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Innovative Treatments for Central Nervous System Disorders

October 2024

Allosteric modulators for human health

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Addex Overview

High value programs reaching significant milestones	➢ GABAB PAM for cough ready to enter IND enabling studies ➢ Dipraglurant for post-stroke/TBI[1] recovery – Phase 2 ready ➢ Neurosterix portfolio advancing towards IND enabling studies
20% equity interest in spin-out company, Neurosterix	➢ Leading allosteric modulator drug discovery platform – Validated & differentiated pharmacological approach ➢ Preclinical portfolio of high value programs – Lead program: M4 PAM for schizophrenia ➢ $63M series A financing in April 2024 led by Perceptive Advisors
High value industry partnership driving future value	➢ GABAB PAM for SUD[2] partnered with Indivior entering IND enabling studies – $330M in milestones & tiered royalties from high single digit to low double digit
Strong balance sheet & top tier US investors	➢ Dual listed on SIX Swiss Exchange & US Nasdaq Capital Market ➢ CHF 3.79M ($4.20M) cash at June 30, 2024 – April 2024 Neurosterix spin-out: CHF 5M cash received in April 2024 & reduced future cash burn ➢ Cash runway extended beyond 2026

[1]TBI = Traumatic brain injury
[2]SUD = Substance use disorder

Pipeline of In House Discovered Programs

Molecule / MoA	Partner	Stage				Milestone
		Discovery	IND Studies	Phase 1	Phase 2a	
Dipraglurant (mGlu5 NAM)		Post-stroke/TBI recovery				Ready to start Phase 2a study*
ADX71149 (mGlu2 PAM)	janssen	Indication under evaluation				Indication under review
$GABA_B$ PAM	INDIVIOR	Substance use disorders				IND enabling studies expected to start H1 2025
$GABA_B$ PAM		Chronic cough				IND enabling studies ready to start in 2025*
20% Neurosterix LLC – Advancing a focused CNS Pipeline						
M4 PAM		Schizophrenia and other psychosis				Start IND enabling studies in H2 2024
mGlu7 NAM		Mood disorders				Start IND enabling studies in H2 2025
mGlu2 NAM		Cognition				Enter clinical candidate selection in H1 2025
Undisclosed		CNS				Start Lead optimization in H1 2025

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* Timings subject to financing/partnering
TBI = Traumatic brain injury
NAM = Negative Allosteric Modulator

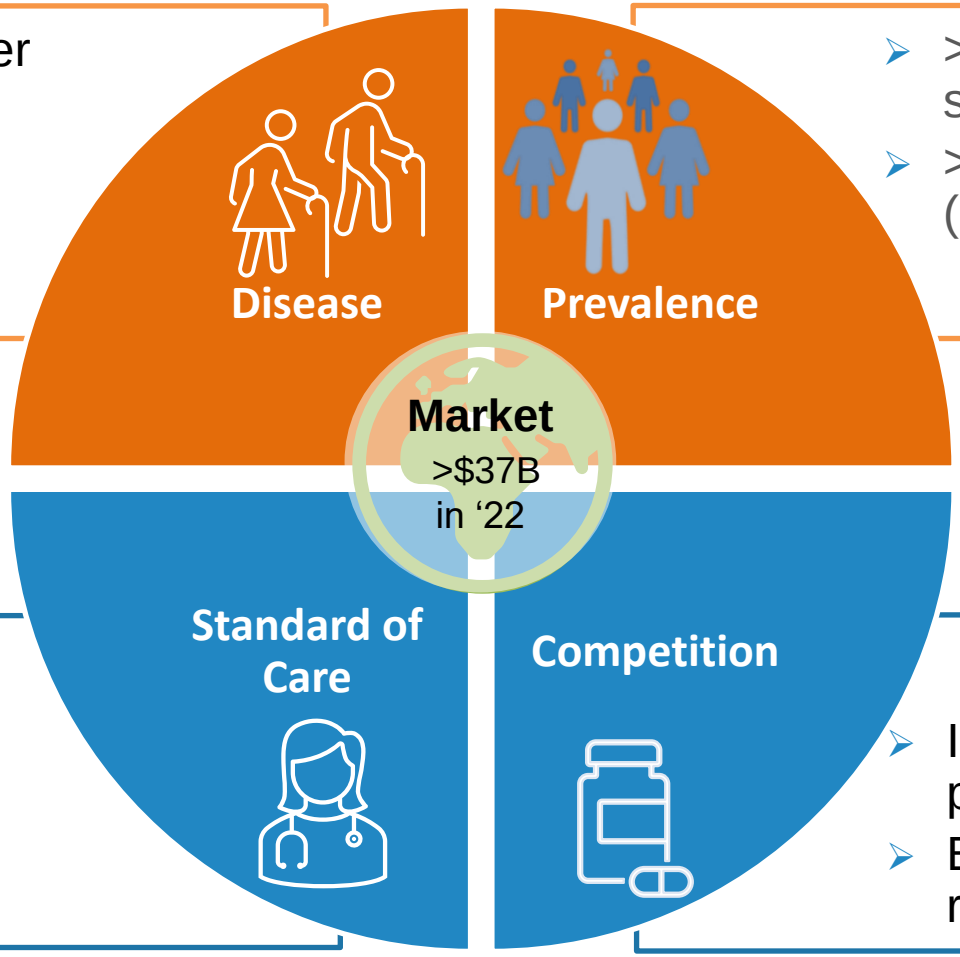
PTSD = Post-traumatic stress disorder
PAM = Positive Allosteric Modulator

Dipraglurant (mGlu5 NAM) for Post-Stroke / TBI Recovery

Targeting neuroplasticity early in rehabilitation to promote recovery

Post Stroke / TBI Recovery - Unmet Medical Need & Commercial Opportunity

- Many stroke /TBI patients suffer motor and somatosensory impairment
- Potential chronic disability & low quality of life



- >101 million ischemic stroke survivors worldwide[1]
- >12 million new strokes/yr (1 every 3 seconds)[1]

- Rehabilitation therapies: e.g. physiotherapy, speech, communication and cognitive
- Majority never fully recover

- Intense early rehabilitation promotes recovery
- But, no approved drugs to support rehabilitation therapies

Urgent medical need to promote sensorimotor recovery in post-stroke patients

[1]World Stroke Association 2022

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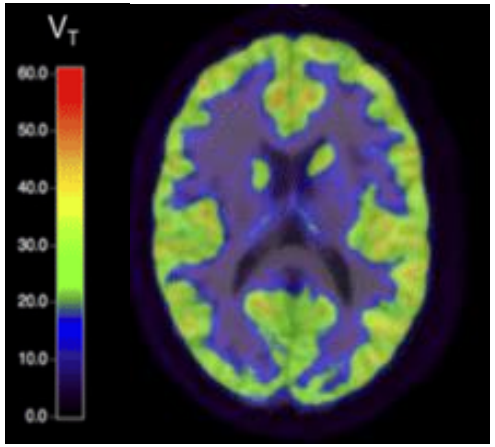
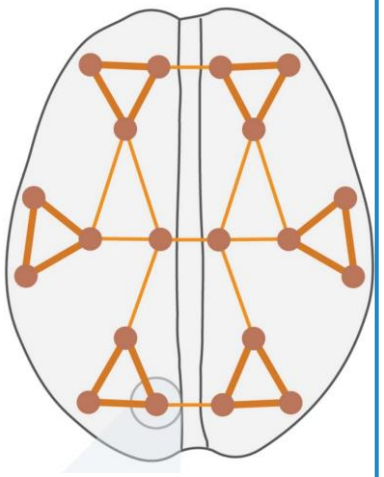
mGlu5: An Innovative Target for Post-Stroke Recovery

