Innovative Treatments for
Central Nervous System Disorders

Allosteric modulators for human health
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<table>
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<tr>
<th>Addex Overview</th>
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<tr>
<td><strong>Dipraglurant for dyskinesia in Parkinson’s disease</strong></td>
<td>➢ Pivotal registration program on track to dose patients in Q1 2020</td>
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<td></td>
<td>➢ US PD-LID market estimated at $4.2B</td>
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<td></td>
<td>➢ FDA Orphan Drug Designation granted in PD-LID</td>
</tr>
<tr>
<td><strong>Validating partnerships with industry</strong></td>
<td>➢ Indivior partnership - $330m in milestones, tiered royalties up to double digit &amp; funded research program</td>
</tr>
<tr>
<td></td>
<td>➢ J&amp;J deal - €109m in milestones &amp; low double digit royalties</td>
</tr>
<tr>
<td><strong>World leading technology platform</strong></td>
<td>➢ “Allosteric modulators” are a validated &amp; differentiated pharmacological approach to address drug targets</td>
</tr>
<tr>
<td></td>
<td>➢ Proprietary biological screening assays and chemical library</td>
</tr>
<tr>
<td><strong>Deep pipeline of first / best in class programs</strong></td>
<td>➢ In-house discovered pipeline</td>
</tr>
<tr>
<td></td>
<td>➢ Creating future partnership opportunities</td>
</tr>
<tr>
<td></td>
<td>➢ Driving long term growth</td>
</tr>
<tr>
<td><strong>Strong balance sheet</strong></td>
<td>➢ 32.8M shares traded on the SIX Swiss Stock Exchange – ADXN</td>
</tr>
<tr>
<td></td>
<td>➢ Cash of CHF36.7M at 30 June 2019</td>
</tr>
<tr>
<td></td>
<td>➢ Runway through 2021</td>
</tr>
</tbody>
</table>
Experienced Leadership Team

**Tim Dyer**
CEO / CFO
Co-Founder of Addex
Formerly with PwC
UK Chartered Accountant

**Dr Roger Mills**
Chief Medical Officer
Developed Nuplazid in PD Psychosis
30 years in Pharma industry including Pfizer, Gilead and Acadia Pharmaceuticals

**Dr Robert Lutjens**
Head of Discovery Biology
Member of Addex founding team
Formerly with Glaxo & Scripps Research Institute

**Dr Jean-Philippe Rocher**
Head of Discovery Chemistry
Member of Addex founding team
Formerly with Pierre Fabre, GSK and Mitsubishi

**Vincent Lawton**
Chairman
Former European Head of Merck & Co.
Former MHRA Board member

**Ray Hill**
Board member
Former Executive Director Merck & Co.

**Jake Nunn**
Board member
Former Partner New Enterprise Associates

**Isaac Manke**
Board member
Partner New Leaf Venture Partners

Experienced Board of Directors
# Extensive Pipeline Driving Long-Term Growth

<table>
<thead>
<tr>
<th>Molecule / MoA</th>
<th>Indication</th>
<th>Partner</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dipraglurant-IR (mGlu5 NAM)</td>
<td>PD-LID</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Top line data Q3 2021</td>
</tr>
<tr>
<td>Dipraglurant-ER (mGlu5NAM)</td>
<td>Dystonia</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>ADX71149 (mGlu2 PAM)</td>
<td>Epilepsy</td>
<td>janssen</td>
<td></td>
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<td></td>
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<tr>
<td>GABA&lt;sub&gt;B&lt;/sub&gt; PAM</td>
<td>Addiction</td>
<td>INDIVIOR</td>
<td></td>
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<tr>
<td></td>
<td>CMT1A</td>
<td></td>
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<tr>
<td>mGlu7 NAM</td>
<td>Post-traumatic stress disorder</td>
<td>eurostars</td>
<td></td>
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<td></td>
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<tr>
<td>mGlu2 NAM</td>
<td>Mild neurocognitive disorders</td>
<td></td>
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<tr>
<td>mGlu4 PAM</td>
<td>Parkinson’s disease</td>
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<tr>
<td>mGlu3 PAM</td>
<td>Neurodegenerative disorders</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**Lead Program** Entering US Pivotal Study and Multiple Orphan Drug Opportunities

NAM = Negative Allosteric Modulator  
IR = Immediate Release  
ER = Extended Release
What are Allosteric Modulators?

- **Negative Allosteric Modulator (NAM)**: Reduces signal inside the cell.
- **Positive Allosteric Modulator (PAM)**: Increases signal inside the cell.

