



## Corporate Overview

March 11, 2024

**NASDAQ: CRVO** 

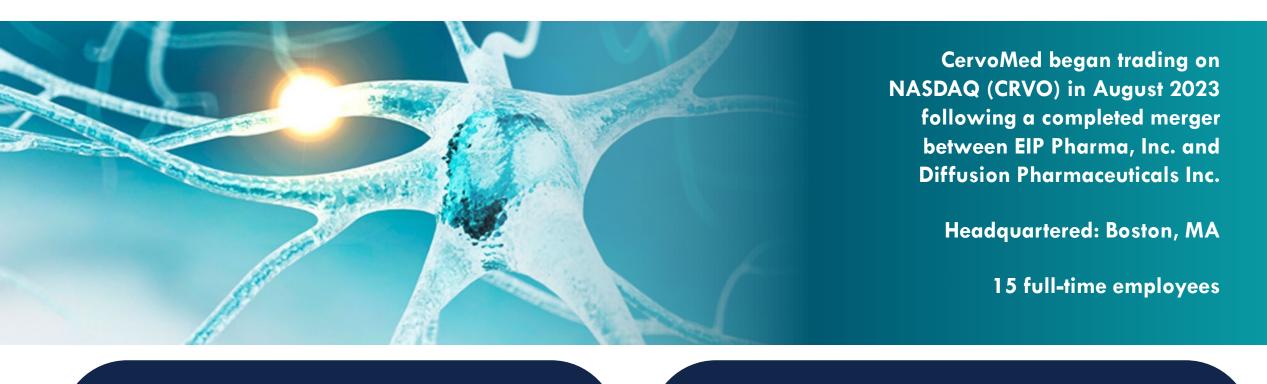
## Forward-Looking Statements

This presentation includes express and implied forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, regarding the intentions, plans, beliefs, expectations or forecasts for the future of CervoMed Inc. (the "Company"), including, but not limited to: the therapeutic potential of neflamapimod in DLB or any other indication; the anticipated timing and achievement of clinical and development milestones, potential discussions with regulatory authorities related to the Initial and Extension phases and clinical development of and approval process for neflamapimod, the initiation of any future clinical trials, or the commercial approval, if any, of neflamapimod by the FDA or any other regulatory authority; any other expected or implied benefits or results, including that any initial clinical results observed with respect to neflamapimod in the AscenD-LB Trial or RewinD-LB Trial will be replicated in later trials; the Company's clinical development plans and related timelines, including; the timing of the initiation of any phase 3 study or other additional clinical trials evaluating neflamapimod in DLB, including as a result of the Company's need to acquire sufficient funding therefor; the potential commercial opportunity of neflamapimod, if approved; and the Company's anticipated cash runway. Terms such as "believes," "estimates," "anticipates," "expects," "plans," "aims," "seeks," "intends," "may," "might," "could," "might," "will," "should," "approximately," "potential," "target," "project," "contemplate," "predict," "forecast," "continue," or other words that convey uncertainty of future events or outcomes may identify these forward-looking statements. Although there is believed to be reasonable basis for each forward-looking statement contained herein, forward-looking statements by their nature involve risks and uncertainties, known and unknown, many of which are beyond the Company's control and, as a result, actual results could differ materially from those expressed or implied in any forward-looking statement. Particular risks and uncertainties include, among other things, those related to: the Company's available cash resources and the availability of additional funds on acceptable terms; the Company's ability to design, initiate, enroll, execute, and complete its planned studies evaluating neflamapimod; the likelihood and timing of any regulatory approval of neflamapimod or the nature of any feedback the Company may receive from the U.S. Food and Drug Administration; the Company's ability to maintain its listing on the Nasdag Capital Market, as well as comply with applicable Nasdag rules and regulations; the market price of the Company's securities, which may be volatile due to a variety of factors, including, but not limited to: changes in the competitive and highly regulated industry in which the Company operates; the issuance of additional shares of the Company's common stock, including upon the issuance of outstanding warrants or otherwise; variations in operating performance across competitors; changes in laws and regulations affecting the Company's business; the ability to implement business plans, forecasts, and other expectations in the future; general economic, political, business, industry, and market conditions, inflationary pressures, and geopolitical conflicts, including the continued availability of funding for the U.S. federal government to support disbursements under the Company's grant from the National Institute on Aging; and the other factors discussed under the heading "Risk Factors" in the Company's most recent Annual Report on Form 10-K for the year ended December 31, 2023 filed with the U.S. Securities and Exchange Commission ("SEC") on March 29, 2024, and other filings that the Company may file from time to time with the SEC. Any forward-looking statements in this presentation speak as of March 10, 2025 (or such earlier date as may be identified) and the Company does not undertake any obligation to update such forward-looking statements to reflect events or circumstances after this date, except to the extent required by law.



