



THARIMMUNE

Unlocking Immunology for a Better Tomorrow

January 2024

Nasdaq: THAR | tharimmune.com

Forward-Looking Statement

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding Tharimmune, Inc.'s (the "Company's" or "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/A for the year ended December 31, 2022 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 presentation represent the Company's views as of the date of this presentation. 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 presentation.

Experienced Leadership with a Successful Track Record

Randy Milby

CEO & Chairman

- Randy is a highly experienced biopharmaceutical executive
- Former CEO of CorMedix, Inc. (Nasdaq: CRMD)
- Senior executive across marketing and operations at DuPont and DuPont Merck
- Equity research analyst at Goldman, Sachs & Co. covering the biotechnology sector
- Bristol-Myers Squibb
- Captain, US Army Medical Service Corps.

Sireesh Appajosyula

Chief Operating Officer

- Seasoned executive with over 20 years of experience in large and small biopharma.
- Entrepreneur & drug developer with operational experience responsible for overseeing preclinical & clinical programs
- Led operations and portfolio strategy of numerous companies while responsible for fundraising ~\$90 M.
- Aventis (acq. by Sanofi), Critical Therapeutics (acq. by Chiesi) Amgen, Salix (acq. by Bausch).

Leonard Mazur

Director

- Executive Chairman of the Board of Directors and Secretary of Citius Pharma (Nasdaq: CTXR)
- Secretary of Citius' majority-owned subsidiary NoveCite, Inc.
- Accomplished and seasoned biopharma executive with multiple successful start-ups and successful exits.
- Co-founded Akrimax, Triax and Genesis Pharmaceutical

Lynne Bui, M.D.

Director

- President, Chief Executive Officer and member of the board of directors of Khloris Biosciences, Inc.
- Board-certified hematologist oncologist, seasoned entrepreneur, angel investor and drug developer.
- Led clinical development from preclinical IND to Phase 1 to 3 registration for multiple drugs in oncology.
- Senior level positions Exelixis, Onyx Pharmaceuticals, and Intellikine

Kelly Anderson.

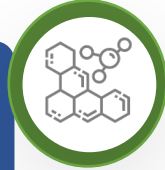
Director

- Chief Executive Officer of CXO Executive Solutions, a specialized executive talent solutions company.
- Formerly partner at C Suite Financial Partners, a financial consulting firm serving, private, private equity, entrepreneurial and family office and government firms.
- Served in senior financial executive posts at companies including Mavenlink, Ener-Core, Fisker Automotove, T3 Motion and The First American Corporation.
- Currently serves on the Board of AgEagle Aerial Systems Inc., Tomi Environmental Solutions and Concierge Technologies

Overview: TH104 for Chronic Pruritis “Itch”

Clinical-Stage Company

- TH104 for chronic pruritus in primary biliary cholangitis
- High unmet need for chronic pruritis in multiple diseases



Issued Patents

- Two issued US Patents
- Several pending in the USA and Rest-of-World



+ Clinical Feedback from FDA

- Ex-US clinical data with positive FDA feedback
- Validated primary endpoint by several approved drugs



IND Approved Feb. '23

- Phase 1 initiated with topline readout in 2Q24
- Phase 2 start with topline readout by 4Q24/1Q25



CMC: Ready for Clinical Trials

- Phase 1: CMC complete; GMP facility (*FDA inspected*)
- Scalable clinical and commercial CMC



Capital Efficient Runway

- Experienced leadership team
- ~\$10 million spend to complete phase 2 trial



TH104 Target Product Profile

Indication

- Moderate-to-severe chronic pruritis in patients diagnosed with Primary Biliary Cholangitis (PBC)

Mechanism & Dosage

- Nalmefene embedded in a proprietary transdermal buccal film
- Modulating μ -opioid & kappa opioid receptor as well as inhibiting IL-17
- Once-daily dosing at night

Clinical Timelines

- Multiple ex-US Phase 1 trials complete with confirmatory data
- Phase 1 PK bridging study in US with topline data expected in 2024
- Phase 2a study planned as a 28-d placebo-controlled trial in 2024

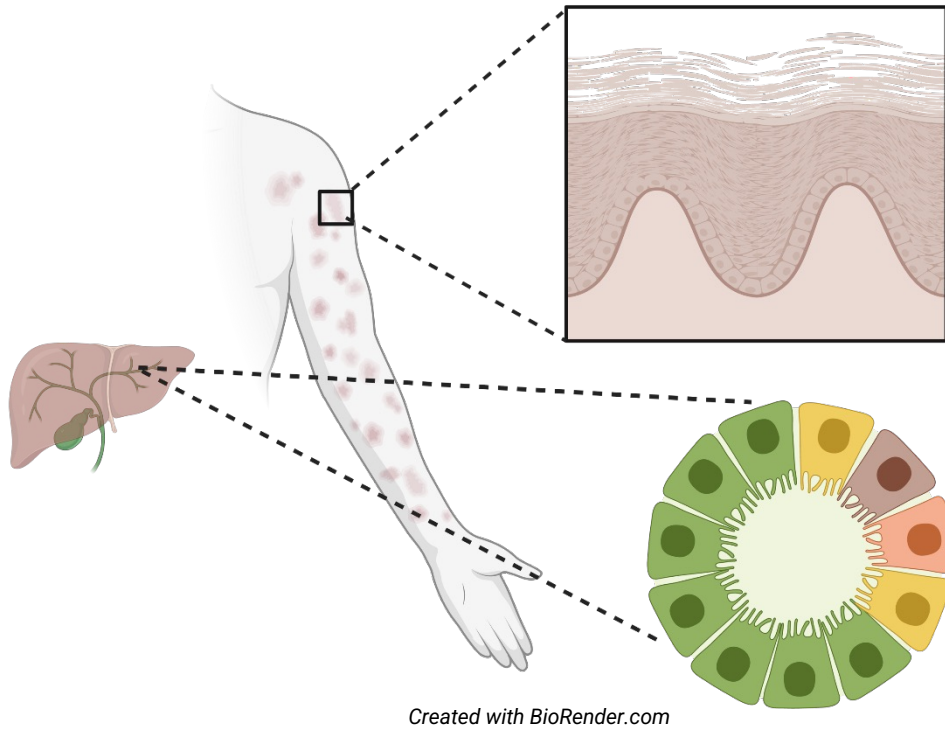
Efficacy

- Primary endpoint: safety and tolerability
- Secondary endpoint:
 - Reduction of pruritis using validated scale worst-itch numerical rating scale (WI-NRS), pending FDA discussions