Healthy brain

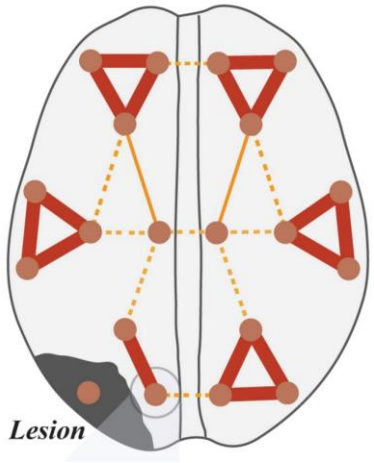


mGlu5 brain distribution



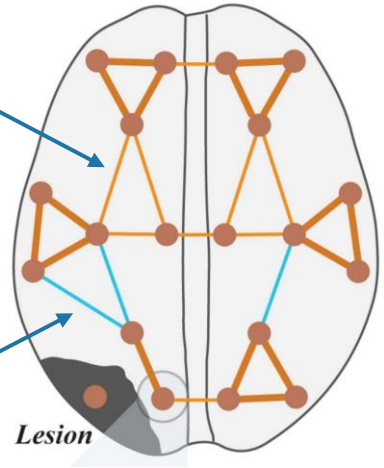
Good inter & intra-nodal connectivity

mGlu5 NAM supports post-stroke recovery



Recovery

+ mGlu5 NAM



mGlu5

- Densely expressed in the brain
- Involved in neural plasticity
- Modulates excitation/inhibition equilibrium

Lesion effects:

- Confined neural tissue necrosis
- Network disruption & module segregation
- Imbalance in excitation/inhibition

mGlu5 NAM promotes synaptic plasticity

- Cortical reorganization & new functional pathways (a)
- Connectivity changes toward pre-lesion state (b)
- Restoration of excitation/inhibition equilibrium

Adapted from DOI: 10.3389/fnsys.2021.806544

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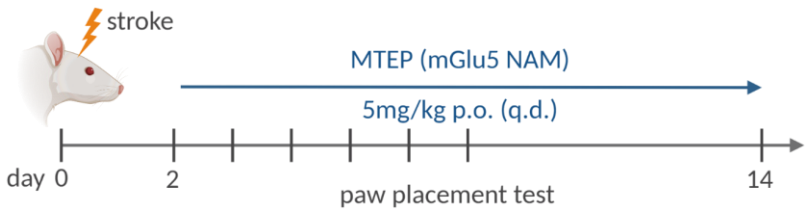
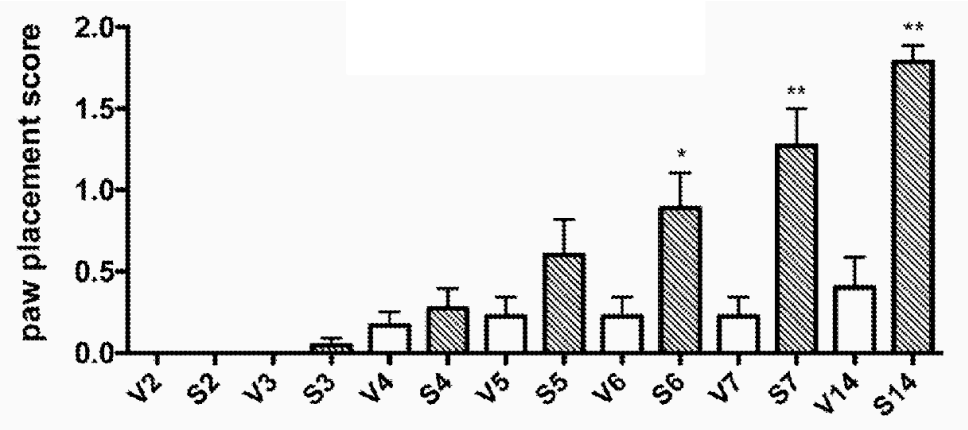
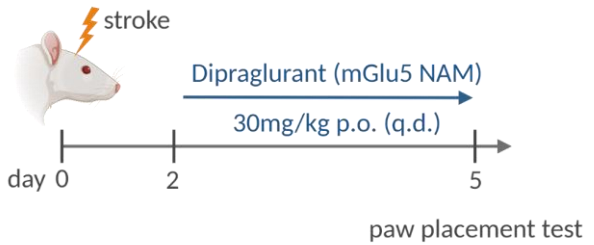
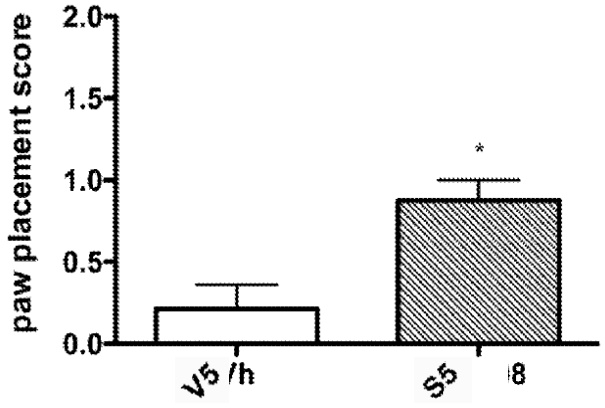
Preclinical Data: mGlu5 Inhibition Promotes Post-Stroke Recovery





MTEP treatment resulted in a significant recovery of functional control





Dipraglurant significantly restored functional control in a one-week experiment

Dipraglurant enhanced functional brain recovery in a rat model of experimental stroke

