Immunic THERAPEUTICS

Progressive Multiple Sclerosis R&D Day

November 5, 2026
Virtual

NASDAQ: IMUX

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Virtual Progressive Multiple Sclerosis R&D Day: Today's Speakers

Immunic Speakers



Erik Lundgren, MBA
Chief Executive Officer



Jason Tardio, MBA
President & Chief Operating Officer



Michael A. Panzara, MD, MPH
Chief Medical Officer



Hella Kohlhof, PhD
Co-Founder & Chief Scientific Officer

Featured Experts



Jiwon Oh, MD, PhD, FRCPC
University of Toronto



Maria Pia Sormani, PhD
University of Genoa

Moderator



Jessica Breu
Vice President Investor Relations and Communications

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Vidofludimus Calcium – Targeting Key Unmet Needs in Progressive MS

Agenda Virtual Progressive Multiple Sclerosis R&D Day

12:30 - 12:35	**Welcome and Introduction**	Erik Lundgren Chief Executive Officer
12:35 - 12:45	**Expert Talk: Unmet Needs and Progression in MS**	Jiwon Oh, MD, PhD, FRCPC University of Toronto
12:45 - 12:55	**Vidofludimus Calcium's Differentiated Mode of Action: Direct Nurr1 Activator**	Hella Kohlhof, PhD Co-Founder & Chief Scientific Officer
12:55 - 01:05	**Expert Talk: Patient Populations, Imaging and Fluid Biomarkers in Progressive MS**	Jiwon Oh, MD, PhD, FRCPC University of Toronto
01:05 - 01:15	**Expert Talk: Clinical Trial Design and Endpoints in Progressive MS**	Maria Pia Sormani, PhD University of Genoa
01:15 – 01:25	**Vidofludimus Calcium in Progressive MS: Phase 2 CALLIPER Trial and Planned Phase 3 Trial**	Michael A. Panzara, MD, MPH Chief Medical Officer
01:25 - 01:35	**Commercial Opportunity for Vidofludimus Calcium in Progressive MS**	Jason Tardio President & Chief Operating Officer
01:35 - 01:40	**Outlook: Upcoming Milestones for Vidofludimus Calcium in MS**	Erik Lundgren Chief Executive Officer
01:40 - 02:00	**Q&A Session**	

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Welcome and Introduction

Erik Lundgren I Chief Executive Officer

Immunic: Pivoting to a Fully Integrated Multiple Sclerosis Company

Advancing a Potentially Differentiated Oral MS Therapy to Address High Unmet Needs

Lead Asset

Vidofludimus Calcium
(IMU-838)

Near-Term Value Inflection in Relapsing Multiple Sclerosis

Significant Upside Potential in Progressive Multiple Sclerosis

Building a Leading, Fully Integrated Commercial Multiple Sclerosis Organization

Driven by the Needs of People with Multiple Sclerosis

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Vidofludimus Calcium Is Being Developed as a Franchise Opportunity Spanning Relapsing and Progressive MS

PROGRAM	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	STATUS	NEXT MILESTONE
Vidofludimus Calcium (IMU-838)	Relapsing MS ENSURE-1					Both trials fully enrolled	Top-line data for both trials expected December 2026
Vidofludimus Calcium (IMU-838)	Relapsing MS ENSURE-2					Both trials fully enrolled	Top-line data for both trials expected December 2026
Vidofludimus Calcium (IMU-838)	**Progressive MS** Phase 3					In preparation	Initiation of Phase 3 trial ongoing, first-patient-enrolled expected H1/2027
Vidofludimus Calcium (IMU-838)	Relapsing-Remitting MS EMPhASIS					Trial met primary and key secondary endpoints OLE ongoing	Additional OLE data expected
Vidofludimus Calcium (IMU-838)	**Progressive MS** CALLIPER					Numerically reduced CDW, signals for CDI* OLE ongoing	Additional OLE data expected
IMU-381	Neurologic Diseases Nurr1 Platform					Candidate screening	Lead candidate identification











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* Primary percent brain volume change endpoint not met

MS: multiple sclerosis; Nurr1: nuclear receptor-related-1; OLE: open-label extension; CDW: confirmed disability worsening; CDI: confirmed disability improvement; IND: Investigational New Drug

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Building a Leading MS Company: A Phased Commercial Strategy

Relapsing MS Establishes Commercial Foundation; Progressive MS Drives Long-Term Value Creation

BUILD THE COMMERCIAL FOUNDATION (2026-2028)

Launch a differentiated oral DMT into the U.S. relapsing MS market while establishing Immunic as a fully integrated commercial biotechnology company

SCALE & GENERATE CASH FLOW (2028-2032)

Commercial success in relapsing MS funds continued pipeline and data generating investments while strengthening commercial capabilities and organizational scale

BECOME A GLOBAL MS LEADER (2032+)

Capture a substantially larger market opportunity through expansion into progressive MS reinforcing Immunic's position as a leading global MS company

Our strategy is to use the U.S. relapsing MS opportunity to build a profitable, fully integrated commercial organization that serves as the platform for long-term global leadership in MS.

MS: multiple sclerosis; DMT: disease-modifying therapy

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Expert Talk: Jiwon Oh, MD, PhD, FRCPC

Medical Director, Barlo Multiple Sclerosis Program
Waugh Family Chair in MS Research
Staff Neurologist, St. Michael's Hospital Scientist,
Keenan Research Centre of the Li Ka Shing Knowledge Institute
Associate Professor, Division of Neurology, University of Toronto

Vidofludimus Calcium's Differentiated Mode of Action: Direct Nurr1 Activator

Hella Kohlhof, PhD I Co-Founder & Chief Scientific Officer

Nurr1 (NR4A2) Is a Transcription Factor Linked to Neuroprotection and Regulation of Inflammatory Signaling

Nurr1 (NR4A2)

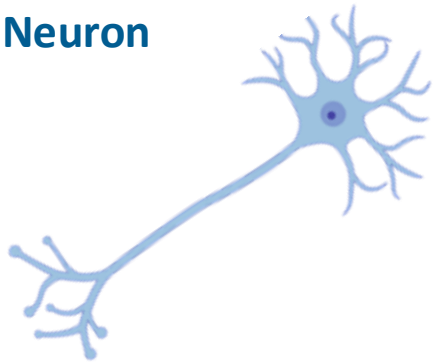
Microglia



Astrocyte



Neuron



Member of the NR4A family of orphan nuclear receptor transcription factors and expressed in neurons, microglia and astrocyes[1-3,5]

Regulates transcriptional programs involved in neuronal maintenance and survival[2,3]

Via its expression in midbrain dopaminergic neurons, cortical and subicular glutamatergic neurons, Nurr1 is associated with different neurological diseases beyond MS, such as Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), schizophrenia and neurodevelopmental disorders.[3,8]

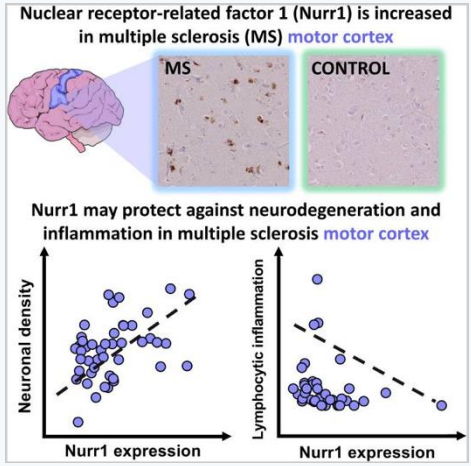
Emerging evidence supports a potential role in MS[4-6]

Relapsing MS

- Reduced Nurr1 expression in relapsing MS is associated with higher relapse rate and higher EDSS[7]
- Nurr1 expression normalizes during pregnancy, coinciding with reduced MS disease activity[6]

Progressive MS – Nurr1 in the motor cortex[4]

- In postmortem MS motor cortex, higher Nurr1 expression is associated with greater neuronal preservation
- Nuclear Nurr1 in layer III correlated with older age at death, longer disease and longer time to wheelchair.