Safety & Outcomes

- Generally safe and well tolerated: treatment-emergent adverse events (TEAEs) were mild, transient and self-limiting
- Potential to improve QOL & sleep quality by reducing nocturnal pruritis

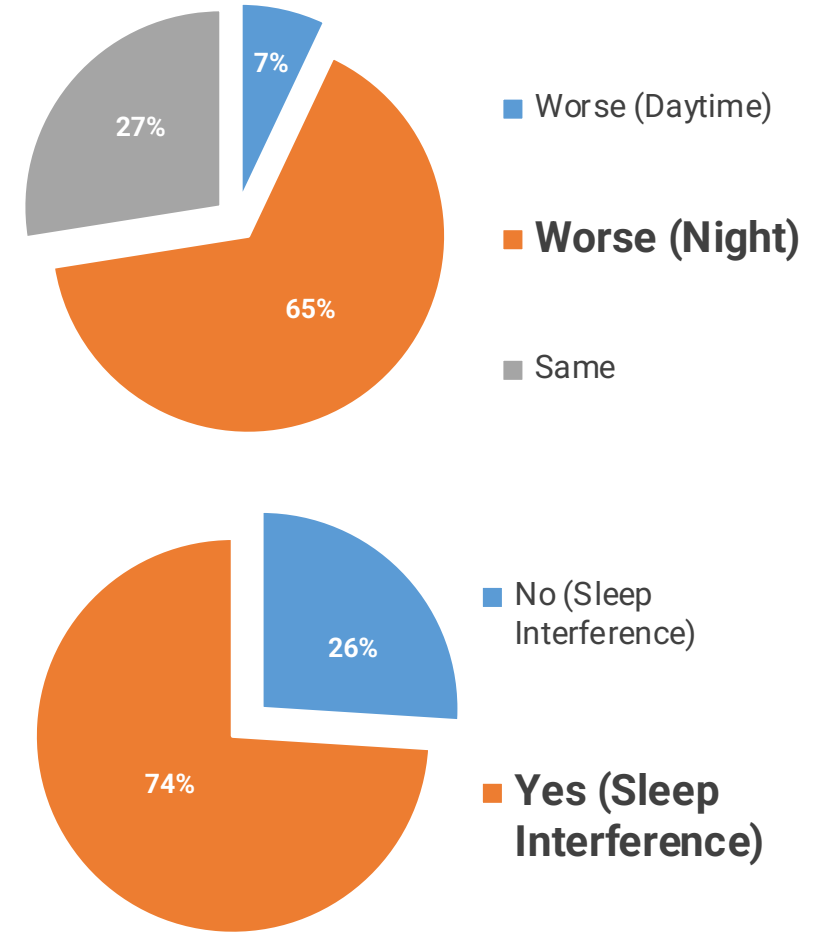
Initial Indication: *Chronic Pruritis (itching)* in PBC



Pruritis is common; **more than 70% of Primary Biliary Cholangitis (PBC) patients affected by pruritis**¹

PBC is a chronic disease where **bile ducts in the liver** are eventually dysfunctional; the bile builds up and causes liver damage.⁴

Nocturnal Pruritus³



- PBC is an **orphan disease** in the USA and Europe
- Affects men & women (rate higher in women: ~ 1 in 1,000 > 40 years old)²
- **65% of patients** have “worse **nocturnal** pruritus”³

1. Gungabissoon U, et al. BMJ Open Gastro 2022;**9**:e000857. doi:10.1136/bmjgast-2021-000857
2. <https://www.healthywomen.org/condition/primary-biliary-cholangitis-pbc>
3. Rische et. al. Itch in Primary Biliary Cholangitis: A Patients' Perspective Acta Derm Venereol 2008; 88: 34-37
4. <https://www.niddk.nih.gov/health-information/liver-disease/primary-biliary-cholangitis/definition-facts>

Chronic Pruritis Highly Prevalent in Liver Diseases



>70%

of PBC patients affected by pruritus at some point during their disease course²

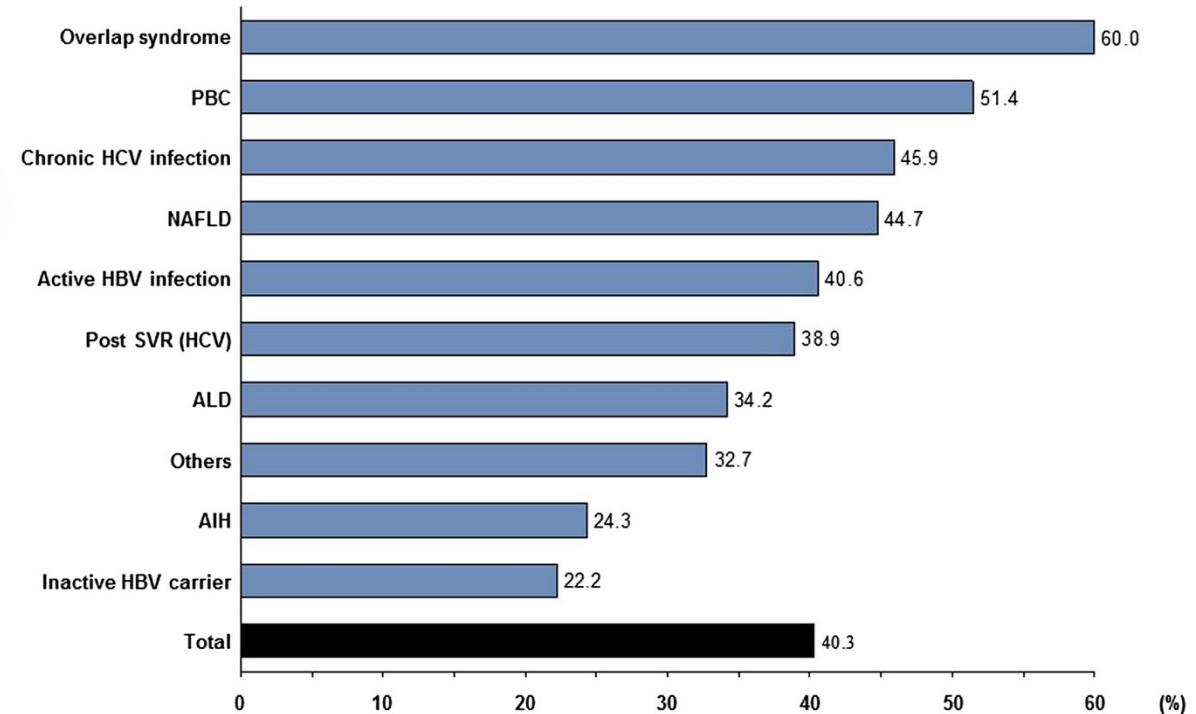
~4.4 million patients suffer from liver disease in the USA¹



