Addex Corporate Presentation

Baader Helvea Swiss Equities Conference

10-11 January 2019

Tim Dyer, CEO

Innovative Treatments for Central Nervous System Disorders

SIX: ADXN

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Addex Overview

Dipraglurant for Parkinson's Disease

- Registration trials scheduled to start in H2 2019
- US PD-LID market estimated at $4.2B
- FDA Orphan Drug Designation granted in PD-LID

Validating Partnerships with Industry

- Indivior PLC worth - $330m in milestones, tiered royalties up to double digit & funded research program
- J&J worth €109m in milestones & low double digit royalties

World Leading Technology Platform

- "Allosteric modulators" are a validated & differentiated pharmacological approach
- Proprietary biological screening assays and chemical library

Deep Pipeline of first /best in class programs

- Driving long term growth
- Creating future partnership opportunities with industry

Strong balance sheet

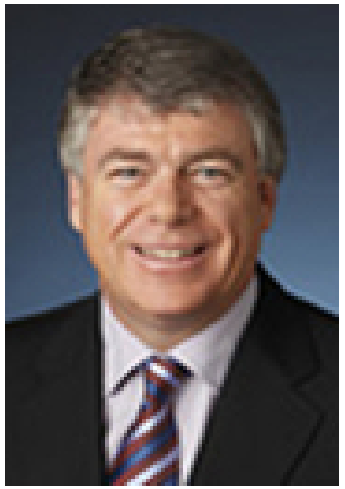
- 28.6M shares traded on the SIX Swiss Stock Exchange – ADXN
- Cash of CHF41.7m at 31 December 2018
- Runway through 2021

Experience Leadership Team

Tim Dyer

CEO / CFO

- Co-Founder of Addex
- Formerly with PwC
- UK Chartered Accountant



Dr Roger Mills

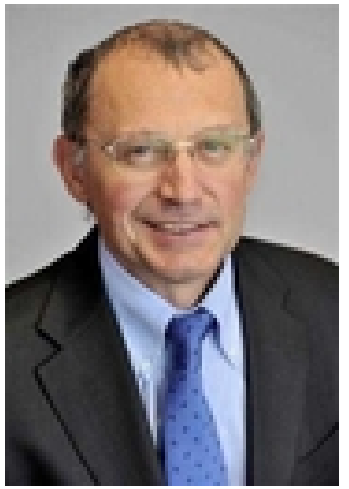
Chief Medical Officer

- Formerly with Acadia Pharmaceuticals
- Developed Nuplazid in PD Pyschosis
- 30 years in Pharma industry including Pfizer and Gilead

Dr Robert Lutjens

Co-Head of Discovery (Biology)

- Member of Addex founding team
- Formerly with Glaxo & Scripps Research Institute



Dr Jean-Philippe Rocher

Co-Head of Discovery (Chemistry)

- Member of Addex founding team
- Formerly with Pierre Fabre, GSK and Mitsubishi

Clinical Stage Pipeline with Lead Program Entering US Pivotal Study

Multiple Orphan Drug Opportunities

Molecule / MoA	Preclinical	Phase 1	Phase 2	Phase 3 Pivotal
Dipraglurant-IR *(mGluR5 NAM)*	Parkinson's disease levodopa-induced dyskinesia			
Dipraglurant-ER *(mGluR5 NAM)*	Focal cervical dystonia			
ADX71149 *(mGluR2 PAM)*	Epilepsy			
ADX71441 *(GABAB PAM)*	Addiction			

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	Patient Groups, Government and Academic Collaborators
GABAB PAM	Charcot-Marie-Tooth 1A			
mGluR7 NAM	Psychosomatic Disorders (PTSD)			Innosuisse /CHUV
mGluR2 NAM	Mild Cognitive Impairment			Neuromed Institute
mGluR4 PAM	Parkinson's Disease			Innosuisse / CHUV
mGluR3 PAM	Neurodegenerative Disorders			Neuromed Institute
TrkB PAM	Neurodegenerative Disorders			Innosuisse/Uni Geneva & MJFF

