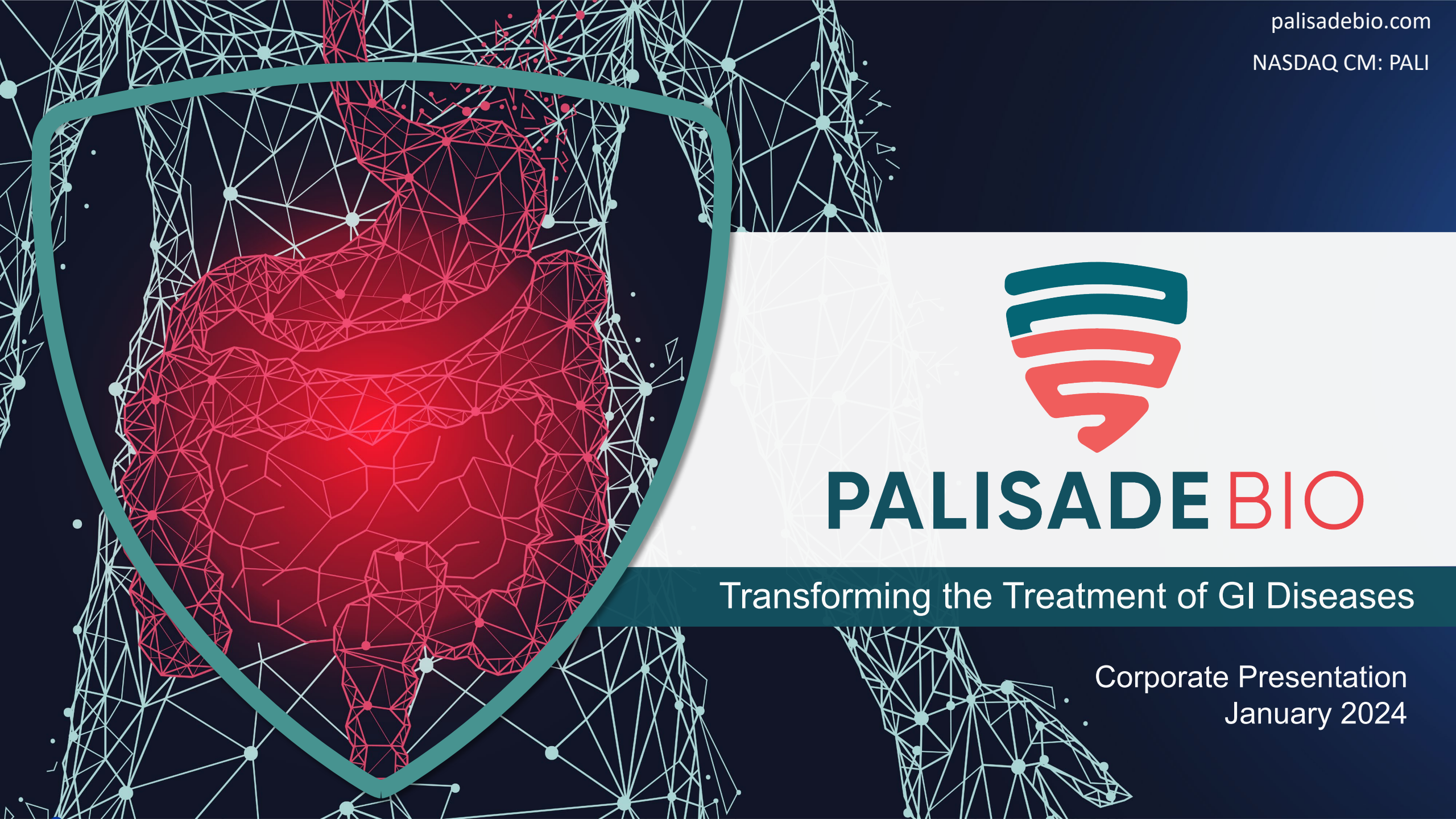
palisadebio.com

NASDAQ CM: PALI



PALISADE BIO

Transforming the Treatment of GI Diseases

Corporate Presentation
January 2024

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 commence human clinical trials of PALI-2018, the potential for PALI-2108 to transform the current standard of care, strategy, potential of PALI-2018 to be covered by a patient's pharmacy benefit, 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 anticipated 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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Investment Highlights

Developing novel therapeutics for serious chronic gastrointestinal diseases, with a targeted approach that transforms the treatment landscape

KEY HIGHLIGHTS

Recent transaction jumpstarts into high-value IBD market

Clinically validated PDE4 target utilized by multiple Big Pharma players

Rapidly advancing towards Phase 1 initiation in 2024 for treatment of Ulcerative Colitis

Sufficient capital to execute on strategy and achieve significant milestones into 2025

Our Oral IBD Development Pipeline

Oral Prodrug Therapies that Act Locally at Site of Disease

Program	Discovery	IND/CTA-Enabling	Phase 1	Phase 2	Phase 3	Highlights
PALI-2108	Ulcerative Colitis					Ongoing IND/CTA-enabling tox studies Rapidly advancing towards IND/CTA filing in 2024
PALI-1908	Fibro Stenotic Crohn's Disease					Lead optimization complete Significant overlap with PALI-2108 IND/CTA filing in 2024

Platform Technology Provides Opportunity to Grow Pipeline Organically and Target Additional High-Value Gastrointestinal Diseases

Strategic Shift in Prioritization to Newly Licensed Assets for Treatment of Inflammatory Bowel Diseases

giiant pharma

We entered into an exclusive worldwide licensing agreement to develop and commercialize proprietary oral prodrug therapies that act locally targeting multi-billion-dollar IBD market

Company Secured Favorable Terms:

100% Exclusive Worldwide Rights	**Milestones Starting at Phase 1**	**Locally Acting PDE4 Inhibitor Developed by Merck Scientists**	**Prodrug Formulations to Locally Deliver the Active Ingredient**

Big Pharma is Active in IBD and Spending Big Dollars for Earlier Stage Programs

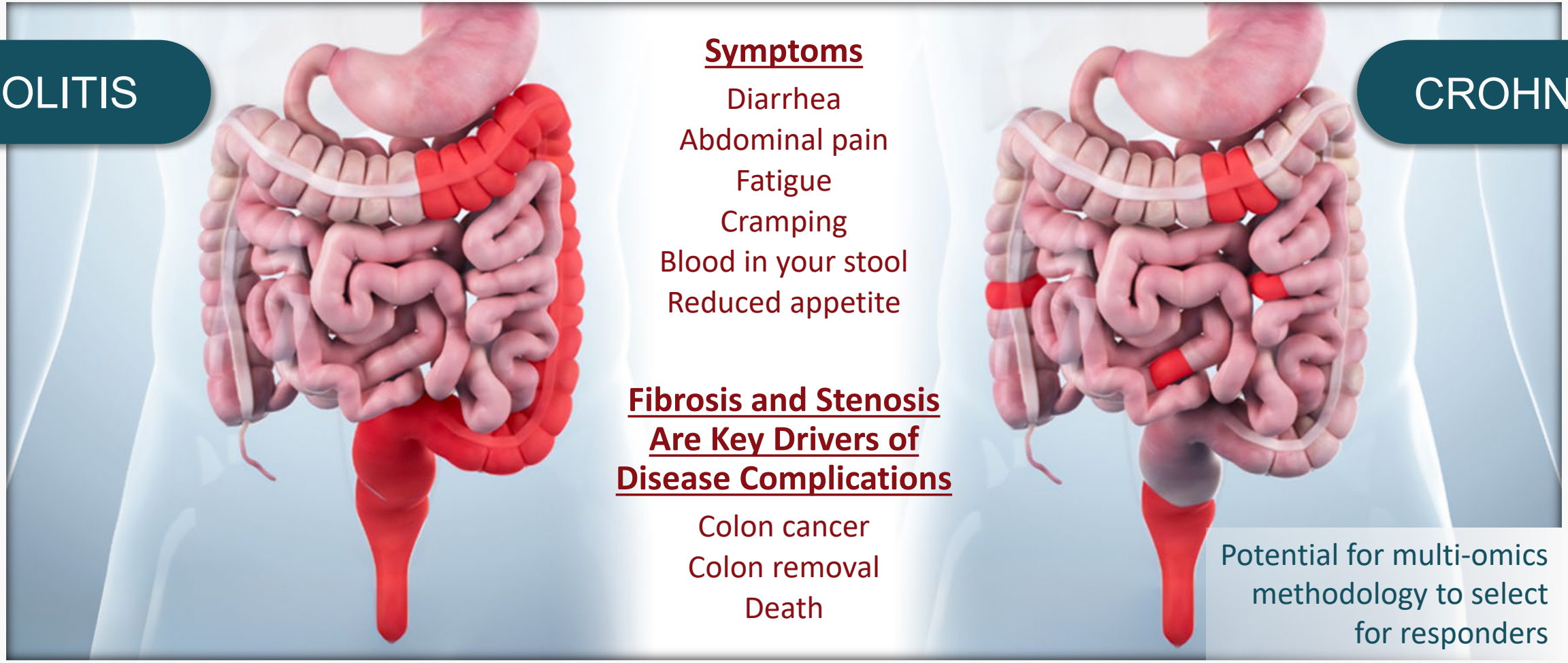
Company	Acquirer	Date	Lead Asset	Phase at Deal	MOA	Upfront	Total Deal	Royalties	Current Status
Telavant	Roche	Oct 2023	RVT-3101	Phase 3 Ready	Anti-TL1A Mab	**$7.1 Billion**	**$7.2 Billion**	NA	Phase 3 Prep
teva	sanofi	Oct 2023	TEV'574	Phase 2b	Anti-TL1A MAb	**$500 Million**	**$1.5 Billion**	50/50 JV	Active
Recludix Pharma	sanofi	Jul 2023	Pre-IND Candidates	Preclinical	STAT6 Inhibitor (IL-4, IL-13)	**$125 Million**	**$1.3 Billion**	Potential for 50/50	Active
Prometheus Biosciences	MERCK	Apr 2023	PRA023	Phase 2	Anti-TL1A Mab	**$10.8 Billion**	**$10.8 Billion**	NA	Phase 3 Prep
ARENA PHARMACEUTICALS	Pfizer	Dec 2021	Etrasimod	Phase 3 Ready	Oral S1P	**$6.7 Billion**	**$6.7 Billion**	NA	Approved (Oct 2023)
Protagonist Therapeutics	Johnson&Johnson	May 2017	JNJ-2113 (PN-235)	Preclinical	Oral IL-23 peptide	**$50 Million**	**$990 Million**	6-10%	Phase 2/3 Ongoing

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

COLITIS

CROHN'S



Symptoms

Diarrhea
Abdominal pain
Fatigue
Cramping
Blood in your stool
Reduced appetite

Fibrosis and Stenosis Are Key Drivers of Disease Complications

Colon cancer
Colon removal
Death

Potential for multi-omics methodology to select for responders

Source: Mayo Foundation for Medical Education and Research. (2022, September 3). *Inflammatory bowel disease (IBD)*. Mayo Clinic. https://www.mayoclinic.org/diseases-conditions/inflammatory-bowel-disease/symptoms-causes/syc-20353315

IBD is a Large and Growing Market

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

Novel Therapeutics Demonstrating Safety and Efficacy are Likely to Gain Market Share

