# Unraveling the Mysteries of the Brain to Treat Neuroscience Diseases

**August 2023** 

2Q 2023 Financial Results & Business Update



### Forward-Looking Statements

This presentation contains forward-looking statements that are based on management's beliefs and assumptions and on information currently available to management. In some cases, you can identify forward-looking statements by the following words: "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve risks, uncertainties and other factors that may cause actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this presentation, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain.

Forward-looking statements in this presentation include, but are not limited to, statements about: the potential attributes and benefits of our product candidates; the format, timing and objectives of our product development activities and clinical trials; the timing and outcome of regulatory interactions, including whether activities meet the criteria to serve as registrational; the ability to compete with other companies currently marketing or engaged in the development of treatments for relevant indications; the size and growth potential of the markets for product candidates and ability to serve those markets; the rate and degree of market acceptance of product candidates, if approved; and the sufficiency of our cash position.

We cannot assure you that the forward-looking statements in this presentation will prove to be accurate. Furthermore, if the forward-looking statements prove to be inaccurate, the inaccuracy may be material. Actual performance and results may differ materially from those projected or suggested in the forward-looking statements due to various risks and uncertainties, including, among others: clinical trial results may not be favorable; uncertainties inherent in the product development process (including with respect to the timing of results and whether such results will be predictive of future results); the impact of COVID-19, the post-COVID environment and other factors on the timing, progress and results of clinical trials; our ability to recruit and enroll suitable patients in our clinical trials, including the effectiveness of mitigation measures; whether and when, if at all, our product candidates will receive approval from the FDA or other regulatory authorities, and for which, if any, indications; competition from other biotechnology companies; uncertainties regarding intellectual property protection; and other risks identified in our SEC filings, including those under the heading "Risk Factors" in our Quarterly Report on Form 10-Q filed with the SEC on May 3, 2023 and our subsequent SEC filings.

In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. The forward-looking statements in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation.



### Cerevel: Becoming the premier neuroscience company

New Executives Ron Renaud - President & Chief Executive Officer
Susan Altschuller, Ph.D. - Chief Financial Officer
Paul Burgess - Chief Business Development and Strategic Operations Officer

### Pipeline Progress

#### **Emraclidine:**

- Two robust Phase 2 EMPOWER trials in schizophrenia Data 2H 2024
- Phase 1 healthy elderly volunteer trial to support development in ADP Ongoing

### **Darigabat:**

- Phase 2 REALIZE trial in focal epilepsy Data mid-year 2024
- Phase 2 ADAPT trial in panic disorder Initiated

### **Tavapadon:**

Three Phase 3 TEMPO trials in Parkinson's – Data beginning 1H 2024

Capital

- Cash, cash equivalents and marketable securities of \$825.1M as of 6/30/2023
- Disciplined spending with cash resources expected to **support operations into 2025**



### **CEREVEL: Unraveling the Mysteries of the Brain**

A Deliberate and Differentiated Approach to Treating Neuroscience Diseases



#### **Targeted Neurocircuitry**

Cerevel unlocks new treatment opportunities by precisely identifying and targeting the neurocircuitry that underlies a given neuroscience disease.

#### **Receptor Subtype Selectivity**

Cerevel is selectively targeting only the receptor subtype(s) related to the disease physiology, to minimize undesirable off-target effects while maximizing activity.

### Differentiated Pharmacology

Cerevel designs full and partial agonists, antagonists, and allosteric modulators that can precisely fine-tune the receptor pharmacology and neurocircuit activity without over-activation or over-suppression of the endogenous physiologic range.



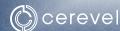
### Deep Pipeline with Multiple Upcoming Value Inflections

Multiple Assets Across All Stages of Development

Large Patient
Populations with
High Unmet Need

LEAD PROGRAMS	CANDIDATE SELECTION	IND	PHASE 1	PHASE 2	PHASE 3	Timing
Tavapadon		Adju	nctive Parkinson's	Monotherapy Park	inson's 👩	Data 1H and 2H 2024
Emraclidine			Schizop	hrenia O		Data 2H 2024
Emraclidine	Alzheimer's Dise	ease Psychosis	0			Initiated 4Q 2022
Darigabat			Ep	oilepsy O		Data Mid-Year 2024
Darigabat			Panic Di	sorder O		Initiated 2Q 2023
CVL-871			Dementia-Related	Apathy 🧿		Under Review
EARLY STAGE of PRECLINICAL H						
CVL-354 (KORA)			0			
PDE4 Inhibitor						
M4 Agonist						

