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Loop Bio – Executive summary

PROBLEM

10M+ Americans

affected by OCD & tic disorders

Current treatments for treatable patients have poor efficacy and severe side effects (sexual dysfunction, weight gain, movement disorders) — a significant unmet need.

SOLUTION

Novel therapy targeting CSTC Circuit

established safety: over 130M patient exposures to API

Novel 2PAA prodrug targeting the overactive CSTC circuit. Leverages betahistine's proven safety profile, eliminating side effects of SSRIs and antipsychotics. Robust preclinical efficacy in validated models.

OPPORTUNITY

\$3B+ Market

through late clinical development (Emalex and Biohaven)

Ecopipam's expected FDA approval validates the TS market. ~50% OCD comorbidity in TS means one asset addresses both indications. De-risked safety profile makes Loop an attractive acquisition target.

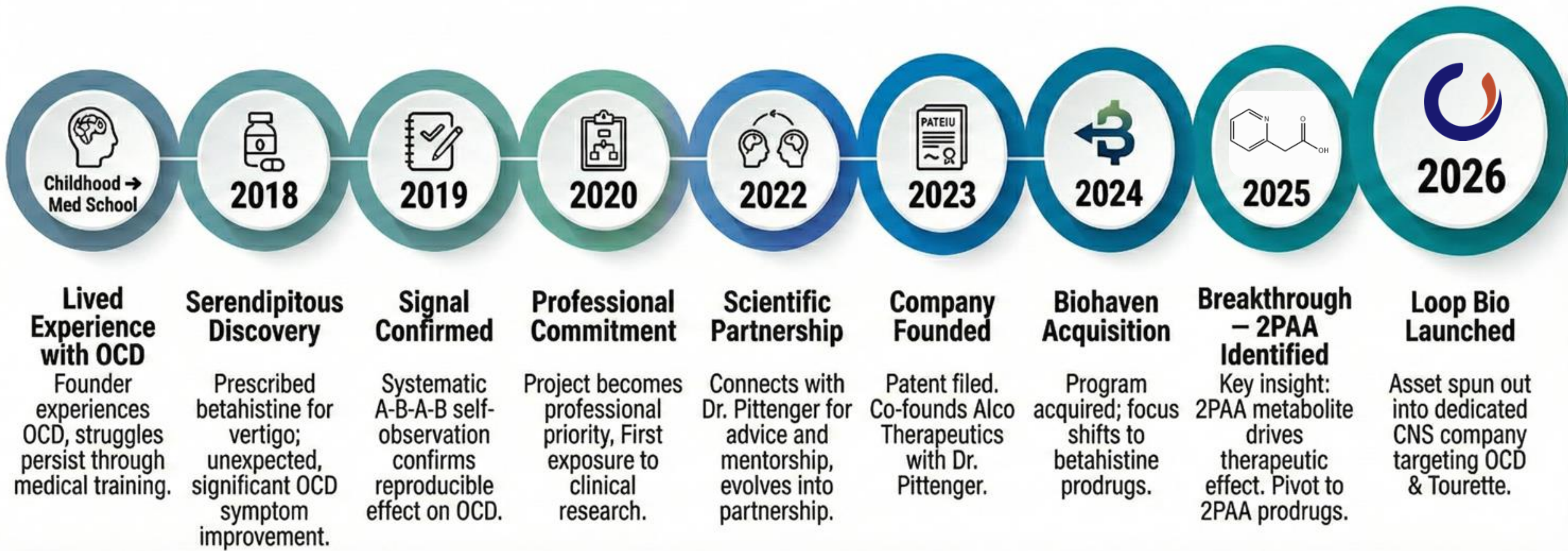
ASK

\$2M through SAFEs

Derisking safety + MoA

9-month runway: tox + CMC + reg package + target ID

From Lived Experience to Loop Bio



The Loop Bio Team

Deep domain expertise across OCD/TS neuroscience and drug development

Nicolas Cuba, MD

Founder & CEO

- Former Founder & CEO, Alco Therapeutics — led successful exit to Biohaven (March 2024)
- Former Associate Research Director — Biohaven
- Leads 2PAA/BTH program since 2020; discovered betahistine's therapeutic effect on OCD

Christopher Pittenger, MD, PhD

Co-founder & SAB Chair

- Mears & Jameson Professor of Psychiatry, Yale — world authority on OCD & TS pathophysiology
- Pioneered histamine & glutamate research in OCD & Tourette Syndrome
- Decades of translational neuroscience: preclinical models through clinical trials

