NASDAQ: PALI
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Next-Generation Precision Therapies for Immune, Inflammatory and Fibrotic Diseases

April 2025
Investor Presentation

Forward Looking Statements

Statements in this presentation that are not statements of historical fact are forward-looking statements. Such forward-looking statements include, without limitation, statements regarding our research and pre-clinical and clinical development plans, expected near and long-term milestones, hypothesis related to PALI-2108, the potential of PALI-2108 to treat inflammatory bowel disease ("IBD"), our ability to successfully complete our current and planned human clinical trials of PALI-2018, the ability of PALI-2108 to achieve market acceptance, the success of our development and business strategy, Insurance company's agreeing to reimburse patients for treatments utilizing PALI-2018, ability to leverage certain regulatory pathways, timing of studies, competitors, regulatory matters, market size and opportunity and our ability to complete certain milestones, including completion of subject enrollment. Words such as "believe," "anticipate," "could," "estimate," "aim," "target," "plan," "expect," "intend," "will," "may," "goal," "potential" and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain these identifying words. These forward-looking statements are based on the beliefs of management of Palisade Bio, Inc. (the "Company") as well as assumptions that may never materialize or prove to be incorrect. Such statements reflect the current views of the Company with respect to future events and are subject to known and unknown risks, including business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company, including, without limitation, risks inherent in developing pharmaceutical products, future results from the Company's ongoing pre-clinical studies and clinical trials, the Company's ability to obtain adequate financing to fund its operations and planned studies and other expenses, trends in the industry, changes in the competitive landscape, delays or disruptions due to the pandemics, the legal and regulatory framework for the industry and future expenditures. In light of these risks and uncertainties, the events or circumstances referred to in this presentation may not occur. The actual results may vary from the anticipated results and the variations may be material. Other factors that may cause the Company's actual results to differ from current expectations are discussed in the Company's filings with the Securities and Exchange Commission, including the section titled "Risk Factors" contained therein. These forward-looking statements should not be taken as forecasts or promises, nor should they be taken as implying any indication, assurance or guarantee that the assumptions on which such forward-looking statements have been made are correct or exhaustive or, in the case of the assumptions, fully stated in this presentation. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this presentation is given. Except as required by law, the Company assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

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Corporate Highlights

Our Mission:

Develop differentiated product candidates targeting immune, inflammatory and fibrotic diseases in established commercial markets where there is significant unmet medical need.

Lead Program, PALI-2108, Targeting Multi-Billion-Dollar IBD Market

PALI-2108

- **Only PDE4 inhibitor in development targeting the terminal ileum and colon** for treatment of UC and FSCD
- **Commercially proven PDE4 target** with potential for superior efficacy and greater tolerability over systemic PDE4 inhibitors
- **Positive preliminary Phase 1a/b data** demonstrating safety, tolerability and PK supporting local bioactivation
- **Precision Medicine CDx test in development** to identify UC patient responders to PDE4 inhibitors, ensuring better treatment outcomes
- **First and only dual-acting anti-inflammatory and anti-fibrotic candidate in development for FSCD** where there are currently no approvals

Development Pipeline

Differentiated product candidates with potential to address shortcomings of existing therapies in established markets

PROGRAM	INDICATION	STATUS	HIGHLIGHTS
PALI-2108 (PDE4 B/D Target)	Ulcerative Colitis (UC)	Phase 1a/b	Completed SAD, MAD, FE and first UC patient Topline data on-track and expected H1 2025 IND and Ph1b/2a expected to commence in Q1 2026
	Fibrostenotic Crohn's Disease (FSCD)	Phase 1a	Leveraging Phase 1a data to accelerate development PoC for fibrotic pathway engagement complete IND and Ph1b/2a expected to commence in Q1 2026

PALI-2108 Upcoming Milestones[1]

INDICATION	Q2 2025	H2 2025	H1 2026	H2 2026
Ulcerative Colitis (UC)	• Phase 1a/b Topline Data	• Pivotal Toxicology Studies • GMP Drug Product Manufacturing	• IND Clearance • Phase 1b/2a First Subject Dosed	• Phase 1b Safety Data • Phase 1b/2a Topline Efficacy Data • Phase 2a First Subject Dosed • Launch Open-Label Extension
Fibrostenotic Crohn's Disease (FSCD)	• Phase 1a/b Topline Data	• Pivotal Toxicology Studies • GMP Drug Product Manufacturing	• IND Clearance • Phase 1b/2a First Subject Dosed	• Phase 1b Safety Data • Phase 2a Induction Readout

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1. The timing of the milestones are estimated, and the actual timing of these milestones may differ than described herein.

PALI-2108

Targeting Multi-Billion-Dollar IBD Market

Ulcerative Colitis (UC) | **Fibrostenotic Crohn's Disease (FSCD)**

Differentiated asset with potential to address important unmet medical needs in large, established IBD market

Inflammatory Bowel Diseases (IBD)

Chronic condition characterized by persistent inflammation in the digestive tract diagnosed in early adulthood with alternating periods of activity and remission.

Market Expected to Grow to **$20B** by 2031[1]

CURRENT IBD MARKET [2,3]

Ulcerative Colitis	Crohn's Disease
1.95 Million Cases	1.63 Million Cases
$7.7 Billion Market	$8 Billion Market

1. Global Data
2. Centers for Disease Control and Prevention; Inflammatory Bowel Disease
3. United European Gastroenterology

A Differentiated Approach to IBD

An oral prodrug designed to treat UC and FSCD by targeting the key enzyme PDE4 locally in intestinal tissues

Key Differentiation

✓ **Oral Dosing**
Preferred by patients and clinicians, important goal for large pharma and supports future oral combination therapies.

✓ **Novel Target**
First therapy designed to target PDE4 enzymes in treating inflammatory and fibrotic bowel diseases.

✓ **Targeted Localized Delivery**
Only PDE4 inhibitor targeting the terminal ileum and colon for UC and FSCD with high local tissue levels and minimal systemic exposure.

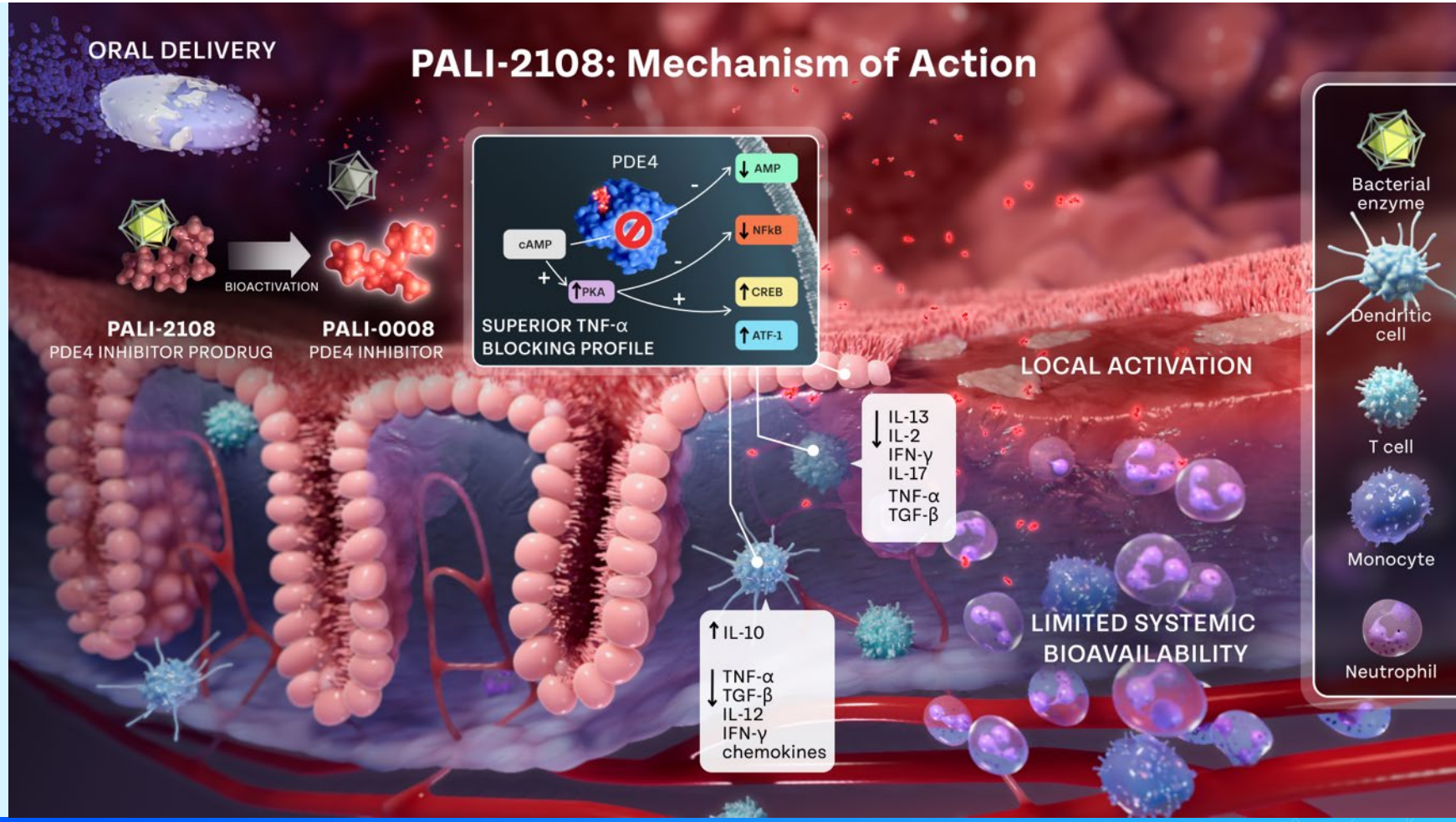
✓ **Improved Tolerability**
Minimizes common PDE4 inhibitor-related side effects, such as CNS and GI toxicity, by ensuring activation only in the affected areas of the gut.

✓ **Precision Medicine for UC Patient Selection**
Employs a biomarker test developed using machine learning for UC patient selection, potentially increasing remission rates.

✓ **Dual-Action Mechanism for FSCD**
Delivers both anti-inflammatory and anti-fibrotic effects in FSCD, where there are no approved therapies, offering a novel treatment approach.