### **Company Overview**

Targeting the Early Stage of the Neurodegenerative Process, Synaptic Dysfunction, to Treat Age-Related Neurologic Disorders



Lead Asset: Neflamapimod licensed from Vertex
Pharmaceuticals; developed for CNS indications by EIP
Pharma/CervoMed

Neflamapimod IP covered by multiple CervoMed-owned issued patents around method of use for various indications and formulations, expiring at various dates through 2039



### **Experienced Leadership Team**

Robert J. Cobuzzi Jr., PhD

Kelly Blackburn, MHA

John Alam, MD

William Elder



President, CEO & Co-Founder, Director

Former Chief Medical Officer and EVP Medicines Development, Vertex

Former Global Head Alzheimer's R&D at Sanofi

Led clinical development of Avonex for multiple sclerosis at Biogen



Chief Financial Officer & General Counsel

Principal Financial Officer of CervoMed since March 2024

General Counsel and Corporate Secretary of Diffusion (2020-23)

J.D. from University of Pennsylvania School of Law, M.S. Finance from Villanova University, B.A. Economics from Tufts University



Chief Operating Officer, Director

President, Chief Executive Officer and Director of Diffusion (2020-23)

More than 25 years of cross-functional leadership and operational experience in pharmaceutical and biotechnology companies, including Endo, Adolor,

Centocor and AstraMerck



SVP, Clinical Development

Former VP, Clinical Affairs at aTyr Pharma; VP, Clinical Development

Operations at Vertex. Led global clinical operations for Kalydeco® for the treatment of cystic fibrosis, Incivek® for hepatitis C, and Velcade® for multiple myeloma

#### **DIRECTORS**

#### Joshua Boger, PhD (Chair)

Executive Chair, Alkeus Therapeutics.
Founder, former CEO, Vertex Pharmaceuticals

#### Sylvie Gregoire, PharmD

Co-Founder; Board member, Novo Nordisk, F2G, Abivax; Former Executive VP, Biogen; Former President, HGT Division, Shire Pharmaceuticals; Former Board member, Revitty, ViFor, Corvidia, Cubist

#### Jeff Poulton (Chair of Audit Committee)

CFO, Alnylam Pharmaceuticals (Nasdaq:ALNY)
Former CFO, Shire Pharmaceuticals; CFO, Indigo Agr.

#### Jane H. Hollingsworth, JD

Managing Partner, Militia Hill Ventures
Former Chairman of the Board, Diffusion
Pharmaceuticals

#### Marwan Sabbagh, MD

Prof. of Neurology at the Alzheimer's and Memory Disorders division of the Barrow Neurological Institute at Dignity Health/St Joseph's Hospital in Phoenix, Arizona

#### Frank Zavrl

Former Board Member, Puma Biotechnology Retired Partner, Adage Capital

#### **SCIENTIFIC ADVISORS**



#### Ole Isacson, MD (Chair)

Prof of Neurology (Neuroscience) Harvard Medical School



#### Lewis Cantley, PhD

Professor of Cell Biology, Harvard Medical School, Dana-Farber Cancer Institute; Laureate, Breakthrough Prize in Life Sciences



#### Jeff Cummings, MD, PhD

Director, Chambers-Grundy Center for Transformative Neuroscience at UNLV

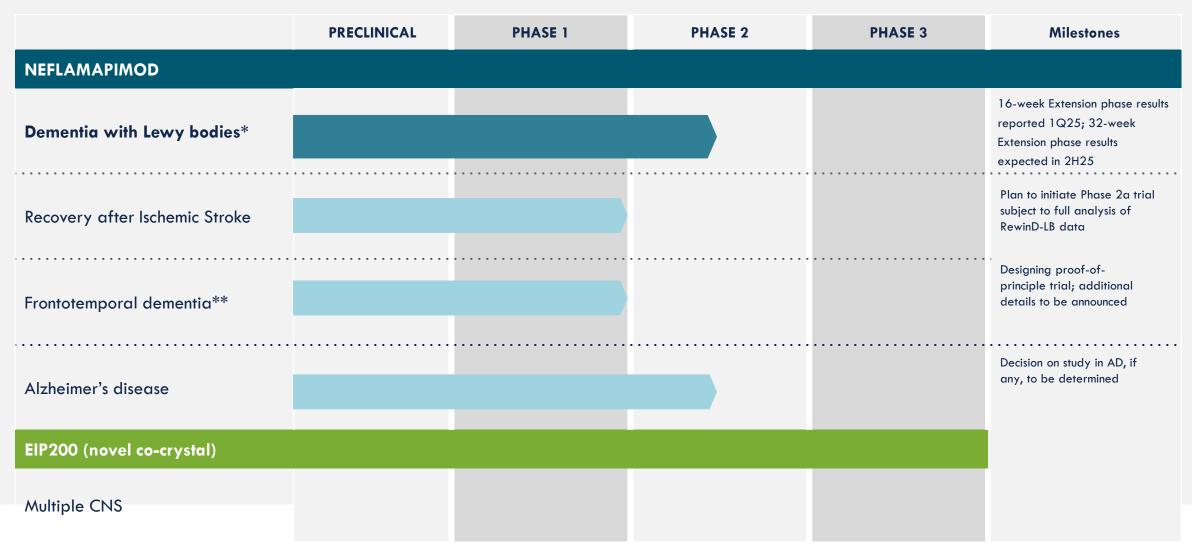


#### Heidi McBride, PhD

Professor, Dept. of Neurology & Neurosurgery, McGill University



## **CervoMed Pipeline**



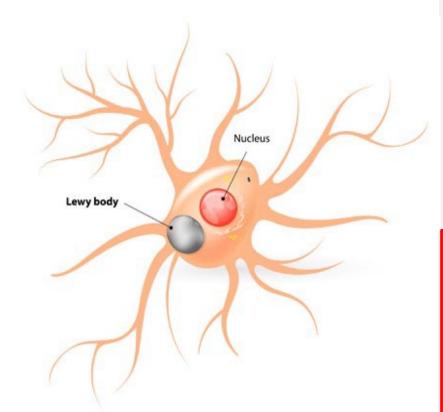


<sup>\*</sup>Received FDA Fast Track designation



<sup>\*\*</sup>Received FDA Orphan Drug designation

### Dementia with Lewy Bodies (DLB)



DLB associated with abnormal deposits ("Lewy bodies") within neurons of a protein called alpha-synuclein in the brain.