Biohaven (NYSE: BHVN)

Shareholder & BOD seat

- Clinical-stage pharma — Neuroscience, Immunology, Oncology; OCD clinical dev experience
- 15% equity stake, 2% royalty rights, Board of Directors seat in Loop Bio
- Acquired Alco Therapeutics IP (2024)

ADVISORY BOARD & CONSULTANTS

Bruce Car, DVM, PhD, DACVP

SAB Member

CSO, Biohaven; fmr CSO Agios Pharmaceuticals

- 25+ years at BMS — progressed ~250 drug candidates, 18+ registrations
- Founded BMS Translational Medicine (300+ scientists)

Matthew State, MD, PhD

Clinical Dev/Neuroscience Consultant

Chair of Psychiatry, UCSF; fmr Yale

- Pioneered genetics underlying autism and Tourette disorder
- Leads Autism Sequencing Consortium & TIC Genetics

Stephan Loose

BD Consultant

Managing Director, Old Street Strategy

- Fractional CBO/CCO across Series A–C neurology & psychiatry biotechs
- BD strategy, valuation modeling, investor deal prep

Ric Stanulis, PhD, DABT

Toxicology Consultant

CEO, Akkeri

- Board-certified toxicologist with over 25 years of nonclinical drug development experience

Problem: Massive Unmet Need in OCD & Tourette Syndrome

No new OCD drugs in 20+ years. Only antipsychotics for TS. Patients deserve better.

OCD

10M+ Americans

- 60% inadequate response to first-line SSRIs
- Higher doses required = worse side effects
- 2nd line: antipsychotics with severe side effects
- \$1.4B market by 2032 (9.7% CAGR)

TOURETTE SYNDROME

400K+ US patients

- 1st line: alpha-2 agonists (small effect, not FDA approved)
- 3 FDA options — all antipsychotics with severe side effects
- Ecopipam Phase 3 success validates market path
- \$6.5B market by 2030 (4.2% CAGR)

>50% of TS patients have comorbid OCD — one asset addresses both indications

TARGET PRODUCT PROFILE

	OCD	Tourette Syndrome
Population	Adjunctive refractory / Monotherapy	2nd-line to moderate-severe / All TS
Endpoints	Y-BOCS II superior to placebo	YGTSS TTS superior to placebo
Safety Edge	No sexual dysfunction or emotional blunting	No movement disorders, sedation, or weight gain
Dosage	Chronic, oral, once daily	

Technology: Small molecule, 2PAA prodrug | **IP:** COM for 150+ NCEs; MOT for 20+ indications; protection to 2047+

WHY NOW

Field wide open

No pharma competitors in late-stage OCD trials

Ecopipam validates TS path

Phase 3 success; expected NDA approval 2026

Psychedelic alternatives 5+ yrs away

No competing novel programs in pipeline

Betahistine to 2PAA: Serendipitous finding from safe therapeutics

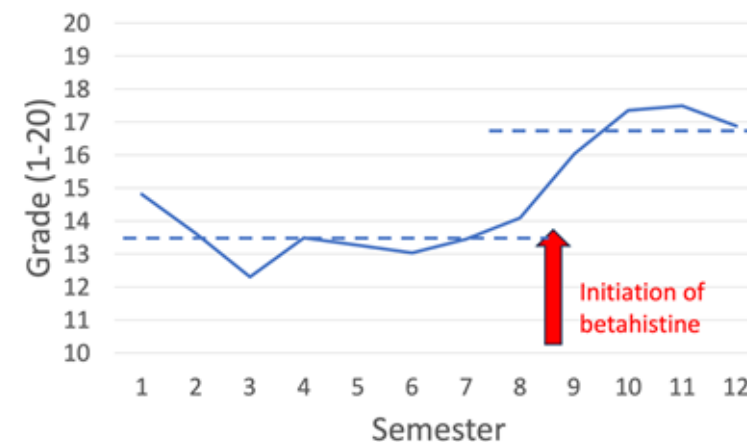
A clinical observation led to a metabolite-driven prodrug strategy supported by ample human data

THE DISCOVERY

- 1 Betahistine prescribed for vertigo worldwide** — 130M+ patient exposures; not available in US
- 2 Serendipitous OCD benefit observed** — marked improvement in function, minimal side effects
- 3 Second patient: 61% Y-BOCS improvement** — clinically significant response
- 4 Metabolite 2PAA identified as active entity** — preclinical models confirm; prodrug strategy initiated