PALI-2108 Only Bio-Activates in the GI System

- Targets PDE4 B/D enzymes
- Prevents break down of intracellular cAMP
- cAMP levels become elevated
- Reduces inflammatory tone and prevents inflammatory cell infiltration within tissues of the ileum and colon



Bioactive Beta-Glucuronidase Produced Ubiquitously by Bacteria in the Gut

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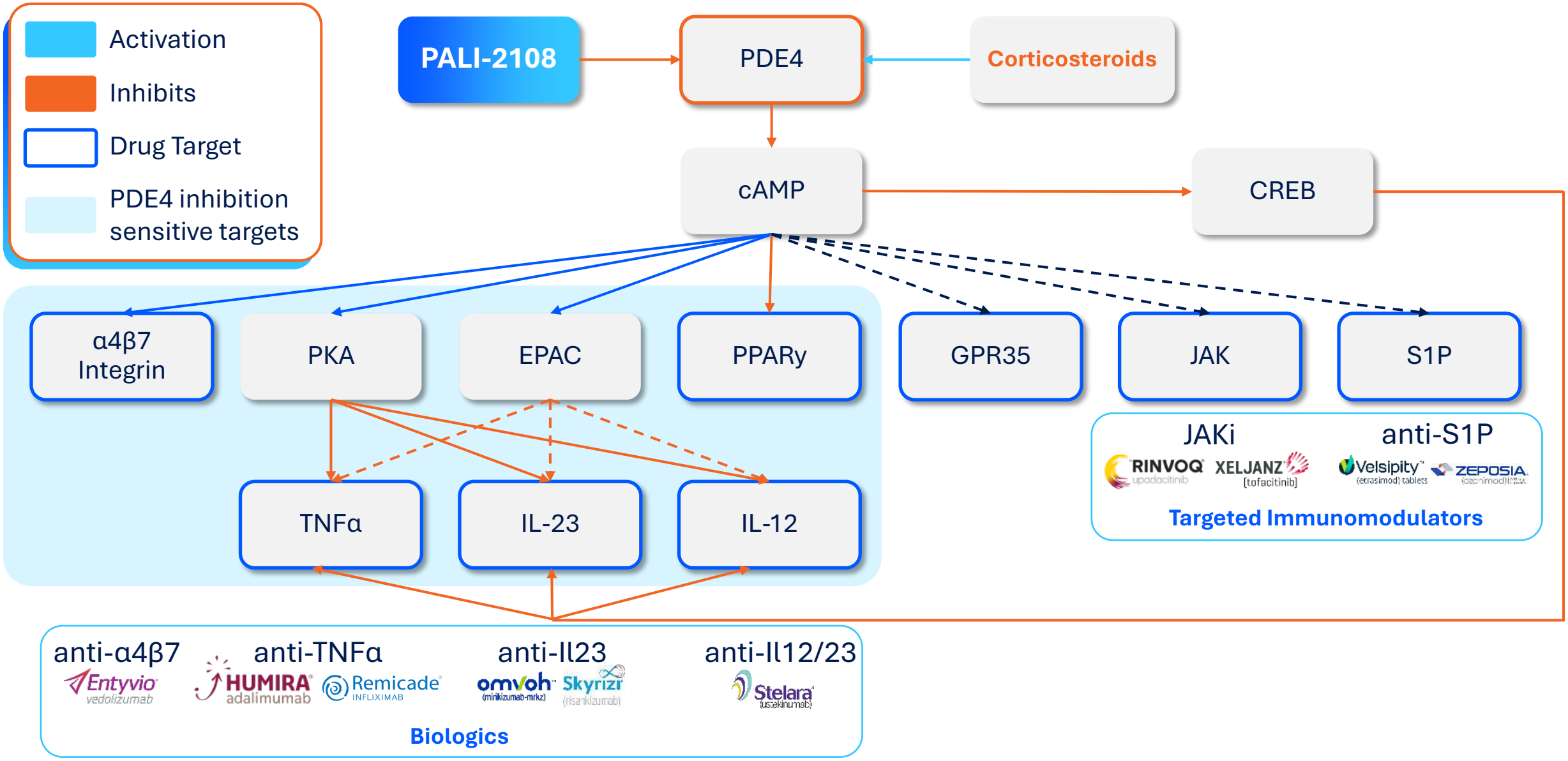
How PDE4 Regulates the UC Therapeutic Targets



PDE4 Inhibitors

Commercially Proven Target Validated for Inflammatory and Fibrotic Diseases

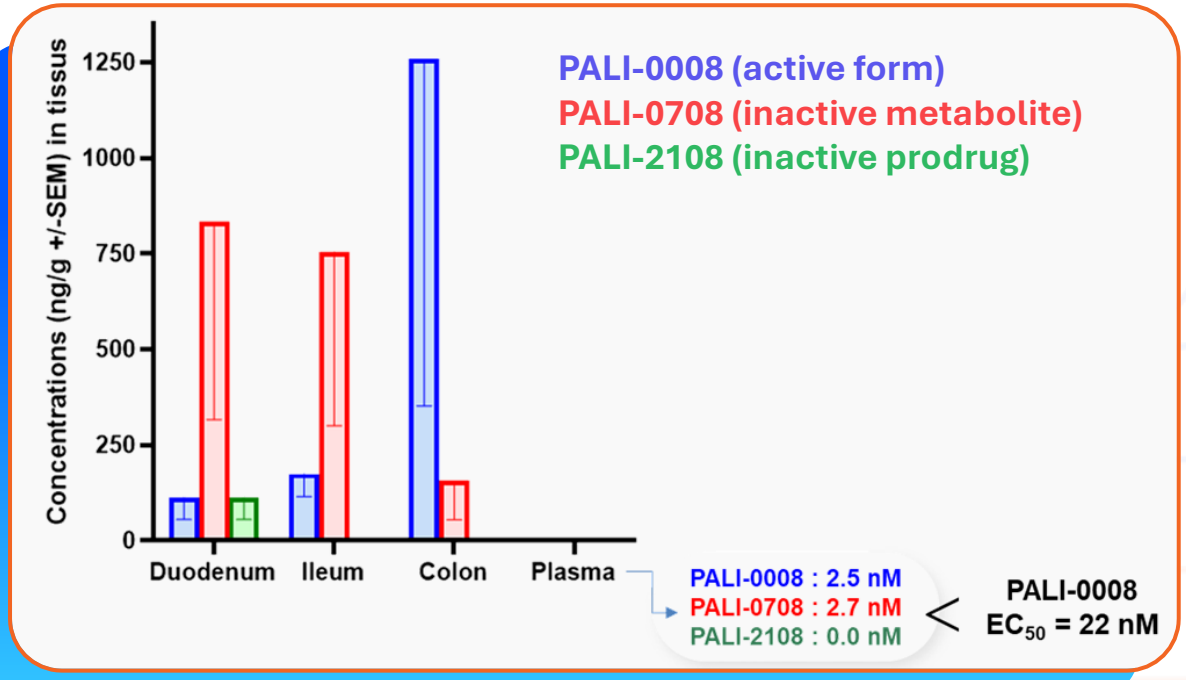
PDE4 is a Commercially Proven Target Validated by Billion Dollar Products in Inflammatory and Fibrotic Disease

PALI-2108 Is the Only PDE4 Inhibitor Designed to Target Terminal Ileum and Colon Give Key Factors Including Mechanism, Formulation and Profile

	PALI-2108	Apremilast	Rofumilast	Orimilast	Nerandomilast
Company	palisadebio	AMGEN	AstraZeneca	UNION THERAPEUTICS	Boehringer Ingelheim
Selectivity	B / D	Pan	Pan	B / D	B
IC50 (B/D)	0.4 / 1.4 nM (1)	12 / 8 nM (2)	0.14 / 0.11 nM (3)	4 / 9 nM (4)	10 / 91 nM (5)
Dose	15-30mg BID	30mg BID	0.5mg BID	30mg BID	18mg BID
Route	Oral	Oral	Oral	Oral	Oral
Target	Terminal ileum and Colon	Systemic	Lung	Systemic	Lung
Indication	Colitis and Crohn's	Psoriasis and Psoriatic Arthritis	COPD	Atopic Dermatitis and Psoriasis	Idiopathic Pulmonary Fibrosis

Limited Systematic Activity in Preclinical Model Provides Potential for Improved Safety Profile

Lack of Plasma Activity is Believed to Mitigate CNS Side Effects, Like Nausea, Which is Seen with Systemic PDE4 Inhibitors



- ✓ Prodrug is released within the ileum and bio-converted by bacterial enzymes in the colon
- ✓ Prodrug is bioactivated within the colon and active PDE4 is locally absorbed
- ✓ Improved therapeutic window enables maximal PDE4 inhibition supporting higher cAMP tissue levels

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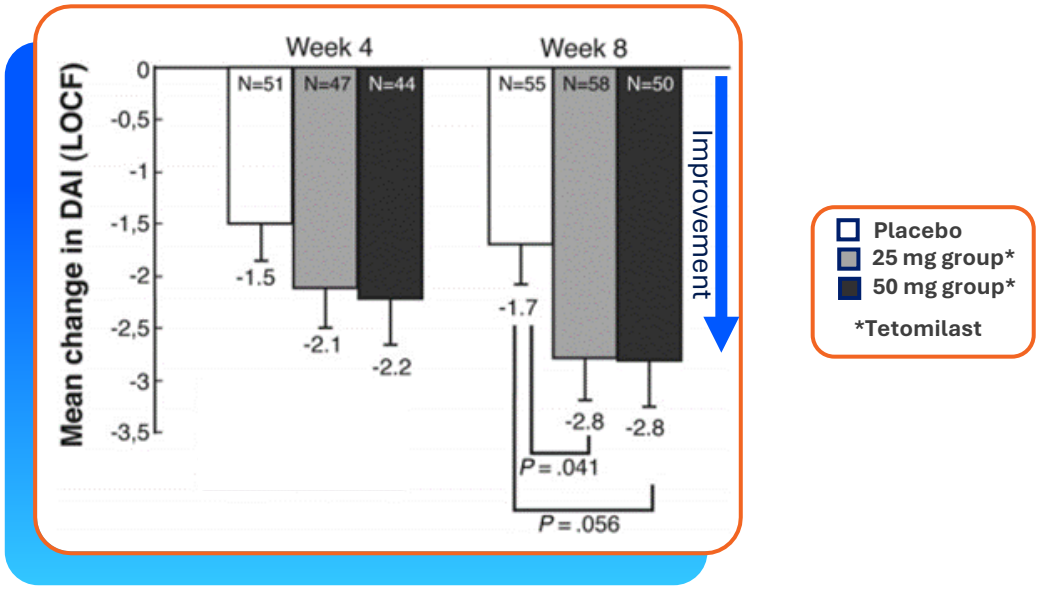
Previously Published Ph2 Studies of Systemic PDE4 Inhibitors Demonstrate Compelling Dose Response and Efficacy

