

# THARIMMUNE

Unlocking Immunology for a  
Better Tomorrow

Corporate Presentation

March 2025

Nasdaq: THAR | [www.tharimmune.com](http://www.tharimmune.com)



# Forward-Looking Statements

Certain statements in this presentation are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, contained in this press release, including statements regarding the timing and design of Tharimmune's future Phase 2 trial, Tharimmune's strategy, future operations, future financial position, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "depends," "estimate," "expect," "intend," "may," "ongoing," "plan," "potential," "predict," "project," "target," "should," "will," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The Company may not actually achieve the plans, intentions, or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements. Factors that may cause such differences, include, but are not limited to, those discussed under Risk Factors set forth in our Annual Report on Form 10-K for the year ended December 31, 2024 and other periodic reports filed by the Company from time to time with the Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent the Company's views as of the date of this release. Subsequent events and developments may cause the Company's views to change; however, the Company does not undertake and specifically disclaims any obligation to update or revise any forward-looking statements to reflect new information, future events or circumstances or to reflect the occurrences of unanticipated events, except as may be required by applicable law. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this release.

# Investment Highlights

Developing **novel treatments for immune-mediated diseases**, with lead programs in primary biliary cholangitis (PBC) and autoimmune conditions



## Clinical-stage Immunology & Inflammation Pipeline

- TH104: First-in-class buccal film delivery of nalmefene for chronic pruritus in PBC (Phase 2-ready)
- TH023: Oral anti-TNF $\alpha$  monoclonal antibody targeting autoimmune diseases (Phase 1-ready)



## Large, Underserved Market Opportunities

- Chronic pruritus in PBC: No FDA-approved therapies, with an estimated >150K US patients
- Oral anti-TNF $\alpha$  opportunity: Potential to disrupt the \$50B+ global autoimmune biologics market



## Proprietary Drug Delivery Innovation

- TH104's buccal film potentially avoids first-pass metabolism while delivering rapid relief
- TH023's oral formulation offers a patient-friendly alternative to injectable TNF- $\alpha$  inhibitors



## Strong Leadership & Clinical Expertise

- Management has a proven track record launching biopharma companies
- Clinical team with extensive experience in drug development



## Near-Term Clinical & Regulatory Milestones

- TH104 Phase 2 ready with HI study initiation planned in 2025
- TH023 Phase 1 study to establish oral bioavailability in 2025

# Product Pipeline

Multiple, De-Risked Shots on Goal

Stage	Candidate	Modality & Indication	Preclinical	Phase 1	Phase 2	Next Milestones
Clinical	<b>TH104</b> MOR/KOR	<b>Buccal Transmucosal Film</b> Avoids first-pass liver effect  <b>Moderate-to-Severe Chronic Pruritus in PBC</b>	Phase 2 Ready*			<b>2025:</b> HI Study Initiation* Ph2 Planning
	<b>TH023</b> Anti-TNF $\alpha$	<b>Oral Infliximab</b> Only approved as IV/SC  <b>Multiple high-value autoimmune indications</b>	Phase 1 Ready†			<b>2H25:</b> CMC Optimization Ph1 Initiation
Development	<b>HS1940</b> PD-1/VEGF	<b>EpiClick™ Technology</b>  <b>Multiple high-value oncology indications</b>				<b>2025:</b> Preclinical studies

MOR = mu opioid receptor; KOR = kappa opioid receptor; TNF $\alpha$  = tumor necrosis factor-alpha;

\*CMC completed; HI – hepatic impairment; TH104 ready to go into Phase 2 in the EU and US with FDA and EMA feedback received

† trial initiation ex-US; Celltrion has right-of-first refusal post clinical study

# Major Unmet Need for Chronic Pruritis (Severe Itching) in PBC

Primary Biliary Cholangitis (PBC) is a rare, chronic autoimmune liver disease that leads to bile duct damage and progressive liver failure

**>150,000**  
US cases

Orphan  
Disease in  
US and EU

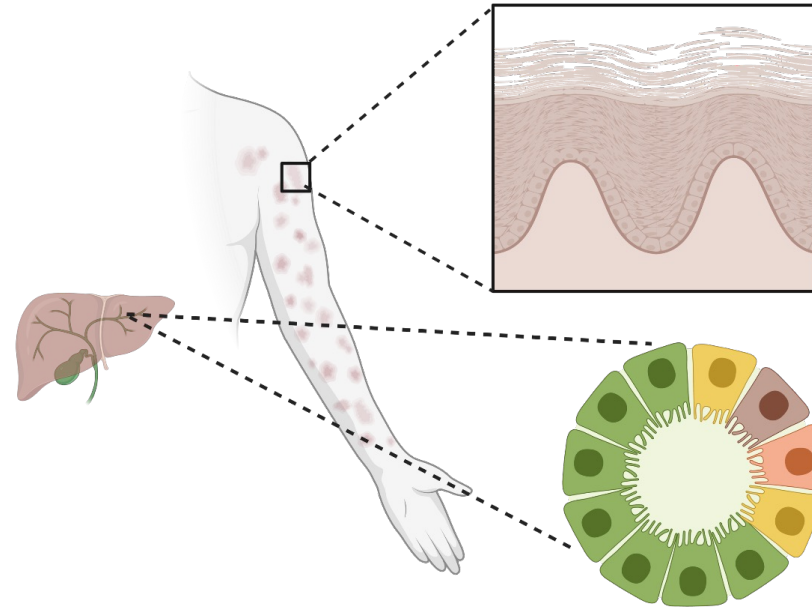
**>200,000**  
Global cases

**~90%**

PBC cases are  
women

**~65%**

Have worse  
nocturnal pruritis



**More than  
70% of PBC  
patients  
affected by  
pruritis<sup>1</sup>**

PBC is a chronic disease where bile ducts in the liver are eventually dysfunctional; the bile builds up and causes liver damage<sup>4</sup>

## Current Treatment Gaps

- Limited options: No convenient FDA-approved therapies for PBC-related pruritis
- Existing treatments have suboptimal efficacy or cause significant side effects
- Significant QoL impact: leads to sleep disturbance, anxiety and depression

In patient testimonials, PBC itch is described as **“the worst, most unimaginable itch, like bugs crawling under the skin”**

# Lead Asset – TH104 for PBC Pruritis

TH104 is a proprietary transmucosal buccal film embedded with FDA-approved nalmefene, designed to suppress chronic pruritus in PBC patients

