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Innovative Treatments for Central Nervous System Disorders

December 2022

Allosteric modulators for human health

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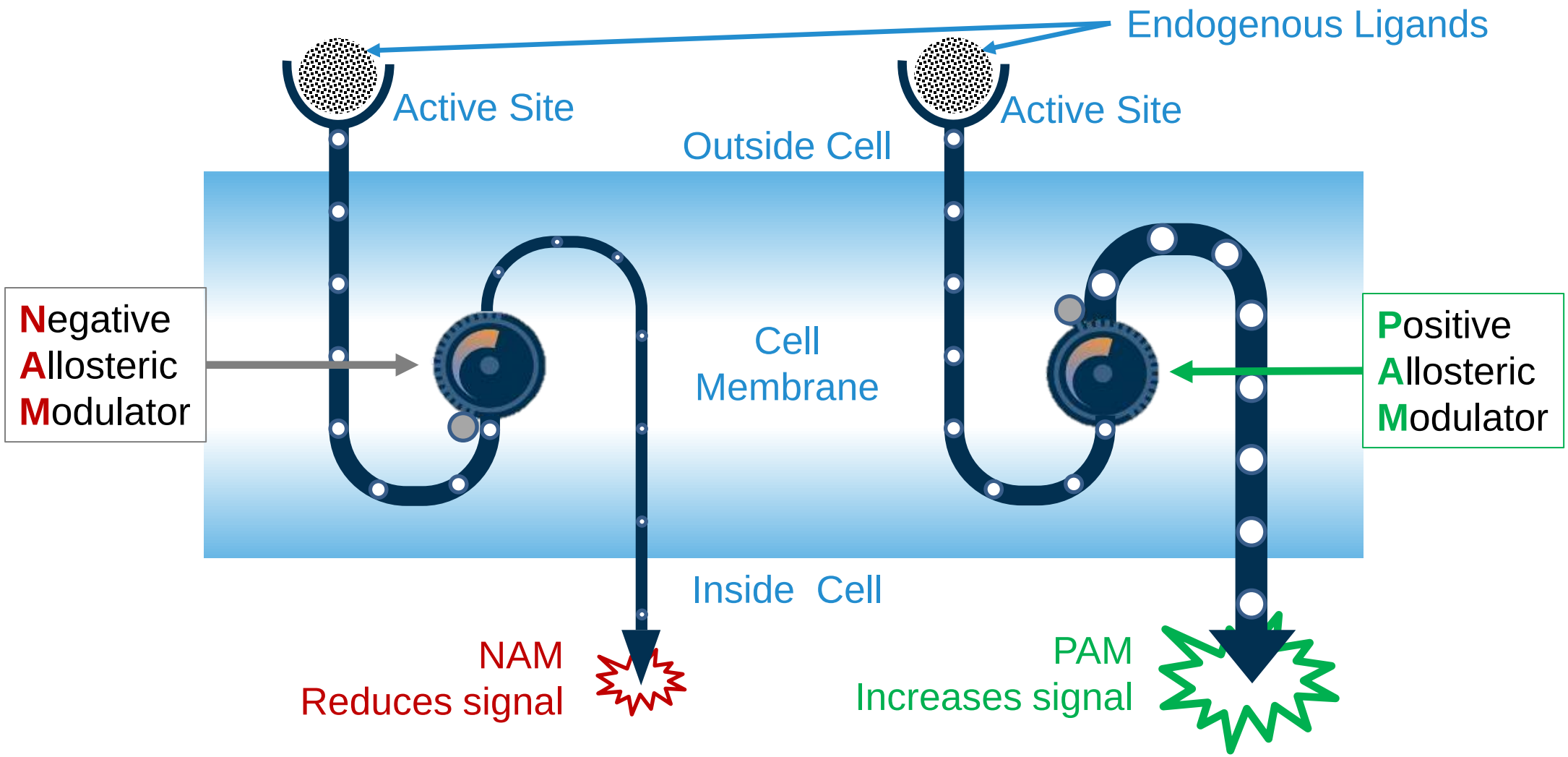
Addex Overview

Multiple high value programs reaching significant milestones	• Phase 2 epilepsy study (J&J) – completion of part 1 expected in Q1 2023 • Dipraglurant (mGlu5 NAM) – Phase 2 ready & indication under evaluation • GABAB PAM for SUD (Indivior), chronic cough, pain & CMT1a • mGlu7 NAM for stress related disorders (PTSD) and schizophrenia
Leading allosteric modulator technology platform	• Validated & differentiated pharmacological approach • Proprietary biological screening assays and chemical library • Track record of delivering novel drug candidates
In house discovered pipeline	• Significant intellectual property portfolio • Multiple novel drug candidates entering clinical candidate selection • Driving long-term growth & future partnership opportunities
Technology validating partnerships with industry	• J&J - €109M in milestones & double-digit royalties • Indivior - $330M in milestones, royalties up to double digit & funded research program
Top tier US investors	• Dual listed on SIX Swiss Exchange & US Nasdaq Capital Market • CHF10.4M cash at September 30, 2022

What are Allosteric Modulators?



Advantages of Allosteric Modulation Versus Orthosteric Drug Discovery

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

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)

Addex Pipeline

Molecule / MoA	Indication	Partner	Pre-clinical	Phase 1	Phase 2	Phase 3	Milestone
ADX71149 (mGlu2 PAM)	Epilepsy	janssen					Completion of part 1 in Q1 2023
Dipraglurant (mGlu5 NAM)	PD-LID, SUD, NDD, pain, post-stroke/TBI rehabilitation						Indication under evaluation
$GABA_B$ PAM	Substance use disorders	INDIVIOR					IND enabling expected 2023
	Chronic cough, pain & CMT1A						IND enabling studies expected 2023
mGlu7 NAM	Stress-related disorders - PTSD	eurostars™					IND enabling studies expected H1 2023
mGlu2 NAM	Mild neurocognitive disorders & depression						IND enabling studies expected H2 2023
M4 PAM	Schizophrenia / other psychosis						
mGlu4 PAM	Parkinson's & autoimmune disorders						
mGlu3 PAM	Neurodegenerative disorders						

NAM = Negative Allosteric Modulator

PAM = Positive Allosteric Modulator

PD-LID = Parkinson's disease levodopa induced dyskinesia
SUD = Substance use disorders
NDD = Neurodevelopmental disorders
TBI = Traumatic brain injury
CMT1A = Charcot-Marie-Tooth disease type 1A
PTSD = Post-traumatic stress disorder