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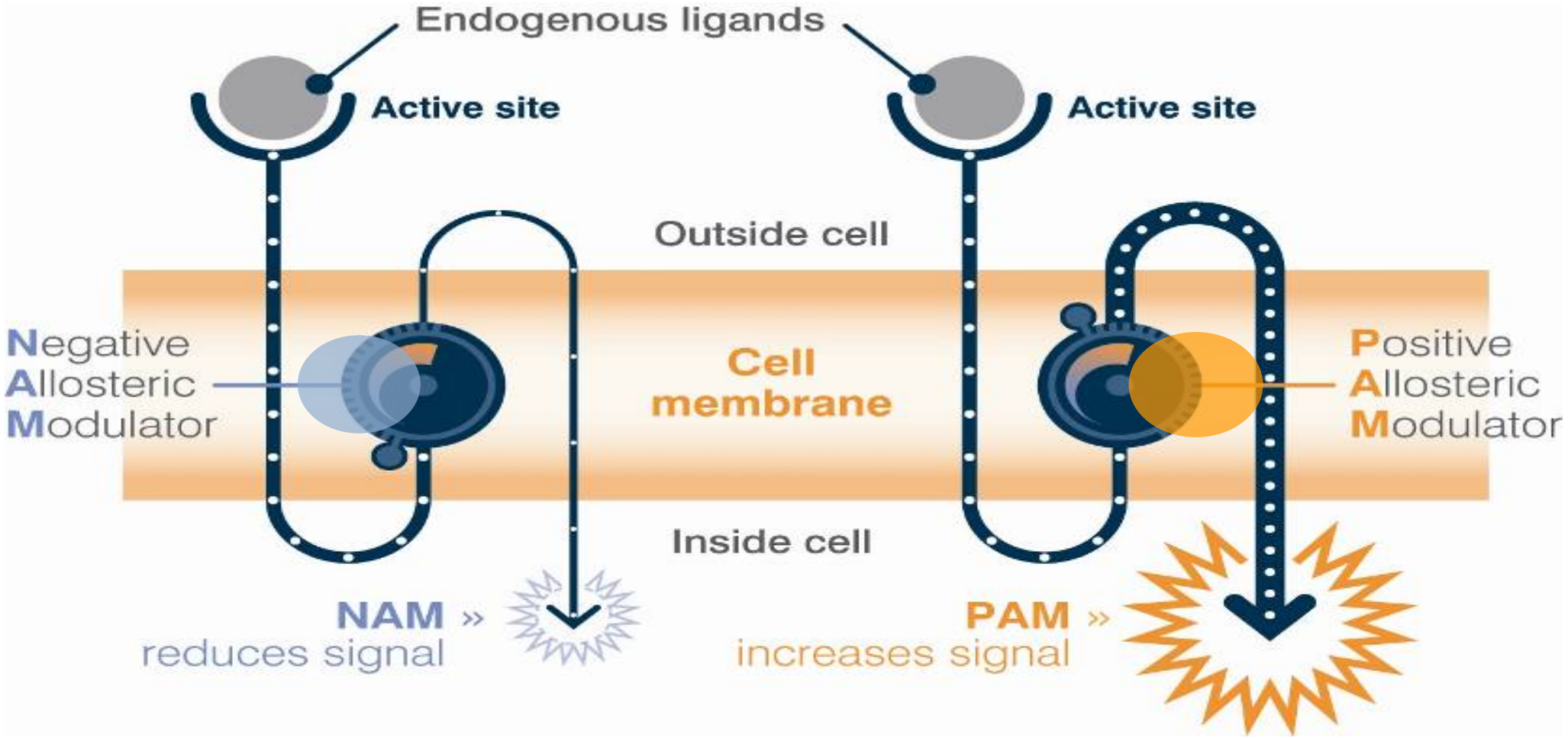
NAM = Negative Allosteric Modulator
PAM = Positive Allosteric Modulator

World Leading Allosteric Modulator Discovery Platform

What are allosteric modulators?



Addex is based on a world leading technology platform

Allosteric Modulation Drug Discovery Platform

- Proven track record
  - Pipeline of in house discovered drug candidates
    - mGluR5 NAM & mGluR2 PAM in clinical studies
    - Novel chemistry for GABAB, mGluR4, mGluR2, mGluR3, mGluR7 and TrKB
  - Proprietary biological tools for screening and medicinal chemistry support
  - Drug like allosteric biased chemical library
  - Significant in-house expertise

- Platform & preclinical strategy
  - Continue to invest in allosteric modulation expertise
  - Leverage platform through collaboration with industry and non-dilutive sources of expertise and funding
  - Focus on advancing preclinical portfolio to clinical candidate selection

Dipraglurant in Parkinson’s Disease

Dipraglurant Scheduled to Start Pivotal Registration Studies in PD-LID

Development & Regulatory Path	➢ Pivotal studies scheduled to start in H2 2019 ➢ Manufacturing & 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, oral small molecule mGluR5 NAM ➢ PK profile mirrors that of L-dopa, making it ideal to treat LID ➢ Inhibits abnormal glutamate stimulation 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