## Asset De-Risked by Improved Formulation

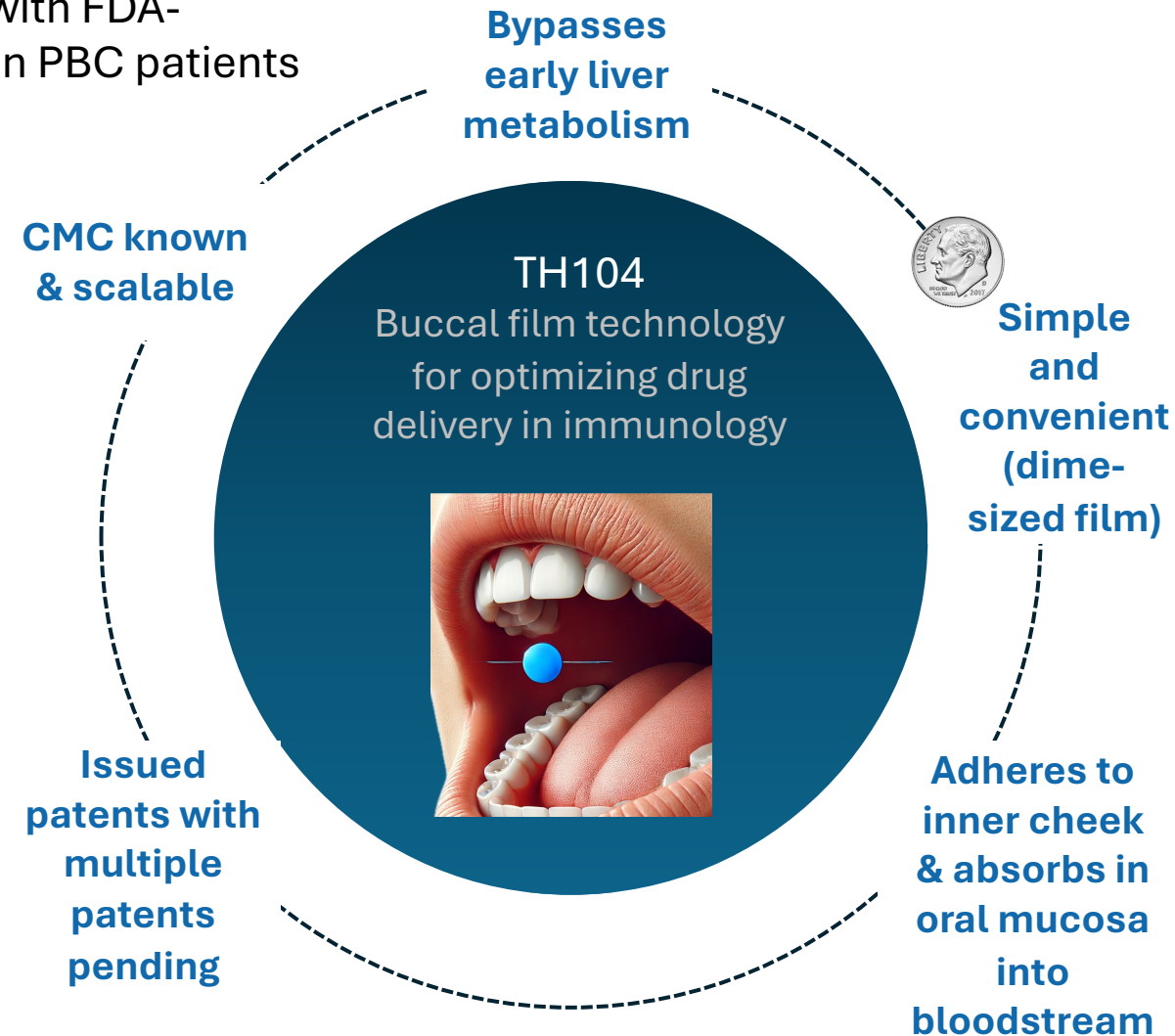
- Active ingredient, FDA-approved (nalmefene), suppresses PBC-induced pruritis
- Buccal delivery potentially avoids early liver metabolism, benefitting liver impaired patients
- Once-daily dosing, rapid onset, high absorption
- Buccal delivery offers comparable bioavailability as IV and oral delivery of nalmefene

## Positive Phase 1 Results

- ✓ All subjects had a mean **33.3% decline** in itch scores after a single dose at 24 hours in an open-label proof-of-concept
- ✓ Significant correlation between blood levels and symptom relief

## Clinical Progress

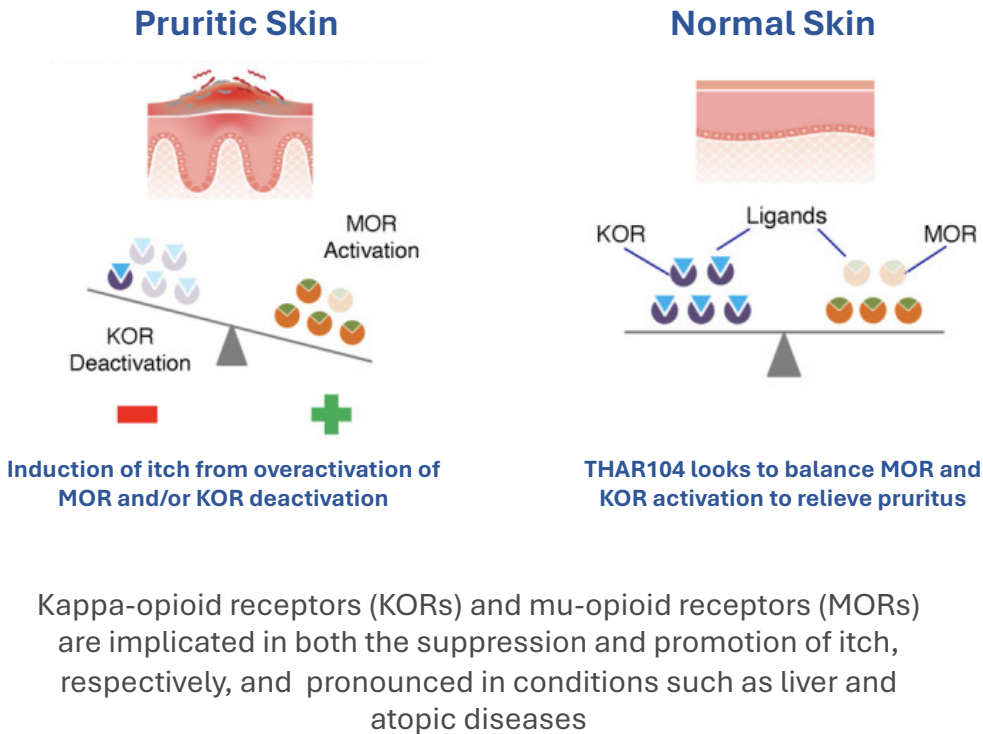
- Positive Phase 1 completed
- Phase 2 initiation planned