Experienced Team

Leadership Team

Tim Dyer	Dr Roger Mills	Dr Robert Lutjens	Dr Jean-Philippe Rocher	Dr Mikhail Kalinichev
CEO / CFO	Chief Medical Officer	Head of Discovery Biology	Head of Discovery Chemistry	Head of Translational Science
Co-Founder of Addex Formerly with PwC UK Chartered Accountant	Developed Nuplazid for PD Psychosis >30 years Pharma industry incl. Pfizer, Gilead and Acadia	Member of Addex founding team Formerly with Glaxo & Scripps Research Institute	Member of Addex founding team Formerly with Pierre Fabre, GlaxoSmithKline and Mitsubishi	Neuropharmacologist with >20 years pharma industry experience Formerly with Ipsen, Lundbeck and GlaxoSmithKline

Non-executive Directors

Vincent Lawton	Ray Hill	Jake Nunn	Isaac Manke
Chairman	Board member	Board member	Board member
Former European Head of Merck & Co. Former MHRA Board member	Former Executive Director Merck & Co.	Venture advisor and former Partner at New Enterprise Associates	General Partner at Acorn Bioventures. Formerly Partner at New Leaf Venture Partners

Scientific Advisory Board

Darryle Schoepp	Mark Bear	Peter Bernstein	Benny Bettler
Chairman of SAB	Picower Prof. of Neuroscience at MIT	Principal, PhaRmaB LLC	Biomedicine Prof. at Basel University
Former leader of Neuroscience research department at Eli Lilly, and at Merck was Neuroscience research therapeutic area leader	Formerly on faculty of Brown University School of Medicine and an Investigator of the Howard Hughes Medical Institute	Formerly with ICI Astra Zeneca Awarded numerous accolades including Fellow of the American Chemical Society	Formerly at Novartis and discovered allosteric modulators at $GABA_B$ receptor and recipient of the Peter Speiser Award

ADX71149 (JNJ-40411813) for Epilepsy
Partnered with Janssen Pharmaceuticals, Inc.

ADX71149 Opportunity in Epilepsy

Large market & unmet medical need	• Market projected to reach $20 billion by 2026* – Keppra market leader with > 2M patients & €800M p.a.** • High proportion of refractory patients (¼ of new patients***) - combination treatments have limited therapeutic benefit • Large underserved patient population in need of improved treatment options
Strong MoA & synergistic effect	• Selective oral mGlu2 PAM demonstrated clear MoA in epilepsy • Showed 35-fold increase in Keppra (SV2A antagonist) efficacy • Potential to reduce Keppra dosing – improve efficacy & reduce side effects
Status of development	• Extensive preclinical and clinical data - 9 Phase 1 and 2 Phase 2 studies • Japan Phase 1 completed in Q4 2021 • Phase 2 POC study ongoing – completion of Part 1 expected in Q1 2023 • 2 year open label extension study initiated in Q3 2022
Strategic Partner Janssen Pharmaceuticals, Inc.	• Eligible to receive €109 million in pre-launch milestones and double digit royalties

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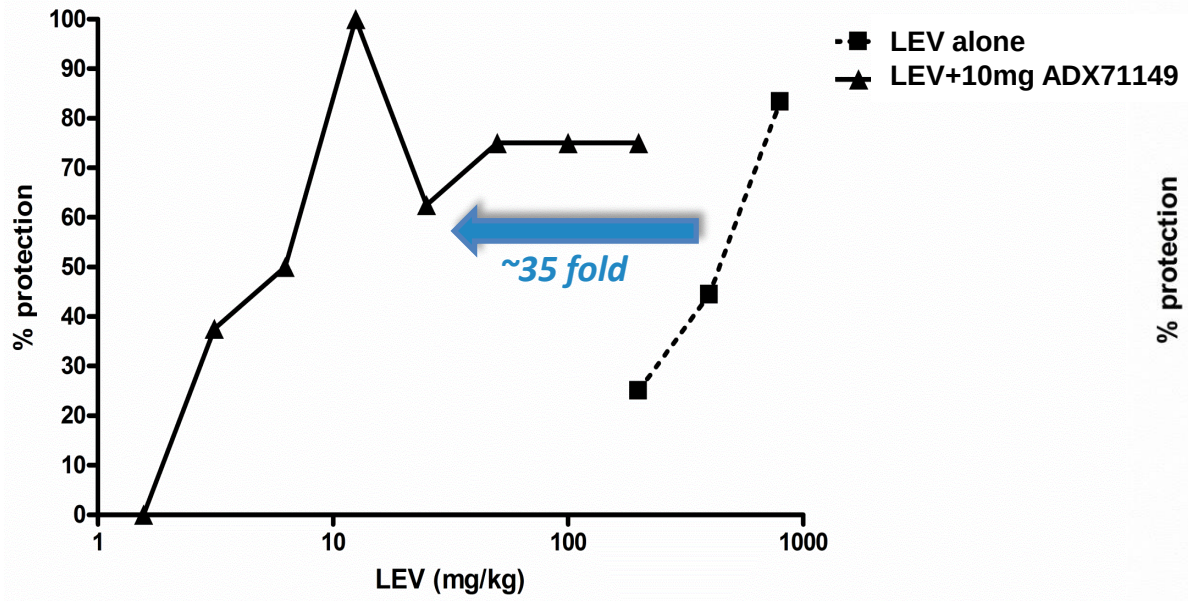
* Fortune Business Insights April 8, 2020
** UCB FY 2020
*** Xue-Ping et al, Medicine July 2019

