Innovative Treatments for Central Nervous System Disorders

April 2024

Allosteric modulators for human health
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# Addex Overview

<table>
<thead>
<tr>
<th>High value programs reaching significant milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ ADX71149 Phase 2 epilepsy study (J&amp;J) - data expected Q2 2024</td>
</tr>
<tr>
<td>➢ GABAB PAM for cough (Addex) &amp; SUD&lt;sup&gt;1&lt;/sup&gt; (Indivior) in CCS&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>➢ Dipraglurant for PD-LID &amp; post-stroke/TBI&lt;sup&gt;3&lt;/sup&gt; recovery – Phase 2 ready</td>
</tr>
<tr>
<td>➢ 20% interest in Neurosterix</td>
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</tbody>
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<table>
<thead>
<tr>
<th>20% equity interest in Neurosterix</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Leading allosteric modulator drug discovery platform</td>
</tr>
<tr>
<td>– Validated &amp; differentiated pharmacological approach</td>
</tr>
<tr>
<td>➢ Preclinical portfolio of high value programs</td>
</tr>
<tr>
<td>– Lead program: M4 PAM for schizophrenia</td>
</tr>
<tr>
<td>➢ $63M series A financing in April 2024 led by Perceptive Advisors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>High value partnerships driving future value</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ J&amp;J - €109M in milestones &amp; double-digit royalties</td>
</tr>
<tr>
<td>➢ Indivior - $330M in milestones, royalties up to double digit &amp; funded research program</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strong balance sheet &amp; top tier US investors</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Dual listed on SIX Swiss Exchange &amp; US Nasdaq Capital Market</td>
</tr>
<tr>
<td>➢ CHF4.8M ($5.2M) cash at September 30, 2023</td>
</tr>
<tr>
<td>– CHF5M funding in received April 2024</td>
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<tr>
<td>➢ Cash runway beyond 2026</td>
</tr>
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<sup>1</sup>SUD = Substance use disorder  
<sup>2</sup>CCS = Clinical candidate selection phase  
<sup>3</sup>TBI = Traumatic Brain Injury
What are Allosteric Modulators?

Endogenous Ligands

Active Site

Outside Cell

Cell Membrane

Active Site

Inside Cell

Negative Allosteric Modulator (NAM) Reduces signal

Positive Allosteric Modulator (PAM) Increases signal

No activation in the absence of the endogenous ligand
## Advantages of Allosteric Modulation Vs Orthosteric Drug Discovery

<table>
<thead>
<tr>
<th></th>
<th>Conventional small molecules</th>
<th>Biologics/peptides</th>
<th>Nucleic acid-based therapies</th>
<th>Gene therapies</th>
<th>Allosteric modulators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selectivity</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>✓</td>
</tr>
<tr>
<td>Differentiated</td>
<td>-</td>
<td>-</td>
<td>+++</td>
<td>+++</td>
<td>✓</td>
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<tr>
<td>pharmacology</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Better potential</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>✓</td>
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<tr>
<td>safety/tolerability</td>
<td></td>
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<td></td>
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<tr>
<td>Non-competitive</td>
<td>-</td>
<td>-</td>
<td>n/a</td>
<td>n/a</td>
<td>✓</td>
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<tr>
<td>mechanism</td>
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<tr>
<td>Respect physiological</td>
<td>-</td>
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<td>✓</td>
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<tr>
<td>rhythm</td>
<td></td>
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<tr>
<td>Oral bioavailability</td>
<td>+++</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>✓</td>
</tr>
<tr>
<td>Crossing BBB</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>✓</td>
</tr>
<tr>
<td>No immunogenicity</td>
<td>+++</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>✓</td>
</tr>
<tr>
<td>Low cost of goods</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>✓</td>
</tr>
</tbody>
</table>

