

THARIMMUNE

Unlocking Immunology for a Better Tomorrow

Corporate Presentation

June 2024



Forward Looking Statements

This presentation contains certain statements which 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 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, 2023 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.

Tharimmune (Nasdaq: THAR) Company Highlights



TH104: De-risked Clinical Program with approved active + novel delivery

Recently completed Phase 1 study. Positive safety readout and topline full readout completed 1H24
Anticipate initiation of Phase 2 in 2024 with potential Registrational Trial ready in 2025



Currently Funded into 2025

Company completed transaction for \$11M public offering in 4Q23



Estimated Large Annual Market Opportunity for Pruritis Expansion

Initial indication: moderate-to-severe chronic pruritus in primary biliary cholangitis
Indication expansion to Pruritogenic Diseases, including atopic dermatitis (>\$15 Billion market)



Expanded Pipeline and Platform Technologies

Bispecific ADC to target novel conformational epitopes on high value validated targets: HER2/HER3
Knob Domains– smallest known antibody fragments targeting undruggable epitopes



IP Protection of Assets

Multiple US Patents with wholly-owned Global commercial rights to pipeline

Pipeline and Anticipated Milestones

Stage	Candidate	Modality & Indication	Preclinical	Phase 1	Phase 2	Anticipated Milestones
Clinical Stage	TH104 MOR/KOR (+ ↓IL-17)	<p>Transmucosal Film : avoids first pass liver effect</p> <p>Moderate-to-Severe Chronic Pruritis in Primary Biliary Cholangitis</p>	<p><i>Phase 2 Ready*</i></p>			<p>2024: 2Q: Ph1 Readout</p> <p>Ph2 Initiation</p> <p>2025: Ph2 Topline Readout</p> <p>Potential Registration Trial Initiation</p>
		<p>Undisclosed Indication</p>	<p><i>Phase 1 Ready*</i></p>			
Early Stage	<p>PD-1/HER2/HER3</p> <p>Multi-specific Knob Domain Platform</p>	<p><i>Bispecific Antibodies/ADCs for multiple solid tumors</i></p>				<p>2024: Pre-clinical Studies</p> <p>2025: IND enabling studies</p>

*Pending discussions with FDA


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Lead Asset:
TH104



Chronic Pruritis Highly Prevalent in Liver Disease Patients

Primary Biliary Cholangitis

Affects 1 in 1,000 women over 40
< 200k US patients¹
(similar in EU4+UK)

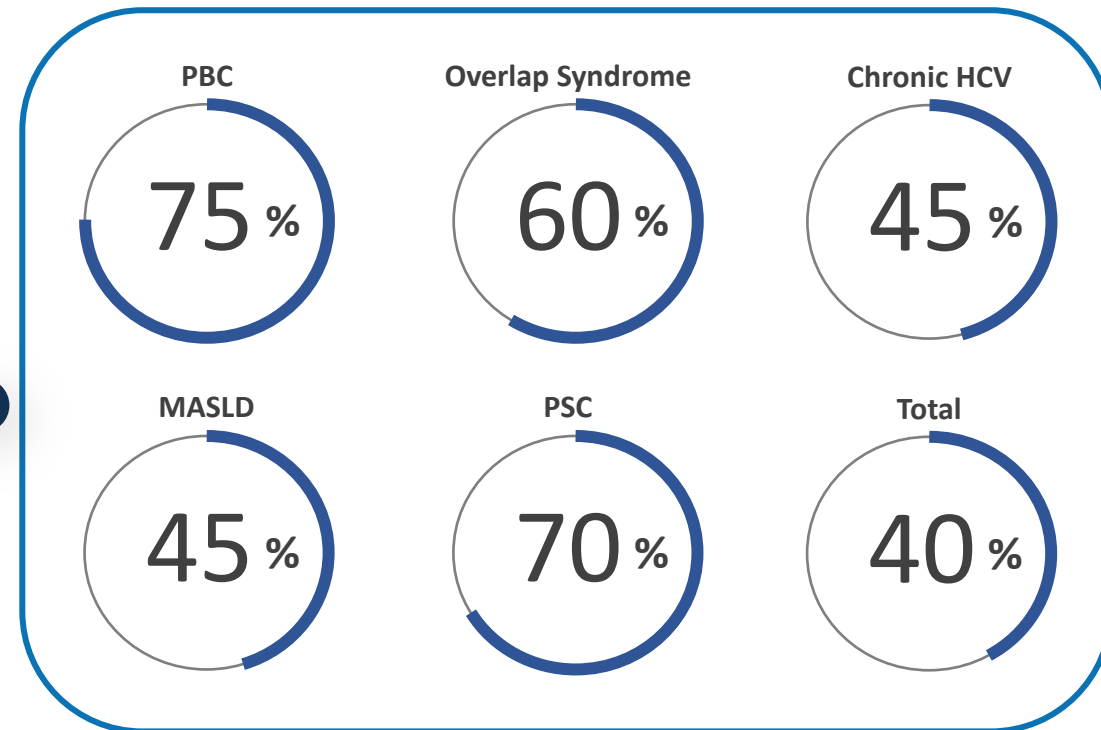


>70%

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



Prevalence of pruritus in liver diseases^{2,3,4}



1. Lu, M et. al. Clin Gastro Hepatol 2018 Aug;16(8):1333-1341.e6. doi: 10.1016/j.cgh.2017.10.018)

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)

4. Nietsche Cholestatic pruritus: a knowledge update, Anais Brasileiros de Dermatologia, Volume 97, Issue 3, 2022.

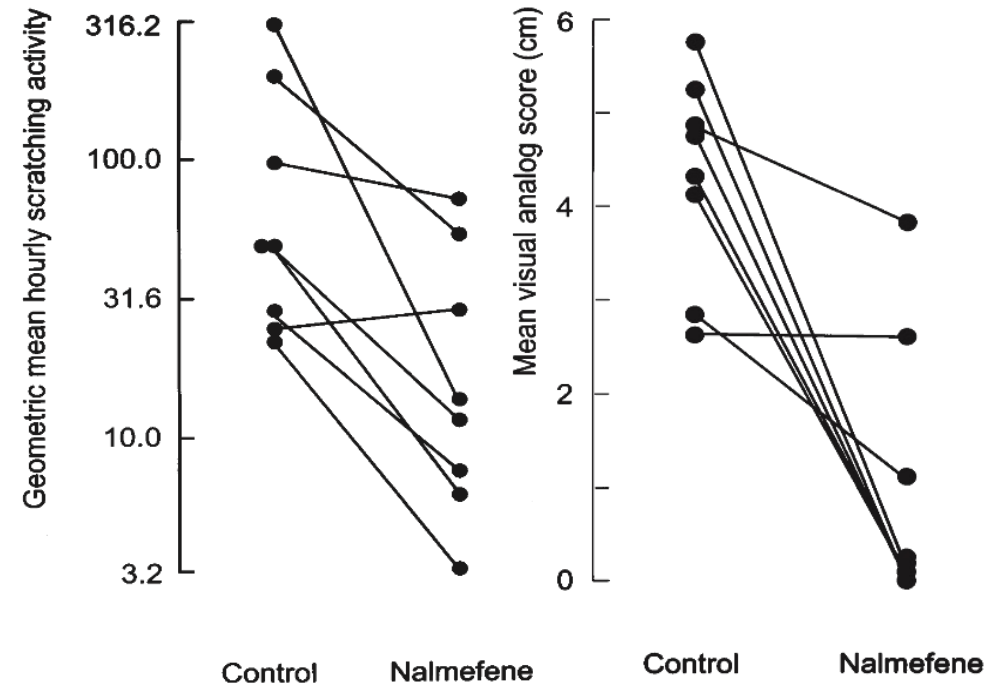
Nalmefene: Established Proof-of-Concept with Limitations

Nalmefene is currently only approved in US as intravenous and intranasal routes for acute use: opioid overdose*

Not ideal for chronic use

Oral route (approved in Europe) explored with high doses potentially due to first pass liver metabolism¹; Efficacy established in PBC patients with pruritus, but avoidance of liver metabolism could be beneficial in liver impaired patients.