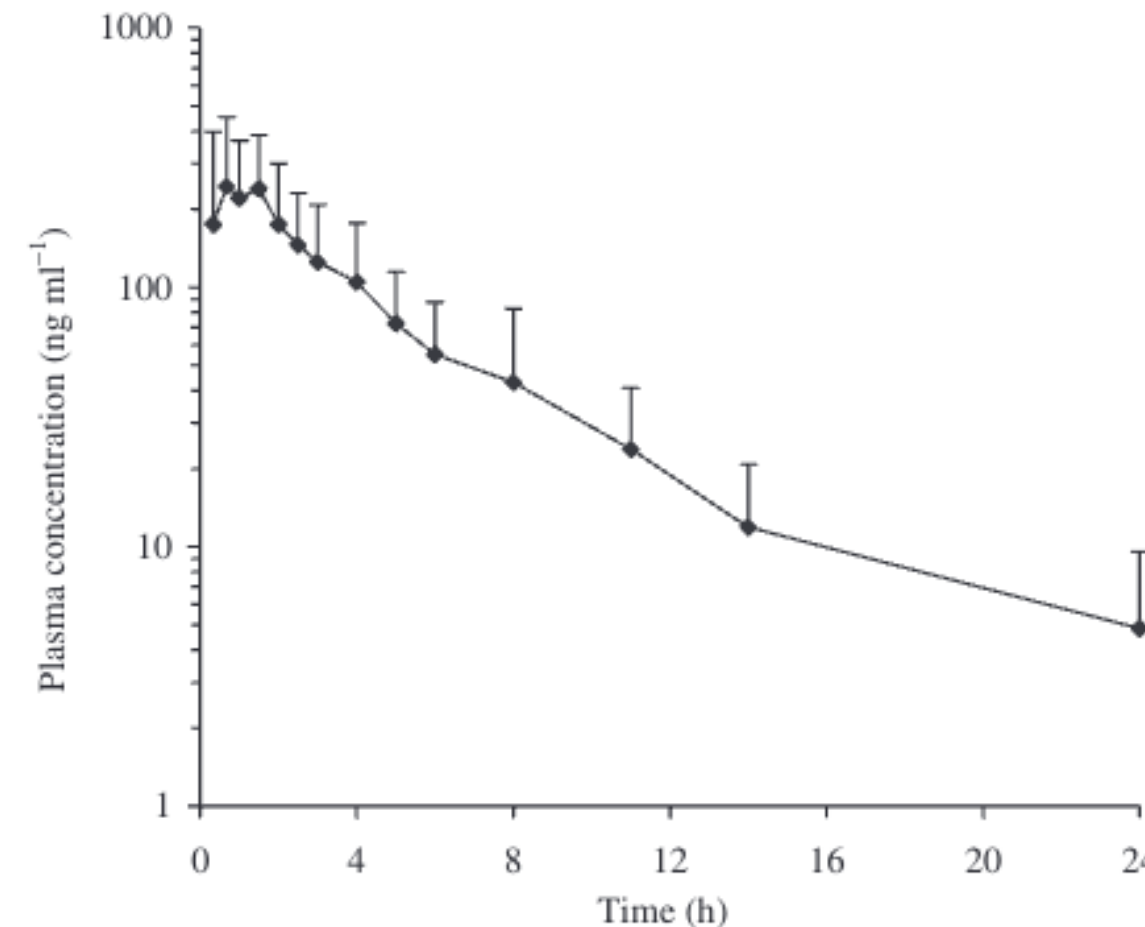
61%

Y-BOCS improvement over 1M of Tx



HUMAN PK DATA (PUBLISHED PHASE 1)

Mean plasma concentration-time curve of 2PAA after oral dose of 24mg betahistine mesylate in 20 healthy volunteers



Parameter	Value (Mean ± SD)
C _{max} (ng/mL)	339.4 ± 213.4
T _{max} (h)	0.98 ± 0.47
AUC _{0-t} (ng·h/mL)	1153 ± 729
AUC _{0-∞} (ng·h/mL)	1196 ± 748
t _{1/2} (h)	5.17 ± 2.66
k _e (1/h)	0.18 ± 0.15
MRT (h)	5.14 ± 0.88
CL/F (L·h ⁻¹ ·kg ⁻¹)	0.44 ± 0.28
V _{dss} /F (L/kg)	2.19 ± 1.19