#### Primary site of pathology is basal forebrain

Clinically, characterized by dementia and  $\geq 2$  of the following: fluctuating attention, visual hallucinations, REM sleep disorder, and/or parkinsonism (motor deficits)<sup>1</sup>

- DLB patients experience rapid clinical worsening, high healthcare costs, low quality of life, and caregivers have high levels of distress. DLB patients progress significantly faster than patients with Alzheimer's disease (AD)

## Treatment Landscape and Unmet Need

- No approved therapies; limited drugs in development
- Current standard of care is cholinesterase inhibitor therapy; only transiently improves cognition & does not impact motor component

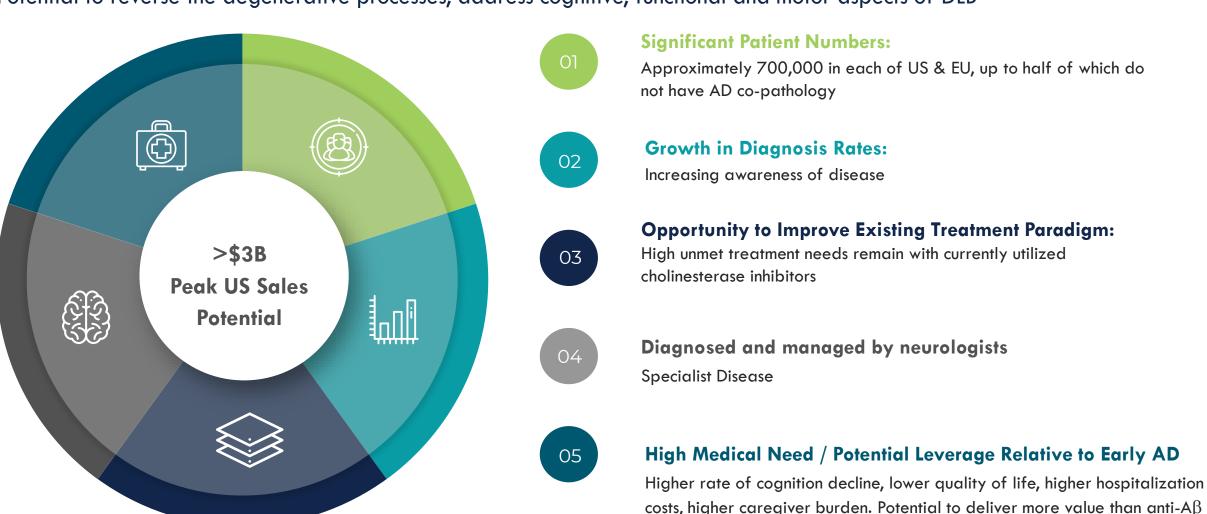
#### **Market Opportunity**

- 3rd most common degenerative
   disease of the brain (after AD and PD)
- 1.4M individuals in US and EU



### DLB is an Indication with High Potential Value

Potential to reverse the degenerative processes, address cognitive, functional and motor aspects of DLB



therapies provide in AD

### Neflamapimod: Targeted Therapy for Diseases of the Basal Forebrain

#### **Preclinical**

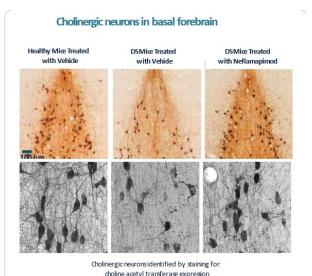
#### Disease processes in basal forebrain reversed with neflamapimod

When administered in mice that develop basal forebrain cholinergic degeneration, neflamapimod:

- ✓ Reduced Rab5 activity and tau phosphorylation
- Reversed loss of cholinergic (ChaT+) neurons in the basal forebrain; and
- ✓ Normalized performance in behavioral tests of cholinergic function<sup>2</sup>

#### Clinical

#### Improvement on multiple clinical endpoints in Phase 2a trial



In AscenD-LB, a 91-patient, 16-week, placebo-controlled Phase 2a trial in patients with DLB neflamapimod:

- √ <u>Improved</u> dementia severity (assessed by Clinical Dementia Rating Sum-of Boxes, CDR-SB, p=0.023 vs. placebo)
- ✓ Improved gait (assessed by Timed Up and Go, TUG, p=0.044 vs. placebo
- ✓ Reduced levels of plasma biomarker of neurodegeneration (glial fibrillary acidic protein (GFAP))
- Results most prominent in patients with DLB without AD co-pathology



## **RewinD-LB Study Overview**



Designed to replicate Phase 2a study results, thereby demonstrating proof-of-concept for neflamapimod as a potential treatment for dementia with Lewy bodies (DLB)

- 16-week double-blind, placebo-controlled (40mg TID or placebo, 1:1) initial phase (Initial phase), followed by 32 weeks of open-label treatment with neflamapimod (Extension phase)
- Primary endpoint: change in Clinical Dementia Rating Sum-of-boxes (CDR-SB)
- Excluded patients with concomitant Alzheimer's disease related pathology, as assessed by plasma ptau181