Nalmefene Suppresses Pruritus in PBC Patients¹



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

Nalmefene therapy was associated with a 75% reduction in hourly scratching activity ($P < .01$)

1. Bergasa N et. al. Oral nalmefene therapy reduces scratching activity due to the pruritus of cholestasis: a controlled study J Am Acad Dermatol 1999;41:431-4
*Tablet formulation approved in Europe for Alcohol Use Disorder

TH104: Proprietary Biodegradable Transmucosal Buccal Film

The Phase 1 study demonstrated TH104 oral film had comparable safety and tolerability to IV

Drug film is dime-sized



Adheres to inner-cheek



TH104: Nalmefene transmucosal film

- Validated mechanism: MOR/KOR activation (+ IL-17 inhibition)
- De-risked CMC using proprietary transmucosal film technology
- Two issued patents with multiple patents pending

TH104
developed by
embedding drug
onto proprietary
transmucosal
film

- Once-Daily Dosing
- Rapid Onset
- High Absorption

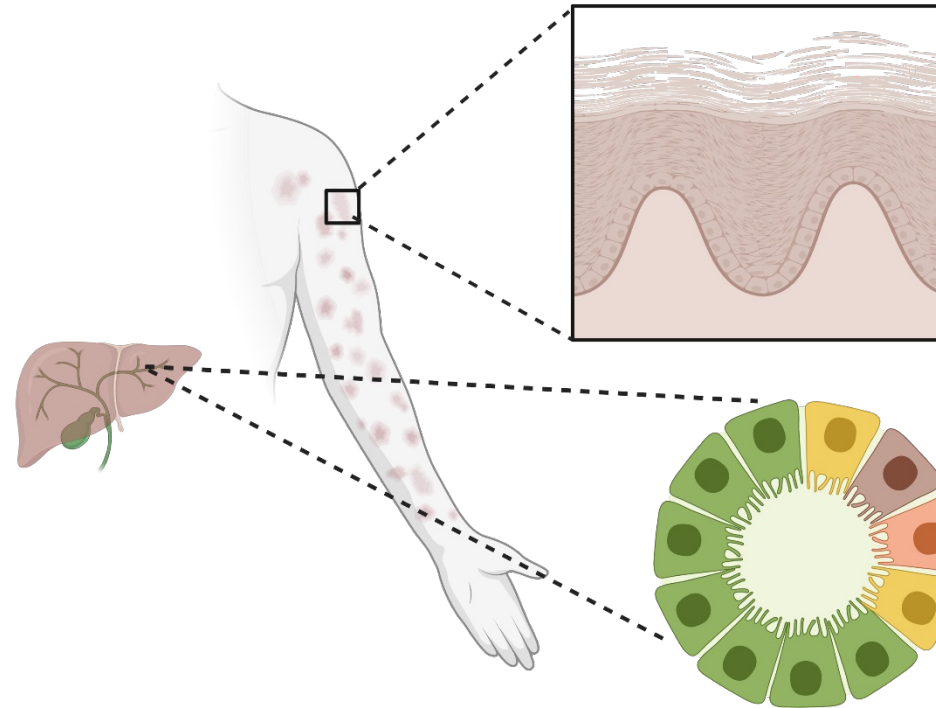
**TH104 designed
to bypass the
liver**
*(no first pass
effect)*

- Absorbed in oral mucosa & distributes to skin
- Designed to treat liver impaired conditions

Initial Indication: Moderate-to-Severe Chronic Pruritus (itching) in PBC

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

- PBC is an **orphan disease** in the USA and Europe, with <200k patients in the US.
- Affects men & women (rate higher in women: ~ 1 in 1,000 > 40 years old)²
- **65% of patients** have “worse **nocturnal pruritus**” with 71% of patients stating a disturbance in their sleep³



More than 70% of Primary Biliary Cholangitis (PBC) patients affected by pruritus¹

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

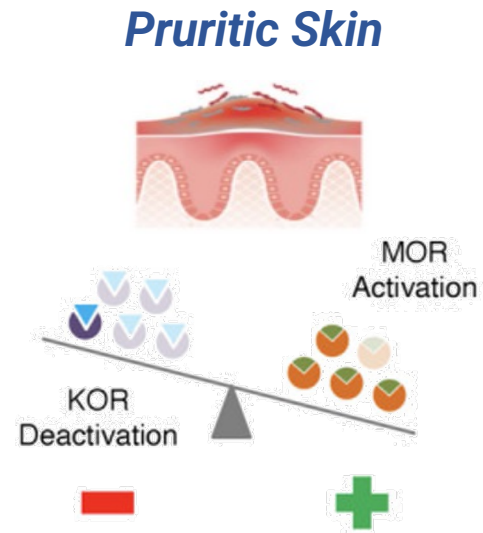
1. Gungabissoon U, et al. BMJ Open Gastro 2022;9:e000857. doi:10.1136/bmjgast-2021-000857

2. <https://www.healthywomen.org/condition/primary-biliary-cholangitis-pbc>

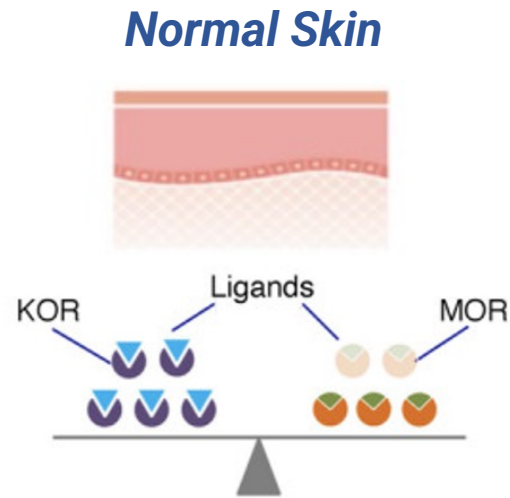
3. Rishe et. al. Itch in Primary Biliary Cholangitis: A Patients' Perspective Acta Derm Venereol 2008; 88: 34-37

4. <https://www.niddk.nih.gov/health-information/liver-disease/primary-biliary-cholangitis/definition-facts>

TH104 Mechanism of Action: Modulation of MOR/KOR



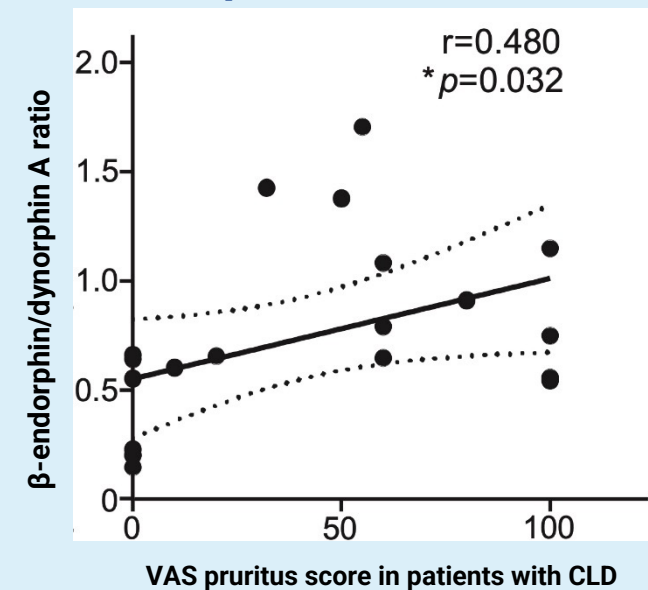
Induction of itch from overactivation of MOR and/or KOR deactivation



THAR104 looks to balance MOR and KOR activation to relieve pruritis

Kappa-opioid receptors (KORs) and mu-opioid receptors (MORs) have been implicated in both the suppression and promotion of itch, respectively, and pronounced in conditions such as liver and atopic diseases