Chen, X Y et al., 2003

Established human safety

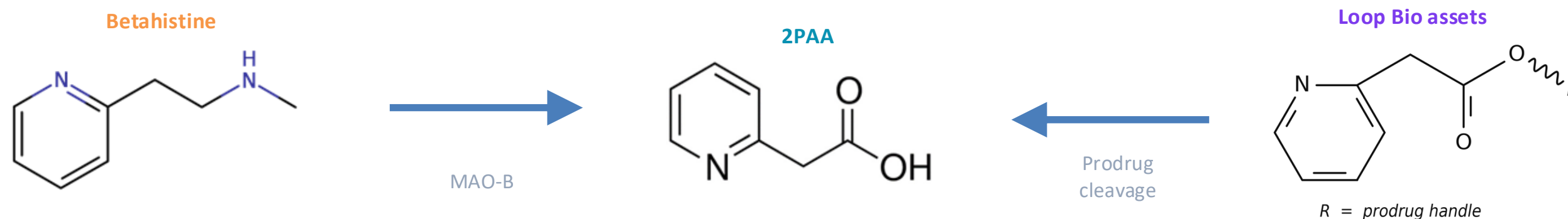
130M+ exposures; ADR rate 1:100,000

Dose-proportional PK in humans

Published Phase 1: safe, tolerable, predictable exposure

Wide therapeutic window

MRSD 24 mg; efficacy range 33–193 mg

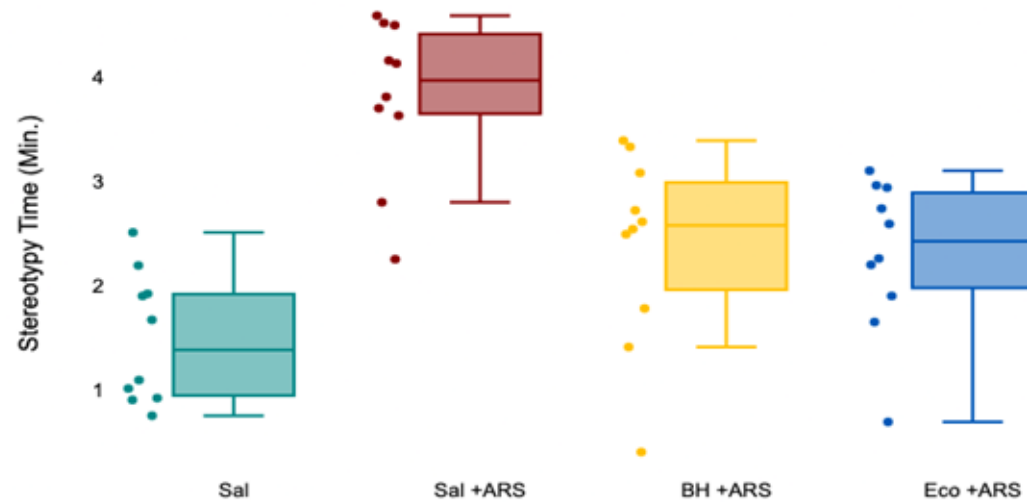


Preclinical Efficacy: Pittenger Lab, Yale University

2+ years of translational work across behavioral, molecular and circuit-level readouts

1 Stress-Induced Stereotypy (ARS)

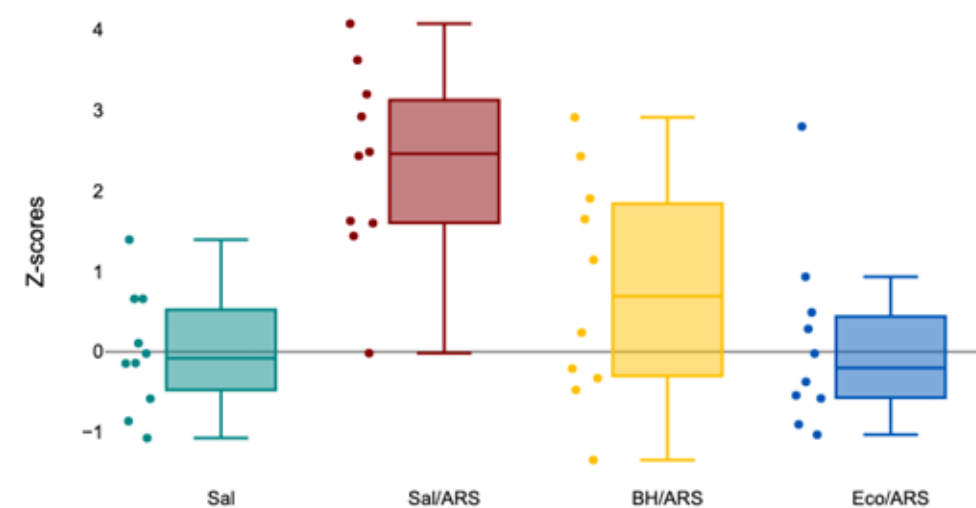
Stereotypy Time after ARS with BH-017594 or Ecopipam Pretreatment



