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Innovative Treatments for Central Nervous System Disorders

October 2019

Allosteric modulators for human health

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Addex Overview

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

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 Pyschosis
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

Experienced Board of Directors

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

Extensive Pipeline Driving Long-Term Growth

Molecule / MoA	Indication	Partner	Pre-clinical	Phase 1	Phase 2	Phase 3	Milestone
Dipraglurant-IR (mGlu5 NAM)	PD-LID						Top line data Q3 2021
Dipraglurant-ER (mGlu5NAM)	Dystonia						
ADX71149 (mGlu2 PAM)	Epilepsy	janssen					
$GABA_B$ PAM	Addiction	INDIVIOR					
	CMT1A						
mGlu7 NAM	Post-traumatic stress disorder	eurostars™					
mGlu2 NAM	Mild neurocognitive disorders						
mGlu4 PAM	Parkinson's disease						
mGlu3 PAM	Neurodegenerative disorders						

Lead Program Entering US Pivotal Study and Multiple Orphan Drug Opportunities

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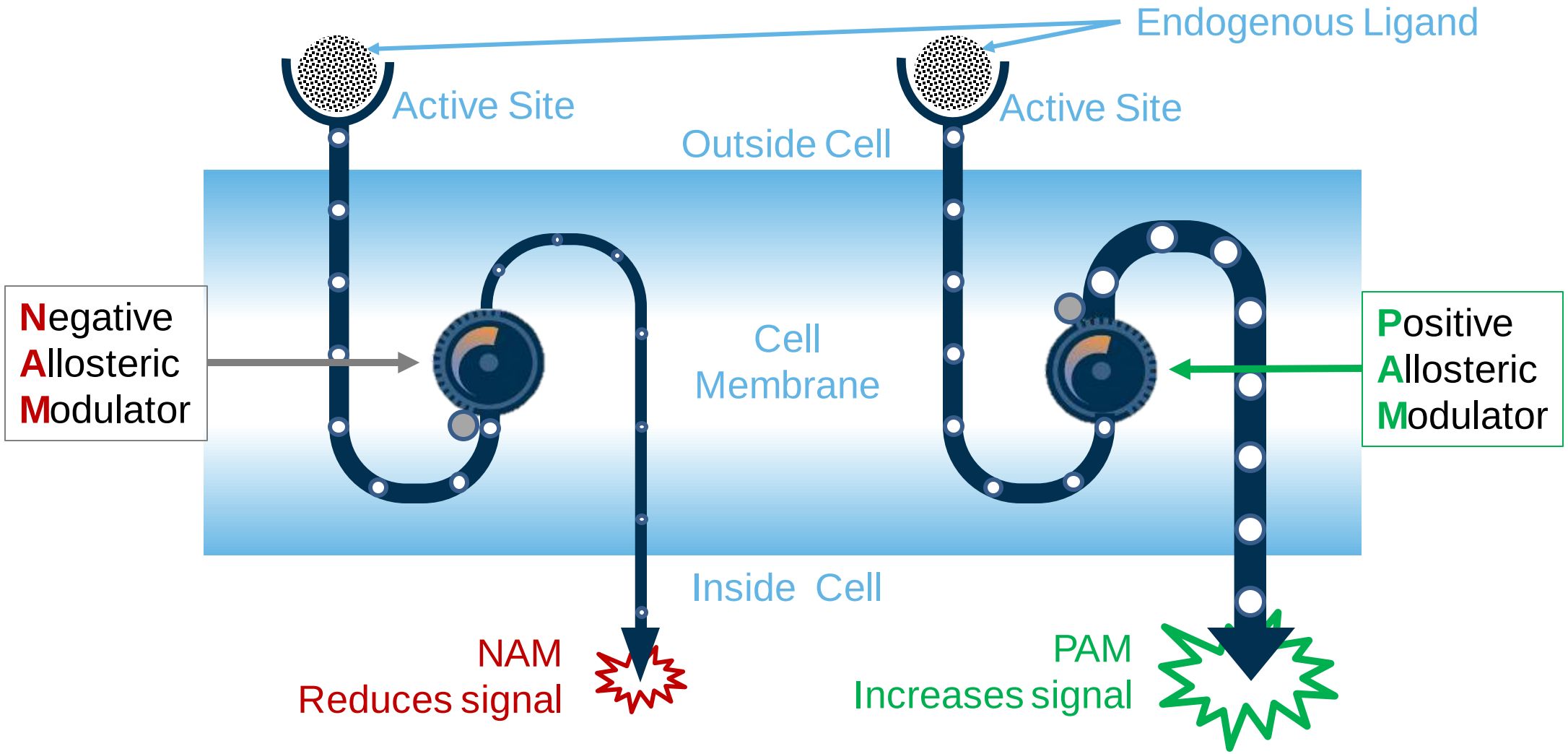
NAM = Negative Allosteric Modulator
PAM = Positive Allosteric Modulator

IR = Immediate Release
ER = Extended Release

What are Allosteric Modulators?