Endogenous Opioids Overexpressed in CLD²



CLD – chronic liver disease

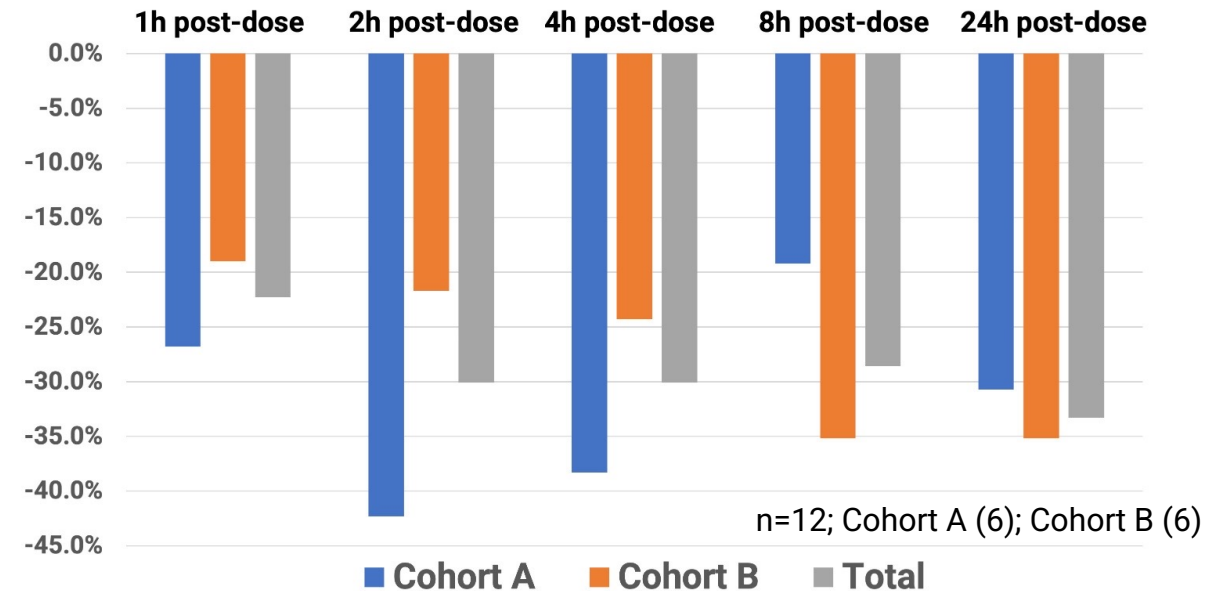
1. Kim, BS, et. al. Role of kappa-opioid and mu-opioid receptors in pruritus: peripheral and central itch circuits. *Exp Dermatol.* 2022; 31: 1900-1907. doi: 10.1111/exd.14669
2. Moniaga CS, et. al. Plasma dynorphin A concentration reflects the degree of pruritus in CLD *Acta Derm Venereol.* 2019 Apr 1;99(4):442-443. doi: 10.2340/00015555-3139.

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

All Patients Responded to TH104

- **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)**
- **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.**

% change from baseline in Worst Itch – Numerical Rating Scale (WI-NRS)



Cohort A: Child-Pugh A Liver Cohort; Baseline WI-NRS = 4.33

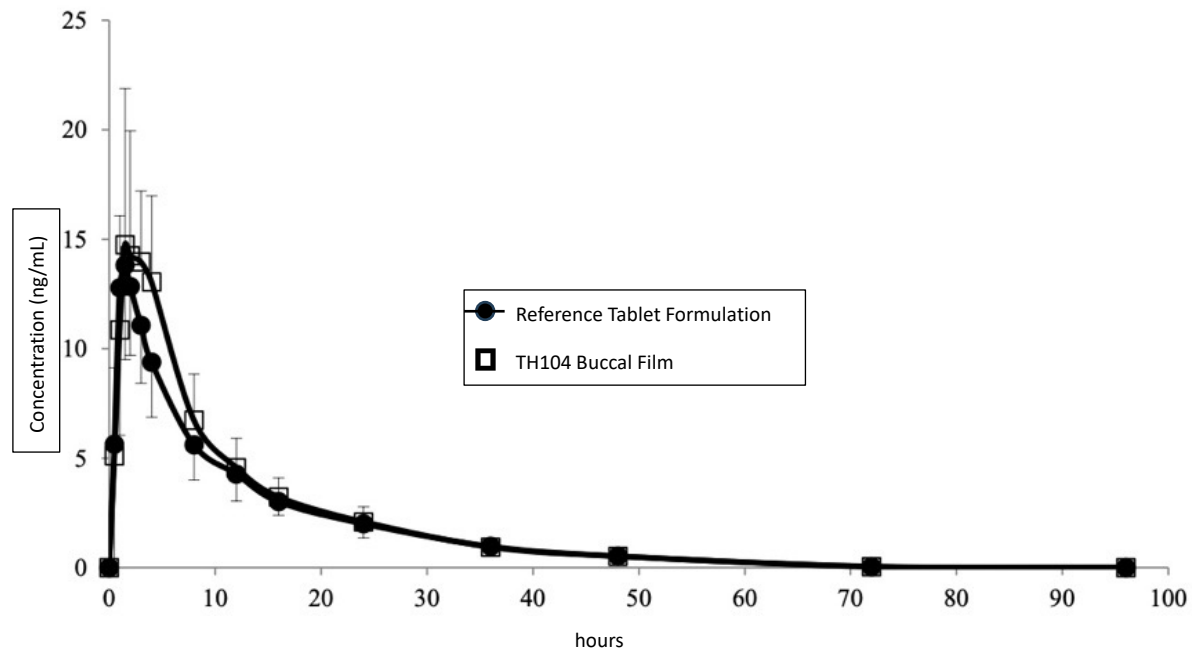
Cohort B: Child-Pugh B Liver Cohort; Baseline WI-NRS = 6.17

Total: Baseline WI-NRS = 5.25

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.

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

Once-daily Dosing, Rapid Onset, High Bioavailability



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

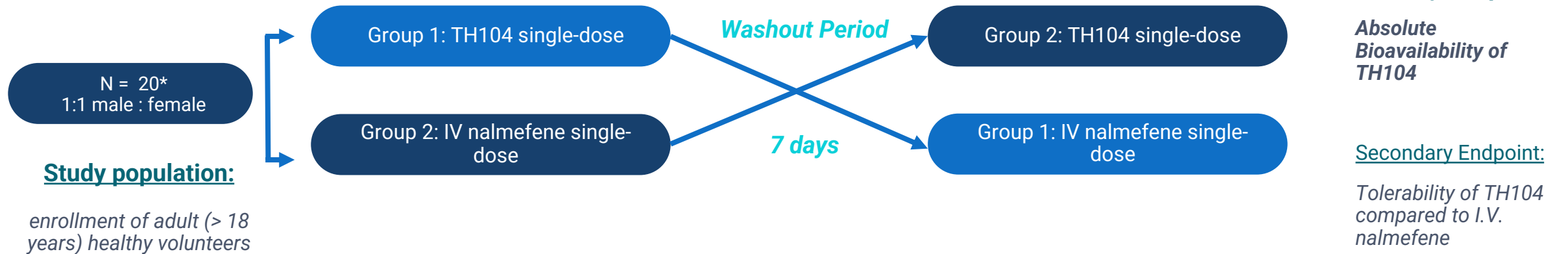
- **Safe:** Well tolerated in all Human Phase 1 Trials
- **Easy to Administer:** Once daily use. Detected in plasma < 15 min
- **Attributes:** The entire product dissolves in minutes

Safety of TH104 in-line with known approved nalmefene formulations

US Phase 1 Study Complete: Positive Safety & Tolerability Reported

Study Design:

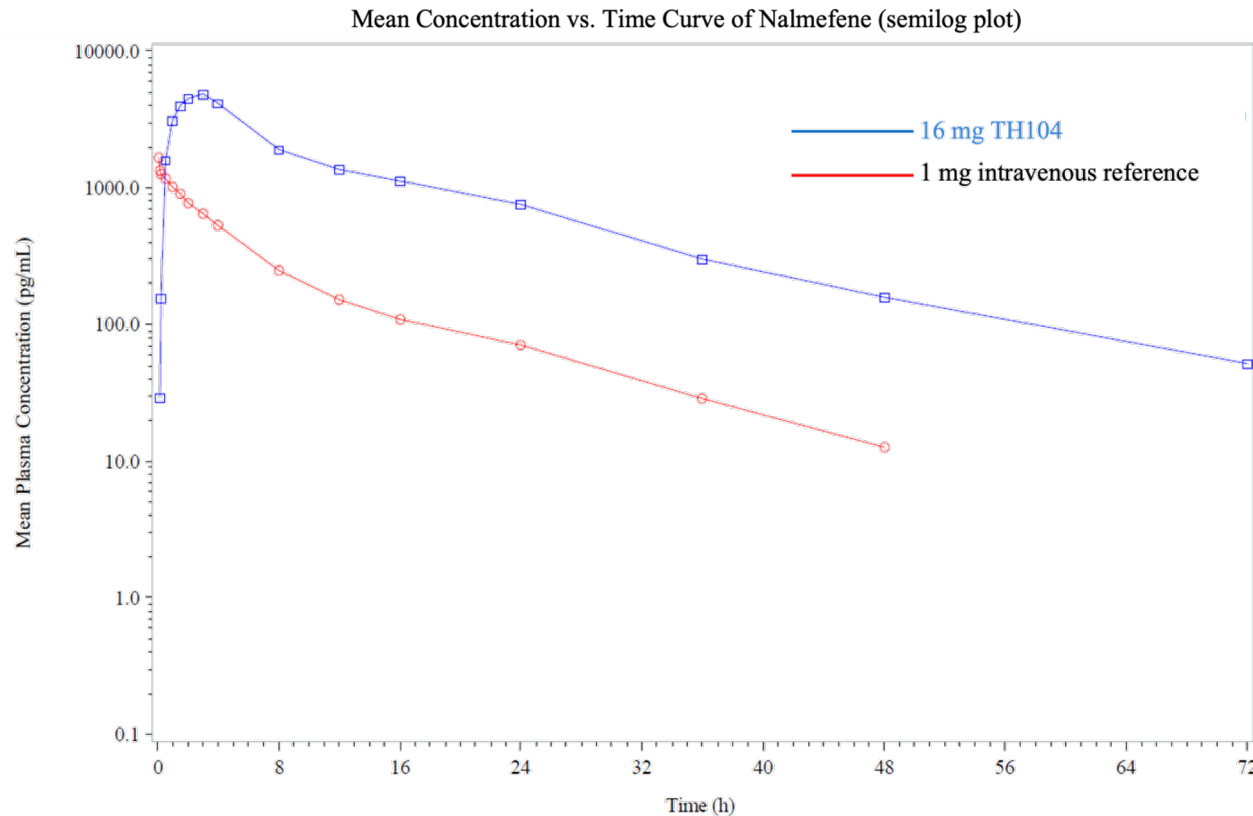
Single-dose, single-center, open-label, randomized, 2-way crossover study (2 treatments, 2 periods and 2 sequences) of TH104 and an intravenous dose of nalmefene injection, with a 7-day washout period between doses.



