



Innovative Treatments for Central Nervous System Disorders

September 2025

Allosteric modulators for human health

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Addex Overview

High value programs reaching significant milestones	<ul style="list-style-type: none">➤ GABAB PAM for cough ready to enter IND enabling studies➤ Dipraglurant for post-stroke/TBI¹ recovery – Phase 2 ready➤ Neurosterix portfolio advancing towards Phase 1 studies
20% equity interest in spin-out company, Neurosterix	<ul style="list-style-type: none">➤ Leading allosteric modulator drug discovery platform<ul style="list-style-type: none">– Validated & differentiated pharmacological approach➤ Preclinical portfolio of high value programs<ul style="list-style-type: none">– 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	<ul style="list-style-type: none">➤ GABAB PAM for SUD² partnered with Indivior - IND enabling studies successfully completed<ul style="list-style-type: none">– \$330M in milestones & tiered royalties from high single digit to low double digit
Strong balance sheet	<ul style="list-style-type: none">➤ Dual listed on SIX Swiss Exchange & US Nasdaq Capital Market➤ CHF 2.8M (\$3.2M) cash at March 31, 2025➤ Cash runway through 2026

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		Substance use disorders				File IND
GABA _B PAM		Chronic cough				IND enabling studies ready to start*

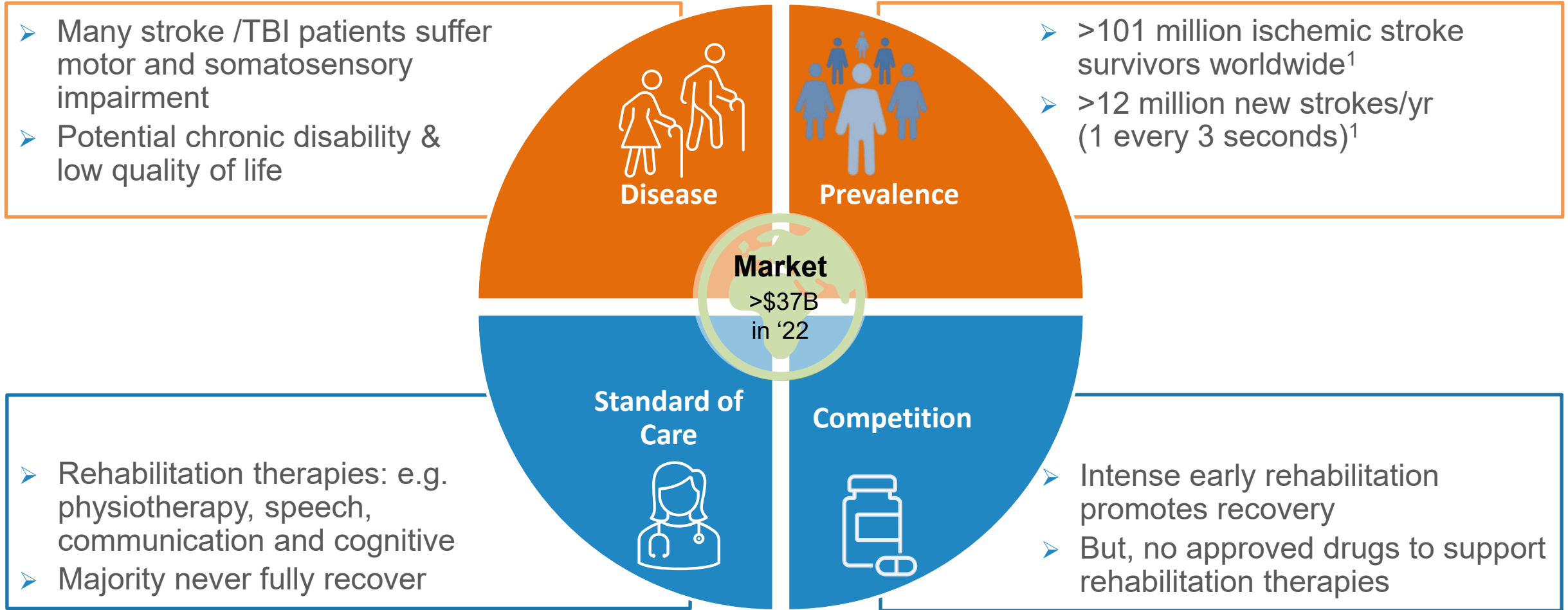
20% Neurosterix LLC – Advancing a focused CNS Pipeline

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

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

*Targeting neuroplasticity early in rehabilitation to promote rebuilding of neuronal connections
and sensorimotor recovery*

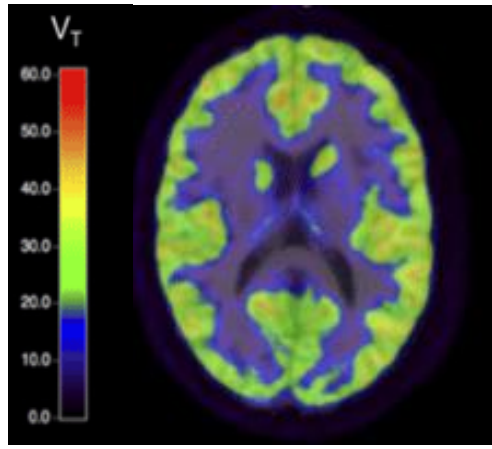
Post Stroke / TBI Recovery - Unmet Medical Need & Commercial Opportunity



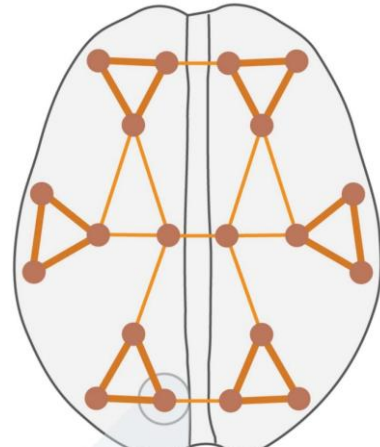
Urgent medical need to promote sensorimotor recovery in post-stroke patients