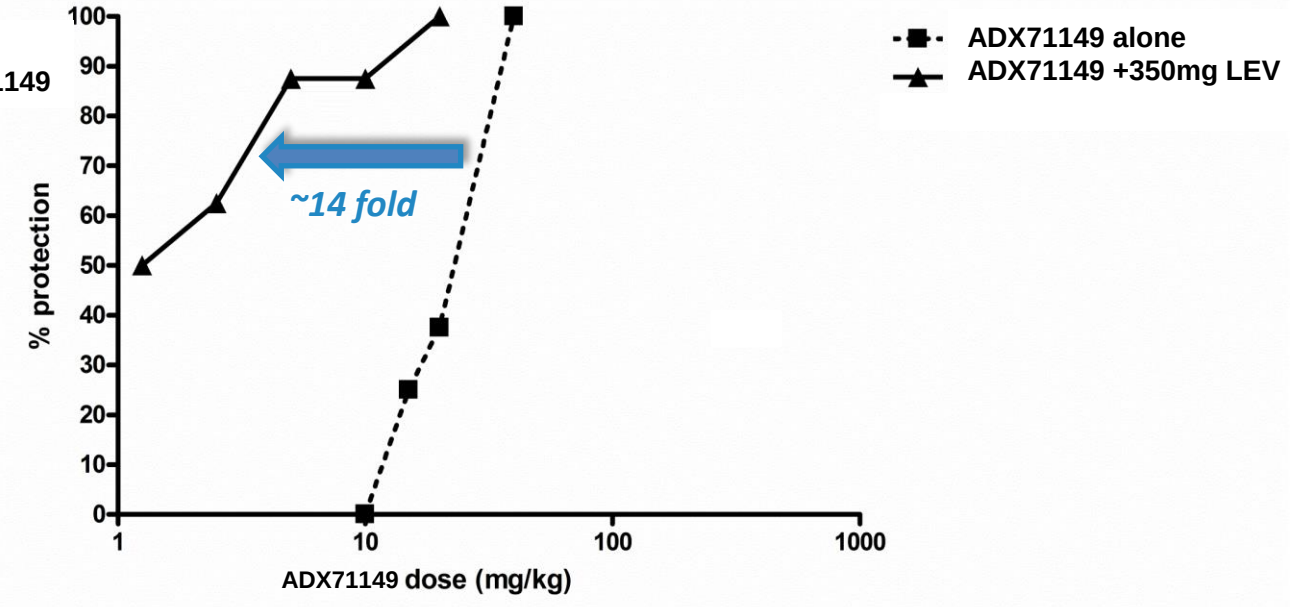
ADX71149 Preclinical Efficacy in Epilepsy - 6Hz Model

- Preclinical validation in pharmaco-resistant mouse epilepsy model with high translational value:

ED_{50} shift of Keppra by adding low dose of ADX71149

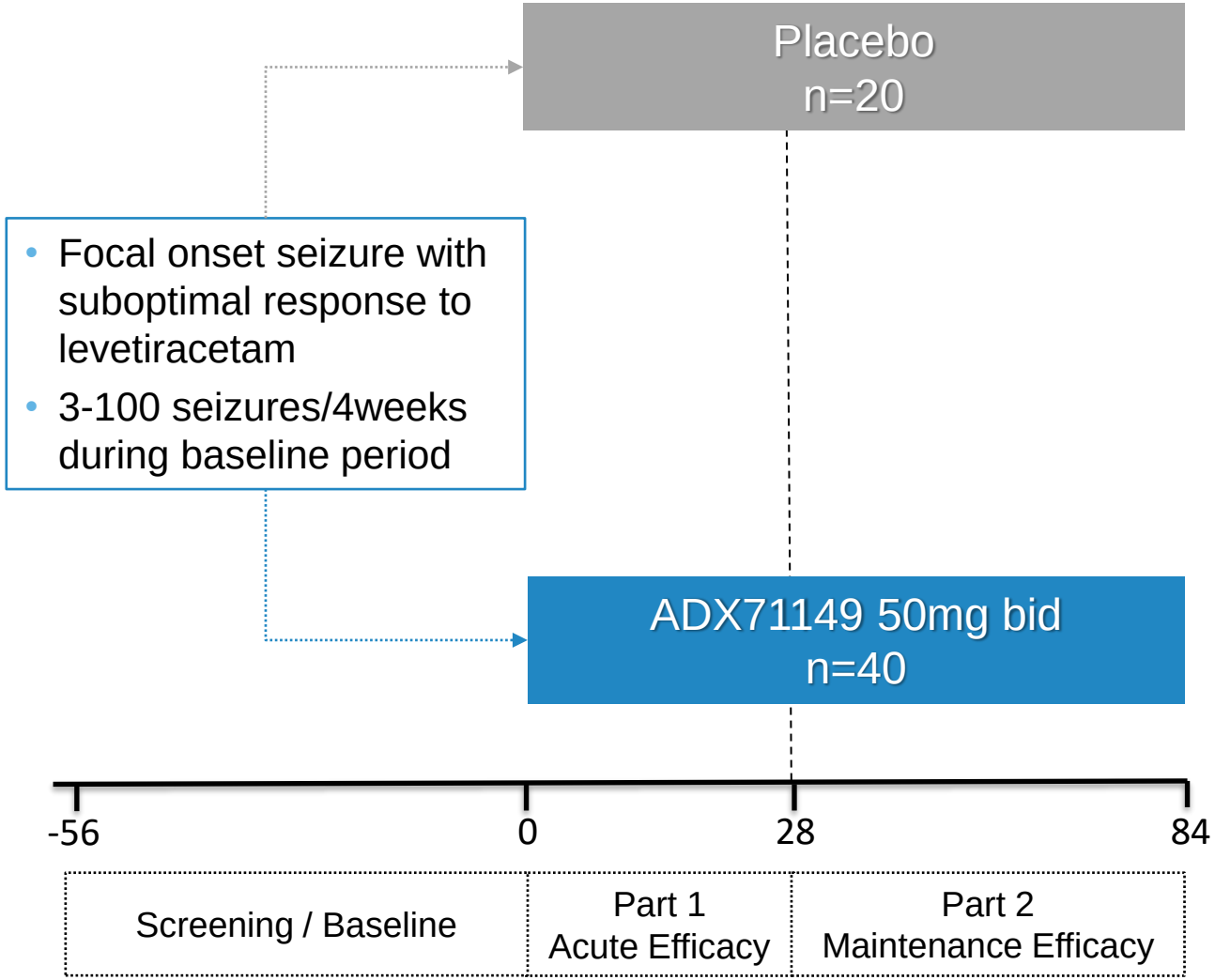


ED_{50} shift of ADX71149 by adding ED_{50} dose of LEV



- 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

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

Data from completion of part 1 expected in Q1 2023

Dipraglurant (mGlu5 NAM) – Phase 2 Ready

Indications Under Evaluation:
PD-LID, SUD, Post-Stroke Recovery, Pain and NDD

Dipraglurant Phase 2 Ready Opportunity in Multiple Indications

Significant target patient populations and commercial opportunities	• PD-LID: 200,000 patients in US, Orphan drug designation granted in US • SUD: 20 million patients in US and 2.2% of adult population worldwide • Pain: up to 10% of adult population are diagnosed with chronic pain every year • TBI & stroke recovery: 5.3 million patients incl. 1 million stroke patients in US • Neurodevelopmental disorders - Fragile X: 50K Fragile X patients in US
Clinically validated approaches	• Dipraglurant (ADX48621) reduced PD-LID in Phase 2 • ADX10059 reduced pain in patients with episodic migraine • Mavoglurant (AFQ056) effects in PD-LID, CUD, AUD, Fragile X, OCD, GERD • Basimglurant (RG-7090; NOE-101) currently in Phase 2 for trigeminal neuralgia
Status of development	• Extensive preclinical and clinical data – 5 Phase 1 and Phase 2 POC in PD-LID completed • Phase 2 ready with >30kg cGMP API and >90kg DP in 100mg & 50mg tablets
Intellectual property	• Composition of matter through June 2025 & strong polymorph patent through 2034 (without extensions) • Potential for additional protection - formulation IP & ODD (granted for PD-LID)