From patent application PCT WO2017/171594A1

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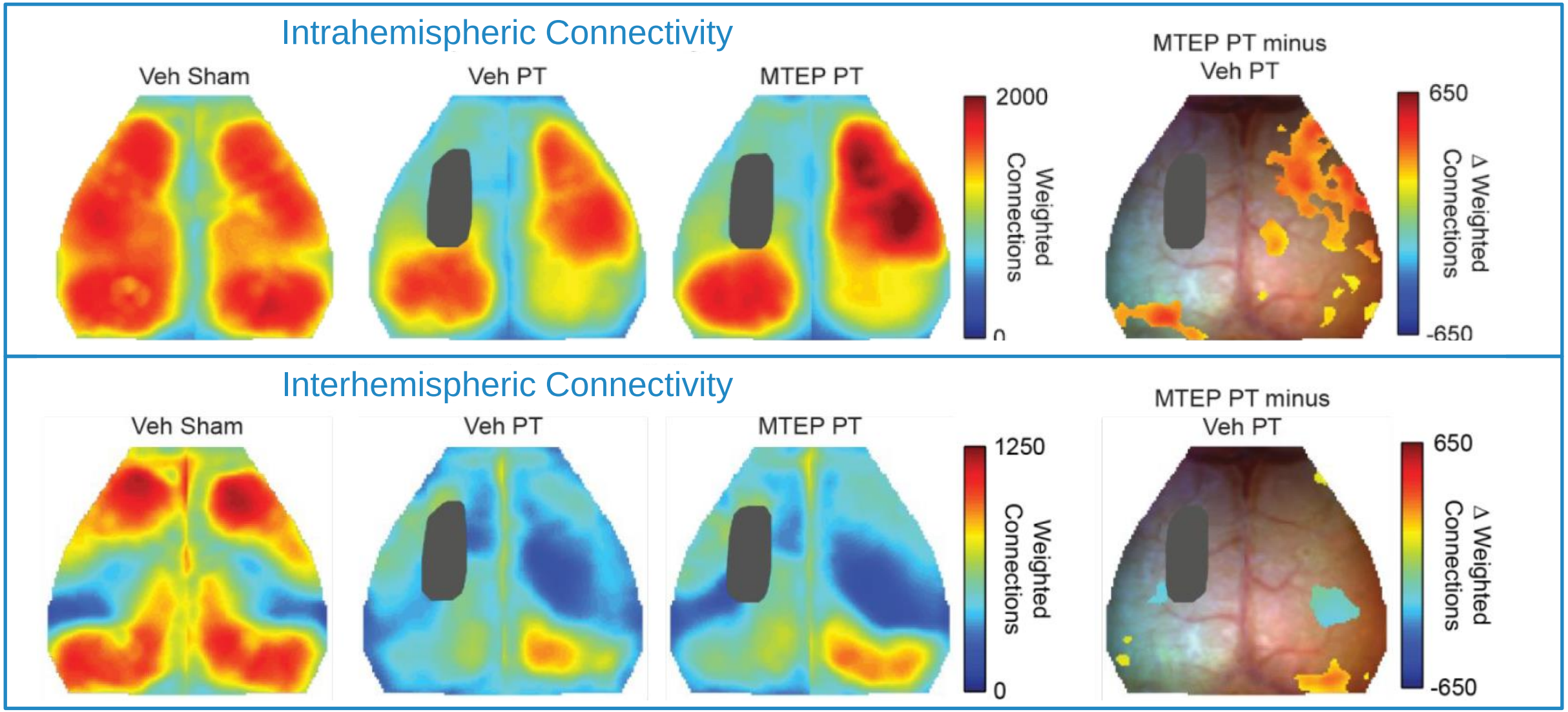
MRI Imaging Data: Post-Stroke Resting State Functional Connectivity



mGlu5 inhibitors promote intra- and inter-hemispheric connectivity following stroke

https://doi.org/10.1093/brain/awad293

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Dipraglurant for Post-stroke/TBI Recovery - Development Status

- Fast onset of action and short half-life
  - Ideally suited for concurrent dosing with rehabilitation
- Extensively profiled Phase 1 studies
  - 5 studies with >100 patients
  - Including receptor occupancy (PET ligand study)
- Phase 2 studies conducted
  - Safe and well tolerated in patients suffering from neurological disease – Parkinson's disease
  - Mild to moderate CNS type AEs at doses < 200mg
  - 7 PD-LID patient exposed >6 months
- CMC Status
  - >30kg API in stock
  - Drug product available in 50mg and 100mg tablets with placebo
- IP
  - Patent through 2034 (without extensions)
  - Use patent of mGlu5 NAMs in treatment of brain damage until 2035 – option to exclusive license

First-in-class program for post-stroke recovery ready to start Phase 2

GABAB PAM for Substance Use Disorders (Indivior Partnership)

Going beyond baclofen to treat substance use disorders with improved safety and tolerability

GABAB PAM for Substance Use Disorder

Large market & unmet medical need	➢ High prevalence;1.8% of US population[1] ➢ Current treatments have undesirable side-effects and prone to relapse ➢ Burden to society in US is >$600B annually[2]
Clinically validated MoA	➢ Baclofen (GABAB agonist) used off label for alcohol use disorder ➢ ADX71441 attenuates alcohol self-administration and relapse to alcohol seeking in rats[3] and alcohol consumption in mice[4] ➢ ADX71441 reduces cocaine self-administration in non-human primates[5]
Status of program and near-term milestone	➢ Funded research phase of collaboration completed ➢ Drug candidate selected for IND enabling studies ➢ Differentiated leads and backups with robust novel IP potential ➢ IND enabling studies expected to start in H1 2025
Strategic partnership with Indivior	➢ Eligible to receive $330 million in milestones and tiered royalties from high single digits to low double digits

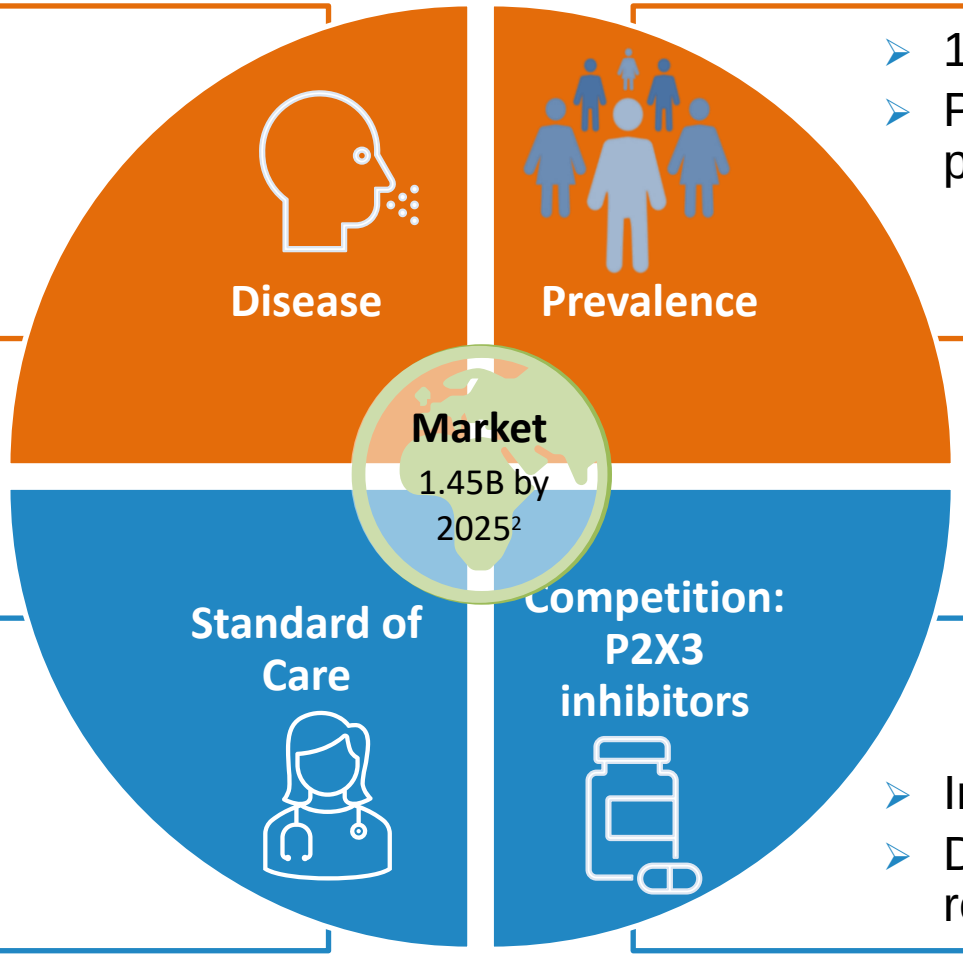
[1]Merikangas et al. 2010
[2]NIDA
[3]Augier et al 2017
[4]Hwa et al 2014
[5]Addex int. report