Palisade Bio Has the Only PDE4 Under Development for UC and CD

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

The IBD Patient Journey

Patients and clinicians search out the most effective therapies with novel mechanism that are not systemically distributed to reduce side effects

> ***~10-35%** of Patients Switch Due to Lack of Efficacy Typically Three to Six Months Following Treatment Indication*
>
> *Only **50%** of Patients Achieve Remission Within a Year; Often Requiring Several Different Treatments*

Source: Crohn's & Colitis Foundation of America, The Facts About Inflammatory Bowel Diseases

ULCERATIVE COLITIS

~40-50%	Of patients have moderate-to-severely active disease
70%	Of patients with active disease will have active disease the next year
30%	Of patients in remission will have active disease the next year
40%	Of patients with long-lasting UC and extensive disease require colectomies

CROHN'S DISEASE

52%	Have uncontrolled active disease
70%	Of mod-severe patients cannot sustain remission on the same drug "patient churn"
15%	Require colectomies
~20-30%	Require surgery within 10 years of diagnosis

Current Standard-of-Care Therapies Have Limited Effectiveness

No Standard Regimen for Managing All IBD Patients
The Approach to Treatment Needs to Be Tailored for the Individual

CURRENT TREATMENT APPROACH

5-ASA is generally first line for ulcerative colitis but not as effective in Crohn's Disease

Corticosteroids: not for long-term use due to significant side effects

Immune-modulating therapies are considered second line for moderate-to-severely active disease

FACTORS THAT DETERMINE TREATMENT APPROACH

Disease severity

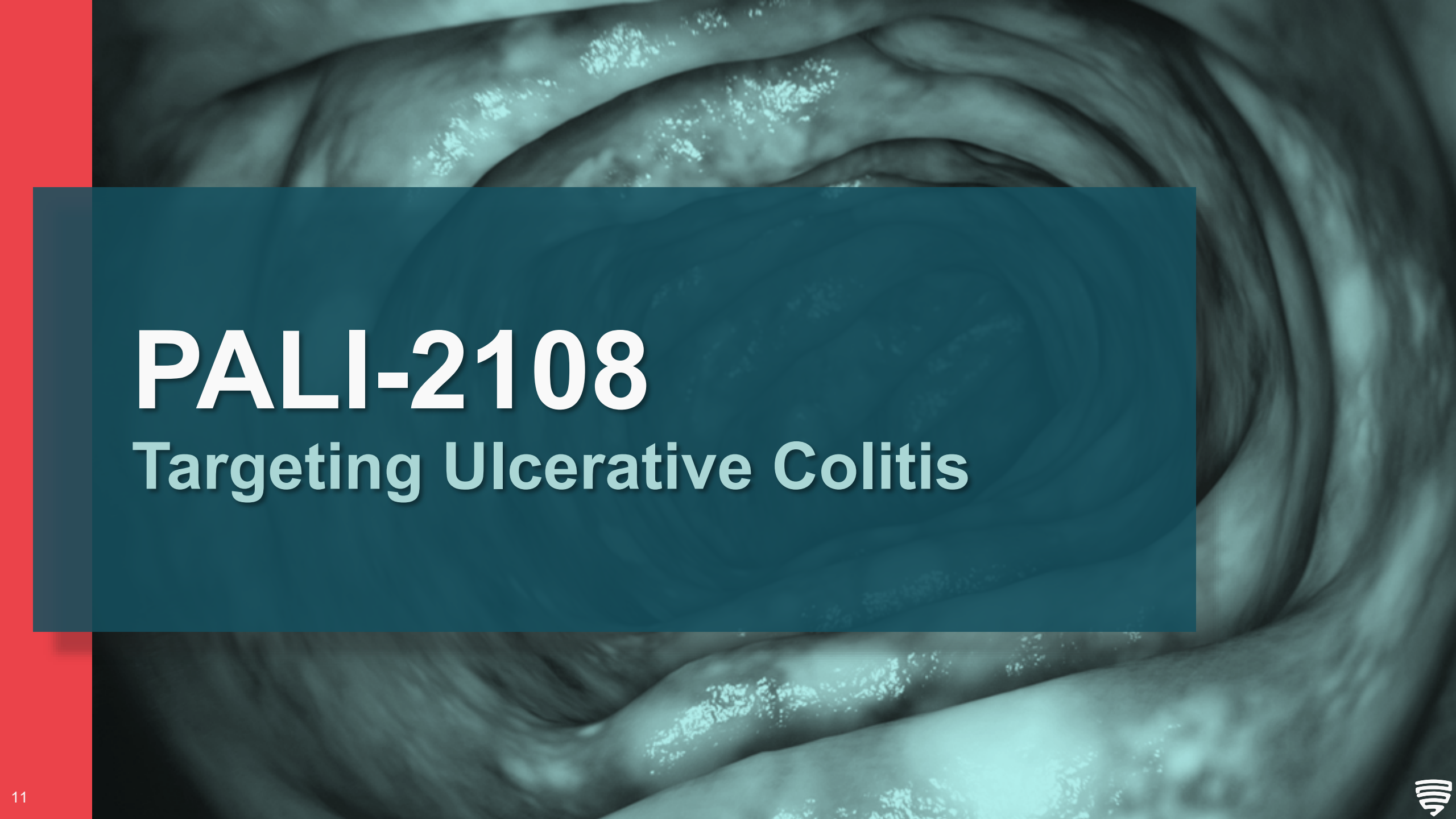
Anatomic location of disease

Previous response to medication

Side effects of medication

Comorbidities

Average **Clinical Remission Rate Only 16%** of Treated Patients After Induction Therapy