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

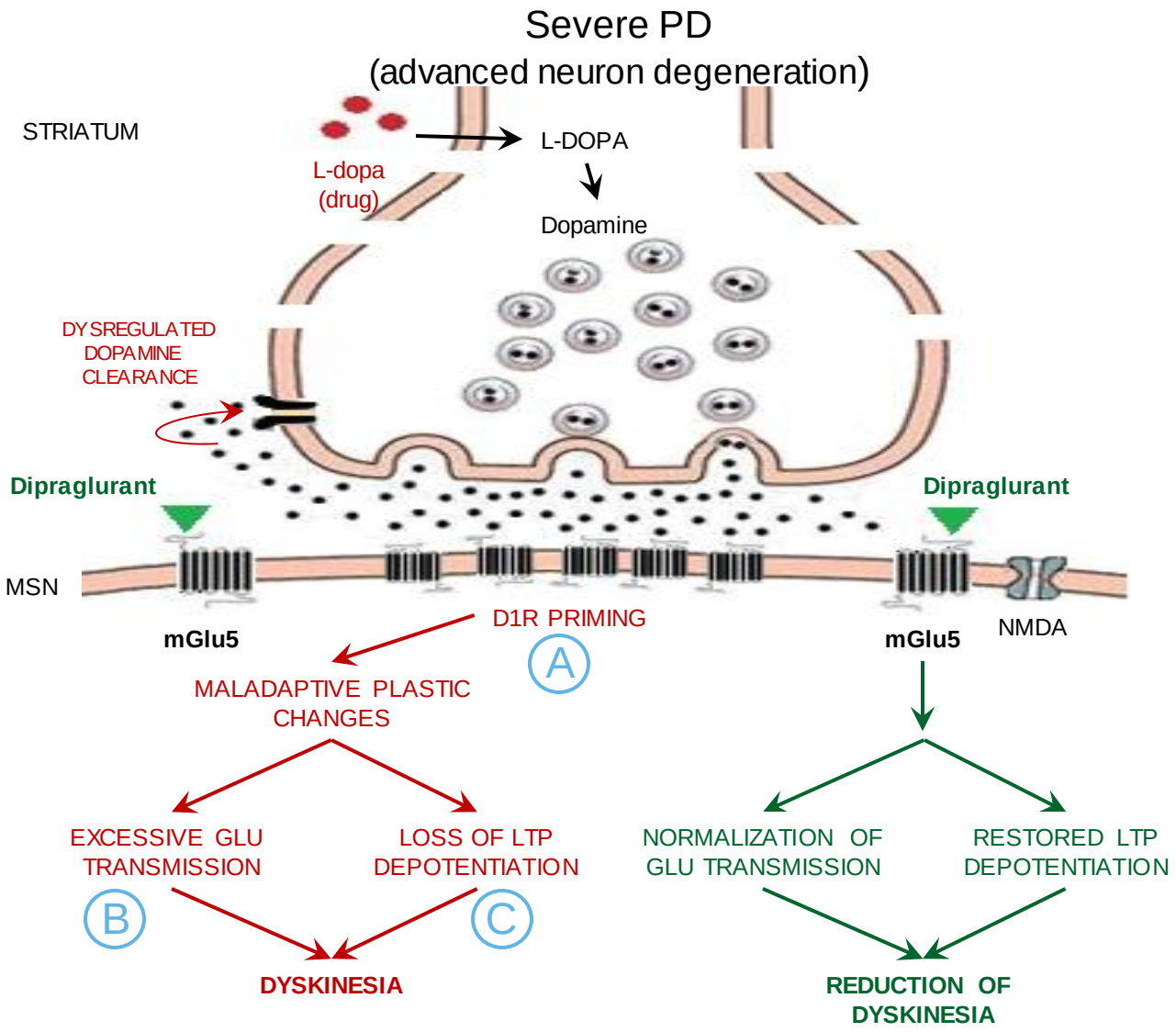
The Dipraglurant Opportunity in Dyskinesia associated with PD

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 Parkinson's disease 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 of PD therapeutics – 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)

Long-term L-dopa use is invariably associated with the development of dyskinesias	➢ 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
LID symptoms: irregular migrating uncontrollable contractions or twisting and writhing due to dystonia, chorea, and choreoathetosis	➢ 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
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
Over time PD drugs become less effective, exacerbated by the emergence of LID	**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**

