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Innovative Treatments for Central Nervous System Disorders

July 2025

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 Phase 1 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 successfully completes IND enabling studies ➢ $65M 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 - IND enabling studies successfully completed – $330M in milestones & tiered royalties from high single digit to low double digit
Strong balance sheet	➢ Dual listed on SIX Swiss Exchange & US Nasdaq Capital Market ➢ CHF 2.8M ($3.2M) cash at March 31, 2025 ➢ Cash runway through 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)		Brain injury recovery - post-stroke / TBI				Ready to start Phase 2a study*
ADX71149 (mGlu2 PAM)		Indication under evaluation				New indication selection
$GABA_B$ PAM	INDIVIOR	Substance use disorders				File IND
$GABA_B$ PAM		Chronic cough				IND enabling studies ready to start*
20% Neurosterix LLC – Advancing a focused CNS Pipeline						
M4 PAM		Schizophrenia and other psychosis				Start Phase 1 in H2 2025
mGlu7 NAM		Mood disorders				IND enabling studies ongoing
mGlu2 NAM		Cognition				Enter clinical candidate selection in H2 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

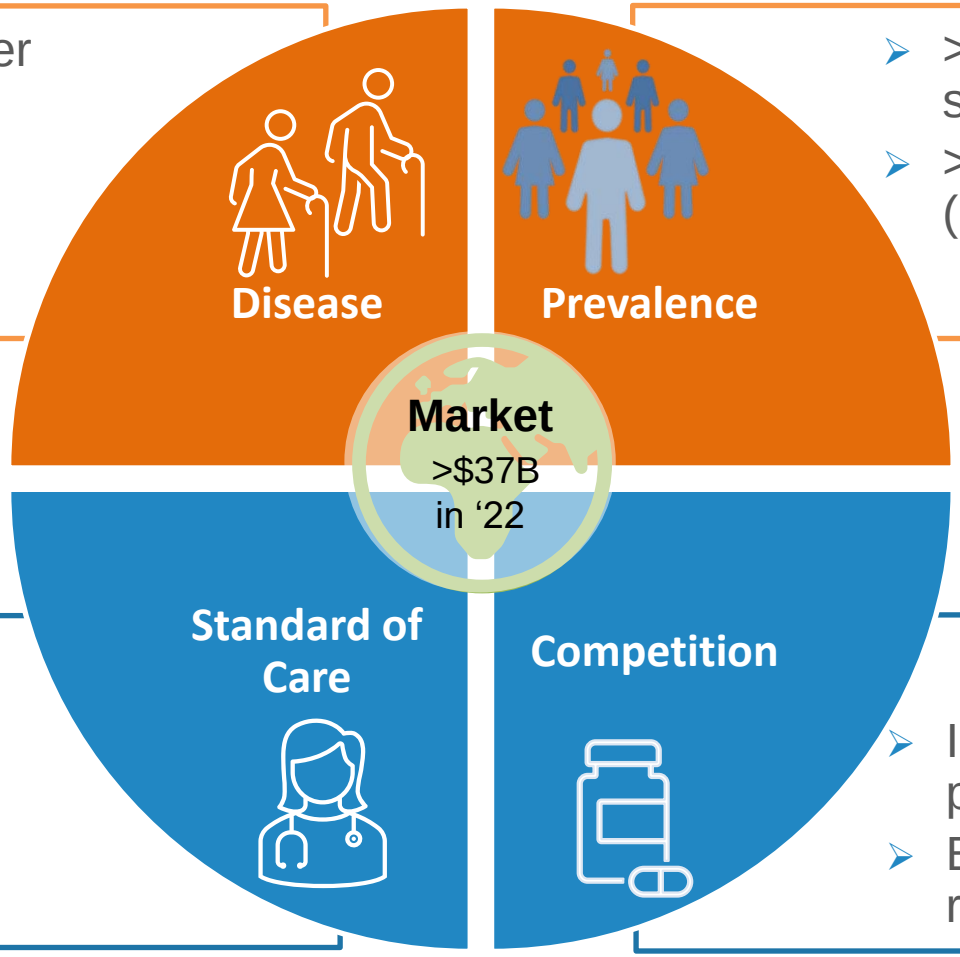
PTSD = Post-traumatic stress disorder
PAM = Positive Allosteric Modulator

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

Targeting neuroplasticity early in rehabilitation to promote rebuilding of neuronal connections and sensorimotor 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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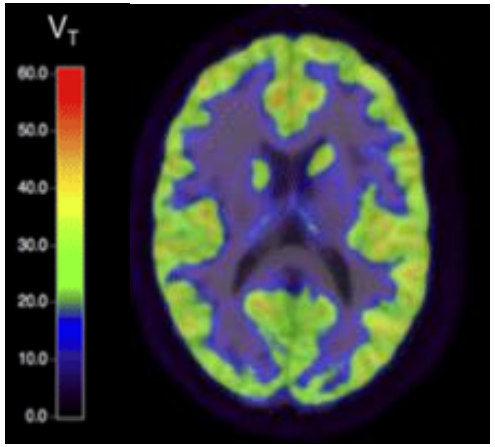
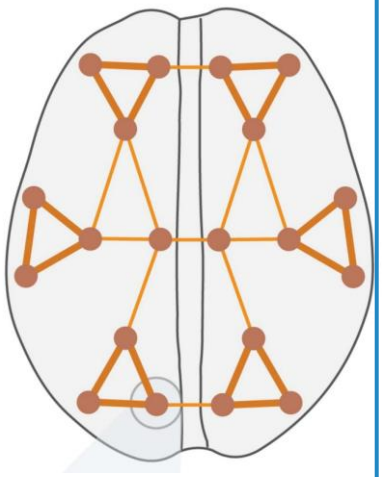
mGlu5: An Innovative Target for Brain Injury Recovery

