Addex Corporate Presentation

April 2018

Innovative Treatments for Central Nervous System Disorders

SIX: ADXN

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Our Story on a Page

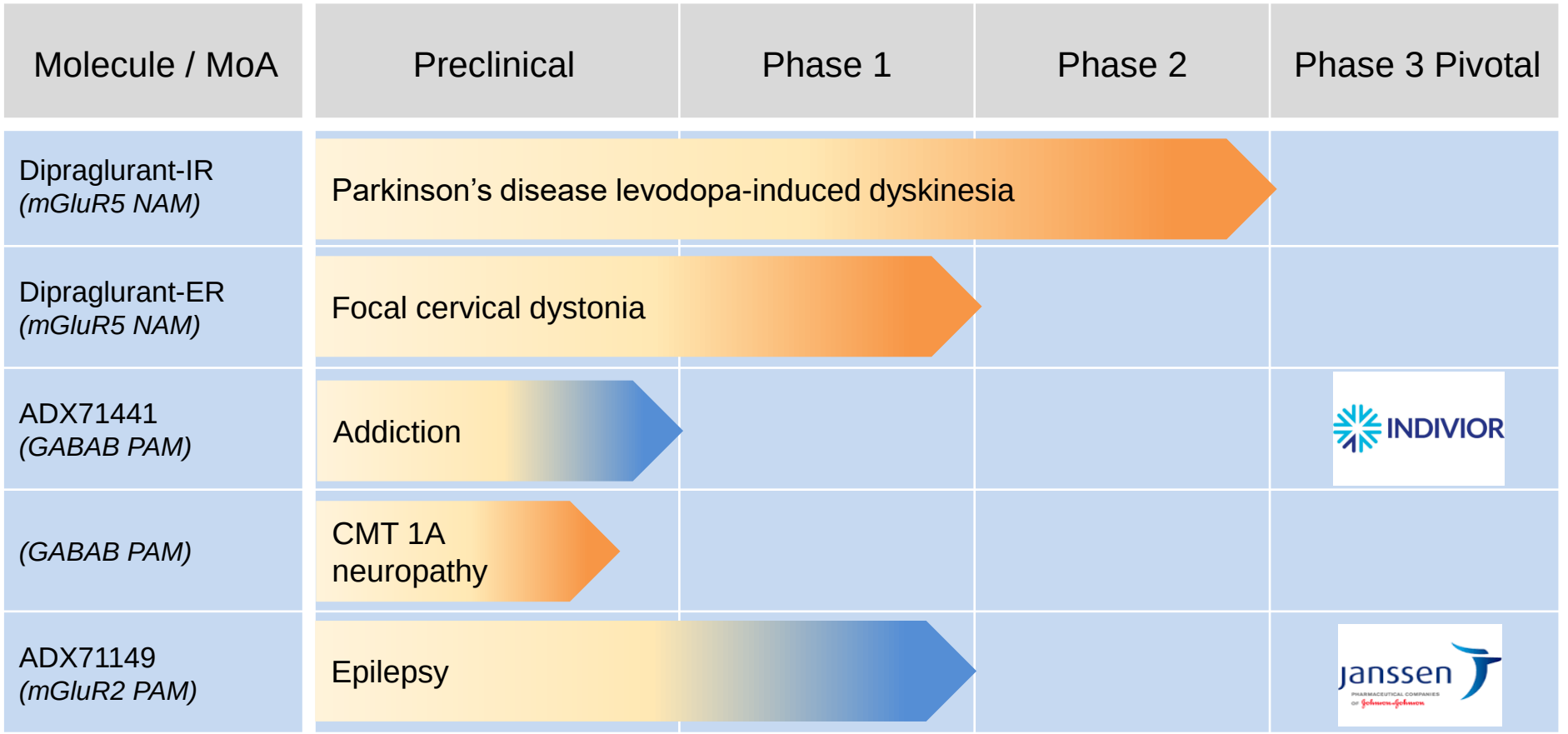
Important Unmet Need in PD-LID	➢ >1M PD patients in US of which > 170,000 have Levodopa-Induced-Dyskinesia (LID); 90% experience LID after 9-15 years of L-dopa exposure ➢ Adamas' Gocovri (reformulated generic amantadine): Approved Aug 2017 – safety profile similar to generic
Dipraglurant: Unique Mechanism of Action	➢ First-in-class, selective, oral small molecule - negative modulator at mGluR5 ➢ PK profile mirrors that of L-dopa, making it ideal to treat LID ➢ Inhibits abnormal glutamate stimulation during L-dopa dosing
Development & Regulatory Path	➢ Phase 2: clinically meaningful & statistically significant efficacy - good safety & tolerability. Reduced "OFF time" and increased "ON time" without dyskinesia ➢ Precedented regulatory path in US. Phase 3 expected to start H2:2018 with 2 pivotal studies. NDA submission 2022
Significant Commercial Opportunity	➢ US LID market estimated at $4.2B ➢ Dipraglurant US peak sales estimated at $1.4B (30% market share) ➢ Significant recent increase in pricing of PD therapeutics – Nuplazid at $26K p.a. and Gocovri at $28.5K p.a.
Strong IP Position	➢ Composition of matter through June 2025 & strong polymorph patent through 2034 without patent extensions ➢ US FDA orphan drug designation in PD-LID, additional patent strategies expected to provide further market exclusivity
Financials	➢ ~ CHF90mm market cap (ADXN on SIX Swiss Stock Exchange) ➢ Cash balance of ~ CHF45 mm (as of 30 June 2017); runway through 2021 ➢ No debt