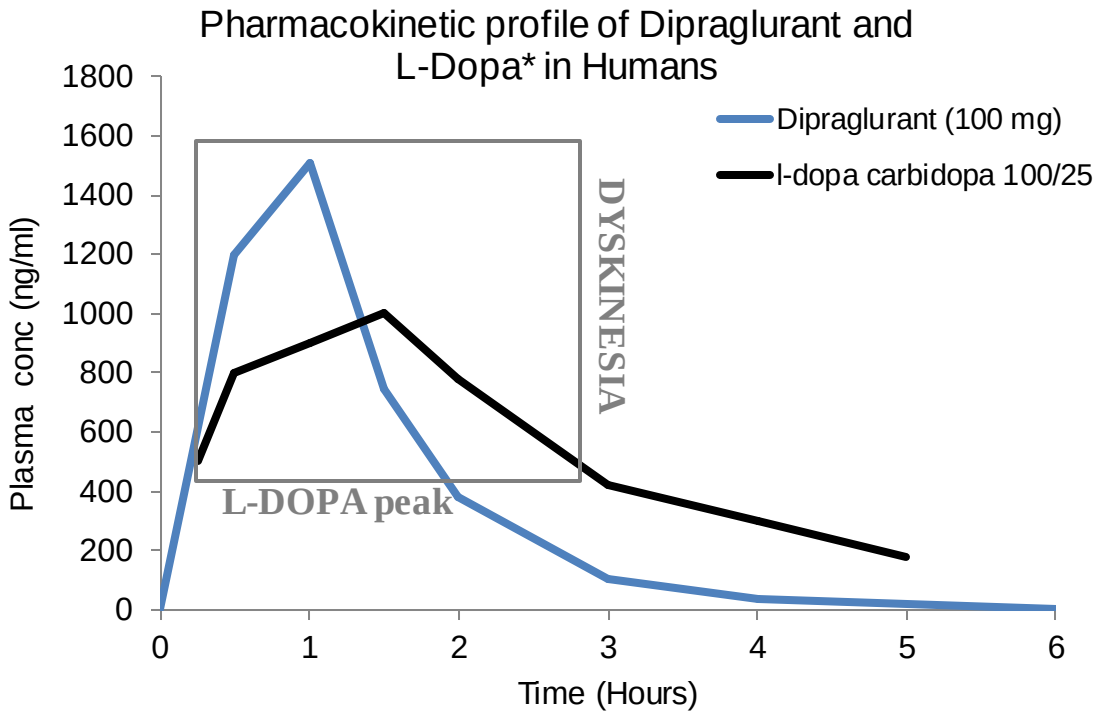
Dipraglurant - Overview and Mechanism of Action