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
  - GOCOVRI® price: $34K p.a., Nuplazid® price: $45K p.a.
  - 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

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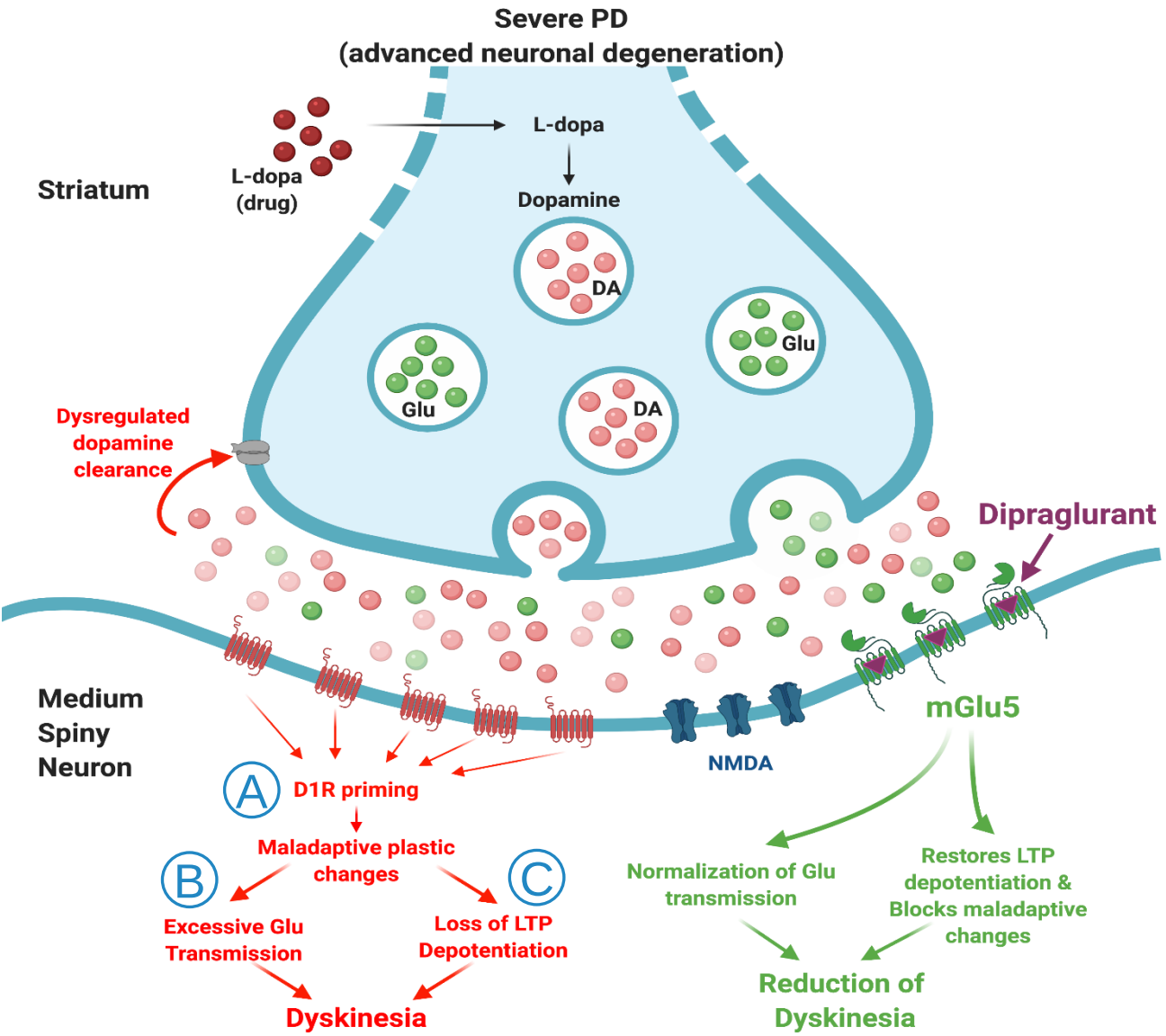
* www.drug.com

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**

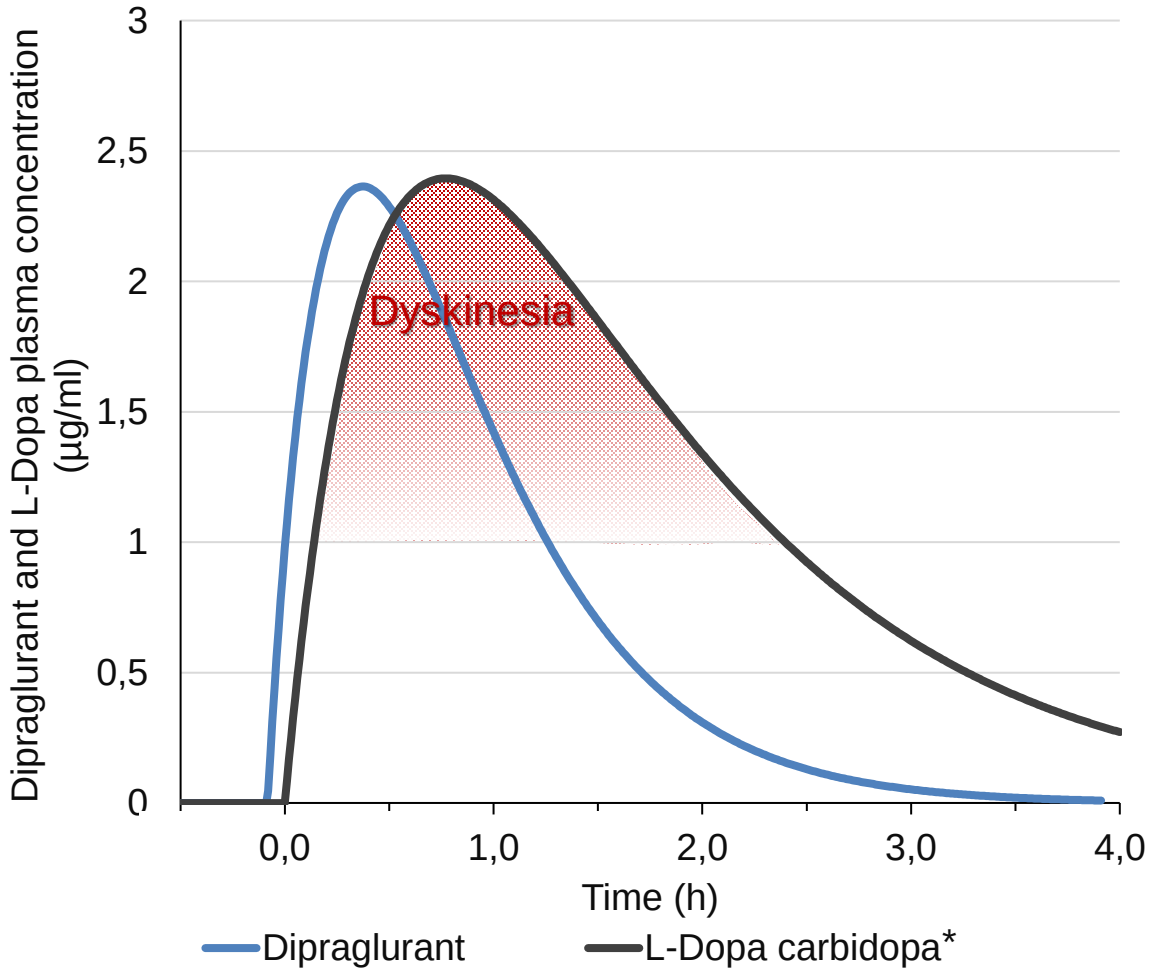
MoA Rationale for Targeting mGlu5 Inhibition in PD-LID