mGlu5: An Innovative Target for Brain Injury Recovery

Healthy brain



mGlu5 brain distribution

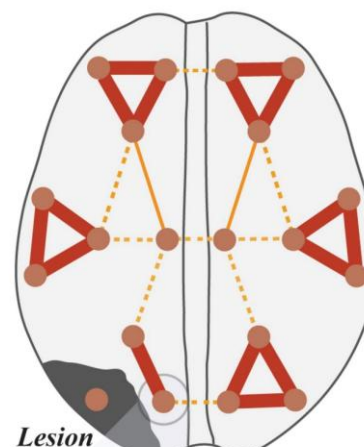


Good inter & intra-nodal connectivity

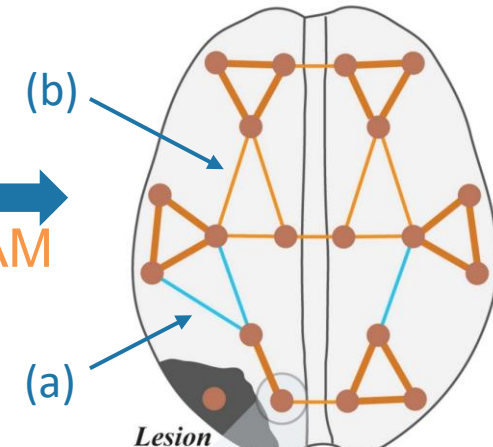
mGlu5

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

mGlu5 NAM supports rebuilding of neuronal connections



Recovery
+ mGlu5 NAM



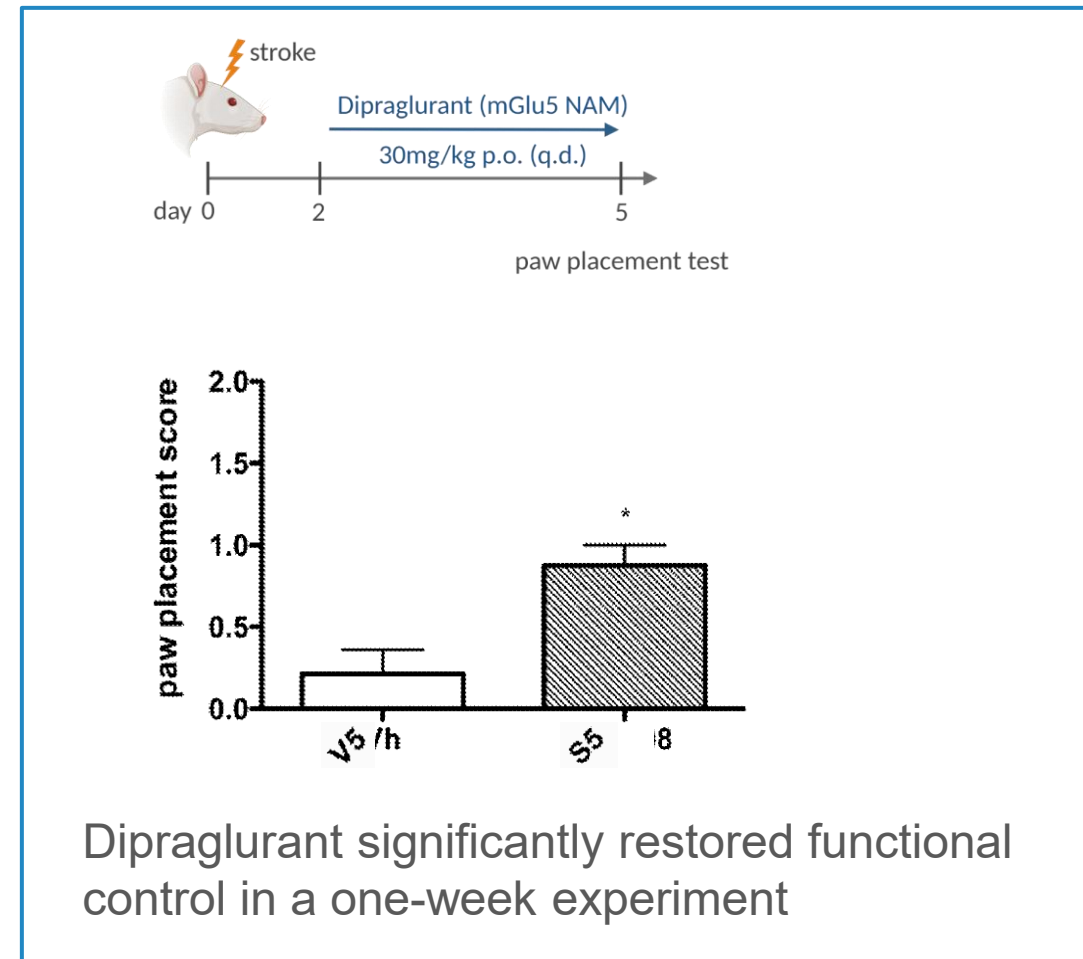
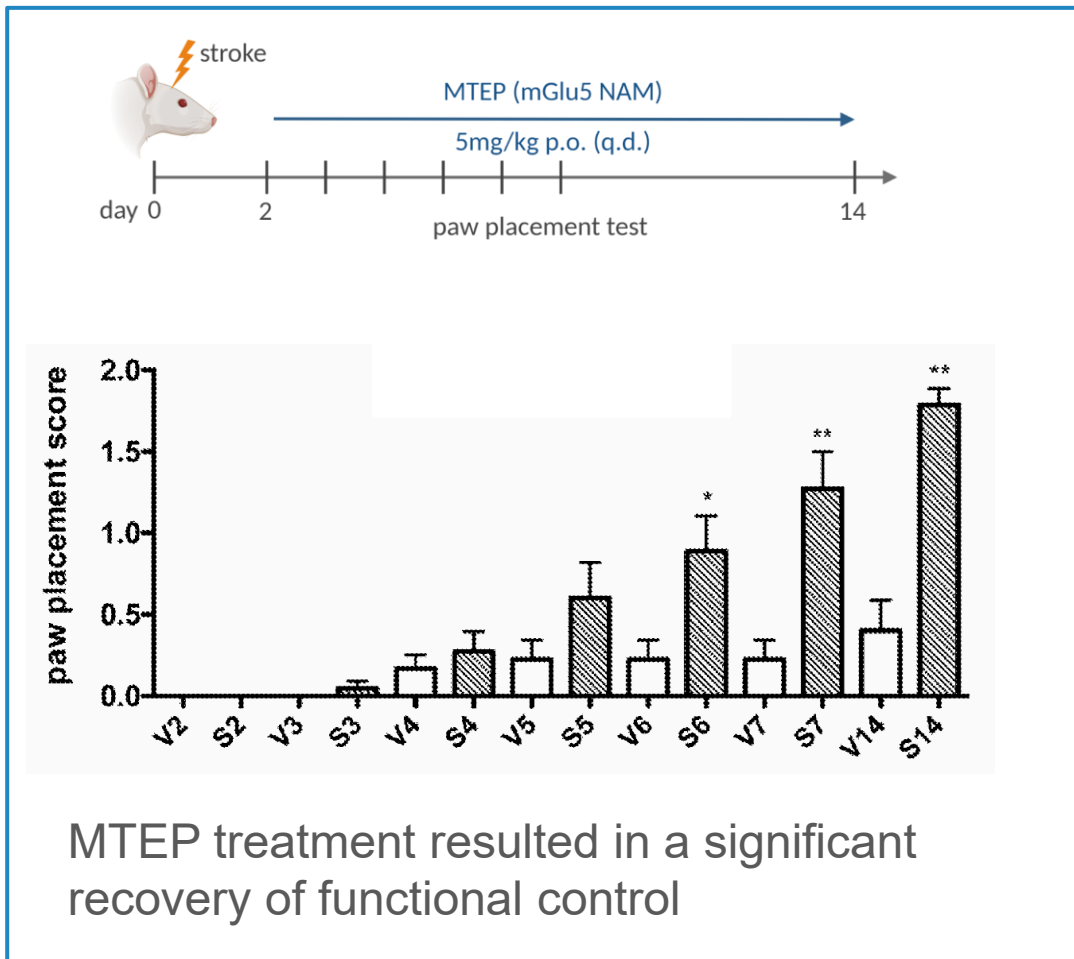
Lesion effects:

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

mGlu5 NAM promotes synaptic plasticity

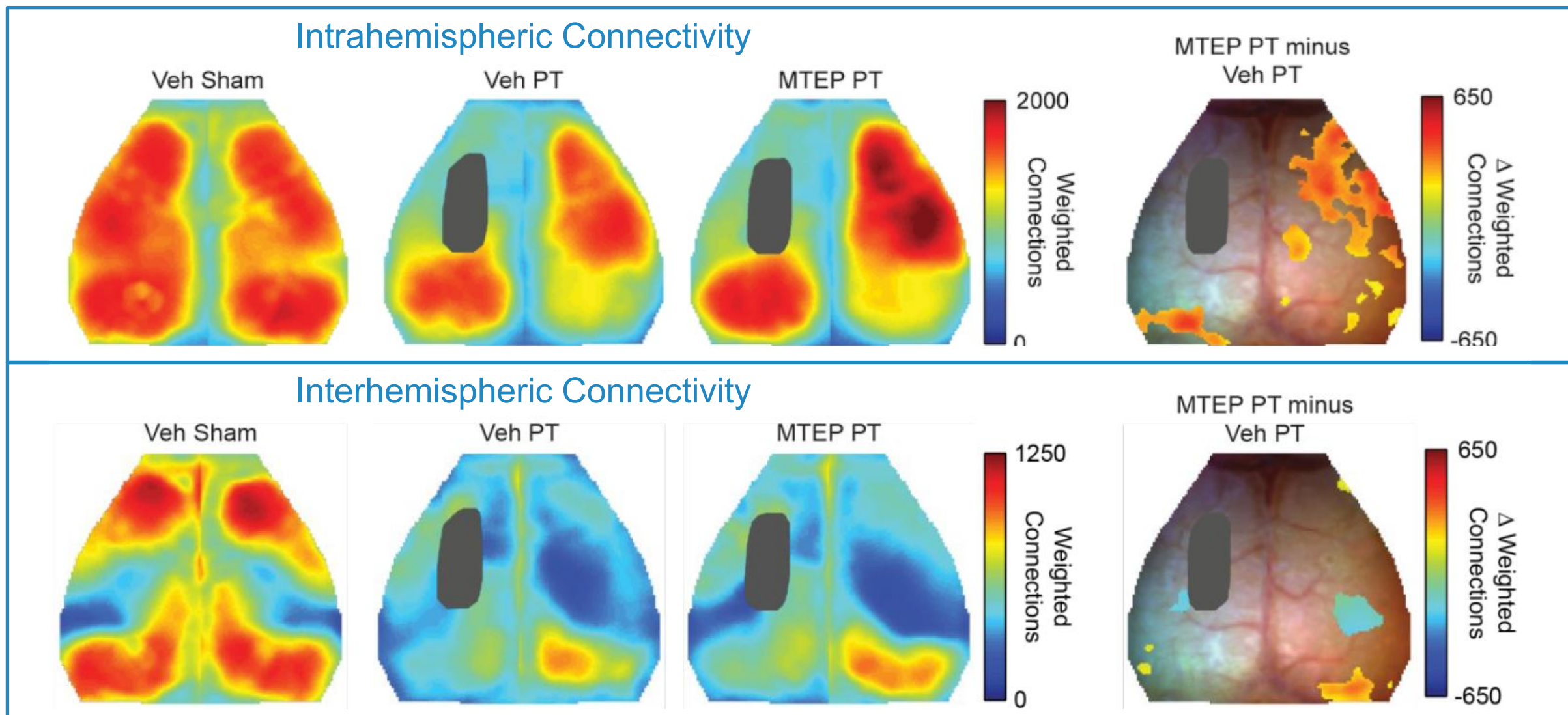
- Cortical reorganization & new functional pathways (a)
- Connectivity changes toward pre-lesion state (b)
- Restoration of excitation/inhibition equilibrium

Preclinical Data: mGlu5 Inhibition Promotes Post-Stroke Recovery



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

MRI Imaging Data: Post-Stroke Resting State Functional Connectivity



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

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

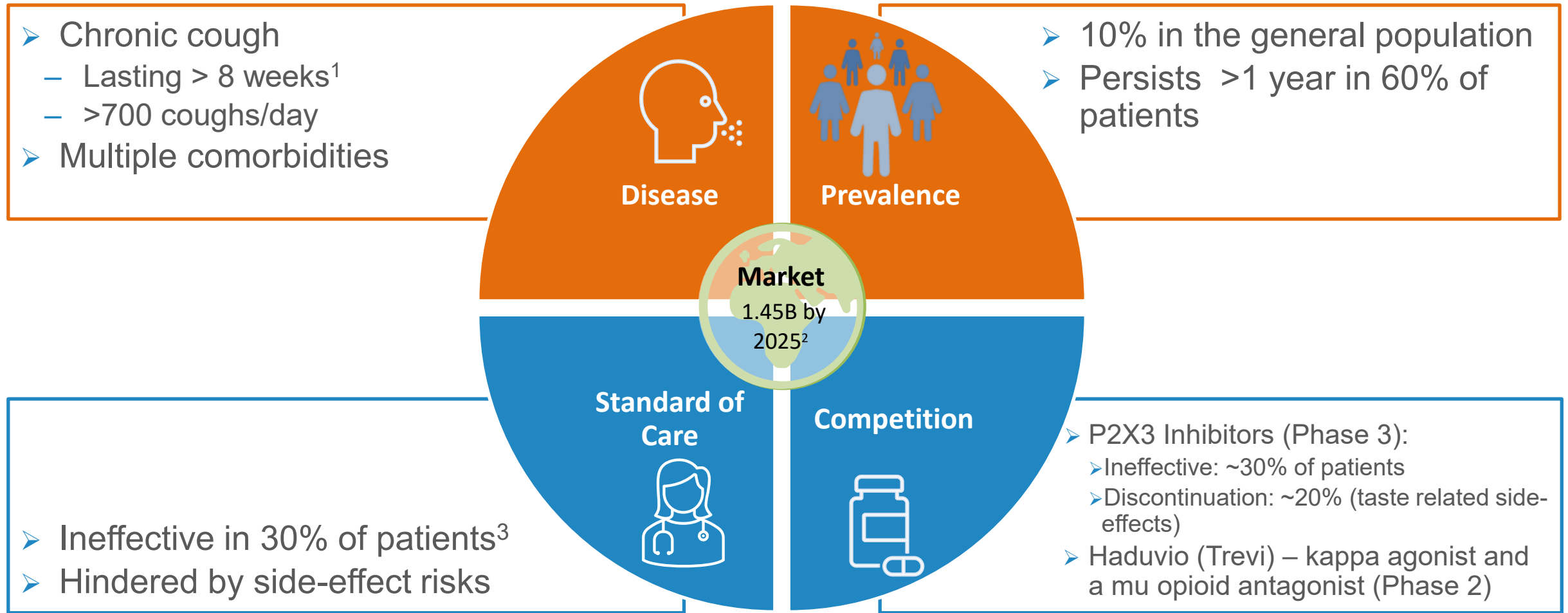
GABAB PAM for Substance Use Disorder

Large market & unmet medical need	<ul style="list-style-type: none">➤ High prevalence: 1.8% of US population¹➤ Current treatments have undesirable side-effects and prone to relapse➤ Burden to society in US is >\$600B annually²
Clinically validated MoA	<ul style="list-style-type: none">➤ Baclofen (GABAB agonist) used off label for alcohol use disorder➤ ADX71441 attenuates alcohol self-administration and relapse to alcohol seeking in rats³ and alcohol consumption in mice⁴➤ ADX71441 reduces cocaine self-administration in non-human primates⁵
Status of program and near-term milestone	<ul style="list-style-type: none">➤ Funded research phase of collaboration completed<ul style="list-style-type: none">➤ Drug candidate successfully completed IND enabling studies➤ Differentiated leads and backups with robust novel IP potential➤ IND filing ongoing
Strategic partnership with Indivior	<ul style="list-style-type: none">➤ Eligible to receive \$330 million in milestones and tiered royalties from high single digits to low double digits

GABAB PAM for Chronic Cough

Going beyond baclofen to treat cough with improved safety and tolerability

Cough - Unmet Medical Need and Commercial Opportunity



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

Pharmacological treatment of chronic cough – efficacy vs tolerability

GABAB



Use / side-effects	Dextro-metorphan	Opioids	Nalbuphine (Phase 2)	Gabapentin & pregabalin	Amitriptyline	P2X3*	GABAB	
							Agonist Baclofen	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 camlipixant¹
- ** 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