- 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**

LTP = Long Term Potentiation
MSN = Medium Spiny Neurons

Dipraglurant PK is a Key Advantage for Treating LID

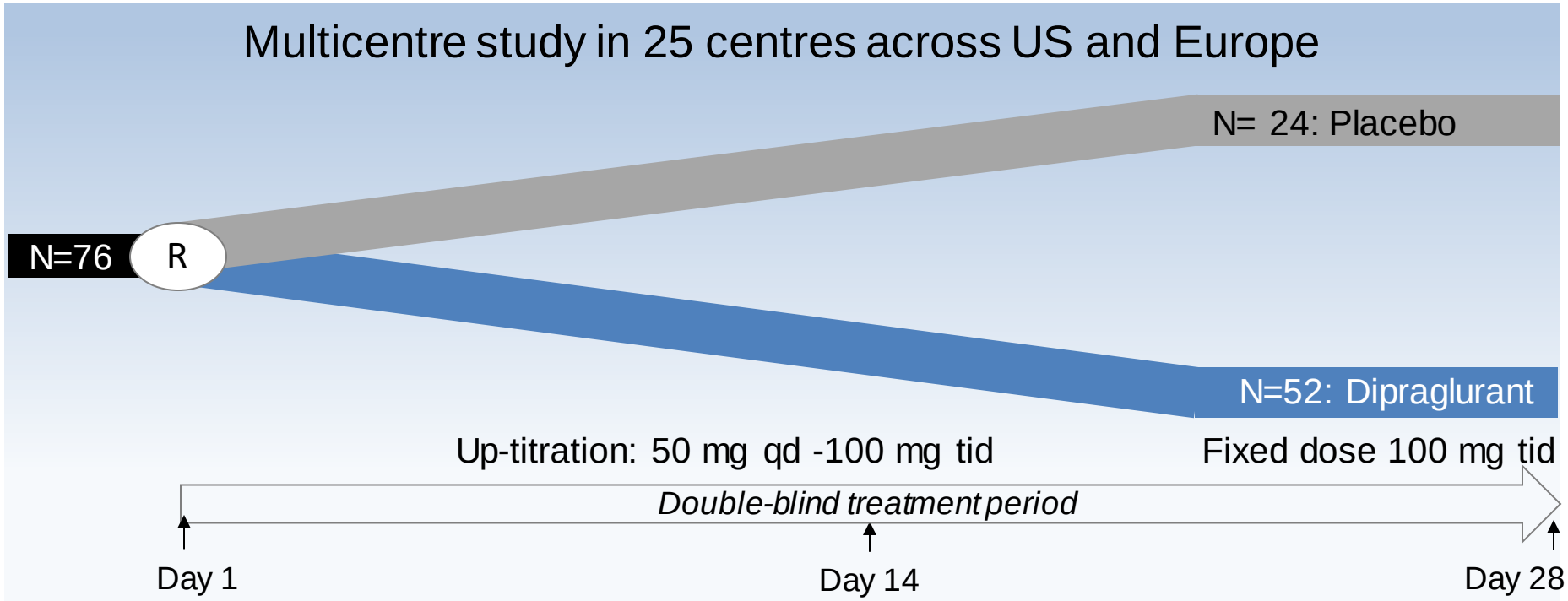


- Dyskinesia symptoms are correlated to peak levels of levodopa therapy
- PK profile of dipraglurant mirrors that of levodopa
- **Dipraglurant inhibits abnormal glutamate stimulation during peak levodopa dose but releases the receptor during normal glutamate activity**

PK profile differentiates dipraglurant from other treatments

* Clinical Neuropharmacology Vol 22 No.1 pp.24-29

Dipraglurant EU and US Phase 2a Study in LID



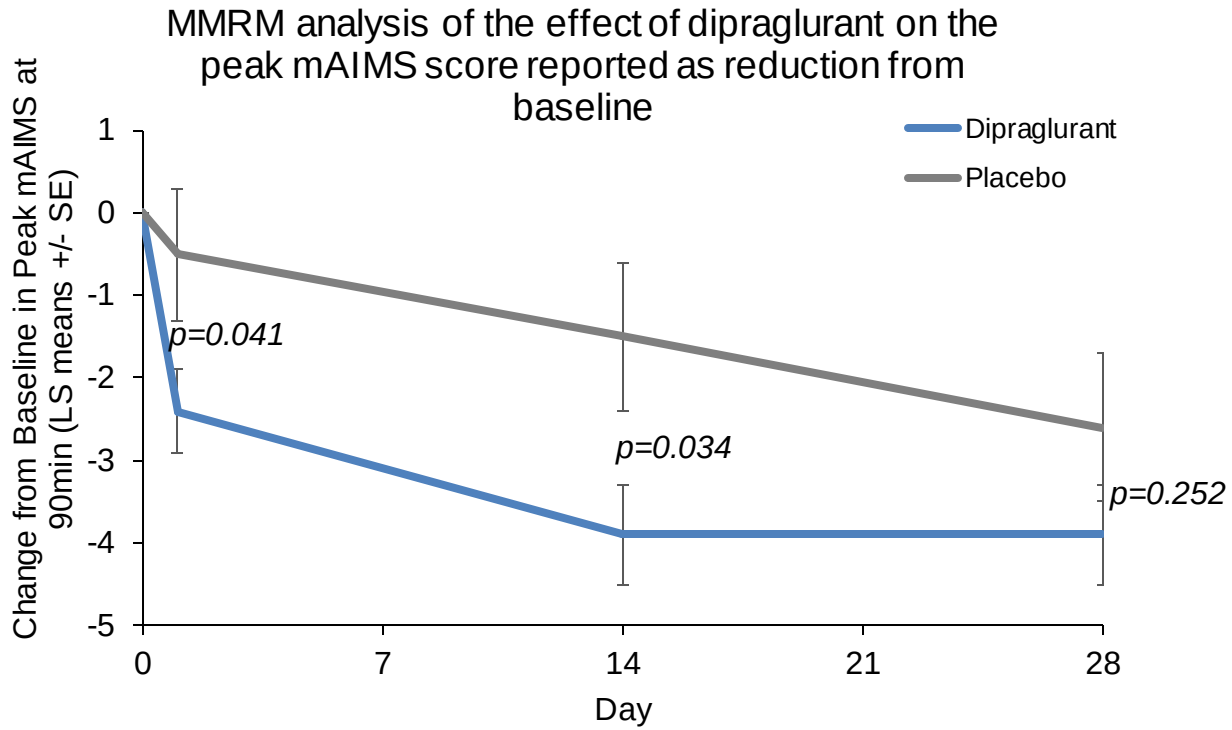
Days		1-3	4-7	8-13	14-16	17-21	22-28
Dose/mg	AM			50	50	50	100
	Noon	50	50	50	100	100	100
	PM		50	50	50	100	100
	Daily	50	100	150	200	250	300