# TH104 Mechanism of Action: Dual Modulation of Receptors

## Growing Market Opportunity Unlocked by Addressing Root Causes

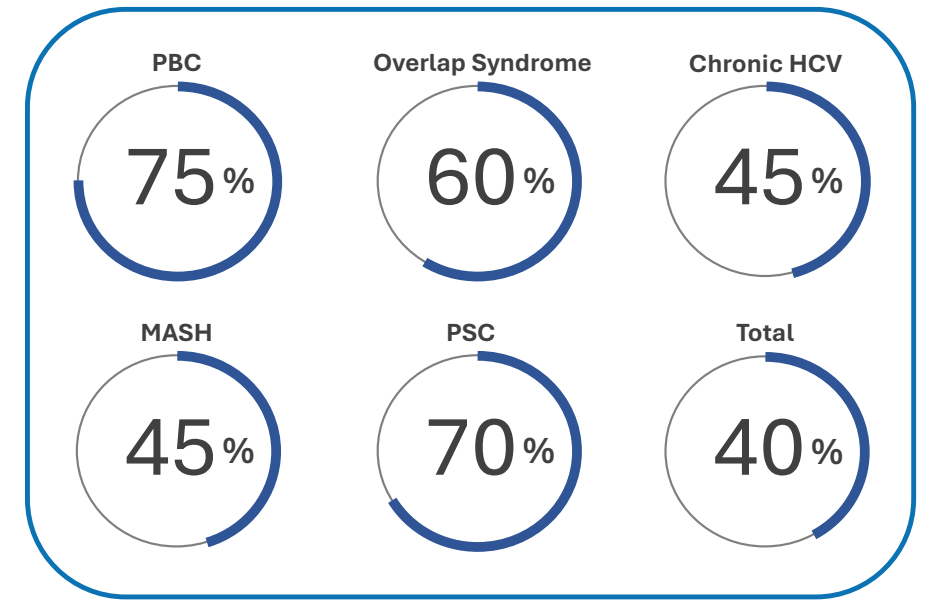
1 TH104 functions by **restoring the opioid receptor activation imbalance** implicated in promoting itch across many liver diseases



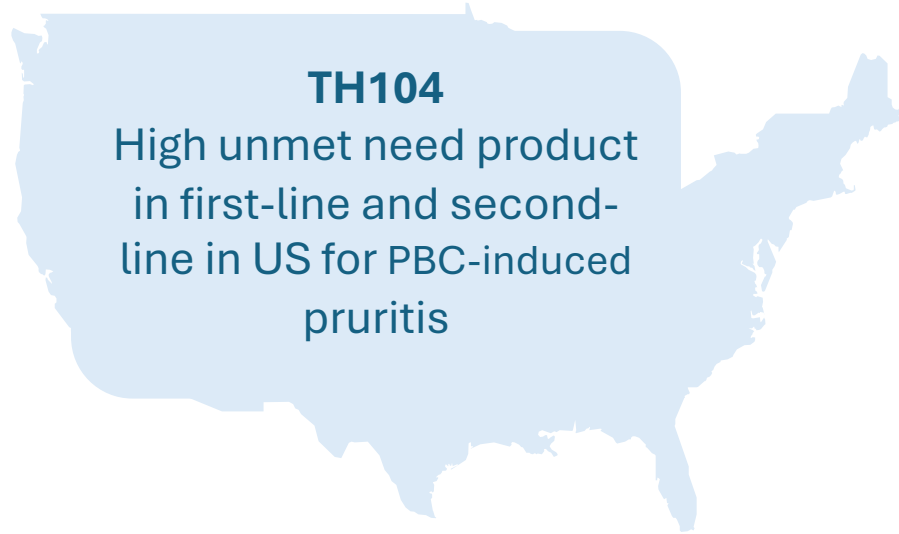
2 This unlocks **clinical potential across multiple indications** with PBC being the first

### Prevalence of pruritus in liver diseases<sup>2,3,4</sup>

**~1.7 million patients**



# TH104 – Market Opportunity and Differentiation



Global PBC treatment market valued at ~\$2.5B and expected to grow

Global chronic pruritus treatment market projected to exceed \$7B by 2030 (across multiple conditions, including liver disease)

Treatment	Mechanism	Limitations	TH104's Advantage
✗ Bile acid binders (e.g., cholestyramine)	Reduce bile salts	Poor tolerability, GI side effects	Buccal film avoids GI issues
✗ Rifampin	antibacterial, PXR agonist	Hepatotoxicity concerns	Improved safety profile
✗ Opioid antagonists (e.g., naltrexone)	Central opioid modulation	Liver metabolism	Lower systemic exposure
✓ TH104	Dual opioid receptor modulation	Targeted delivery, generally safe, non-invasive	Potential best-in-class therapy

## Regulatory & Commercial Potential for TH104

- **Regulatory pathway:** FDA approval pathway under 505b2 path with de-risked active
- **Physician & patient adoption:** non-invasive, easy-to-administer therapy more compelling
- **Improved formulation:** first buccal delivery treatment targeting PBC pruritis specifically



# TH023 - Oral Anti-TNF $\alpha$ for Autoimmune Diseases

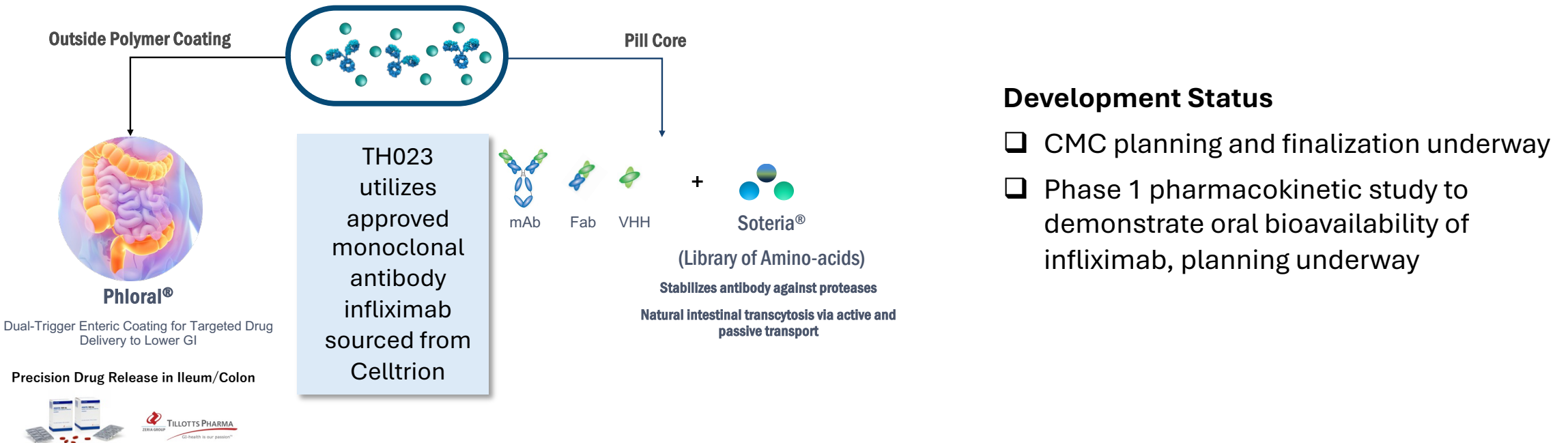
Oral infliximab, a gold standard for multiple autoimmune diseases