No serious adverse events reported during this study. No subjects discontinued the study due to adverse events. No subjects exhibited abnormal results for the visual examinations of the buccal mucosa pre- or post-dosing with TH104 buccal film

*All 20 subjects completed TH104 buccal dosing, while 19 of 20 subjects also completed the intravenous dosing

TH104 Demonstrated Favorable Pharmacokinetic Profile Compared to IV Dosing



Pharmacokinetic profile of oral transmucosal delivery of TH104 was comparable to intravenous delivery of reference drug

PK Profile:

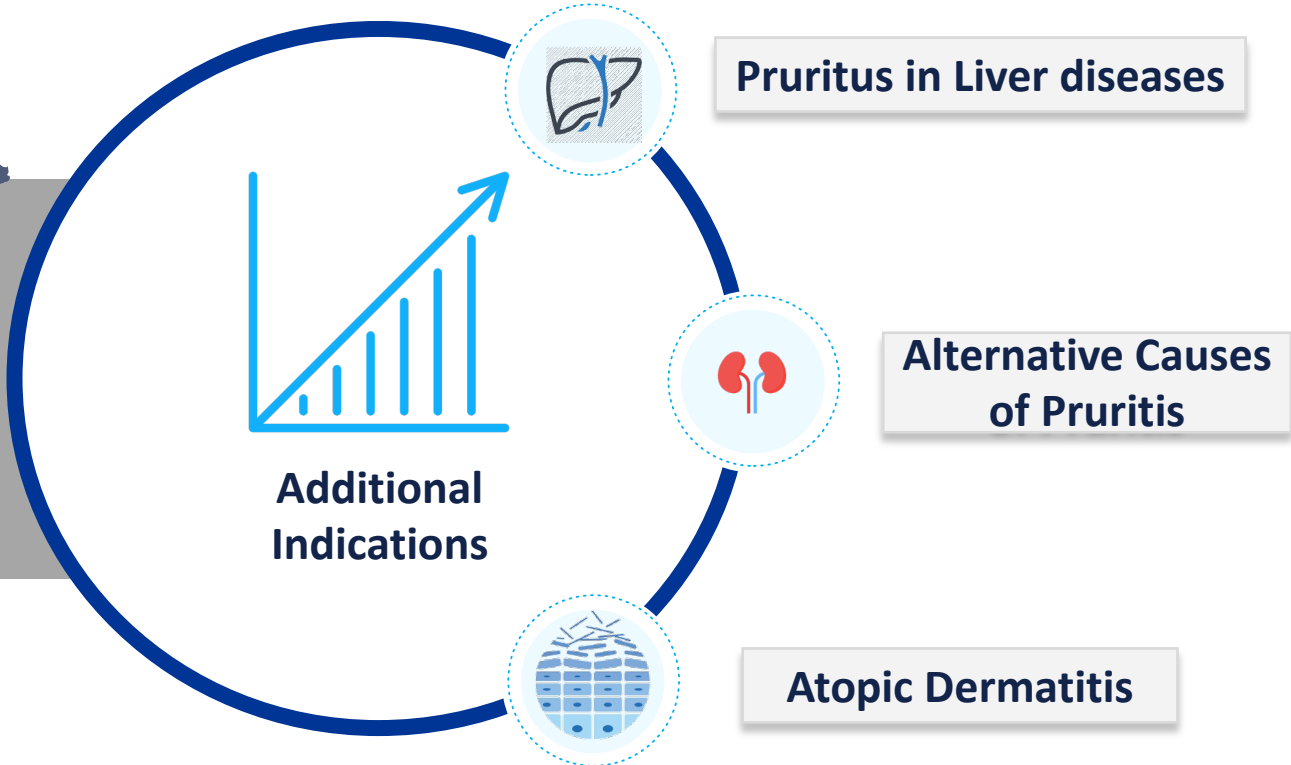
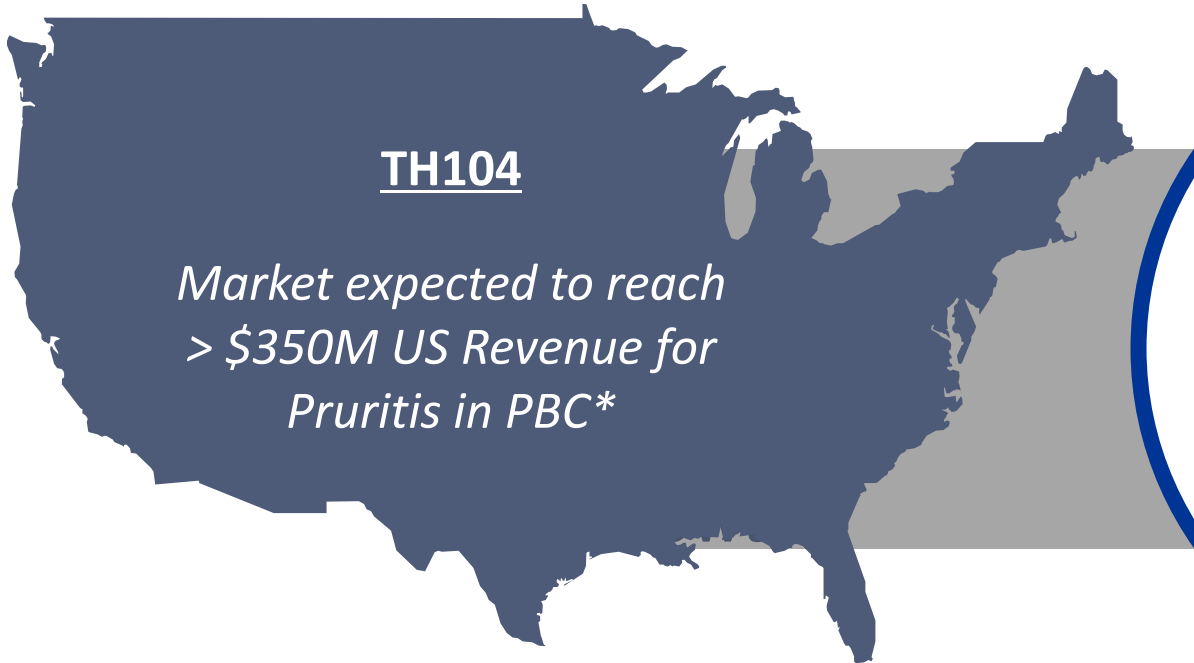
- Primary endpoint of the absolute bioavailability*: 0.459 (45.9%)
- Median time to maximum concentration (C_{max}): 2.0 hours
- Mean half-life ($T_{1/2}$): 14 hours

AE Profile:

- Treatment emergent adverse events (TEAEs) reported in 8 subjects (40.0%) in TH104 group; 7 subjects (36.8%) in IV
- All reported TEAEs were considered mild in severity
- Most frequently reported TEAE in both groups was dizziness (4 TH104 group; 7 intravenous)
- TEAEs reported in at least 2 subjects in any treatment group were nausea (3 in each group) and somnolence (3 in each group).