While Phase 2 Studies Validate PDE4 Target in UC, Adverse Events Limited Dose Selection and Complicated Potential Advancement in UC

Mild-to-Moderate Active UC[1]



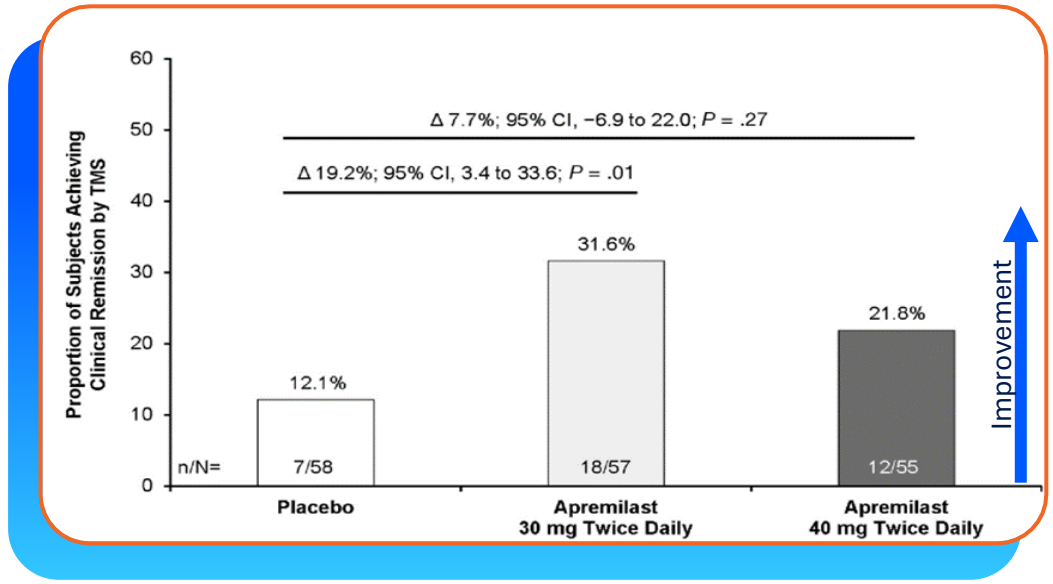
1. Schreiber et al. Gastroenterology. 2007 (not PALI data)

Significant improvement in disease activity index (DAI) at Week 8

Significant improvement in clinical remission rate

Adverse Events (AEs) were most frequently nausea, headache and vomiting

Moderate-to-Severely Active UC[2]



2. Danese et al. Clin Gastro and Hep. 2020 (not PALI data)

Significant improvement in clinical remission rate of 19.2%

Adverse Events (AEs) were most frequently headache and nausea

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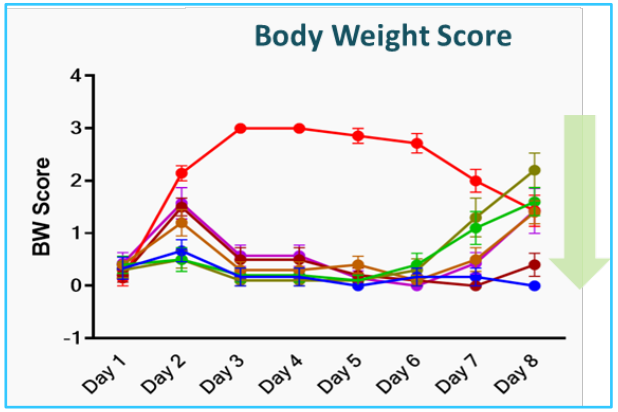
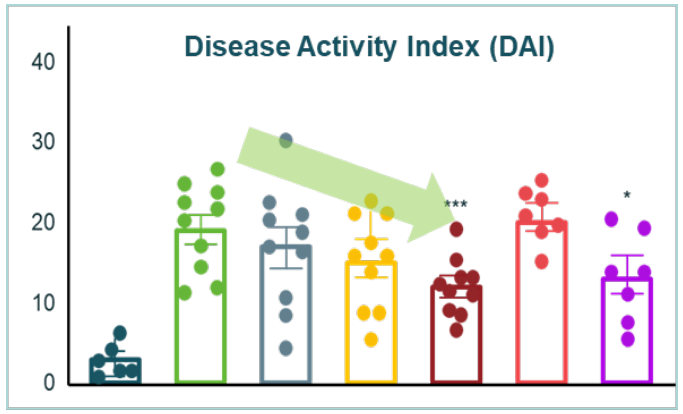
PALI-2108 Demonstrated Improved Efficacy Over Standard of Care and Systematic PDE4 Inhibitors in DSS Colitis Mouse Model

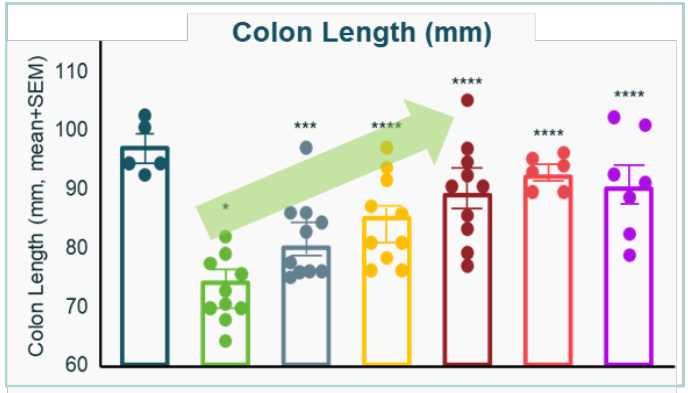
Dose Dependent Efficacy Response in DSS Colitis Mouse Model





<0.05,***p<0.001, ****p<0.0001: Dunnett's test compared to 4%DSS+Vehicle

- Non-Treatment naive
- 4% DSS + Vehicle (PO)
- 4% DSS + PALI-2108/ 40mg/kg (PO)
- 4% DSS + PALI-2108/ 80mg/kg (PO)
- 4% DSS + PALI-2108/ 160mg/kg (PO)
- 4% DSS + Cyclosporin A 80mg/kg (PO)
- 4% DSS + Apremilast/ 25mg/kg (PO)



****p<0.0001,***p<0.0001, *p<0.05: Dunnett's test compared to DSS+Vehicle

PALI-2108 showed dose-dependent improvements in clinical outcome measures and superior to Standard of Care

PALI-2108 demonstrated highly significant improvements in clinical measures such as body weight score, Disease Activity Index (DAI), and colon length

While apremilast showed efficacy, it was at a dose not well tolerated in UC patients including headache, nausea, and diarrhea*

*Danese et al

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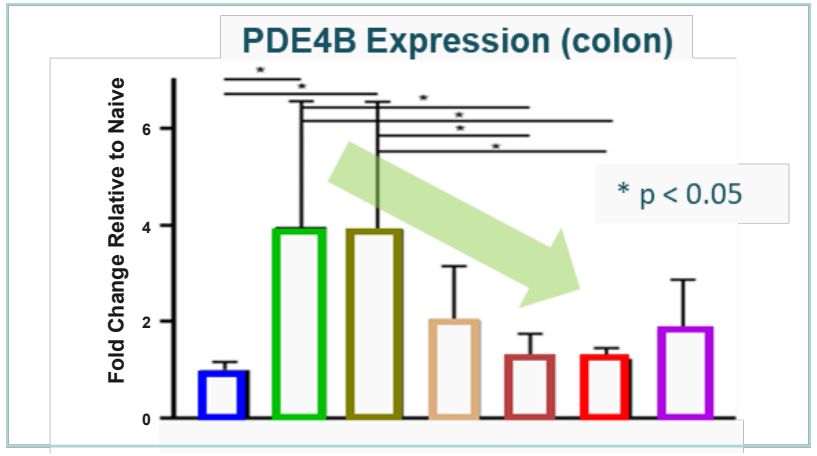
PALI-2108 Demonstrated Improved Efficacy Over Standard of Care and Systematic PDE4 Inhibitors in DSS Colitis Mouse Model

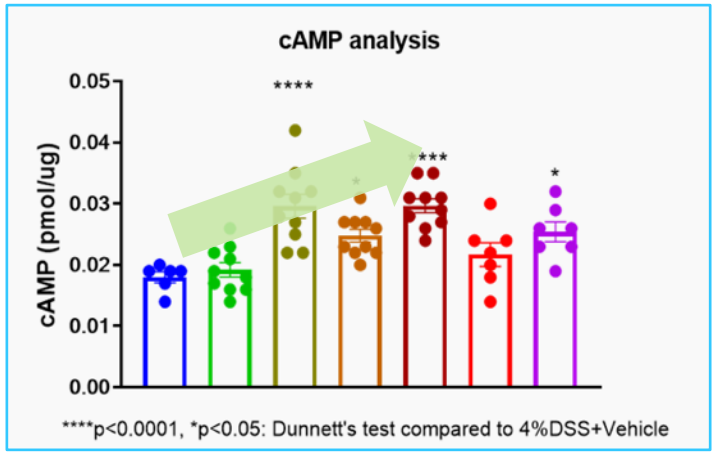
Dose Dependent Efficacy Response in DSS Colitis Mouse Model

Dose dependent reductions in colon tissue PDE4B Expression (mRNA) in response to increasing PALI-2108 dose

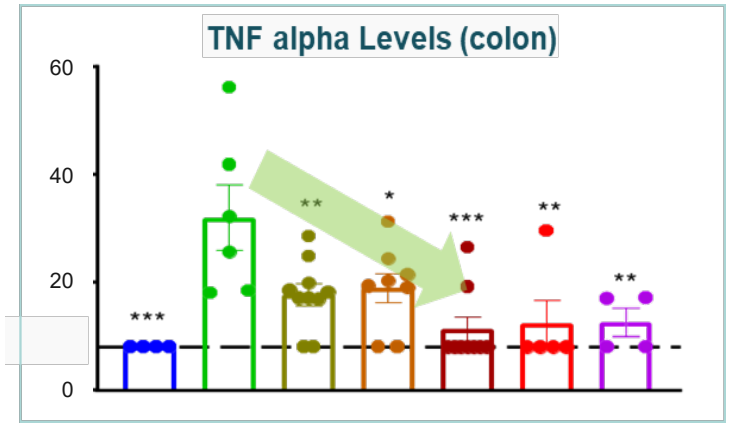
Dose dependent increases in colon tissue cAMP in response to increasing PALI-2108 dose