- **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

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

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

Clear dose response but need to manage placebo

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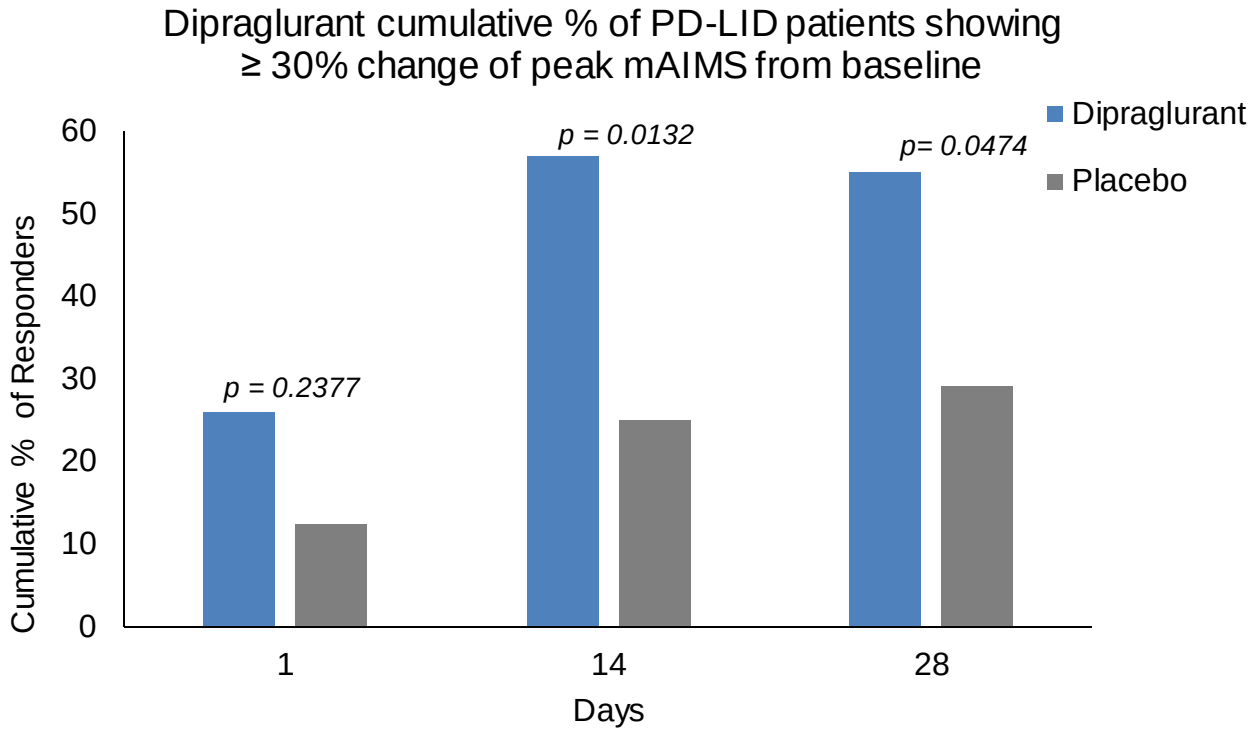
Responder Analysis Demonstrates Dipraglurant Significant Benefit



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	55.1%	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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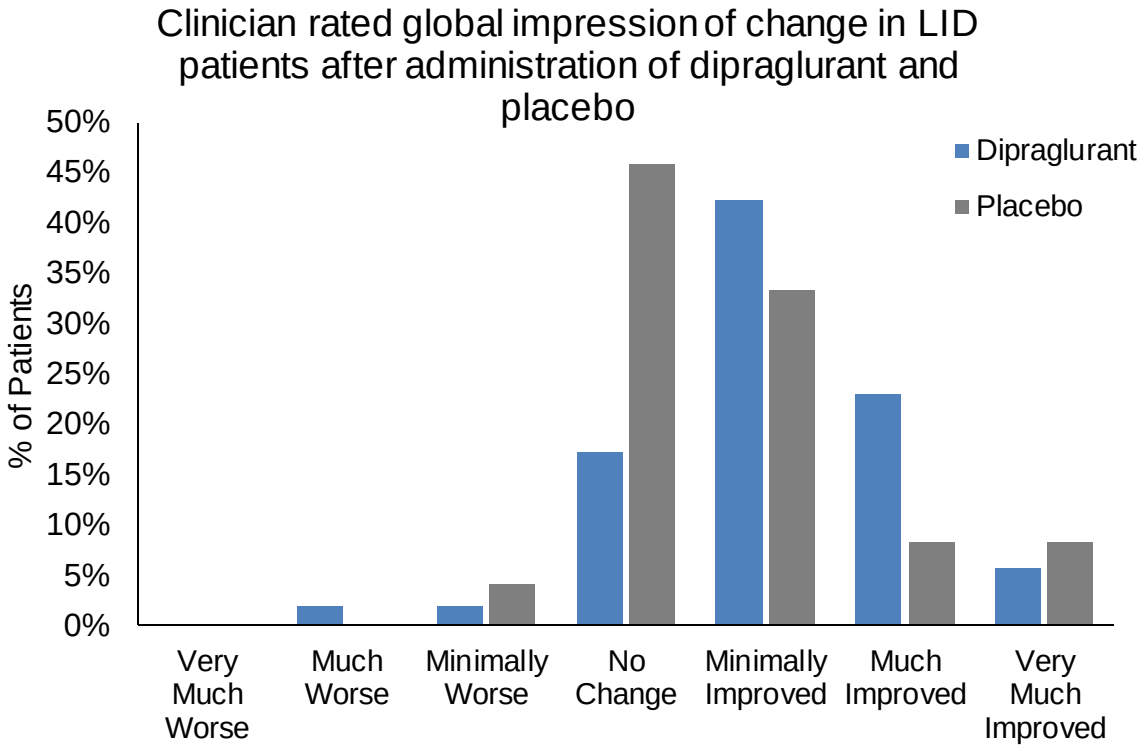
Clinician Rated Global Impression of Change - Dyskinesia