* fraction (or percentage) of the administered dose absorbed into the systemic circulation compared to an equivalent intravenous dose of nalmefene

Primary Biliary Cholangitis Associated Pruritis Market



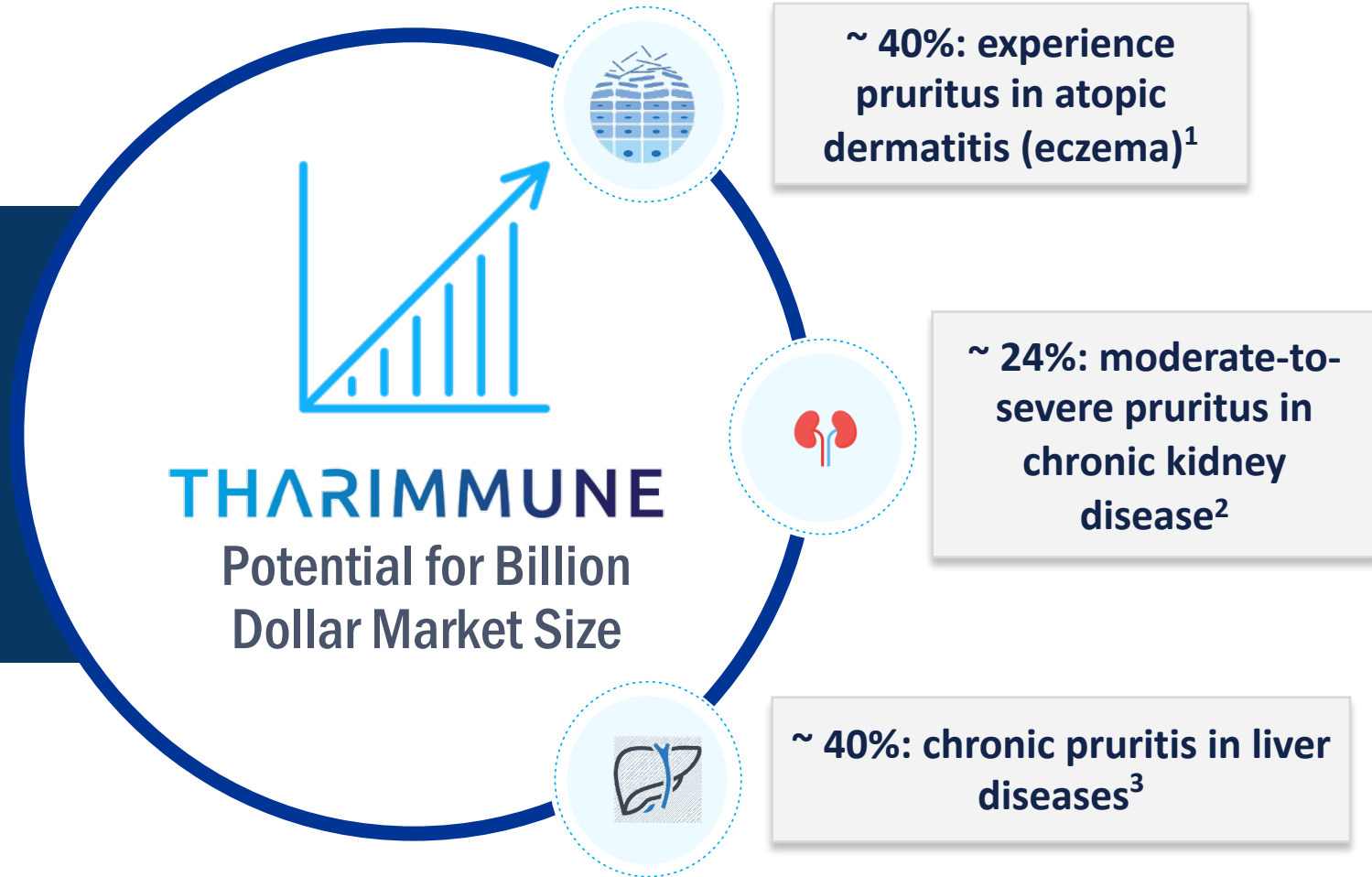
*Based on Company Assumptions: 40% of patients in PBC market suffering from chronic moderate-to-severe pruritis; TH104 addresses 1st Line (ursodeoxycholic acid) and 2L (obeticholic acid + potential seldelapar and/or elafibranor markets)

Indication Expansion to Inflammatory Pruritogenic Diseases

2.7 M atopic dermatitis patients experience from pruritus¹

1.3 M chronic kidney disease patients suffer from pruritus⁴

1.7 M chronic liver disease patients affected by chronic pruritus⁴



1. Atopic Dermatitis in America Study. Asthma and Allergy Foundation of America and National Eczema Association
2. Sukul et. al. Pruritus 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. Tables of Summary Health Statistics for U.S. Adults: 2018 National Health Interview Survey. National Center for Health Statistics. 2019

PBC and Pruritis Competitive Landscape¹

PBC Treatments



\$4.3B Acquisition

Lead Asset: seldelapar for the treatment of PBC



GNFT MC:\$180mm

Lead Asset: elafibranor for treatment of PBC, does not treat pruritis. €120m upfront and up to €360m in milestone payments via licensing deal with Ipsen



Acquisition by Alfasigma

Lead Asset: obeticholic acid second-line treatment for PBC which generated revenue of \$152 million in 1H 2023

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Once daily buccal treatment for moderate-to-severe pruritus in PBC

Company has commercial applicability in PBC pruritis and other pruritic pathologies

Pruritis Treatments



\$942m Acquisition by Ipsen

Lead Asset: odevixibat Approved in 2021 in the U.S. for the treatment of pruritis in pediatric patients with progressive familial intrahepatic cholestasis



MIRM MC:\$1.2B

Lead Asset: maralixibat Oral solution for the treatment of cholestatic pruritis in patients five and older with progressive familial intrahepatic cholestasis



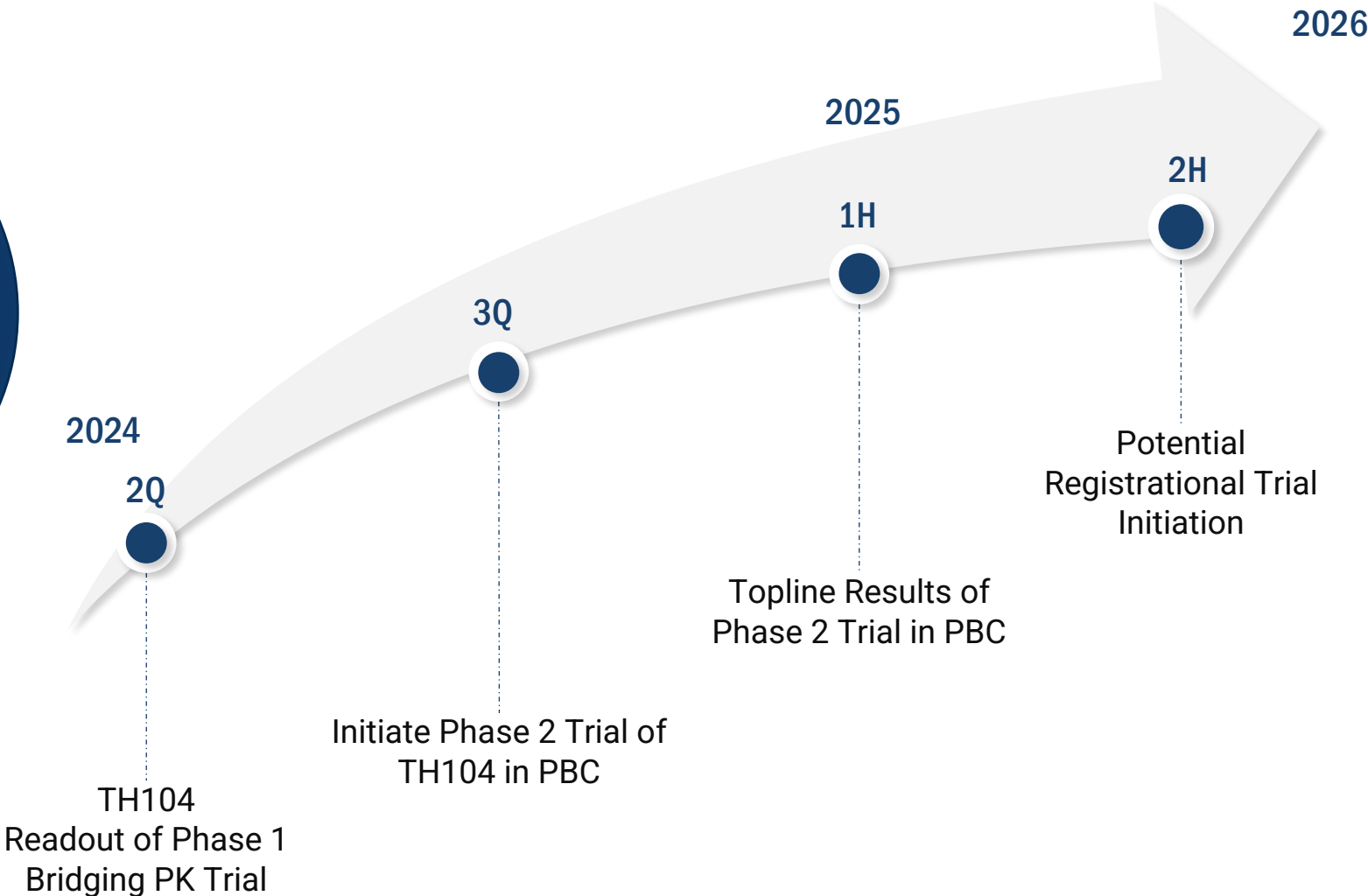
Peak MC: \$1.46B

Lead Asset: difelikefalin Injection for moderate-to-severe pruritis associated with chronic kidney disease in adults undergoing hemodialysis.