Dose dependent reductions in colon tissue TNF-alpha levels which were normalized on average and in most animals





- Non-Treatment naive
- 4% DSS + Vehicle (PO)
- 4% DSS + PALI-2108/ 40mg/kg (PO)
- 4% DSS + PALI-2108/ 80mg/kg (PO)
- 4% DSS + PALI-2108/ 160mg/kg (PO)
- 4% DSS + Cyclosporin A 80mg/kg (PO)
- 4% DSS + Apremilast/ 25mg/kg (PO)



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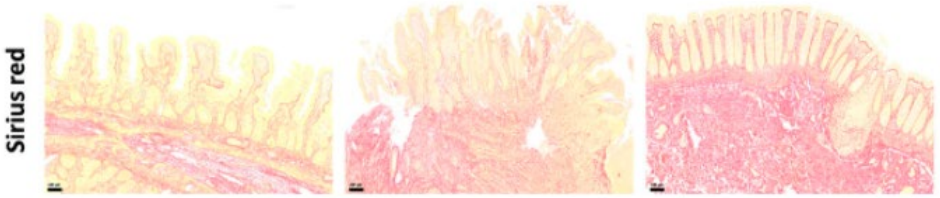
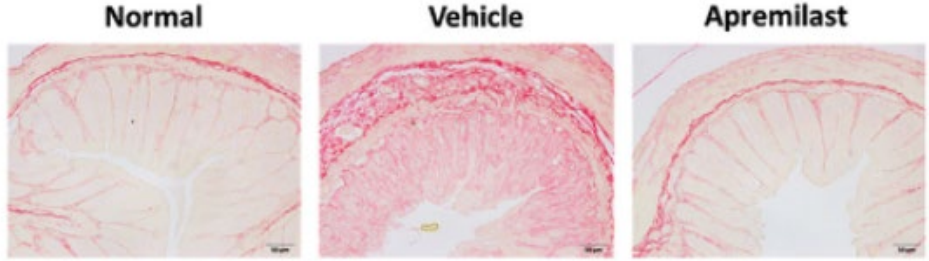
PALI-2108 Demonstrated Dose Response on Fibrotic Pathways

PDE4 Inhibitor Effect on Fibrotic Pathways

Evidence of Collagen Deposition in Biopsies of UC Patients

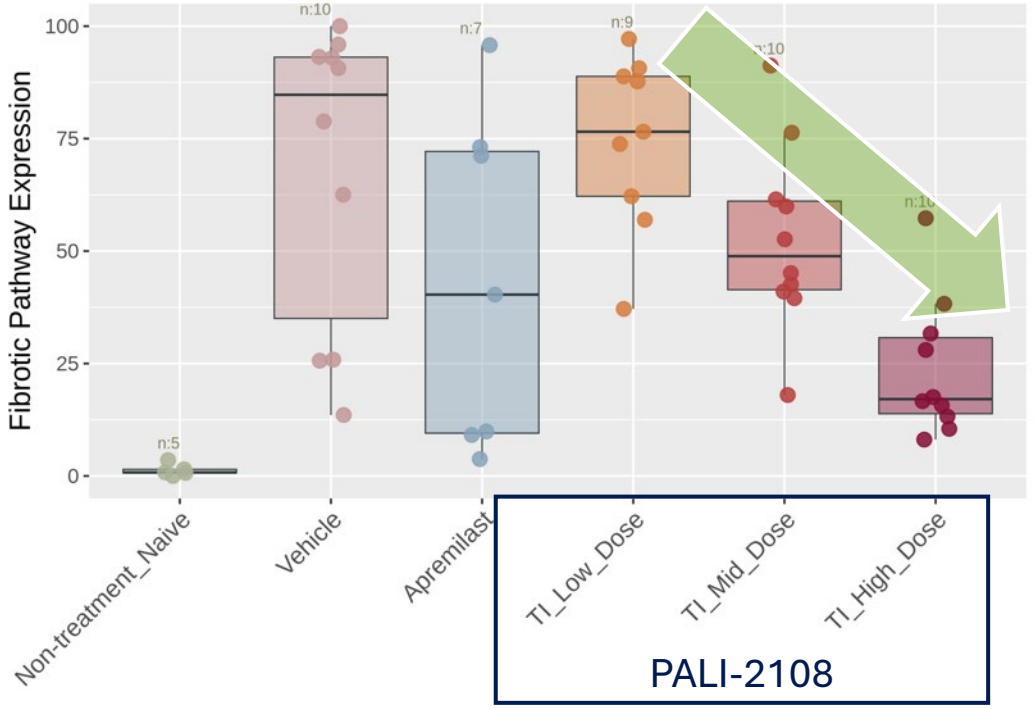


PDE4 Inhibitor Attenuates Collagen Deposition and Reverses Activation of Mucosal Fibroblasts

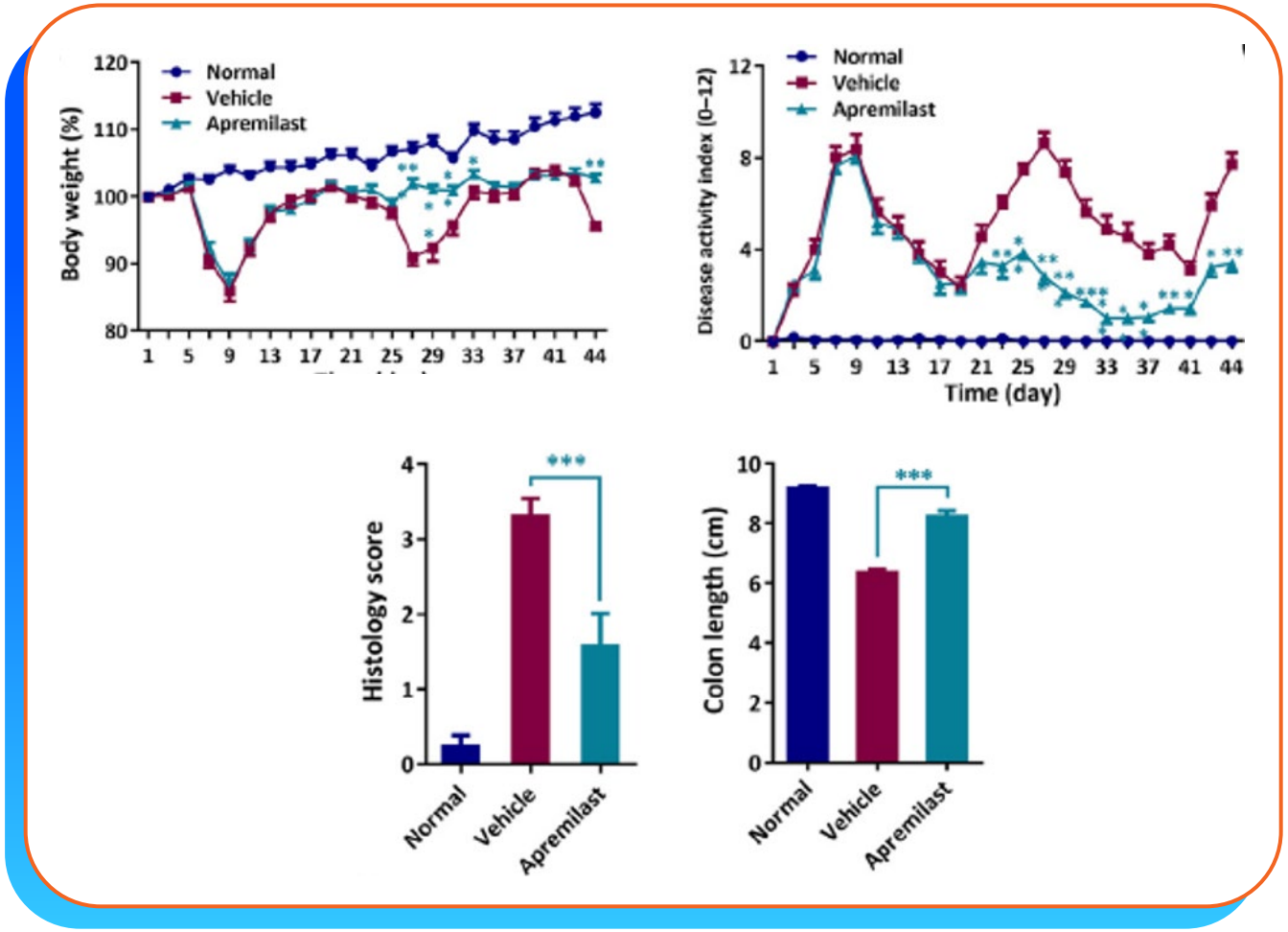


*Li et al.

PALI-2108 Demonstrated Greater Antifibrotic Effect Compared to Apremilast



PDE4 Inhibitors Effective at Improving Clinical Symptoms and Fibrotic Biomarkers in Chronic DSS Mouse Model



Significantly improved clinical measures including body weight, disease activity, colon length and intestinal fibrosis biomarkers[1]

PDE4 inhibition prevents breakdown of cAMP inhibiting fibroblast functions including mitigating tissue remodeling[1]

PDE4 inhibition has particularly effective anti-fibrotic effects in the presence of TGF-beta-induced fibroblast stimulation[2]