PALI-2108
Targeting Ulcerative Colitis

Ulcerative Colitis Competitive Landscape

Most Effective Therapies Have Black Box Warning, New Therapies Are Not as Effective

Drug	Company	Placebo-Adjusted Clinical Remission	Overall Remission Rate	Indication	FDA Approval	Route of Administration	Safety Considerations
Remicade® INFLIXIMAB	janssen	24% (ACT1)	38.8% (ACT1)	Moderate-to-severely active UC with inadequate response or intolerance to standard therapies	2005	Injectable	***BLACK BOX WARNING***
RINVOQ® upadacitinib	abbvie	21% (U-ACHIEVE)	26% (U-ACHIEVE)	Moderate-to-severely active UC with inadequate response to (TNF) blockers	2022	Injectable	***BLACK BOX WARNING***
Entyvio® vedolizumab	Takeda	11.5% (GEMINI I)	16.9 (GEMIMI I)	Moderate-to-severely active UC with inadequate response to (TNF) blockers	2014	Injectable	Risk of PML
Skyrizi® risankizumab-rzaa	abbvie	14.1% (INSPIRE)	20.3% (INSPIRE)	Moderate-to-severely active UC with inadequate response to conventional or biologic	2023	Injectable	URTI, headache, fatigue
ZEPOSIA® (ozanimod) 0.92 mg capsules	Bristol Myers Squibb	10.3% (TOUCHSTONE)	16.3% (TOUCHSTONE)	Moderate-to-severely active UC	2021	Oral	URTI, UTI, back pain, liver enzymes
XELJANZ® (tofacitinib)	Pfizer	10.3% (OCTAVE 1)	18.5% (OCTAVE 1)	Moderate-to-severely active UC with inadequate response to (TNF) blockers	2018	Oral	***BLACK BOX WARNING***
HUMIRA® adalimumab	abbvie	9.3% (ULTRA I)	18.5% (ULTRA I)	Moderate-to-severely active UC with inadequate response or intolerance to standard therapies	2012	Injectable	***BLACK BOX WARNING***

Potential Future Ulcerative Colitis Competitive Landscape

UC Market is Expected to Evolve By 2028 with New Therapies

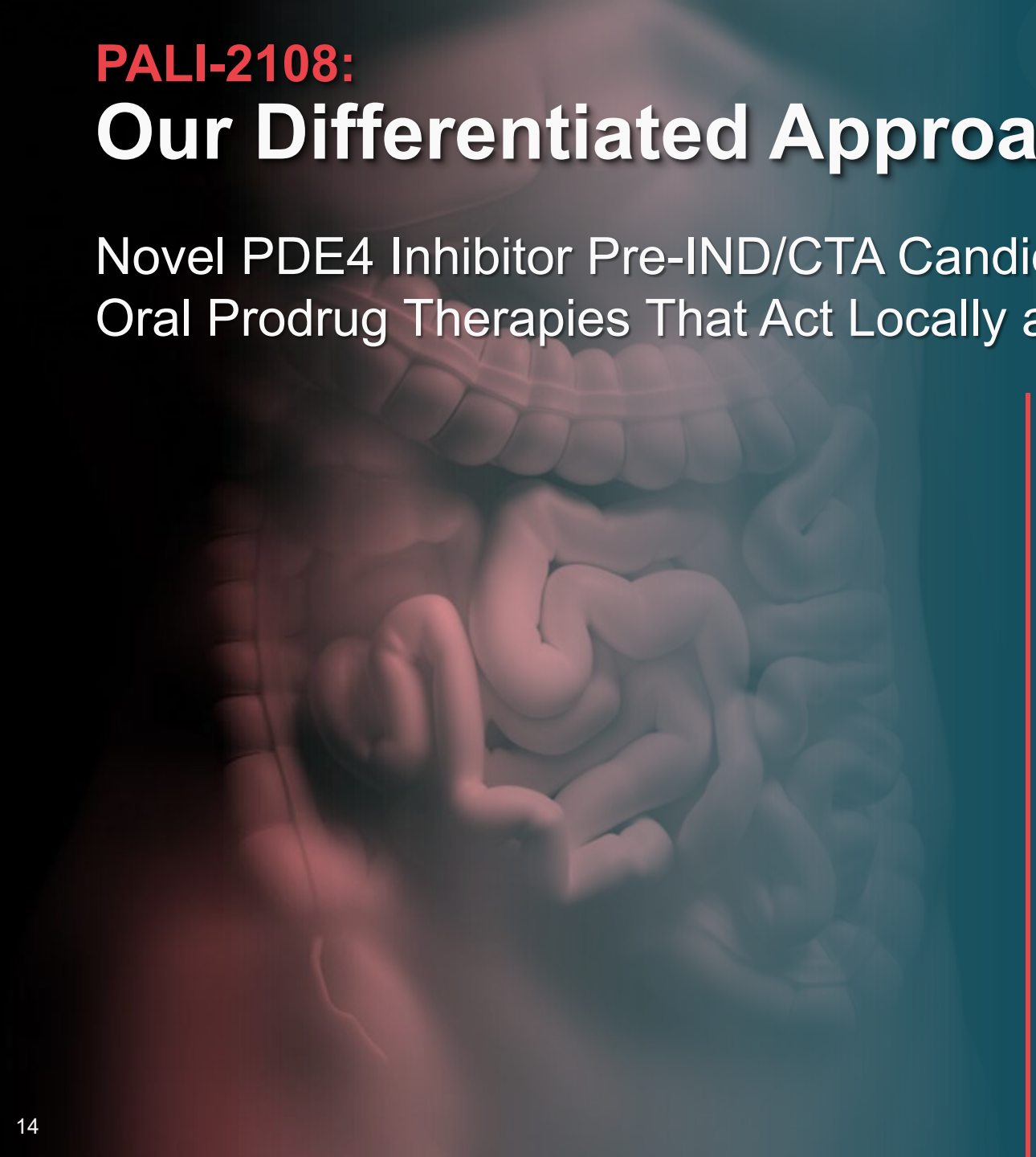
We Believe PALI-2108 Has a Significant Advantage Over Current Projections and has Potential to Take Significant Market Share