~1.7 million patients suffer from pruritus in liver disease²



Prevalence of pruritus in liver diseases³



1. Center for Disease Control and Prevention - Summary Health Statistics: National Health Interview Survey, (2018), Table A-4a, page 1-9.

2. Gungabissoon U, et al. BMJ Open Gastro 2022;9:e000857. doi:10.1136/bmjgast-2021-000857

3. Oeda, S, et al. Prevalence of pruritus in patients with chronic liver disease: A multicenter study, Hepatology Research, 48: E252-E262, (2018)

Indication Expansion to Inflammatory Pruritogenic Diseases



~ 40%: experience pruritus in atopic dermatitis (eczema)¹

2.7 M patients suffer from moderate to severe pruritus¹



~ 24%: moderate-to-severe pruritus in chronic kidney disease²

1.3 M patients suffer from pruritus with CKD⁵



~ 40%: chronic pruritis in liver diseases³
with >70% with pruritus in PBC at some point in their disease course⁴

1.7 M patients affected by chronic pruritus⁵

1. [Atopic Dermatitis in America Study](#). Asthma and Allergy Foundation of America and National Eczema Association
2. Sukul et. al. [Pruritis and patient-reported outcome in non-dialysis CKD](#) Clin J Am Soc Nephrol. 2019 May 7; 14(5): 673–681
3. Oeda, S, et al. [Prevalence of pruritus in patients with chronic liver disease](#): A multicenter study, Hepatology Research, 48: E252–E262, (2018)
4. Gungabissoon U, et al. [Disease burden of PBC and associated pruritis based on cross-sectional US claims analysis](#) BMJ Open Gastro 2022;9:e000857
5. Villarroel MA, Blackwell DL, Jen A. [Tables of Summary Health Statistics for U.S. Adults](#): 2018 National Health Interview Survey. National Center for Health Statistics. 2019

Proprietary Transmucosal Film Technology

TH104 embedded in a novel, proprietary film - easily adhering to the inner cheek (*transmucosal delivery*)



Drug film is dime-sized



TH104 is developed by embedding drug onto a proprietary transmucosal film

- PK compatible with once-a-day dosing using film technology
- Fast onset
- High absorption

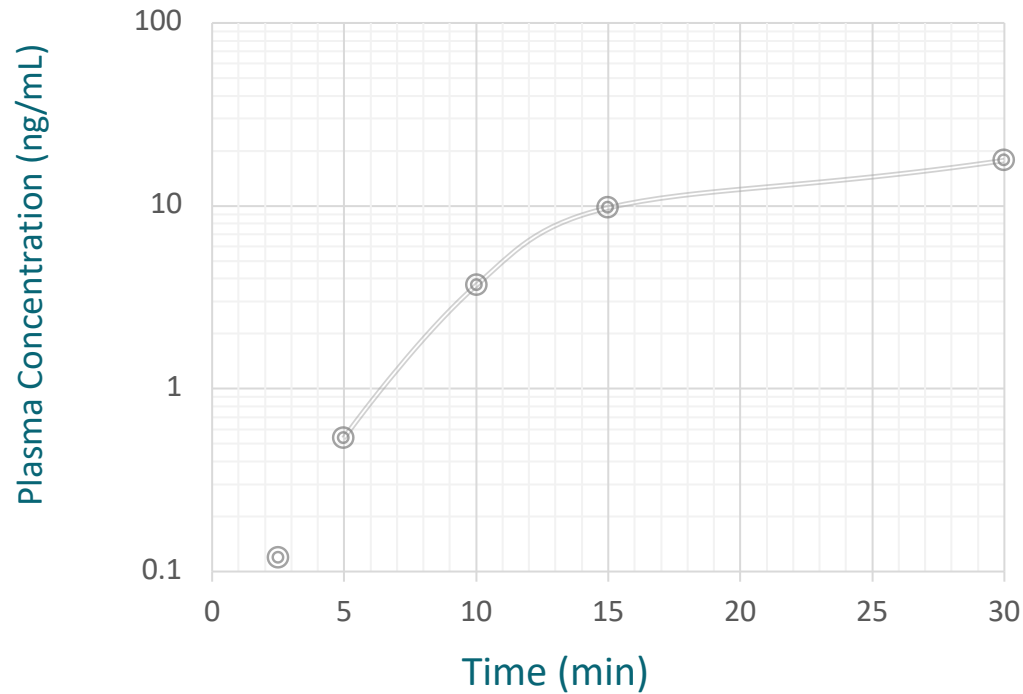
TH104 bypasses the liver (*no first pass effect*)

- Drug is systemically absorbed faster & distributed to the skin
- important in treating rare and chronic liver disease related conditions in which impaired liver disrupts drug metabolism