1. Li et al. 2021
2. Togo et al. 2009

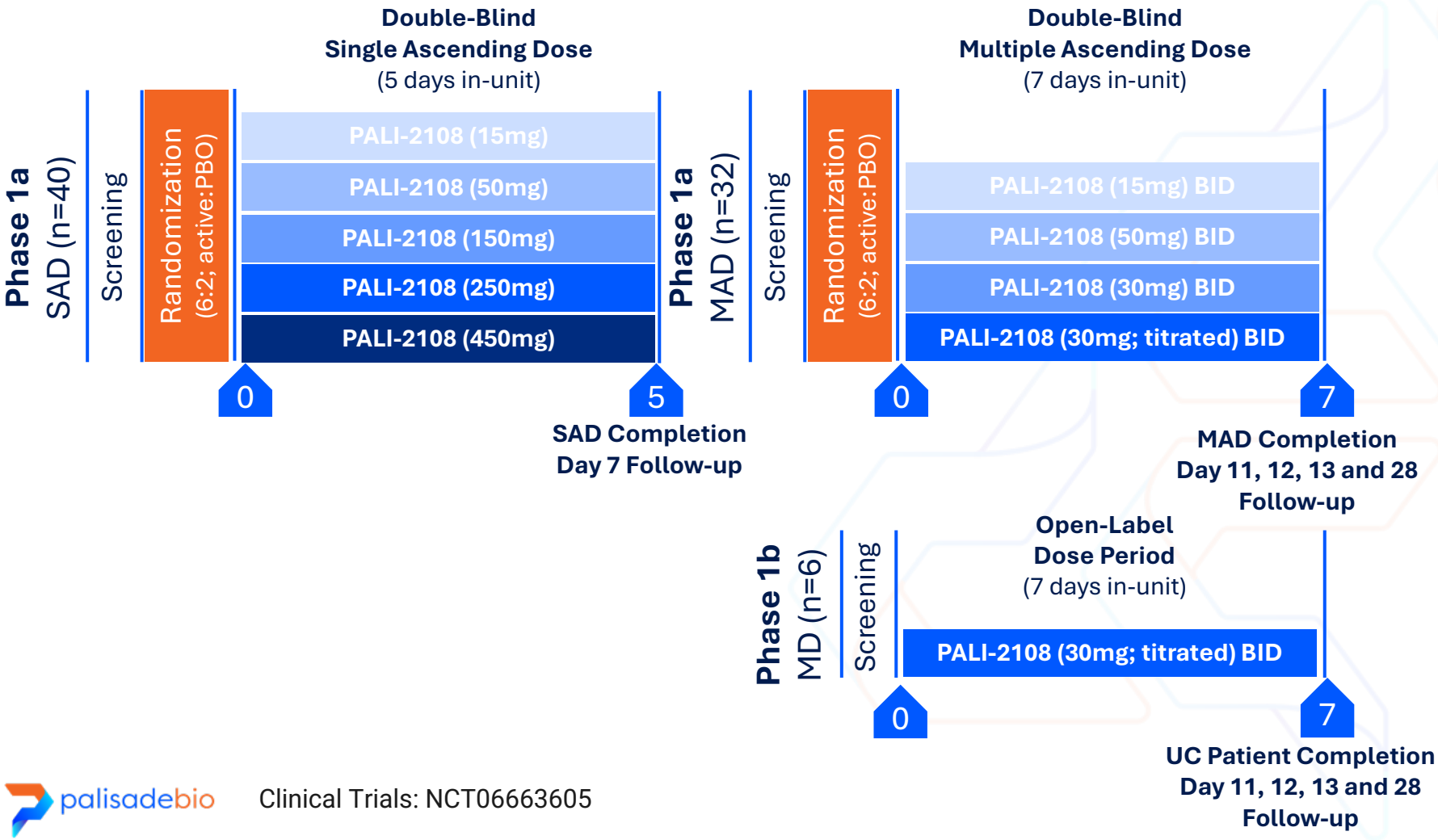
PALI-2108 Phase 1a/b

SAD/MAD Study Design and Preliminary Findings

Ongoing Ulcerative Colitis Phase 1a/b Study

Double-Blind, Placebo-Controlled, Safety, Tolerability, Pharmacokinetics and Pharmacodynamics Study of PALI-2108 in Healthy Volunteers and Open-Label Study of a Patient Cohort with Ulcerative Colitis

Topline Data Expected Q2 2025



Single Ascending Dose (n~40)

- Primary Endpoint
  - Safety and tolerability
- Secondary Endpoints
  - PK including Tmax, Cmax and T1/2

Multiple Ascending Dose (n~32)

- Primary Endpoint
  - Safety and tolerability
- Secondary Endpoints
  - PK including plasma and tissue C SS and colon : plasma ratio

Multiple Dose UC Cohort (n~6)

- Pharmacokinetic Endpoints
  - Plasma, colon tissue, urine, stool including plasma and tissue C SS and colon : plasma ratio
- Pharmacodynamic Endpoints
  - Fecal calpro, calpro epitope, hsCRP, colon tissue PDE4s, cAMP, TLC, and histology

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Clinical Trials: NCT06663605

PALI-2108 Was Safe and Well-Tolerated in Phase 1 Safety Study

Single Ascending Dose (SAD)

- **Doses: 5mg, 15mg, 50mg, 250mg, 450mg**
- Safe and well-tolerated with no SAEs, no lab or EKG TEAEs
- Few minor TEAEs at the highest dose (450mg, >10x therapeutic dose)

Multiple Ascending Dose (MAD)

- **15mg BID:** Safe and well-tolerated with no SAEs, lab or EKG TEAEs, and no TEAEs overall
- **30mg BID (titrated):** Safe and well-tolerated with no SAEs, lab or EKG AEs, and one TEAEs (headache)
  - Impressive tolerability despite high PDE4 potency and extended half-life (enabling QD maintenance dosing)
- **30mg BID:** Safe and well-tolerated with no SAEs, lab or EKG AEs, and few minor TEAEs in getting to SS
  - TEAEs resolved at SS, confirming tachyphylaxis and the potential for a titration schedule
- **50mg BID:** Highest MAD dose evaluated
  - No SAEs, no lab or EKG AEs, and few minor reversible AEs
  - Single grade 3 AE with voluntary withdrawal

Multiple Dosing (MD) in UC Patients

- PDE4 inhibitors typically require titration due to tachyphylaxis
- **30mg BID (titrated):** Safe and well-tolerated with no SAEs, lab or EKG AEs
  - Single minor TEAE at 25mg resolved, and 30mg at SS was well tolerated

Targeted Approach:

✓PALI-2108 is **potent PDE4 B/D specific inhibitor**
~10x potency of Union's Orimilast (AD & Psoriasis)

- ✓ ~20x potency of Amgen's Apremilast (Psoriasis & PA)
- ✓ ~20x potency of Boehringer's PDE4B (2x ongoing Ph3 studies in IPF; next anti-fibrotic blockbuster)

✓PALI-2108 **targets the terminal ileum and colon**

- ✓ Orimilast PDE4 B/D MR targets systemic distribution (30mg BID)
- ✓ Apremilast Pan-PDE4 IR targets systemic distribution (30mg BID)
- ✓ Boehringer's PDE4B targets the lung tissues (18mg BID)

PALI-2108 Preliminary Findings:

- ✓ Safe & well-tolerated with exceptional tolerability given high potency at repeat dosing of 15mg & 30mg BID
- ✓ Potential to be the safest and best tolerated oral PDE4 inhibitor
- ✓ PK targeting ileum and colon enables treatment of Ulcerative Colitis and Crohn's Disease

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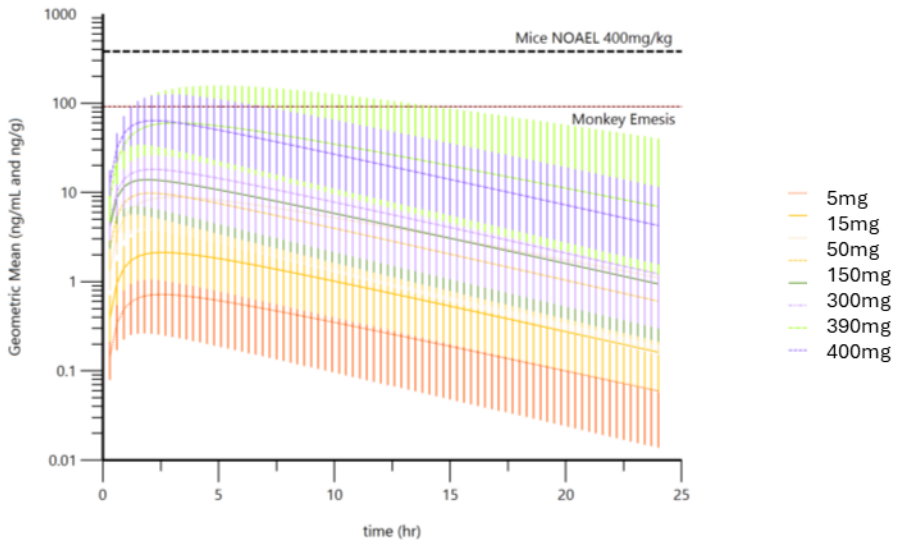
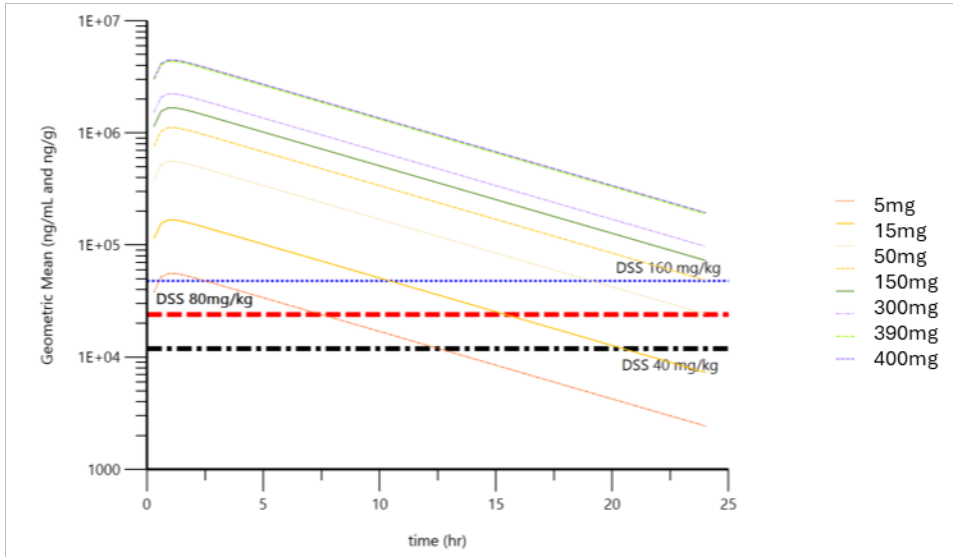
Drafted on Preliminary Blinded Data

PALI-2108 PK Modeling Demonstrates Dosing Relationship to Therapeutic Window

Plasma active PDE4 in healthy volunteers and UC patients



Colon tissue active PDE4 in healthy volunteers and UC patients



Preliminary Observations from MAD and Therapeutic Window (PopPK Dose Simulations):

- ✓ **15mg dose**: Achieves mean concentrations above highest colon tissue levels in DSS efficacy studies for 12 h supporting BID dosing.
- ✓ **50mg dose**: Achieves mean concentrations above the above highest colon tissue levels in DSS efficacy studies for 24 hours even supporting QD dosing.
- ✓ **PopPK simulations:** Suggests a target therapeutic window of **15-30mg BID or 50mg QD**, with both low (15mg) and high (30mg) BID doses sufficient to achieve effective colon tissue concentrations, supporting PDE4 inhibition, increased cAMP and TNF-α suppression.