Plus several undisclosed targets, including those with disease-modifying potential



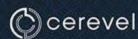
### **EMRACLIDINE**

Highly selective M4 Positive Allosteric Modulator (PAM) with the goal of effectively treating psychosis-related symptoms and improving tolerability compared to standard of care

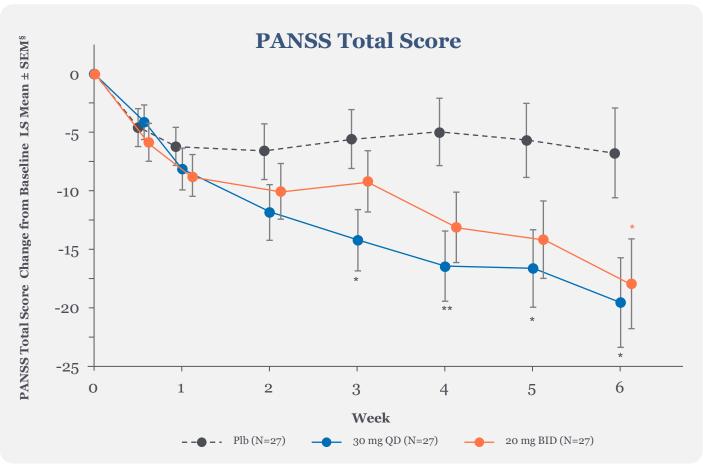
Schizophrenia

**Alzheimer's Disease Psychosis** 





### Emraclidine: Phase 1b Data Demonstrated Antipsychotic Activity



- Clinically meaningful improvements in PANSS total score
- Statistically significant difference in PANSS total score versus placebo\*
- Clinically meaningful improvements in both PANSS Positive and PANSS Negative subscales
- Generally well tolerated

Published in The Lancet



<sup>\*</sup> P<0.05 vs Placebo \*\* P<0.01 vs Placebo

### **Emraclidine EMPOWER Program**



### Comprehensive program to characterize dose range, assess efficacy and tolerability

### **EMPOWER Program Overview:**

### Two adequately-powered 3-arm Phase 2 trials

- N=372 per trial
- Two doses of emraclidine in each trial
  - Trial 001: 10 mg / 30 mg once-daily & pbo
  - Trial 002: 15 mg / 30 mg once-daily & pbo
- Designed to fully characterize the dose range

### Prioritizing key registration-enabling activities

- Hepatic and renal insufficiency clinical trials
- 8-week ambulatory blood pressure monitoring trial
- CMC manufacturing scale-up
- Nonclinical safety pharmacology

### Initiated 52-week OLE trial with both roll-over and de novo patients\*\*

### **Key Features:**

#### **Inclusion criteria**

- Adults (18-65) with schizophrenia who are experiencing an acute exacerbation or relapse of psychotic symptoms
- PANSS total score 85-120, inclusive
- CGI-S ≥4