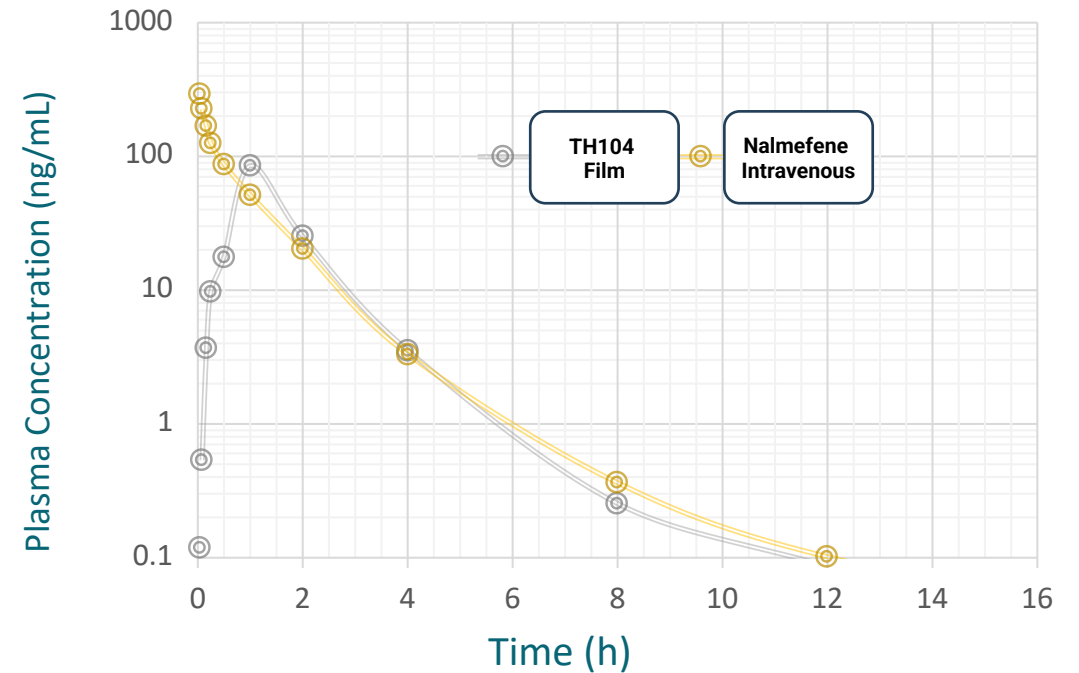
TH104 Offers Once-a-Day, Fast Onset, High Bioavailability

Once-daily Dosing, Rapid Onset (10 min), High Bioavailability (>70%)

Pharmacokinetic Profile of TH104 in Beagle Dogs (N=12)

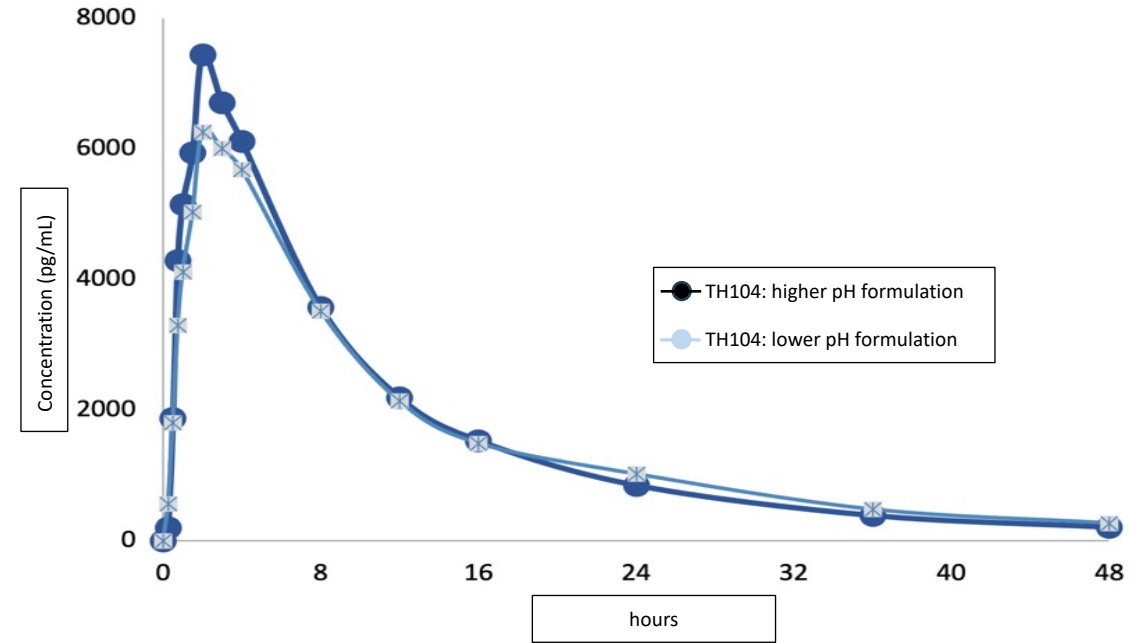
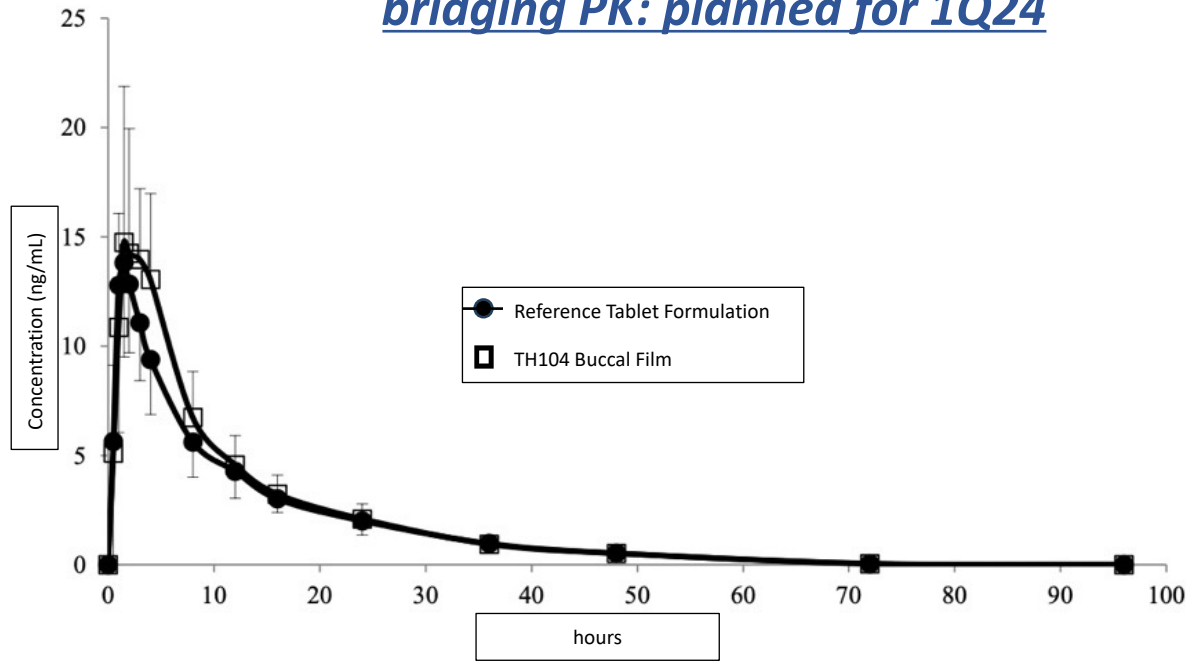