A potential protective role of the nuclear receptor-related factor 1 (Nurr1) in multiple sclerosis motor cortex: a neuropathological study[4]

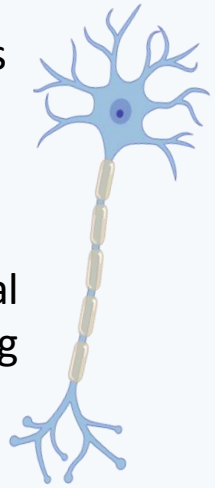
1. Safe S, et al. J Steroid Biochem Mol Biol. 2016;157:48-60; 2. Montarolo F, et al. Int J Mol Sci. 2019;20(19):4858; 3. Jeon SG, et al. Aging Dis. 2020;11(3):705-724; 4. Pansieri J, et al. Brain Commun. 2023;5(2):fcad072; 5. Saijo K, et al. Cell. 2009;137(1):47-59; 6. Gilli F, et al. PLoS One. 2010;5(1):e8962; 7. Gilli F, et al. Arch Neurol. 2011;68(7):879–888; 8. García-Yagüe ÁJ, Cuadrado A. International Journal of Molecular Sciences. 2023;24(15):12280 / Nurr1: nuclear receptor-related factor 1; NR4A2: nuclear receptor subfamily 4 group A member 2; MS: multiple sclerosis; EDSS: Expanded Disability Status Scale

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Vidofludimus Calcium: A Differentiated Dual Mechanism Approach to MS

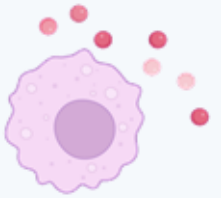
Direct Nurr1 Activator

- **Nurr1 activation may support neuronal resilience under inflammatory and oxidative stress.**
- Preclinical findings suggest vidofludimus has both direct and indirect neuroprotective mechanisms.
  - ***In vitro*:** In cell culture assays, vidofludimus calcium promoted neuronal survival and reduced neurotoxic signaling of activated microglia and astrocytes.
  - ***In vivo*:** In EAE, vidofludimus calcium increased BDNF levels and expression of Nurr1-regulated target genes consistent with Nurr1 pathway activation.



Selective DHODH Inhibitor

- **Vidofludimus calcium selectively inhibits DHODH limiting *de novo* pyrimidine synthesis.**
  - **Immune effects:** DHODH inhibition preferentially affects highly metabolically active immune cells and contributes to anti-inflammatory effects with no indication of immunosuppression.
  - **Antiviral effects**: DHODH inhibition may also have antiviral relevance, including effects on EBV reactivation.



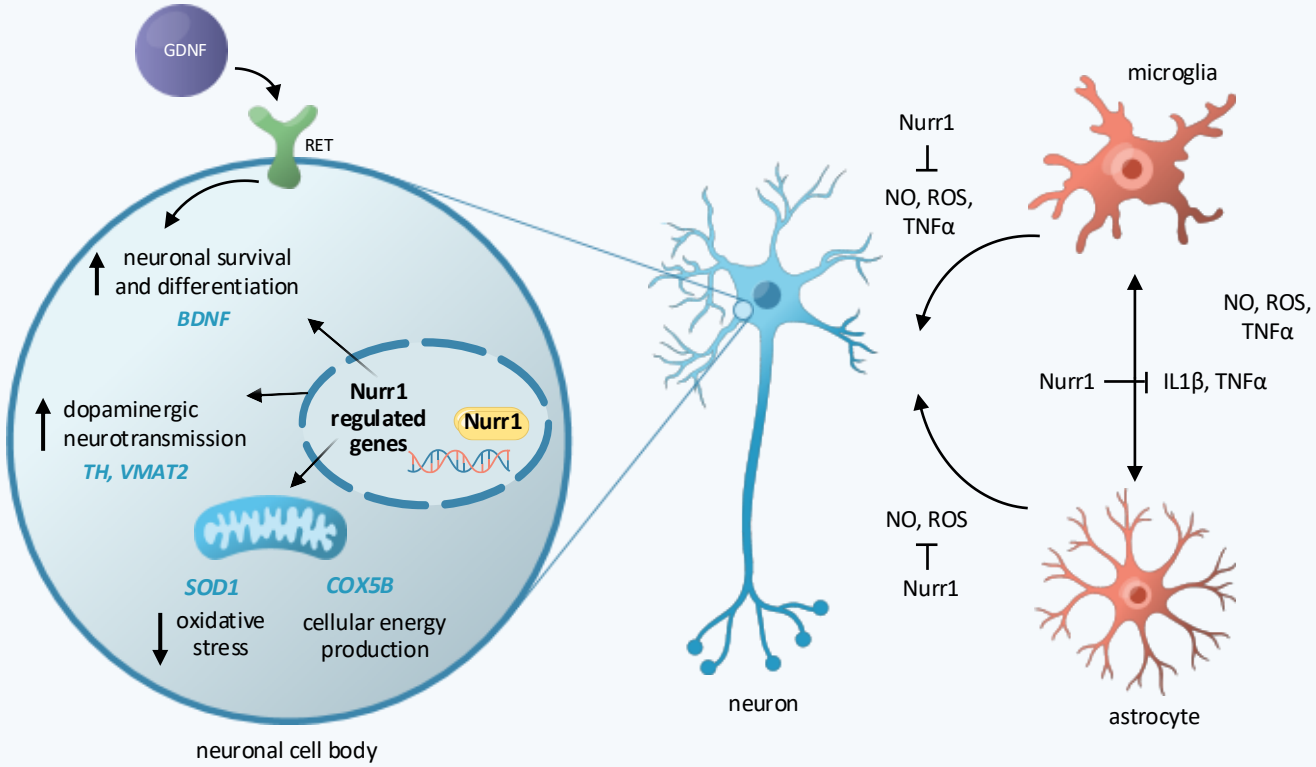
B and T cells



1. Muehler A, et al. Multi Scler Relat Disord. 2020:43:102129; 2. Vietor J, et al. J Med Chem. 2023;66(9):6391-6402; 3. Lopez-Garcia U, et al. Commun Chem. 2025;8(1):15; 4. Jafari, M E, et al. Presented at: ACTRIMS Forum 2026; Poster P317 / MS: multiple sclerosis; Nurr1: nuclear receptor-related 1; DHODH: dihydroorotate dehydrogenase; EAE: experimental autoimmune encephalomyelitis; BDNF: brain-derived neurotrophic factor; EBV: Epstein-Barr virus

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Nurr1 Is a Nuclear Receptor Involved in Neuroprotection



Nurr1 activation

- mediates neuronal survival and function
- prevents microglia/astrocyte-driven neurotoxicity in the brain

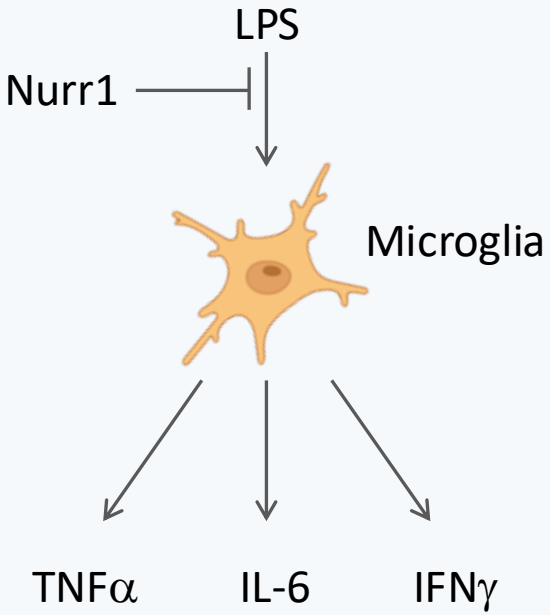
Vietor et al., Journal of Medicinal Chemistry 2023 66 (9), 6391-6402; Schiro et al., 2022, Frontiers in Neurology, adapted from Willems S, Merk D. J Med Chem. 2022;65(14):9548-9563