### Allosteric modulators

- Address:
  - “Undruggable” targets, such as GPCRs, RTKs, cytokine receptors and enzymes
  - mAb and peptide drug targets with oral small molecules
  - Offer exquisite selectivity and superior safety profile
  - Are suitable for chronic treatment as potency maintained over prolonged periods
  - Require a distinct HTS and characterization approach to discovering small molecule allosteric modulators
  - Proven clinical approach (diazepam, cinacalcet, etc)
Advancing a Broad Allosteric Modulator Pipeline in Neuroscience

<table>
<thead>
<tr>
<th>Molecule / MoA</th>
<th>Partner</th>
<th>Stage</th>
<th>Milestone</th>
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<tbody>
<tr>
<td>Clinical Stage Assets</td>
<td></td>
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<tr>
<td>ADX71149 (mGlu2 PAM)</td>
<td>Janssen</td>
<td>Discovery</td>
<td>Data expected Q2 2024</td>
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<td></td>
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<td>IND Studies</td>
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<td>Phase 1</td>
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<td>Phase 2</td>
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<tr>
<td>Dipraglurant (mGlu5 NAM)</td>
<td></td>
<td>Discovery</td>
<td>Ready to start Phase 2b/3 study*</td>
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<td>IND Studies</td>
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<td>Phase 1</td>
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<td>Phase 2</td>
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<tr>
<td>Dipraglurant (mGlu5 NAM)</td>
<td></td>
<td>Discovery</td>
<td>Ready to start Phase 2a study*</td>
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<td>IND Studies</td>
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<td>Phase 1</td>
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<td>Phase 2</td>
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<tr>
<td>Preclinical Programs</td>
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<tr>
<td>GABA_B PAM</td>
<td>INDIVIOR</td>
<td>Discovery</td>
<td>IND enabling studies expected to start H2 2024</td>
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<td>Phase 2</td>
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* Timings subject to financing/partnering

PAM = Positive Allosteric Modulator

TBI = Traumatic brain injury

NAM = Negative Allosteric Modulator
ADX71149 (JNJ-40411813) for Epilepsy

Partnered with Janssen Pharmaceuticals, Inc
# ADX71149 - Opportunity in Epilepsy

<table>
<thead>
<tr>
<th>Large market &amp; unmet medical need</th>
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<tbody>
<tr>
<td>➢ Market projected to reach $20 billion by 2026(^1)</td>
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<tr>
<td>- Keppra &amp; Briviact net sales in 2022 of €1.2 billion treating 2M patients(^2)</td>
</tr>
<tr>
<td>➢ High proportion of refractory patients (¼ of new patients(^3)) - combination treatments have limited therapeutic benefit</td>
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<tr>
<td>➢ Large underserved patient population needing improved treatment options</td>
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<tr>
<th>Strong MoA &amp; synergistic effect</th>
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<tr>
<td>➢ Selective oral mGlu2 PAM demonstrated clear MoA in epilepsy</td>
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<tr>
<td>➢ Showed 35-fold increase in Keppra (SV2A antagonist) efficacy</td>
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<tr>
<td>➢ Potential to reduce SV2A antagonist dosing – improve efficacy &amp; reduce side effects</td>
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<tr>
<th>Status of development</th>
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<tr>
<td>➢ Phase 2 study ongoing</td>
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<tr>
<td>- Cohort 1 (60 patients) completed</td>
</tr>
<tr>
<td>- Cohort 2 (50 patients) recruitment completed - November 2023</td>
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<tr>
<td>➢ Open label extension study ongoing</td>
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<tr>
<th>Strategic Partner Janssen Pharmaceuticals, Inc.</th>
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<tr>
<td>➢ Eligible to receive €109 million in pre-launch milestones and double-digit royalties</td>
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1 Fortune Business Insights April 8, 2020  
2 UCB FY 2022  
3 Xue-Ping et al, Medicine July 2019
Keppra efficacy increased 35-fold when administered with a low dose of ADX71149.

Low dose of Keppra leads to 14-fold increase in efficacy of ADX71149.