Pharmacokinetic Profile of TH104 in Beagle Dogs (N=12)



TH104 in Healthy Volunteers in Phase 1 Studies (ex-US)

ex-US human data de-risks Phase 1 bridging PK: planned for 1Q24



- **Safe:** Completed all necessary non-clinical studies.
- **Easy to Administer:** Once daily use. Film rapidly sticks in less than 5 seconds to the inner lining of the cheek
- **Attributes:** The entire product dissolves in minutes
- **Regulatory: US IND Granted in February 2023**
- **Ex-US Clinical Data de-risks US Phase 1; IND approved in USA**

Adverse Events (N=12)	Total AE Mild	Total AE Moderate	Total AE Severe
Dizziness	5	0	0
Headache	1	1	0
Somnolence	10	0	0
Nausea	3	0	0
Vomiting	2	0	0

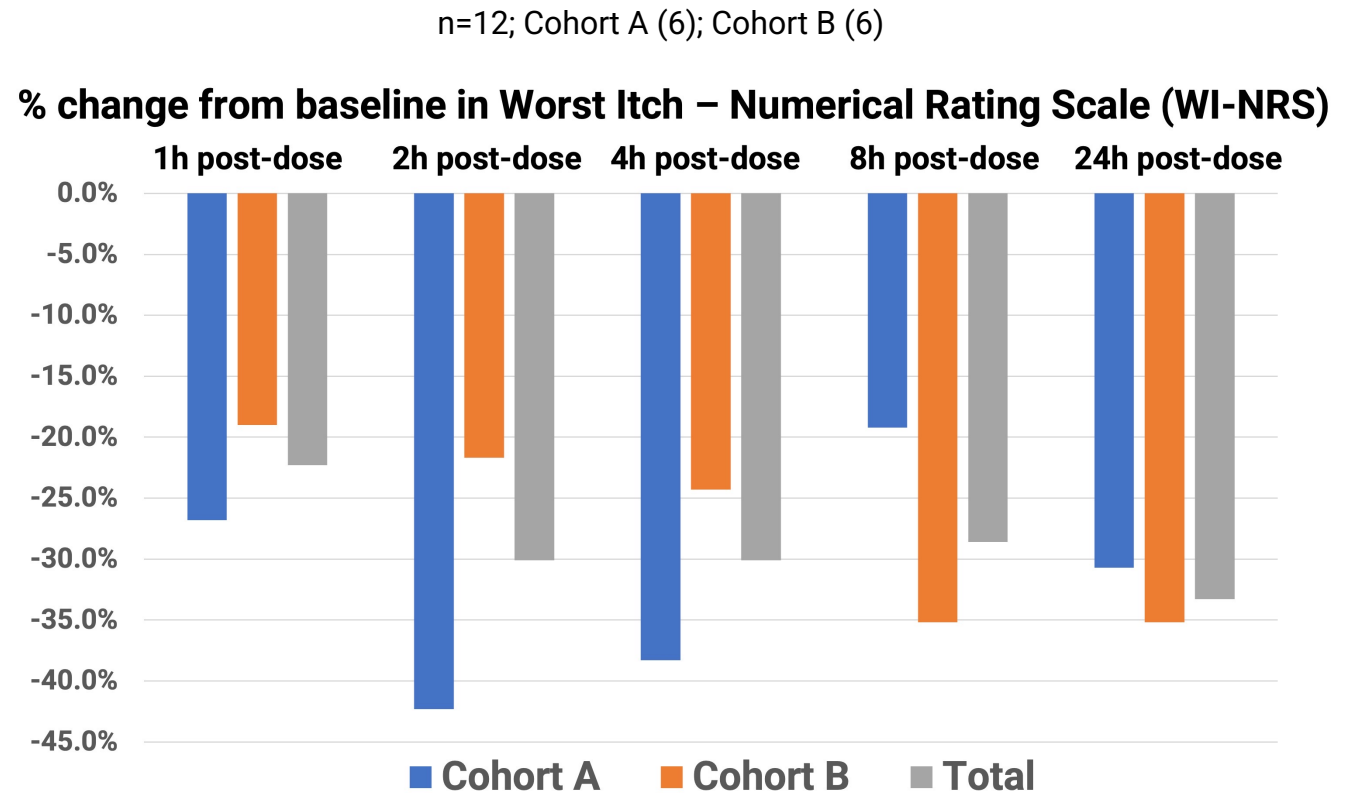
Safety of TH104 in-line with known approved nalmefene formulations

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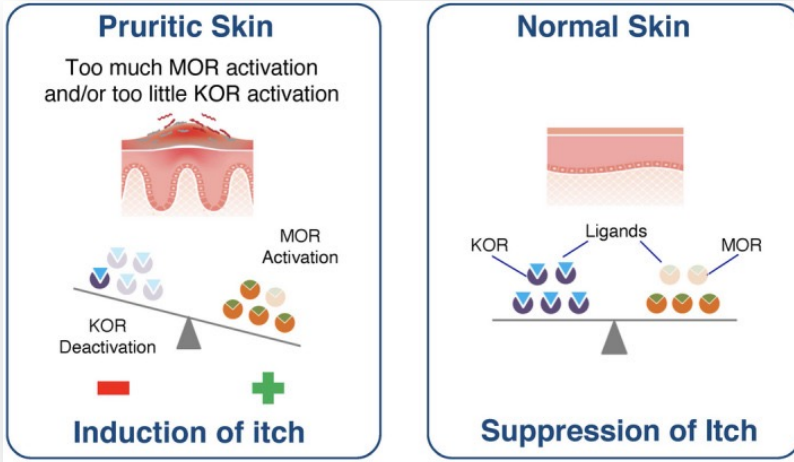
TH104 Phase 1 in Chronic Liver Disease (CLD) ex-US

