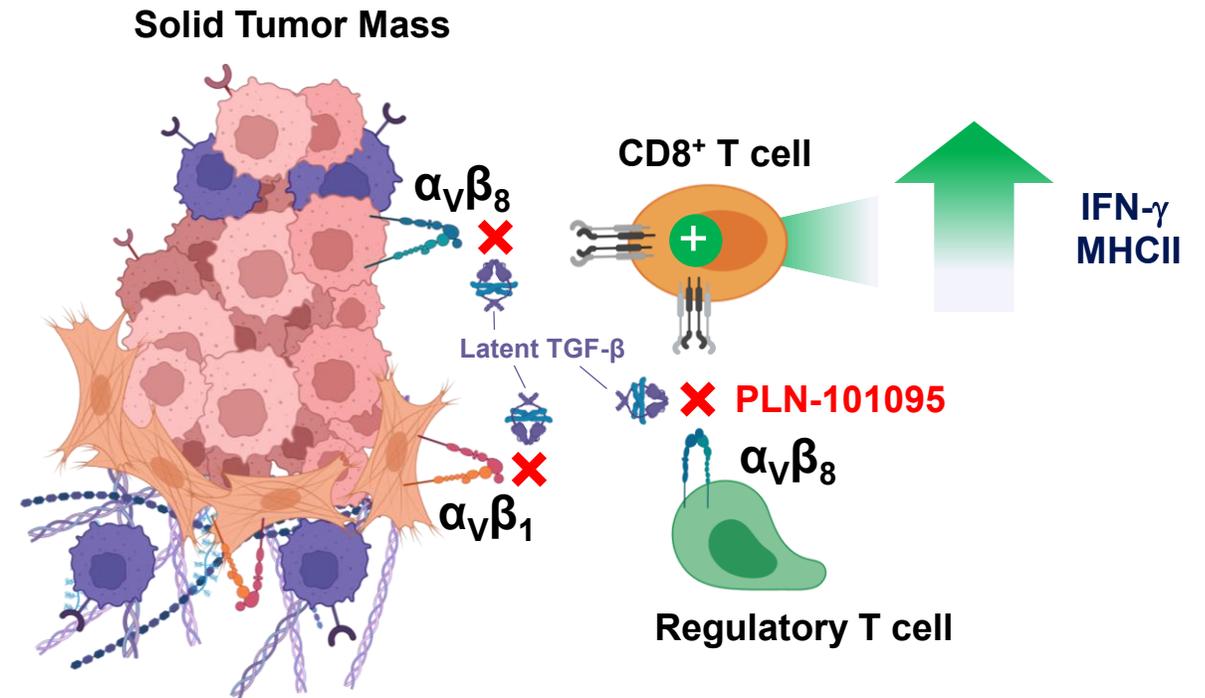
CR, confirmed complete response; PR, confirmed partial response; SD, stable diseases; PD, progressive diseases; BOR, best overall response; PFS: progression free survival.
Rates of PRs and acquired resistance estimated from US PI for approved PD-1 regimens.