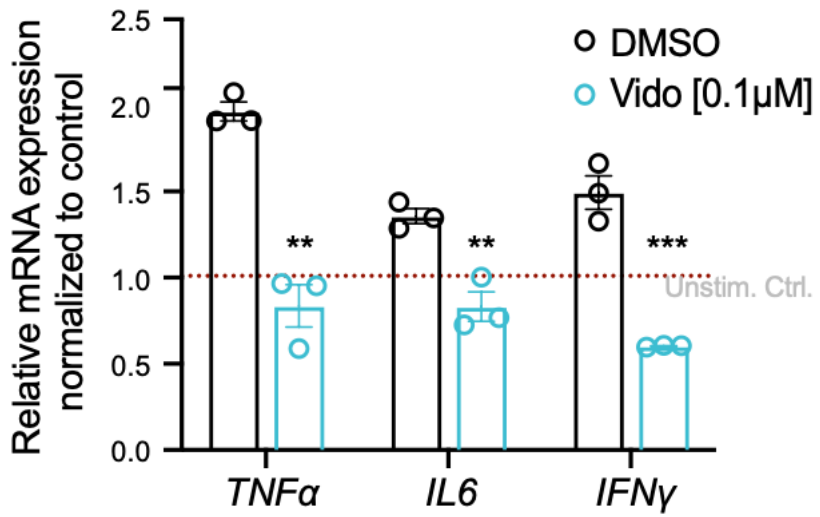
Nurr1: nuclear receptor-related 1; GDNF: glial cell line-derived neurotrophic factor; BDNF: brain-derived neurotrophic factor; RET: receptor tyrosine kinase; TH: tyrosine hydroxylase; VMAT2: vesicular monoamine transporter 2; SOD1: superoxide dismutase 1; COX5β: cytochrome c oxidase subunit 5 beta; NO: nitric oxide; ROS: reactive oxygen species; TNFα: tumor necrosis factor alpha; IL1β: interleukin-1 beta; NO: nitric oxide; ROS: reactive oxygen species

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Vidofludimus Calcium Reduced Microglia Activation

Nurr1 can prevent antigen-induced activation of microglia and subsequent production of pro-inflammatory cytokines in the brain. Vidofludimus calcium attenuated LPS-stimulated IL-6, TNFα and IFNγ production in human HMC3 microglial cells at low doses of 100 nM.

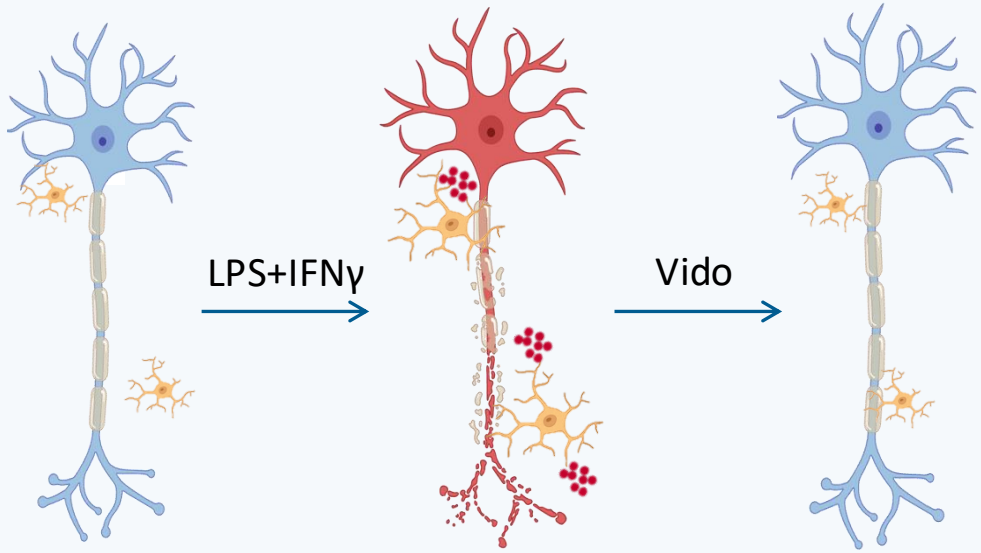




Unpublished data: Sun lab, City of Hope, Duarte; 2023; illustration created in BioRender.com / Nurr1: nuclear receptor-related 1; LPS: lipopolysaccharide; IL-6: interleukin-6; TNFα: tumor necrosis factor alpha; IFNγ: interferon gamma; HMC3: human microglial clone 3; mRNA: messenger ribonucleic acid; DMSO: dimethyl sulfoxide

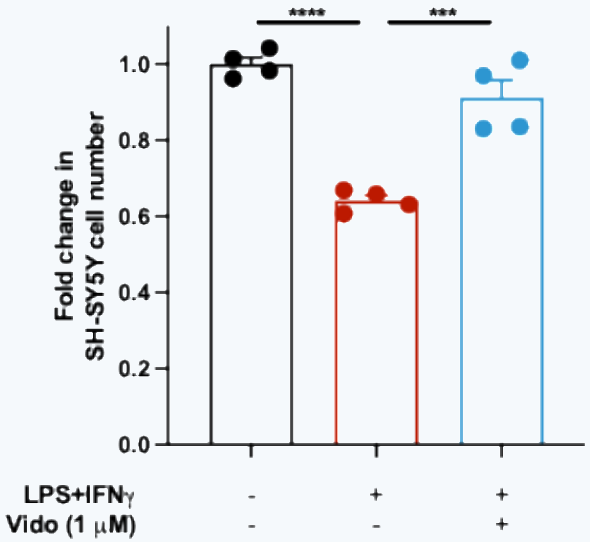
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Vidofludimus Calcium Increased Neuronal Viability Under Neuroinflammatory Condition (Neuron-Microglia Co-Culture)



Co-culture of activated microglia and neurons results in destruction of neurons.

Neuron-microglia co-culture



Vidofludimus calcium was associated with increased neuronal viability in inflammatory co-culture.

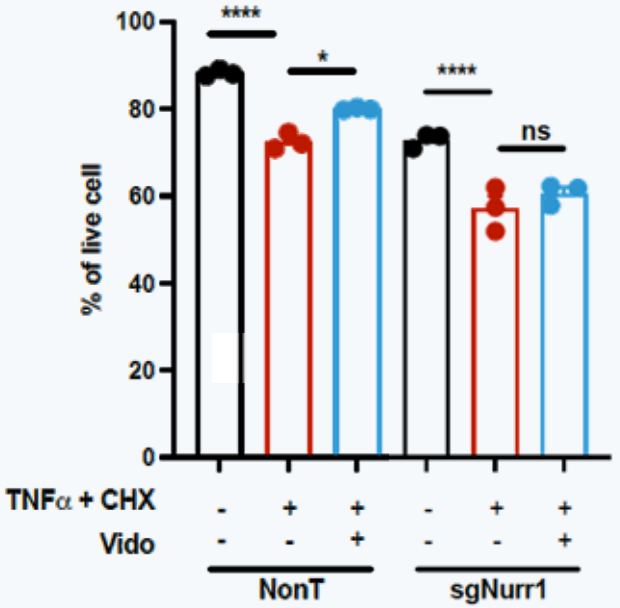
Performed at City of Hope, USA, Zuoming Sun

LPS: lipopolysaccharide; IFNγ: interferon gamma; SH-SY5Y: human neuroblastoma line

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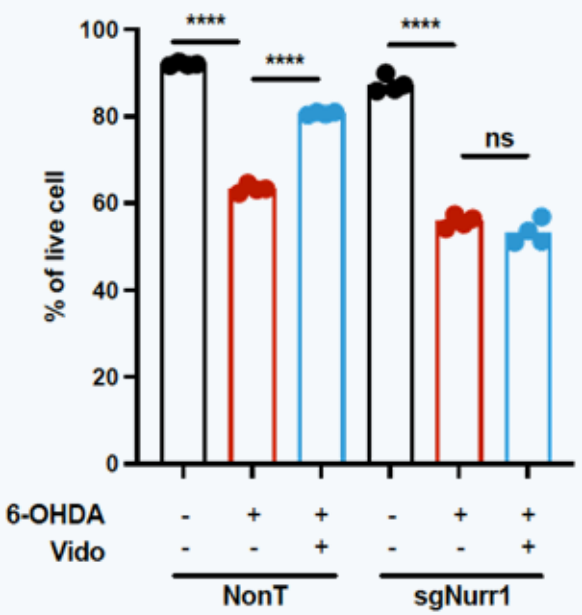
Vidofludimus-Associated Improved Neuronal Survival Requires Nurr1