## What is it?

- TH023 is a first-in-class oral formulation of infliximab, an anti-TNF $\alpha$  monoclonal antibody targeting autoimmune diseases
- Designed to provide the **benefits of biologics without injections**
- Developed using proprietary oral antibody delivery platform licensed from Intract Pharma

## How it works

- TNF $\alpha$  is a key driver of inflammation in autoimmune diseases
- TH023 blocks TNF $\alpha$  activity, reducing inflammation in conditions like RA and Crohn's
- Oral formulation offers a non-invasive alternative to IV or subcutaneous TNF inhibitors



## Development Status

- CMC planning and finalization underway
- Phase 1 pharmacokinetic study to demonstrate oral bioavailability of infliximab, planning underway

# TH023 – Market Opportunity

A \$50B+ Market Ready for Innovation

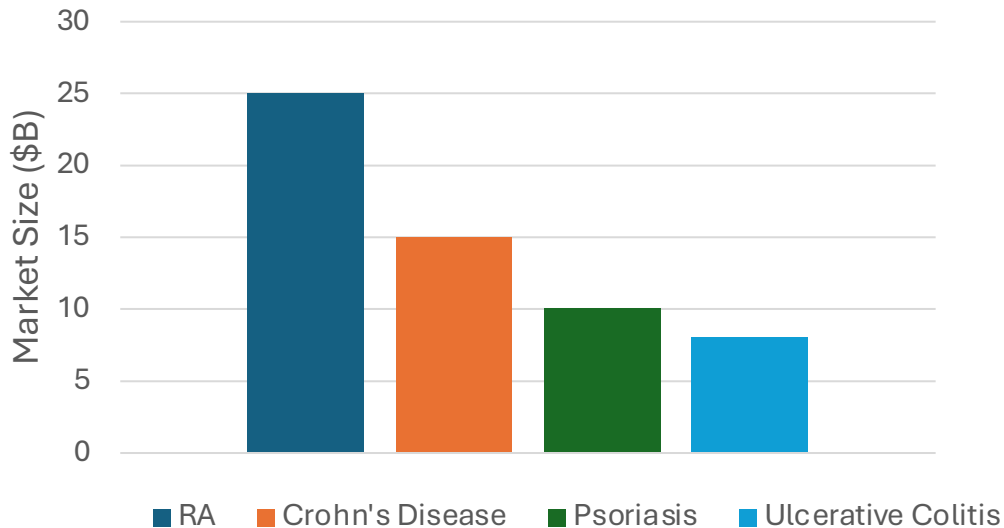
## Existing Market Size

~\$47B

Generated annually by TNF $\alpha$  inhibitors (e.g., Humira, Remicade)

- Rheumatoid arthritis (RA), Crohn’s disease, psoriasis, ulcerative colitis (UC) are primary indications

Autoimmune Disease Market Components (2024)



## Unmet Need

- **High patient burden with injectables** (pain, needle phobia, side effects)
- **Biologic adoption barriers:** Cost, physician administration requirements
- **Oral therapy could increase patient compliance & accessibility**

## Potential to Disrupt a Multibillion-Dollar Market

- ✓ **Market Shift to Oral Biologics:** if TH023 proves efficacy and bioavailability, it could capture market share from injectables
- ✓ **Potential Competitive Differentiation: A daily oral anti-TNF $\alpha$  could**
  - ✓ Enhance adherence
  - ✓ Improve patient quality of life
  - ✓ Lower costs for healthcare systems

# TH023 – Market Opportunity

## TNFα Competitive Comparison

Therapy	Delivery	Dosing Frequency	Patient Burden	Peak Sales
<b>TH023 (Tharimmune)</b>	<b>Oral</b>	<b>Daily / as needed</b>	<b>Low - no injections</b>	<b>High potential</b>
Humira® (AbbVie)	Injection	Every 2 weeks	Moderate – painful injections	\$21B
Remicade® (Janssen)	IV infusion	Every 6-8 weeks	High – hospital visits required	\$4B
Simponi® (Janssen)	Injection	Monthly	Moderate	\$2.5B

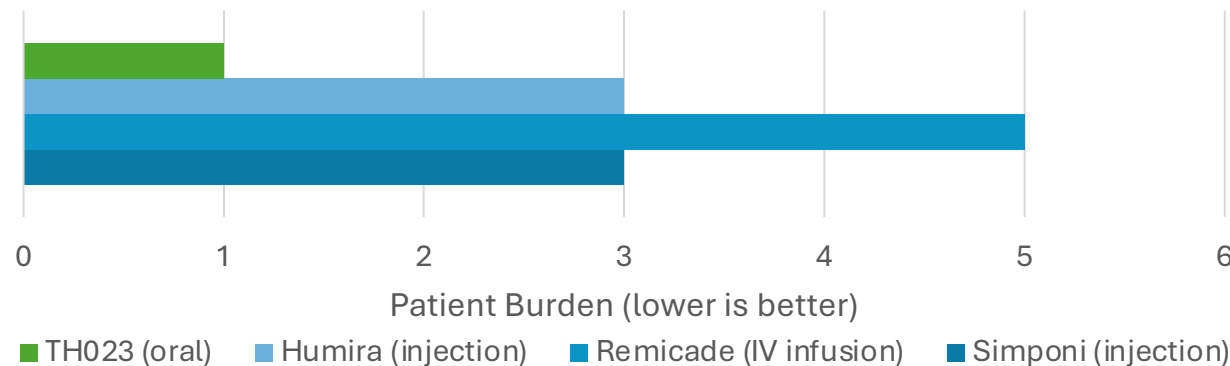
### Dosing & Administration Burden

- **Humira (Injection):** Biweekly or monthly self-administered injection
- **Remicade (IV):** Requires infusions administration every 6-8 weeks (high burden)
- **Simponi (Injection):** Monthly subcutaneous injection
- ✓ **TH023 (Oral): Daily pill, offering a non-invasive alternative**