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

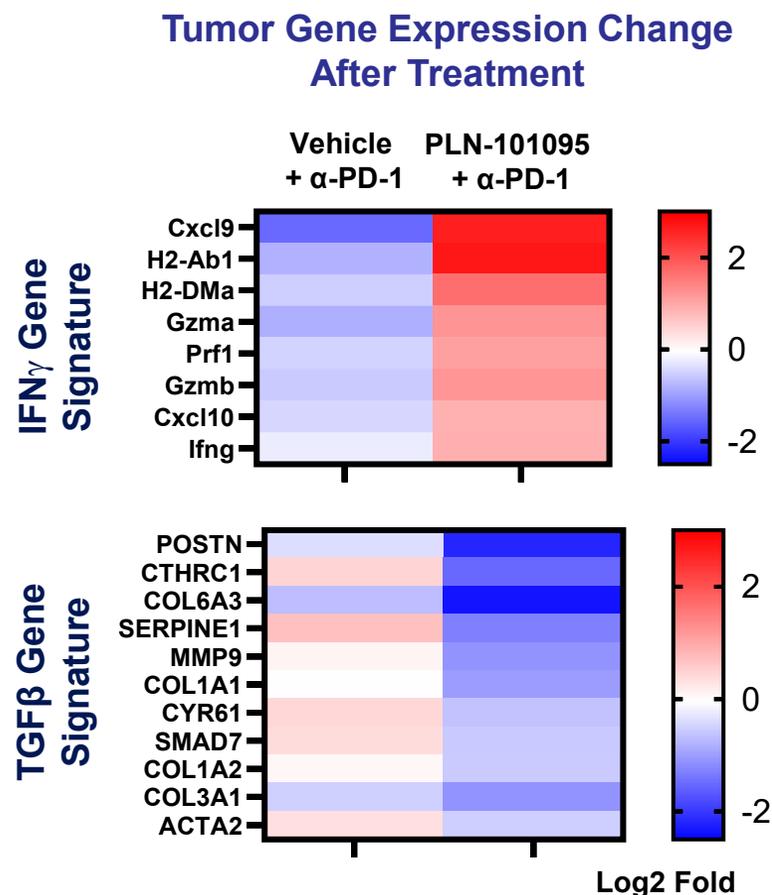


Integrin inhibition of $\alpha_v\beta_8$ and $\alpha_v\beta_1$ blocks activation of TGF- β to reduce immunosuppression leading to a new or reinvigorated cancer immune response

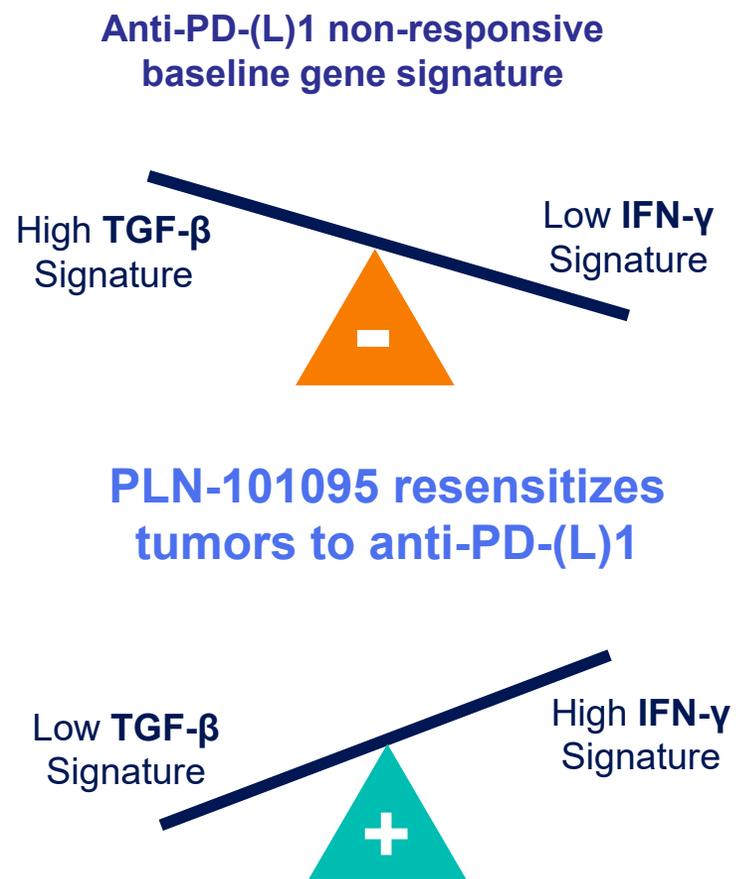
Mechanism of Action in Solid Tumors

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



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





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 population¹ 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)