Addex is based on a world leading technology platform.
Potential benefits of Allosteric Modulation Approach

- Novel, orally available drug class
- Superior receptor sub-type selectivity
- Potentially more GPCR targets – address intractable targets
- Re-address well characterized and clinically validated GPCR targets
- Potentially improved safety
- Clinical use in combination
Dipraglurant in Parkinson’s Disease
The Dipraglurant Opportunity in Dyskinesia associated with PD

| Clear Development & Regulatory Path | Pivotal studies on track to dose patients in Q1 2020  
| | Manufacturing and planning ongoing  
| | Precedented FDA regulatory path |
| Unmet Need and Significant Commercial Opportunity in PD-LID | >1M PD patients in US of which >170,000 have dyskinesia  
| | US LID market estimated at $4.2B  
| | Dipraglurant US peak sales estimated at $1.4B  
| | Pricing – Nuplazid at $30K p.a. and Gocovri at $28.5K p.a. |
| Dipraglurant: Unique Mechanism of Action | First-in-class, selective, orally available small molecule mGlu5 NAM  
| | PK profile mirrors that of L-dopa, making it ideal to treat LID  
| | Inhibits hyperglutamatergic state during L-dopa dosing |
| Strong IP Position | Composition of matter through June 2025 & strong polymorph patent through 2034 without extensions  
| | US FDA orphan drug designation in PD-LID |
Levodopa-Induced Dyskinesia in Parkinson’s Disease (PD-LID)

<table>
<thead>
<tr>
<th>Topic</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term L-dopa use is invariably associated with the development of dyskinesias</td>
<td>Dopamine replacement does not lead to dyskinesia per se, but lowers the triggering threshold for symptoms. Dyskinesias result from the neurodegenerative process that underlies PD. LID can become as disabling as the PD symptoms themselves.</td>
</tr>
<tr>
<td>LID symptoms: irregular migrating uncontrollable contractions or twisting and writhing due to dystonia, chorea, and choreoathetosis</td>
<td>This can be painful, lead to weight loss, fatigue and exhaustion, with increased risk for falls and injuries. Leading to withdrawal from social interaction, isolation, frustration, depression, reduced quality of life and increased burden on caregiver.</td>
</tr>
<tr>
<td>Prevalence of LID is related to disease duration</td>
<td>Within 4-6 years of L-dopa treatment, LID is experienced by &gt;40% of patients. By 9-15 years of L-dopa treatment, LID affects 90% of PD patients. Next-generation L-dopa will not negate LID.</td>
</tr>
<tr>
<td>Over time PD drugs become less effective, exacerbated by the emergence of LID</td>
<td>The doctor is faced with a balancing act where drug and dosing regimens must be continually optimized in order to ensure adequate symptom control while minimizing intolerable side effects.</td>
</tr>
</tbody>
</table>
Dipraglurant - Overview and Mechanism of Action

- Loss of substantia nigra neurons combined with the non-physiological, pulsatile stimulation of dopamine receptors are at the basis of LID development.

In the striatum, **LID is the result of:**
- **A** D1 receptor priming
- **B** Excess glutamate transmission
- **C** Loss of LTP depotentiation

- Metabotropic glutamate receptors are attractive drug targets due to their modulatory action to normalize glutamatergic activity and restoration of LTP depotentiation.

- mGlu5 receptors are implicated in the control of glutamate transmission.

- Preclinical and clinical data show that mGlu5 blockade controls dyskinesia.

- Dipraglurant is an oral small molecule active as a highly selective negative allosteric modulator at the mGlu5 receptor with the potential to treat LID.

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**Legend:**
- **L-DOPA**
- **D1R PRIMING**
- **mGlu5**
- **NMDA**
- **DYSREGULATED DOPAMINE CLEARANCE**
- **LOSS OF LTP DEPOTENTIATION**
- **DYSKINESIA**
- **EXCESSIVE GLUTAMATE TRANSMISSION**
- **NORMALIZATION OF GLUTAMATE TRANSMISSION**
- **RESTORED LTP DEPOTENTIATION**
- **REDUCTION OF DYSKINESIA**

**Abbreviations:**
- LTP = Long Term Potentiation
- MSN = Medium Spiny Neurons
- PD = Parkinson’s Disease
Dipraglurant PK is a Key Advantage for Treating LID

- Dyskinesia symptoms are correlated to peak levels of levodopa therapy
- PK profile of dipraglurant mirrors that of levodopa
- Dipraglurant inhibits abnormal glutamate stimulation during peak levodopa dose but releases the receptor during normal glutamate activity

PK profile differentiates dipraglurant from other treatments
**Dipraglurant EU and US Phase 2a Study in LID**