### Patient Burden Ranking

- ✓ **Lower burden = More convenience & better adherence**
- ✓ Oral treatment (TH023) **minimizes administration barriers** vs. injections/IV infusions

TH023 vs TNFα Biologic Competitors



# TH023 – Market Opportunity

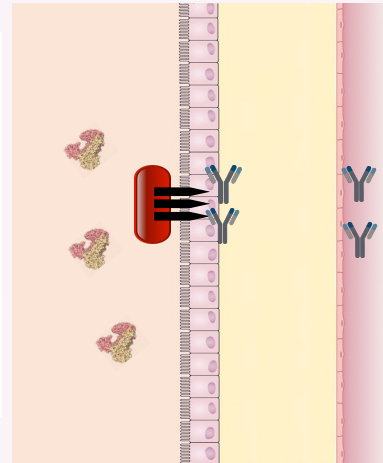
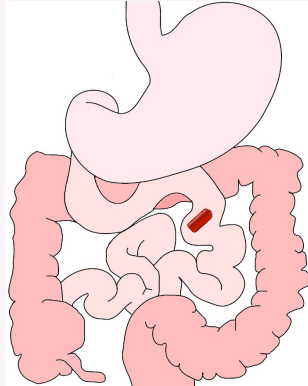
## Oral Biologics Delivery Platform Compared to Other Technologies in Development

### Orally Ingestible Devices

Rani  
THERAPEUTICS

BIORA™  
Therapeutics

BIO>GRAIL



Drug Loaded Needles

- ✗ No enzyme protection if deployment fails
- ✗ CMC/COGS/safety challenges
- Injection into tissue for systemic delivery hampered by deployment failures

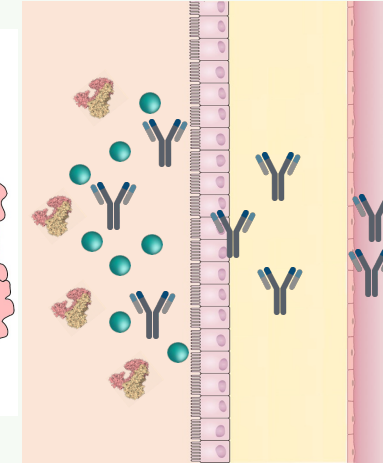
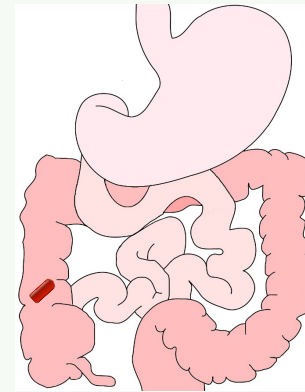
### Oral Antibody Platform Technology

Intract  
Pharma



+

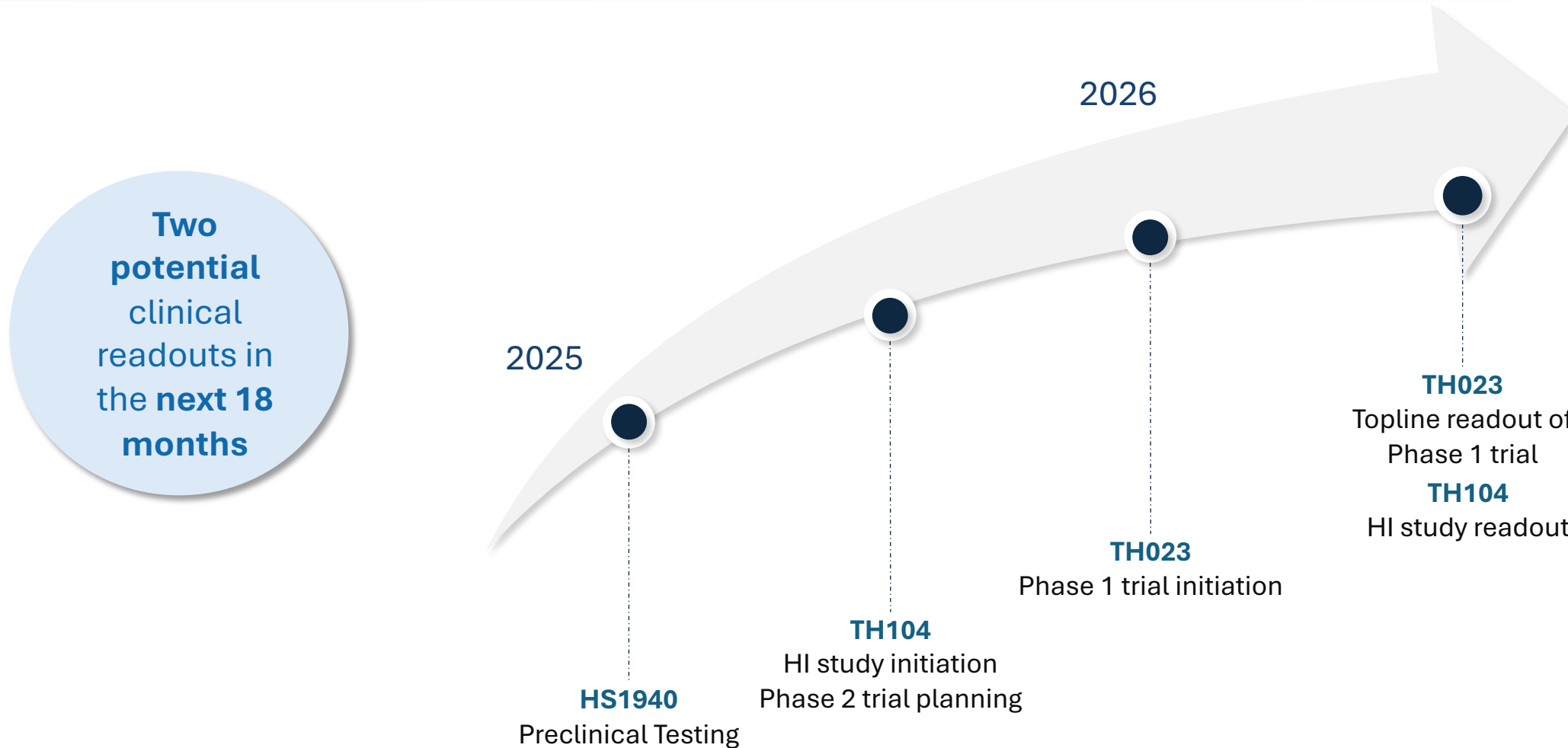
THARIMMUNE



Enzyme Stabilizer +  
Amino Acids

- ✓ Enzyme protection for high local tissue exposure
- ✓ CMC/COGS
- Modest permeation enhancement