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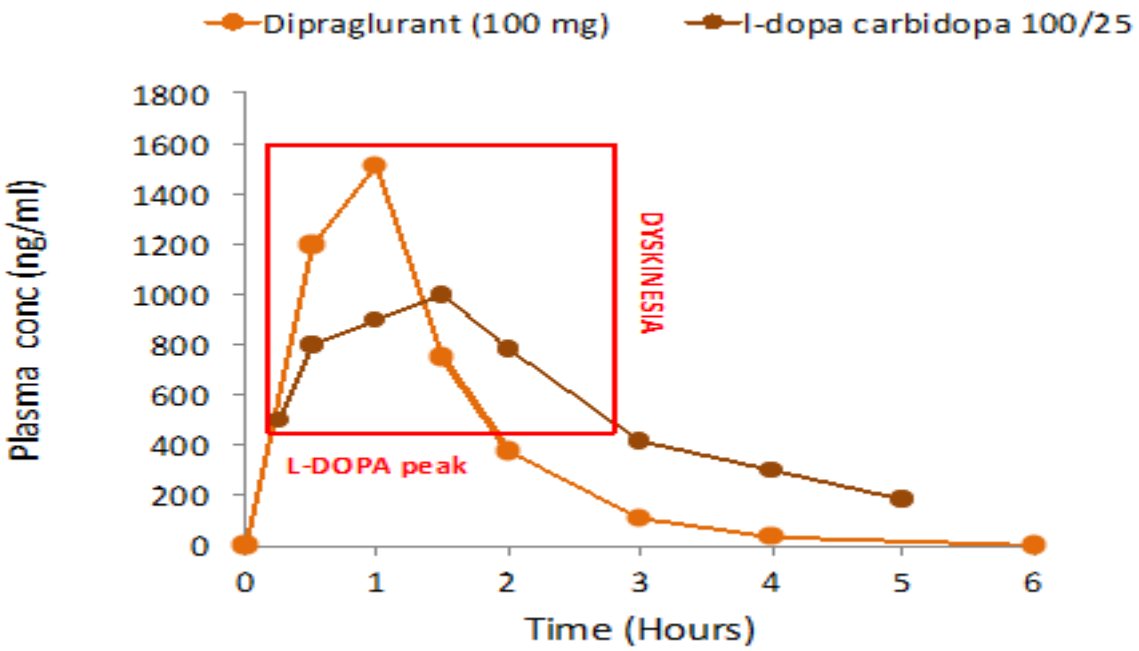
Levodopa-Induced Dyskinesia in Parkinson's Disease (PD-LID)

- Dyskinesia is related to disease duration and result from the neurodegenerative process that underlies PD
  - 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
- Dopamine replacement does not lead to dyskinesia per se, but lowers the triggering threshold for symptoms
- Patients present with irregular migrating uncontrollable contractions or twisting and writhing due to dystonia, chorea, and choreoathetosis.
- Dyskinesia is as disabling as PD symptoms:
  - 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 PK is a Key Advantage for Treating LID