True synergistic effect specific only to SV2A antagonists.
ADX71149 Phase 2a Epilepsy Study

- Double blind placebo controlled
- Establish 28-day seizure count (over 56-day baseline period)
- Primary endpoint: time to monthly baseline seizure count
- Period 1: 4-week acute efficacy phase
- Period 2: 8-week maintenance efficacy phase
  - Subjects who do not reach or exceed their monthly baseline seizure count in Part 1 continue double-blind treatment during Part 2
- Evaluating 2 doses in 110 patients
- Cohort 1 (60 patients) completed Part 1 & 2
- Following review of unblinded data of Cohort 1 Part 1 IRC* recommended to continue study
- Cohort 2 (50 patients): recruitment completed in November 2023

Data expected Q2 2024

*IRC = Independent interim review committee
Dipraglurant (mGlu5 NAM) for Post-Stroke Recovery

Targeting neuroplasticity early in rehabilitation to promote recovery
Urgent medical need to promote sensorimotor recovery in post-stroke patients

Post stroke many suffer motor and somatosensory impairment
Potential chronic disability & low quality of life

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

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

➢ >101 million ischemic stroke survivors worldwide\(^1\)
➢ >12 million new strokes/yr (1 every 3 seconds)\(^1\)

➢ Disease

➢ Prevalence

➢ Market
>$37B in '22

➢ Standard of Care

➢ Competition

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

1\(^{\text{World Stroke Association 2022}}\)
# mGlu5: An Innovative Target for Post-Stroke Recovery

## mGlu5 Brain Distribution

- 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 equilibrium

## mGlu5 NAM Promotes Synaptic Plasticity

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

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Adapted from DOI: 10.3389/fnsys.2021.806544

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*Figures show healthy brain connectivity and lesion effects with mGlu5 NAM support.*
Dipraglurant enhanced functional brain recovery in a rat model of experimental stroke

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

From patent application PCT WO2017/171594A1
mGlu5 inhibitors promote intra- and inter-hemispheric connectivity following stroke

https://doi.org/10.1093/brain/awad293
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
  - 7.5kg 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
Dipraglurant for Levodopa-Induced Dyskinesia in Parkinson’s Disease (PD-LID)
First-in-class program ready to start Phase 2b/3
Compelling Rationale to Develop Dipraglurant for PD-LID

➢ Large underserved patient population in need of improved treatment options

➢ Significant commercial opportunity with limited competition
  – 1M Parkinson’s disease patients in US of which >170,000 have dyskinesia
  – Orphan drug designation granted for dipraglurant in US
  – US LID market estimated at $4B

➢ Strong mechanistic rationale for blocking mGlu5 to inhibit glutamate signalling

➢ Supportive pre-clinical data and Phase 2 clinical data

➢ PK profile ideally suited for treatment of LID

➢ Dipraglurant is active on same biological pathway as amantadine (inc. GOCOVRI®)
  – Decreases glutamatergic tone
  – Unlike amantadine, dipraglurant:
    • Restores synaptic plasticity to prune aberrant signalling
    • Highly selective with limited off target activity

➢ Novartis mGlu5 NAM (AFQ056) data supportive of mGlu5 target & rationale for dipraglurant PK profile
**Disability and Impact of PD-LID**

| Invariably associated with long-term L-dopa use | Dyskinesias caused by neurodegeneration  
Dopamine replacement lowers the triggering threshold for symptoms  
LID can become as disabling as the PD symptoms themselves |
|-----------------------------------------------|----------------------------------------------------------------------------------|
| Symptoms include dystonia, chorea, and choreoathetosis | Uncontrollable muscle contractions, twisting and writhing  
Painful and severely disabling  
Causes fatigue/exhaustion and increased risk for falls and injuries  
Social withdrawal, reduced quality of life and increased burden on caregiver |
| Prevalence related to disease duration | >40% of patients experience LID within 4-6 years of L-dopa treatment  
Increases to 90% after 9-15 years  
Patients treated with next-generation L-dopa will still experience LID |
| PD drug efficacy wanes over time - exacerbated by emergence of LID | Treatment becomes a balancing act requiring constant adjustments to ensure symptom control & minimize intolerable side effects |
Loss of substantia nigra neurons combined with the non-physiological, pulsatile stimulation of dopamine receptors with L-dopa are at the basis of LID development.