**Multicentre study in 25 centres across US and Europe**

- **N= 76**
- **R= Randomization**

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

**Fixed dose:** 100 mg tid

- **Day 1**
- **Day 14**
- **Day 28**

### Dose/mg

<table>
<thead>
<tr>
<th>Days</th>
<th>1-3</th>
<th>4-7</th>
<th>8-13</th>
<th>14-16</th>
<th>17-21</th>
<th>22-28</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM</td>
<td></td>
<td></td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>Noon</td>
<td><strong>50</strong></td>
<td>50</td>
<td>50</td>
<td><strong>100</strong></td>
<td>100</td>
<td><strong>100</strong></td>
</tr>
<tr>
<td>PM</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Daily</td>
<td>50</td>
<td>100</td>
<td>150</td>
<td>200</td>
<td>250</td>
<td>300</td>
</tr>
</tbody>
</table>

**Primary objective:**
- safety & tolerability

**Secondary objective:**
- exploratory efficacy:
  - Modified Abnormal Involuntary Movement Scale (mAIMS) on Day 1, 14 and 28
  - Unified Parkinson’s Disease Rating Scale (UPDRS)
  - Clinician and Patient Global Impression of Change (CGIC & PGIC)
  - Pharmacokinetics (PK)
  - Patient diaries of ON & OFF time

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

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Coordinating Investigator: Prof Olivier Rascol at University Hospital, Toulouse, France

N= Number of patients; R= Randomization
Dipraglurant had a statistically significant effect on the first day.

Dipraglurant reduced dyskinesia compared to placebo at all visits over the 28 days.

Placebo response confounded significance at day 28.

Dose titration contributed to placebo response (patients only on full dosage for last 7 days).

No placebo-mitigating techniques deployed in study.

Clear dose response but need to manage placebo.
A 30% reduction in mAIMS is clinically meaningful
- One patient was able to hold & read a newspaper for the first time in years
- Another patient had improved speech and became more easily intelligible

Responder analysis reinforces robustness of dipraglurant anti dyskinetic effect

<table>
<thead>
<tr>
<th>Responder analysis (≥30% change of peak mAIMS from baseline)</th>
</tr>
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<tbody>
<tr>
<td>Midday dose</td>
</tr>
<tr>
<td>Day 1 (50 mg)</td>
</tr>
<tr>
<td>Day 14 (100 mg)</td>
</tr>
<tr>
<td>Day 28 (100 mg)</td>
</tr>
</tbody>
</table>
Clinician Rated Global Impression of Change - Dyskinesia

- Relatively simple scale that reflects everyday clinical practice
- Assessment by treating physician and thus is a more objective assessment than the more subjective mAIMS
- Assessment performed at end of study compared to baseline

Greater improvement in dyskinesia with dipraglurant according to clinicians (p<0.05)

<table>
<thead>
<tr>
<th></th>
<th>Dipraglurant</th>
<th>Placebo</th>
</tr>
</thead>
<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>
</tr>
</tbody>
</table>
Pattern of motor complications of dipraglurant patients over the course of a day, as reported in patients’ diaries

After 4-week treatment with dipraglurant:

- ON time with dyskinesia **reduced** during the day
- ON time without dyskinesia **increased** and maintained during the day
Dipraglurant Demonstrated Good Safety and Tolerability in PD Patients

- Adverse events were common in both treatment groups (dipraglurant 88.5%, pbo 75%)
- The majority of patients completed the dose escalation regimen
- Most common AEs:

<table>
<thead>
<tr>
<th></th>
<th>Dipraglurant</th>
<th>Placebo</th>
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</thead>
<tbody>
<tr>
<td>Worsening Dyskinesia</td>
<td>21%</td>
<td>12.5%</td>
</tr>
<tr>
<td></td>
<td>(15.3%*)</td>
<td></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>
</tbody>
</table>

* 3 of the 11 patients who reported “worsening dyskinesia” did so only in the follow up period (i.e. when not taking the drug). Thus the dyskinesia recurred only after therapy had stopped. Therefore the adjusted AE% is 15.3% for dipraglurant arm vs.12.5% for placebo arm.