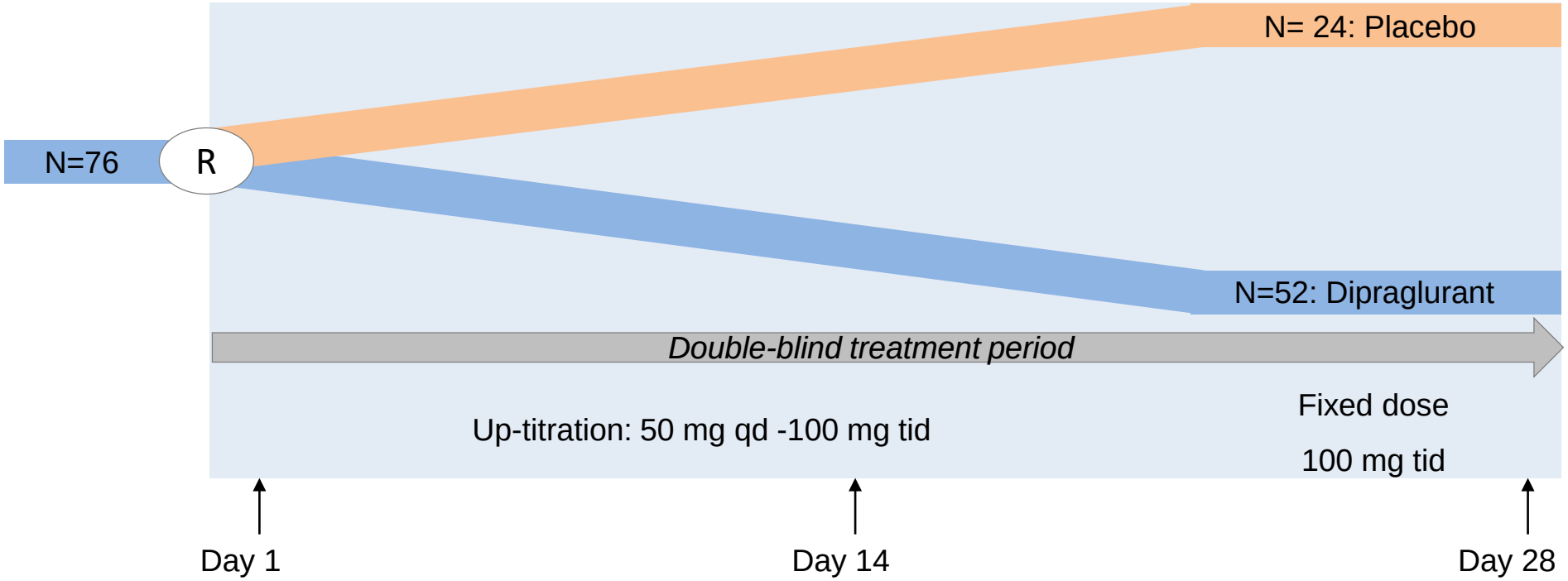


- Dyskinesia symptoms are correlated to peak levels of levodopa therapy
- PK profile of dipraglurant mirrors that of levodopa
- **Dipraglurant inhibits abnormal glutamate stimulation during peak levodopa dose but releases the receptor during normal glutamate activity**

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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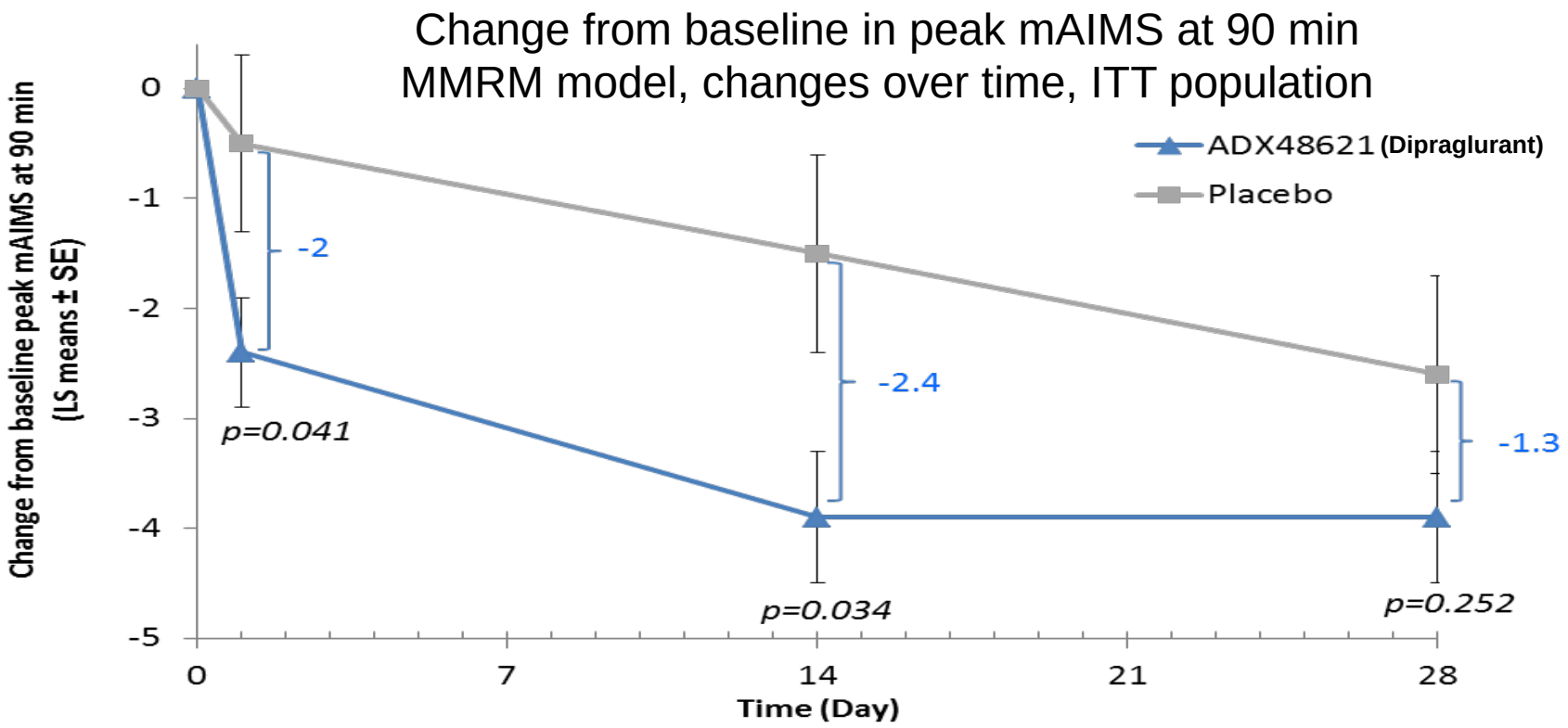
Dipraglurant Reduces LID Severity by 30%