#### Results of Initial phase of study presented at ILBDC\*:

- No discernible differences between neflamapimod 40mg TID and placebo treatment groups during the Initial phase of the clinical study
- Measured trough plasma drug concentrations during this phase were similar to those seen with a lower dose of 40mg BID in earlier studies, a potential explanation for why these results were discordant from prior Phase 2a study in DLB
- Analyses to date suggest the lower-than-expected bioavailability during Initial phase was related to the age of the capsules utilized during this phase of the study

With the introduction of a newer batch of capsules in the ongoing Extension phase of the study, mean trough plasma drug concentration achieved the targeted threshold

## Overview of Batch of Capsules in RewinD-LB Study

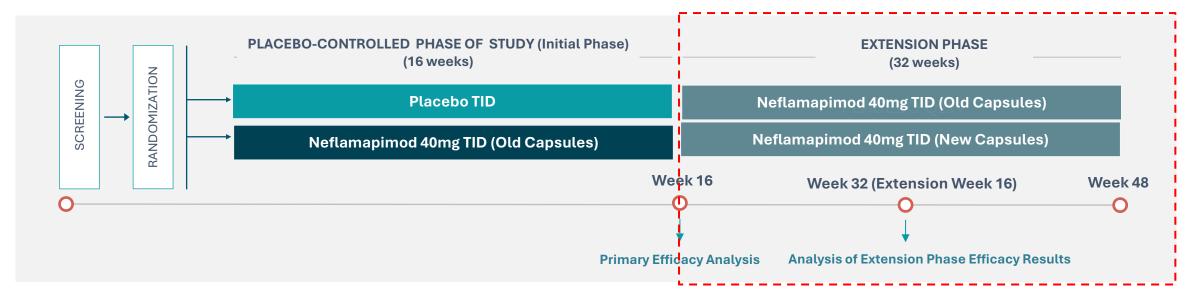


	Old Capsules	New Capsules
Use in RewinD-LB	Placebo-controlled ("Initial") phase and in Extension	Extension only
Production Date	October 2020 (Age of 3 to 4 years during period of utilization in RewinD-LB)	March 2023 (Age < 2 years during first 16 weeks of Extension)
In Vitro Properties	Lower dissolution kinetics	Expected dissolution kinetics
Mean Trough Plasma Drug Concentration during RewinD-LB	3.9 ng/mL, which is similar to that seen with 40mg BID in prior studies	Attained targeted threshold of 5 ng/mL

Manufacturing processes were identical between both the old and new capsules

## **Week 16 Extension Phase Analysis**





#### **PARTICIPANTS**

Dementia with Lewy bodies (DLB) by consensus criteria

Global CDR score of 0.5 or 1.0

Absence of AD co-pathology, as defined by screening ptau181 < 2.4 pg/mL

#### **COMPARISONS**

Outcomes during treatment in the Extension with old capsules vs. treatment with new capsules

Comparison in participants treated with new capsules during Extension with outcomes with placebo administration during Initial phase

#### **CLINICAL OUTCOME MEASURES**

- Primary: Clinical Dementia Rating Sum of Boxes (CDR-SB)
- Secondary:
  - Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change (ADCS-CGIC)
  - Timed Up and Go (TUG) test
  - Neuropsychological Test Battery (NTB)

## 



#### Positive effects with new capsules on multiple clinical endpoints:

- Significant improvement on primary efficacy endpoint, change in CDR-SB, both vs. old capsules (p<0.001) during 1st 16 weeks of the Extension and vs. placebo (p=0.003) utilizing all data in the study through to week 32 (includes placebo-controlled phase and 1<sup>st</sup> 16 weeks of the Extension)
- Significant improvement on ADCS-CGIC in comparison to old capsules (p=0.035) during the Extension and in a within-subject comparison to placebo treatment (p=0.035)
- Trend towards improvement in TUG vs. old capsules during at week 16 of Extension; no discernible effects on NTB
- Greater positive clinical effect in participants with levels of plasma ptau181 < 2.2 pg/mL $^{1}$

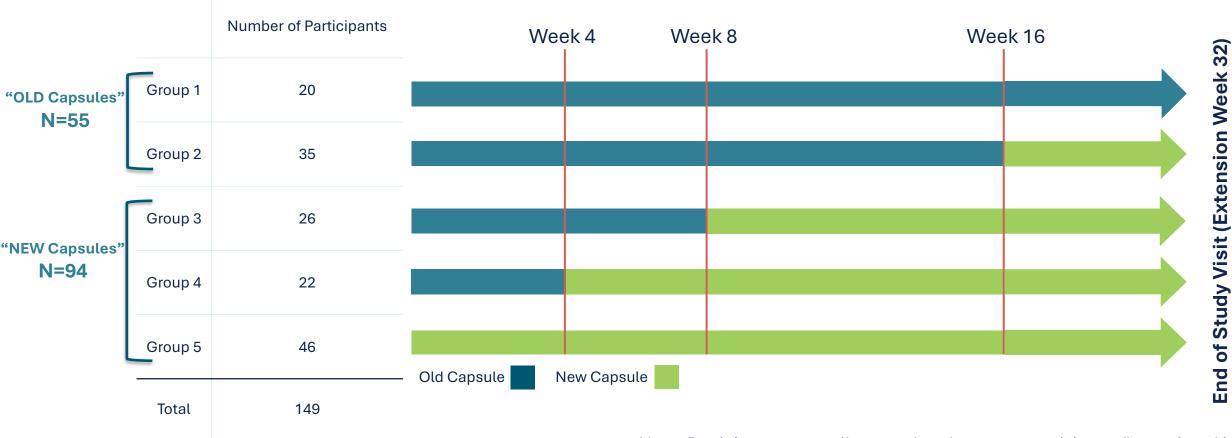
#### Old and new capsules have similar overall safety/tolerability profile