Drug	Company	Placebo-Adjusted Clinical Remission	Overall Remission Rate	Indication	FDA Approval	Route of Administration	Safety Considerations
Velsipity™ (etrasimod) tablets	abbvie	11% (ELEVATE UC 12)	26% (ELEVATE UC 12)	Moderate-to-severely active UC	2023	Oral	Elevated LFTs and headache
Tremfya® (guselkumab)	Johnson&Johnson	9.5% (QUASAR 1)	25.7% (QUASAR 1)	Moderate-to-severely active UC	Phase 3	Injectable	URTI, headache, infection
Stelara® (ustekinumab)	Johnson&Johnson	19.8% (UNIFI)	43.8% (UNIFI)	Moderate-to-severely active UC	2022	Injectable	URTI, headache, infection
omvoh™ (mirikizumab-mrkz) 300 mg/15 mL infusion 100 mg/mL injection	Lilly	15% (LUCENT)	24% (LUCENT)	Moderate-to-severely active UC	2023	Injectable	URTI, headache, infection

PALI-2108:

Our Differentiated Approach to Ulcerative Colitis

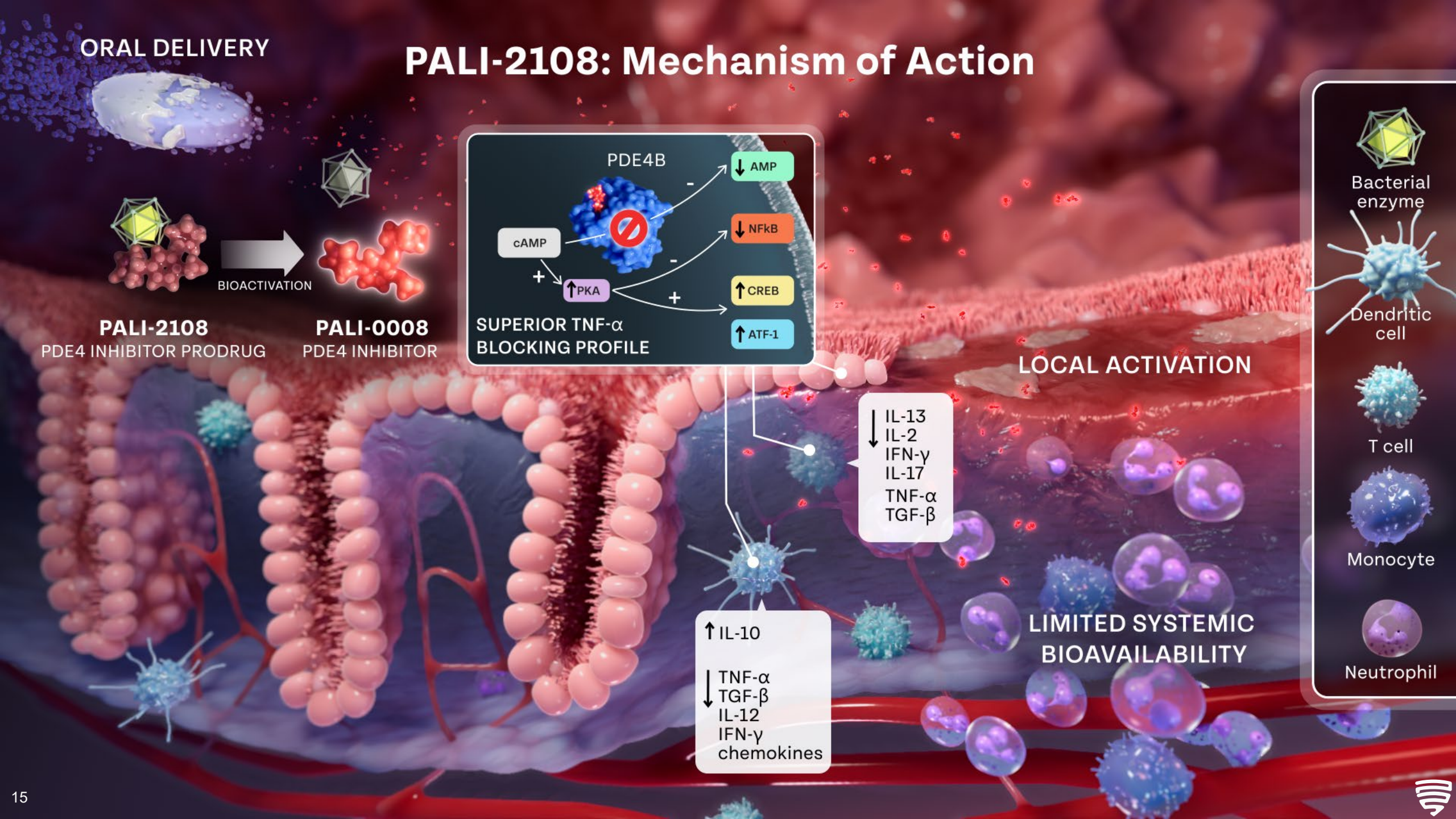
Novel PDE4 Inhibitor Pre-IND/CTA Candidate
Oral Prodrug Therapies That Act Locally at Site of Disease