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Drafted on Preliminary Blinded Data

PALI-2108

A Precision Medicine Approach to IBD

From Trial-and-Error to Precision Medicine

Current Treatment Challenges

Non-targeted approaches with unpredictable responses

Lack of personalization leads to suboptimal outcomes

Effective treatment delayed

The PDE4 CDx Solution

Molecular profiling identifies likely responders

Personalized treatment selection

Better outcomes with optimized therapy

Transformative Impact

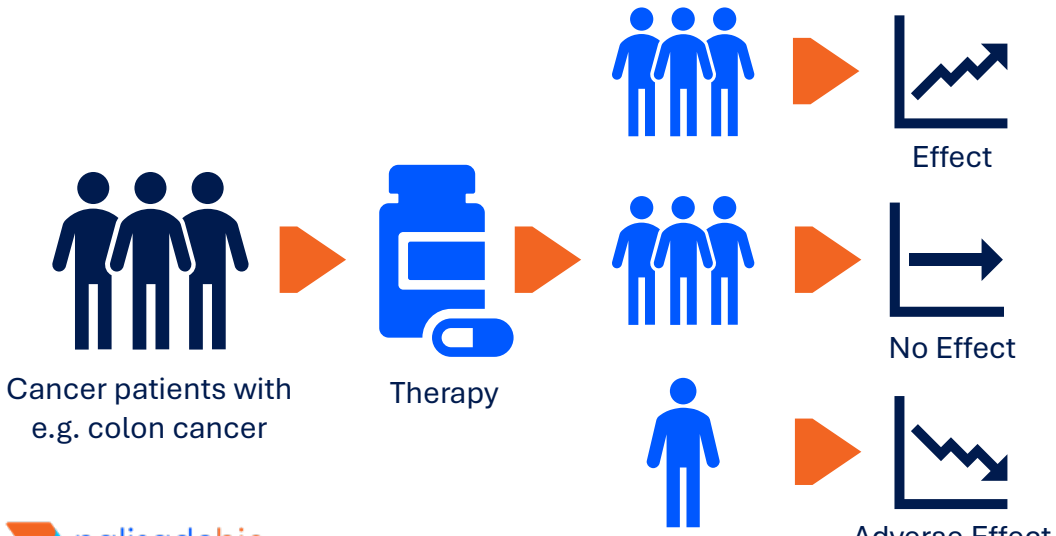
Parallel to HER2 CDx success in breast cancer

Shift from broad immunosuppression to targeted PDE4 inhibition

Faster and more effective treatment pathway

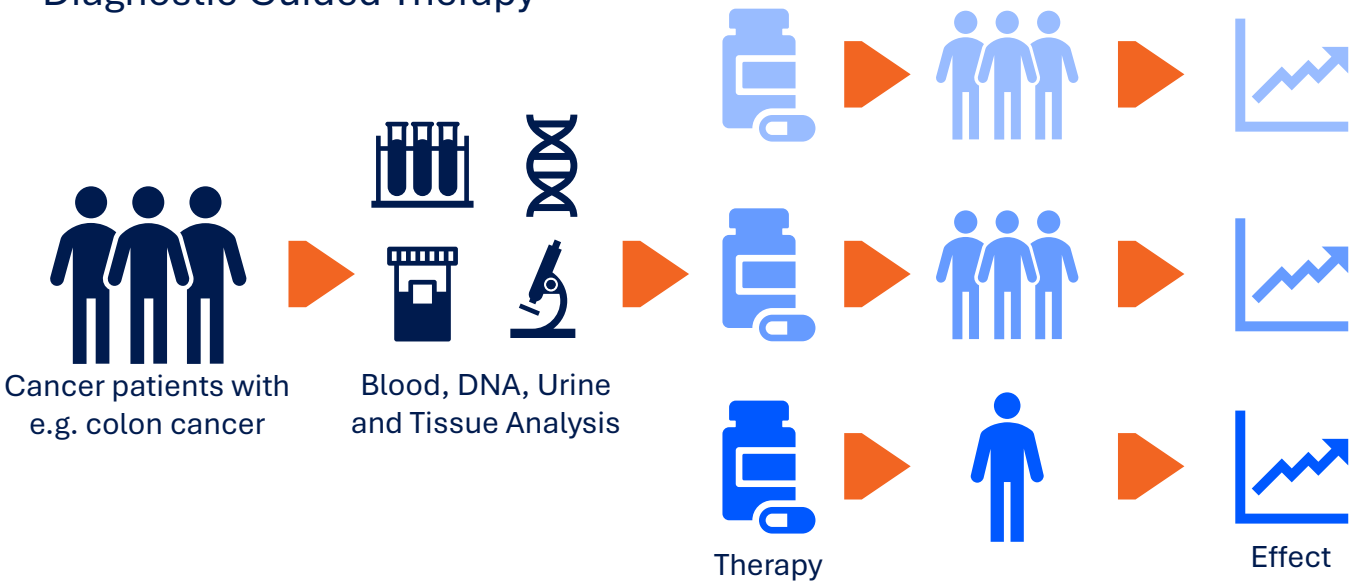
Traditional Medicine

Trial and Error Based on Algorithm



Precision Medicine

Diagnostic Guided Therapy



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Precision Medicine-Based Approach

Machine Learning Technology for Patient Selection

Targeting Patients with Elevated PDE4 Activity (PDE4-Related Biomarkers) to Potentially Enhance Responder Population

Process

Identify Markers of Colitis → **RNAseq DiffExp** → **Top Ranked Genes (U or D)** → **Top Ranked in Multiple Studies** → **Relation with PDE4**

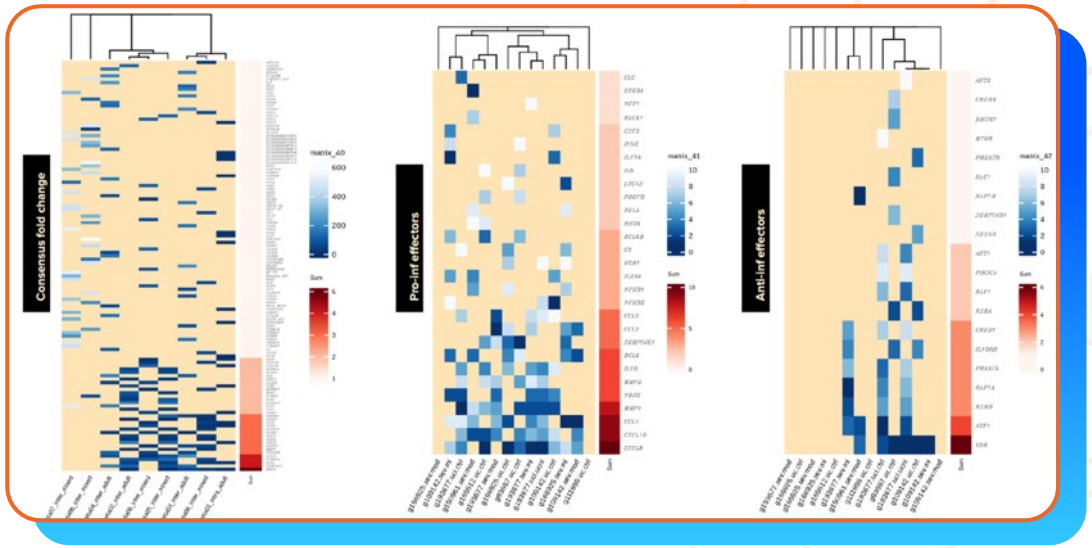
Output

Identified pool of PDE4-effector genes predictive of potential patient response to PDE4 inhibitor

Genes ranked by weights were selected from meta-analysis, pro-inflammatory and anti-inflammatory

Generate a weighted sum DAS score

Meta-Analysis



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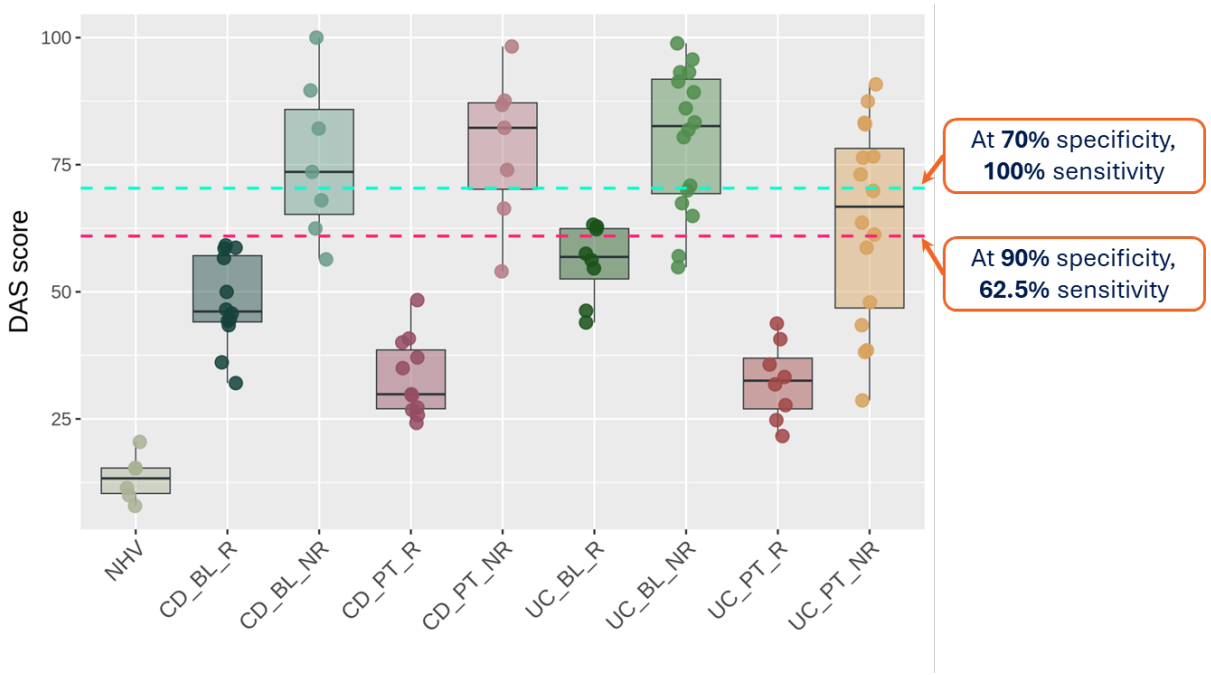
Precision Medicine Test with PDE4-Related Biomarkers Could Be a Breakthrough for IBD Treatment



Treatment in this dataset was with Infliximab (anti-TNF). PDE4 inhibitors act at a higher level on the inflammatory cascade and our DAS score was selected based on PDE4 inhibitor effectors and thus designed to perform specifically for the selection of PDE4 responders.