### **Primary endpoint**

Change from baseline in PANSS total score at Week 6

#### **Key secondary endpoint**

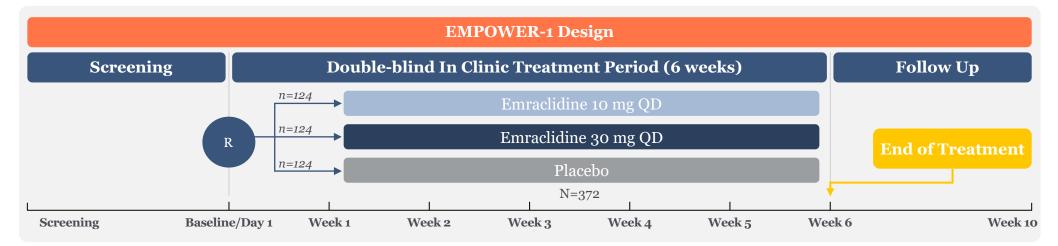
• CGI-S

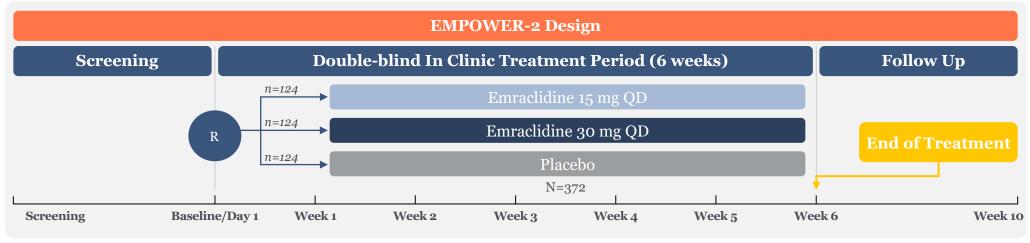
#### **Other endpoints**

- PANSS subscale scores and Marder Factor scores
- PANSS responder rate\*
- SF-6D (QOL) and BACS (cognition)



### Emraclidine EMPOWER Clinical Trial Designs: Data Expected 2H 2024





EMPOWER-3: 52-week open-label extension trial ongoing



### Emraclidine: Initiated Healthy Elderly Trial for Development in ADP



FDA Fast Track designation granted for treatment of hallucinations and delusions associated with Alzheimer's disease psychosis

#### **Phase 1 MAD Trial**

- **Objective** Evaluate safety, tolerability, and PK in healthy elderly participants
- Trial will inform future development as potential once-daily dosing option without need for titration in Alzheimer's disease psychosis
- Trial Design Testing dose ranges 2-30mg QD;
   14-days of treatment
- **Inclusion Criteria** Male and female subjects, aged 65 to 85 years

#### **Emraclidine: Potential for Differentiation**

- Potential **once-a-day** treatment option with **no titration**
- Possibility as a well-tolerated therapy in a disease area with no currently approved treatment options
- Substantial unmet need: ~6M diagnosed Alzheimer's disease patients; ~40% present with symptoms of psychosis
- FDA Fast Track designation granted in recognition of unmet medical need



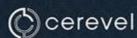
### **DARIGABAT**

Selectively targeting specific subunits of the GABA<sub>A</sub> receptor with the goal of providing anticonvulsant and anxiolytic activity with enhanced tolerability and potential for reduced abuse liability

**Epilepsy** 

**Panic Disorder** 

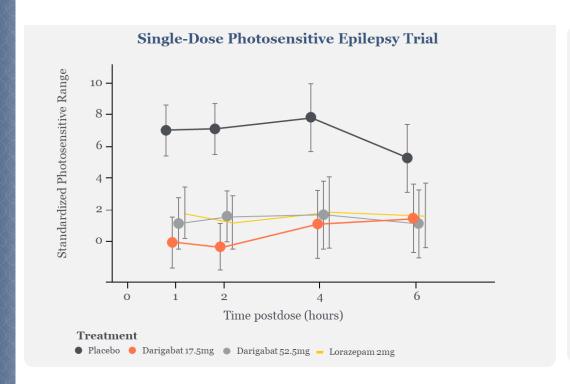




### Darigabat: REALIZE POC Epilepsy Trial Ongoing; Data Mid-Year 2024

Prior proof-of-principle photoepilepsy trial of darigabat demonstrated anticonvulsant activity comparable to lorazepam at ~60% and 80% RO

Current Phase 2 REALIZE focal epilepsy trial intended to establish proof of concept (POC) and tolerability profile and support development in additional epilepsy indications





### Darigabat Data Showed a Favorable Side Effect Profile Relative to Benzodiazepines

### **Multiple doses of darigabat**

Phase 1 MAD Study (Protocol: B7431011)

Phase 1 MAD Study – only mild AEs and limited somnolence up to 42.5 mg BID

Able to achieve >80% receptor occupancy without significant somnolence observed

Benzodiazepines achieve 10% to 15% receptor occupancy with significant somnolence observed