# Anticipated Key Upcoming Milestones



# Leadership

## Executive Team



**Randy Milby**  
Chief Executive Officer



**Sireesh Appajosyula**  
Chief Operating Officer



**Don Kim**  
Chief Financial Officer



**Nir Barak, MD**  
Chief Medical Advisor



## Board of Directors

**Randy Milby**  
Chairman of the Board



**Leonard Mazur**  
Director



**Lynne A Bui**  
Director



**Sireesh Appajosyula**  
Director



**Kelly Anderson**  
Director



**Sanam Parikh**  
Director



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# Appendix: TH104

## Phase 1 Chronic Liver Disease (CLD) Study Results

### All Patients Responded to TH104

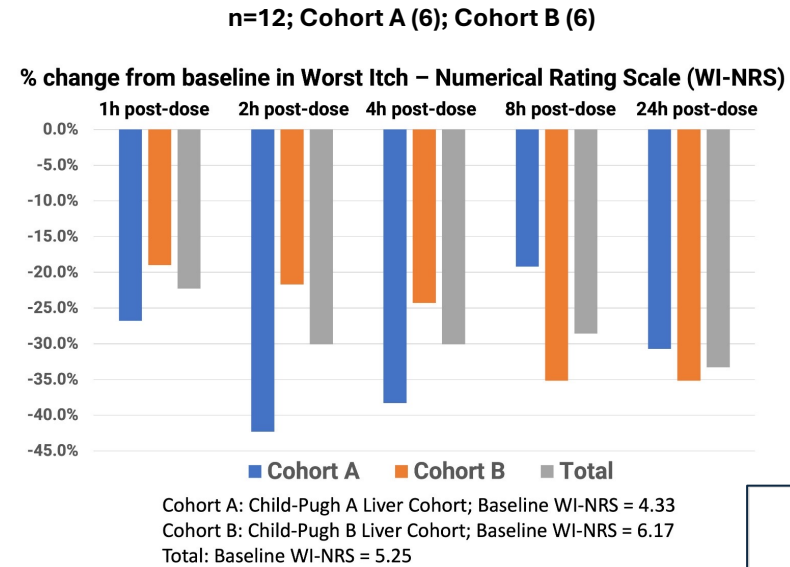
Single-dose, single-center, open-label, randomized, study conducted in India in two different cohorts

Primary outcome measure: safety and tolerability of a buccal dose in CLD patients

At 24-hours, Groups A & B had mean declines of 30.7% & 35.2%, respectively in pruritus scores. **All 12 subjects had a mean decline of 33.3% in itch scores after a single dose at 24-hours** post dosing

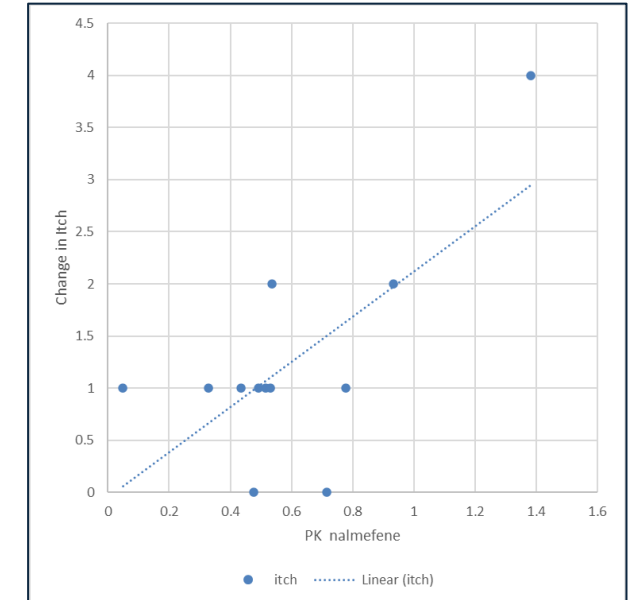
The correlation coefficient between TH104 AUC and change in itch,  $r$ , was 0.7060, with a  $p$ -value of 0.0103 and a 95% confidence interval for  $r$  of 0.2220 to 0.9108.

Poster titled "4348: Correlation Between the Pharmacokinetics of TH104 and Pruritus Relief in Patients with Cholestatic Pruritus," presented at the 75<sup>th</sup> American Association for the Study of Liver Diseases (AASLD) Annual Conference at The Liver Meeting® 2024, November 15-18 in San Diego



The Worst Itch Numerical Rating Scale (WI-NRS) is a validated scale with 11 numbers - 0 representing “no itch” to 10 representing “worst imaginable itch”; patients are asked to pick the number corresponding to the intensity of their pruritus.

**Significant correlation shown between blood levels and symptom relief; TH104 was well tolerated with no unexpected treatment-emergent adverse events**