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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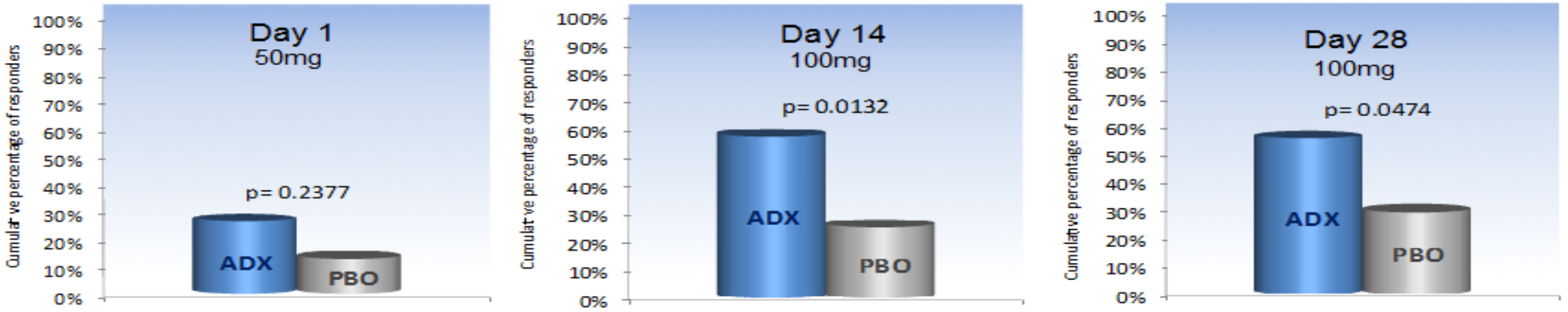
Responder Analysis Demonstrates Dipraglurant Significant Benefit