Experienced Team

- Executive Management:
  - Tim Dyer, CEO / CFO
    - Co-founder of Addex, formerly with PwC
  - Roger Mills, CMO
    - Formerly with Acadia Pharmaceuticals
  - Robert Lutjens, Head of Discovery
    - Formerly with Glaxo, The Scripps Res Inst.
- Team of Experts:
  - Thierry Duvauchelle
    - Medical Director; Former CEO Aster-Cephac
  - Hilde Williams
    - Regulatory Affairs, Former SVP Regulatory Acadia Pharmaceuticals
  - Ron Lawrence
    - CMC; Formerly with GSK
  - Tim Hammond
    - Toxicology; Former VP AstraZeneca
  - Sonia Poli
    - Translational Science; Formerly with Roche
- Clinical Advisors:
  - PD-LID
    - Michael J. Fox Foundation for Parkinson's Research
    - Dr. Erwan Bézard
    - Prof. Chris Goetz
    - Prof. Stuart Isaacson
  - Dystonia
    - Dystonia Medical Research Foundation
    - Prof Hyder Jinnah
    - Prof. Antonio Pisani
    - Dr. Jan Teller
- Board Members:
  - Vincent Lawton, Chairman
    - Former European Head of Merck & Co., MHRA
  - Ray Hill
    - Former Executive Director at Merck & Co.

Clinical Stage Pipeline with Registration Trial-Ready Program

Multiple Orphan Drug Opportunities



NIH NIAAA

NIH National Institute on Drug Abuse

DYSTONIA MEDICAL RESEARCH FOUNDATION

CMTA Charcot-Marie-Tooth Association

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

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NAM = Negative Allosteric Modulator
PAM = Positive Allosteric Modulator

Extensive Preclinical Stage Pipeline for Long-Term Growth

Molecule / MoA	Hit to Lead	Lead Optimization	Clinical Candidate	Collaboration Partners
mGluR4 PAM	Parkinson's disease, addiction, autoimmune disease			NIH National Institute on Drug Abuse; CHUV
mGluR2 NAM	Depression, stroke			NEUROMED I.R.C.C.S. ISTITUTO NEUROLOGICO MEDITERRANEO
FSH / LH NAM	Endometriosis, uterine fibrosis, polycystic ovarian disease			LMU KLINIKUM DER UNIVERSITÄT MÜNCHEN; INRA SCIENCE & IMPACT
mGluR7 NAM	Psychosomatic disorders (PTSD)			CHUV
mGluR3 PAM / NAM	Neurodegeneration			NEUROMED I.R.C.C.S. ISTITUTO NEUROLOGICO MEDITERRANEO
TrkB PAM	Neurodegener.			UNIVERSITÉ DE GENÈVE FACULTÉ DE MÉDECINE; THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

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Upcoming Development Milestones

Milestone	Timing
Dipraglurant – LID Phase 3 Registration Program	
Study 301 – start dosing	H2 2018
Study 301 – results	H1 2020
Study 302 – start dosing	H1 2020
Study 302 – results	H2 2021
Dipraglurant – Focal Cervical Dystonia Phase 2 POC	
Study 202 – start dosing	H1 2018
Study 202 – results	H1 2019
ADX71441 – Addiction (Partnered with Indivior)	
Phase 1 (NIDA sponsored study) – start dosing	H2 2018
Phase 1 (NIDA sponsored study) – results	H1 2019

Dipraglurant in PD-LID: What Has Changed Since 2012?

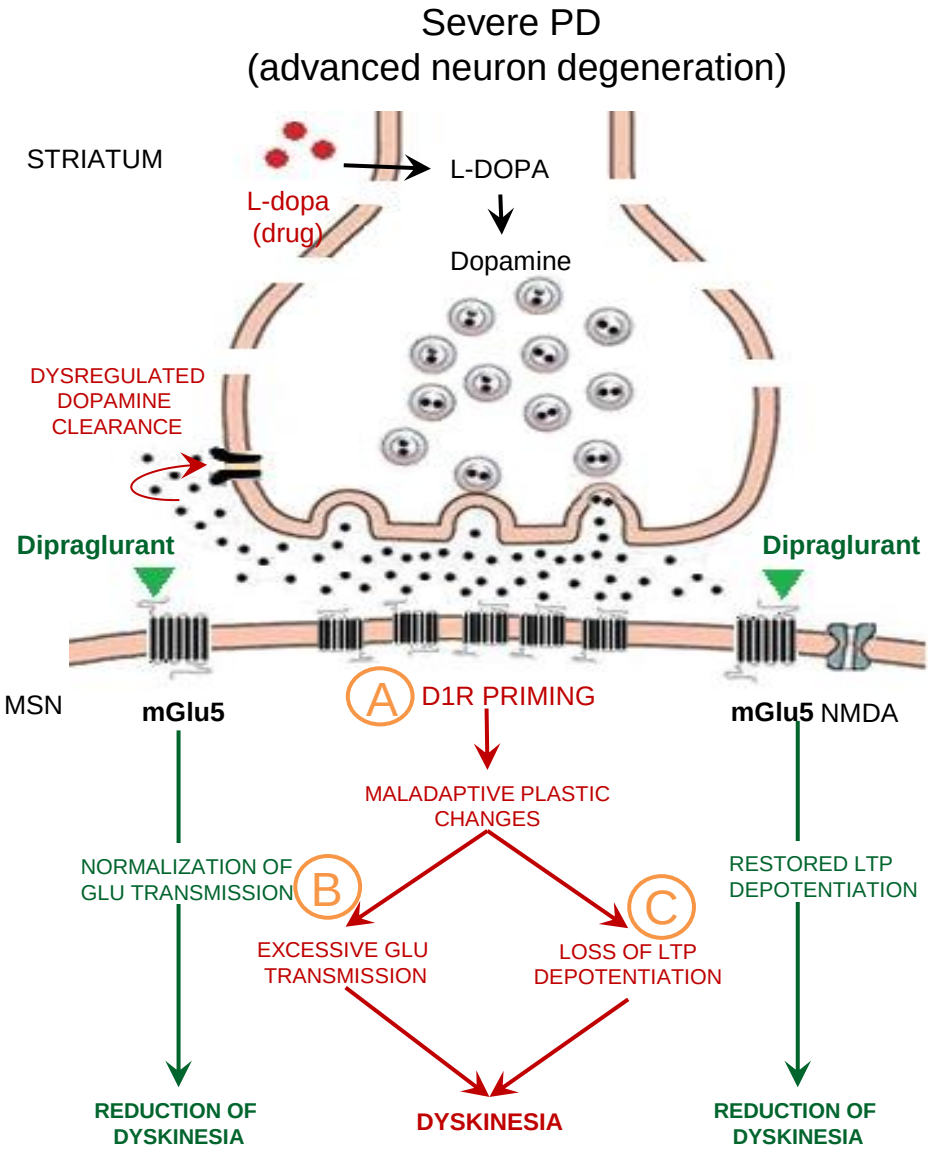
	2012	2018
PD-LID US Market Size	• Patient numbers unclear • Pricing in range of $3K-$4K pa • Less than $400mm	• 170K PD-LID patients in US • Pricing expected in range of $20K-$30K pa based on recent pricing of Nuplazid, Ingrezza and Gocovri • $4.2bn PD-LID market opportunity in US
Dipraglurant Development Plan	• Regulatory path unclear • 3 studies anticipated (Ph2b and 2 Ph3) • Efficacy endpoint – mAIMs (prone to placebo response)	• Precedented regulatory path in LID - Gocovri • Post FDA interaction – only 2 registration studies • Efficacy endpoint – UdysRS (developed for LID and includes objective clinician assessment)
Competition	• Dipraglurant 2nd in class behind mavoglurant (Novartis) • Long-acting amantadine (ADS-5102)	• Dipraglurant now 1st in class – mavoglurant terminated • Gocovri approved 24th August 17, but safety profile similar to generic amantadine
Dipraglurant Data	• Efficacy signal poorly understood • Placebo effect in Ph2 POC • No placebo mitigating factors included • Short-acting PK profile viewed as negative	• New FDA required analysis highlights robustness of efficacy signal • Placebo effect understood and mitigating factors built into registration studies • PK profile mirrors L-dopa – recognized by KOLs as a key advantage
Exclusivity	• Patent on composition of matter expires in 2025	• Orphan drug designation – additional 7 years of protection • Additional patents filed to extend protection to 2034