Healthy brain

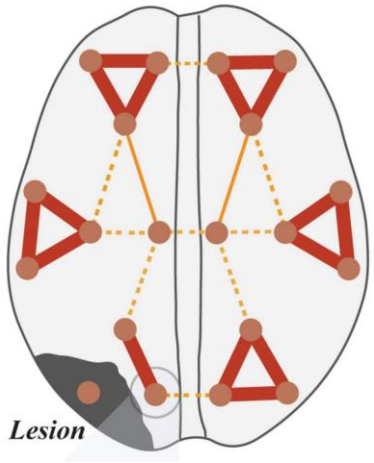


mGlu5 brain distribution



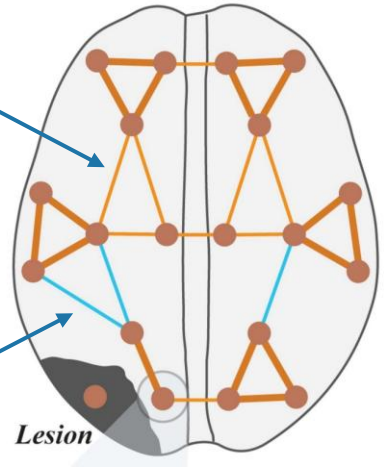
Good inter & intra-nodal connectivity

mGlu5 NAM supports rebuilding of neuronal connections



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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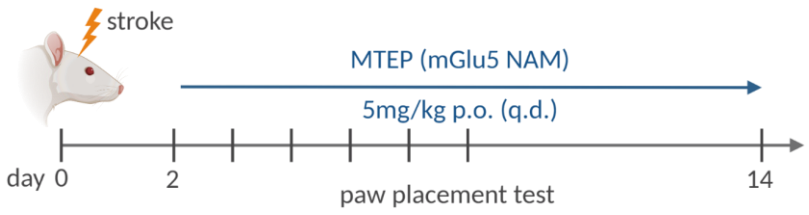
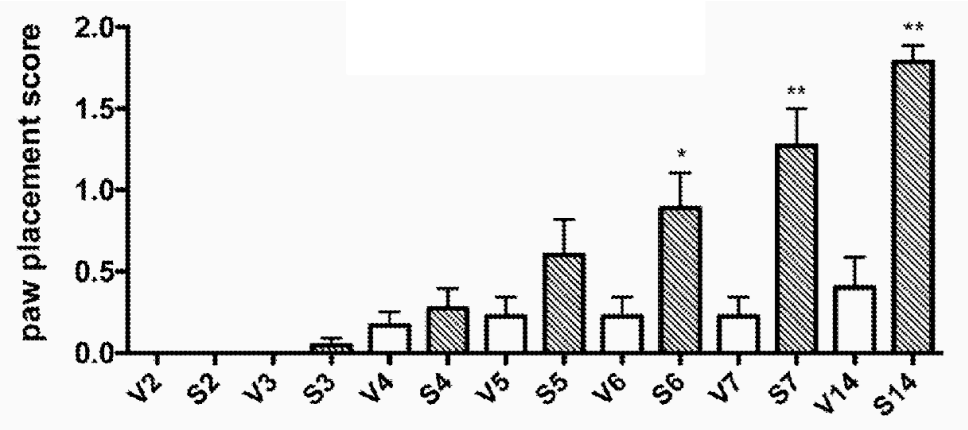
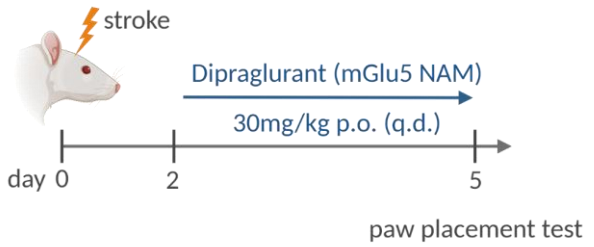
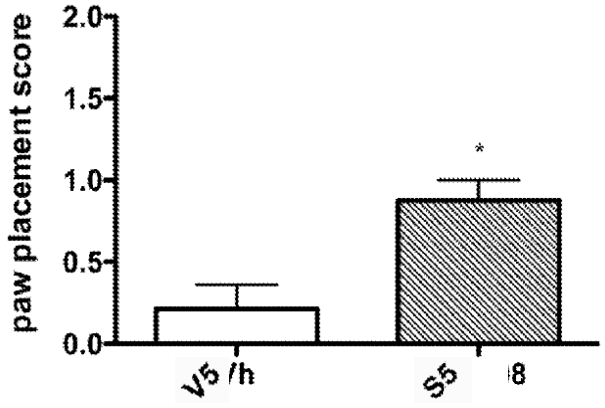
Preclinical Data: mGlu5 Inhibition Promotes Post-Stroke Recovery





MTEP treatment resulted in a significant recovery of functional control



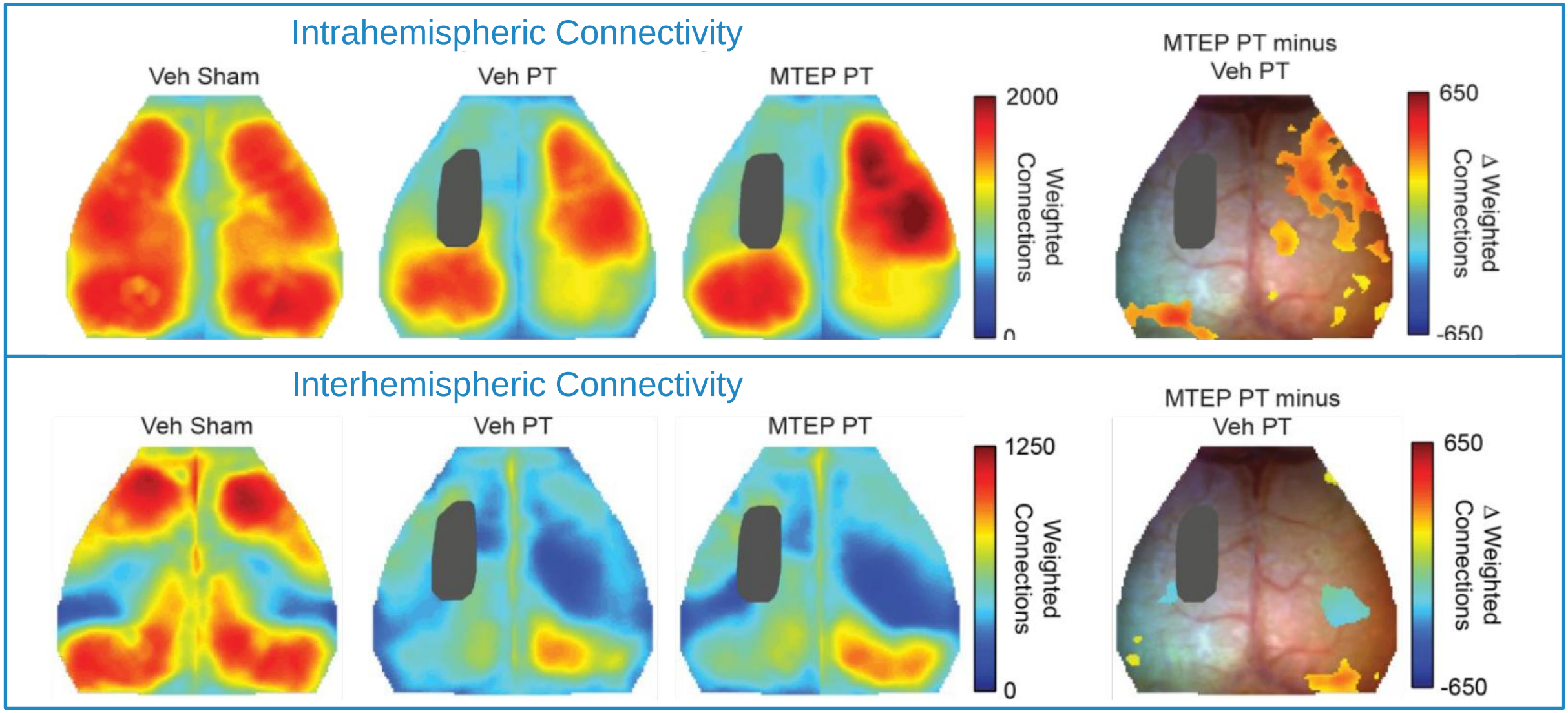


Dipraglurant significantly restored functional control in a one-week experiment

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

From patent application PCT WO2017/171594A1

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 protection through 2037 (without extensions)

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 successfully completed IND enabling studies ➢ Differentiated leads and backups with robust novel IP potential ➢ IND filing ongoing
Strategic partnership with Indivior	➢ Eligible to receive $330 million in milestones and tiered royalties from high single digits to low double digits