- 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

LTP = Long Term Potentiation
D1R = D1 dopamine receptor
Glu = glutamate DA = dopamine

Dipraglurant PK is a Key Advantage for Treating LID



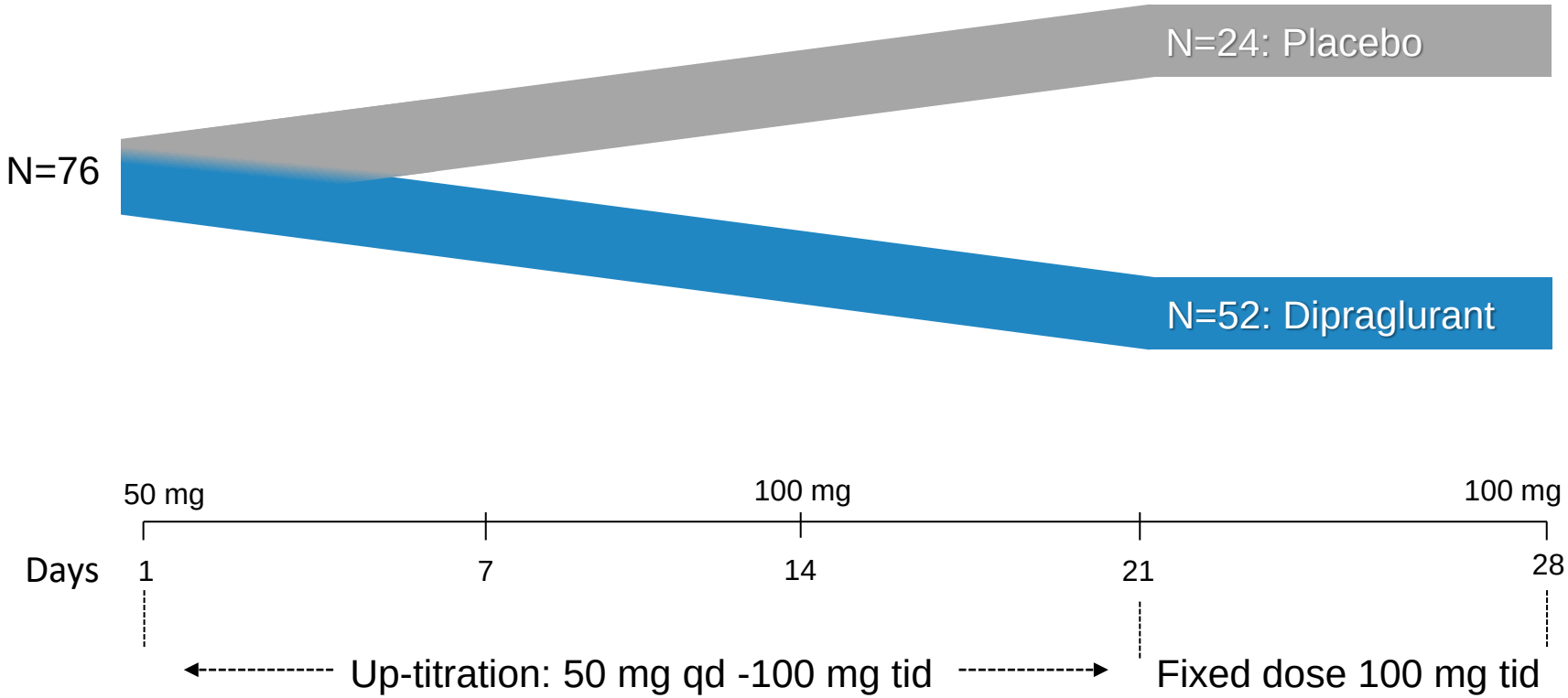
- Dyskinesia symptoms are correlated to peak levels of L-dopa
- PK of dipraglurant allows control of glutamatergic tone ahead of L-dopa Cmax