Lower incidence of falls during the Extension with the new capsules (p=0.025 vs. old capsules and p=0.007 vs. placebo in participants with baseline plasma ptau181 < 2.2 pg/mL)

## Dosing Groups in Extension Phase of RewinD-LB Study







**Extension Week 16 Completion Rate** 

Old (Groups 1-2) 87.3%

New (Groups 3-5) 91.5%

Note: Participants were all aware that they were receiving neflamapimod in the Extension phase (i.e. treatment was "open label"), but neither they nor study site personnel were aware if they were receiving old or new capsules

## Primary Outcome Measure: Change in CDR-SB



- "Gold standard" for evaluating severity and progression of dementia
- Primary endpoint for many Phase 3 clinical studies in early Alzheimer's Disease (AD)
- Best performer for evaluating treatment effects in the Phase 2a study of neflamapimod in DLB

Clinical Dementia Rating Sum of Boxes (CDR-SB, Total Score = 0-18)

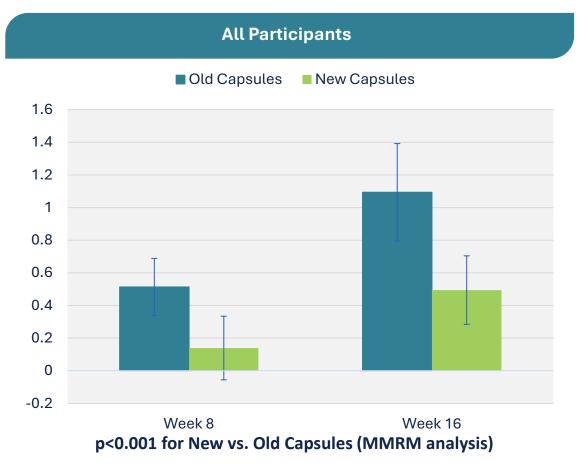
#### **Cognitive Domains:**

- Memory (0-3)
- Orientation (0-3)
- Judgement and Reasoning (0-3)

#### **Functional Domains:**

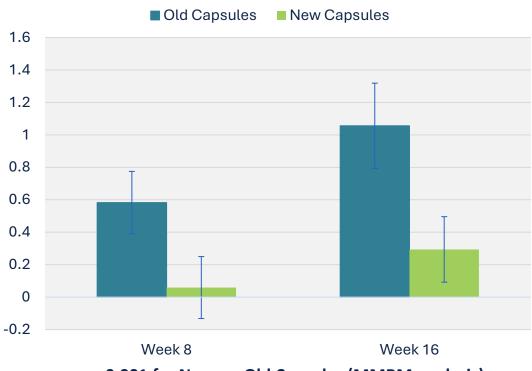
- Community Affairs (0-3)
- Home & Hobbies (0-3)
- Personal Care (0-3)

## Mean Change from Baseline in CDR-SB in First 16 Weeks of Extension



Number of Participants		
Old Capsules	75	48
New Capsules	62	84

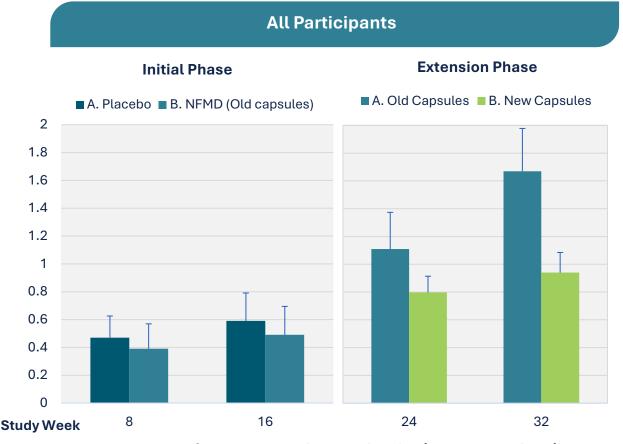
#### Participants with Screening ptau181 < 2.2 pg/mL



p<0.001 for New vs. Old Capsules (MMRM analysis)

Number of Participants		
Old Capsules	66	45
New Capsules	52	67

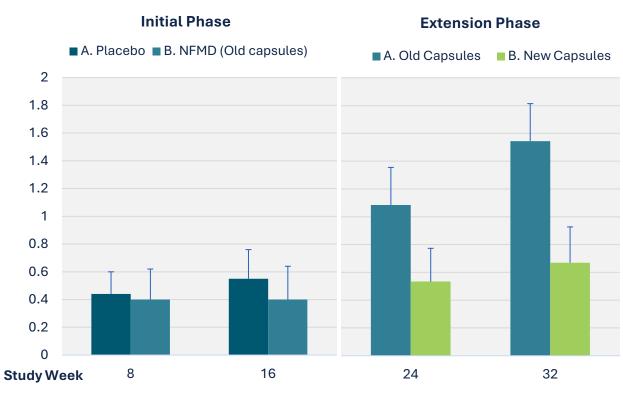
## Mean Change in CDR-SB from Baseline to Week 32 (Week 16 of Extension)