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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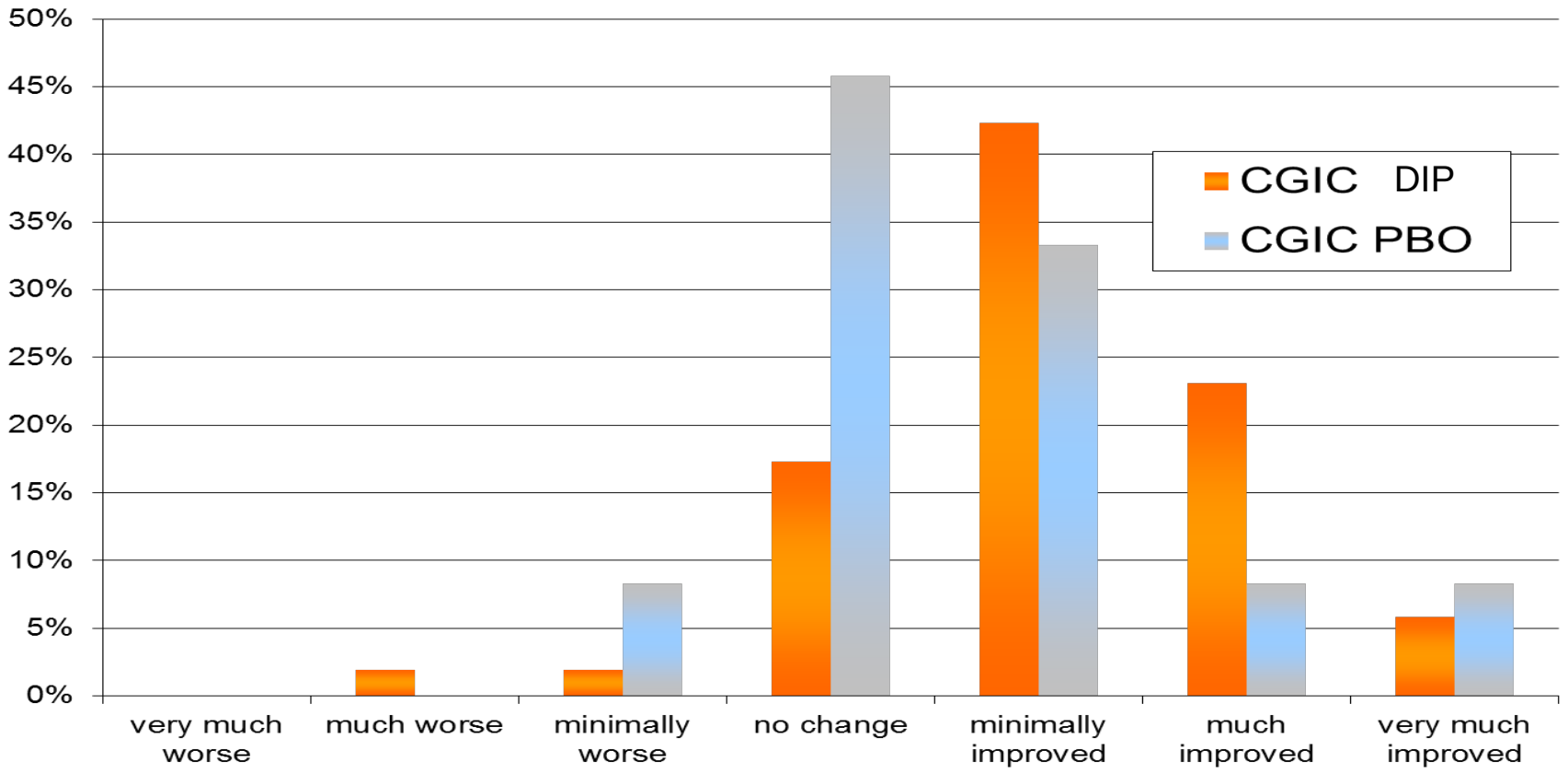
Clinician Rated Global Impression of Change - Dyskinesia