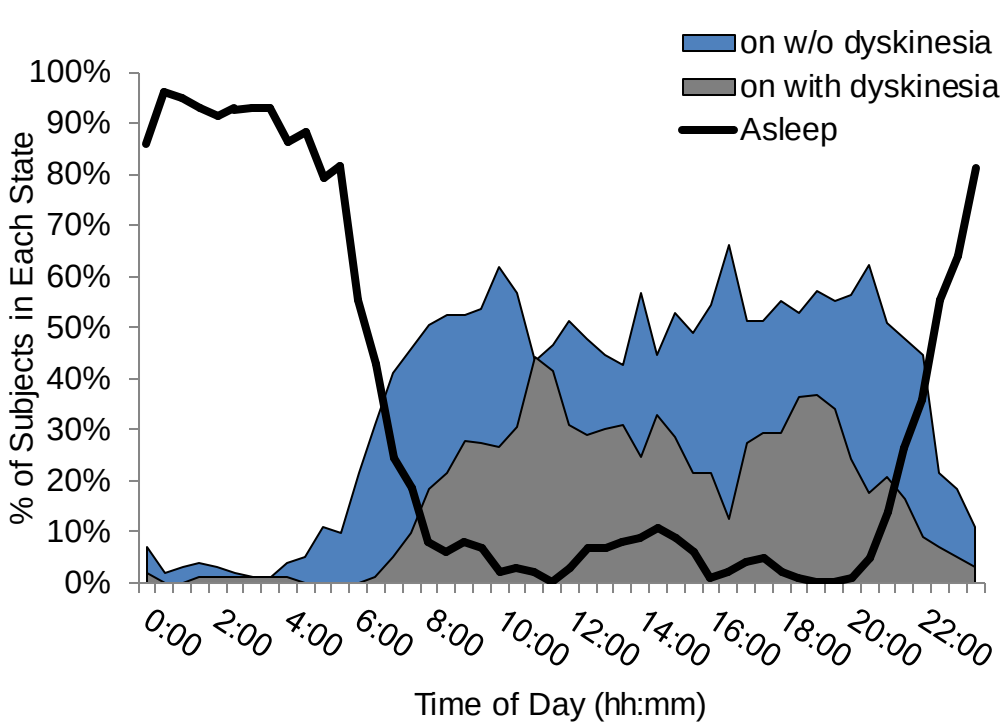
	Dipraglurant	Placebo
Improved (p<0.05)	71.2%	49.9%
No change	17.3%	45.8%