P=0.003 for New Capsules vs. placebo (MMRM analysis)

	Number of Participants				
	Week 8	Week 16	Week 24	Week 32	
Group A	78	77	49	48	
Group B	77	74	89	84	

#### Participants with Screening ptau181 < 2.2 pg/mL



p<0.001 for New Capsules vs. placebo (MMRM analysis)

Number of Participants				
	Week 8	Week 16	Week 24	Week 32
Group A	66	67	47	45
Group B	62	62	73	68

## **New Capsules Improves Outcome on CDR-SB**



#### Analysis of Change in CDR-SB during First 16 Weeks of Extension in New vs. Old Capsules

	Mean (95% CI) Difference* between New and Old Capsules	P-Value
All Participants	-0.73 (-1.14, -0.32)	p<0.001
Participants with screening ptau181 < 2.2 pg/mL	-0.81 (-1.23, -0.39)	p<0.001

## Analysis of Change in CDR-SB During First 32 Weeks of Study (includes Initial phase + First 16 weeks of Extension)

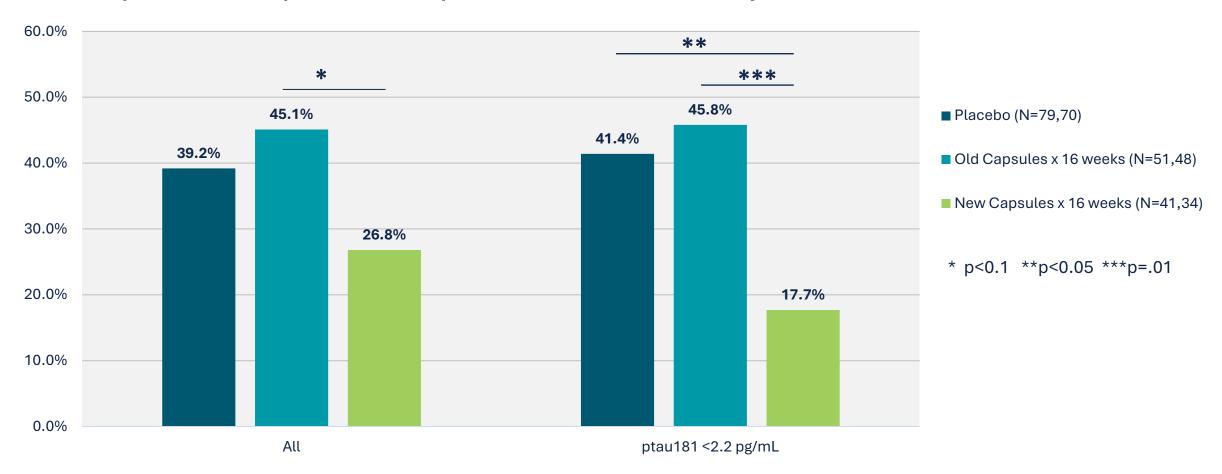
	Old Capsules		New Capsules	
	Mean Difference* to Placebo (95% CI)	P-Value	Mean Difference* to Placebo (95% CI)	P-Value
All Participants	0.00 (-0.28, 0.29)	0.97	-0.45 (-0.78, -0.15)	p=0.003
Participants with screening ptau181 < 2.2 pg/mL	-0.06 (-0.36, 0.23)	0.67	-0.57 (-0.88, -0.25)	p<0.001

Linear Mixed-Effects Model for Repeated Measures (MMRM) with baseline CDR-SB, Sex, Age and MMSE as covariates \*Negative indicates improvement