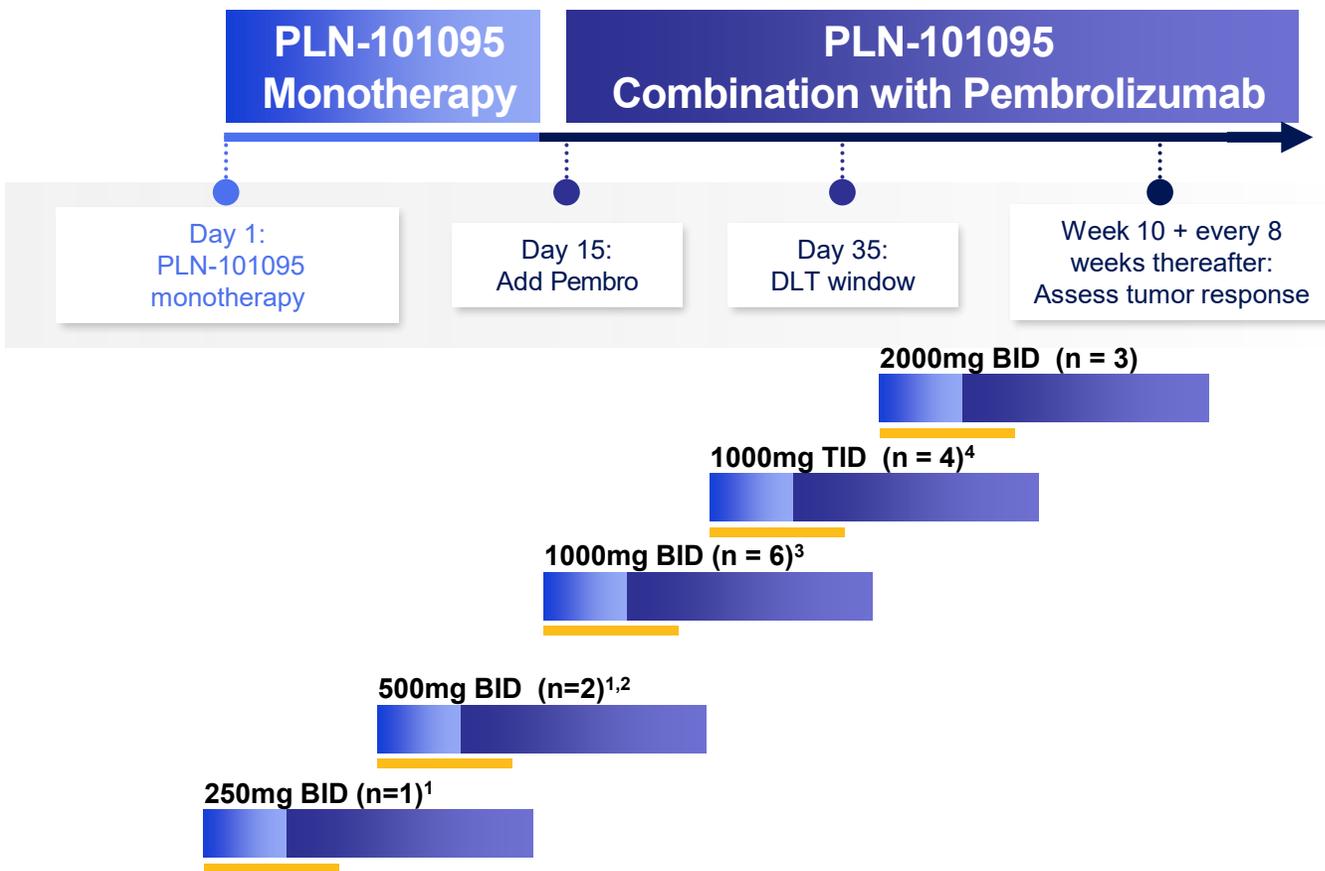
Circulating biomarker IFN- γ was identified as a potential early predictor of treatment response