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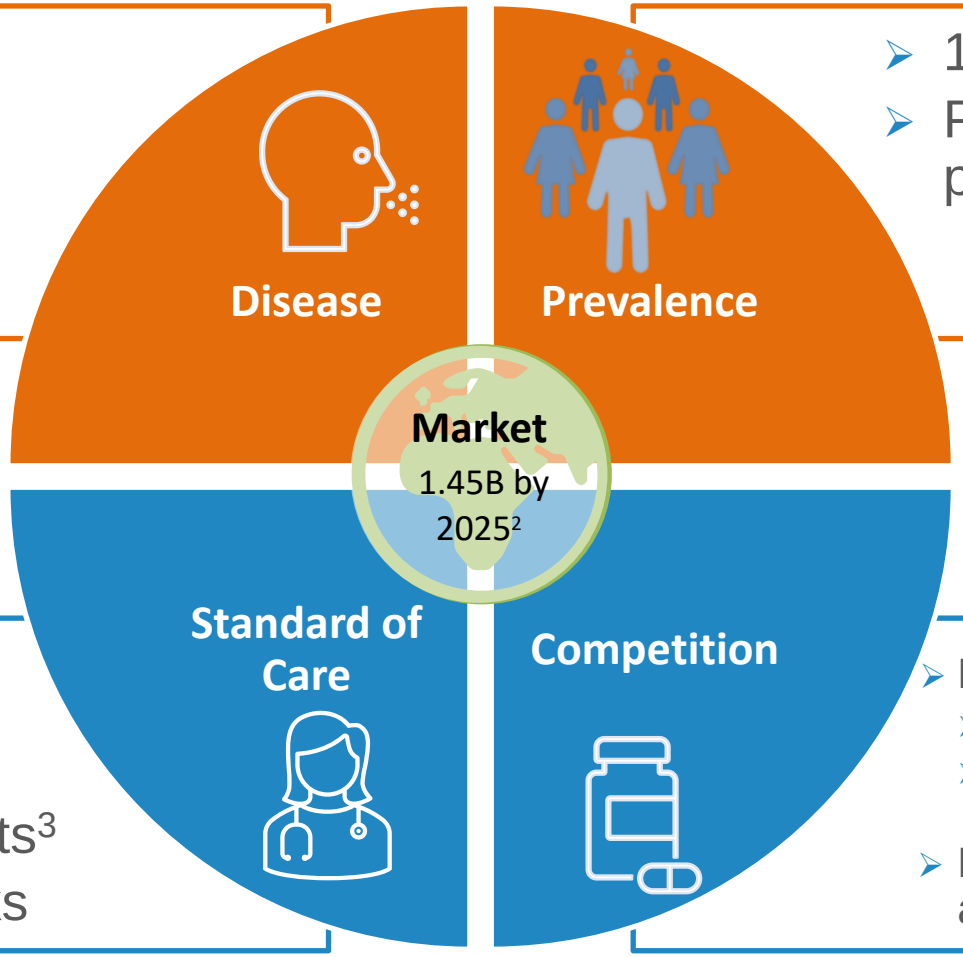
[1]Merikangas et al. 2010
[2]NIDA
[3]Augier et al 2017
[4]Hwa et al 2014
[5]Addex int. report

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
- Persists >1 year in 60% of patients

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

- P2X3 Inhibitors (Phase 3):
  - Ineffective: ~30% of patients
  - Discontinuation: ~20% (taste related side-effects)
- Haduvio (Trevi) – kappa agonist and a mu opioid antagonist (Phase 2)

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

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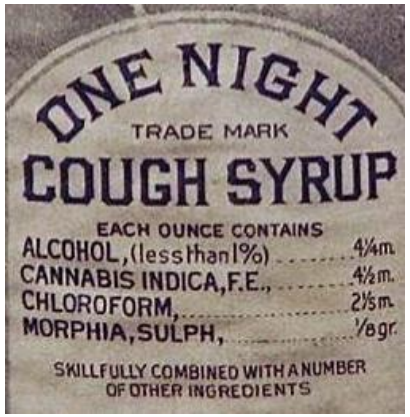
Pharmacological treatment of chronic cough – efficacy vs tolerability



Use / side-effects	Dextro-metorphan	Opioids	Nalbuphine (Phase 2)	Gabapentin & pregabalin	Amitriptyline	P2X3*	GABAB Agonist Baclofen	GABAB Addex PAM
Treatment type	Chronic	Acute	?	Acute	Acute	Chronic	Chronic+	Chronic
Risk of Abuse	Yes	Yes	No	Yes	Yes	No	No	No
Respiratory	No	Yes	Yes	Yes	Yes	No	Yes	No
Other CNS	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Gastrointestinal	Yes	Yes	No	No	No	No	No	No
Taste-related	No	No	No	No	No	Yes**	No	No

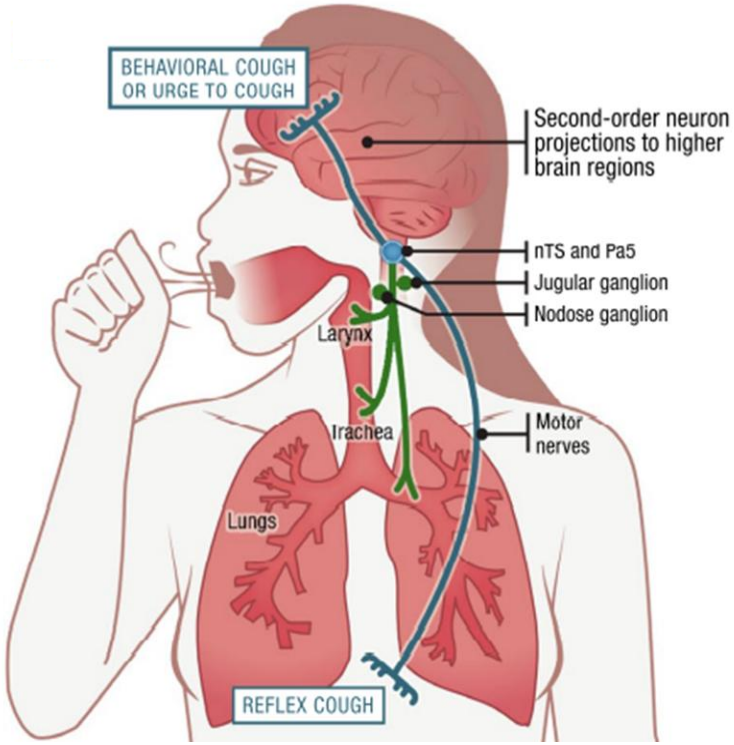
- P2X3 inhibitors
  - *Taste-related side effects observed in up to 97% of patients treated with gefapixant- expected to be less with camlipixant[1]
  - ** Both ineffective in up to 30% of patients
- GABAB agonist baclofen
  - Most patients discontinue due to poor tolerability

GABAB PAM has the potential to offer a best-in-disease efficacy and tolerability profile

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

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

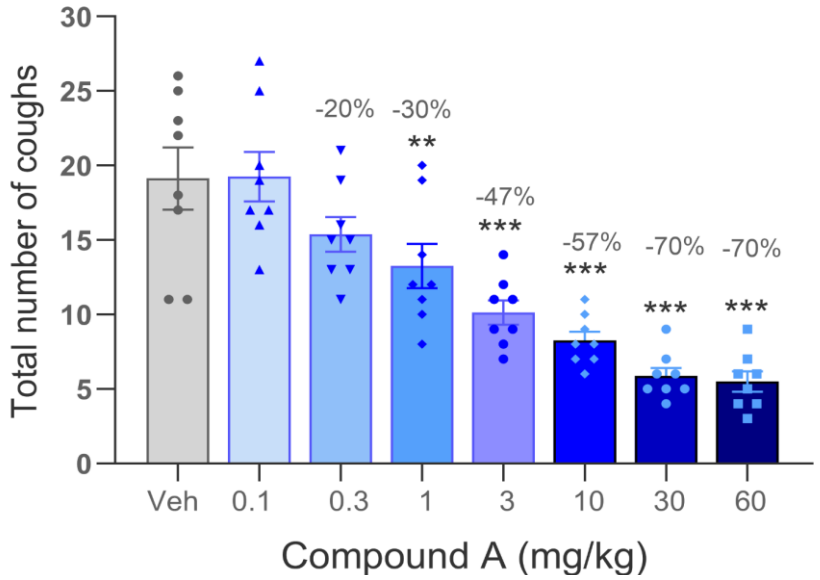
- Addex has a range of diverse potent and selective GABAB PAMs that were explored for cough indications
- Clinical candidate selected:
  - Favorable developability
  - Pre-IND activities completed
  - CMC completed
- In vivo proof-of-concept in a broad range of cough models demonstrated
  - Consistent 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*