- 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)**

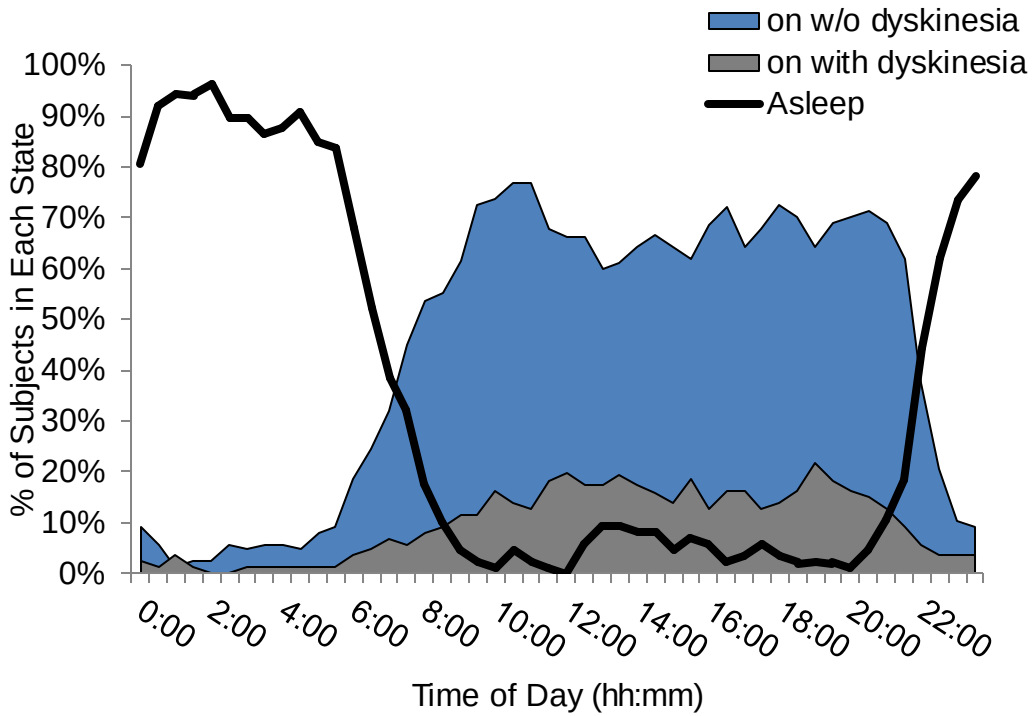
Patient Diaries – Improvement Throughout the Waking Day

Pattern of motor complications of dipraglurant patients over the course of a day, as reported in patients' diaries

Baseline (n=42)



Week 4 (n=42)



After 4-week treatment with dipraglurant:

- ON time with dyskinesia **reduced** during the day
- ON time without dyskinesia **increased** and maintained during the day

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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:

	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)

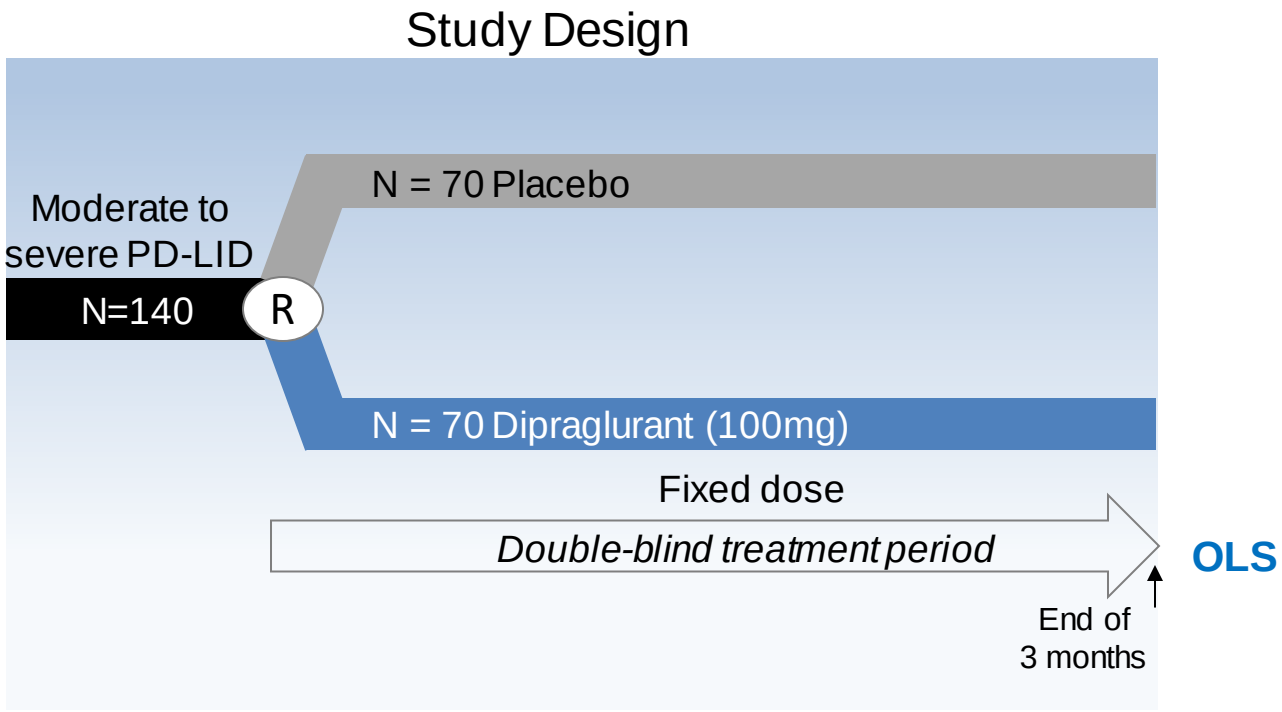
Safety profile suitable for continued development in PD (KOLs and DSMB)