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

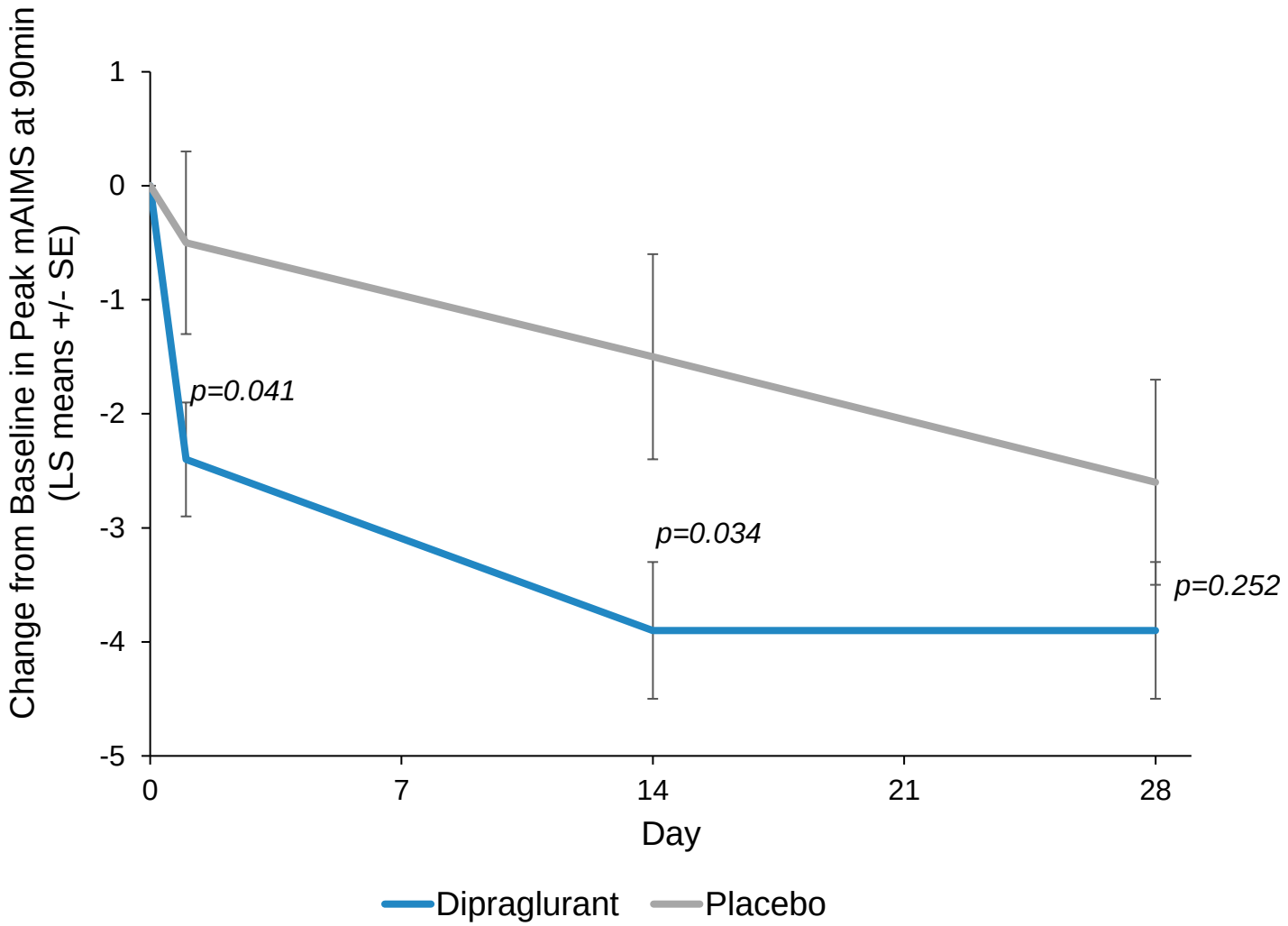
Dipraglurant Phase 2a Study in LID (in US and Europe)



- **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

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		
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%

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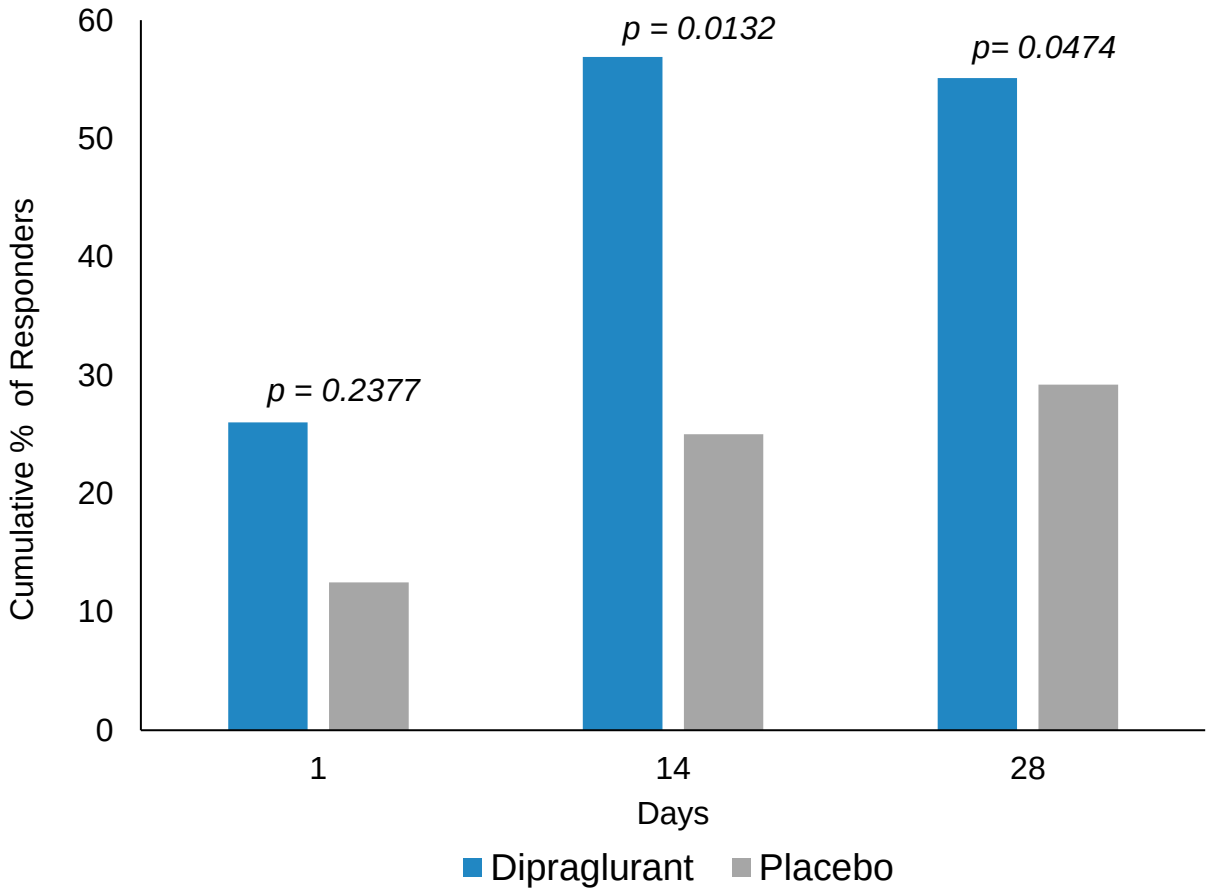
Responder Analysis Demonstrates Dipraglurant Significant Benefit