GABAB Receptor - Validated Target in Cough

➤ GABAB receptor

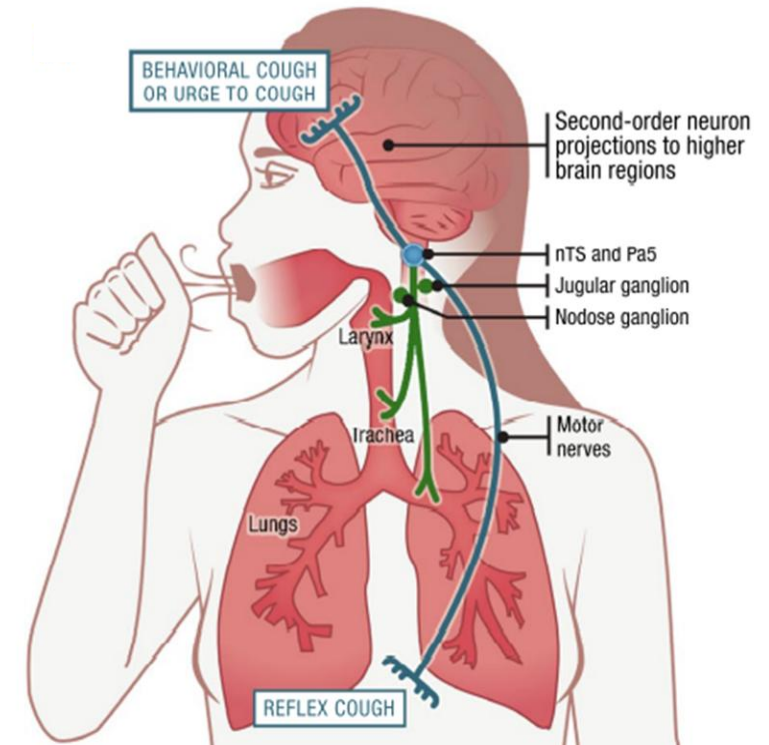
- Expressed throughout the cough neural circuit
- Activation reduces neuronal excitability
- Potential for broad application in cough patients

➤ 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

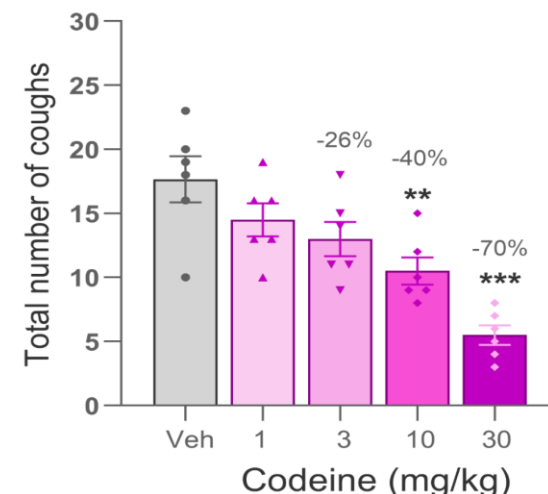
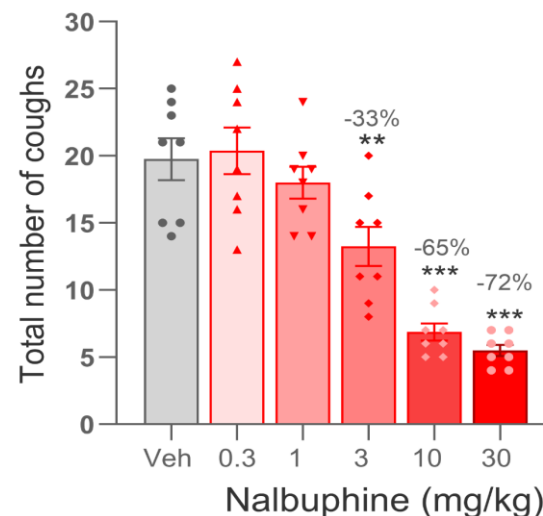
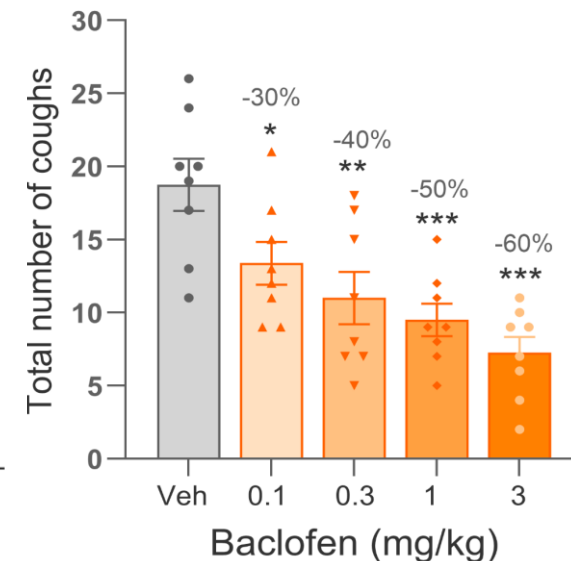
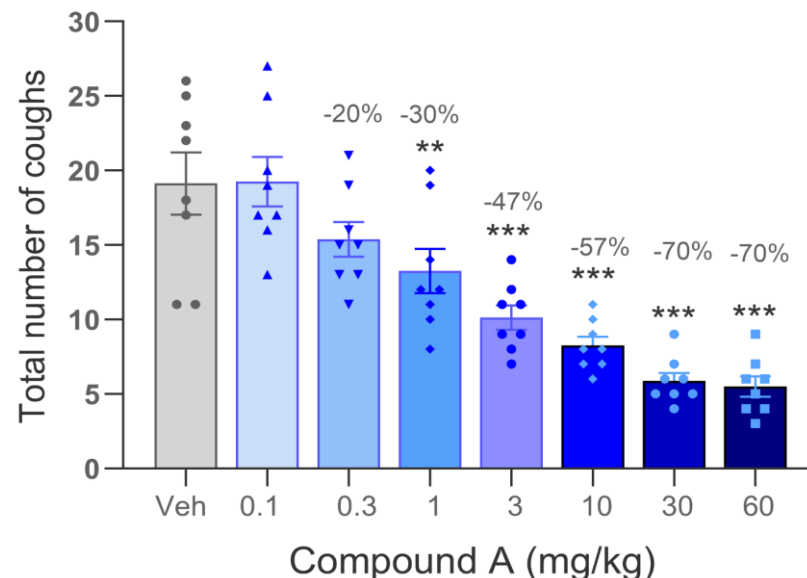
GABAB PAM for Cough – Program Status

- 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 ED₅₀ 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*

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

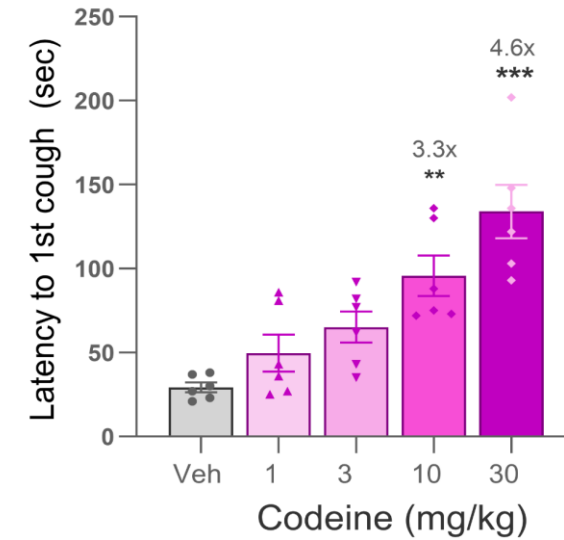
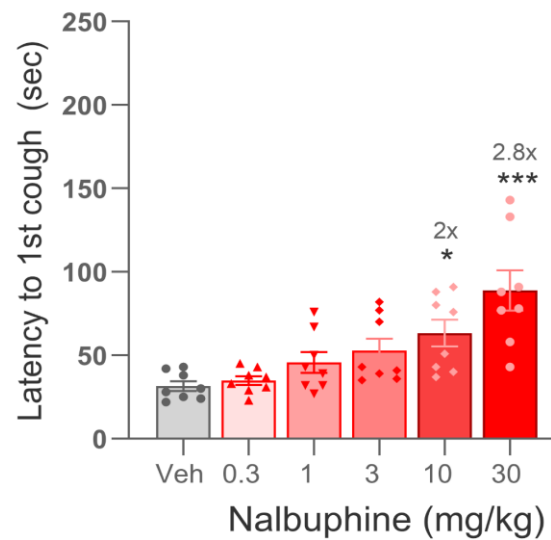
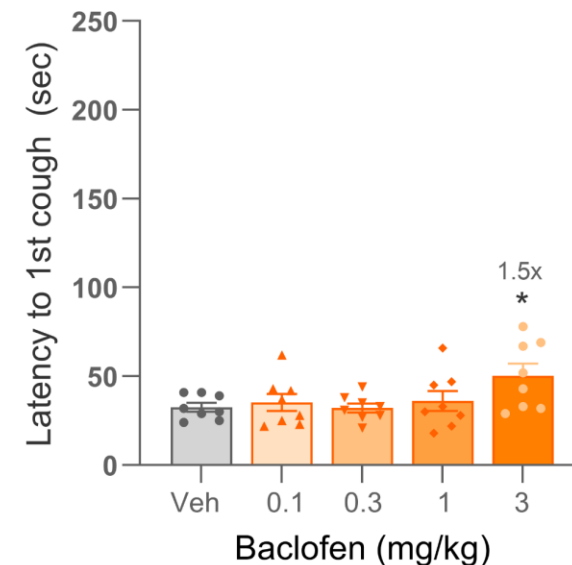
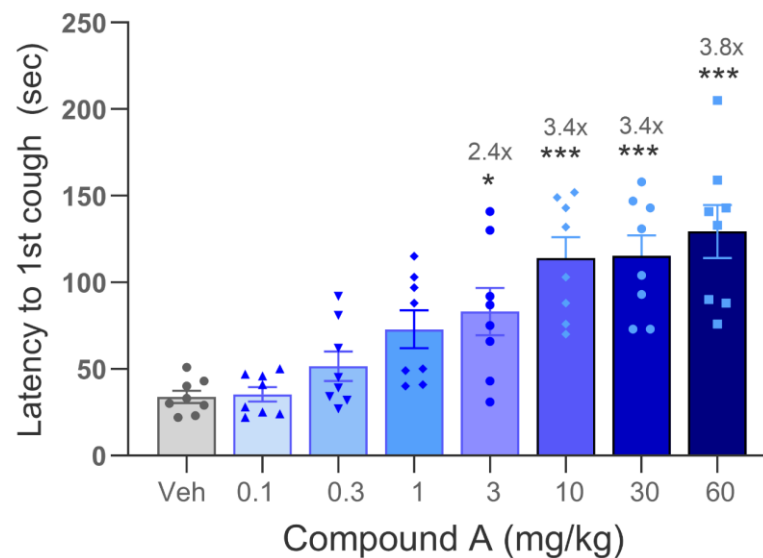