## **Progression Over 16 Weeks**

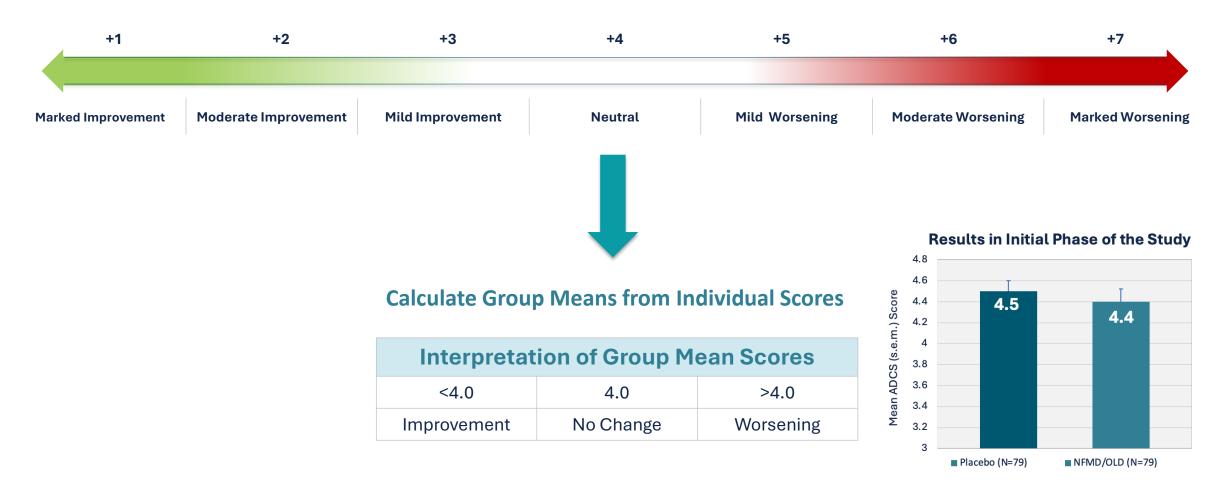


#### **Proportion of Participants with ≥ 1.5-point increase in CDR-SB or Early Termination**



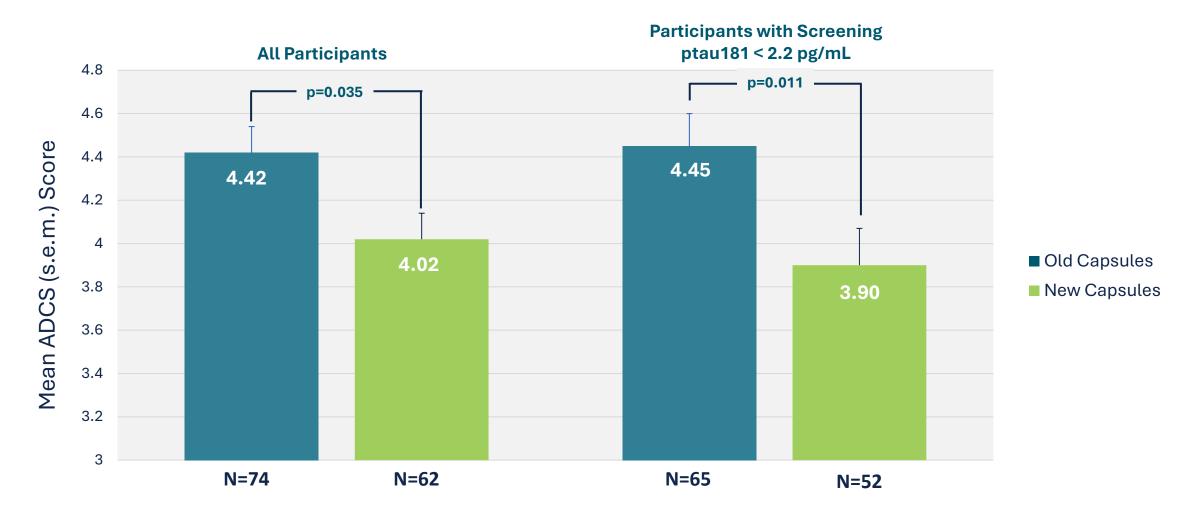
Placebo is during 16-week Initial phase of the study; Old and New Capsules during first 16 weeks of the Extension