In the striatum, LID is the result of:

- **D1 receptor priming**
- **Excess glutamate transmission**
- **Loss of LTP depotentiation**

mGlu5 receptor is an attractive target due to its modulatory action - normalizing glutamatergic activity and restoring LTP depotentiation.

Inhibiting mGlu5 decreases excess glutamatergic tone thereby controlling dyskinesia.

Dipraglurant is an oral, highly selective NAM of the mGlu5 receptor.

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MoA Rationale for Targeting mGlu5 Inhibition in PD-LID

LTP = Long Term Potentiation
D1R = D1 dopamine receptor
Glu = glutamate  DA = dopamine
Dipraglurant PK is a Key Advantage for Treating LID

➢ Dyskinesia symptoms are correlated to peak levels of L-dopa

➢ PK of dipraglurant allows control of glutamatergic tone ahead of L-dopa Cmax

Dipraglurant normalizes abnormal glutamate stimulation during peak levodopa dose

Dipraglurant peaks ahead of L-dopa for optimal LID control

* Pharm Sci (www.cspscanada.org) 20, 226 - 238, 2017
Dipraglurant Phase 2a Study in LID (in US and Europe)

**Up-titration:**
- 50 mg qd - 100 mg tid
- Fixed dose 100 mg tid

**N=76**
- N=24: Placebo
- N=52: Dipraglurant

**Primary objective:**
- safety & tolerability

**Secondary objective exploratory efficacy:**
- Modified Abnormal Involuntary Movement Scale (mAIMS) on days 1, 14 and 28
- Clinician Global Impression of Change (CGIC)
- Patient diaries of “On” & “Off” time

**Measured acute effect of mid-day dose on days 1, 14 and 28**

N=24: Placebo
N=52: Dipraglurant
Dipraglurant Improves LID by 30%

- Statistically significant effects: Day 1 (50mg) and Day 14 (100mg)
- Improvement maintained through Day 28
- Increasing placebo response caused significance to be lost at Day 28
- No placebo mitigation in study

Mean % change of peak mAIMS from baseline

<table>
<thead>
<tr>
<th>Midday dose</th>
<th>Dipraglurant</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 (50 mg)</td>
<td>19.9%</td>
<td>4.1%</td>
</tr>
<tr>
<td>Day 14 (100 mg)</td>
<td>32.3%</td>
<td>12.6%</td>
</tr>
<tr>
<td>Day 28 (100 mg)</td>
<td>31.4%</td>
<td>21.5%</td>
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</tbody>
</table>
Responder Analysis Demonstrates Dipraglurant Significant Benefit

Percent of patients with ≥ 30% improvement on mAIMS

Reinforces robustness of dipraglurant anti-dyskinetic effect

![Bar Chart]

**Responder analysis (≥30% change of mAIMS from baseline)**

<table>
<thead>
<tr>
<th>Midday dose</th>
<th>Dipraglurant</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 (50 mg)</td>
<td>n=13 26.0%</td>
<td>n=3 12.5%</td>
</tr>
<tr>
<td>Day 14 (100 mg)</td>
<td>n=29 56.9%*</td>
<td>n=6 25.0%</td>
</tr>
<tr>
<td>Day 28 (100 mg)</td>
<td>n=27 55.1%*</td>
<td>n=7 29.2%</td>
</tr>
</tbody>
</table>