- **Single-dose, single-center, open-label, randomized, study** of TH104 transmucosal buccal film conducted in India in two different cohorts
- Primary outcome measure: safety and tolerability of a buccal dose of TH104 in CLD patients
- Secondary objective: **response for clinical efficacy for pruritus or “debilitating itching” using a validated endpoint, the Worst Itch-Numerical Rating Scale (WI-NRS)**
- The WI-NRS is a validated numerical rating scale with 11 numbers anchored at 0 representing “no itch” to 10 representing “worst imaginable itch” which are displayed, and patients are asked to pick the number corresponding to the intensity of their pruritus.
- **Enrolled 2 types of CLD patients** including subjects with Child-Pugh A (Cohort A) and Child-Pugh B (Cohort B) categorized CLD
- At 24-hours post dosing, Group A and Group B achieved a mean decline of 30.7% and 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 of TH104.**



Cohort A: Child-Pugh A Liver Cohort; Baseline WI-NRS = 4.33
 Cohort B: Child-Pugh B Liver Cohort; Baseline WI-NRS = 6.17
 Total: Baseline WI-NRS = 5.25

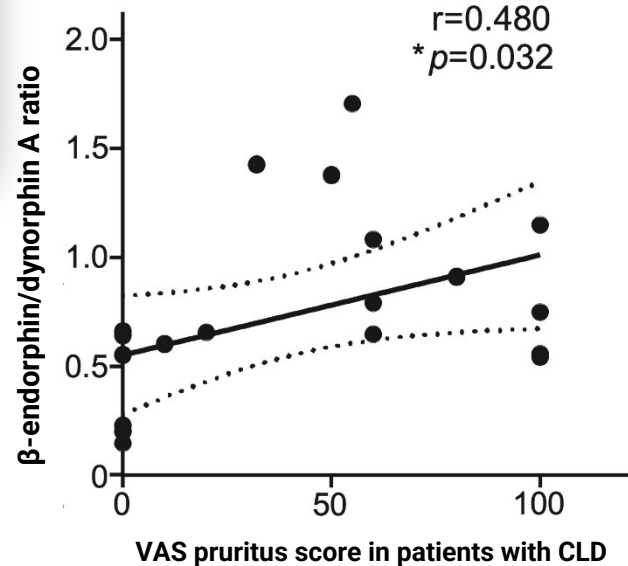
Mechanism of Action: Modulation of MOR/KOR



Itch circuitry is imbalanced in certain pruritogenic conditions such as liver and atopic diseases¹

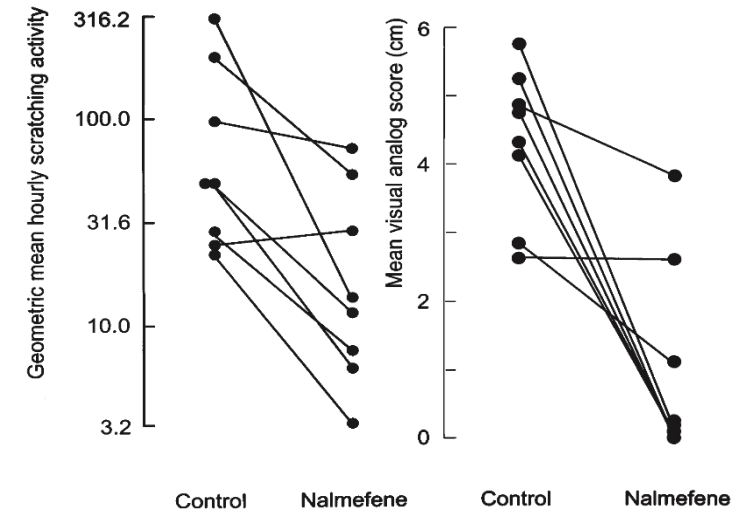
MOR – mu opioid receptor
KOR – kappa opioid receptor

Endogenous Opioids Overexpressed in CLD²



CLD – chronic liver disease

Nalmefene Suppresses Pruritus in PBC Patients³



Oral dose ranging from 40 to 240 mg BID x 12 weeks

- 8 patients who received at least 1 course of nalmefene available for comparison with corresponding control data, (a course of placebo and/or at baseline)
- Nalmefene therapy was associated with a 75% reduction in hourly scratching activity ($P < .01$)
- Achieved decrease in the mean of a visual analogue score of the perception of pruritus in all 8 patients (mean decrease 77%, $P < .01$).

TH104 Could Suppress Inflammation in PBC

IL-17 expression in PBC patients in liver tissues is significant¹

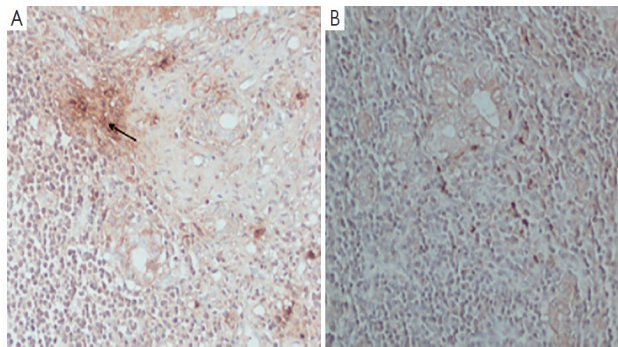
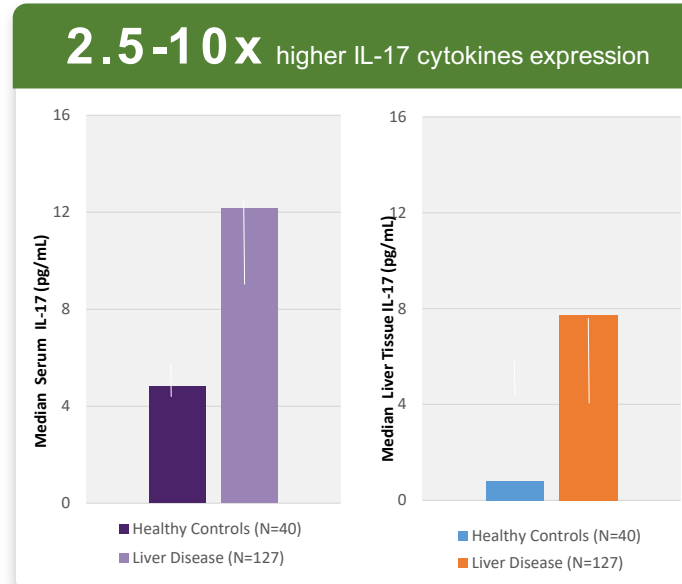


Figure 2 IL-17 expression in liver tissue of primary biliary cirrhosis (PBC) group and healthy control group (immunohistochemical staining, $\times 200$). (A) PBC group; (B) healthy control group. Arrows indicate IL-17 positive cells in PBC liver tissue.