TNFα+CHX



Control Nurr1 KD

6-OHDA



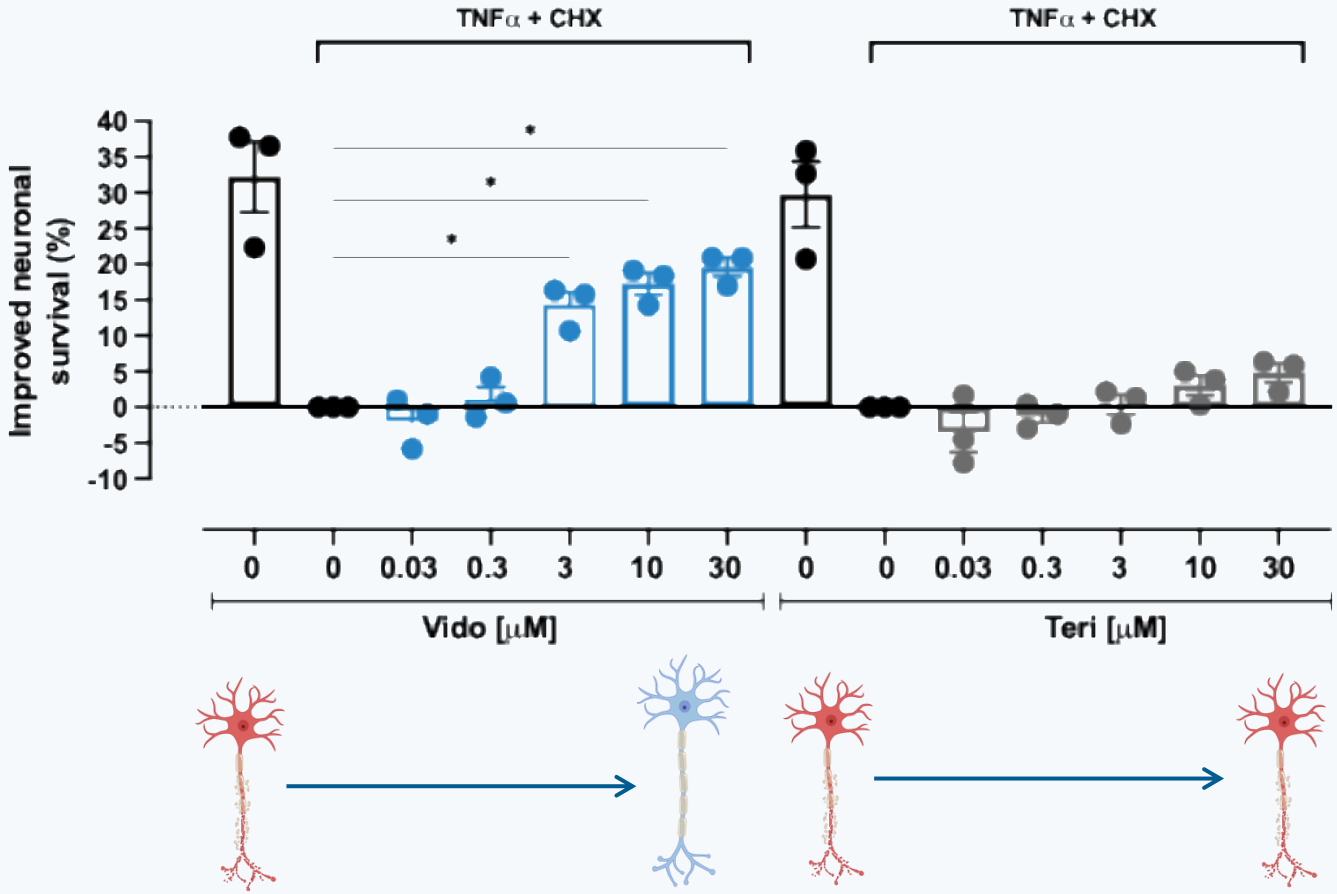
Control Nurr1 KD

CRISPR-mediated Nurr1 knockdown abolished the neuronal survival benefit of vidofludimus calcium under different models of apoptosis in SH-SY5Y line.

Performed at City of Hope, USA, Zuoming Sun; vidofludimus 1 uM / Nurr1: nuclear receptor-related 1; TNFα: tumor necrosis factor alpha; CHX: cycloheximide; 6-OHDA: 6-hydroxydopamine; NonT: non-targeted control; sgNurr1: single-guide RNA targeting Nurr1/Nr4a2; KD: kockdown; CRISPR: clustered regularly interspaced short palindromic repeats; SH-SY5Y: human neuroblastoma line

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Vidofludimus Calcium Improved Neuronal Survival Under Apoptotic Stress, Whereas Teriflunomide Did Not



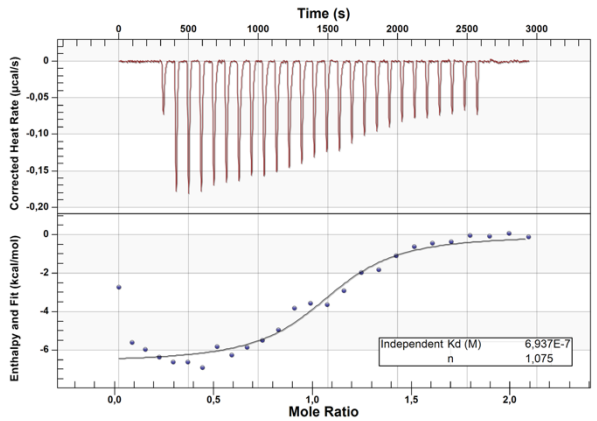
In this preclinical test system, teriflunomide did not significantly improve survival of neuronal cells.

Performed at City of Hope, USA, Zuoming Sun
TNFα: tumor necrosis factor alpha; CHX: cycloheximide

Is Every DHODH Inhibitor a Nurr1 Agonist? – NO!

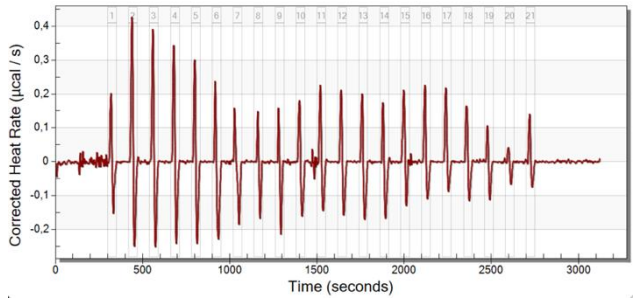
ITC

ISOTHERMAL TITRATION CALORIMETRY



Vidofludimus Calcium

→ Binding signal detected

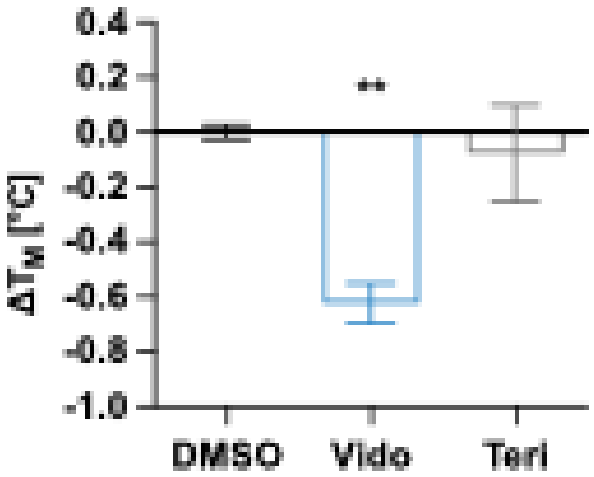


Teriflunomide

→ No measurable binding detected

DSF

DIFFERENTIAL SCANNING FLUORIMETRY



ΔT_M (melting temperature) shifts indicate ligand-Nurr1 interaction

Vidofludimus calcium induces a ΔT_M shift; teriflunomide does not

Performed at LMU, Munich, Daniel Merk; vidofludimus calcium, 1568 and 2054 (Immunic Nurr1 agonists), teriflunomide (DHODH inhibitor, approved as Aubagio® in MS), 4A7C301 (Nurr1 agonist, µM activity)
DHODH: dihydroorotate dehydrogenase; Nurr1: nuclear receptor related 1; ΔTM : change in protein melting temperature; DSMO: dimethyl sulfoxide