- Acute restraint stress model — validated OCD/TS behavioral readout
- BTH, 2PAA, prodrug & ecopipam all reduce stereotypy
- Effect comparable to ecopipam positive control
- Dose-dependent response observed

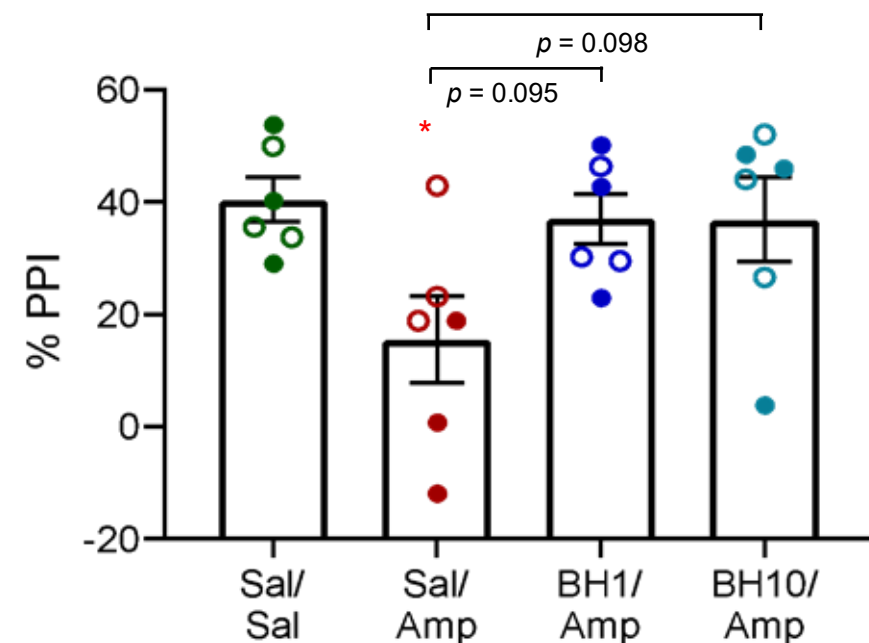
2 c-Fos Circuit Mapping

C-fos Levels in Amygdala after ARS with BH-017594 or Ecopipam Pretreatment



- Immediate early gene expression in CSTC circuit regions
- Modulates activity in key OCD/TS brain regions
- Decreased stereotypy correlates with circuit normalization
- Consistent across BTH, 2PAA, prodrug and ecopipam

3 Prepulse Inhibition (PPI)

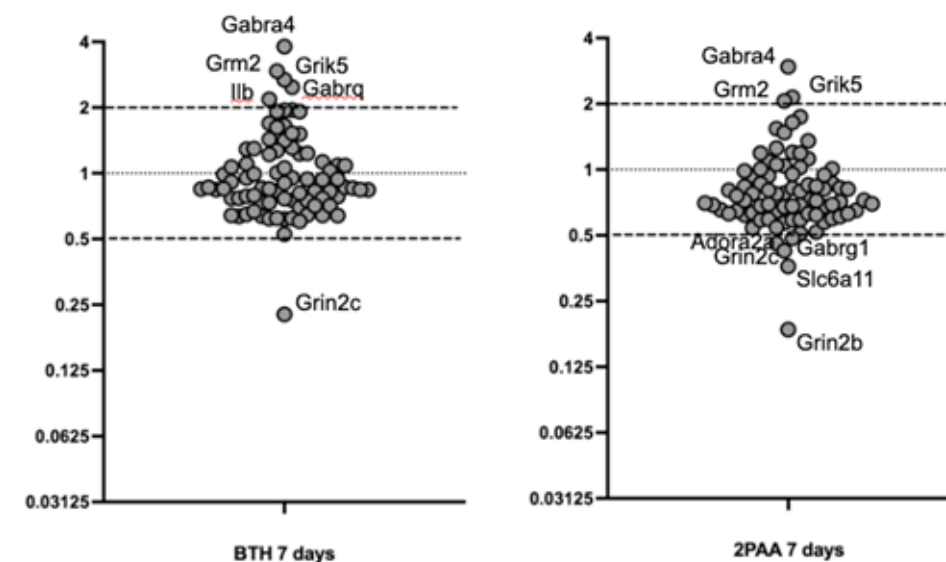


- Sensorimotor gating — translational TS biomarker
- Sensorimotor gating deficit is a hallmark of TS
- Validated cross-species translational measure
- Assesses impact on sensory filtering circuits