GABAB PAM for Chronic Cough

Going beyond baclofen to treat cough with improved safety and tolerability

Cough - Unmet Medical Need and Commercial Opportunity

- Chronic cough
  - Lasting > 8 weeks[1]
  - >700 coughs/day
- Multiple comorbidities



- 10% in the general population[4]
- Persists >1 year in 60% of patients

- Ineffective in 30% of patients[3]
- Hindered by side-effect risks

- Ineffective in ~30% of patients
- Discontinuation in ~20% (taste related side-effects)

High unmet medical need for an efficacious and safe treatment of cough

[1]Morice et al. *Eur Respir Rev* 2021
[2]Cough Remedies Market Share, Size and Industry Growth Analysis 2021 - 2026 (industryarc.com)
[3]Ryan *Expert Opin Pharmacother* 2018
[4] Song WJ, Chang YS, Faruqi S, et al. 2015.

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Standard of Care in Cough - Strengths and Weaknesses

Use / side-effects	Dextro-metorphan	Opioids	Gabapentin & pregabalin	Amitriptyline	P2X3*	GABAB Agonist Baclofen	GABAB Addex PAM
Treatment type	Chronic	Acute	Acute	Acute	Chronic	Acute	Chronic
Risk of Abuse	Yes	Yes	Yes	Yes	No	No	No
Respiratory	No	Yes	Yes	Yes	No	Yes	No
Other CNS	Yes	Yes	Yes	Yes	No	Yes	No
Gastrointestinal	Yes	Yes	No	No	No	No	No
Taste-related	No	No	No	No	Yes**	No	No

- P2X3 inhibitor Gefapixant
  - * Ineffective in 30% of patients
  - ** Taste-related side effects observed in up to 97% of patients, leading to discontinuation in up to 20% of patients[1]

A highly selective and targeted GABAB PAM has the potential to offer best-in-disease efficacy and tolerability profile suitable for chronic treatment

[1]Niimi et al. *Allergology International* 2022

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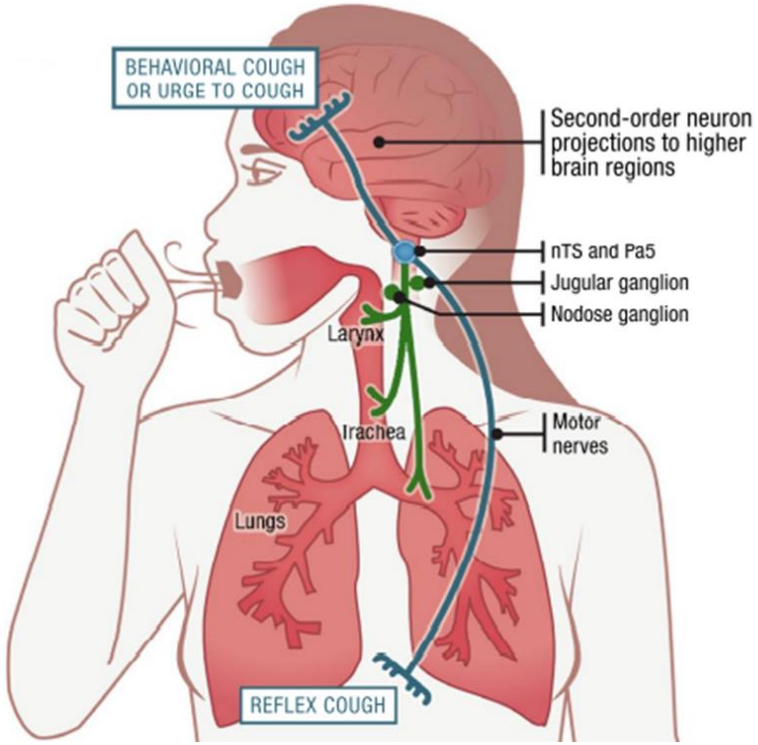
GABAB Receptor - Validated Target in Cough

- GABAB receptor
  - Expressed throughout the cough neural circuit
  - Activation reduces neuronal excitability
  - Potential for broad application in cough patients
- Baclofen, an orthosteric agonist
  - Used off-label in patients with chronic cough
  - Clinical studies with cough patients showed efficacy
  - Efficacious in healthy volunteer and multiple preclinical models
- Selective GABAB PAM
  - Differentiated pharmacology
  - Improved efficacy and tolerability demonstrated in preclinical models
  - Absence of receptor desensitization with chronic treatment



The anatomical mediators of cough (1)