*statistically significant

\[ p = 0.2377 \]

\[ p = 0.0132 \]

\[ p = 0.0474 \]
Significant Improvement on CGI-C

- Simple scale reflecting clinical assessment by treating physician
- More objective than mAIMS
- Assessed at end of study compared to baseline
- Supports use of UDysRS in pivotal program

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<thead>
<tr>
<th></th>
<th>Dipraglurant</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>Improved (p&lt;0.05)</td>
<td>71.2%</td>
<td>49.9%</td>
</tr>
<tr>
<td>No change</td>
<td>17.3%</td>
<td>45.8%</td>
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Dipraglurant Demonstrated Good Safety and Tolerability in PD Patients

- Adverse events common in both treatment groups (dipraglurant 88.5%, placebo 75%)

- Most common AEs:

<table>
<thead>
<tr>
<th></th>
<th>Dipraglurant</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>Worsening Dyskinesia</td>
<td>21% (15.3%*)</td>
<td>12.5%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>19%</td>
<td>12.5%</td>
</tr>
<tr>
<td>Nausea</td>
<td>19%</td>
<td>0%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>15%</td>
<td>4%</td>
</tr>
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- AEs led to discontinuation in 2 patients (dipraglurant 100 mg)

- Fewer AEs at 50 mg (Weeks 1 and 2) 53% vs 58% placebo compared to 100 mg (Weeks 3 and 4) 73% vs 63% placebo

- No treatment effects on ECG, HR, BP, haematology and biochemistry

Safety profile supports continued development in PD-LID (KOLs and DSMB)
Dipraglurant PD-LID - Development Status

➢ Fast onset of action and short half-life
  - Ideally suited normalizes abnormal glutamate stimulation during peak levodopa dose

➢ 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 PD-LID patients with 7 patients exposed >6 months
  - Significant improvement in peak mAIMS from baseline (at days 1 & 14)
  - Significant improvement seen in responder analysis
  - Significant Improvement on CGI-C
  - Pivotal registration study started in June 2021 and stopped in June 2022 due to poor enrolment related to COVID-19

➢ CMC Status
  - >30kg API in stock & 7.5kg 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 PD-LID ready to start Phase 2b/3
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

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<th>Large market &amp; unmet medical need</th>
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<tbody>
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<td>➢ High prevalence; 1.8% of US population(^1)</td>
</tr>
<tr>
<td>➢ Current treatments have undesirable side-effects and prone to relapse</td>
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<tr>
<td>➢ Burden to society in US is &gt;$600B annually(^2)</td>
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<thead>
<tr>
<th>Clinically validated MoA</th>
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<tr>
<td>➢ Baclofen (GABAB agonist) used off label for alcohol use disorder</td>
</tr>
<tr>
<td>➢ ADX71441 attenuates alcohol self-administration and relapse to alcohol seeking in rats(^3) and alcohol consumption in mice(^4)</td>
</tr>
<tr>
<td>➢ ADX71441 reduces cocaine self-administration in non-human primates(^5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Status of program and near-term milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Addex is executing Indivior funded GABAB PAM research program</td>
</tr>
<tr>
<td>➢ Multiple compounds in late clinical candidate selection phase</td>
</tr>
<tr>
<td>➢ Differentiated leads and backups with robust novel IP potential</td>
</tr>
<tr>
<td>➢ IND enabling studies expected to start in 2024</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strategic partnership with Indivior</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Eligible to receive $330 million in milestones and tiered royalties from high single digits to low double digits</td>
</tr>
<tr>
<td>➢ Conducting a funded research program to discover novel GABAB PAMs</td>
</tr>
<tr>
<td>– Right to select compounds for development in reserved indications</td>
</tr>
</tbody>
</table>

\(^1\) 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

- Ineffective in 30% of patients\(^3\)
- Hindered by side-effect risks

- 10% in the general population\(^4\)
- Persists >1 year in 60% of patients

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

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

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\(^1\) 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.
### Standard of Care in Cough - Strengths and Weaknesses