	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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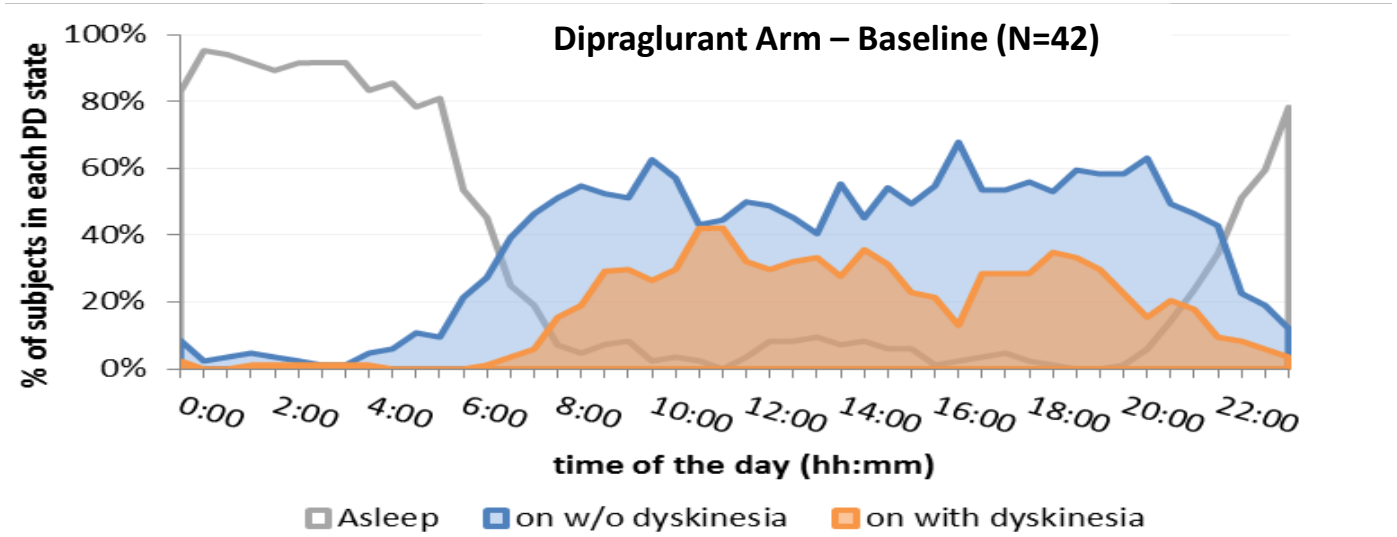
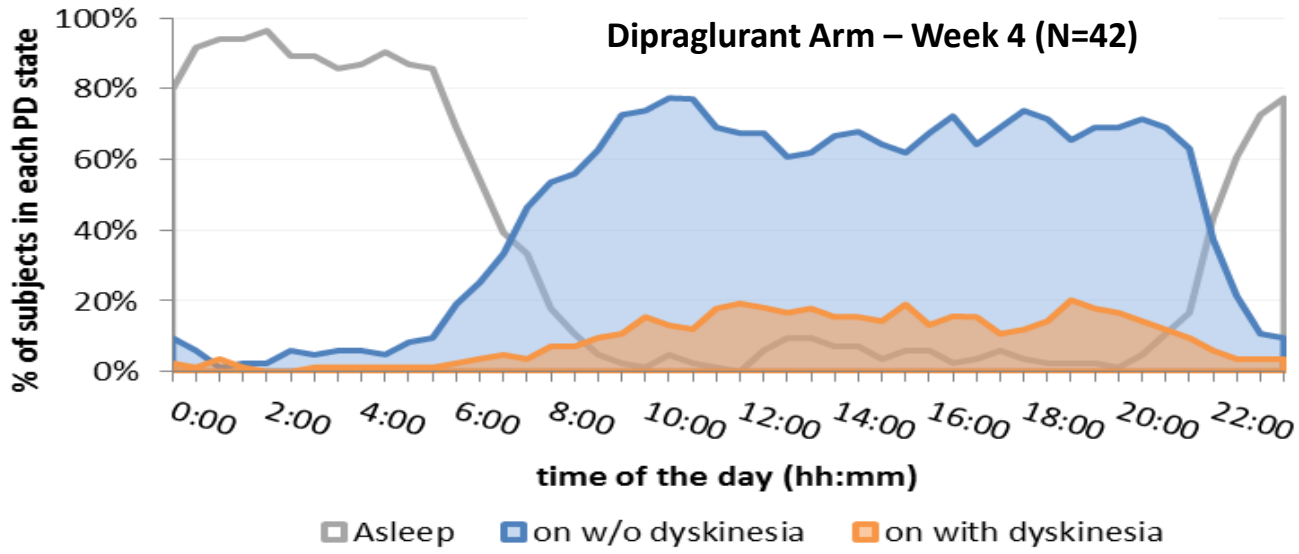
Patient Diaries – Improvement Throughout the Waking Day



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

- Dipraglurant 50 and 100 mg doses demonstrated safety and satisfactory tolerability in Parkinson’s disease patients