Dipraglurant in Parkinson's Disease

Levodopa-Induced Dyskinesia in Parkinson's Disease (PD-LID)

- Long-term L-dopa use is invariably associated with the development of dyskinesias - as disabling as the PD symptoms themselves
- Prevalence of LID is related to disease duration
  - Within 4-6 years of L-dopa treatment, LID is experienced by >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
- Dyskinesias result from the neurodegenerative process that underlies PD.
- Dopamine replacement does not lead to dyskinesia per se, but lowers the triggering threshold for symptoms.
- Patients with LID present with irregular migrating uncontrollable contractions or twisting and writhing due to dystonia, chorea, and choreoathetosis.
- Over time PD drugs become less effective, exacerbated by the emergence of LID, which limits tolerability of the drugs
- The constant dyskinetic movements can be painful, lead to weight loss, fatigue and exhaustion, with increased risk for falls and injuries.
- Patients are embarrassed and withdraw from social interaction leading to isolation, frustration and depression.
- This diminishes the patient's quality of life but it also significantly increases the burden on the caregiver.
- 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.

Dipraglurant - Overview & 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 *Abnormal 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 mGluR5 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**

LTP = Long Term Potentiation

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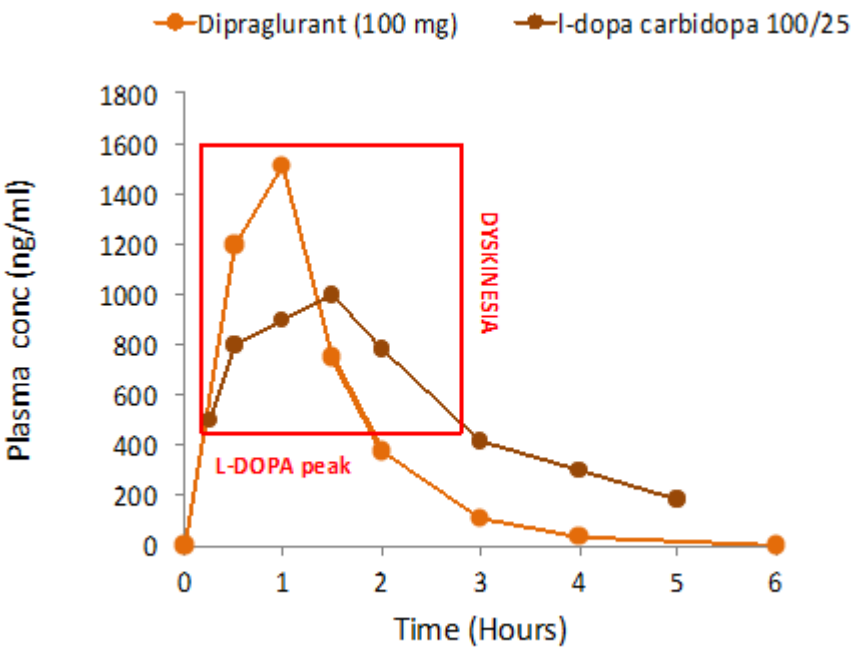
Dipraglurant PK is a Key Advantage for Treating LID