<table>
<thead>
<tr>
<th>Use / side-effects</th>
<th>Dextrometorphan</th>
<th>Opioids</th>
<th>Gabapentin &amp; pregabalin</th>
<th>Amitriptyline</th>
<th>P2X3*</th>
<th>GABAB</th>
<th>Addex PAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment type</td>
<td>Chronic</td>
<td>Acute</td>
<td>Acute</td>
<td>Acute</td>
<td>Chronic</td>
<td>Acute</td>
<td>Chronic</td>
</tr>
<tr>
<td>Risk of Abuse</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Respiratory</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Other CNS</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Taste-related</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes**</td>
<td>No</td>
</tr>
</tbody>
</table>

- **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

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

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1Niimi 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

GABAB PAM offers potential for improved treatment for cough patients

1 Mazzone and McGargey Clin Pharm Ther 2021
Target Product Profile, Project Status and Development Plan

➢ A first-in-class GABAB PAM to treat Cough
  – Once-a-day oral dosing suitable for chronic treatment
  – Reduction in cough bouts and severity and improvement in quality of life
  – Superior tolerability with no taste related side-effects

➢ Status of program: clinical candidate selection
  – Potent, highly selective compounds with good developability properties identified
  – In vivo PoC with PK/PD confirmed in multiple preclinical models of cough with comparable efficacy to P2X3 inhibitors

Development Plan

<table>
<thead>
<tr>
<th>2024</th>
<th>2025</th>
<th>2026</th>
<th>2027</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCS</td>
<td>IND-enabling studies</td>
<td>Phase 1 &amp;1b</td>
<td>Phase 2a (18 Months)</td>
</tr>
</tbody>
</table>

On track for first-in-human studies in 2025

Timings beyond CCS are subject to funding/partnering
Addex Financials and Stock
Financials and Stock

➢ Cash at September 30, 2023: CHF4.8M (USD5.2M)
  – CHF5M from sale of Neurosterix

➢ No debt

➢ Traded on SIX Swiss Exchange: ADXN (ISIN:CH0029850754)

➢ ADS representing 120 shares traded on Nasdaq: ADXN (ISIN: US00654J206; CUSIP: 00654J206)

➢ 125.19M outstanding shares
  – Armistice Capital LLC – 26.81%
  – New Enterprise Associates – 3.11%

➢ 184.35M shares incl. treasury shares (247.60M fully diluted)
  – Management & board holds – 11.23%

➢ Analyst coverage:
  – HC Wainwright - Raghuram Selvaraju
  – valuationLab - Bob Pooler
  – Baader Helvea AG - Leonildo Delgado
  – ZKB – Edouard Riva

* Percentage of ownership calculated based on shares and warrants divided by fully diluted shares
| **Multiple high value partnerships** | ➢ Phase 2 epilepsy study (J&J) expected to read-out data in Q2 2024  
➢ GABAB PAM for substance use disorder (Indivior) in clinical candidate selection  
➢ 20% equity interest in Perceptive Advisors led company, Neurosterix |
| **In house programs driving future value** | ➢ Dipraglurant - post-stroke recovery Phase 2 ready to start  
➢ Dipraglurant – PD-LID Phase 2 ready to start  
➢ GABAB PAM for chronic cough in clinical candidate selection |
| **Solid foundation** | ➢ Partnerships with industry leaders - JnJ & Indivior  
➢ Top tier US investors - Armistice Capital, NEA and NLV  
➢ Dual listed SIX Swiss exchange & US Nasdaq  
➢ Strong balance sheet and cash runway through 2026 |
| **Promising outlook** | ➢ Data from Phase 2 epilepsy study - data expected Q2 2024  
➢ GABAB PAM - start IND enabling studies in 2024  
➢ Dipraglurant Phase 2 expected to start in 2024  
➢ Neurosterix lead program, M4 PAM - start IND enabling studies in 2024 |