*the highest dose without effects on respiratory rate

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%

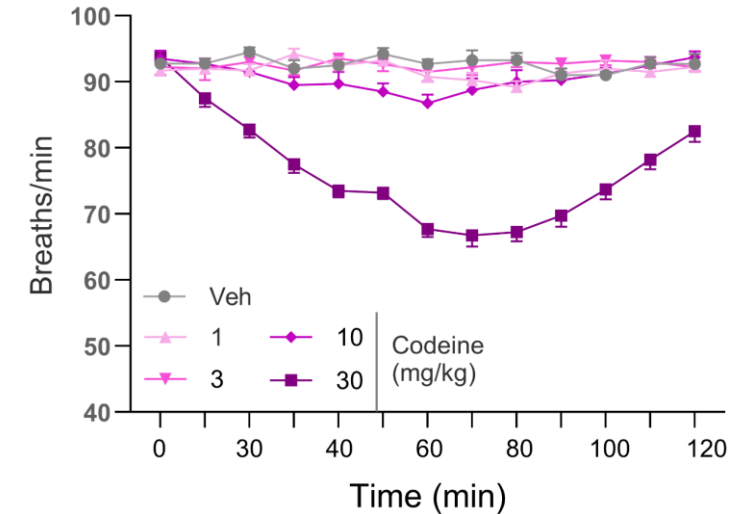
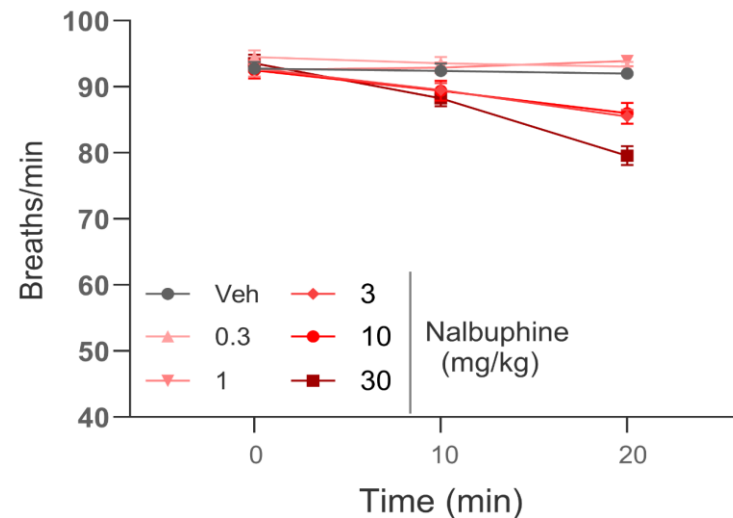
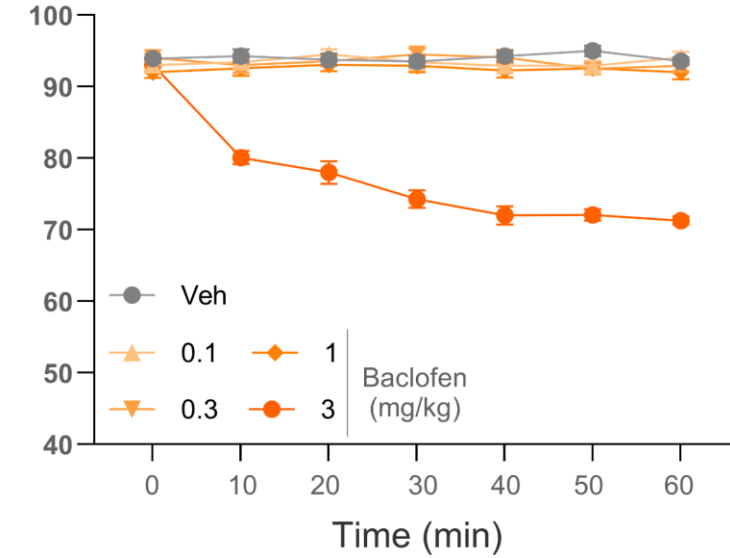
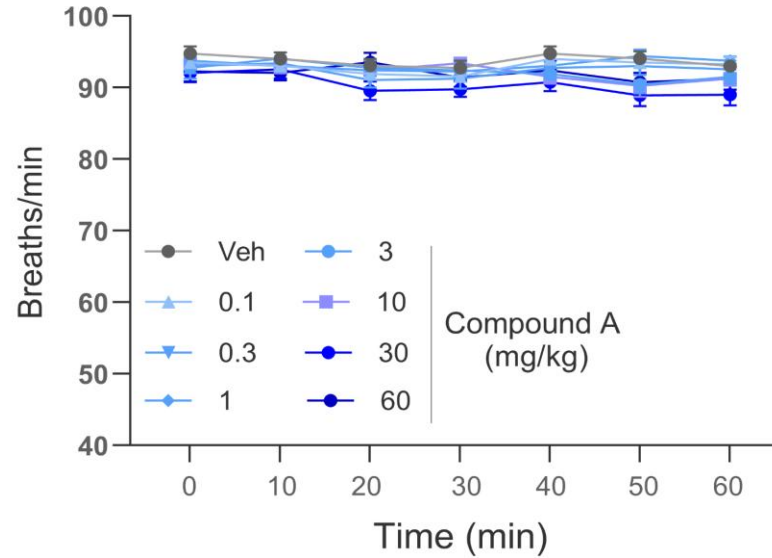
- Compound A results in a dose-dependent increase in cough latency reaching maximal effects similar or better than with other compounds