GABAB PAM offers potential for improved treatment for cough patients

[1]Mazzone and McGargey *Clin Pharm Ther* 2021

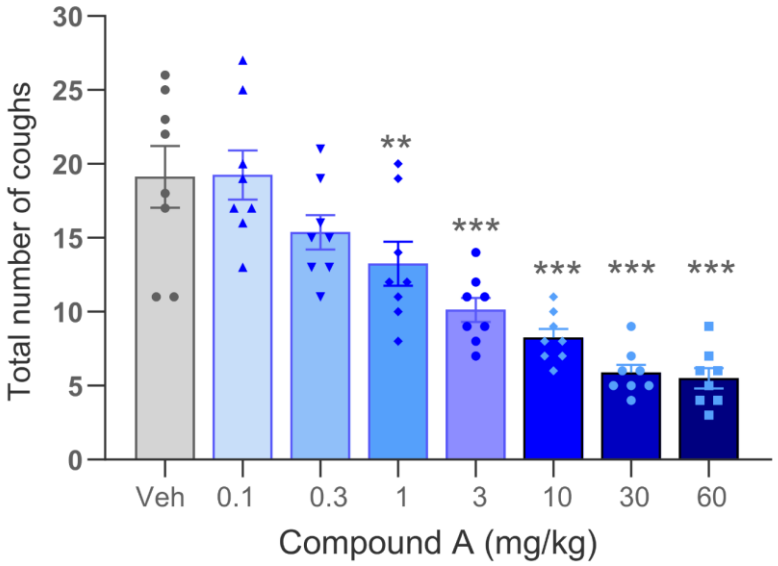
GABAB PAM for Cough – Program Status

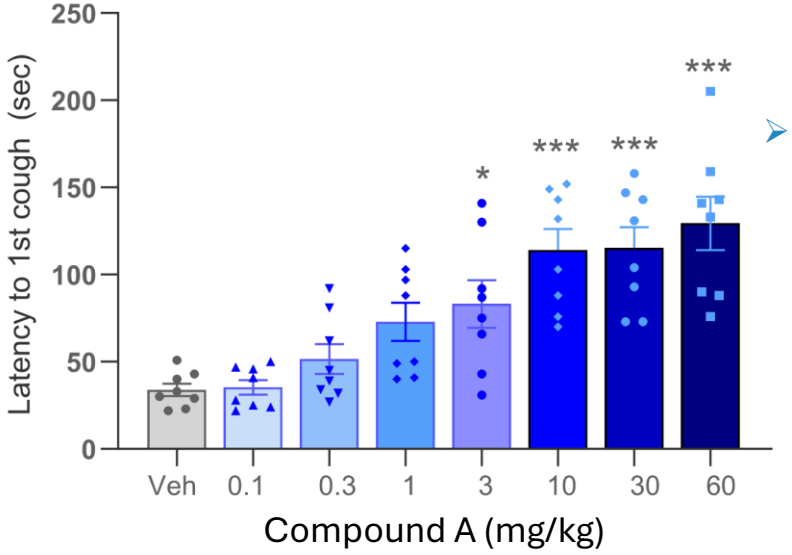
- Addex has a range of diverse potent and selective GABAB PAMs that were explored for cough indications
- Clinical candidate selected:
  - Favourable developability
  - Pre-IND activities completed
  - CMC completed
- In vivo proof-of-concept in a broad range of cough models demonstrated
  - Consistent MED of 1 mg/kg and ED_{50} of 6 mg/kg in cough frequency
  - No signs of tolerance after sub-chronic (7-day) treatment
  - Similar to a P2X3 inhibitor
  - No marked changes in respiratory rate, body temperature and growth hormone release up to 60 mg/kg across experiments
- IND enabling studies planned to start in 2025*

* Timings subject to financing/partnering

Antitussive Effects of Cpd A vs Baclofen in Citric Acid Induced Cough

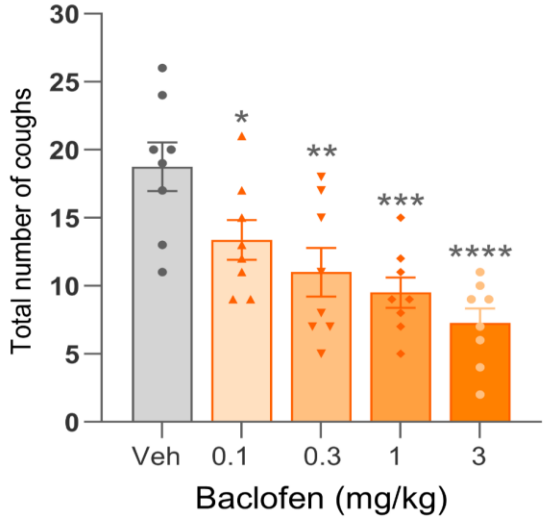
Compound A

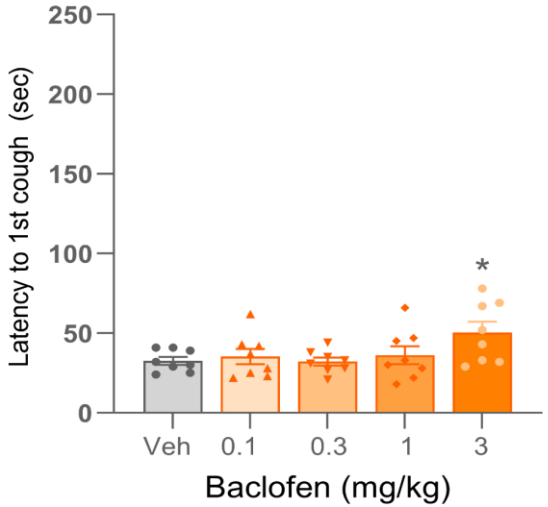




- Compound A results in dose-dependent reductions in cough frequency and increases in cough latencies

BACLOFEN





- Baclofen affects only cough frequencies

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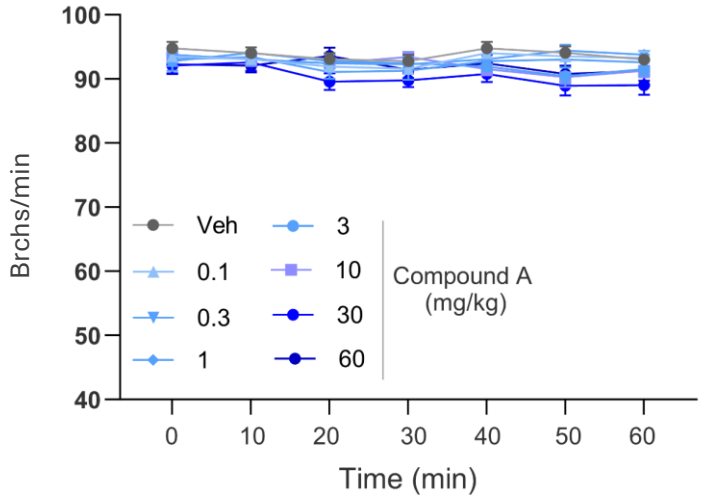
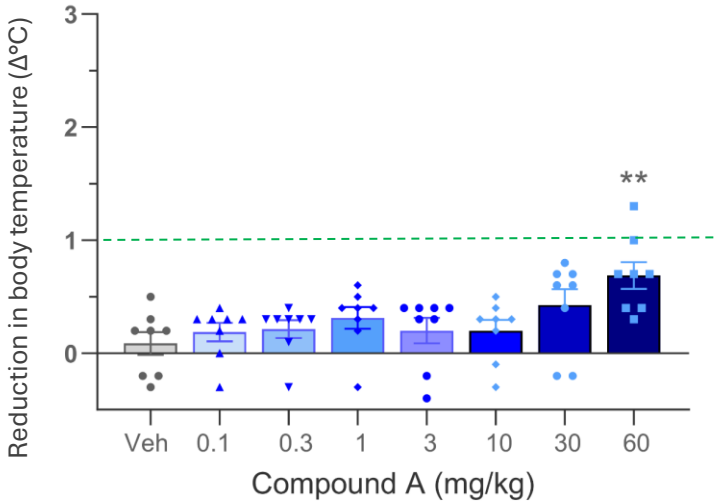
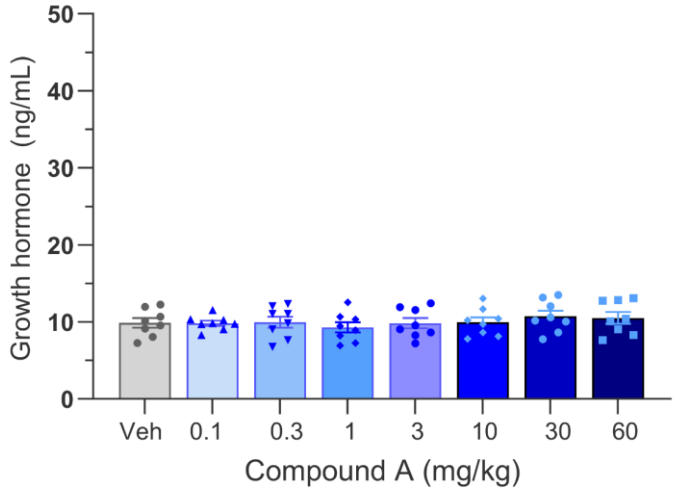
Compound A vs baclofen on Biomarkers Related to Side-effects