- AEs caused discontinuation in 2 patients taking dipraglurant 100 mg
- AEs at the 50 mg dose level (wk 1 and 2) were less frequent – 53% vs 58% pbo than at the 100 mg dose level (wk 3 and 4) – 73% vs 63% pbo
- No treatment effects on any safety monitoring variables (ECG, HR, BP, haematology and biochemistry)

Safety profile suitable for continued development in PD (KOLs and DSMB)
The Phase 2b/3 trial is fully funded and expected to report out in Q3 2021

Primary endpoint: UDysRS – more sensitive to treatment effect than mAIMS (Goetz, 2008) and less prone to placebo response (Goetz, 2013)

Implementing measures to manage placebo response is a priority

Considering Fast-Track and/or Breakthrough Therapy applications after first pivotal study readout
Dipraglurant First Pivotal PD-LID Study (301)

**Study Design**

- **N=140**
  - **R** Fixed dose
  - **N = 70 Placebo**
  - **N = 70 Dipraglurant (100mg)**
  - **Double-blind treatment period**

**Moderate to severe PD-LID**

**OLS**

- **End of 3 months**

**Study Design**

- **Primary objective is efficacy in reducing LID**
  - Change over time in UDysRS at 3 months
- **Secondary objectives**
  - Change over time in MDS-UPDRS Part III
  - Patient diaries, on & off time
  - CGI-S
  - Safety and tolerability
Dipraglurant Confirmatory Phase 3 PD-LID Study (303)

- **Primary objective** efficacy in reducing LID
  - Change over time in UDysRS at 3 months
- **Secondary objectives**
  - Change over time in UDysRS at 6 months
  - Change over time in MDS-UPDRS Part III
  - Patient diaries, on & off time
  - CGI-S
  - Pharmacokinetics (PK)
  - Safety and tolerability

**Study Design**

- **N=140**
- **R= Randomisation**
- **LID= L-Dopa induced dyskinesia**
- **OLS= Open label study**

- **N = 70 Placebo**
- **N = 70 Dipraglurant (100mg)**

- Fixed dose
- **Double-blind treatment period**
- **End of 3 months**
- **End of 6 months**

- **Moderate to severe PD-LID**

- **End of 6 months**
  - **N = 70 Placebo**
  - **N = 70 Dipraglurant (100mg)**
# Dipraglurant LID Opportunity

<table>
<thead>
<tr>
<th>LID has a large unmet need and market opportunity</th>
</tr>
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<tbody>
<tr>
<td>➢ &gt; 170K LID patients in US</td>
</tr>
<tr>
<td>➢ ~$1.4bn US market opportunity for dipraglurant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Limited competition – only one FDA approved medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Gocovri (reformulation of generic amantadine): Approved on 24th August 17, safety profile similar to generic</td>
</tr>
<tr>
<td>➢ Dipraglurant 1st in class highly selective oral monotherapy</td>
</tr>
<tr>
<td>➢ Improved safety profile</td>
</tr>
<tr>
<td>➢ Ideal PK profile mirrors levodopa – recognized by KOLs as key advantage</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Clear development plan with precededented regulatory path</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Precedented regulatory path paved by Gocovri (Adamas)</td>
</tr>
<tr>
<td>➢ Two registration trials (301 and 303) with Open Label Study</td>
</tr>
<tr>
<td>➢ UDysRS – more sensitive to treatment effect than mAIMS and less prone to placebo response (Goetz 2013)</td>
</tr>
<tr>
<td>➢ Implementing measures to manage placebo response is a priority</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strong patent and market exclusivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ NCE and polymorph patent provide protection through 2034 without extensions and data exclusivity</td>
</tr>
<tr>
<td>➢ Orphan Drug Designation – 7 years of market exclusivity</td>
</tr>
</tbody>
</table>
Financials
Financials and Stock

- **Cash runway through 2021**
  - Cash of CHF36.7M at 30 June 2019
  - Fully funded through dipraglurant study 301 readout

- **Market capitalization:** approx. CHF45M

- **No debt**

- **Traded on SIX Swiss Exchange:** ADXN (ISIN:CH0029850754)

- **32,848,635 shares outstanding 44.6M (fully diluted)**
  - New Enterprise Associated - 13.91%
  - New Leaf Venture Partners - 4.86%
  - CAM Capital - 4.86%
  - Credit Suisse Asset Management - 4.87%
  - Management & board holds -14% (fully diluted basis)

- **Analyst coverage:**
  - Van Leeuwenhoek - Marcel Wijma
  - valuationLab - Bob Pooler
  - ZKB - Dr. Michael Nawrath
## Upcoming Major Development Milestones

<table>
<thead>
<tr>
<th>Milestone</th>
<th>Timing</th>
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</thead>
<tbody>
<tr>
<td>Dipraglurant – LID Phase 3 Registration Program</td>
<td></td>
</tr>
<tr>
<td>Complete manufacturing of Drug Product</td>
<td>Q4 2019</td>
</tr>
<tr>
<td>Study 301 – Start dosing</td>
<td>Q1 2020</td>
</tr>
<tr>
<td>Study 301 – Top line data</td>
<td>Q3 2021</td>
</tr>
</tbody>
</table>
ALLOSTERIC MODULATORS FOR HUMAN HEALTH

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