4 Gene Expression (qPCR)

Saline vs BTH (10 mg/kg)

Saline VS 2PAA (75 mg/kg)



- Molecular readouts in CSTC regions post-treatment
- Mouse GABA and Glutamate PCR Array in Dorsal Striatum after BTH or 2PAA subchronic (7d) dosing
- Broadly concordant profiles: 4/6 BTH-regulated genes changed in the same direction with 2PAA.

Key finding: BTH, 2PAA, 2PAA prodrug lead, and ecopipam all mitigate stress-induced stereotypy while modulating relevant brain circuitry



Betahistine Improves Cognitive Outcomes: Clinical Evidence

Wang et al. 2021

RCT in Schizophrenia

N = 89, double-blind, 12 weeks
Betahistine 72 mg/day

MCCB composite: p = 0.003
Verbal learning: p = 0.02
Visual learning: p = 0.001

No change in PANSS — cognitive effect is independent of antipsychotic symptom control.

Barak et al. 2016

RCT with Olanzapine in HV

N = 48 healthy women, double-blind
Betahistine 144 mg/day + olanzapine 10 mg

37% ↓ weight gain (p = .049)
60% ↓ somnolence (p = .042)

Improved outcomes alongside antipsychotics.

Nogura et al. 2019

Cognition Crossover RCT in HV

N = 38, crossover, object recognition task
Betahistine 108mg once

Improved overall correct ratio (OR 1.11)
Significant participant x drug interaction effect
Improved performance of poor placebo performers and middle-range IQ subjects

Improves cognition in healthy volunteers

Nishii et al. 2025 Meta-Analysis: 11 RCTs (n = 754), 6 H3-targeting drugs

Only betahistine improved cognition (SMD = -0.61; -0.48 working memory; -0.62 verbal learning). **Other H3R antagonists: no benefit.**

Tolerability fingerprint: other H3R-ANTs/IAs showed **2.18× insomnia** and **3.5× discontinuation from AEs** vs. placebo. Betahistine: no tolerability issues.

Why? Betahistine is a 2PAA prodrug — the clinical effect is driven by 2PAA, not H3 antagonism. The absence of H3-class AEs is the fingerprint of a different mechanism.