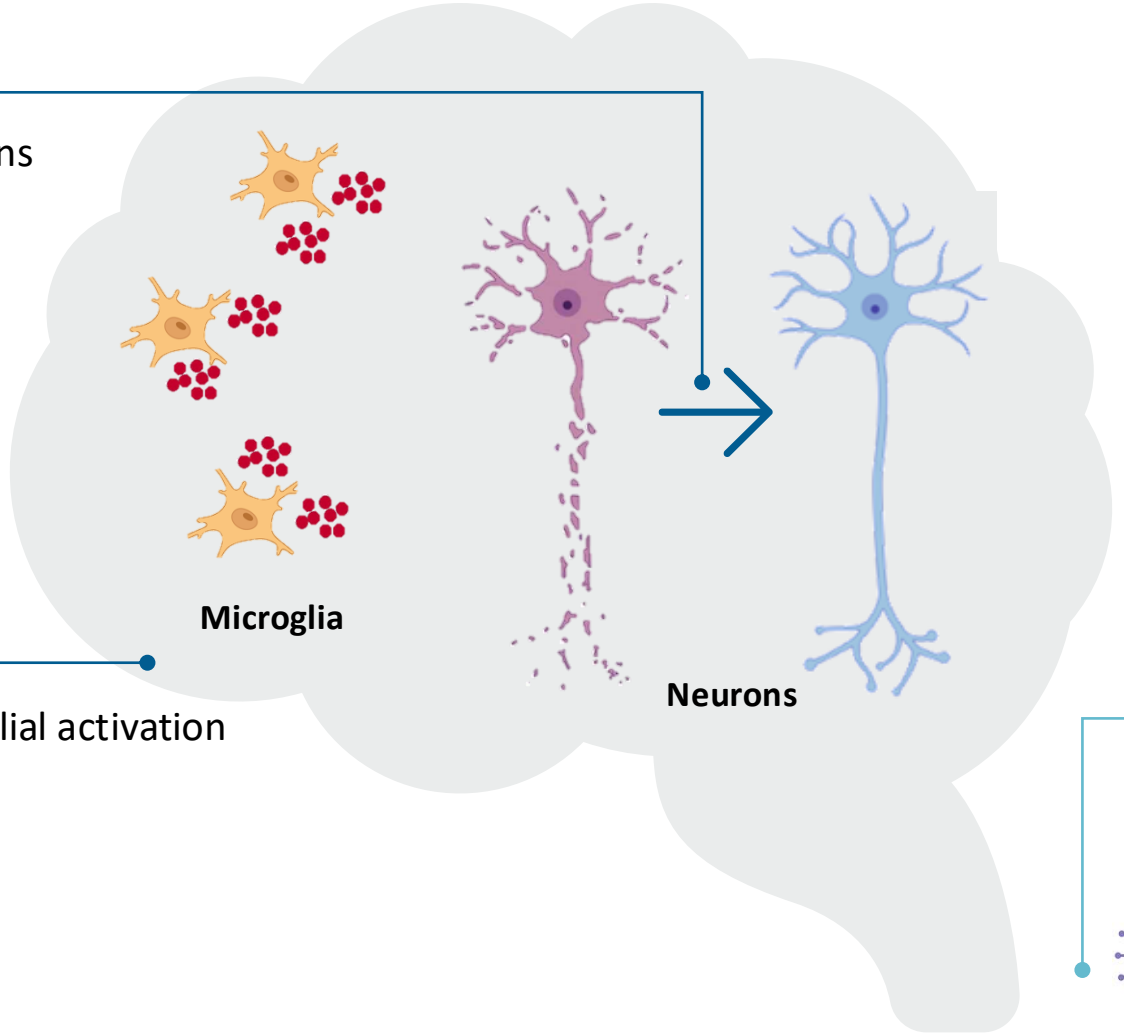
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Vidofludimus Calcium: Nurr1 Activation and Selective DHODH Inhibition

Improving survival of neurons

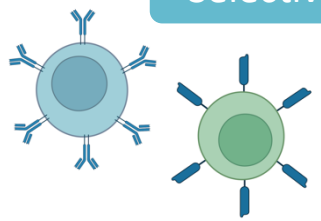
Direct Nurr1 Activation

Reducing neurotoxic microglial activation



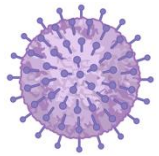
Targeting metabolically active T & B cells

Selective DHODH Inhibition



B & T cells

Inhibition of EBV-associated B-cell responses



Nurr1: nuclear receptor related 1; DHODH: dihydroorotate dehydrogenase; EBV: Epstein-Barr virus

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Expert Talk: Jiwon Oh, MD, PhD, FRCPC

Medical Director, Barlo Multiple Sclerosis Program
Waugh Family Chair in MS Research
Staff Neurologist, St. Michael's Hospital Scientist,
Keenan Research Centre of the Li Ka Shing Knowledge Institute
Associate Professor, Division of Neurology, University of Toronto

Expert Talk: Maria Pia Sormani, PhD

Professor of Biostatistics
University of Genoa, Italy

Phase 2 CALLIPER Trial of Vidofludimus Calcium in Progressive MS

Michael A. Panzara, MD, MPH I Chief Medical Officer

Progressive MS: Potential to Change Treatment Paradigm

Limited Treatment Options Available to Date With Many Patients Continuing to Worsen Despite Treatment

Progressive MS

~175K Diagnosed Patients in the U.S.[1,2]

- Key unmet needs remain, with limited treatment options available for patients with progressive MS.
- Compared with RRMS, progressive MS is clinically associated with greater symptom severity and functional impairment, higher rates of unemployment and hospitalization, greater economic burden and a more substantial impact on health-related quality of life.[3,4]
- Clinicians are increasingly focused on slowing disability progression and preserving neurological function beyond relapse control.
- High unmet need for targeted therapies with novel mechanisms that potentially address the underlying biology of progression.

- **New treatments** should tackle the processes responsible for the continuous accumulation of disability in progressive MS, rather than acute relapses.
- PIRA accounts for most disability progression in patients with progressive MS.

- **Vidofludimus calcium's Nurr1 mechanism** is targeted to preserve neurons and improve neuronal function.
- Initiation of a Phase 3 clinical trial in progressive MS based on the CALLIPER Phase 2 data is ongoing, with first-patient-enrolled expected in H1/2027.

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1. Multiple Sclerosis Disease Landscape and Forecast Research Report by Decision Resources Group Part of Clarivate 2. Immunic analysis 3.Gross HJ, Watson C. Neuropsychiatr Dis Treat. 2017;13:1349–1357
4. Chataway J, Murphy N, Khurana V, Schofield H, Findlay J, Adlard N. Curr Med Res Opin. 2021;37(6):995–1004
MS: multiple sclerosis; RRMS: relapsing-remitting MS; PIRA: progression independent of relapse activity; Nurr1: nuclear receptor-related-1

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Progression in MS Is Increasingly Seen as a Continuum of Common Underlying Pathological Processes

MS patients share qualitatively similar (but quantitatively different) pathological features regardless of clinical course

- Inflammation and neurodegeneration present at disease onset, regardless of progressive vs. relapsing onset
- Substantial proportion of disability progression independent of relapses (described as PIRA)

2024 revision of McDonald diagnostic criteria established a unified framework for diagnosis

- Single diagnostic criteria now applied using clinical, imaging, CSF findings to fulfill dissemination in space to establish MS diagnosis regardless of relapsing or progressive onset

Revision of MS disease course descriptors (Lublin-Reingold criteria) underway with a focus on these common underlying pathological processes rather than clinical descriptions

Therefore, perfect environment to move forward with a study design that incorporates these concepts to establish an effect on MS progression with a potentially neuroprotective compound

MS: multiple sclerosis; PIRA: progression independent of relapse activity; CSF: cerebrospinal fluid

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CALLIPER: Phase 2 Clinical Trial in Progressive MS

Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial (NCT05054140)

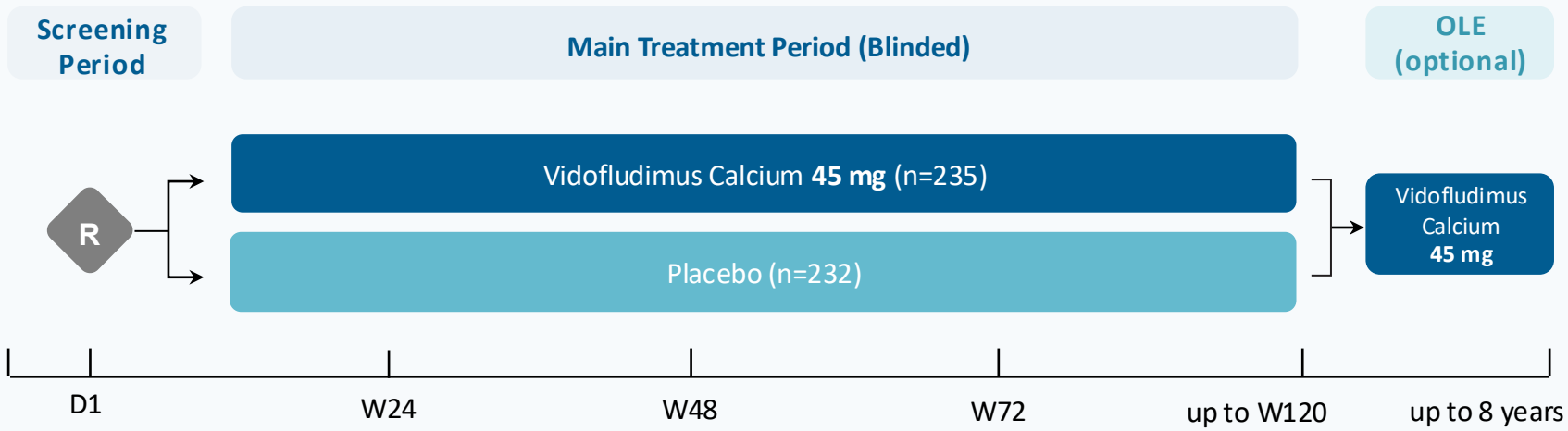
467 Adult Patients Randomized, >340 Patients Continuing in OLE*