*the highest dose without effects on respiratory rate

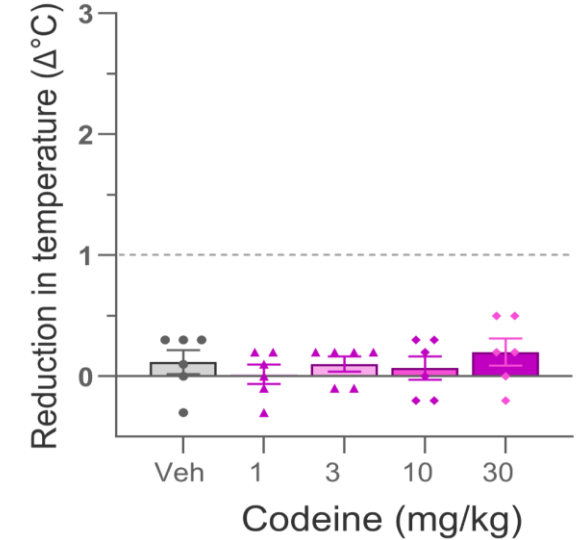
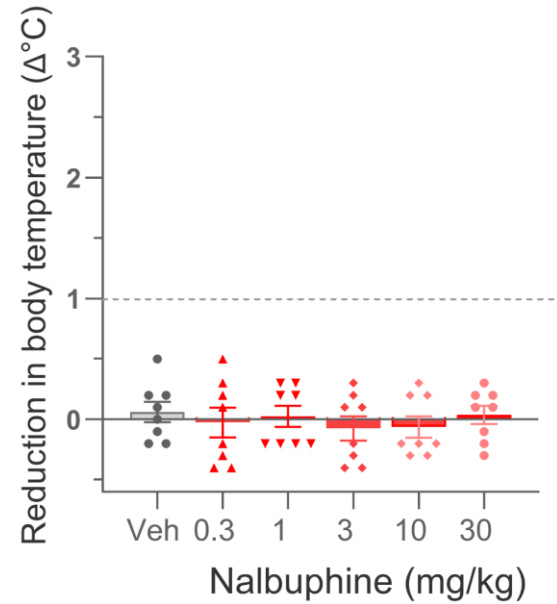
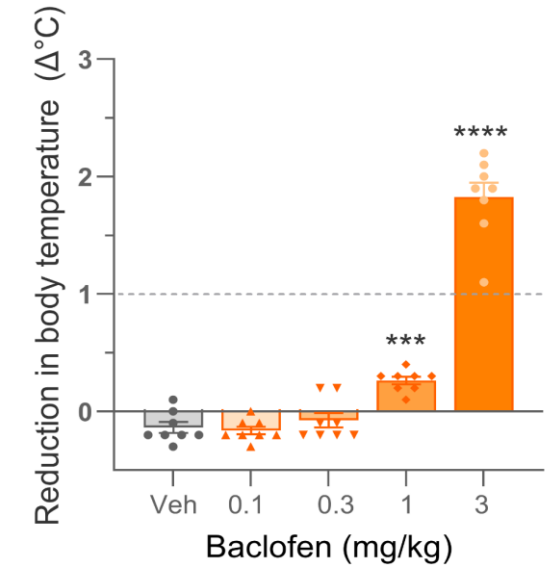
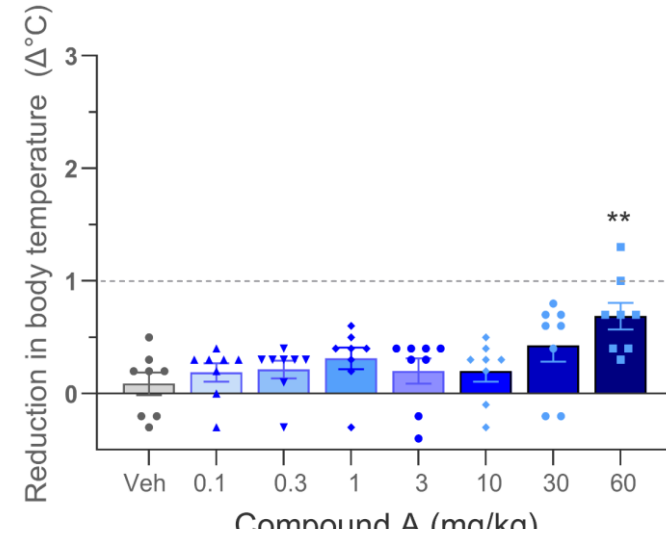
Citric Acid Cough in Guinea Pigs – Respiratory Rate

- 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



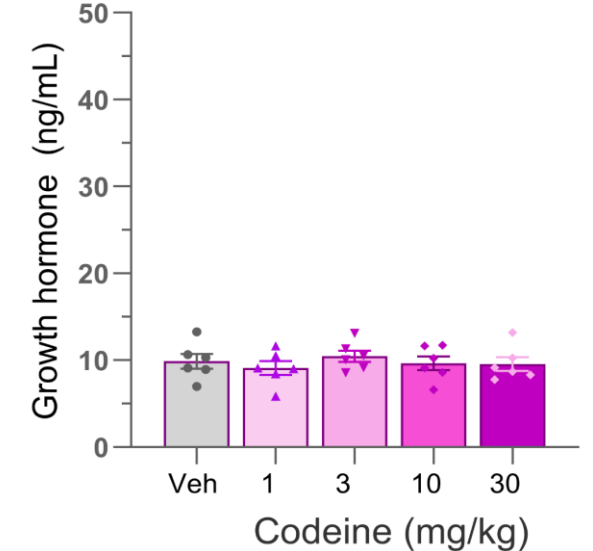
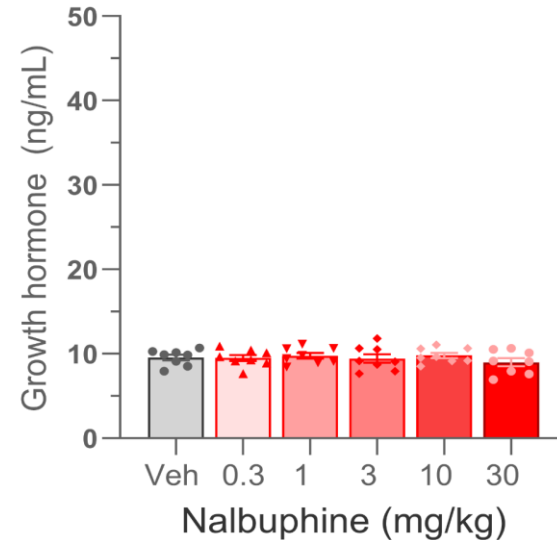
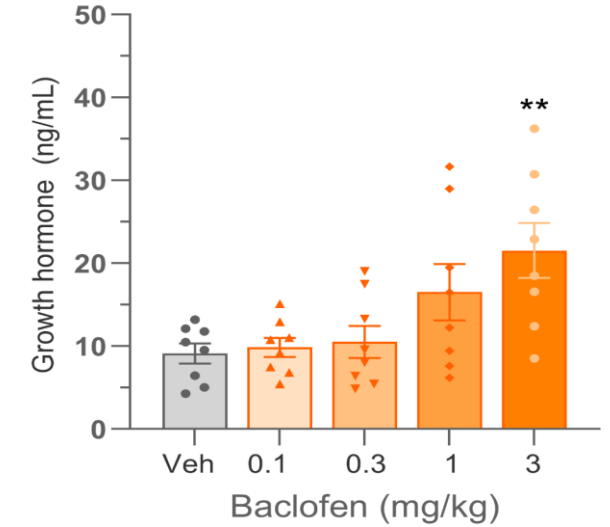
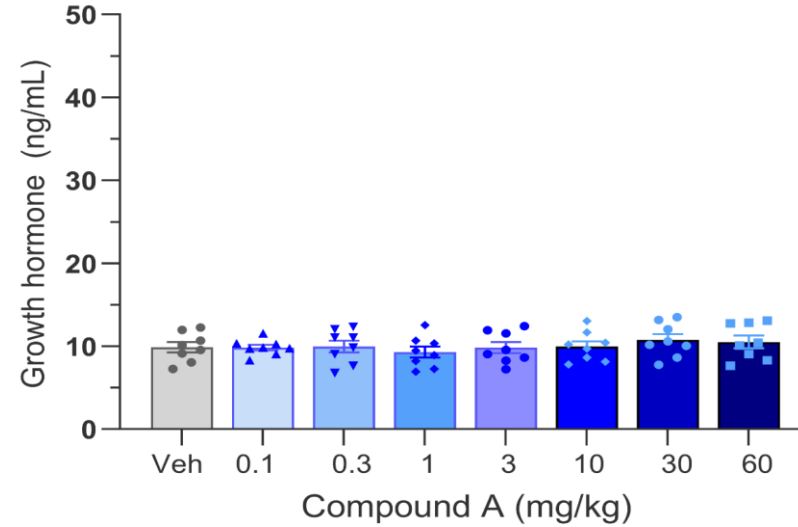
Citric Acid Cough in Guinea Pigs – Reduction in Body Temperature