Percent of patients with ≥ 30% improvement on mAIMS

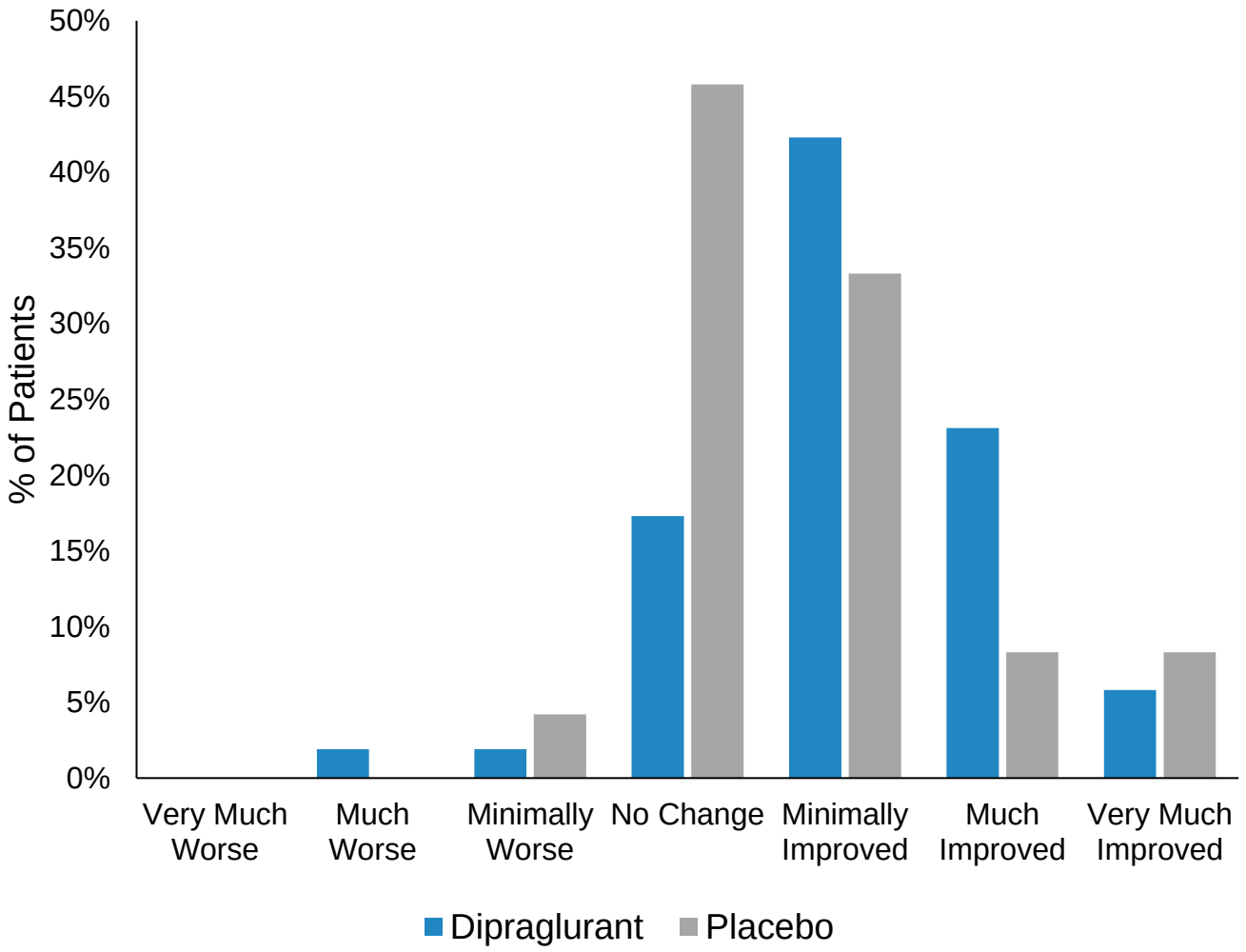


Responder analysis (≥30% change of mAIMS from baseline)				
Midday dose	Dipraglurant		Placebo	
Day 1 (50 mg)	n=13	26.0%	n=3	12.5%
Day 14 (100 mg)	n=29	56.9%*	n=6	25.0%
Day 28 (100 mg)	n=27	55.1%*	n=7	29.2%

*statistically significant

Reinforces robustness of dipraglurant anti-dyskinetic effect

Significant Improvement on CGI-C



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

- 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

Dipraglurant Demonstrated Good Safety and Tolerability in PD Patients

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

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

* 3 of 11 AEs of “worsening dyskinesia” occurred in the follow up period (i.e., after drug discontinuation). On treatment incidence = 15.3% dipraglurant, 12.5% placebo

- 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 – Status of Development

- Pivotal registration program
  - Study 301 & 12-month Open Label Study (302) terminated in June 2022 due to slow recruitment rate attributed to COVID related constraints

- Future development under evaluation, including:
  - PD-LID
  - Substance use disorder
  - Neurodevelopment disorders
  - Pain
  - Post-stroke / TBI recovery

GABAB PAM for Substance Use Disorders (Indivior Partnership) & Chronic Cough

GABAB PAM for Substance Use Disorder

Large market & unmet medical need	• High prevalence;1.8% of US population* • Current treatments have undesirable side-effects and prone to relapse • Burden to society in US is >$600B annually**
Clinically validated MoA	• Baclofen (GABAB agonist) used off label for alcohol use disorder • ADX71441 attenuates alcohol self-administration and relapse to alcohol seeking in rats*** and alcohol consumption in mice**** • ADX71441 reduces cocaine self-administration in NHP*****
Status of program and near-term milestone	• Addex is executing Indivior funded GABAB PAM research program • Multiple compounds in late clinical candidate selection phase • Differentiated leads and backups with robust novel IP potential • IND enabling studies expected to start in 2023
Strategic partnership with Indivior	• Eligible to receive $330 million in milestones and tiered royalties from high single digits to low double digits • Conducting a funded research program to discover novel GABAB PAMs – Right to select compounds for development in reserved indications

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* Merikangas et al. 2010
** NIDA
*** Augier et al 2017
**** Hwa et al 2014
***** Addex int. report

Addex GABAB PAM for Chronic Cough

Large market & unmet medical need	• Widespread prevalence – Up to 10% of adult population worldwide* – More prevalent (10-20%) in Europe, America and Australia than in Asia (5%)* • Opioid drugs (codeine) offer suboptimal relief and are linked to undesirable side effects, including abuse potential
Clinically validated MoA	• Baclofen (GABAB agonist) reduced chronic cough in multiple clinical studies • Baclofen is used off-label as a treatment of chronic cough • Baclofen showed efficacy in animal models of chronic cough**
Status of development	• Multiple compounds in late clinical candidate selection phase • Potential for safer and better tolerated therapeutic approach to baclofen
Intellectual property & near-term milestone	• Differentiated leads and backups with good IP potential – Independent IP from Indivior collaboration • IND enabling studies expected to start in 2023