Inclusion Criteria

- Patients aged 18 to 65 years
- PPMS or SPMS diagnosis (revised McDonald criteria 2017)
- EDSS score at screening between 3.0 and 6.5
- No relapse in the last 24 months before randomization
- Evidence of disability progression

Disease Subtypes at Baseline

- naSPMS: 57.4% (n=268)
- PPMS: 32.5% (n=152)
- aSPMS: 10.1% (n=47)



>70 sites in North America, Western, Central and Eastern Europe

Endpoints

Primary:

Annualized rate of percent brain volume change (PBVC) during main treatment period up to 120 weeks

Secondary include:

Time to 24-week confirmed disability worsening, including composite and EDSS-based measures

Exploratory:

Clinical and MRI endpoints

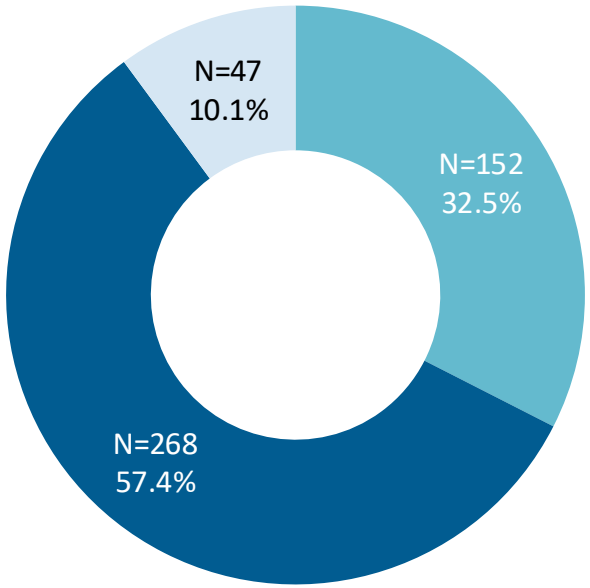
* as of May 2026 / MS: multiple sclerosis; PPMS: primary progressive MS; SPMS: secondary progressive MS; na: non-active; a: active; OLE: open-label extension; EDSS: Expanded Disability Status Scale; MRI: magnetic resonance imaging; R: randomization; D: day; W: week

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CALLIPER: Patient Demographics and Baseline Characteristics

Total Study Population of 467 Enrolled Patients

Progressive Disease Subtypes



Total N=467

- Primary progressive MS
- Non-active secondary progressive MS
- Active secondary progressive MS

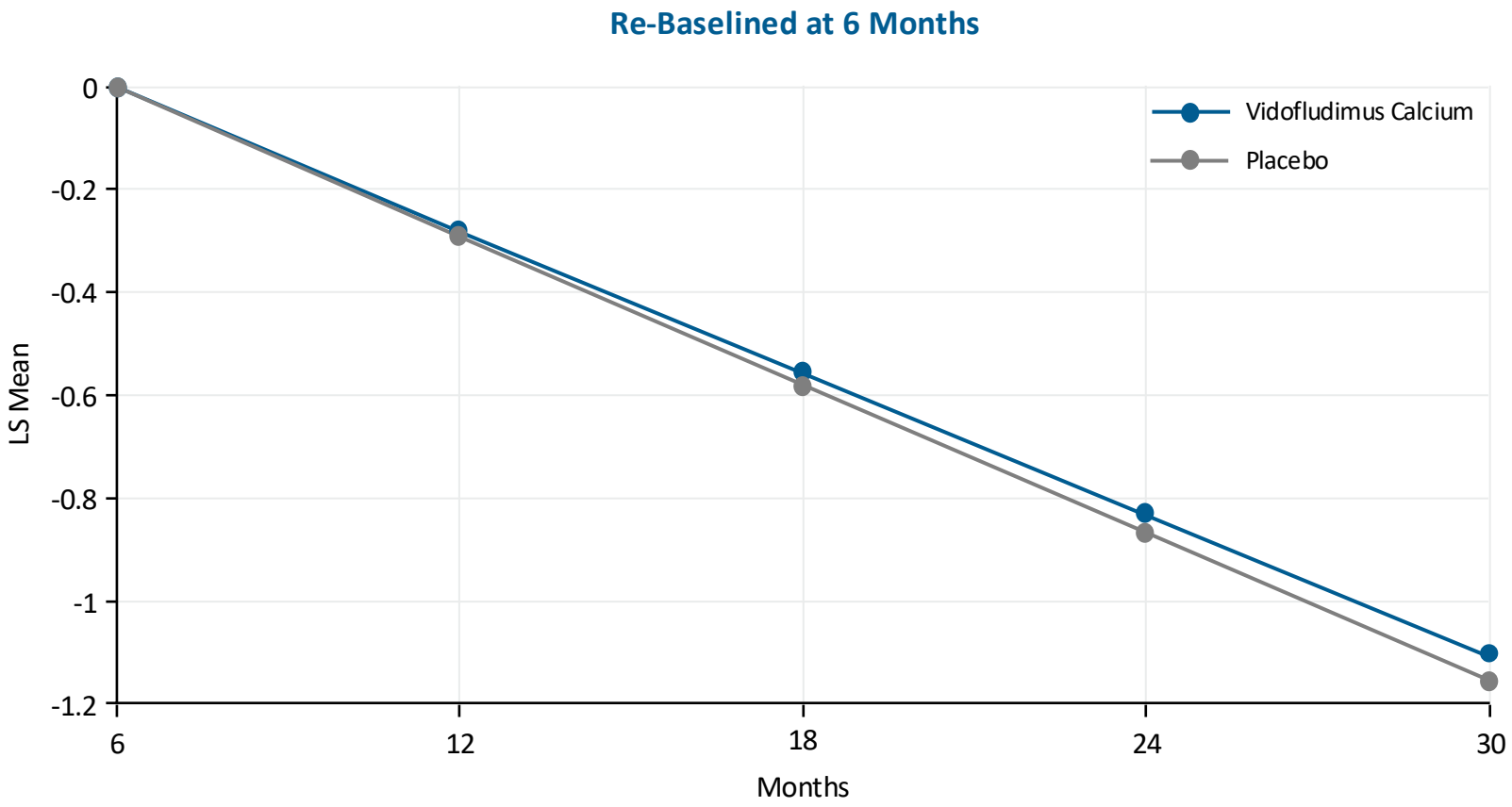
Baseline Patient Characteristics

Age [years], median (min-max)	**51.0 (21-65)**
Gender (n and % female)	**302 (64.7%)**
Race (n and % White)	**460 (98.7%)**
BMI [kg/m^2], median (min-max)	**24.85 [14.0 - 46.6]**
SDMT [points], median (min-max)	**40 [8-80]**
EDSS at Visit 1, median (min-max)	**5.5 [2.5-6.5]**
MS relapses during last 24 months, median (min-max)	**0.0 [0-1]**
Gd+ lesions at baseline MRI (%)	**16.3%**
Treatment duration, median	**589 days**

Baseline characteristics initially assessed by the investigators when patients entered screening based on history. These data summarize the disease subtype as assessed per diagnosis at screening visit 1. A small number of patients changed their subtype (in particular from non-active to active disease) due to events during the screening period. Definition non-active SPMS (according to CALLIPER protocol): no evidence of relapse in the last 24 months before randomization, AND patients showing no evidence of Gd+ MRI lesions in the brain or spinal cord in the last 12 months; definition non-relapsing SPMS: no evidence of relapse in the last 24 months before randomization / BMI: body mass index; SDMT: Symbol Digit Modalities Test; EDSS: Expanded Disability Status Scale; Gd+: gadolinium-enhancing; MRI: magnetic resonance imaging; N: number of patients evaluated