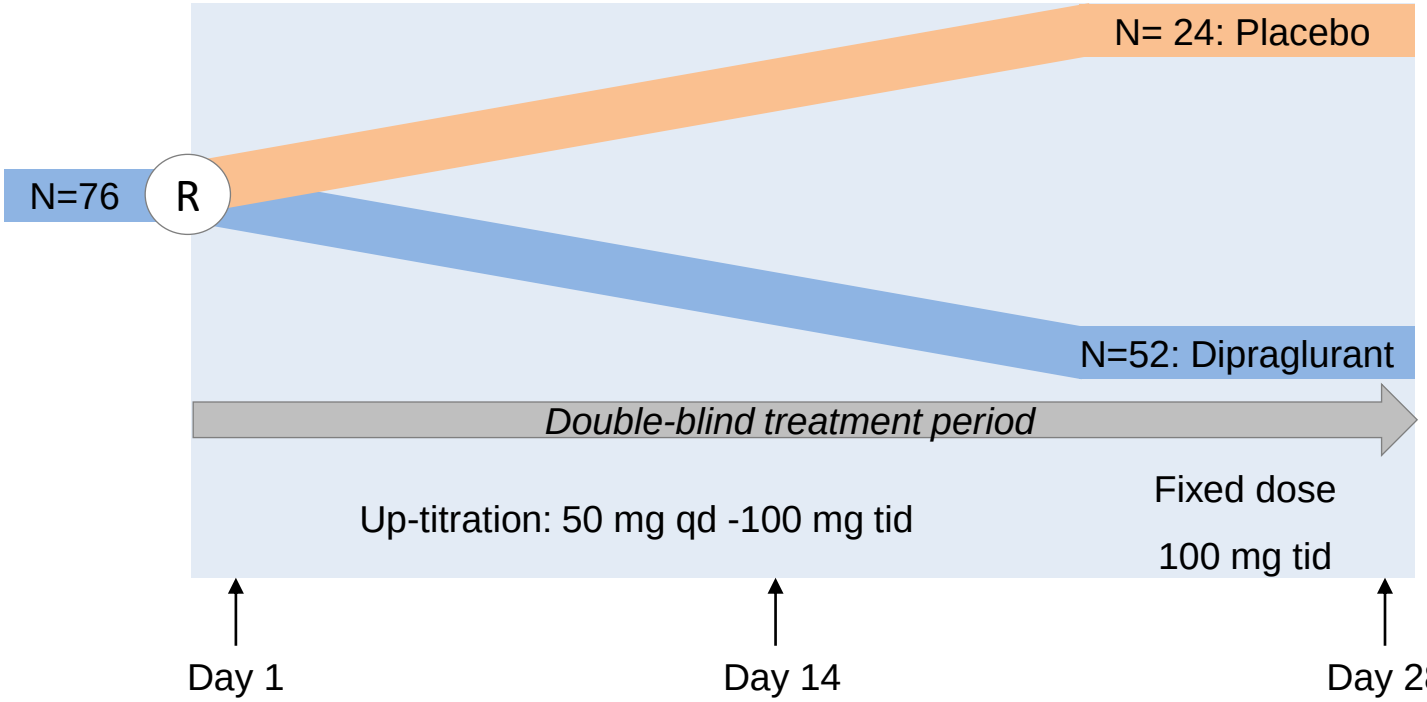


- Dyskinesia symptoms are correlated to peak levels of levodopa therapy
- PK profile of dipraglurant mirrors that of levodopa
- **Dipraglurant inhibits abnormal glutamate stimulation during peak levodopa dose but releases the receptor during normal glutamate activity**

Dipraglurant PK/PD Profile is Ideal for Treating LID

Dipraglurant EU and US Phase 2a Study in LID

Multicentre study in 25 centres across US and Europe



- **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

Days		1-3	4-7	8-13	14-16	17-21	22-28
Dose/mg	AM			50	50	50	100
	Noon	50	50	50	100	100	100
	PM		50	50	50	100	100
	Daily	**50**	**100**	**150**	**200**	**250**	**300**

N= number of patients; R= randomization
Coordinating Investigator: Prof Olivier Rascol at University Hospital, Toulouse, France

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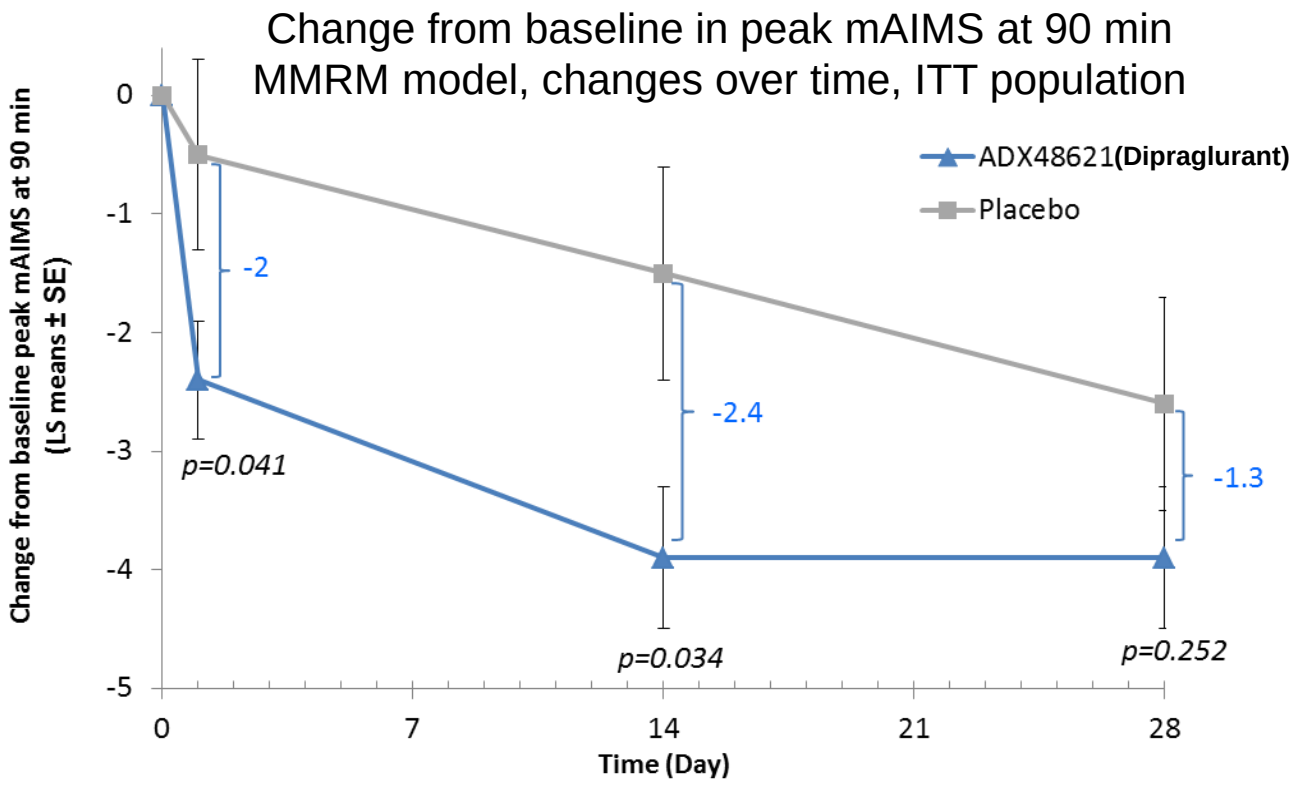
Dipraglurant Reduces LID Severity by 30%