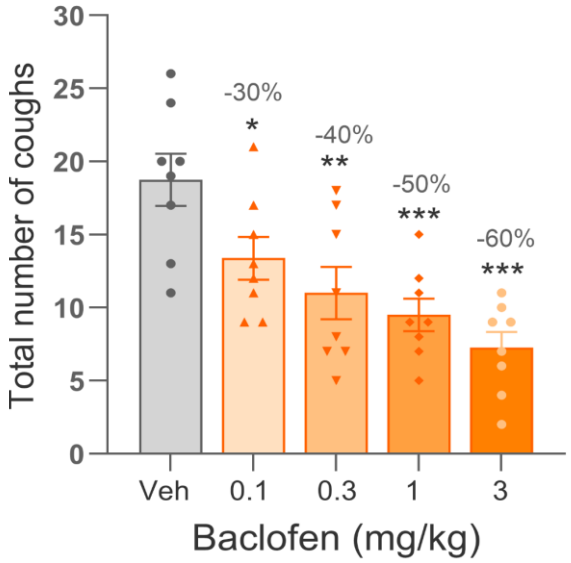
* Timings subject to financing/partnering

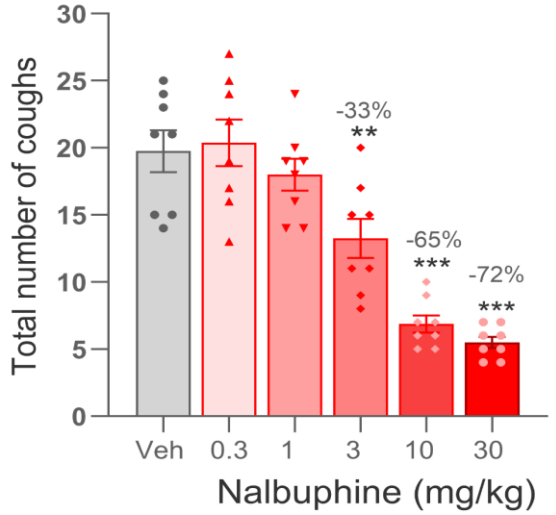
Citric Acid Cough in Guinea Pigs – Total Number of Coughs

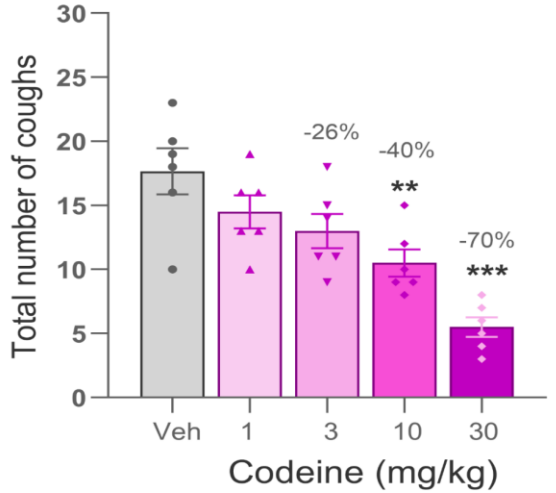
Compound	ED50 (mg/kg)	Max Efficacy	Max Efficacy*
Compound A	5.96	70%	70%
Baclofen	0.93	60%	50%
Nalbuphine	7.57	70%	65%
Codeine	12.6	70%	40%

- Compound A results in a dose-dependent reduction in cough number reaching maximal effects similar or better than with other compounds









*the highest dose without effects on respiratory rate

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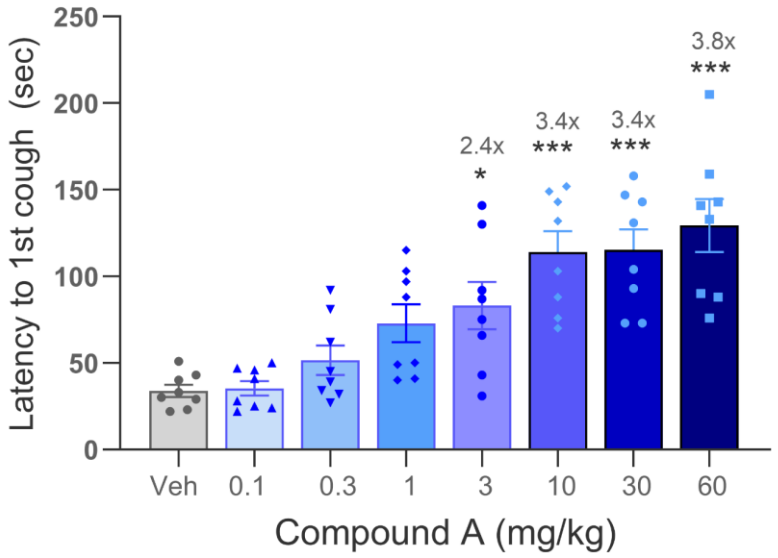
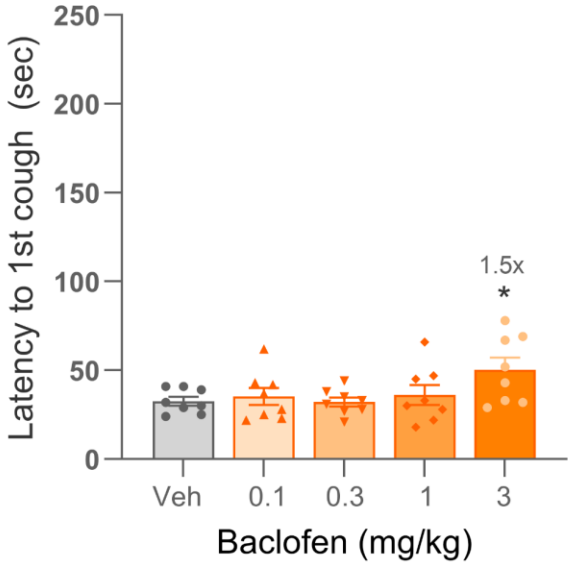
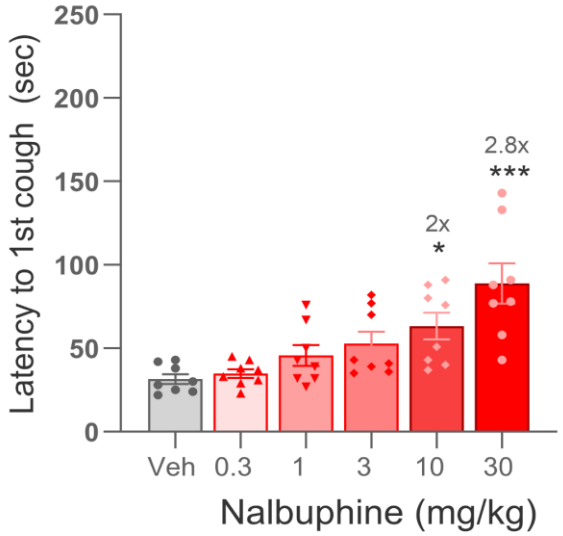
Citric Acid Cough in Guinea Pigs – Latency to First Cough

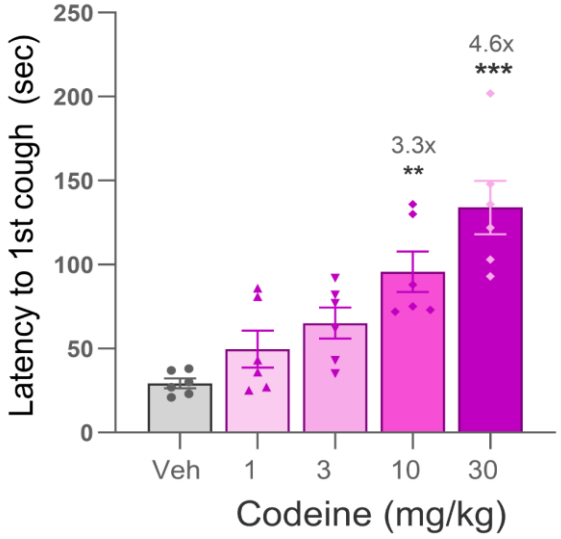
Compound	ED50 (mg/kg)	Max Efficacy	Max Efficacy*
Compound A	5.20	282	282%
Baclofen	8.58	54	10%
Nalbuphine	31.78	182	100%
Codeine	4.91	357	226%