No evidence of withdrawal effects

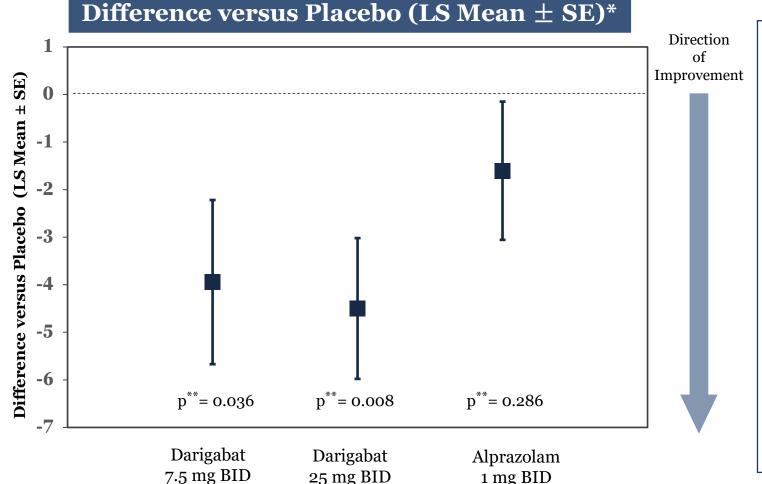
	Reaction	Week 1 (Titration)	Week 2 (Maintenance)	Week 3 (Maintenance)	Follow-up
Placebo	No Reaction	4/4	4/4	3/4	4/4
	Dizziness	-	-	1/4	-
	Somnolence	-	-	-	-
25 mg BID (~80% RO <sup>(1)</sup> )	No Reaction	5 / 8	7/8	8/8	8 / 8
	Dizziness	2/8	1/8	-	-
	Somnolence	3/8	-	-	-
42.5 mg BID (>80% RO <sup>(1)</sup> )	No Reaction	4/7	6/7	6/7	6/7
	Dizziness	3 / 7	1/7	1/7	1/7
	Somnolence	-	-	-	-



No somnolence observed following titration through doses of 42.5 mg BID



### Positive Data in Phase 1 Acute Anxiety Trial: Change in Panic Symptoms List Score (PSL-IV) at Day 8



#### • Darigabat 7.5 mg BID:

3.9-point improvement versus placebo at the end of 8-day treatment (9.9 on 7.5 mg BID versus 13.8 on placebo in PSL-IV total score increase following CO<sub>2</sub> challenge) with p\*\*=0.036

#### Darigabat 25 mg BID:

4.5-point improvement versus placebo at the end of 8-day treatment (12.5 on 25 mg BID versus 17.0 on placebo in PSL-IV total score increase following CO<sub>2</sub> challenge) with p\*\*=0.008

#### Alprazolam 1 mg BID:

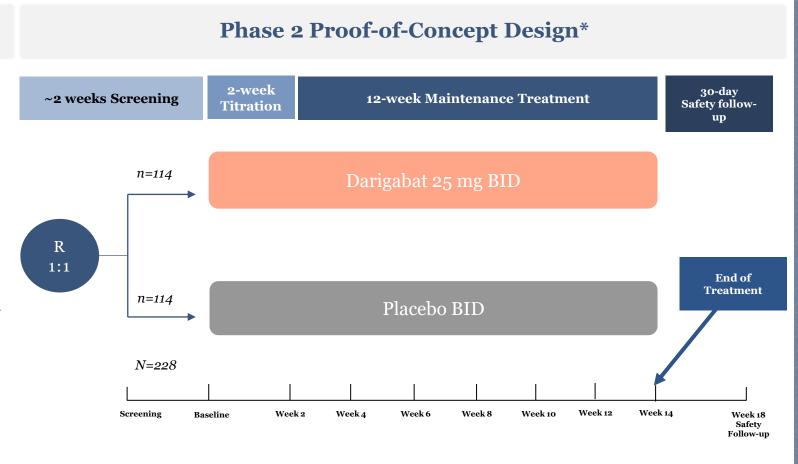
1.6-point improvement versus placebo at the end of 8-day treatment (14.5 on alprazolam 1 mg BID versus 16.1 on placebo in PSL-IV total score increase following  $CO_2$  challenge) with  $p^{**}$ =0.286