Mean % change of peak mAIMS from baseline		
Midday dose	Dipraglurant	Placebo
Day 1 (50 mg)	19.9%	4.1%
Day 14 (100 mg)	32.3%	12.6%
Day 28 (100 mg)	31.4%	21.5%

- 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:
  - No centralized raters
  - No independent raters
  - Rater not blinded to visit number
  - Patients were more moderate than severe

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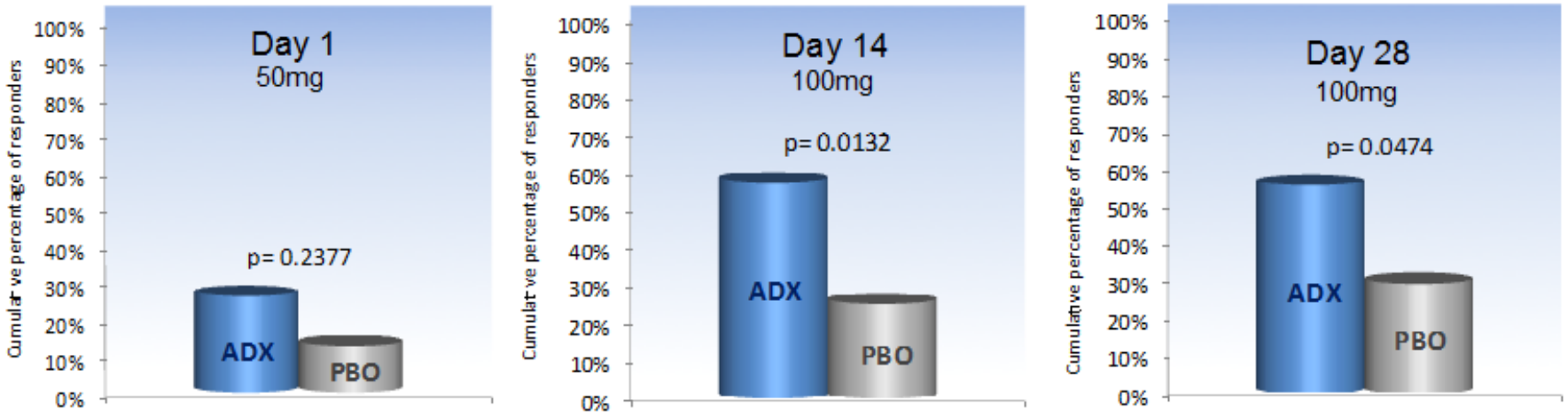
Responder Analysis Demonstrates Dipraglurant Significant Benefit

Cumulative % of Patients Showing ≥ 30% Change of Peak mAIMS from Baseline



Responder analysis (≥30% change of peak mAIMS from baseline)					
Midday dose	Dipraglurant		Placebo		p-value
Day 1 (50 mg)	n=13	26.0%	n=3	12.5%	0.2377
Day 14 (100 mg)	n=29	56.9%	n=6	25.0%	0.0132
Day 28 (100 mg)	n=27	55.3%	n=7	29.2%	0.0474