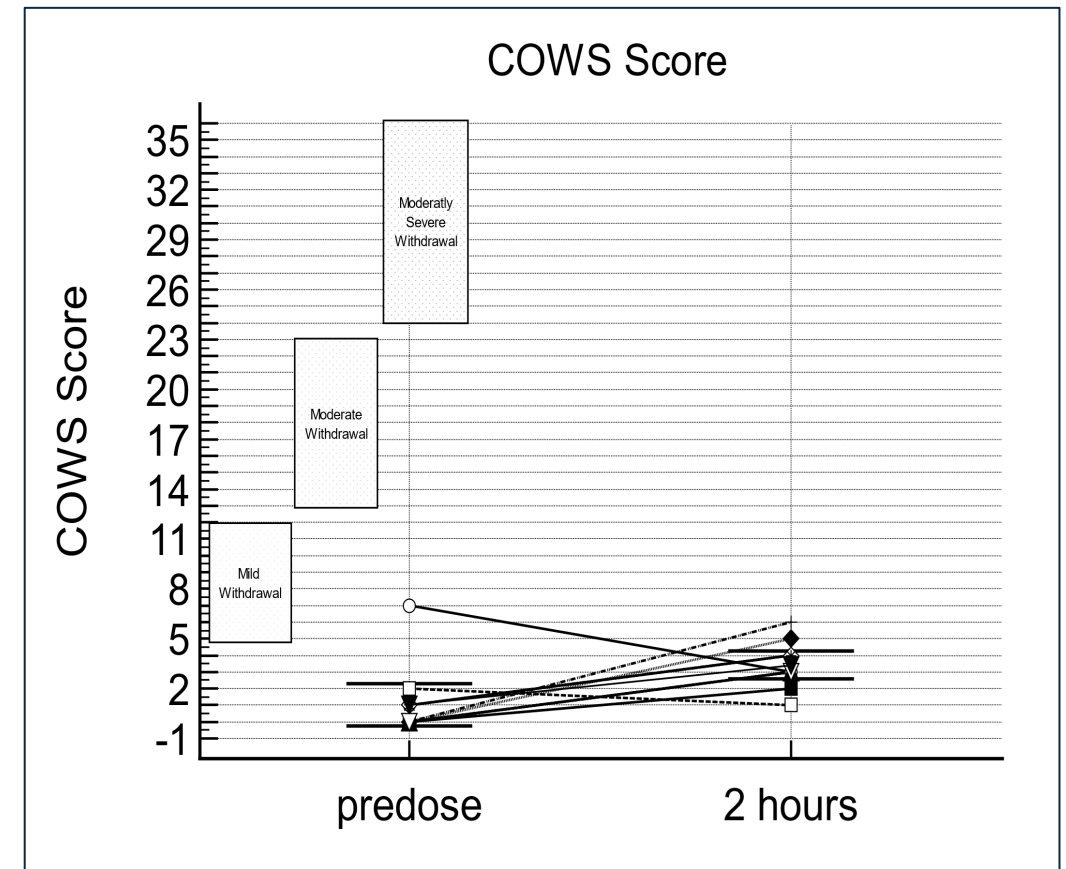


# Appendix: TH104

Withdrawal Symptoms were not seen in CLD patients given TH104

✓ TH104 did not induce withdrawal symptoms in CLD patients after a single low dose

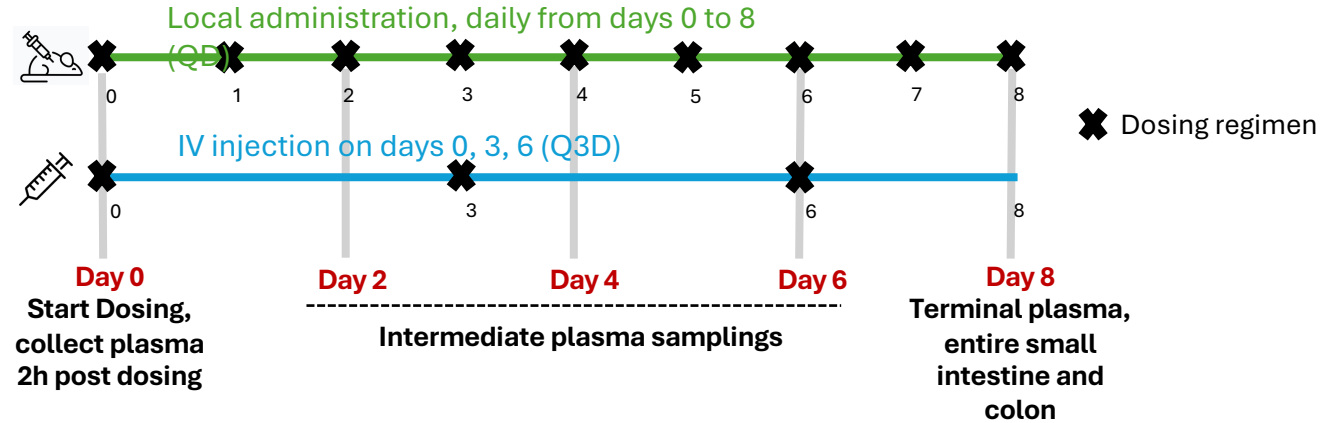
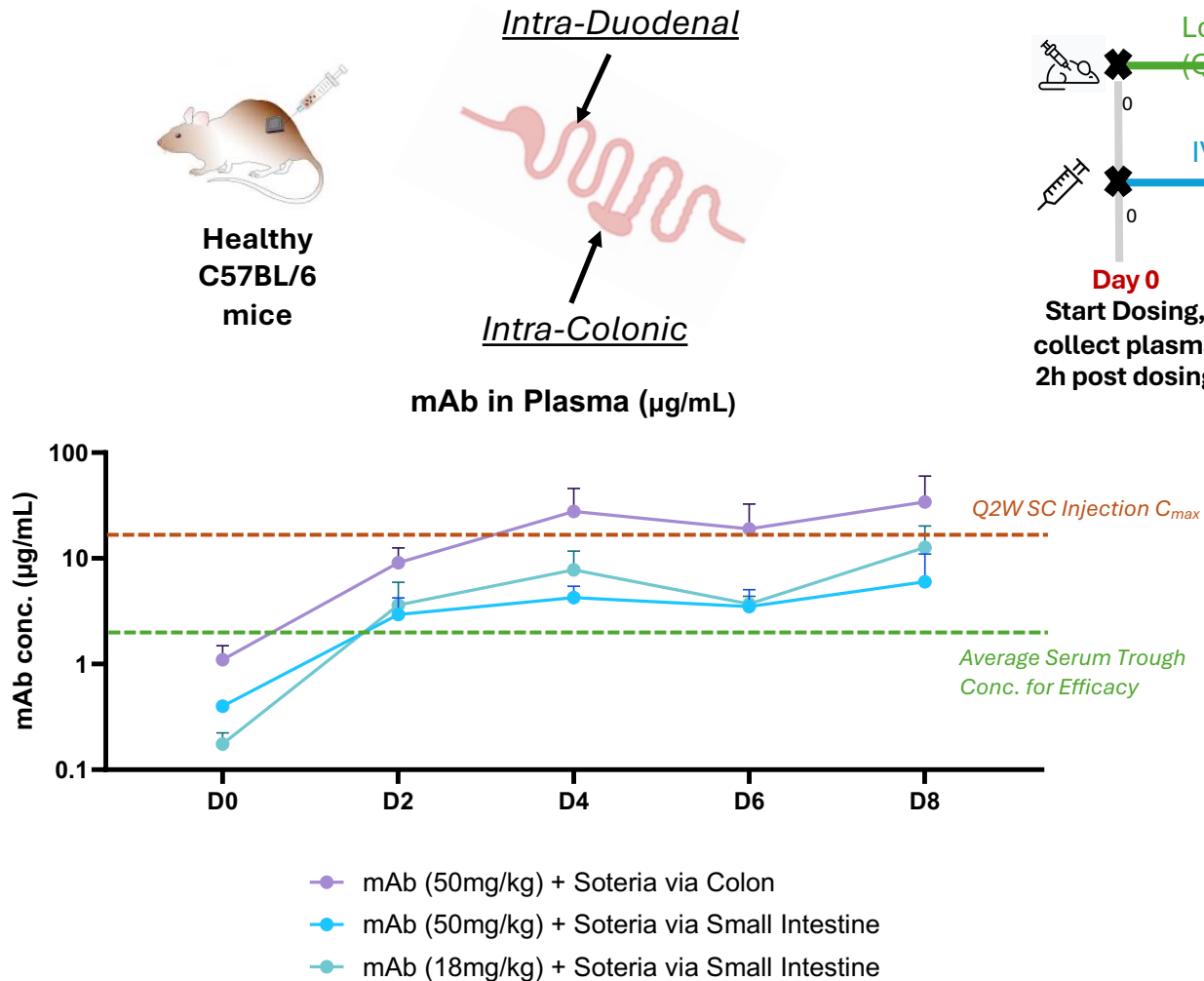
- Assessment of patients for withdrawal symptoms used the Clinical Opiate Withdrawal Scale (COWS)
- The COWS is an 11-item clinician-administered scale for inpatient and outpatient settings to rate common signs and symptoms of opiate withdrawal and monitoring
- **Study results indicate the use of TH104 2 mg in patients with mild and moderate cholestatic liver disease is safe and tolerable and not associated with opioid withdrawal syndrome**