- 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 ($\geq 30\%$ tumor reduction); uPR, unconfirmed partial response ($\geq 30\%$ tumor reduction)

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)

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

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

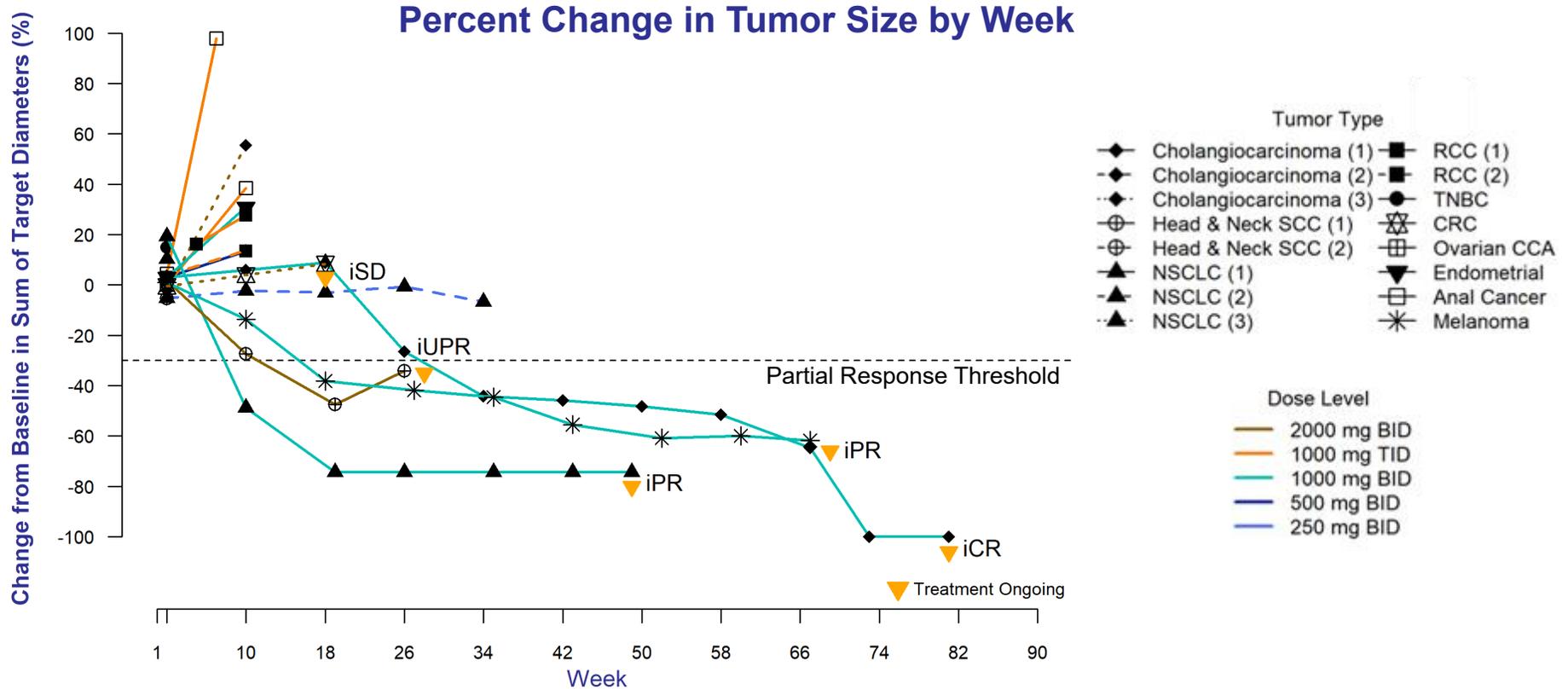
- Rash was the most common TEAE with all events mild or moderate in severity
- Two participants discontinued PLN-101095 due to TEAEs
 - Immune-mediated hepatitis (DLT, Cohort 3)
 - Grade 2 dermatitis bullous (Cohort 4)