- 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

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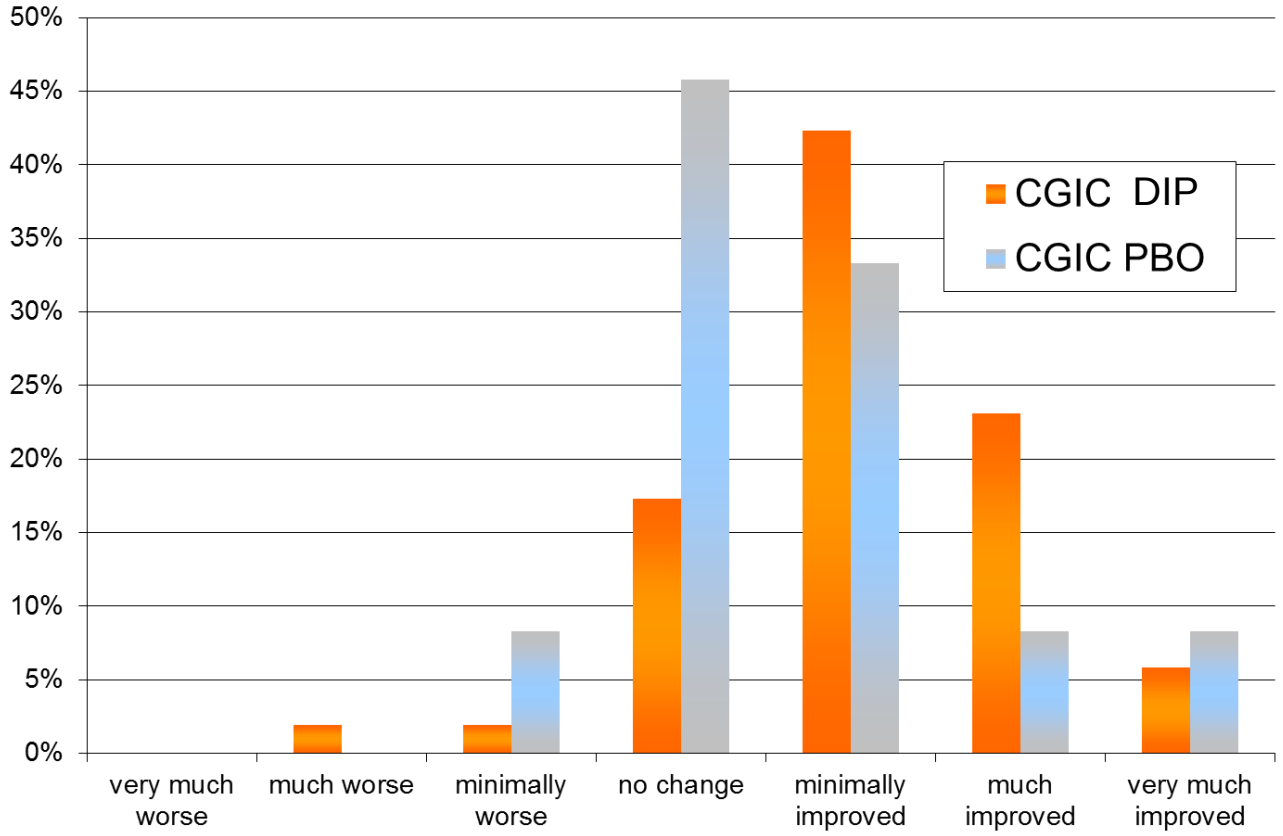
Clinician Rated Global Impression of Change - Dyskinesia



	Dipraglurant	Placebo
Improved (p<0.05)	71.2%	49.9%
No change	17.3%	45.8%

- 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)**

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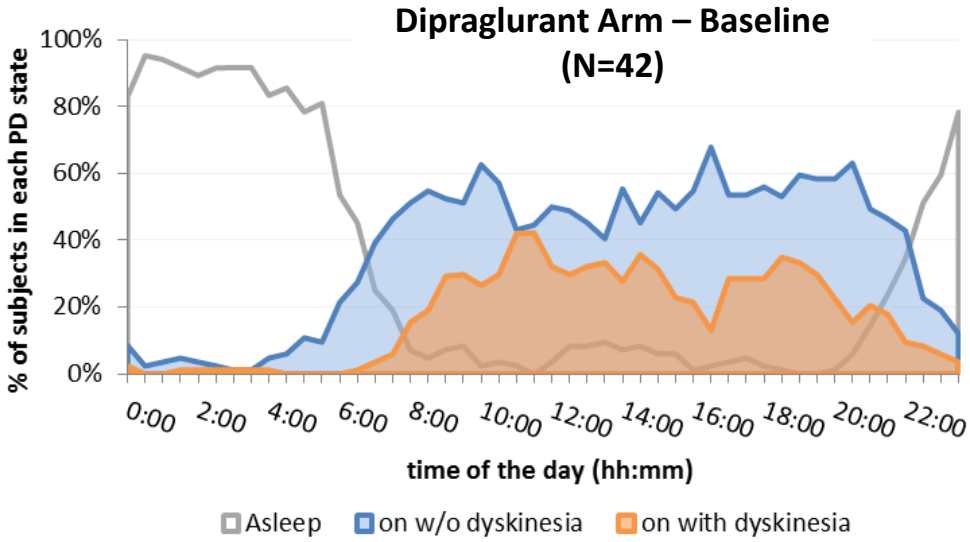
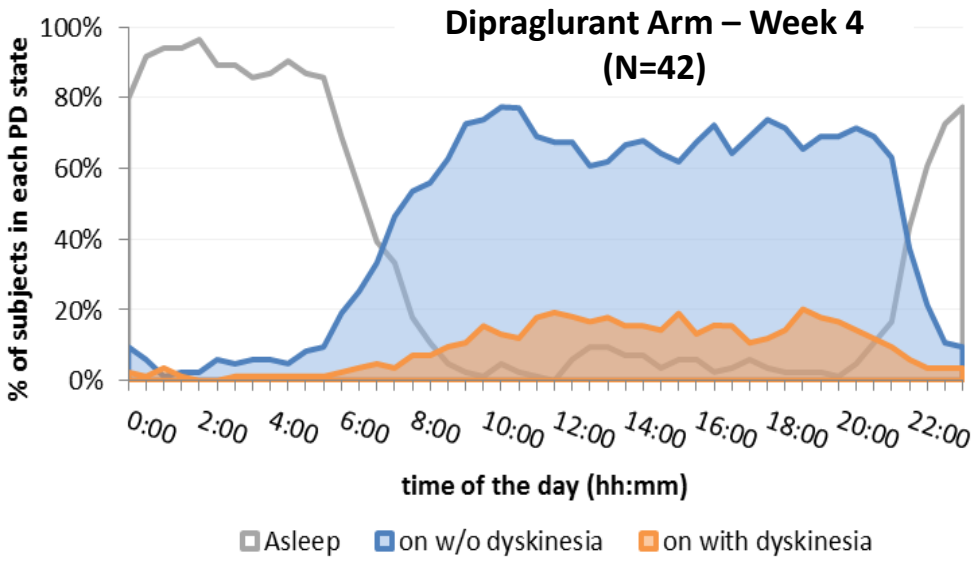
Patient Diaries – Improvement Throughout the Waking Day



After 4-week treatment with dipraglurant:

- ON time <u>with dyskinesia</u> **reduced** during the day
- ON time <u>without dyskinesia</u> **increased** and maintained during the day