- 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 contrast 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

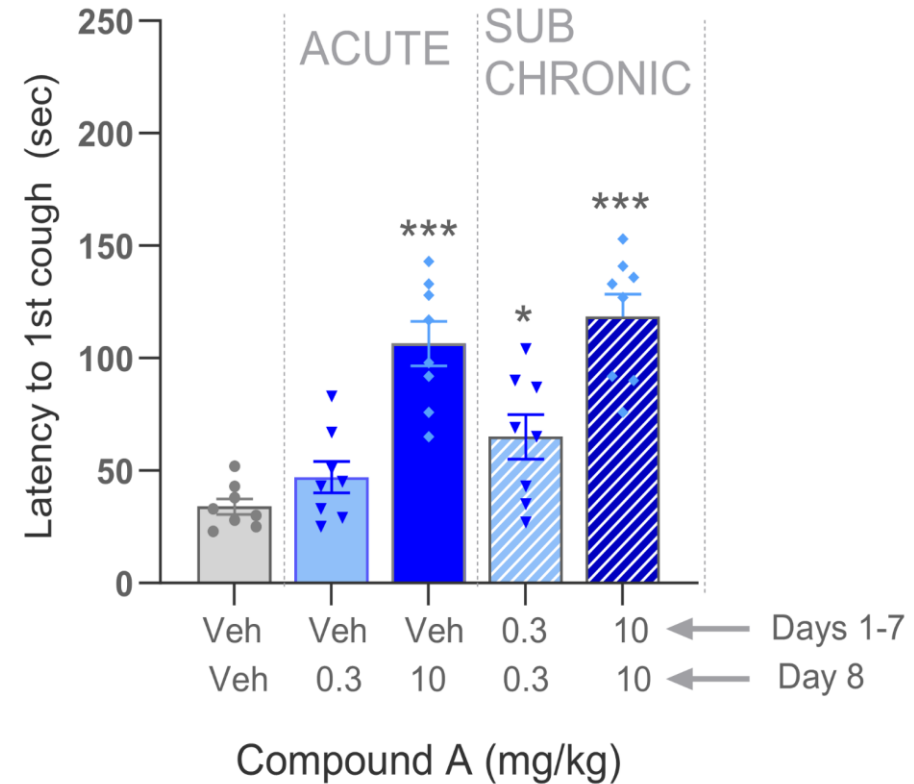
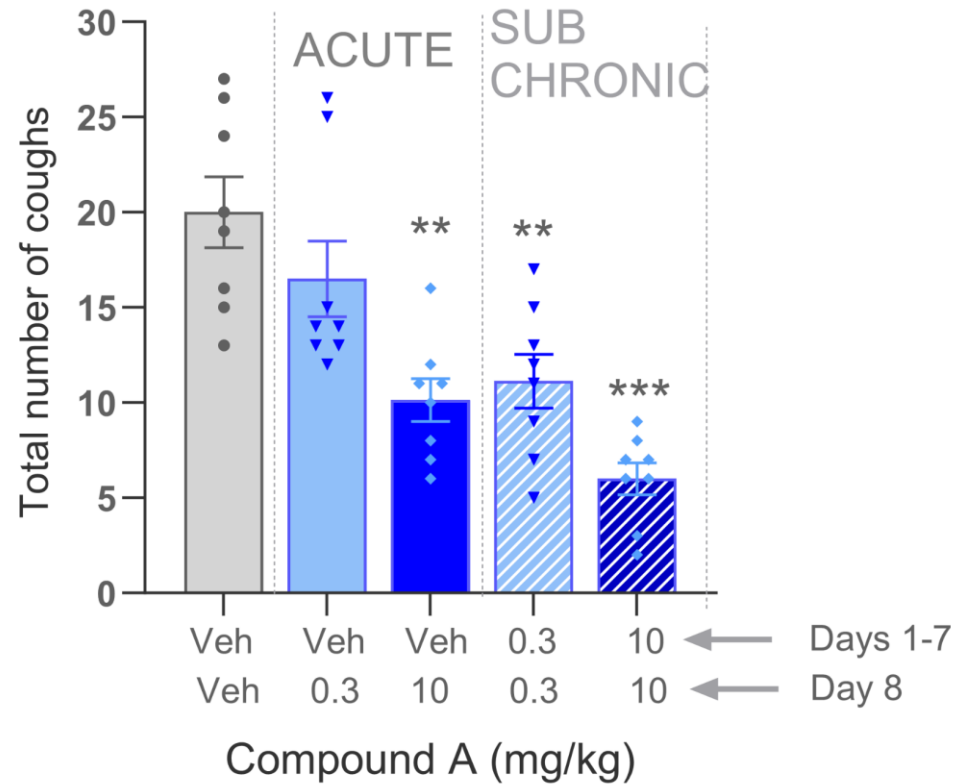