Prodrug Development - Robust IP Portfolio

Comprehensive protection until 2047+

150+

NCEs

Composition of matter claims for BTH and 2PAA prodrugs

20+

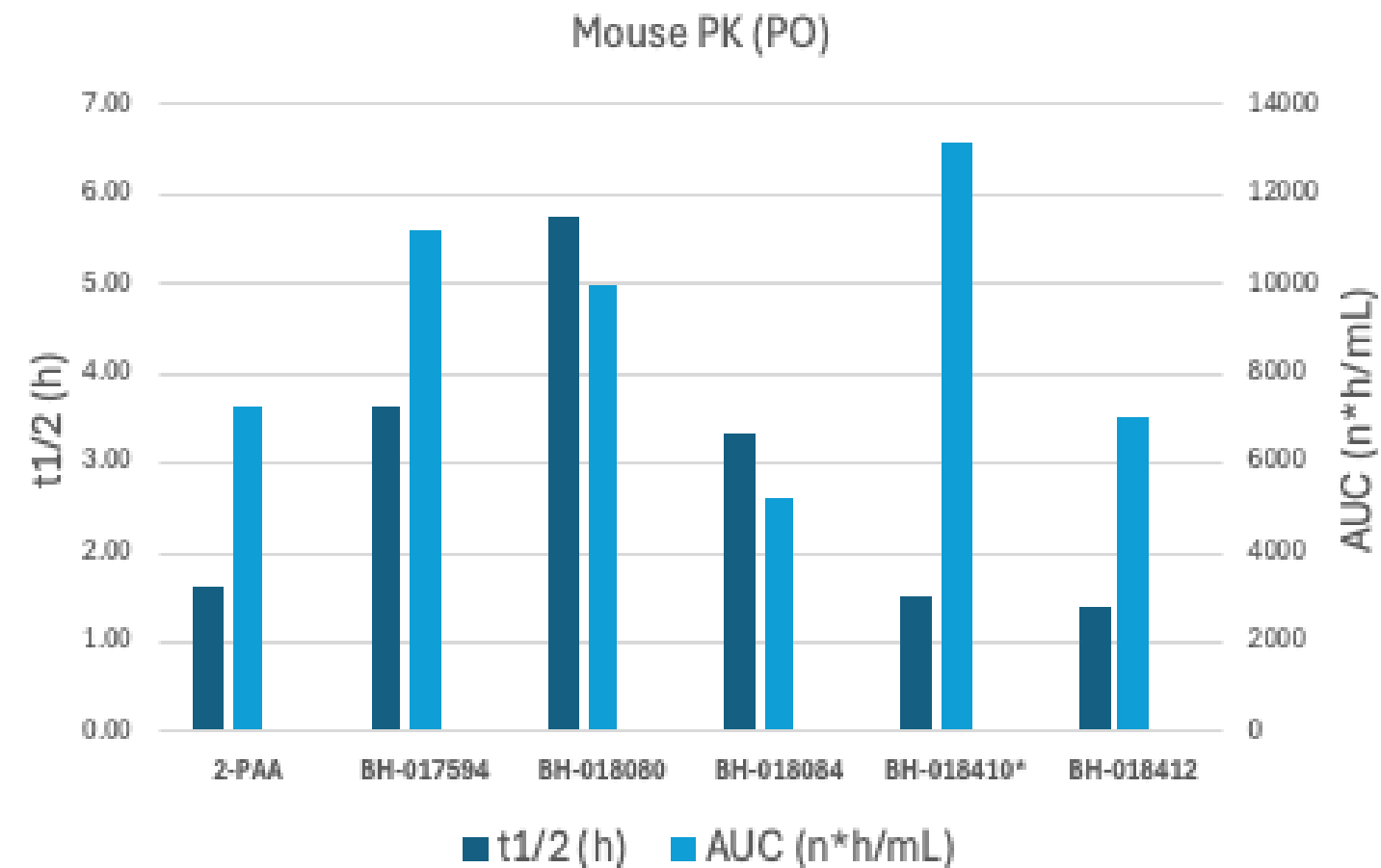
Indications

MOT claims for OCD, tic disorders, and glutamate excitotoxicity disorders

2047+

Coverage

Comprehensive protection with 20+ years of exclusivity remaining



Capital-efficient virtual model

Lean operation focused on speed and strategic oversight

IN-HOUSE

CEO – Full-Time Execution

- Spearhead project & strategic oversight
- Vendor management & project integration
- Investor relations & fundraising

Board of Directors (5 seats, 3 open)

- Corporate strategy & milestone review
- Financial oversight & capital allocation
- Partnership & exit strategy