Phase 3 Trial On-Track to Start Dosing in Q1 2020

- The Phase 3 trial is fully funded and expected to report out in Q3 2021
- Considering Fast-Track and/or Breakthrough Therapy applications after first pivotal study readout
- 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:

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

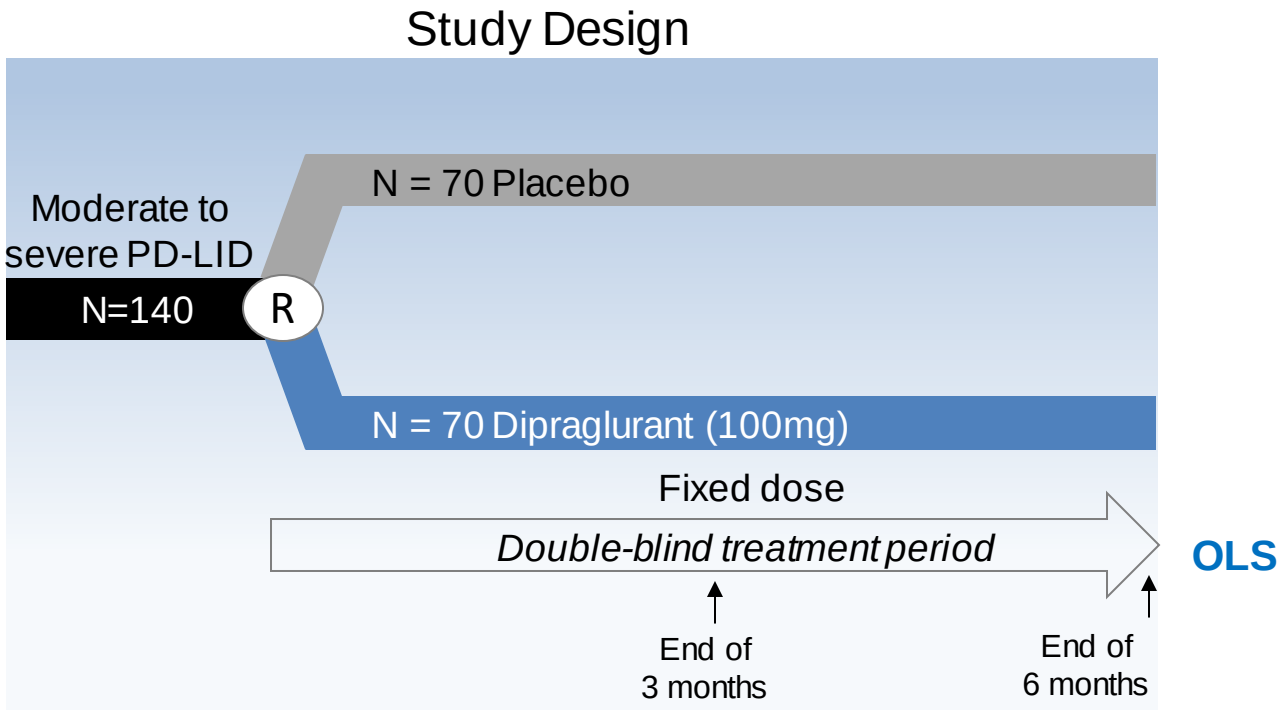
Dipraglurant First Pivotal PD-LID Study (301)



- 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

N= Number of patients
LID= L-Dopa induced dyskinesia
R= Randomisation
OLS = Open label study

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

N= Number of patients
LID= L-Dopa induced dyskinesia
R= Randomisation
OLS = Open label study

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
	  ➢ Ideal PK profile mirrors levodopa – recognized by KOLs as key advantage

Clear development plan with precedented regulatory path	➢ Precedented regulatory path paved by Gocovri (Adamas) ➢ Two registration trials (301 and 303) with Open Label Study ➢ UDysRS – more sensitive to treatment effect than mAIMS and less prone to placebo response (Goetz 2013) ➢ Implementing measures to manage placebo response is a priority
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
  - Cash of CHF36.7M at 30 June 2019
  - Fully funded through dipraglurant study 301 readout
- 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
- Market capitalization: approx. CHF59M
- No debt

Upcoming Major Development Milestones

Milestone	Timing
Dipraglurant – LID Phase 3 Registration Program	
Complete manufacturing of Drug Product	Q4 2019
Study 301 – Start dosing	Q1 2020
Study 301 – Top line data	Q3 2021

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ALLOSTERIC MODULATORS FOR HUMAN HEALTH

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