Citric Acid Cough in Guinea Pigs – Growth Hormone

- 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

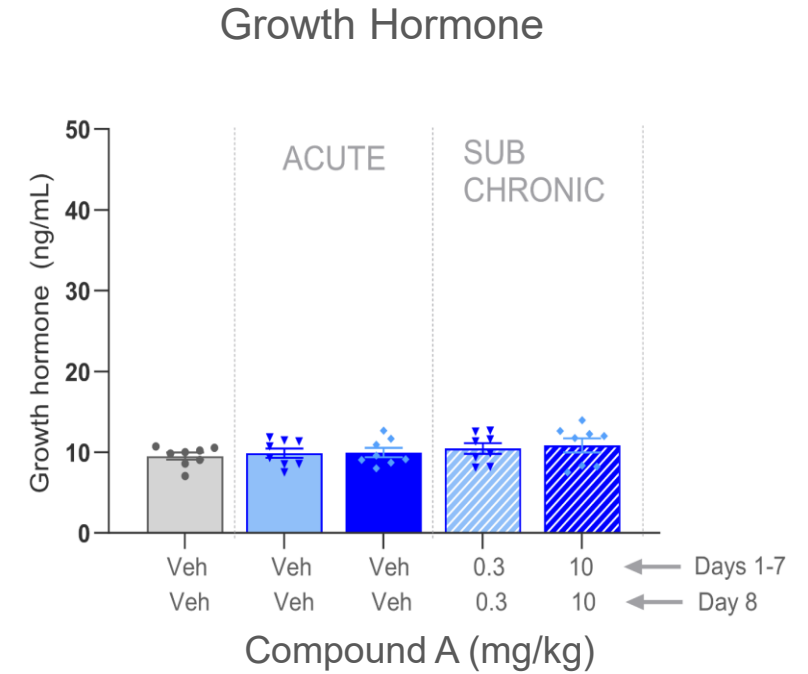
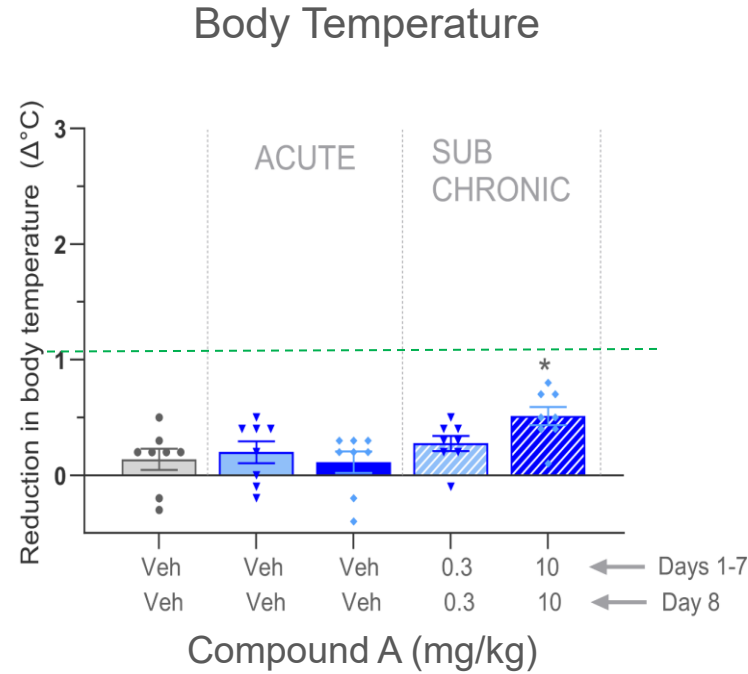
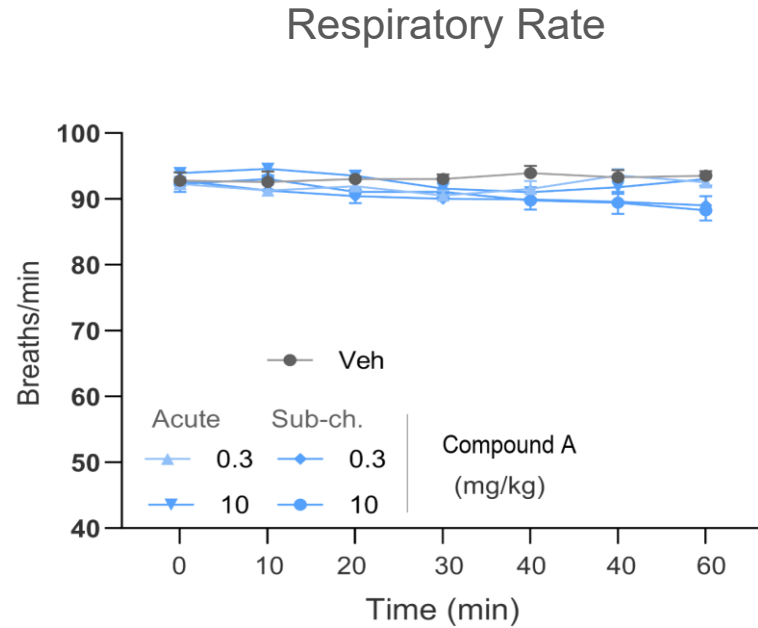


Citric Acid Induced Cough: Acute vs Sub-chronic Treatment



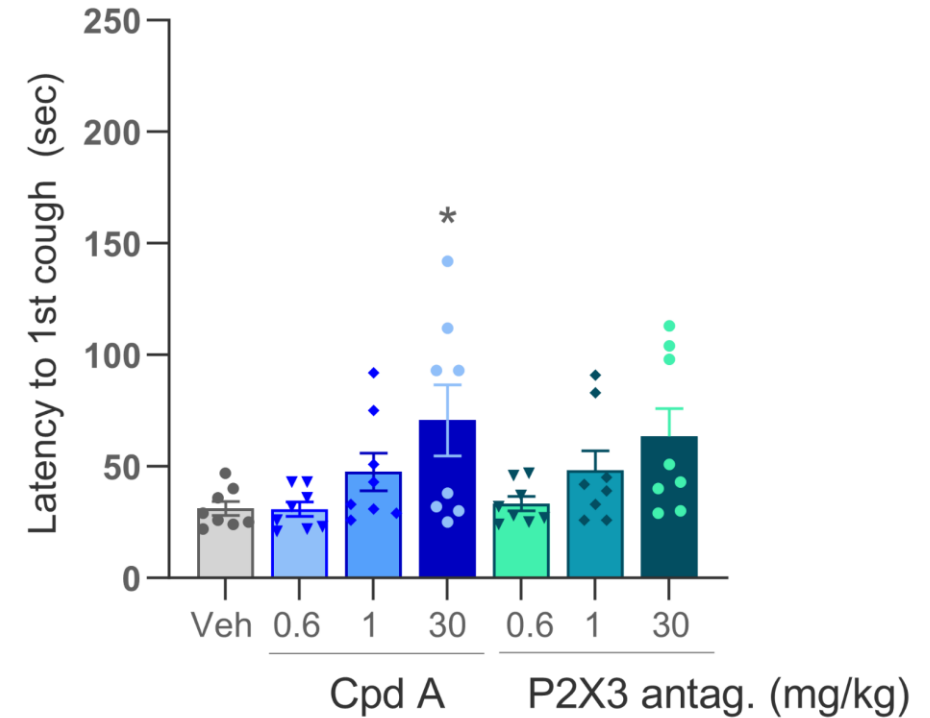
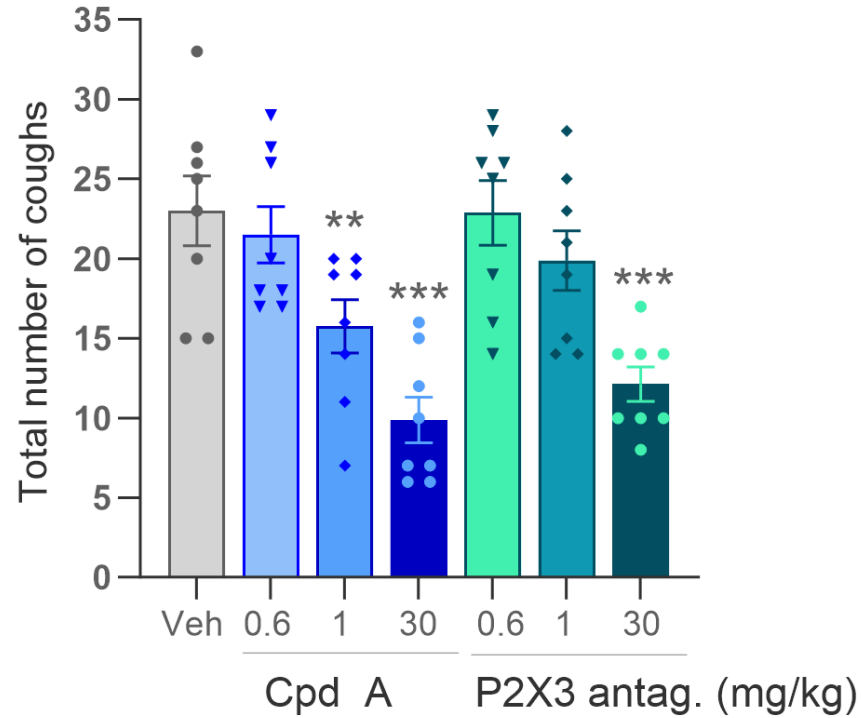
- There are no signs of tolerance in antitussive efficacy of Compound A after sub-chronic (7-day) treatment.
- A trend of reduced MED following sub-chronic treatment is seen in cough frequency and latency.

Citric Acid Induced Cough: Sub-chronic Treatment Tolerability Readouts



➤ 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

- 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

Summary

Multiple high value partnerships	<ul style="list-style-type: none">➤ 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	<ul style="list-style-type: none">➤ 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	<ul style="list-style-type: none">➤ Partnerships with industry leaders - Indivior➤ Dual listed SIX Swiss exchange & US Nasdaq➤ Cash runway through 2026
Promising outlook	<ul style="list-style-type: none">➤ 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<ul style="list-style-type: none">– Lead program, M4 PAM – Phase 1 expected to start in H2 2025



ALLOSTERIC MODULATORS FOR HUMAN HEALTH

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