KEY DIFFERENTIATION

- ✓ Oral Dosing
- ✓ Locally Active
- ✓ Limited Systemic Activity (improved safety)
- ✓ Superior Cytokine Blocking Profile
- ✓ Potential of Breakthrough Clinical Efficacy
- ✓ Potential for Precision Medicine Approach

PALI-2108: Mechanism of Action



PALI-2108 Data Highlights

✓**Exclusively** selective for PDE4 limiting the potential for off-target effects

✓**Isoenzyme inhibition profile** comparable to marketed anti-inflammatory and anti-fibrotic PDE4 inhibitor

✓**20 times more potent** as a TNFα inhibitor than apremilast in human whole blood

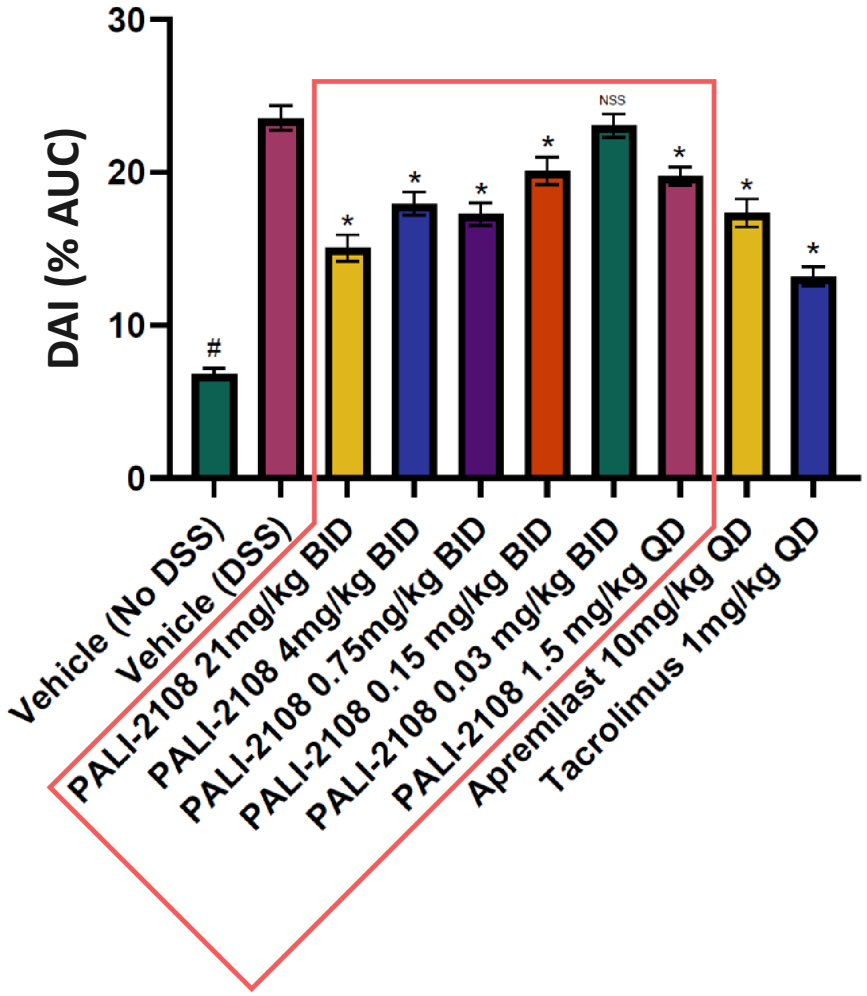
✓**Demonstrated PDE4 target engagement** comparable to apremilast *in vivo*

✓Shown to be **locally bioactivated** in the colon in **human studies**

✓**Preclinical** data demonstrating prodrug significantly **limit systemic drug exposure** and CNS toxicity

✓Shown to be **effective** and demonstrated a **dose response** across multiple preclinical studies

DSS Mouse Proof of Efficacy Study



* Statistically Significant Compared to DSS Vehicle

PDE4 is an Established Dual Acting (Pleiotropic) Anti-Inflammatory and Anti-Fibrotic Target

AstraZeneca

COPD (Roflumilast; AstraZeneca): Anti-fibrotic indications such as chronic obstructive pulmonary disease

AMGEN

Psoriasis and Psoriatic Arthritis (Apremilast; Amgen): Anti-inflammatory indications validated by approved drug Otezla

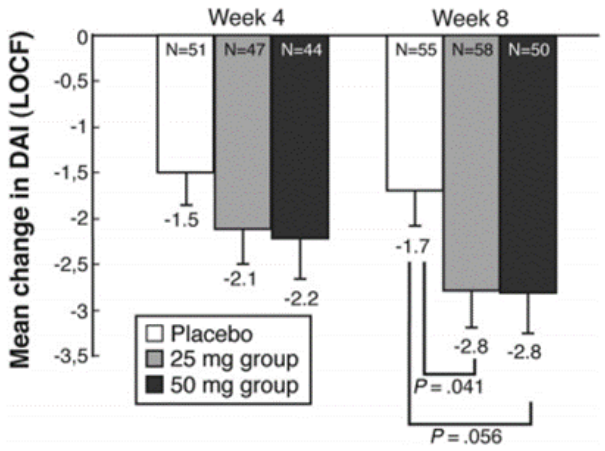
Boehringer Ingelheim

Idiopathic Pulmonary Fibrosis (BI 1015550; Boehringer Ingelheim): Under evaluation in global Phase 3 study (FIBRONEER) for idiopathic pulmonary fibrosis

Demonstrated High Potential for Locally Acting PDE4

Two Placebo-Controlled Randomized Trials Have Been Conducted

Mild-to-Moderate Active UC[1]