Table 9 IL-17 expression levels in liver tissues of each group

Cytokine	Primary biliary cirrhosis (PBC) group (n=20)	Healthy control group (n=4)	P value
IL-17	7.74 \pm 2.06	0.82 \pm 0.39	P<0.01

IL-17 Overexpressed in PBC¹

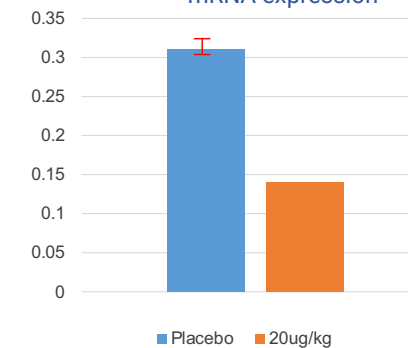


TH104 has the potential to suppress the high IL-17 expression in PBC patients

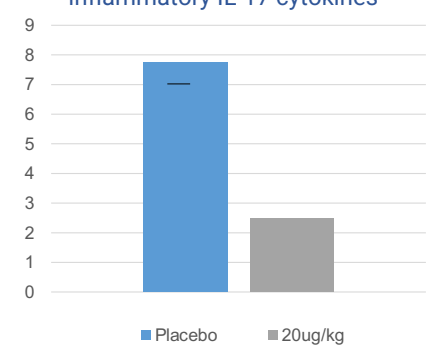
Nalmefene Shows Anti-IL-17 Effects

Anti-inflammatory Activity of *nalmefene* in Sprague Dawley Rats

nalmefene inhibits TLR4 mRNA expression



nalmefene reduces inflammatory IL-17 cytokines



De-Risked US Phase 1 Study Initiated in 1Q24

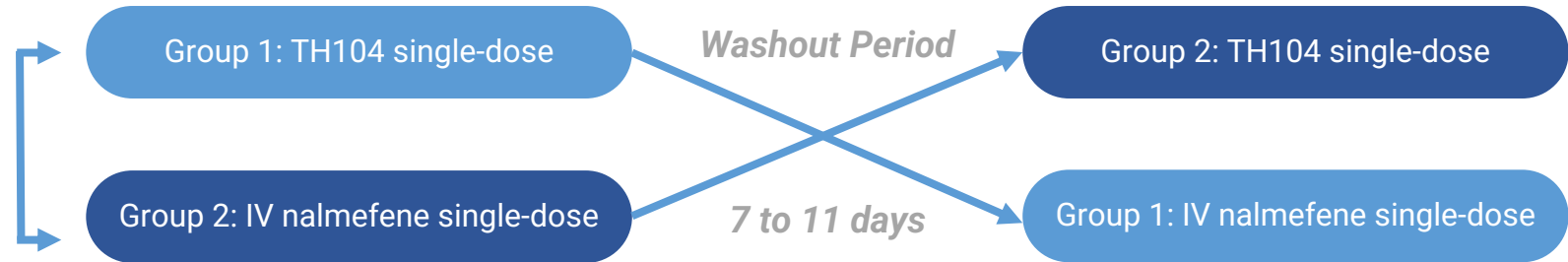
Study population:

enrollment of adult (> 18 years)
healthy volunteers

N = 16
1:1 male:female

Primary Endpoint:
**Absolute Bioavailability
of TH104**

Secondary Endpoint:
**Tolerability of TH104
compared to I.V.
nalmeferene**

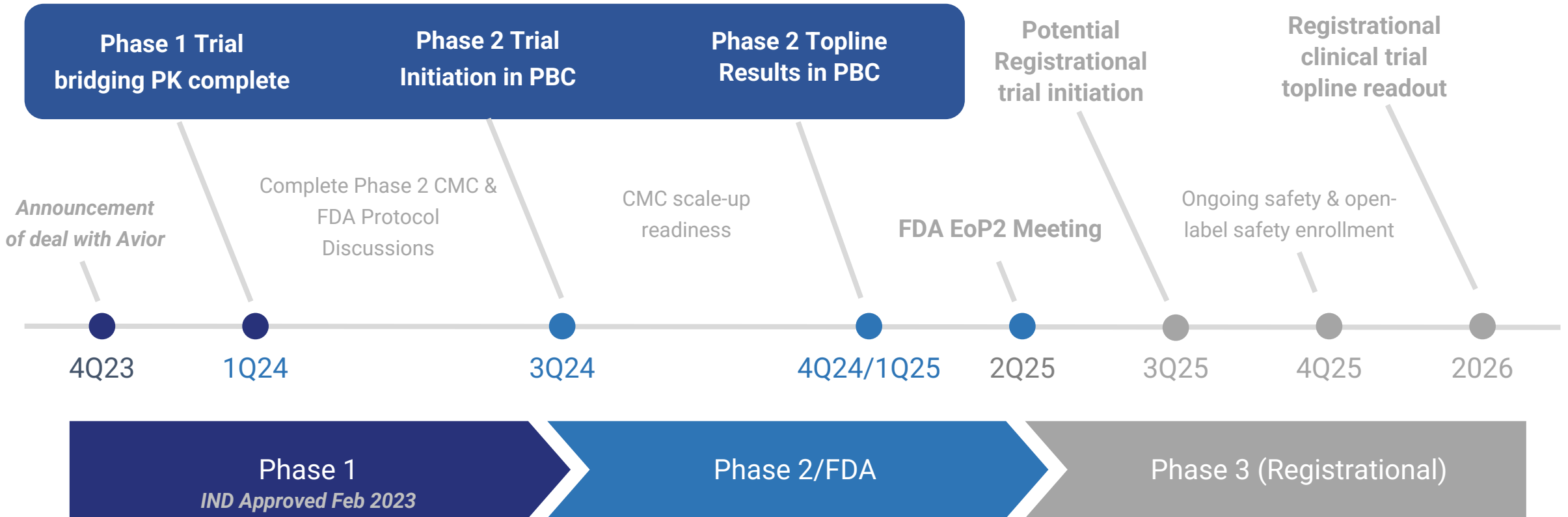


Timeline: completion in 1Q24; topline readout 2Q24

*This is a single-dose, single-center, open-label, randomized, 2-way crossover study (2 treatments, 2 periods and 2 sequences) of TH104 (a buccal formulation of nalmeferene) and an intravenous dose of nalmeferene injection, with a least 7 days washout period between doses. Sixteen (16) normal healthy volunteers (8 male and 8 female volunteers) will participate in the study. Study drug will be given under fasting conditions.

Anticipated Major Milestones Over 24 months

Significant milestones over next year

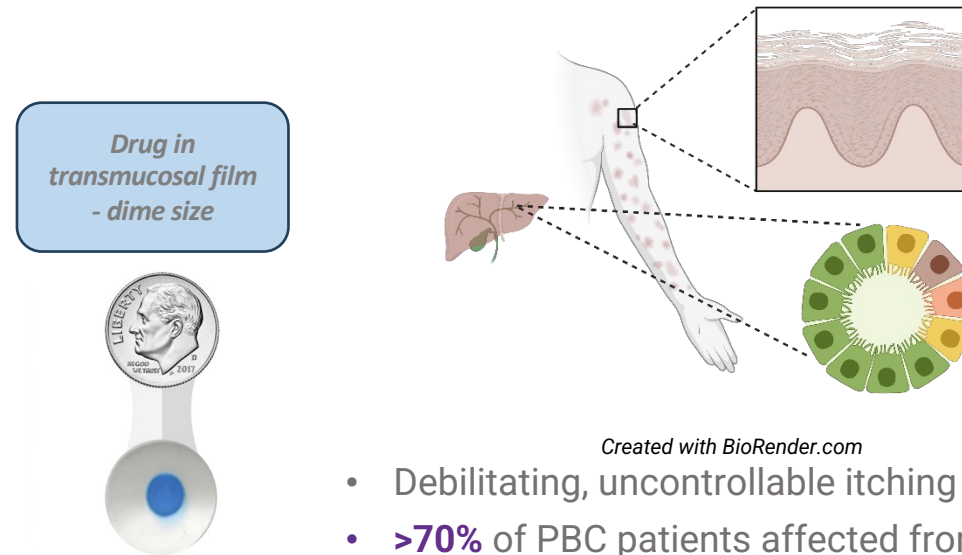


Anticipated Timeline: After alignment with FDA Post Phase 1 Trial

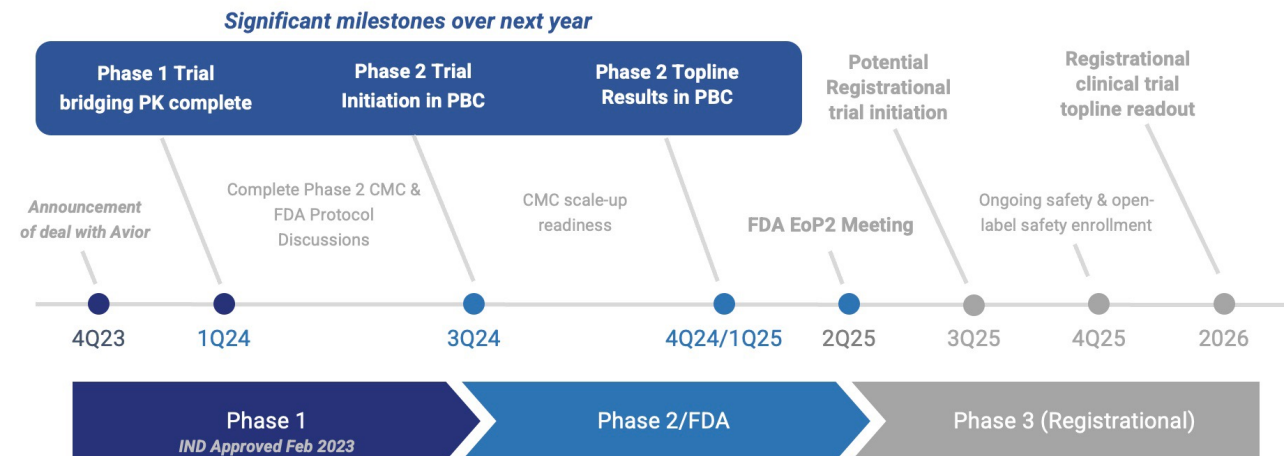
Phase 2 Launch in 2024 for *Chronic Pruritis in PBC*

- Clinically de-risked, **safe, small molecule**
 - US IND approved in Feb 2023
 - Phase 1 PK trial in 2024
 - Phase 2 efficacy readout by 4Q24/1Q25
- Indication: **chronic pruritis in PBC**
 - Primary biliary cholangitis (PBC) is an orphan liver disease
 - Validated approval endpoint (*same used by Regeneron's Dupixent*)
- Expand into other liver diseases and inflammatory pruritogenic conditions
 - **Atopic dermatitis** >\$15 Billion market
 - Multiple published clinical series showing reduction in pruritis
- **Active drug (nalmefene): transmucosal film product**
 - Validated mechanism: MOR/KOR activation & IL-17 inhibition
 - De-risked CMC using proprietary transmucosal film technology
 - Two issued patents
 - *Nalmefene only approved by i.v. & intranasal route for opioid overdose (acute indication). Not approved as an oral drug¹*

1. FDA Orange Book - Approved Drug Products with Therapeutic Equivalence Evaluations: <https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm>



- Debilitating, uncontrollable itching
- **>70%** of PBC patients affected from pruritus
- **65%** patients have “nocturnal pruritus”



Anticipated Timeline: After alignment with FDA Post Phase 1 Trial

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