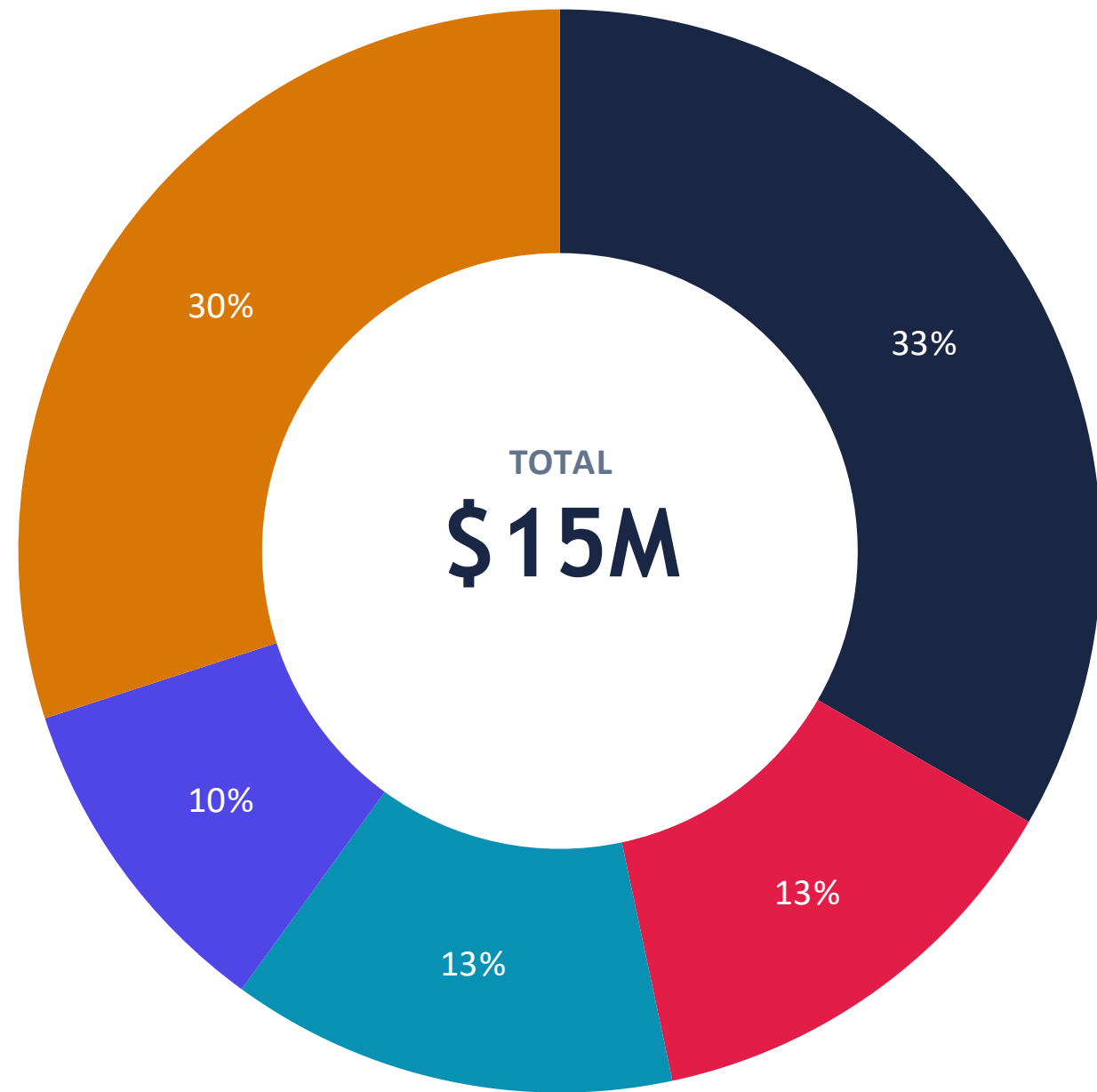
Scientific Advisory Board

- Development strategy & study design
- KOL network & publication strategy

OUTSOURCED

DMPK & IND-Enabling Experiments Chinese or Indian CRO	American non-clinical consultant oversight
CMC & Manufacturing Chinese or Indian CRO/CMO	American CMC consultant oversight
Regulatory & IND Freyr Solutions (India)	Medical writing, regulatory strategy, AI-assisted doc prep
Clinical Development Tier 1 offshore CRO (Australia)	Turnkey Phase 1a; American clinical consultant oversight
BD, Finance & Legal Fractional CFO + Legal Counsel	Financial planning, fundraising, corporate governance

Capital plan: \$2M in SAFEs now → \$13M Series A



Phase 1a Execution SAD, MAD, CSF sampling, clinical ops	\$5M	33.3%
IND-Enabling Non-GLP/GLP tox, CMC, regulatory	\$2M	13.3%
Mechanism Elucidation MOA, biomarkers, translational readouts	\$2M	13.3%
Operations G&A, IP, BD	\$1.5M	10%
Reserve	\$4M	30%

Loop Bio – why invest now?

01

FOUNDERS

Focused & specialized

Founder leading program since 2020. World-leading OCD/TS researcher as co-founder & SAB Chair. Biohaven board seat.

02

MARKET

\$3B+ & untapped

10M+ Americans affected. No new OCD drugs in 20+ years. Ecopipam validates TS path and market. 50% OCD comorbidity in TS.

03

PRODUCT

De-risked safety

130M+ patient exposures. Robust preclinical efficacy. Eliminates sexual, metabolic, and motor side effects of SOC.

04

IP

Protected to 2047+

150+ NCEs with COM claims. 20+ therapeutic indications. Extensive coverage for OCRD and tic disorders.

05

PATH

Bridge to first-in-human

\$2M SAFE funds GLP tox, CMC - Bridges to Phase 1 trials.

Thank You!

"Far and away the best prize that life has to offer is the chance to work hard at work worth doing"

-T. Roosevelt

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