Compound A







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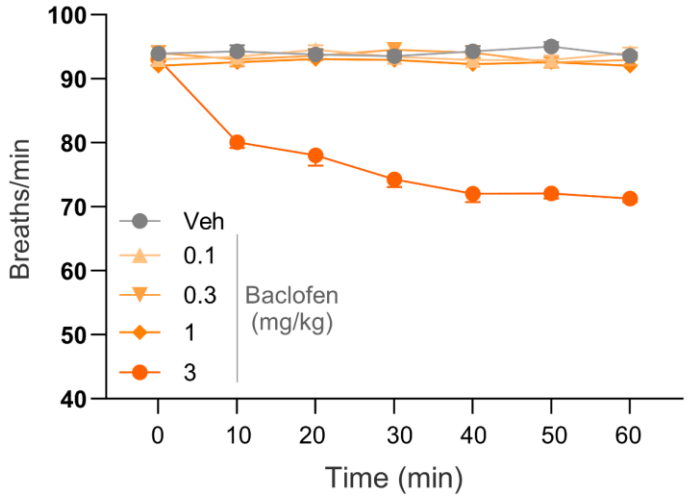

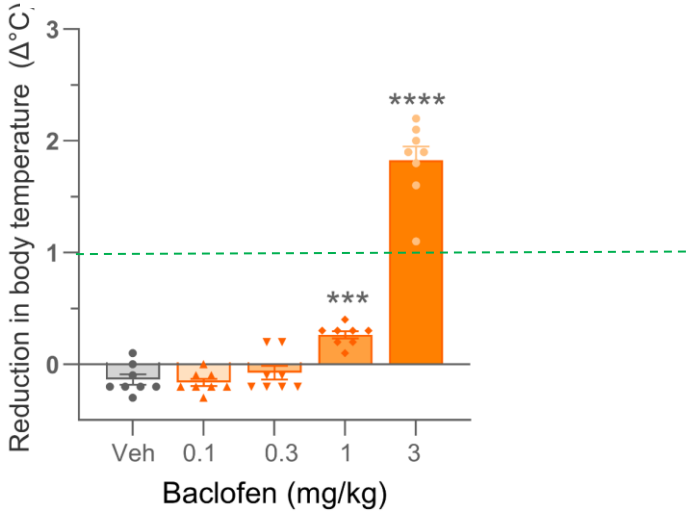

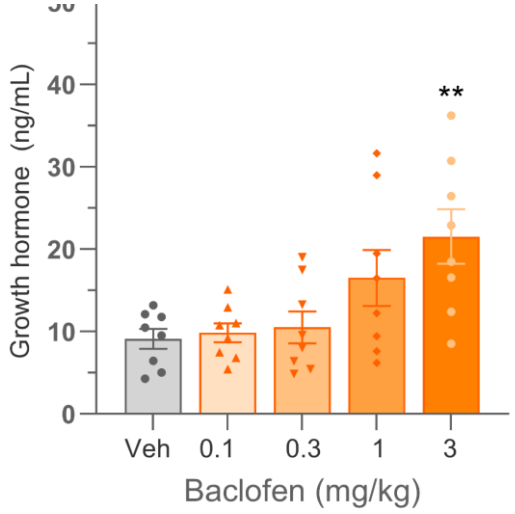

- Compound A has no effect on tolerability-related markers, including respiratory rate, body temperature and GH at up to 60 mg/kg.
- Baclofen showed reductions in respiratory rate, body temperature and increases in growth hormone starting at 3 mg/kg

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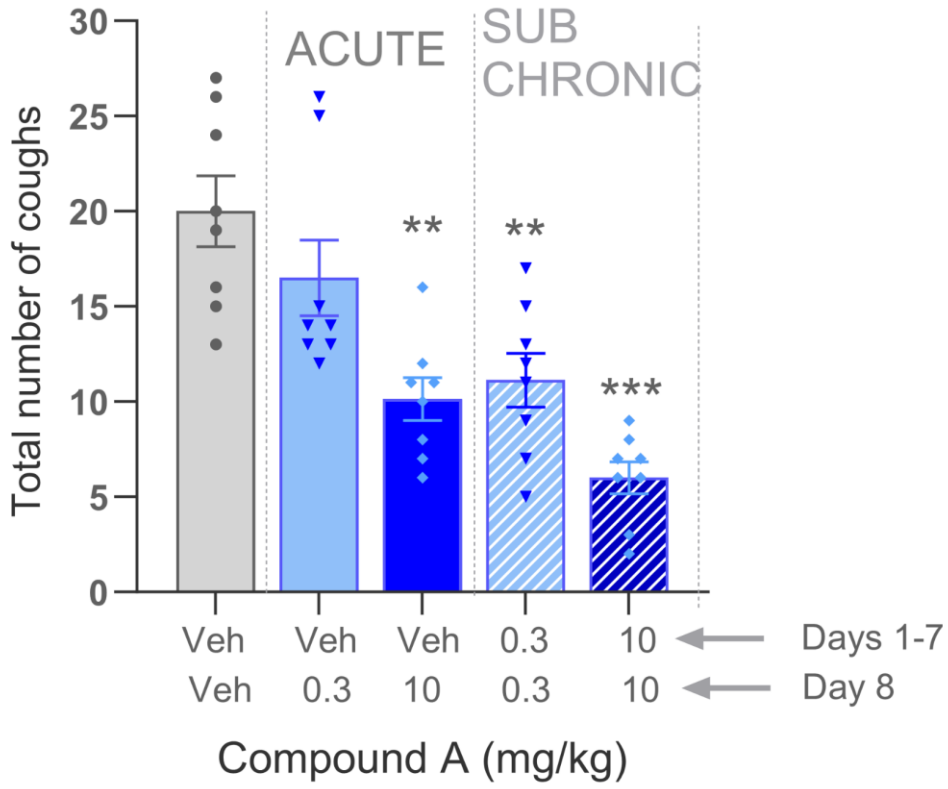
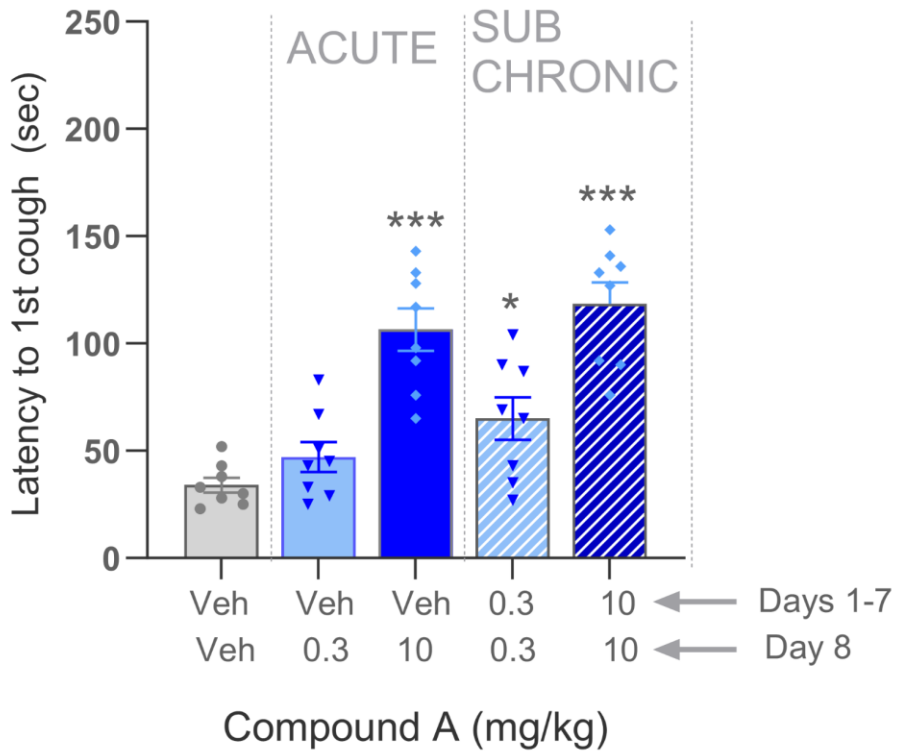
Antitussive Activity of Compound A in Citric Acid Induced Cough: Acute vs Sub-chronic Treatment