Clinical Development Plan

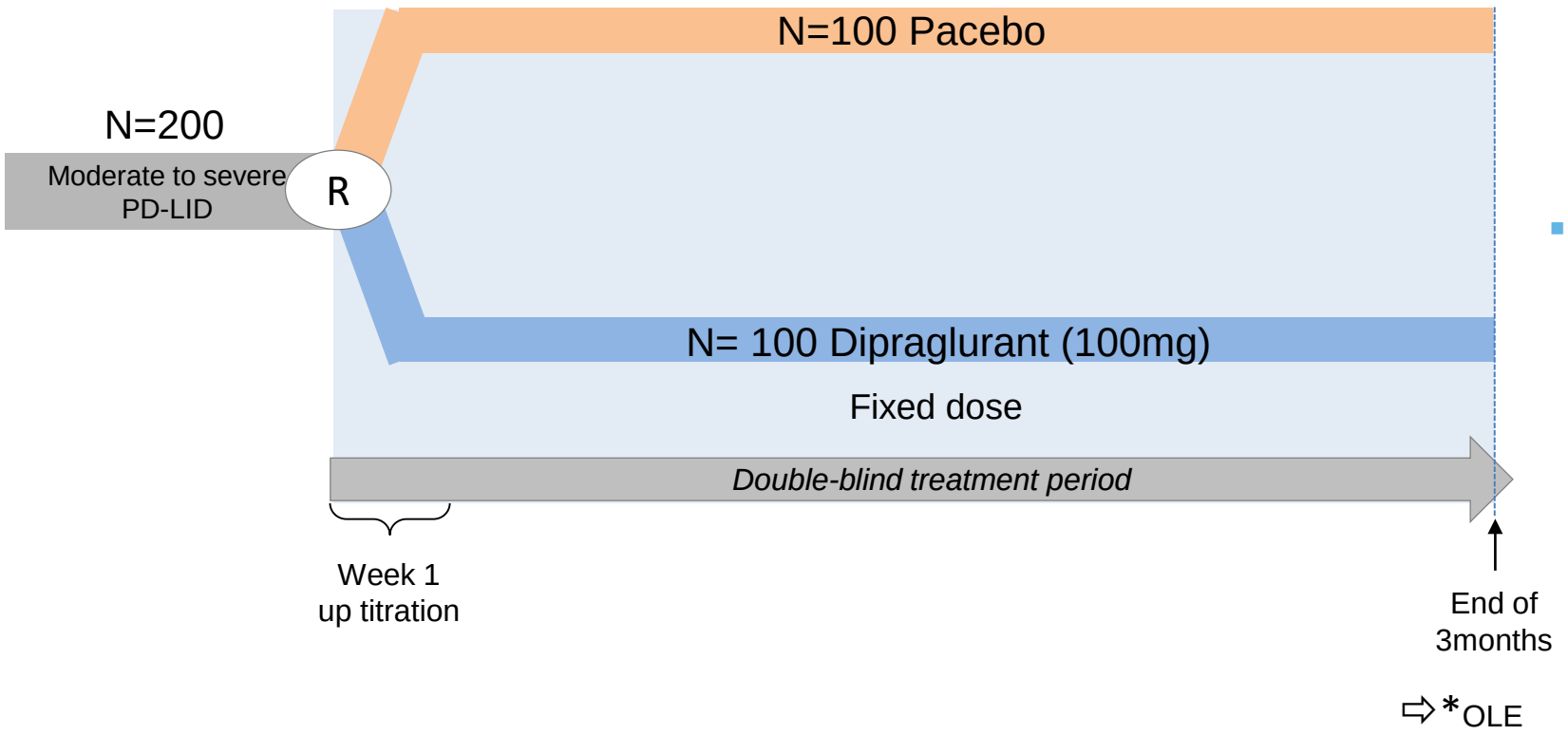
- Pivotal trials:
  - Two studies required for registration
    - Primary endpoint: UDysRS - more sensitive to treatment effect than mAIMS and less prone to placebo response (Goetz 2013)
    - Pivotal Study 1 (301) – 13 weeks
    - Pivotal Study 2 (302) – 26 weeks (primary endpoint at 13 weeks)
  - Open label extension
  - Measure to minimize placebo response integrated in pivotal study design

- Regulatory:
  - Continue to interact with regulatory bodies
  - Consider fast-track / breakthrough applications after first pivotal study

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

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 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

Indivior Partnership

Indivior Partnership on $GABA_B$ PAM for Addiction

- $GABA_B$ is the metabotropic receptor for GABA, main inhibitory neurotransmitter
- Activation of $GABA_B$ is validated through the use of baclofen ($GABA_B$ orthosteric agonist)
  - Approved for the treatment of spasticity
  - Clinical efficacy in alcoholism and Charcot-Marie-Tooth type 1A (CMT1A)
- Positive Allosteric Modulator (PAM) is a differentiated pharmacological approach
  - Potential safety and efficacy advantages – lack of tolerance and less side effects
- Worldwide license and collaboration on $GABA_B$ PAM
- Indivior leading development of ADX71441 in addiction
- Addex leading funded research effort to deliver back up compounds
  - Addex has right to select back up compounds at clinical candidate stage for development in retained indications including CMT1A neuropathy
- Financial terms:
  - Upfront of USD 5 million & USD 4 million research funding over 2 years
  - USD 330 million of development, regulatory and commercial milestones
  - Tiered royalties up to double-digit royalties

Financials

Financials and Stock

- Cash runway through 2021
  - Cash of CHF41.7M at 31 December 2018
- Traded on SIX Swiss Exchange: ADXN (ISIN:CH0029850754)
- 28,564,031 shares outstanding 37.7M fully diluted)
  - New Enterprise Associated – 16%
  - New Leaf Venture Partners – 5.6%
  - CAM Capital – 5.6%
  - Credit Suisse Asset Management – 5.5%
  - Management & board holds - 15% (fully diluted basis)
- Analyst coverage:
  - Van Leeuwenhoek – Marcel Wijma
  - valuationLAB – Bob Pooler
- Market capitalization: approx. CHF60M
- No debt

Upcoming Major Development Milestones

Milestone	Timing
Dipraglurant – LID Phase 3 Registration Program	
Study 301 – start dosing	H2 2019
ADX71441 – Addiction (Partnered with Indivior)	
Phase 1 (NIDA sponsored study) – start dosing	H1 2019

Allosteric modulators for human health

www.addextherapeutics.com