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CALLIPER: Statistical Significance Not Achieved on Primary PBVC Endpoint at Month 30, Although Encouraging Trends on Regional Atrophy



Primary Endpoint: Relative difference of annual PBVC rate at 30 months: 4.7%; 95% CI, -0.285 to 0.379; *P*=0.78

Regional atrophy differences at 30 months favored vidofludimus calcium, although statistical significance not achieved:

- **15.7%** for gray matter
- **10.0%** for cortical gray matter
- **35.0%** for thalamus

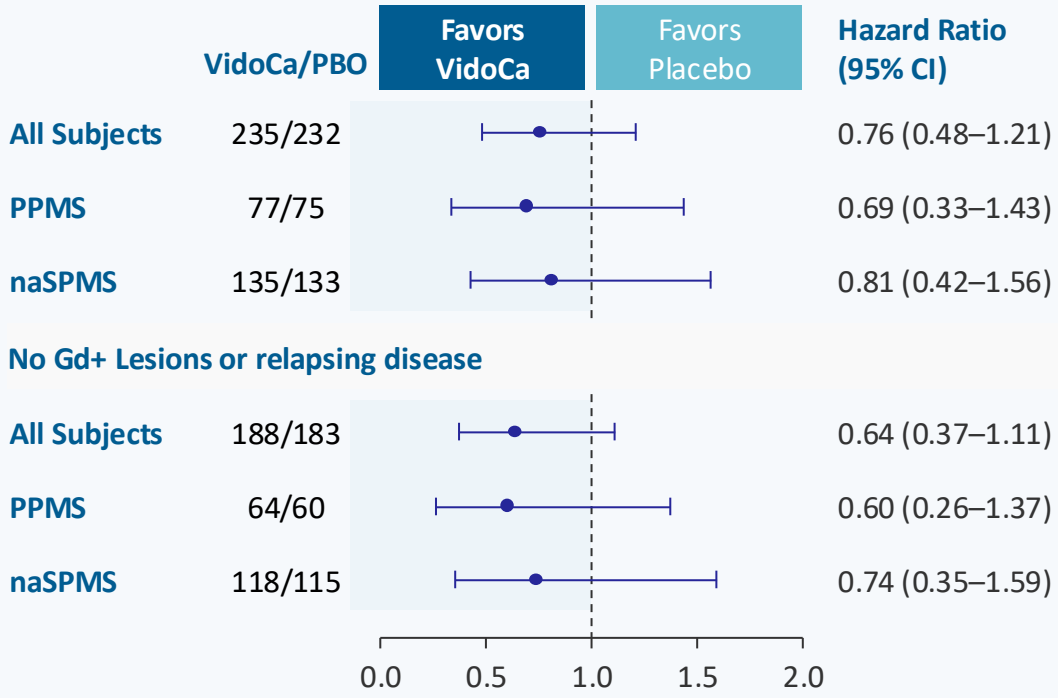
Intent-to-treat patient population (n=467). The annualized rate of PBVC is the population slope within treatment group. The effect estimate of the treatment difference is equivalent to the difference between annualized rates. For the primary estimate, data collected up to 30 days after the onset date of a postbaseline relapse or between the start and 30 days after the end of any rescue medication intake were set to missing. For the calculation of LS means, patients with a valid baseline magnetic resonance image are considered. Missing values are calculated based on the analysis set.

Fox R, et al. Oral presentation: ECTRIMS 2025; 24-26 September 2025; Barcelona, Spain. #O024 / PBVC: Percentage Brain Volume Change; LS: least square

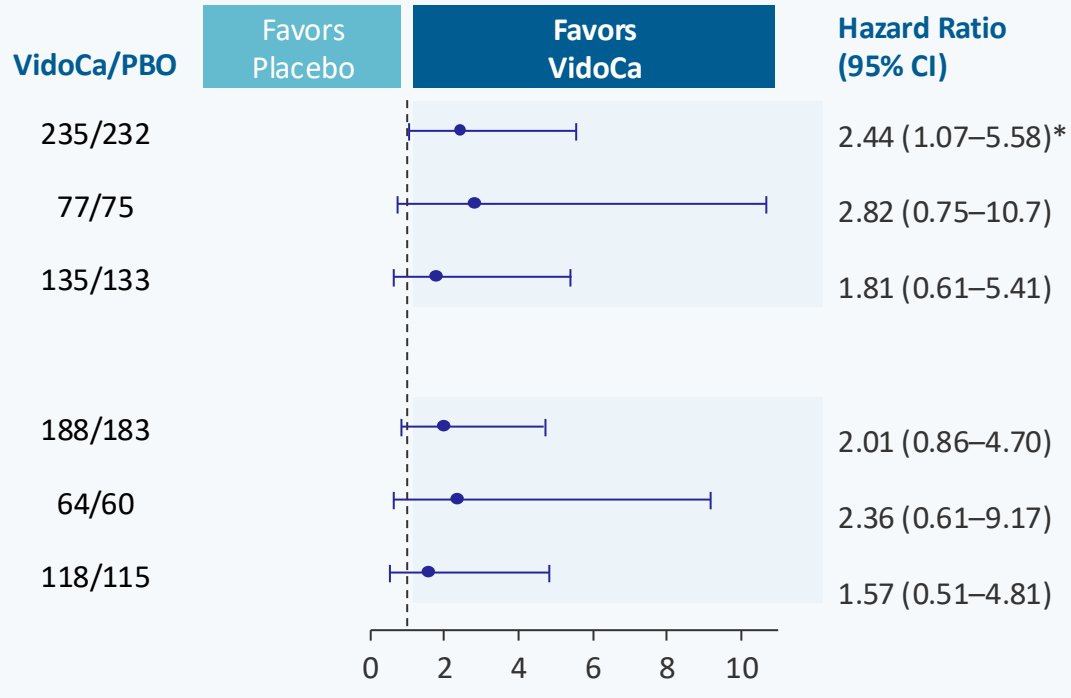
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CALLIPER: Favorable Trends Across Exploratory Disability Outcomes Through Week 120 with a Nominally Significant Effect in CDI

24wCDW



24wCDI



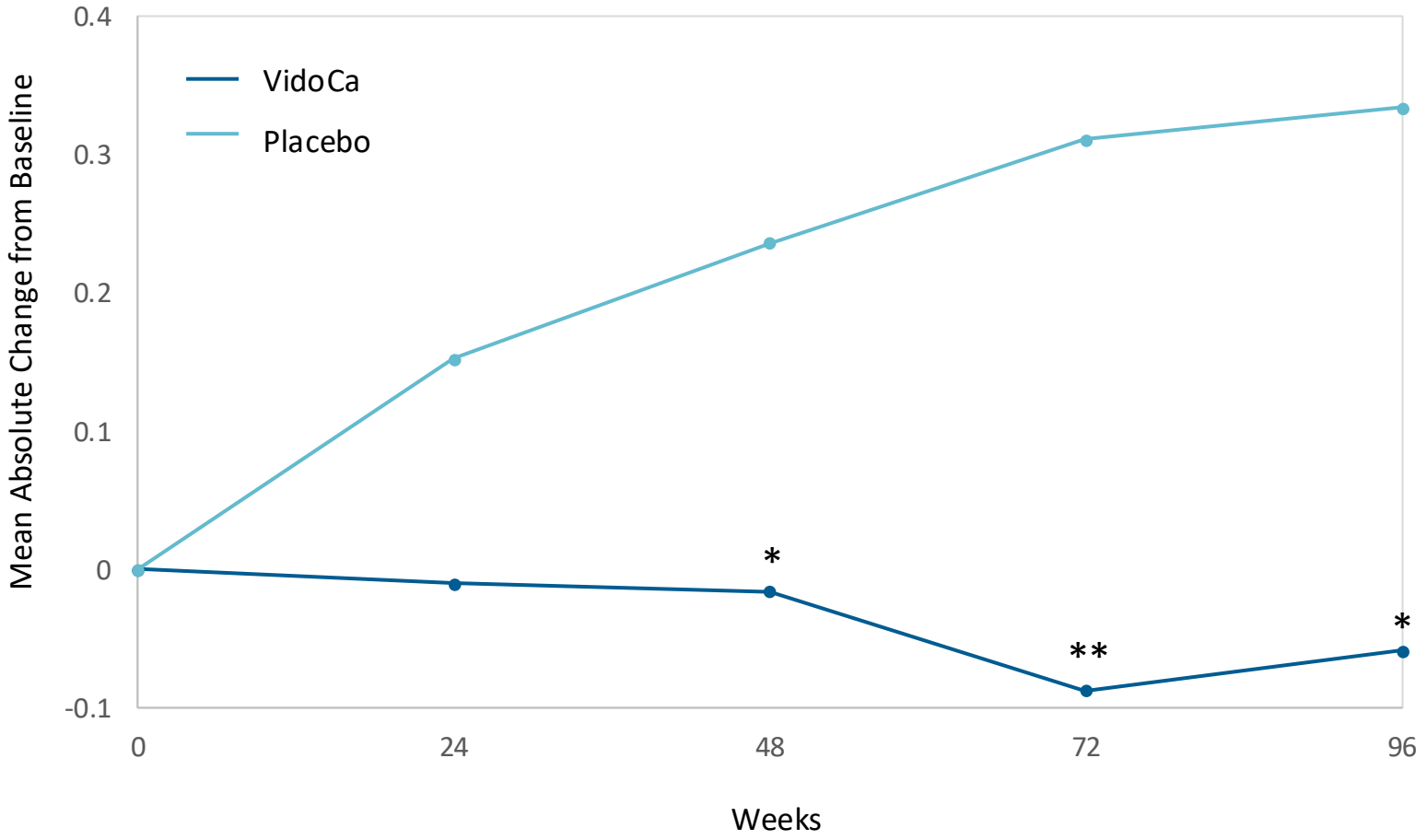
Participants treated with vidofludimus calcium had favorable trends in CDW and a nominally significant effect in CDI (all subjects, *p=0.034). These trends were seen across subgroups.