- Compound A results in a dose-dependent increase in cough latency reaching maximal effects similar or better than with other compounds









*the highest dose without effects on respiratory rate

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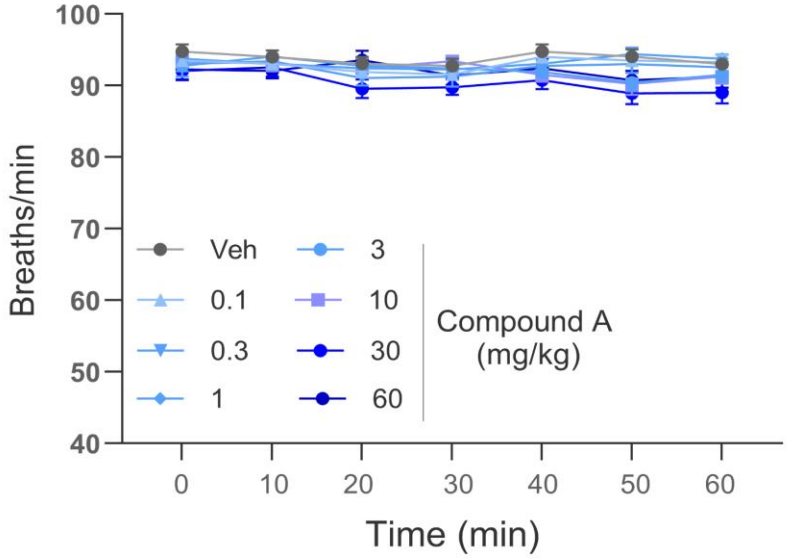
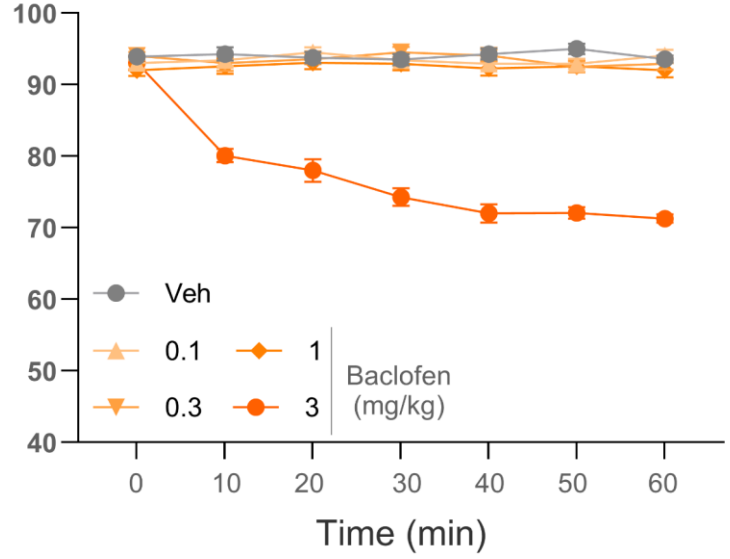
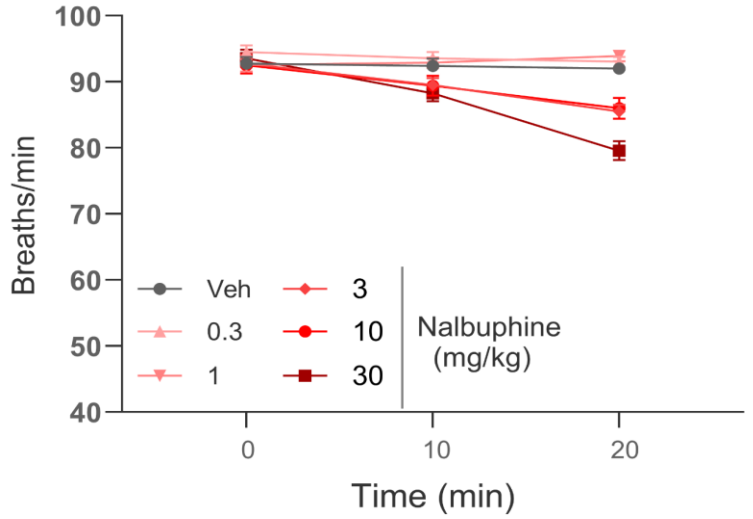
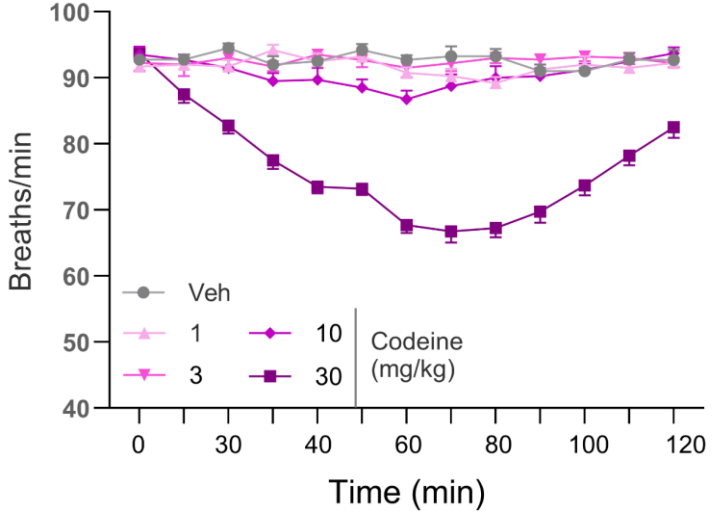
Citric Acid Cough in Guinea Pigs – Respiratory Rate

- Respiratory rate is a biomarker of sedation in rodents as well as humans
- Compound A had no effect on respiratory rate at up to 60 mg/kg, while other compounds resulted in marked reduction in respiratory rate at their highest doses
- Compound A has a superior therapeutic margin
- Sedation and somnolence are side effects reported in the clinic with baclofen, nalbuphine and codeine