1. All data retrieved from public SEC filings

Company's Upcoming Milestones

2 Near Term Clinical Readouts



Experienced Leadership with a Successful Track Record

Executive Team



Randy Milby
Chief Executive Officer



Sireesh Appajosyula
Chief Operating Officer



Thomas Hess, CPA.
Chief Financial Officer



Nir Barak, MD.
Chief Medical Officer



Board of Directors

Randy Milby

Chairman of the Board



Leonard Mazur

Director



Lynne A Bui

Director



Sireesh Appajosyula

Director



Kelly Anderson

Director



THARIMMUNE

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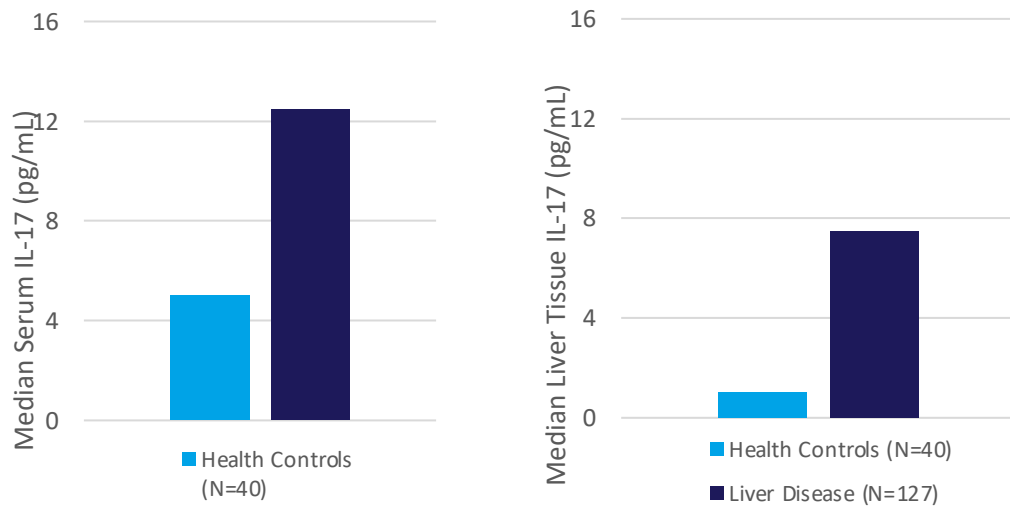
Nasdaq: THAR | tharimmune.com

APPENDIX

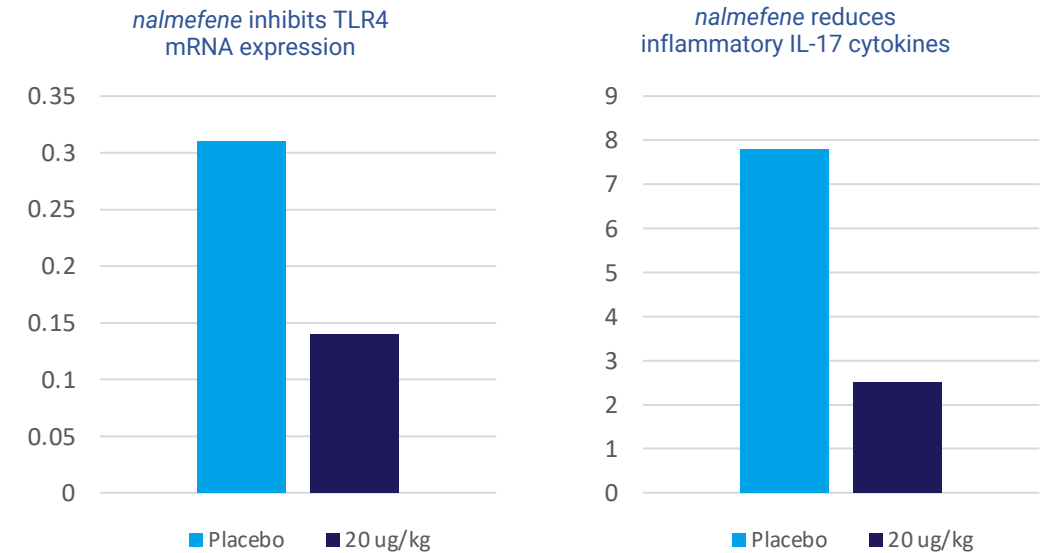


TH104 has the potential to suppress the high IL-17 expression in PBC patients

IL-17 is Overexpressed in PBC¹



Nalmefene Shows Anti-IL-17 Effects²



2.5-10X Higher IL-17 Cytokine Expression in Patients with Liver Disease

Anti-inflammatory Activity of nalmefene in Sprague-Dawley Rats

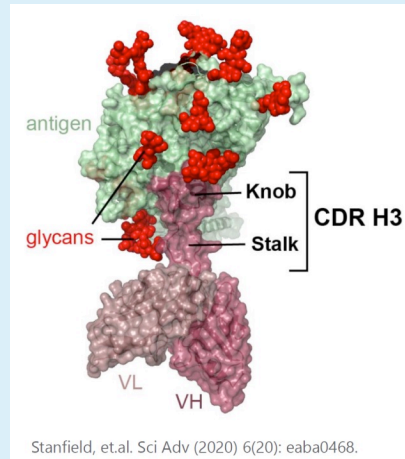
1. Sun, Q et. al. The expression and clinical significance of serum IL-17 in patients with PBC. Ann Transl Med 2019;7(16):389 doi:10.21037/atm.2019.07.100
2. Zhang NL et. al. Effects of nalmefene on TLR4 signaling pathway in rats with LIRi Eur Rev Med Pharmacol Sci 2020; 24:461-468

Knob Platform: Next Generation Knob Domain Therapeutics

KNOB Platform

Transformative platform technology

Multiple targets
First-in-class, modular cow-derived nano antibodies



PNAS

RESEARCH ARTICLE | IMMUNOLOGY AND INFLAMMATION

OPEN ACCESS



The smallest functional antibody fragment: Ultralong CDR H3 antibody knob regions potently neutralize SARS-CoV-2