Dipraglurant 50 and 100 mg Doses Demonstrated Safety and Satisfactory 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:

	Dipraglurant	Placebo
Worsening Dyskinesia	21% (**15.3%***)	12.5%
Dizziness	19%	12.5%
Nausea	19%	0%
Fatigue	15%	4%

* 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)

Summary of Efficacy Data

- Dipraglurant showed a clinical meaningful improvement of dyskinesia
  - Significant improvement of mAIMS on Days 1 and 14
  - Trial design exacerbated placebo response – confounding significance at Day 28
  - Responder analysis (≥30% improvement) demonstrates clinically meaningful and statistically significant benefit on Days 14 and 28
  - Investigator assessed CGIC shows dipraglurant significantly improved dyskinesia over placebo during the study ($p<0.05$)

- Did not impair motor function (UPDRS) – important consideration for FDA

- Dipraglurant effects in patient-reported outcomes:
  - 50-minute reduction in “OFF time” by week 4
  - 2.3 hours more “ON time” without dyskinesia by week 4

Clinical Development Plan

- Pivotal trials:
  - Two studies required for registration
    - Primary endpoint: UDysRS - more sensitive to treatment effect than mAIMS and less prone to placebo response (Goetz 2013)
    - Pivotal Study 1 (301) – 13 weeks – data H1 2020
    - Pivotal Study 2 (302) – 26 weeks (primary endpoint at 13 weeks) – data H2 2021
  - Open label extension: 100 patients exposed for 1 year

- Toxicology:
  - 6 and 9 month toxicology
  - 3 month combination toxicology study in one species before large studies start

- Regulatory:
  - Continue to interact with regulatory bodies in 2018
  - Consider fast-track / breakthrough applications after first pivotal study
  - NDA submission projected for mid 2022

Management of Placebo Response

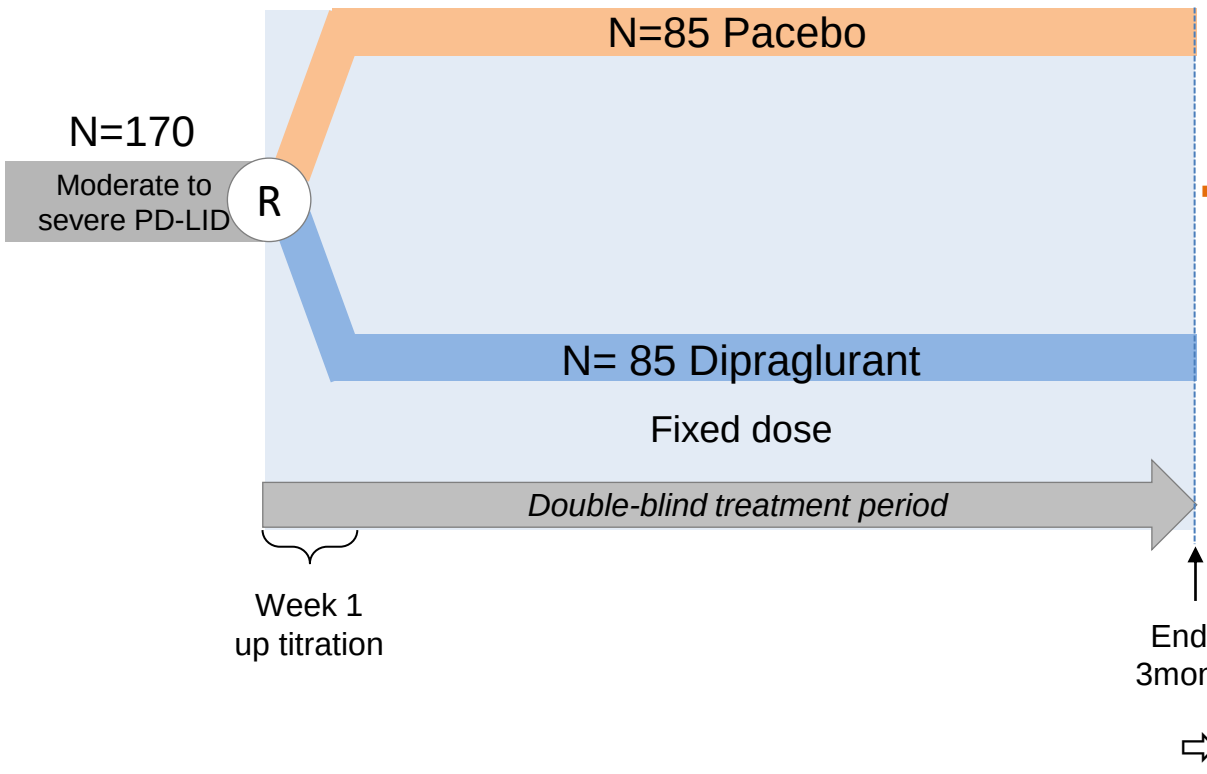
Objective	Strategy
• Minimize rater variability (across and within sites)	• Use independent (centralized) raters
• Reduce expectancy bias	• Raters blinded to visit and do not rate the same patient at baseline and study endpoint
• Exclude patients with minimal symptoms (as more likely to respond to placebo)	• Ensure that symptom score reflects moderate to severe symptoms that warrant therapy • Ensure occur frequently enough for scale sensitivity
• Exclude potential investigator rating inflation	• Independent oversight of screening and use of centralized rater baseline visit score as study entry gate
• Draw placebo response ahead of randomization	• Consider non-pharmacologic intervention during screening period
• Ensure no geographic bias	• Only include countries / sites where centralized rating is feasible