*Song et al. 2015
**Olsen et al. 2021

Addex GABAB PAM for Chronic Pain

Large market & unmet medical need	• Widespread prevalence – Cancer pain - >50% of patients experience pain during cancer treatment* – Trigeminal neuralgia - estimated at 4 to 13 people per 100,000/year** – Pelvic / bladder pain - 6.5% of US women show bladder pain symptoms*** • Suboptimal treatment with opioids, anticonvulsants, antidepressants and anti-inflammatory drugs with significant undesirable side effects
Validated MoA	• Baclofen (GABAB agonist) reduced pain in cancer patients in a range of conditions, including prostate, lung, uterine and breast cancers. • Baclofen is used off-label as a second-line treatment option for trigeminal neuralgia • GABAB PAM ADX71441 reduced bladder pain in *in vivo* PoC in rats****
Status of development	• Multiple compounds in late clinical candidate selection phase • Potential for safer and better tolerated therapeutic approach to baclofen
Intellectual property & near-term milestone	• Differentiated leads and backups with good IP potential – Independent IP from Indivior collaboration • IND enabling studies expected to start in 2023

* van den Beuken-van Everdingen et al. 2016
** Gambeta et al 2020
*** Ness et al 2021
****Cannampalli et al. 2017

Addex GABAB PAM for CMT1a

Large market & unmet medical need	• Prevalence and treatment – CMT1a prevalence is 6.9/100000* – No approved drugs and limited R&D pipeline
Validated MoA	• PXT3003 (fixed-dose combination of three FDA-approved drugs: naltrexone, baclofen, sorbitol) currently in Phase 3 clinical study for CMT1a** • Addex GABAB PAM ADX71441, given chronically (9 weeks) demonstrated *in vivo* proof of concept in transgenic CMT rats – Downregulated pmp22 mRNA, – Reduced the number of hypomyelinated axons – Increased compound muscle action potentials in peripheral nerves
Status of development	• Multiple compounds in late clinical candidate selection phase • Potential for safer and better tolerated therapeutic approach to baclofen
Intellectual property & near-term milestone	• Differentiated leads and backups with good IP potential – Independent IP from Indivior collaboration • IND enabling studies expected to start in 2023

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*Theadom et al 2019
** clinicaltrials.gov

MGlu7 NAM for Stress Related Disorders including PTSD

Addex mGlu7 NAM for Stress Related Disorders (including PTSD)

Large market & unmet medical need	• PTSD affects approximately 3.5% of U.S. adults • Current treatments are primarily based on psychotherapy, medication is nonspecific (off-label use of anxiolytics and antidepressants) and usually ineffective, often with numerous side effects
Novel first in class MoA	• Potential shown in mGlu7 KO mice phenotype and mGlu7 inhibition studies • Preclinical POC demonstrated with Addex mGlu7 NAM: – Fear conditioning model of PTSD in rats – Elevated plus maze and marble burying test of anxiety in mice – Amphetamine-induced hyperactivity test of psychosis in mice
Status of development	• Drug candidate PK/PD established and pre-IND studies completed • Potential breakthrough therapeutic innovation for the treatment of stress related disorders like PTSD
Intellectual property & near-term milestone	• Differentiated leads and backups with good IP potential • IND enabling studies expected to start in H1 2023

MGlu2 NAM for Mild Neurocognitive Disorders and Depression

Addex mGlu2 NAM for mNCD and Depression

Large market & unmet medical need	• Prevalence in 65–69 year olds is 6.7% and 25% in 80–84 year olds* • Donepezil approved for mNCD, but does not work in all patients and has suboptimal tolerability profile
Clinically validated MoA	• Preclinical and post-mortem evidence - blockade of mGlu2 could be of use in diseases linked to low glutamate levels such as Alzheimer's disease and depression • Addex mGlu2NAM demonstrated preclinical PoC: – Scopolamine- and mGlu2/3 agonist-induced cognitive-deficit** – Aspects of pathophysiology of Alzheimer's Disease***
Status of development	• In late lead optimization with established PK/PD – Highly selective to mGlu2 – Potential therapeutic innovation for the treatment mNCD and depression
Intellectual property & near-term milestone	• Differentiated leads and backups with good IP potential • IND enabling studies expected to start in H2 2023

* American Academy of Neurology
** Scopolamine- or LY354740-induced deficit in NOR in rats
*** Intracerebroventricular β-amyloid administration induced deficits in NOR in rats

Addex Financials, Stock and Milestones

Financials and Stock

- Cash at 30 September 2022: CHF 10.4 million ($10.5 million)
- No debt
- Traded on SIX Swiss Exchange: ADXN (ISIN:CH0029850754)
- ADS representing 6 shares traded on Nasdaq: ADXN (ISIN: US00654J107; CUSIP: 00654J107)
- 72.78M outstanding shares*
  - Armistice Capital LLC – 31.00%
  - New Enterprise Associates – 10.30%
  - New Leaf Venture Partners – 3.56%
- 115.34M registered shares incl. treasury shares (150.48M fully diluted)
  - Management & board holds – 18.67% (fully diluted basis)
- Analyst coverage:
  - HC Wainwright - Raghuram Selvaraju
  - valuationLab - Bob Pooler
  - Baader Helvea AG - Leonildo Delgado
  - ZKB - Laurent Flamme

* Percentage of ownership calculated based on shares and warrants divided by outstanding shares

Milestones

Milestone	Timing
ADX71149 for epilepsy	
Phase 2a – study started	June 2021
Phase 2a – completion of part 1 results	Q1 2023
$GABA_B$ PAM for substance use disorders	
Start IND enabling studies	2023
mGlu7 NAM for stress-related disorders – PTSD	
Start IND enabling studies	H1 2023
Dipraglurant new indication selection & start of Phase 2	2023
Partnership for a preclinical program	H1 2023

Summary

Multiple high value programs reaching significant milestones	• Phase 2 epilepsy study (J&J) – completion of part 1 in Q1 2023 • Dipraglurant Phase 2 ready with interest in multiple indications • GABAB PAM for substance use disorder (Indivior) and other indications • mGlu7 NAM for stress related disorders (PTSD)
Technology and capabilities to deliver	• Pioneering allosteric modulation drug development – Proprietary screening assays and unique chemical library • All programs developed in-house, protected with >200 patents
Solid foundation	• Partnerships with industry leaders – JnJ & Indivior • Top tier US investors – Armistice Capital, NEA and NLV • Dual listed SIX Swiss exchange & US Nasdaq
Promising outlook	• Rich news flow in 2022 and beyond – Clinical results expected in Q1 2023 – Multiple drug candidates in CCS

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ALLOSTERIC MODULATORS FOR HUMAN HEALTH