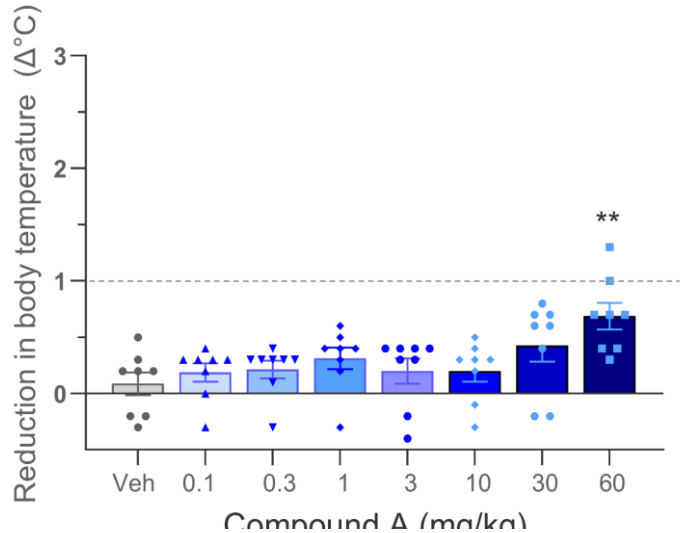


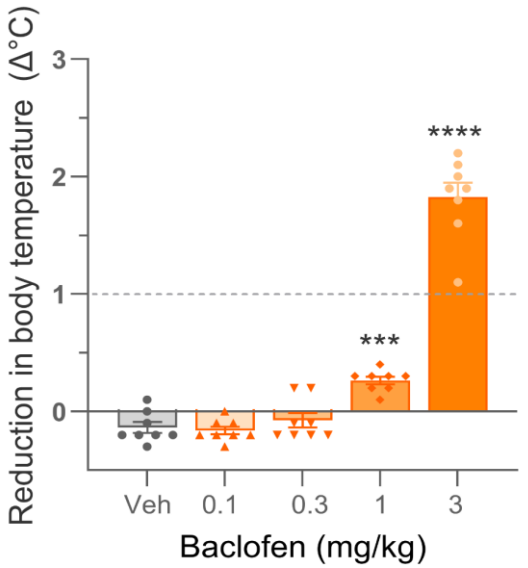


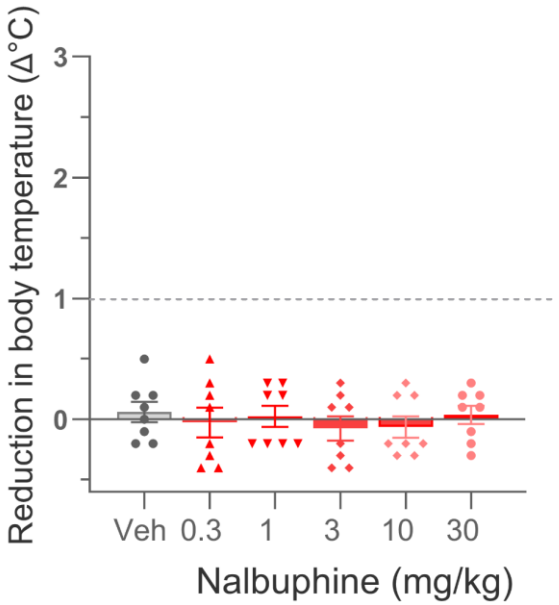


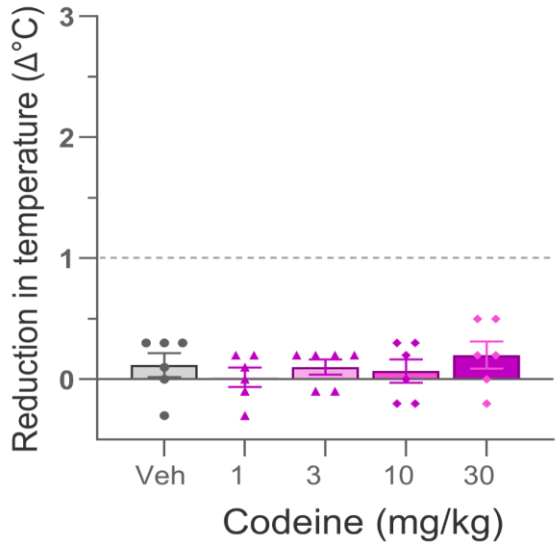
Citric Acid Cough in Guinea Pigs – Reduction in Body Temperature

- Reduction in body temperature is a rodent biomarker of GABAB receptor occupancy in the CNS
- Compound A resulted in a minor (0.7°C) reduction in body temperature only at the highest dose (60 mg/kg), in contract to near 2°C reduction seen with baclofen
- Compound A shows less CNS receptor occupancy than baclofen which explains its improved tolerability profile
- As expected, no effect of Nalbuphine or Codeine









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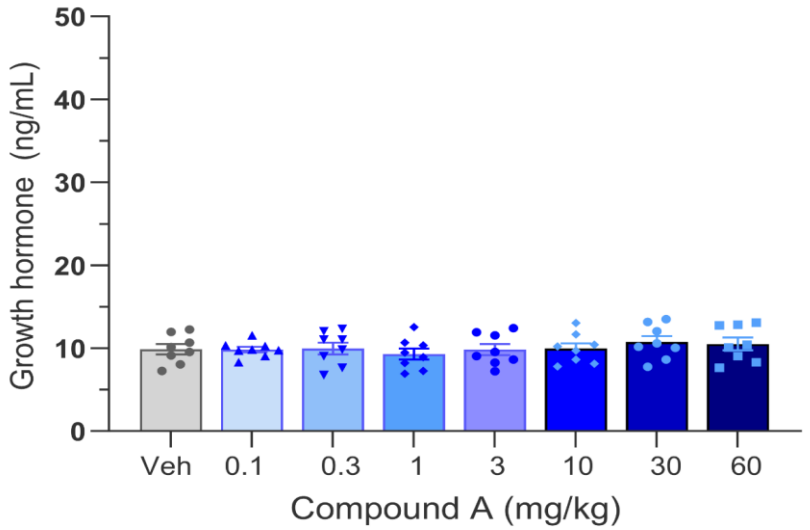
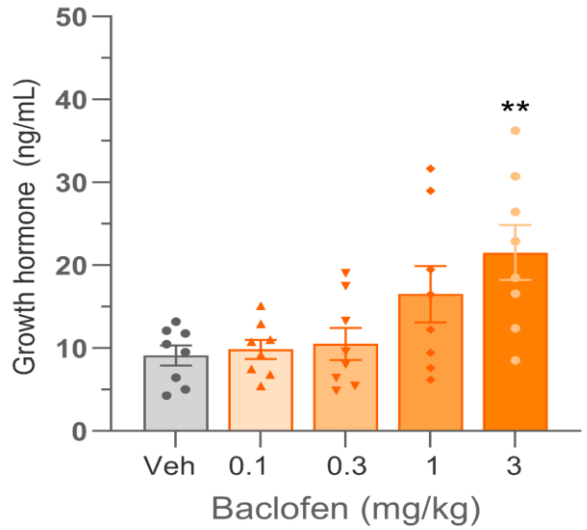
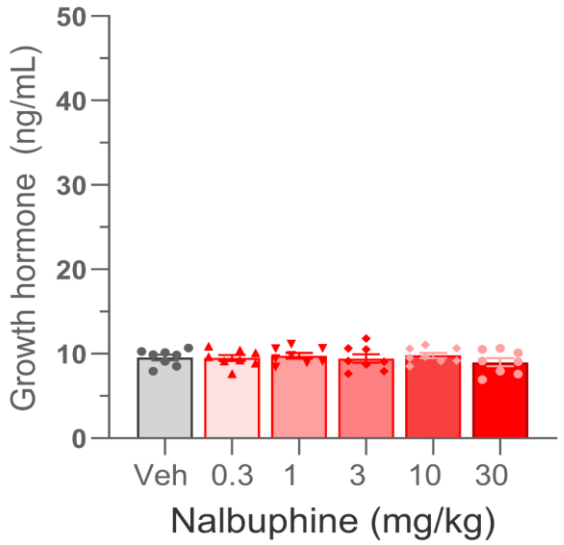
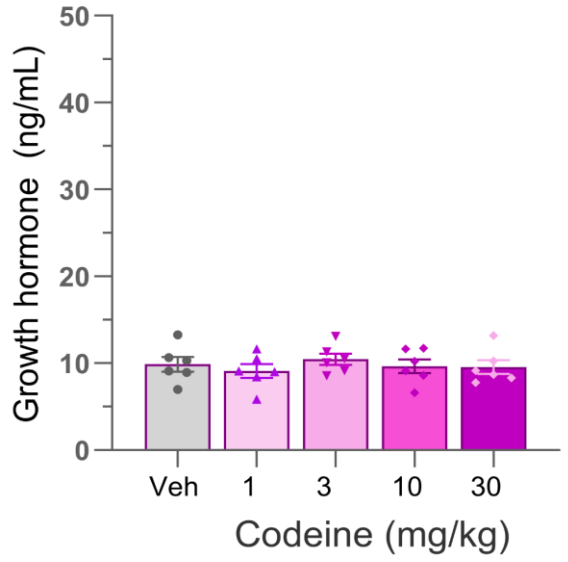
Citric Acid Cough in Guinea Pigs – Growth Hormone