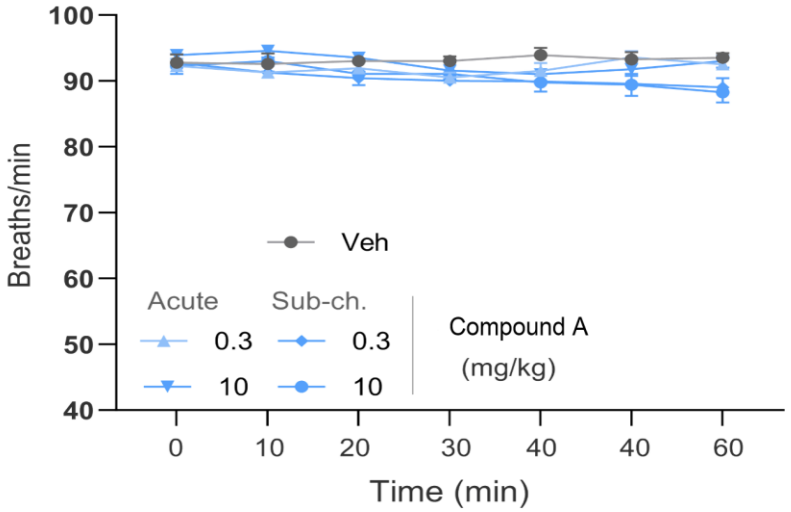


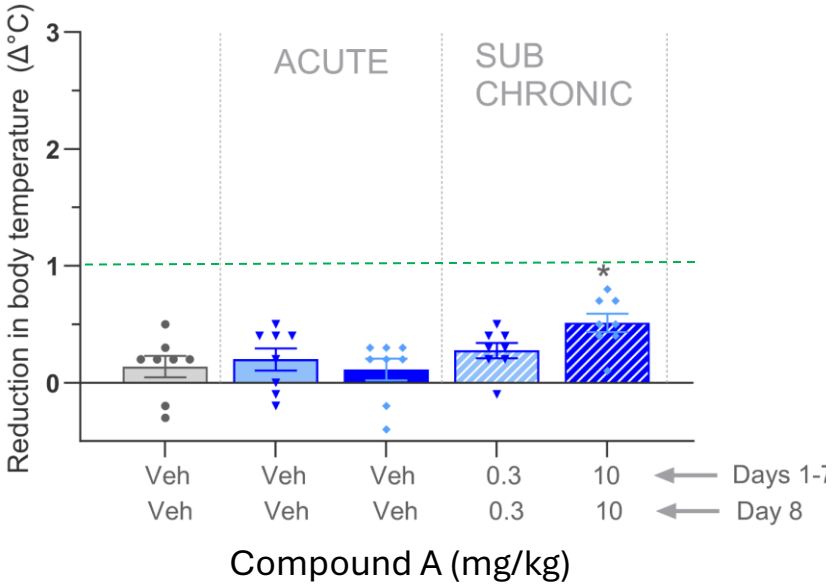


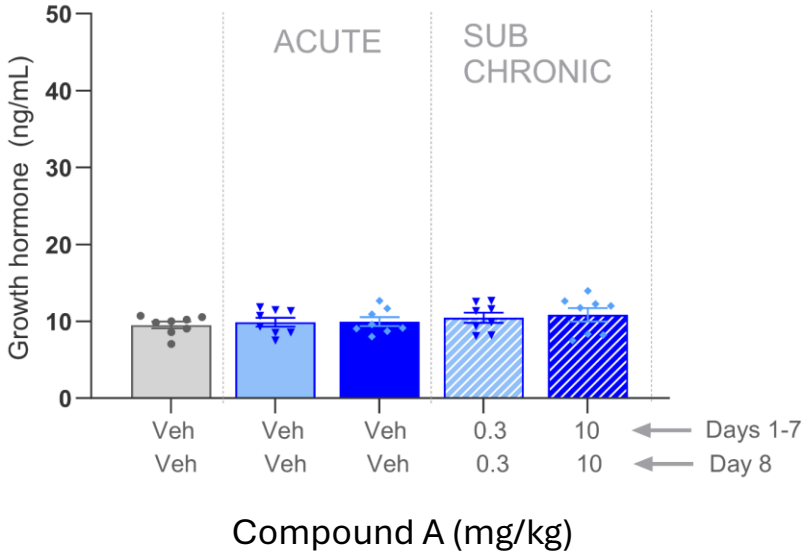
- There are no signs of tolerance in antitussive efficacy of Compound A after sub-chronic (7-day) treatment.
- A trend of reduced MED following sub-chronic treatment is seen in cough frequency and latency.