# Secondary Endpoint: Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change (ADCS-CGIC)



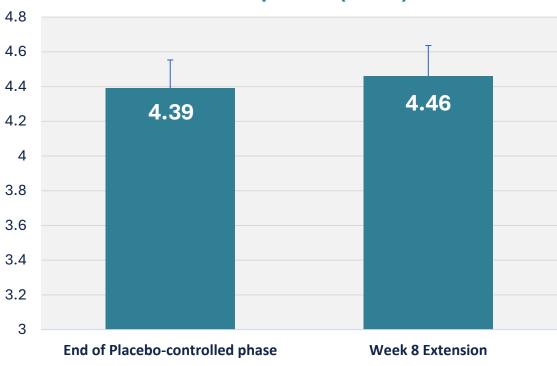


## **ADCS-CGIC** by Capsule Form Administered during Extension Phase

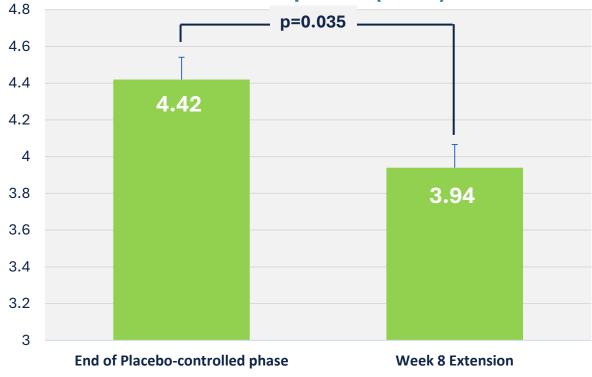


# ADCS-CGIC: Within-participant Comparison in Participants Who Received Placebo in Initial Phase

## Participants who received placebo and then Old Capsules (N=41)



## Participants who received placebo and then New Capsules (N=31)



# Treatment Emergent Adverse Events (TEAE) Seen At Incidence >2% During First 16 Weeks of Extension

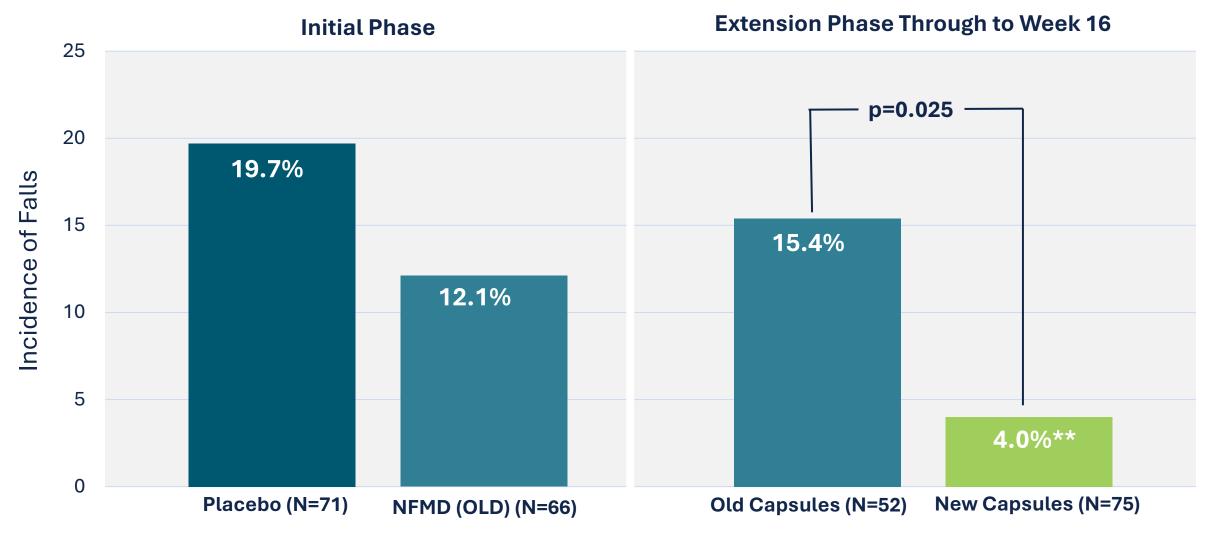
	OLD CAPSULES: GROUPS 1 & 2 (N=55)	NEW CAPSULES: GROUPS 3, 4 AND 5 (N=94)	TOTAL (N=149)
Falls	8 (14.5%)	7 (7.4%)	15 (10.1%)
COVID-19	2 (3.6%)	5 (5.3%)	7 (4.7%)
Headache	1 (1.8%)	5 (5.3%)	6 (4.0%)
<b>Urinary Tract Infection</b>	5 (9.1%)	3 (3.2%)	8 (5.4%)
Diarrhea	4 (7.3%)	3 (3.2%)	7 (4.7%)
Skin Laceration	1 (1.8%)	3 (3.2%)	4 (2.7%)
Hallucination	5 (9.1%)	2 (2.1%)	7 (4.7%)
Fatigue	3 (5.5%)	2 (2.1%)	5 (3.4%)
Confusional State	3 (5.5%)	2 (2.1%)	5 (3.4%)
Arthralgia	2 (3.6%)	1 (1.1%)	3 (2.0%)
Dizziness	3 (5.5%)	1 (1.1%)	4 (2.7%)
AST Increased	3 (5.5%)	1 (1.1%)	4 (2.7%)
ALT Increased	3 (5.5%)	0 (0%)	3 (2.7%)

# TEAE Seen At Incidence >2% During First 16 Weeks of Extension in Participants with Screening ptau181 < 2.2 pg/mL

	OLD CAPSULES: GROUPS 1 & 2 (N=52)	NEW CAPSULES: GROUPS 3, 4 AND 5 (N=75)	TOTAL (N=127)
Headache	1 (1.9%)	5 (6.7%)	6 (4.7%)
COVID-19	2 (3.8%)	4 (5.3%)	6 (4.7%)
Falls	8 (15.4%)	3 (4.0%)*	11 (8.7%)
<b>Urinary Tract Infection</b>	5 (9.6%)	3 (4.0%)	8 (6.3%)
Hallucination	5 (9.6%)	2 (2.7%)	7 (5.5%)
Diarrhea	3 (5.8%)	2 (2.7%)	5 (3.9%)
Fatigue	3 (5.8%)	2 (2.7%)	5 (3.9%)
Confusional State	3 (5.8%)	2 (2.7%)	5 (3.9%)
Skin Laceration	1 (1.9%)	2 (2.7%)	3 (2.4%)
Dizziness	3 (5.8%)	1 (1.3%)	4 (3.1%)
Arthralgia	2 (3.8%)	1 (1.3%)	3 (2.4%)
AST Increased	3 (5.8%)	0 (0%)	3 (2.4%)
ALT Increased	3 (5.8%)	0 (0%)	3 (2.4%)



## Incidence of Falls in Participants with Screening ptau181 < 2.2 pg/mL **During First 16 Weeks of Extension**



## **Next Steps in DLB**



- Present RewinD-LB Data at Scientific Conferences Throughout 2025:
  - AD-PD 2025, Vienna, AT, April 1-5: presentation of Extension Week 16 Results
  - Alzheimer's Association International Conference (AAIC) 2025, Toronto, CA, July 27-31:
     plan to submit
  - American Neurologic Association (ANA), Baltimore MD, Sep 13-16: presentation at Special Interest Group, Neurodegenerative Diseases Therapeutics
  - Clinical Trials in Alzheimer's Disease (CTAD), San Diego, CA, USA Dec 1-4: plan to submit
- Meet with FDA after week 32 Extension (week 48 study overall) data are available to finalize proposed Phase 3 design

### Summary

Late-stage asset with differentiated approach, targeting synaptic dysfunction to treat age-related neurologic disorders

Experienced management team and board of directors

Significant market opportunity in DLB

Key milestones expected over next 12 months

Potential to broaden opportunity through additional indications









## Corporate Overview

March 11, 2024

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