- Growth hormone is a biomarker of GABAB receptor occupancy in the CNS
- Compound A did not increase growth hormone in plasma at up to 60 mg/kg, while baclofen caused more than 2x increases in growth hormone concentration
- Compound A shows less CNS receptor occupancy than baclofen which explains its improved tolerability profile
- As expected, no effect of Nalbuphine or Codeine

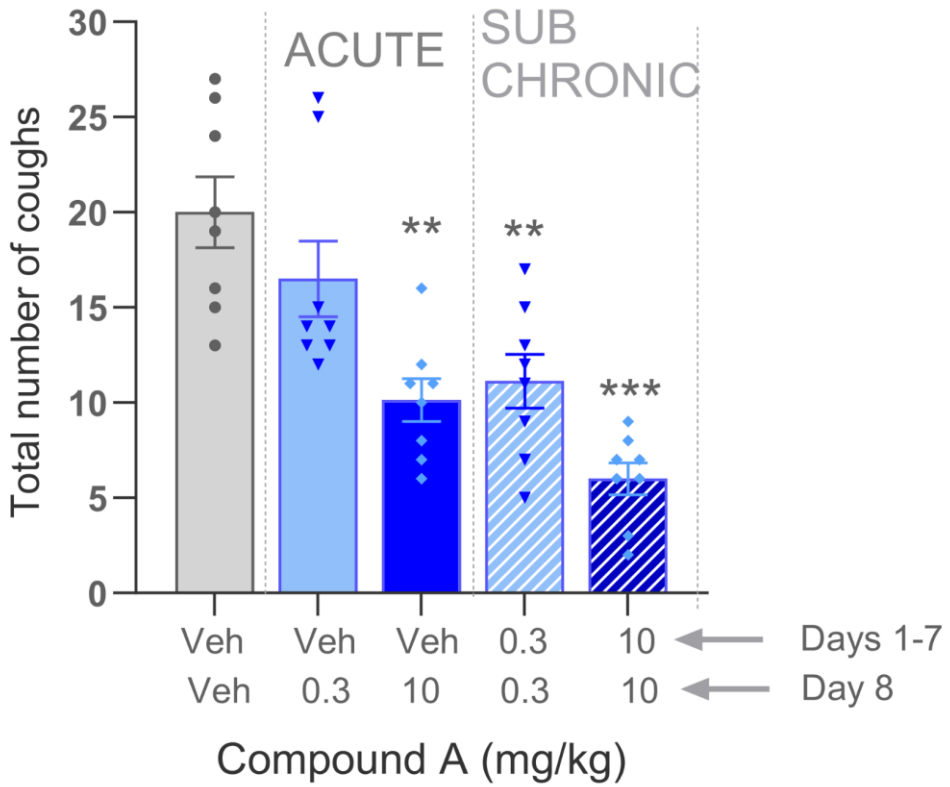


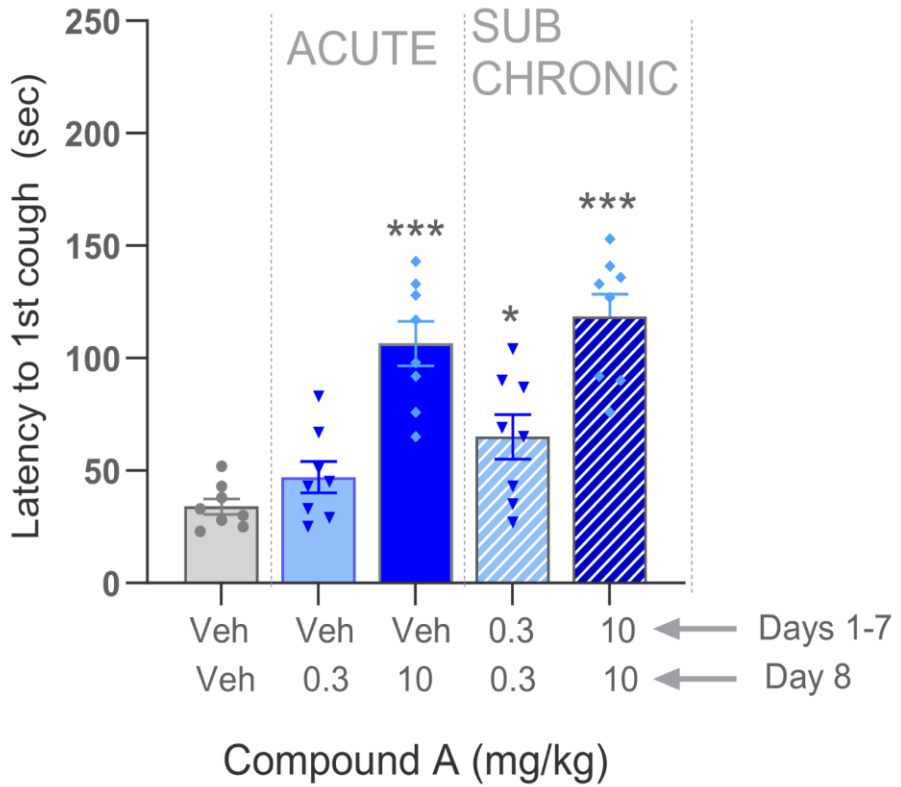






Citric Acid Induced Cough: Acute vs Sub-chronic Treatment





- 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.

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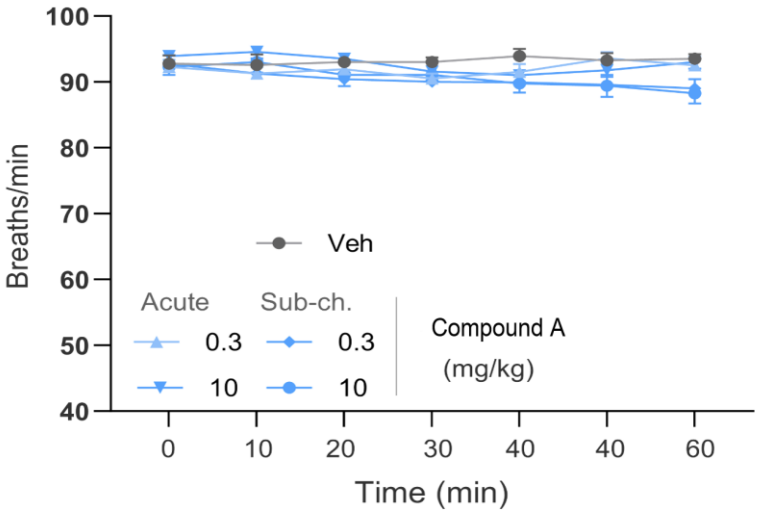
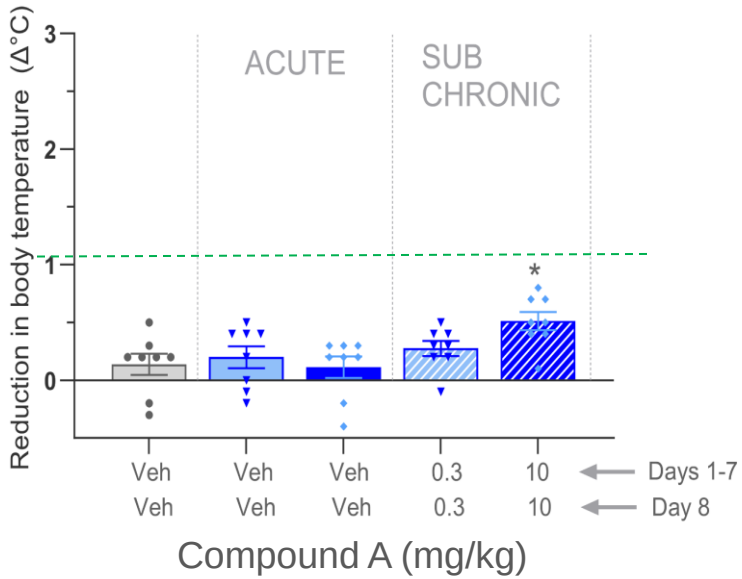
Citric Acid Induced Cough: Sub-chronic Treatment Tolerability Readouts