Dyskinesia Rating Scales: UDysRS verses mAIMS

	UDysRS	mAIMS
Characteristics	• Recommended scale by Movement Disorder Society • FDA regulatory NDA precedent (Adamas - Gocovri) • Contains anchored objective clinician evaluated measures of dyskinesia • UDysRS has both patient-based perceptions of disability and physician assessments of impairment and disability embedded in the single scale • Less prone to placebo effect	• mAIMS alone was identified as suboptimal in detecting treatment-related changes • mAIMS patient driven • More prone to placebo effect
Clinimetric properties	• Validated	• Only the original version has been validated
History	• Developed in 2009 specifically for dyskinesia in PD patients	• Developed in 1970 to assess tardive dyskinesia in psychiatric patients

UDysRS= Unified Dyskinesia Rating Scale

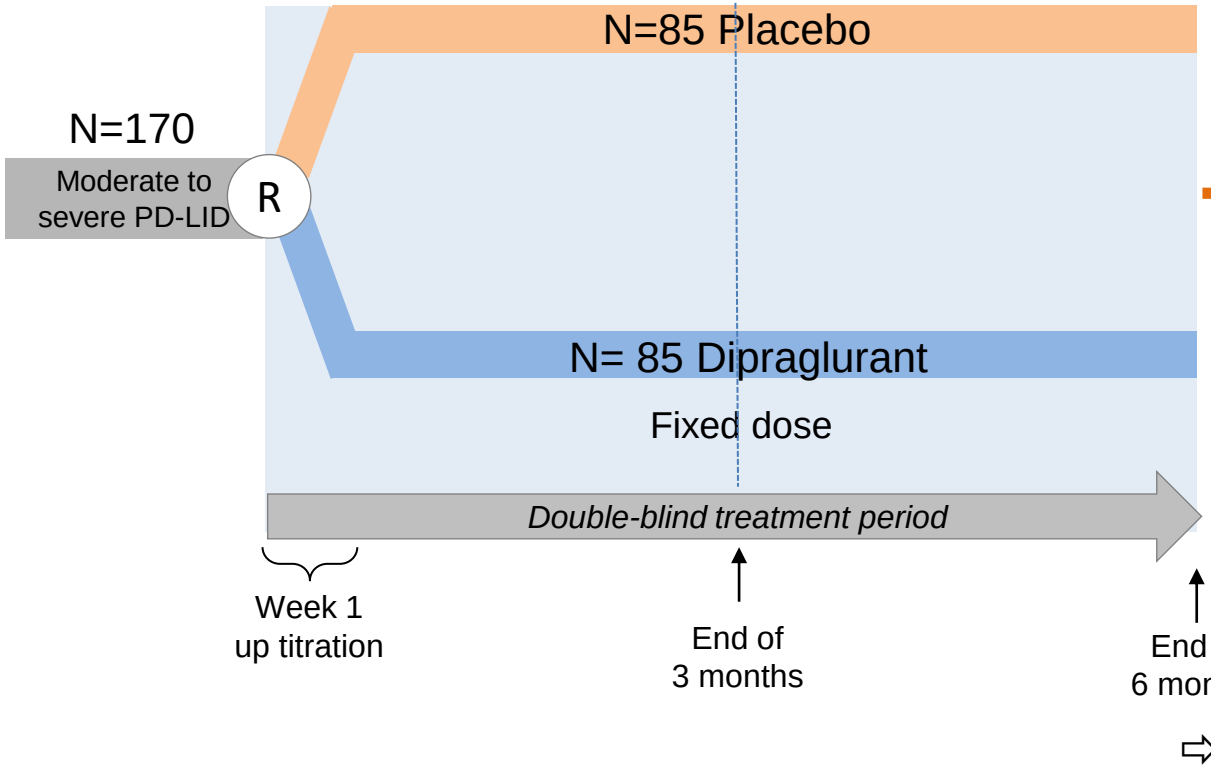
Dipraglurant 1st Pivotal LID Study (301)



- **Primary objective**: efficacy in reducing LID
  - ✓ Change over time in UDysRS (wk13 from baseline)
- **Secondary objective**: safety & tolerability, additional efficacy parameters, PK
  - ✓ Change over time in MDS-UPDRS Part III (Clinician-scored monitored motor evaluation)
  - ✓ Patient diaries, on & off time
  - ✓ CGI-S
  - ✓ Pharmacokinetics (PK)
  - ✓ Safety and tolerability

N= number of patients; R= randomisation; LID= L-Dopa induced dyskinesia; OLE = open label extension

Dipraglurant 2nd Pivotal LID Study (302)



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  - ✓ Pharmacokinetics (PK)
  - ✓ Safety and tolerability

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Dipraglurant LID Opportunity

- LID has a large unmet need and market opportunity
  - > 170K LID patients in US
  - ~$1.4bn US market opportunity for dipraglurant
- Limited competition – only one FDA approved medicine
  - Gocovri (reformulation of generic amantadine): Approved on 24th August 17 – safety profile similar to generic
  - Dipraglurant 1st in class highly selective oral monotherapy – improved safety profile
- Development plan defined
- Precedented regulatory path paved by Gocovri (Adamas)
  - Two registration trials
  - Ideal PK profile mirrors levodopa – recognized by KOLs as key advantage
- Strong patent and market exclusivity
  - NCE and polymorph patent provide protection through 2034 without extensions and data exclusivity
  - Orphan Drug Designation – 7 years of market exclusivity

Financials

Financials and Stock

- Cash runway through 2021
  - Proforma cash of CHF47M at 31 March 2018.
- Traded on SIX Swiss Exchange: ADXN (ISIN:CH0029850754)
- 28,564,031 shares outstanding (37.7M fully diluted)
  - New Enterprise Associates - 16%
  - New Leaf Ventures – 5.6%
  - CAM Capital – 5.6%
  - Management & board holds -10% (fully diluted basis)
- Analyst coverage:
  - LifeSci Capital – David Sherman, Jerry Isaacson
  - Van Leeuwenhoek – Marcel Wijma
  - valuationLAB – Bob Pooler
- Market capitalization: approx. CHF90M
- Tax losses carried forward: CHF190M
- No debt

1 CHF=$1.05

Allosteric modulators for human health

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