Activity of Compound A in a Model of Citric Acid Induced Cough: Sub-chronic Treatment

TOLERABILITY-RELATED READOUTS

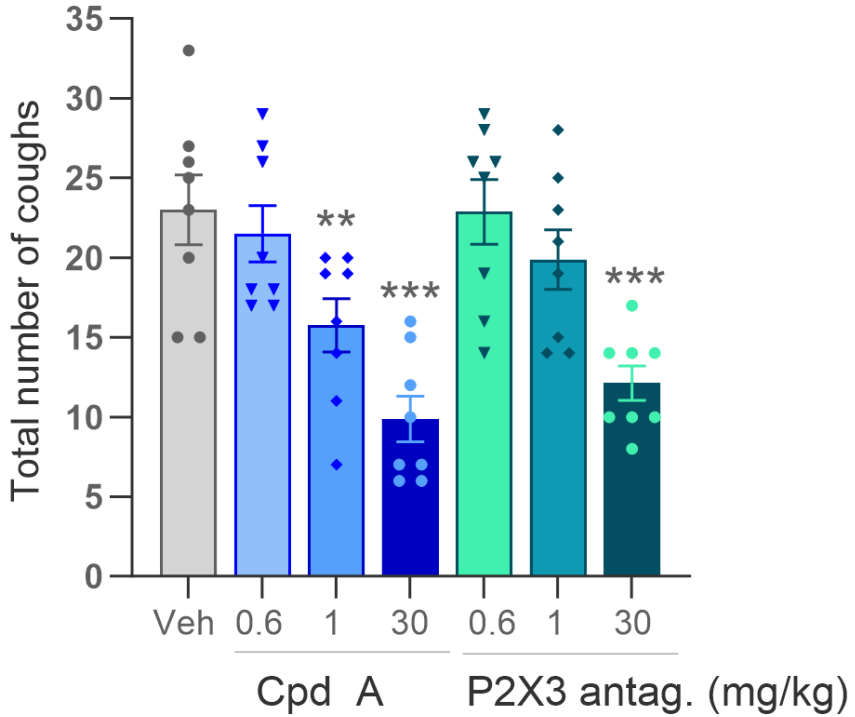


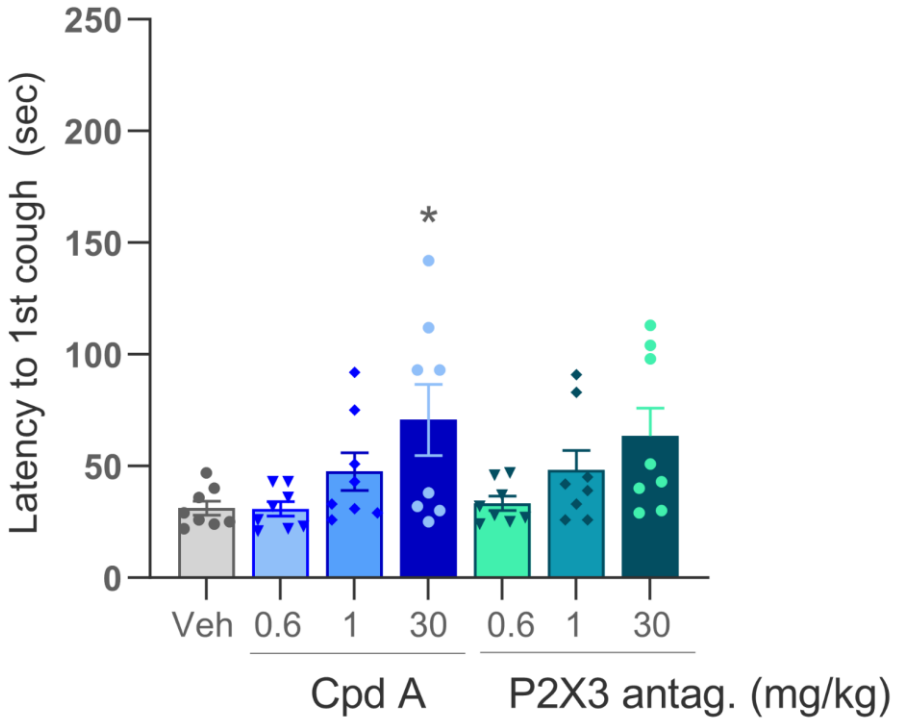




- No marked change in readouts linked to tolerability related markers following sub-chronic dosing of Compound A

Antitussive effects of Compound A vs P2X3 inhibitor in Citric Acid + ATP Induced Cough





- Compound A and a P2X3 inhibitor exhibit similar antitussive efficacy profiles.
- Compound A, similarly to a P2X3 inhibitor, show no marked effect on markers of tolerability, respiratory rate, reduction in body temperature and growth hormone release.

20% Equity Interest in Neurosterix

Well funded preclinical portfolio of high value assets

Neurosterix

- Addex spin-out company
  - Series A funding of $63 million in April 2024 led by Perceptive Advisors
  - Addex contributed allosteric modulator drug discovery platform and portfolio of preclinical programs
  - Addex received CHF5 million and a 20% equity interest
- High value pipeline advancing toward the clinic:
  - M4 PAM for schizophrenia
    - Clinically validated target
    - IND enabling studies expected to start in H2 2024
  - mGlu7 NAM for stress related disorders
    - First-in-class program
    - IND enabling studies expected to start in H1 2025
  - mGlu2 NAM for mild neurocognitive disorders
    - Progressing through lead optimization

Multiple high value programs funded to significant milestones

Addex Financials and Stock

Financials and Stock

- Cash at June 30, 2024:
  CHF 3.79M (USD 4.20M)
  - CHF 5M from sale of Neurosterix received in April 2024
  - Cash runway beyond 2026
- No debt
- Traded on SIX Swiss Exchange: ADXN (ISIN:CH0029850754)
- ADS representing 120 shares traded on Nasdaq: ADXN (ISIN: US00654J206; CUSIP: 00654J206)
- 128.26 M outstanding shares
  - Armistice Capital LLC – 26.13%*
- 184.35M shares incl. treasury shares (254.03M fully diluted)
  - Management & board holds – 13.47%*
- Analyst coverage:
  - HC Wainwright - Raghuram Selvaraju
  - valuationLab - Bob Pooler
  - Baader Helvea AG
  - ZKB – Edouard Riva

* Percentage of ownership calculated based on shares and warrants divided by fully diluted shares

Summary

Multiple high value partnerships	➢ GABAB PAM for substance use disorder (Indivior) candidate selected ➢ 20% equity interest in Neurosterix (backed by Perceptive Advisors)
In house programs driving future value	➢ Dipraglurant - post-stroke/TBI recovery Phase 2a ready to start ➢ GABAB PAM for chronic cough ready to start IND enabling studies ➢ ADX71149 indication under evaluation
Solid foundation	➢ Partnerships with industry leaders - Indivior ➢ Top tier US investors - Armistice Capital ➢ Dual listed SIX Swiss exchange & US Nasdaq ➢ Strong balance sheet and cash runway through 2026
Promising outlook	➢ GABAB PAM - start IND enabling studies in H1 2025 ➢ Dipraglurant Phase 2 ready to start Phase 2 in post-stroke/TBI recovery ➢ 20% holding in Neurosterix – Lead program, M4 PAM - IND enabling studies started Q3 2024

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ALLOSTERIC MODULATORS FOR HUMAN HEALTH