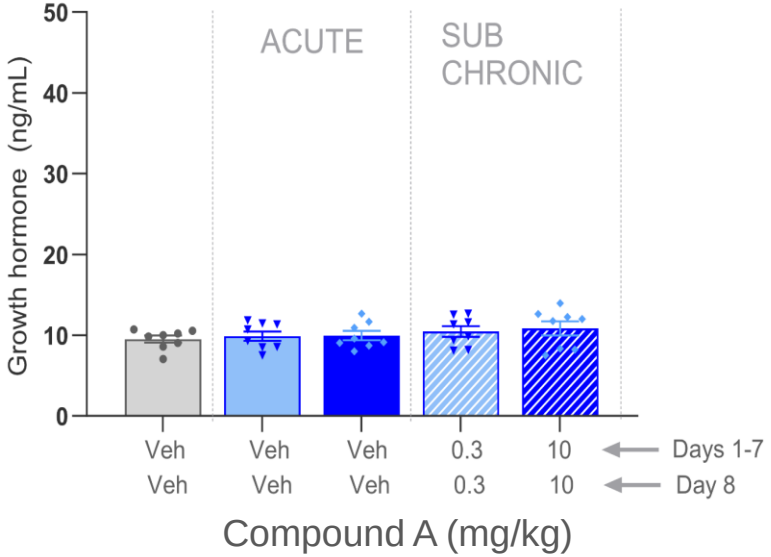
Respiratory Rate



Body Temperature

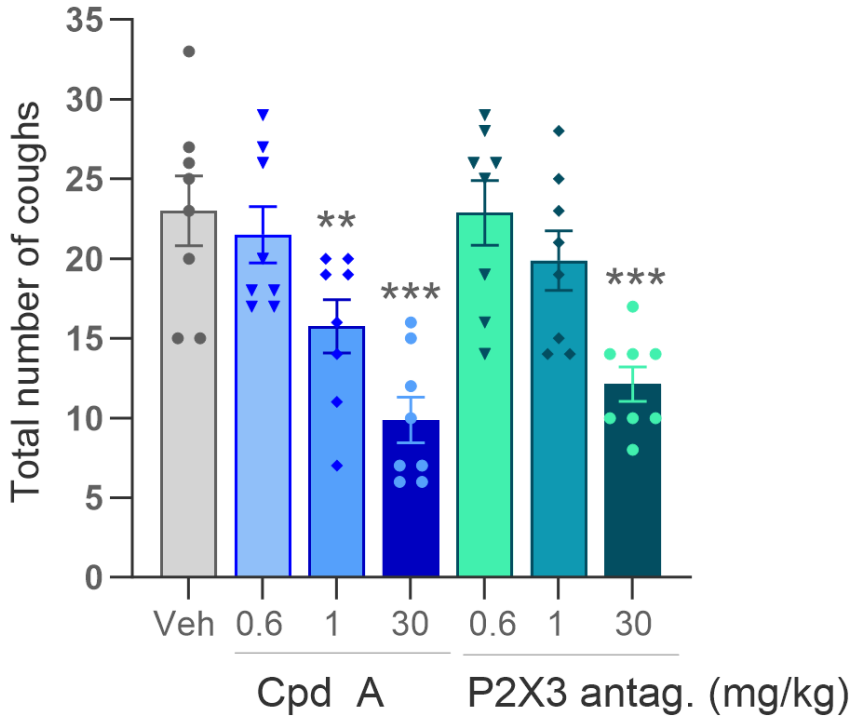


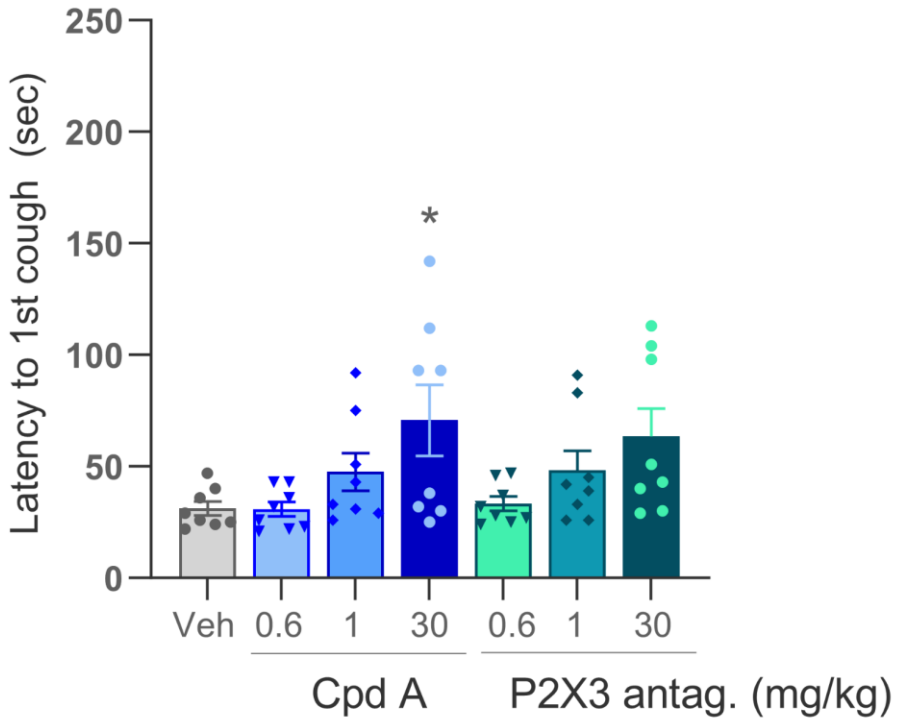
Growth Hormone



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

Compound A vs P2X3 inhibitor - 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 $65 million in 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 successfully completed with Phase 1 scheduled to start in H2 2025
  - mGlu7 NAM for mood disorders
    - First-in-class program
    - IND enabling studies ongoing and expected to complete in H2 2025
  - mGlu2 NAM for mild neurocognitive disorders
    - Progressing through lead optimization – clinical candidate selection expected to start in H2 2025

Multiple high value programs funded to significant value inflection milestones

Addex Financials and Stock

Financials and Stock

- Cash at March 31, 2025: CHF 2.8M (USD 3.2M)
  - Cash runway through 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 – 21.97%*
- 184.35M shares incl. treasury shares (254.03M fully diluted)
  - Management & board holds – 13.46%*
- Analyst coverage:
  - HC Wainwright - Raghuram Selvaraju

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* 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 & IND enabling studies successfully completed ➢ 20% equity interest in Neurosterix (backed by Perceptive Advisors)
In house programs driving future value	➢ Dipraglurant - brain injury recovery Phase 2a ready to start ➢ GABAB PAM for chronic cough ready to start IND enabling studies ➢ ADX71149 (mGlu2PAM) - indication under evaluation
Solid foundation	➢ Partnerships with industry leaders - Indivior ➢ Dual listed SIX Swiss exchange & US Nasdaq ➢ Cash runway through 2026
Promising outlook	➢ GABAB PAM cough program- start IND enabling studies in H2 2025 ➢ Dipraglurant Phase 2 ready to start Phase 2 in post-stroke/TBI recovery ➢ 20% holding in Neurosterix – Lead program, M4 PAM – Phase 1 expected to start in H2 2025

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