Ability to Aid Clinicians in Identifying Patients Who May Better Respond to PALI-2108

Elevated PDE4B-Related Biomarkers: Consistently observed in adult patients in >1600 patients and ~10 studies.

- ✓ Approach featuring five PDE4B-related biomarkers
- ✓ Shown superior performance compared to benchmark
- ✓ Tailored for PDE4 inhibition, providing a targeted solution for enhancing therapeutic outcomes
- ✓ PCR-based assays aimed at potential FDA approval may ensure precision in patient targeting

Development: Used intervention data sets to develop PCR-based assays with RNAseq to standardize TPM values and improve qPCR Ct value correlations, ensuring precise and effective patient targeting.

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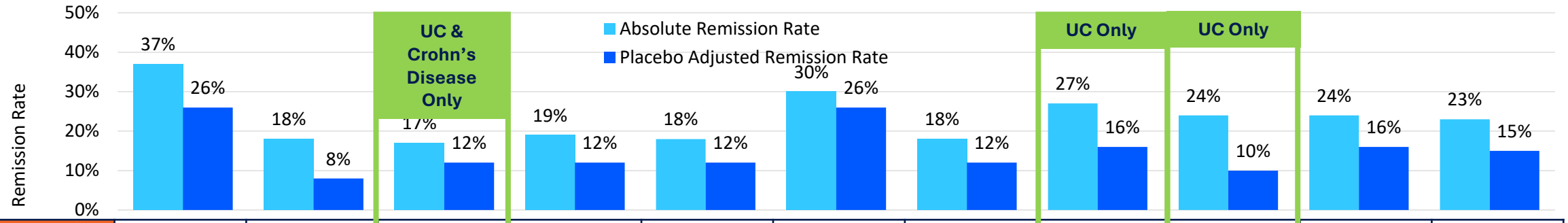
PALI-2108
Ulcerative Colitis

Current Therapies for UC Limited Efficacy with Significant Safety Concerns

Though the number of available therapeutics for moderate-to-severe patients is growing, the placebo-adjusted remission rate remains low, ~10-20%, and many therapies have poor safety profiles

Absolute and Placebo-Adjusted Remission Rates at Completion of Induction (8 to 12 Weeks)



Therapy	Remicade® INFLIXIMAB	HUMIRA® adalimumab	Entyvio® vedolizumab	Stelara® (ustekinumab)	XELJANZ® (tofacitinib citrate)	RINVOQ® upadacitinib	ZEPOSIA® (ozanimod)	Velsipity™ (etrasimod)	omvoh™ (mirikizumab-mrkz)	Skyrizi® risankizumab-rzaa	Tremfya® (guselkumab)
WAC	**$30K**	**$108K**	**$56K**	**$181K**	**$70K**	**$78K**	**$108K**	**$75K**	**$67K**	**$63K**	**$14K**
Target	TNF-α	TNF-α	α4β7	IL-12/23	JAK	JAK	S1PR	S1PR	IL-23p19	IL-23	IL-23
RoA	IV	SC	IV	IV	Oral	Oral	Oral	Oral	IV/SC	IV/SC	IV/SC
Indication	Moderate-to-severe UC refractory to conventional therapy	Moderate-to-severe UC refractory to immuno-suppressants	Moderate-to-severe UC	Moderate-to-severe UC	Moderate-to-severe UC refractory to TNF inhibitors	Moderate-to-severe UC refractory to TNF inhibitors	Moderate-to-severe UC	Moderate-to-severe UC	Moderate-to-severe UC	Moderate-to-severe UC	Moderate-to-severe UC, Moderate-to-severe CD
Adverse Events	**Black box warning:** increased risk of serious infection	**Black box warning:** increased risk of serious infection	Risk of progressive multifocal leukoencephal-opathy	Headache, risk of infection, including of the upper respiratory tract (URT)	**Black box warning:** increased risk of serious infection and adverse CV events	**Black box warning:** increased risk of adverse CV events	Back pain, elevated liver enzymes, risk of infection, including of the URTI and urinary tract	Elevated liver function test and headache	Headache, risk of infection, including of the URT	Headache, risk of infection including of the URT, joint pain, fever, elevated liver enzymes	Risk of infections, including URT tuberculosis (TB), hepatoxicity (liver tox), headache, abdominal pain

Tx's = treatments, SC = subcutaneous, IV = intravenous, Bio = biologic, TNF = tumor necrosis factor, JAK = janus kinase, S1PR = sphingosine-1-phosphate; SAE: serious adverse event; CV: cardiovascular, *based on clinical remission at one year, **at 31 weeks, ^45% 180mg and 41% 360mg; Sources: Back Bay analysis and prior work, Morgan Stanley 5May2023, Stifel 16Mar2023, Inflamm Bowel Dis. 2023 Oct 3;29(10):1633-1647, Inflamm Bowel Dis. 2018 Oct 12;24(11):2461-2467, J Crohns Colitis. 2021 Nov 8;15(11):1846-1851, company press releases for Rinvoq and Zeposia,

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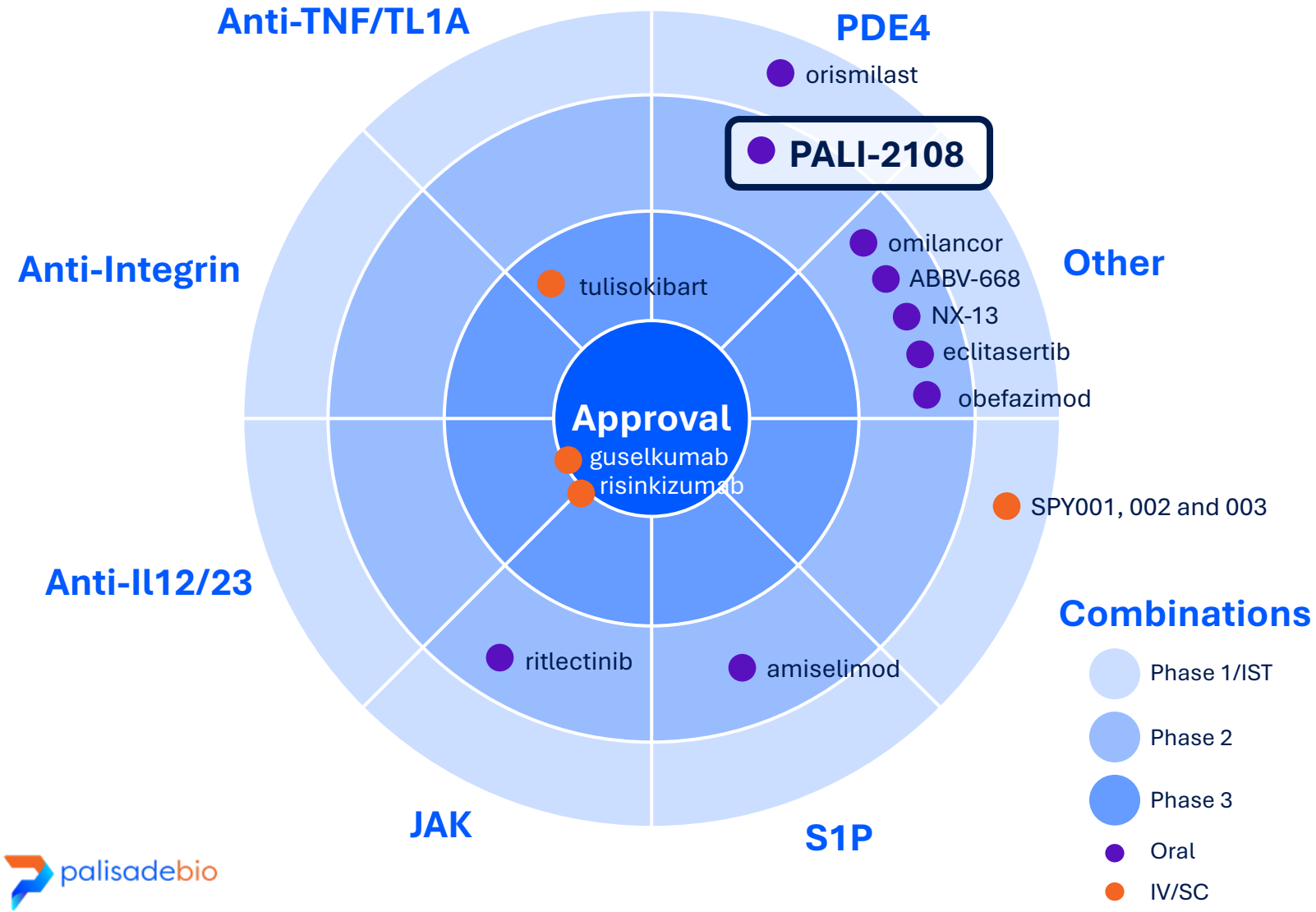
Potential for Best-in-Class and First-in-Class

Candidate			Locally Bioactivated Targeting	Oral Admin Delivery	Extended Release PK Efficacy	Potential for Moderate-Severe UC Efficacy	Potential Precision Medicine Approach Efficacy	Min. Systemic Exposure Safety	No First-Dose Monitoring Safety	No Blackbox warning Safety
PALI-2108	Oral (term ileum and colon-targeted)		✓	✓	✓	✓	✓	✓	✓	✓
Apremilast/Oral ismilast	Oral (systemic)	Stalled or Stopped	✗	✓	✗	✗	✗	✗	✓	✓
Mesalamine / Budesonide	Oral (colon-targeted)	Generic	✓	✓	✓	✗	✗	✓	✓	✓
JAK Inhibitors	Oral (systemic)	RINVOQ upadacitinib XELJANZ (tofacitinib citrate)	✗	✓	✗	✓	✗	✗	✓	✗
S1P Modulators	Oral (systemic)	ZEPOSIA (ozanimod) Velsipity (etrasimod)	✗	✓	✗	✓	✗	✗	✗	✓
Anti-TNF	Injection (SC)	HUMIRA adalimumab Remicade INFLIXIMAB	✗	✗	✓	✓	✗	✗	✓	✓
Anti-IL-23	Injection (IV/SC)	omvoh (mirikizumab-mrkz) Tremfya (guselkumab) Skyrizi risankizumab-rzaa Stelara (ustekinumab)	✗	✗	✓	✓	✗	✗	✓	✗