# Appendix: TH023

TH023 Exceeds Trough Concentration and Matches Subcutaneous Injection  $C_{max}$

## In-vivo PK in Healthy Mice Following QD Dosing for 1wk



**Colon targeting** of mAb showed higher systemic conc. vs **small intestine delivery**, potentially due to better enzymatic stability and active transport receptor engagement

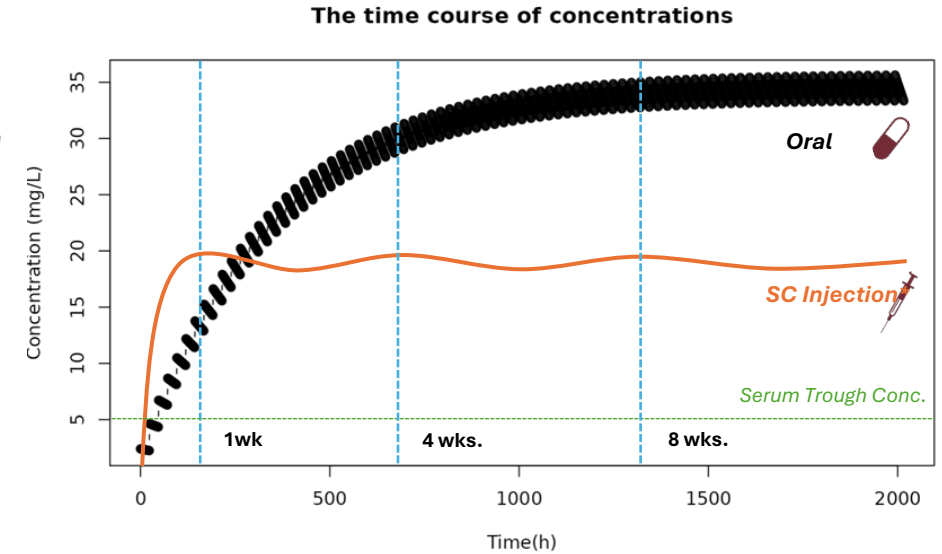
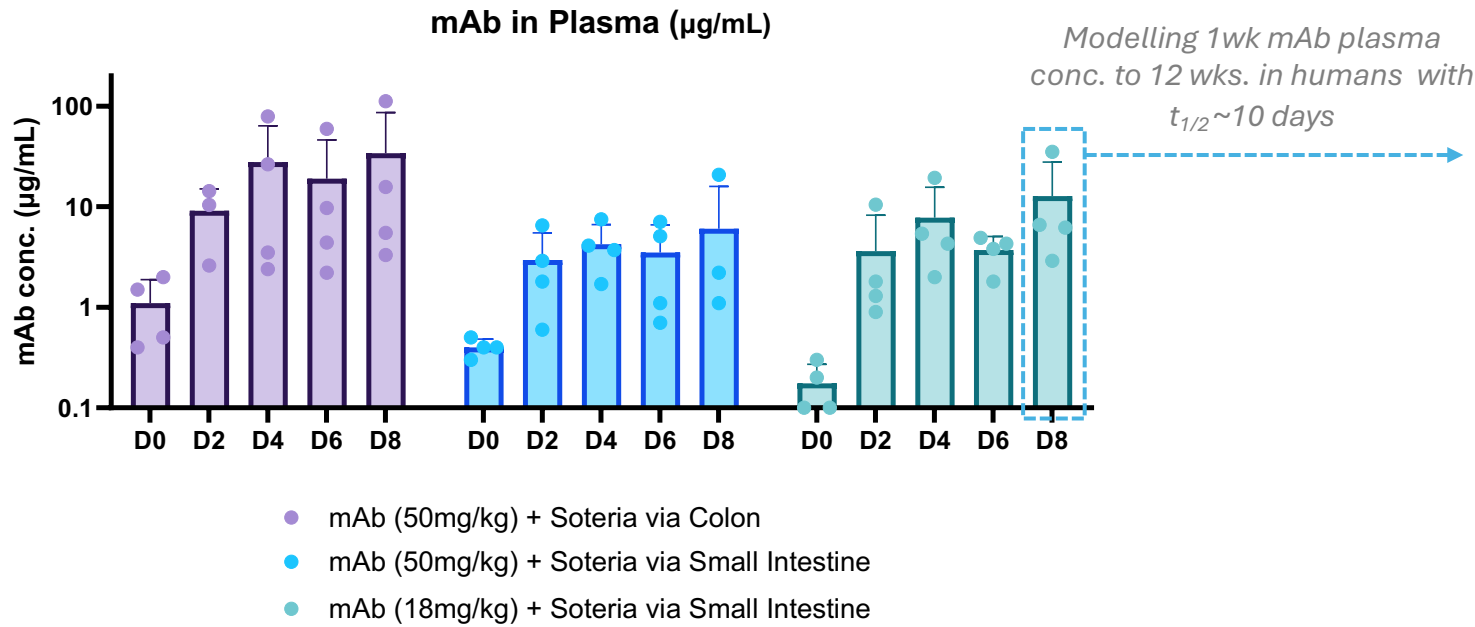
**No dose effect** observed between 50 and 18mg/kg, potentially due to intestinal epithelial transport saturation.

**QD dosing** of antibody enables build-up in plasma levels due to  $t_{1/2}$  of ~3-4 days in mouse.

# Appendix: TH023

## TH023 Systemic Concentration May Exceed Injection Trough and $C_{max}$

### PK Plot with Individual Mouse Data Points



- ✓ All arms reached > therapeutic serum trough concentration for injectable mAbs in humans
- ✓ When 1wk plasma conc. is modelled in humans with a  $t_{1/2}$  of 10days, the mAb concentration surpasses Q2W 240mg SC injection PK profile