### Darigabat: ADAPT Phase 2 Trial in Panic Disorder Underway

#### Overview

- Primary endpoint Proportion of subjects who are free of panic attacks during the last two weeks of the maintenance period
- Key Secondary endpoints:
  - Change from baseline at week 14 in the PDSS score
  - Change from baseline to week 14 in panic attack frequency
- Inclusion Criteria Male and female subjects, aged 18 to 65 years with Panic Disorder (DSM-5) with or without Agoraphobia





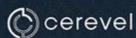
### **TAVAPADON**

Partial agonist selectively targeting the dopamine D1/D5 receptor with the goal of enhancing motor control and improving tolerability compared to standard of care

Monotherapy (Early-Stage) Parkinson's Disease

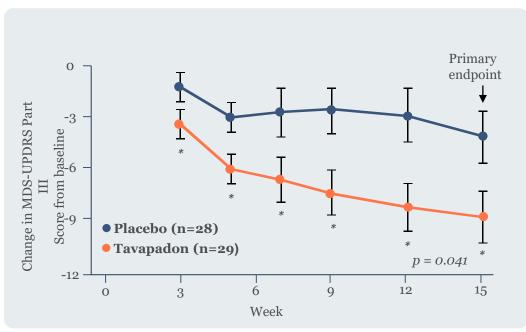
Adjunctive (Late-Stage) Parkinson's Disease





### Tavapadon Targets Direct Motor Pathway To Provide Potential Improved Treatment Option in Parkinson's Disease

In Phase 2, tavapadon demonstrated **4.8 point** MDS-UPDRS III difference vs. placebo at week 15 (p=0.04)¹



Note: Average dose of tavapadon = 9 mg; 11 patients on 15 mg top dose at week 15. Baseline Part III scores of 24.3 (tavapadon) and 25.8 (placebo).

### **Key Findings**

- When measuring MDS-UPDRS Part II + III, tavapadon demonstrated 5.8-point improvement over placebo at week 15 (p=0.02)<sup>1</sup>
- Most common AEs included headache and nausea can be mitigated with titration
- Tavapadon (targeting D1/D5) showed reduced incidence of known D2/D3 side effects:
  - Hallucinations: 0%<sup>2</sup>
  - Hypotension-Related Events: 7%
  - Dizziness: 7%
  - Somnolence: 14%
  - Nausea: 31%



### Tavapadon TEMPO-1 & -2 Monotherapy: Data Expected 2H 2024

Registration-directed program includes three global Phase 3 trials optimally designed to maximize treatment effect

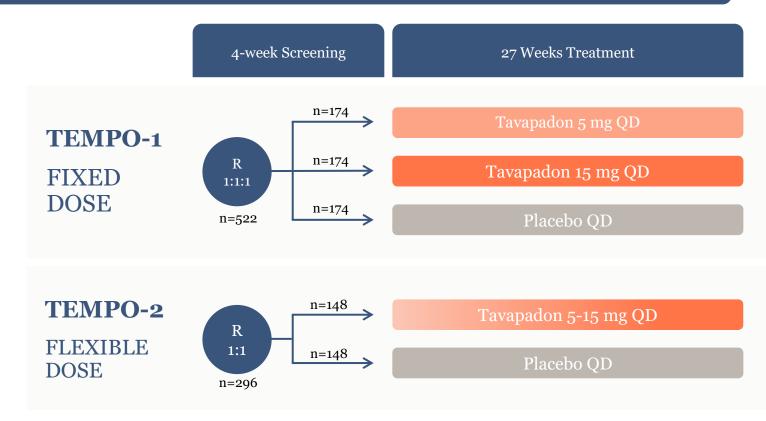
### TEMPO-1 & TEMPO-2: Phase 3

### **Key inclusion criteria**

- Adults 40-80 years old
- Baseline MDS-UPDRS<sup>(1)</sup>
   Part III Score ≥10 and
   Part II Score ≥2
- Modified Hoehn & Yahr<sup>(2)</sup> stage 1 to 2
- No concomitant meds except MAO-B inhibitors