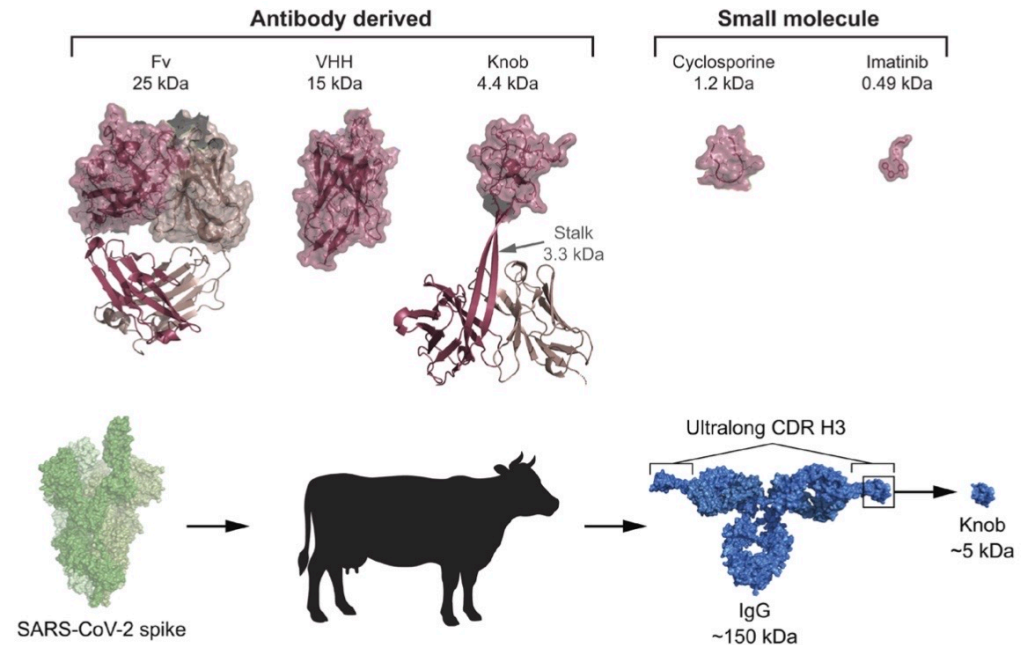
Ruiqi Huang^a, Gabrielle Warner Jenkins^a, Yunjeong Kim^b, Robyn L. Stanfield^c, Amrinder Singh^c, Maria Martinez-Yamout^c, Gerard J. Kroon^c, Jonathan L. Torres^c, Abigail M. Jackson^c, Abigail Kelley^a, Namir Shaabani^d, Baisen Zeng^e, Michael Bacica^f, Wen Chen^f, Christopher Warner^f, Jasmina Radoicic^f, Joongho Joh^g, Krishani Dinali Perera^h, Huldah Sang^b, Tae Kim^b, Jianxiu Yao^b, Fangzhu Zhao^d, Devin Sok^d, Dennis R. Burton^d, Jeff Allenⁱ, William Harriman^o, Waithaka Mwangi^b, Donghoon Chung^h, John R. Tejjaro^d, Andrew B. Ward^c, H. Jane Dyson^c, Peter E. Wright^{cl}, Ian A. Wilson^{cl}, Kyeong-Ok Chang^b, Duncan McGregor^a, and Vaughn V. Smider^{aj,1}

Edited by Andrew C. Kruse, Harvard University, Cambridge

Cows produce antibodies with a disulfide-bonded within ultralong heavy chain third complementa domain is analogous to natural cysteine-rich pept and stable but can accommodate diverse loops immunized cattle with SARS-CoV-2 spike and that could neutralize several viral variants at picon protect from disease in vivo. The independent C and maintained the properties of the parent an SARS-CoV-2 spike was revealed by electron mic spectroscopy, and mass spectrometry and establish as the smallest known recombinant independe other vertebrate antibody fragments, these knobs : domain and have potential as a new class of the:

ultralong CDR3 | knob peptide | phage display | cow ar

The therapeutic response to emerging infectious d several classes of drugs, including biologics and pandemic, initial efforts enabled rapid discovery small molecule drug candidates over a somewha discovery program, the properties of the lead mc



Knobs are Bovine-Derived: Can Be Humanized

Isolation of Knobs

- Mouse and human antibodies use flat binding surfaces formed by CDRs on variable regions of heavy/light chain heterodimers.
- Bovine antibodies feature ultralong CDR-H3 regions that create a "stalk and knob" structure, with the "knob" functioning as an independent binding domain.
- Bovine "knob" components, called Picobodies, are ~4-6 kDa, much smaller than camelid nanobodies, and can target recessed or concave antigenic surfaces.

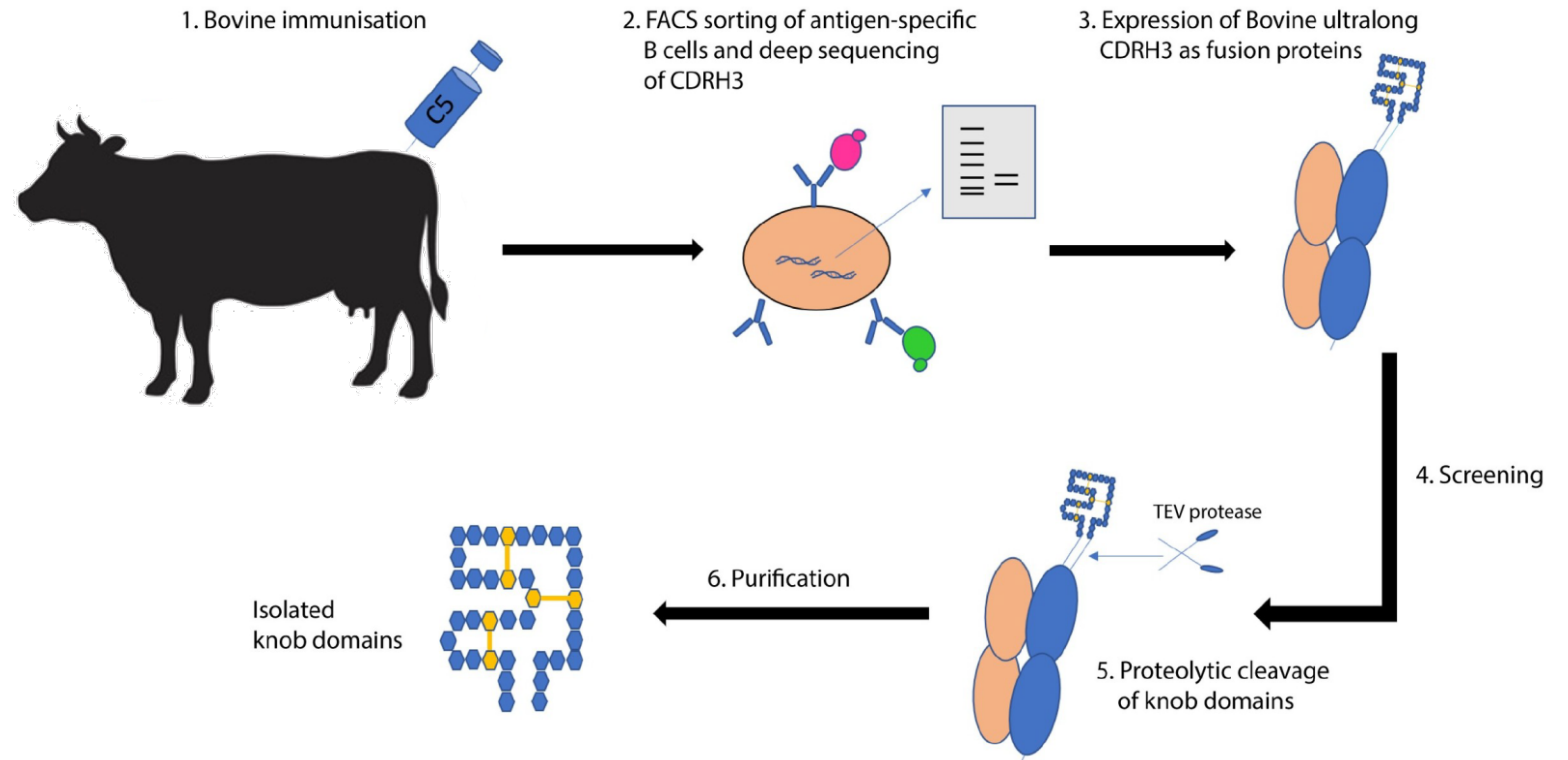
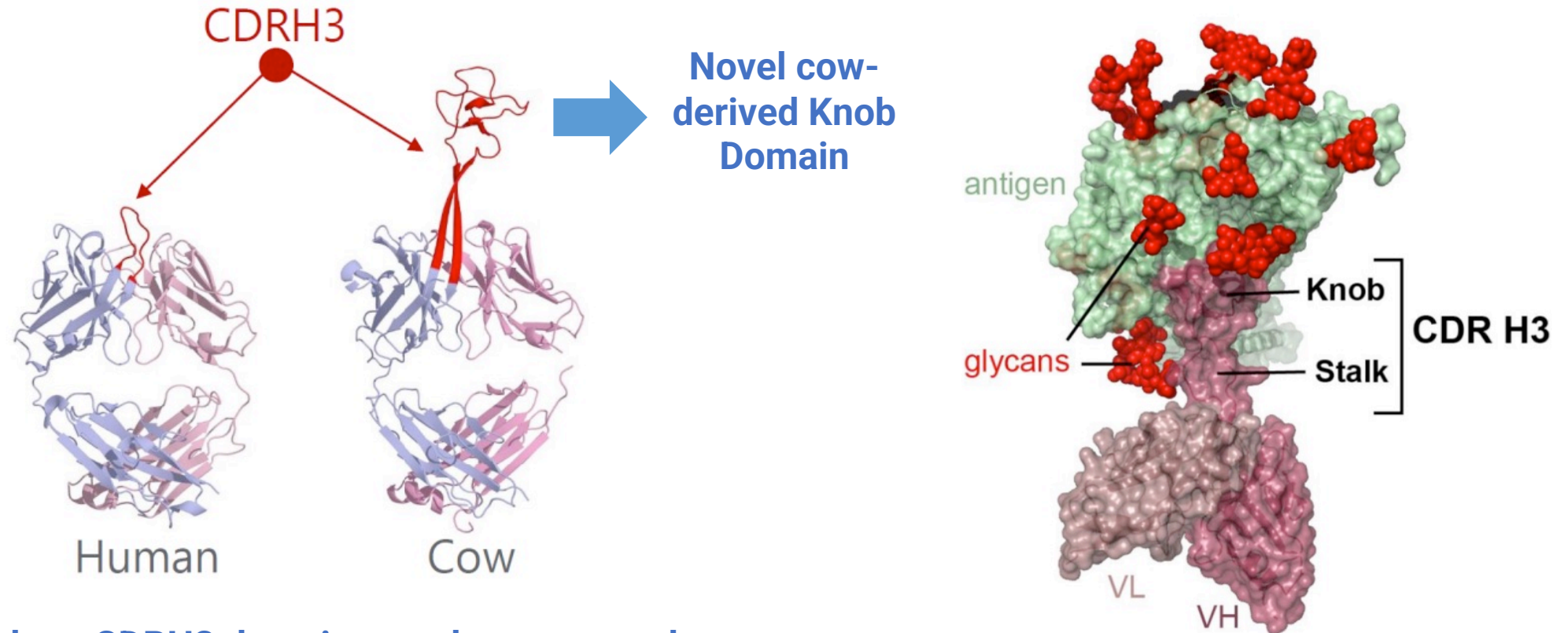