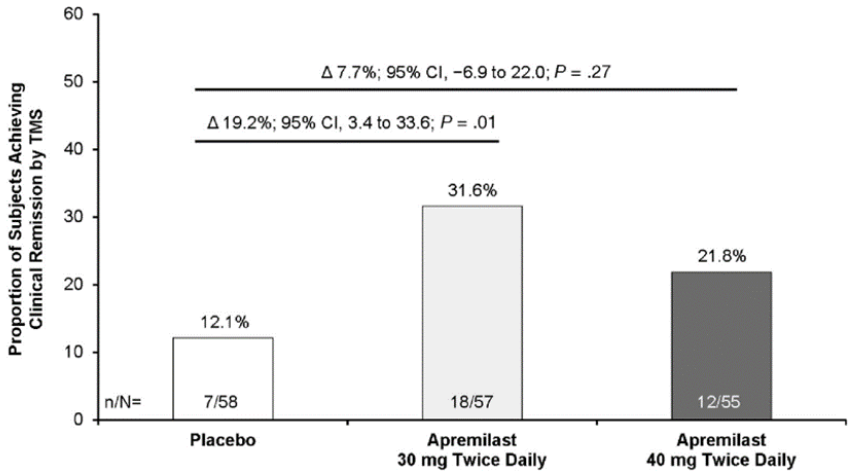


Significant improvement in disease activity index (DAI) at Week 8

Significant improvement in clinical remission rate

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

Moderate-to-Severely Active UC[2]

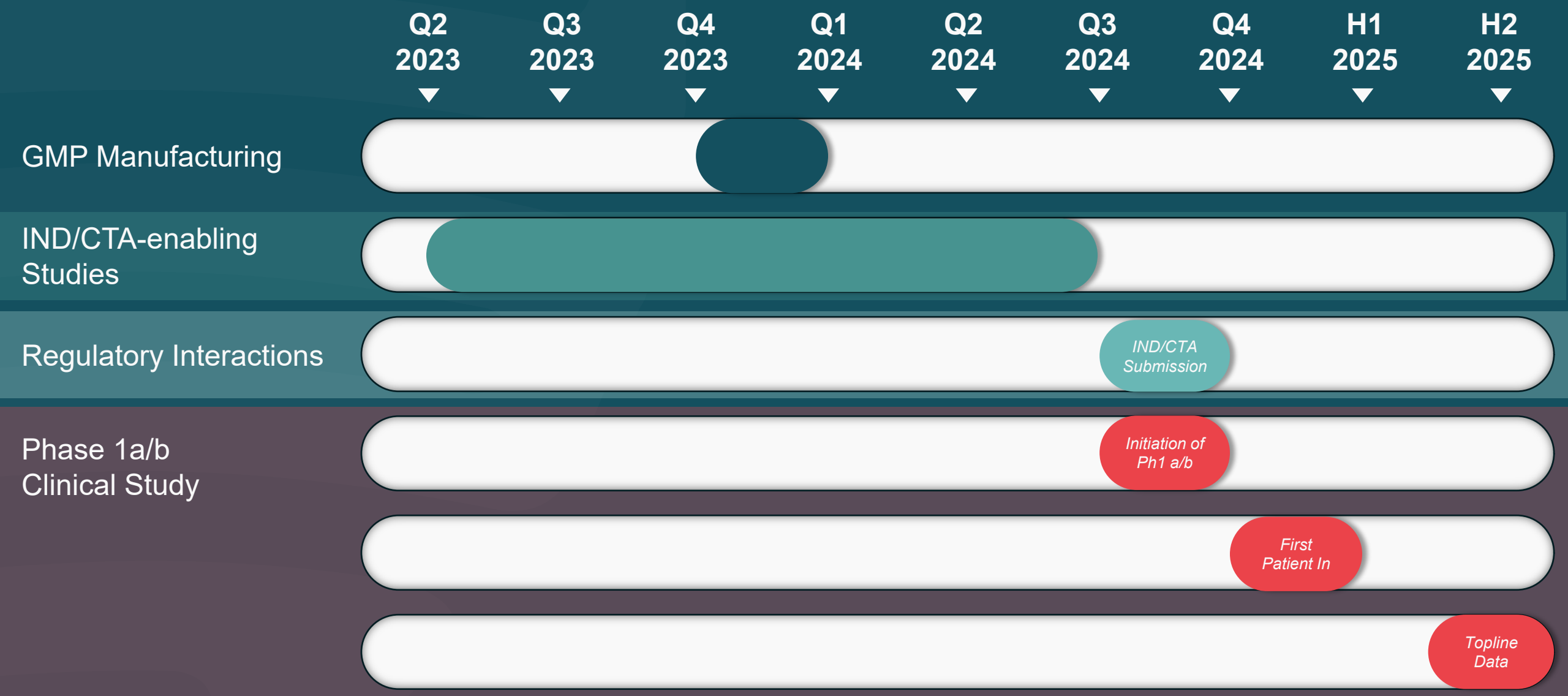


Significant improvement in clinical remission rate of 19.2%

Adverse Events (AEs) were most frequently headache and nausea

1. Schreiber et al.
2. Danese et al.

PALI-2108 Development Plan Through Phase 1a/b



Precision Medicine Approach

Precision Medicine Approach for Selecting Patients Most Likely to Respond to PDE4 Therapy in UC

PROTEOMICS

Changes at the protein level for immune biomarkers, PDE4 expression and PDE4 associated proteins

TRANSCRIPTOMICS

RNA sequencing of colon tissue to identify expression changes

GENOMICS

Identify mutations or SNPs in genes that contribute to cAMP levels in colon tissue (PDE4, IL-22, AhR, Nrf2, HO-1). Utilize existing UC databases to develop a risk score to predict patient response to PDE4