### **Primary endpoint**

 Change in MDS-UPDRS Parts II+III



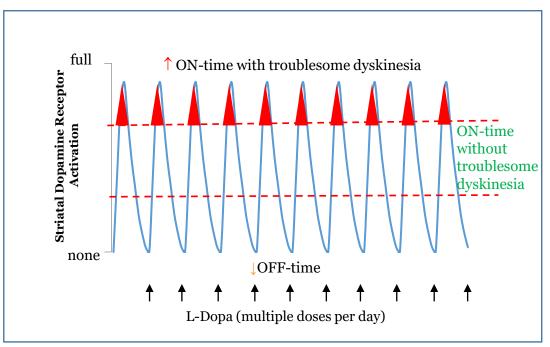


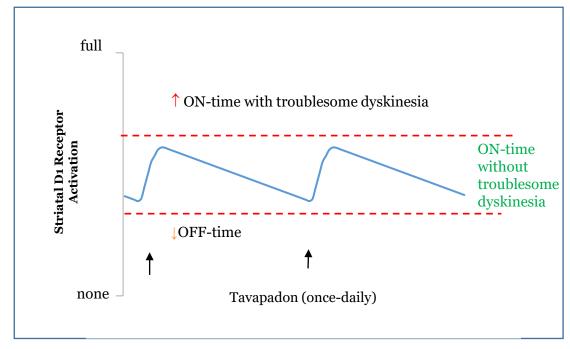
### In Late PD, Goal is to Control Motor Fluctuations and Dyskinesias Driven by L-Dopa

### L-Dopa vs. Tavapadon in Late-Stage PD<sup>1</sup>

L-Dopa is a **FULL** agonist with **SHORT** half-life

Tavapadon is a **PARTIAL** agonist with **LONG** half-life







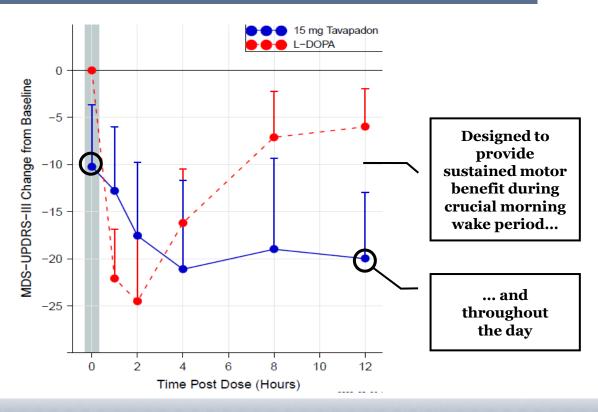
30-40% of patients experience dyskinesias within 5 years on L-Dopa<sup>2</sup> 40% experience OFF-time within 3-5 years on L-Dopa<sup>2</sup>



## Predictable 24-hour Activity → Sustained Effect: Once Daily, Oral Dosing

In an open-label Phase 1b trial, tavapadon demonstrated motor improvement on par with L-Dopa, sustained due to its 24-hour half-life

### Study 1005: Tavapadon in Late-Stage PD<sup>1</sup>





### Tavapadon TEMPO-3 Adjunctive: Data Expected 1H 2024



Registration-directed program includes three global Phase 3 trials optimally designed to maximize treatment effect

### TEMPO-3: Phase 3

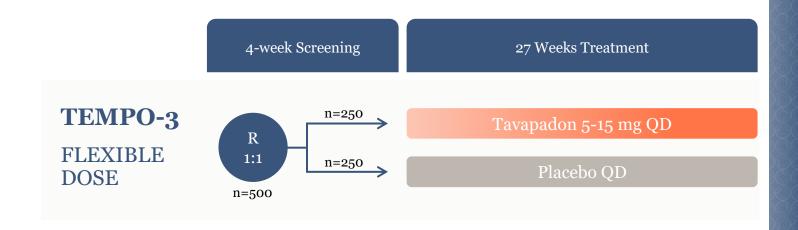
### Adjunct to levodopa

### **Key inclusion criteria**

- Adults 40-80 years old
- At least 2.5 hours OFF-time on 2 consecutive days at baseline
- Modified Hoehn & Yahr<sup>(1)</sup> stage 2 to 3, with response to L-Dopa

### Primary endpoint

 Change in ON-time without troublesome dyskinesia



### Thank You

Contact:

### Matt Calistri

Investor Relations matthew.calistri@cerevel.com