PALI-2108: Potential for First-in-Class and Best-in-Class in Ulcerative Colitis



Strong Preference for Oral Therapies

- Oral medications patient preference and driving market growth
- Robust oral therapy pipeline with multiple acquisitions for early phase this year
- Novel therapies being explored: RIPK1, JAK/TEC, NLRX1

PDE4 is a Validated Target in UC

- Aprimilast POC with ~31% Clinical Remission (p=0.01) and Orimilast ~33% Clinical Remission despite AEs
- Current formulations limited by narrow therapeutic window
- PALI-2108 is the ONLY colon-targeted PDE4 for UC

Competition from Biologics Unlikely to Disrupt

- Late-stage antibodies unlikely to disrupt current treatment paradigm
- Early-stage antibody combinations face significant hurdles:
  - Unproven safety profile
  - Complex development pathway
  - Higher cost burden

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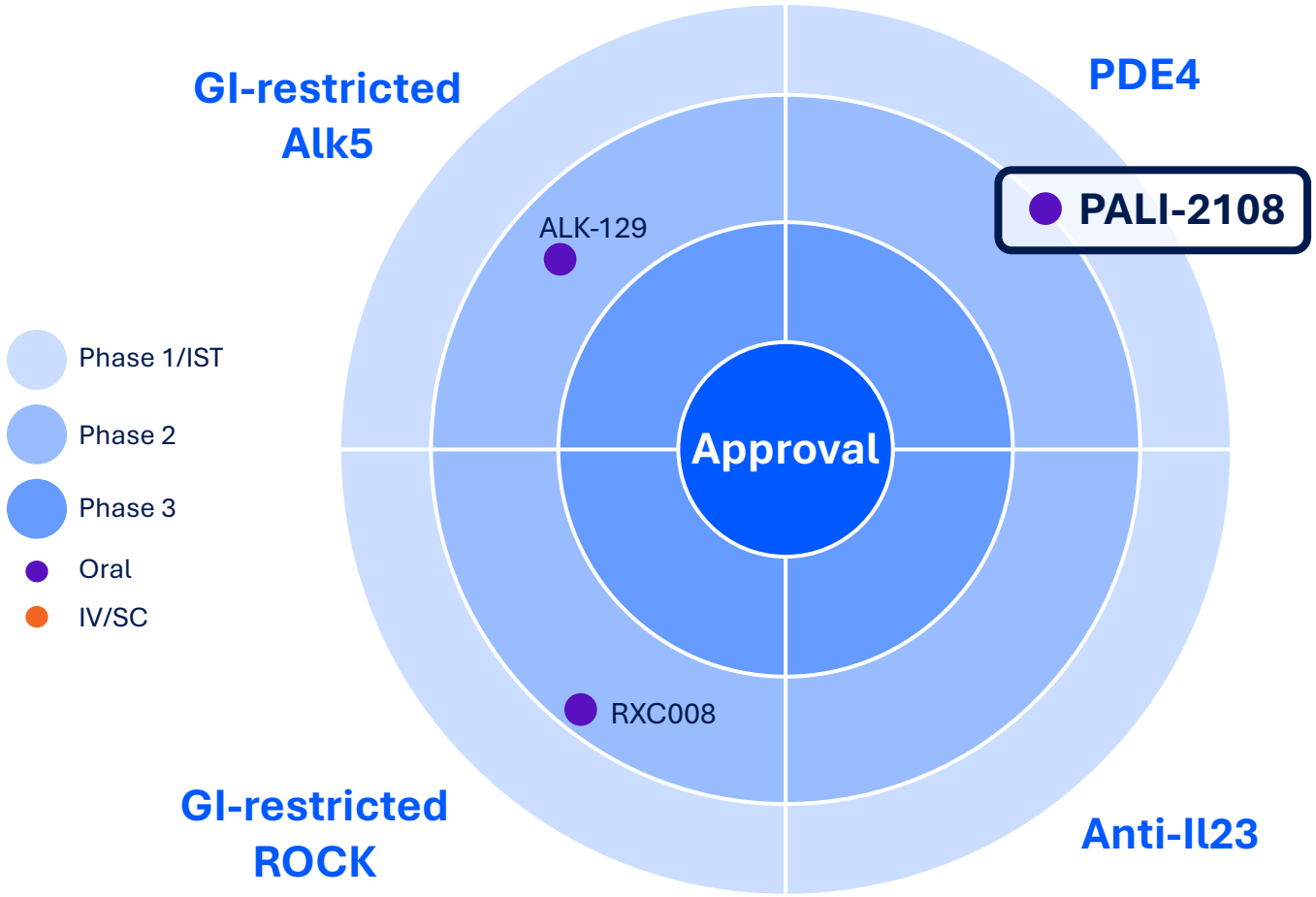
PALI-2108
Fibrostenotic Crohn's Disease (FSCD)

Opportunity to Be First and Best-in-Class and ONLY Anti-Inflammatory and Anti-Fibrotic in Development for Fibrostenotic Crohn's Disease (FSCD)

Candidate			Potential for Fibrostenotic CD Efficacy	Locally Acting Targeting	Oral Admin Delivery	Extended Release PK Efficacy	Commercially Proven Anti-Inflammatory Efficacy	Commercially Proven Anti-Fibrotic Efficacy	Min. Systemic Exposure Safety
PALI-2108	Oral (term ileum and colon-targeted)	palisadebio	✓	✓	✓	✓	✓	✓	✓
RXC008	Oral (GI-restricted)	Redx	✓	✓	✓	✗	✗	✗	✓
ALK-129	Oral (GI-restricted)	AgomAb Therapeutics	✓	✓	✓	✗	✗	✗	✓

PALI-2108: ONLY Anti-Inflammatory AND Anti-Fibrotic in Development for Fibrostenotic Crohn's Disease

Strong Positioning to Be First-in-Class and Best-in-Class



Preference for Oral Therapies on SOC

- Orals are clear patient preference

Anti-fibrotic drugs will be added to SOC

- Anti-fibrotic drugs to be added to stable SOC treatment for prevention of stricture, obstruction and surgery in patients with ileocecal strictures

Competition from GI-restricted Candidates

- GI-restricted (due to toxicity) ALK5 in development by Agomab and in Ph2.
- GI-restricted pan ROCK (due to toxicity) in development by Redx and preparing for Ph2.
- **PALI-2108 has significant differentiation and advantage as ONLY anti-inflammatory AND anti-fibrotic in development.**

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Corporate Overview

Capitalization

Capitalization (As of Dec. 31, 2024)	Common Stock Equivalents
Common Stock	2,768,646
Warrants (WAEP $6.49)[1]	4,718,213
Pre-Funded Warrants (WAEP $0.0001)	2,027,000
Stock Options (WAEP $166.48)	50,674
PSUs	2,952
Preferred Stock[2]	8
Total Fully Diluted	9,567,493

$9.8M

Cash

As of December 31, 2024

1. 6,748 warrants are subject to price reset provisions.
2. 8 common shares issuable upon conversion of 200,000 Series A Convertible Preferred Stock.

Program Team

JD Finley, MT
CEO

Mitch Jones, MD, PhD
CMO

Joerg Heyer, PhD
Head of Translational Science and Medicine

Adarsh Patel, MS, MBA
Assoc. Director, Technical Operations

Christophe Mellon, PhD
CMC & Medicinal Chemistry

Jon Daniels, PhD
Safety & Tox & Reg (Consultant)

Patrick Colin, B. Pharm, PhD
Clinical Dev/Ops (Consultant)

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Clinical Advisory Board

Bruce Sands MD, MS
Dr. Burrill B. Crohn Professor of Medicine, Icahn School of Medicine at Mount Sinai and System Chief, Division of Gastroenterology, Mount Sinai Health System

Icahn School of Medicine at Mount Sinai

Florian Rieder, MD
Associate Staff in the Department of Gastroenterology, Hepatology and Nutrition, as well as an Investigator in the Department of Pathobiology at the Cleveland Clinic

Cleveland Clinic

Brian Feagan, MD, FRCPC
Professor of Medicine at the Schulich School of Medicine & Dentistry at the University of Western Ontario, gastroenterologist at London Health Sciences Centre in Ontario, Canada.

Schulich MEDICINE & DENTISTRY

Why PALI, Why Now

✓ First & Only PDE4 Inhibitor for UC & FSCD

Only PDE4 inhibitor targeting the terminal ileum and colon for Ulcerative Colitis (UC) and Fibrostenotic Crohn's Disease (FSCD), addressing significant unmet medical needs in both indications.

✓ Near-Term Clinical Milestones

Multiple near-term clinical milestones and opportunities for data, including Phase 1b/2a trials in UC and FSCD, with data expected in the next 12-18 months, offering potential for major value inflection.

✓ Improved Efficacy & Tolerability

Novel prodrug approach designed to enhance efficacy and tolerability by targeting local PDE4 B/D inhibition, minimizing systemic exposure, and reducing the potential for common adverse effects.

✓ Precision Medicine for UC Patient Selection

Precision medicine approach utilizing a machine learning-driven CDx test to identify UC responders, optimizing patient selection and improving treatment outcomes.

✓ First-in-Class FSCD Therapy

First potential approval for treating FSCD, with the only dual-action anti-inflammatory and anti-fibrotic candidate currently in development for this indication. Commercial successes and ongoing Phase 3 programs provide significant risk reduction for PDE4 as a potent anti-inflammatory and anti-fibrotic target.

✓ Oral Dosing Advantage

Oral formulation preferred by both patients, improving compliance, and clinicians, improving marketability, and supporting the development of future combination therapies.

✓ De-Risked Investment Opportunity

Clinically de-risked target, with significant differentiation, addressing unmet medical needs in exciting indications, a strong regulatory pathway, and clear near-term milestones, reducing investment risk.

NASDAQ: PALI
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Next-Generation Precision Therapies for Immune, Inflammatory and Fibrotic Diseases