Fig 2. Schematic representation of the method for the isolation of knob domain peptides. Immunisation of cattle with human C5 is used to elicit an immune response (step 1). An antigen-specific response is isolated through FACS of immune cells, using 2 populations of fluorescently labelled C5 (step 2). Cells that are double positive for C5 are sorted into a polyclonal mixture. After RT-PCR, PCR primers specific to CDRH3 are used to create a CDRH3 library. Ultralong CDRH3 are identified using deep sequencing and expressed as cleavable fusion proteins (CDRH3-ScFc or Fab-CDRH3) (step 3). After screening (step 4), TEV protease can be used to excise the knob domain peptides (step 5), which are purified using RP-HPLC (step 6). CDRH3, heavy-chain complementarity-determining region 3; FACS, fluorescence-activated cell sorting; RP-HPLC, reversed-phase high-performance liquid chromatography; RT-PCR, reverse transcription polymerase chain reaction; ScFc, single-chain Fc; TEV, Tobacco etch virus.

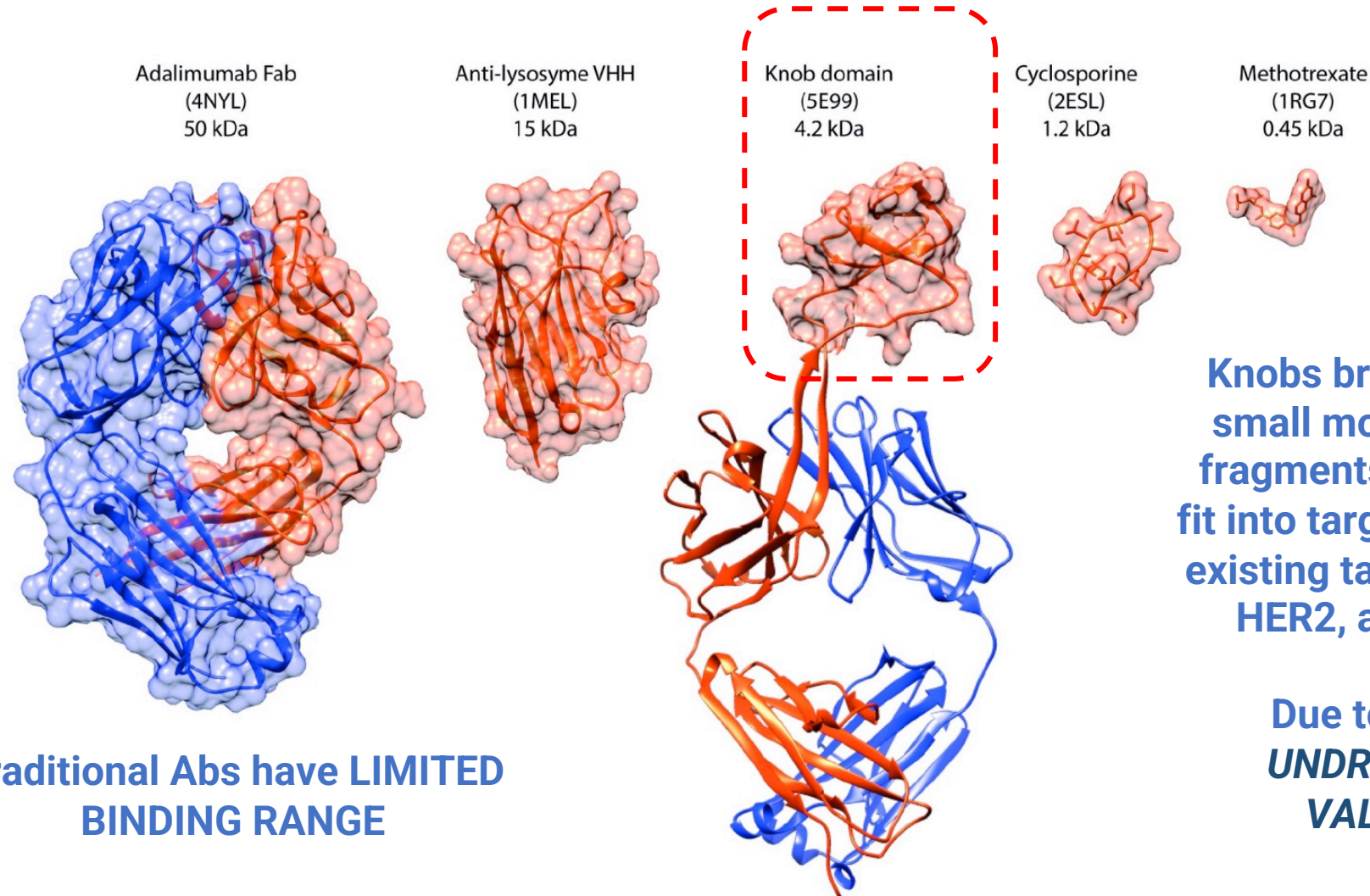
<https://doi.org/10.1371/journal.pbio.3000821.g002>

Novel Structures of Knobs with Ultralong CDR Domains



These long CDRH3 domains can be expressed onto humanized Ab frameworks or Ab-Drug Conjugates

Knobs are Much Smaller than Traditional Antibodies



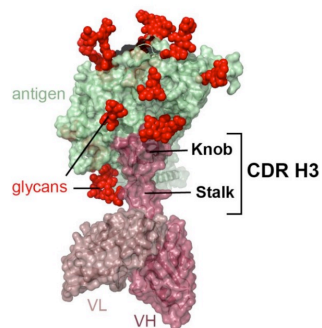
Knob Platform: Next Generation Knob Domain Therapeutics

KNOB Platform

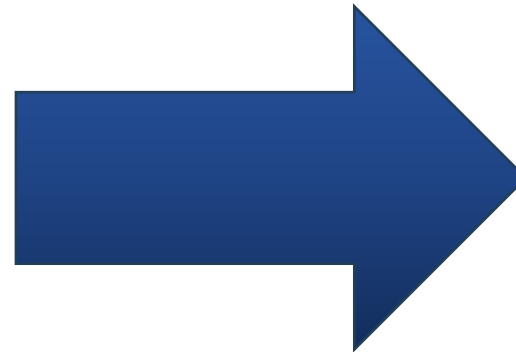
Transformative platform technology

Multiple targets

First-in-class, modular humanized, cow-derived nano antibodies



Stanfield, et.al. Sci Adv (2020) 6(20): eaba0468.



- ✓ Proprietary knobs can be utilized to create bi-, tri-, -tetra specific antibodies
- ✓ May be synergistic as single-domain agents to improve efficacy of existing treatments (e.g. PD-1 Abs)
- ✓ Can be developed onto IgG scaffolds to create ADCs
- ✓ Can be developed into a new class of agents using a variety of Ab backbones