Pharmacokinetics

- Dose dependent increases in exposures observed
- Doses \geq 1000 mg BID achieved sustained 24-hour IC₉₀ 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 responders¹

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

60% of ICI Secondary Refractory Participants Experienced Disease Stabilization or Tumor Reduction with a Median Duration of treatment of 10 months²

	<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

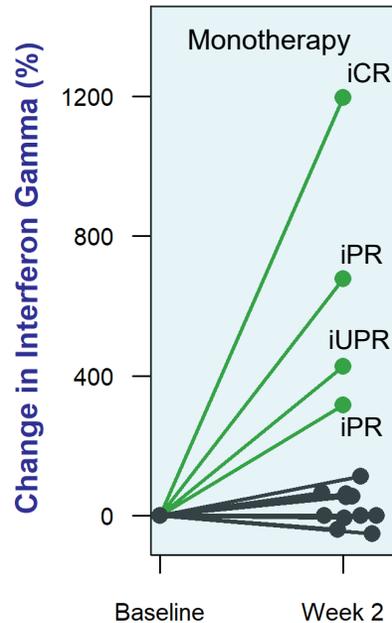
² As of November 30, 2025 for those still on treatment and as of first scan with progression for those with best overall response of stable disease

iCR, confirmed complete response by IRECIST; 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

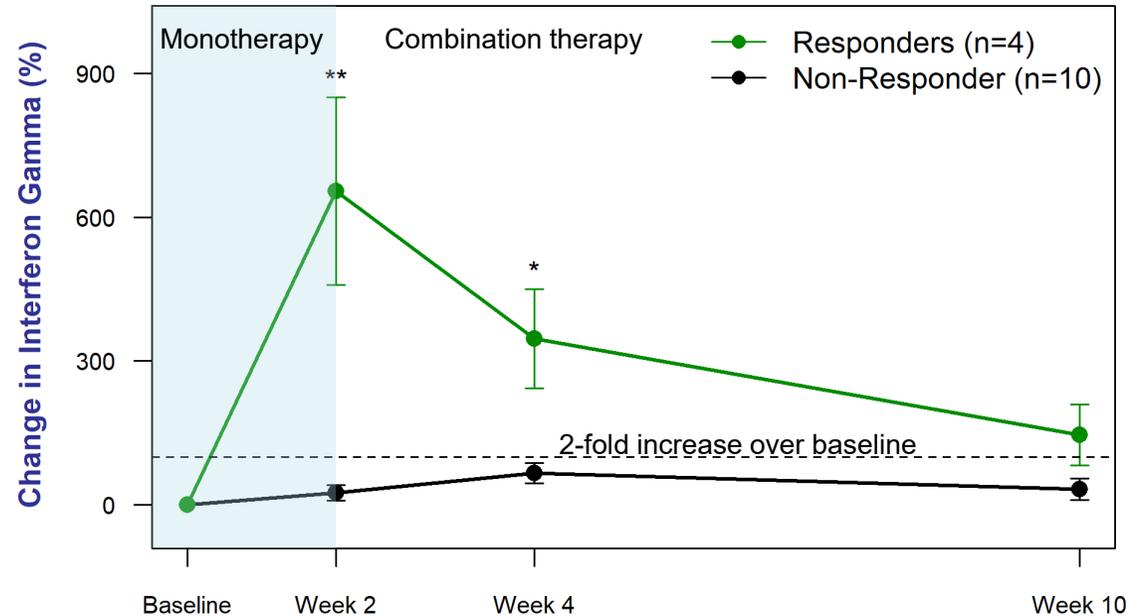
Clinical Response to PLN-101095 is Associated with Elevated Plasma IFN- γ Levels Following 14-day PLN-101095 Monotherapy

Percentage Change from Baseline in Plasma IFN- γ

By Subject at Week 2



Mean (\pm SE) Change over 10 Weeks



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

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