- ✓ Elevated express of PDE4 in chronic UC patients correlates with disease activity by Mayo score[1]
- ✓ Elevated expression of inflammatory cytokines has been shown in chronic UC patients[1]
- ✓ PDE4 expression and cytokine levels are normalized following PDE4 inhibition in mice[1]
- ✓ UC patients with elevated PDE4B expression in colon tissue respond better to therapies that target these pathways[2]

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

Significant IP Portfolio Through 2042

Composition of Matter Patent Family
PCT/CA2021/050725

National Phase Entry of PCT
December 2022

National Phase Entry
US, Canada, China, Japan, Mexico, Australia, EU (France, Germany, Italy, Spain, UK, etc.), South Korea

Composition of Matter Coverage Until 2042+

FDA Regulatory Exclusivity Coverage for 8 Years

Potential to File Additional Patents
- Formulation patients
- Methods of use
- Platform

Program Team

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abbvie Allergan AstraZeneca BIORA Therapeutics Bristol Myers Squibb decīphera

Deloitte. FINCH THERAPEUTICS intrinsik Laurent PHARMA MERCK VERTEX

Financial Snapshot

Strong Financial Position with Cash to Fund Operations into 2025

$15.3M
Cash
As of September 30, 2023

~$5M
Market Cap[1]

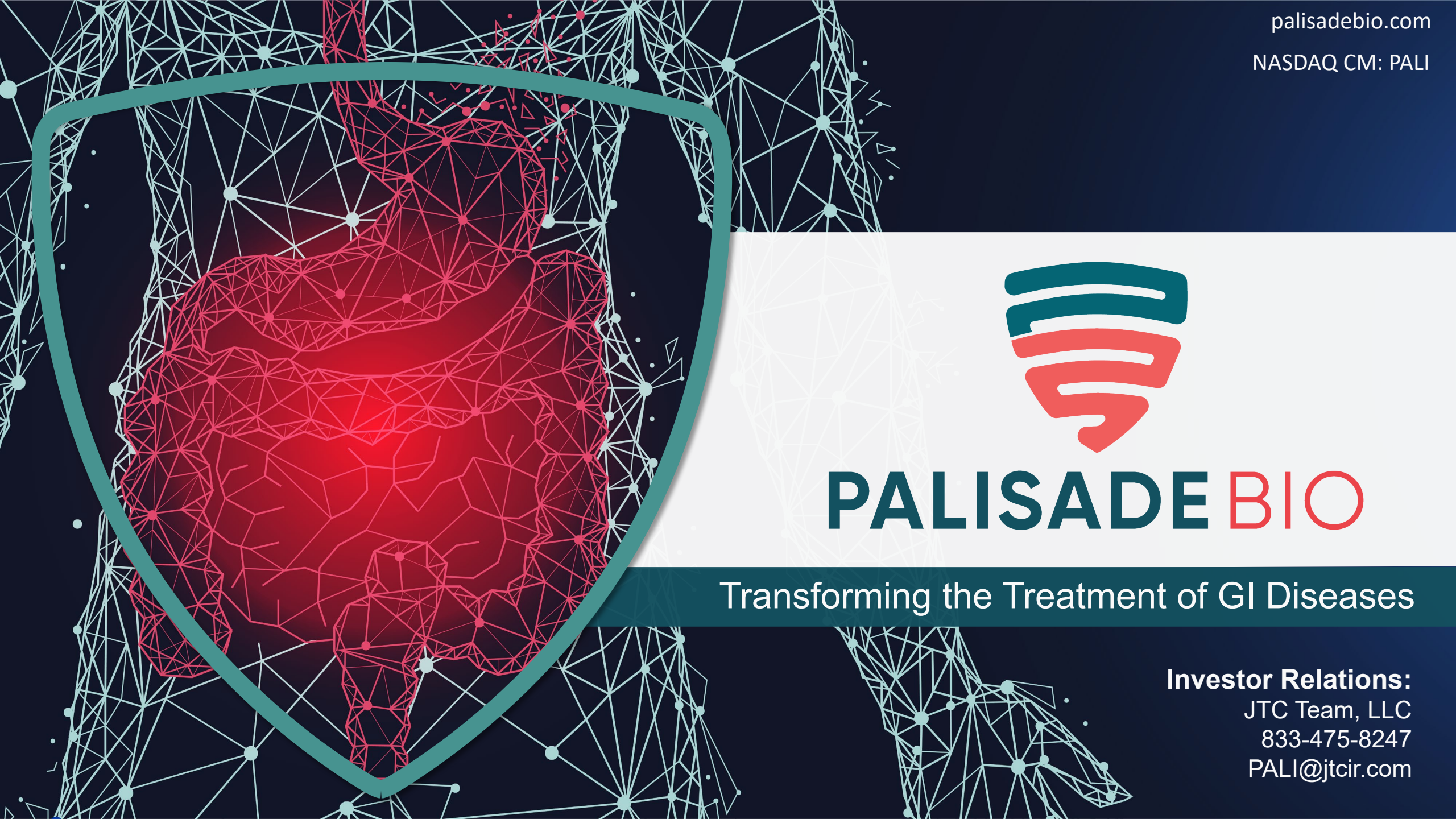
~193K
Volume[1]

1: As of January 24, 2024, with a closing price of $0.53 and total number of shares outstanding of 9,217,129

Investment Summary

Developing novel therapeutics for serious chronic gastrointestinal diseases, with a targeted approach that transforms the treatment landscape

- Oral therapeutics addressing UC and CD in high-value IBD market
- Growing body of data demonstrating locally acting, locally acting approach improves efficacy and safety
- PDE4 target validated by multiple approved products
- Demonstrated significant interest from Big Pharma
- Sufficient capital to fund operations into 2025



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PALISADE BIO

Transforming the Treatment of GI Diseases

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