24wCDW with applied imputation (performed as sensitivity analysis) for participants who discontinued the double-blind main treatment period due to disease progression and who had already achieved 12wCDW confirmation. 24wCDW is defined as patients with worsening in EDSS sustained over at least 22 weeks (154 days). Full CALLIPER population: total of 73 events. / Fox R, et al. Oral presentation: ECTRIMS 2025; 24-26 September 2025; Barcelona, Spain. #O024 / MS: multiple sclerosis; PPMS: primary progressive MS; naSPMS: non-active secondary progressive MS; 24wCDW: 24-week confirmed disability worsening; 24wCDI: 24-week confirmed disability improvement; VidoCa: vidofludimus calcium; PBO: placebo; CI: confidence interval; Gd+: gadolinium-enhancing

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CALLIPER: Exploratory MRI Endpoint Through Week 96

Mean Volume Change in New/Enlarging T2 Lesions



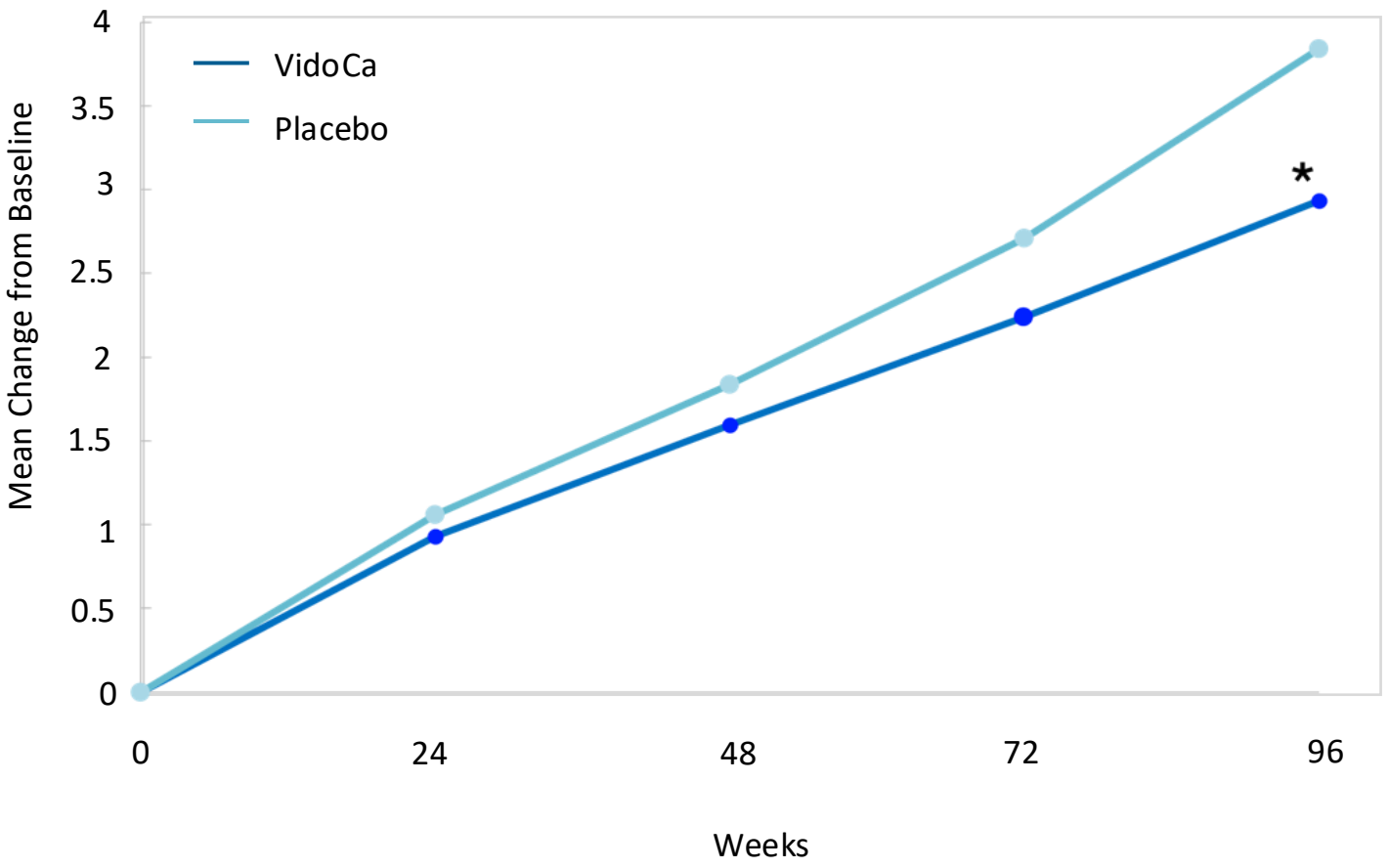
- Mean absolute volume of new/enlarging T2 lesions through week 96: A nominal significant reduction in T2 lesion volume was seen at weeks 48, 72, and 96 in the vidofludimus calcium arm compared to placebo (nominal *p<0.05, **p<0.005).
- Fewer patients on vidofludimus calcium had any new/enlarging T2 lesions at week 72 (18.5% vs 30.0%) and at week 96 (41.2% vs 50.2%).

Number of patients included in arithmetic mean change calculation (in cm^3): Baseline 466 (VidoCa 234, placebo 232), W24 436 (VidoCa 217, Placebo 219), W48 409 (VidoCa 206, placebo 203), W72 369 (VidoCa 189, placebo 180), W96 198 (VidoCa 103, placebo 95). Ranked ANOVA test with factors for treatment and stratification factors used at randomization and baseline value as a continuous covariate. The test and associated *p* value for the test of row mean differences is presented. / Sciacca, et al. Poster presented at: ACTRIMS Forum 2026. Poster P1 30 / MRI: magnetic resonance imaging; VidoCa: vidofludimus calcium

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CALLIPER: Exploratory MRI Endpoint Through Week 96

Mean Change from Baseline in Number of Slowly Expanding Lesions (SELs)



- The mean number of newly detected SELs increased over time in both groups but was lower with vidofludimus calcium than placebo throughout 96 weeks.
- At week 96, least-square mean SEL count was 2.935 with vidofludimus calcium versus 3.840 with placebo (nominal $p<0.05$).

Least Square Mean Number of SELs Per MRI Examination		
Weeks	**Vidofludimus Calcium**	Placebo
Baseline	0	0
24	0.932	1.060
48	1.597	1.837
72	2.239	2.711
96	2.935	3.840

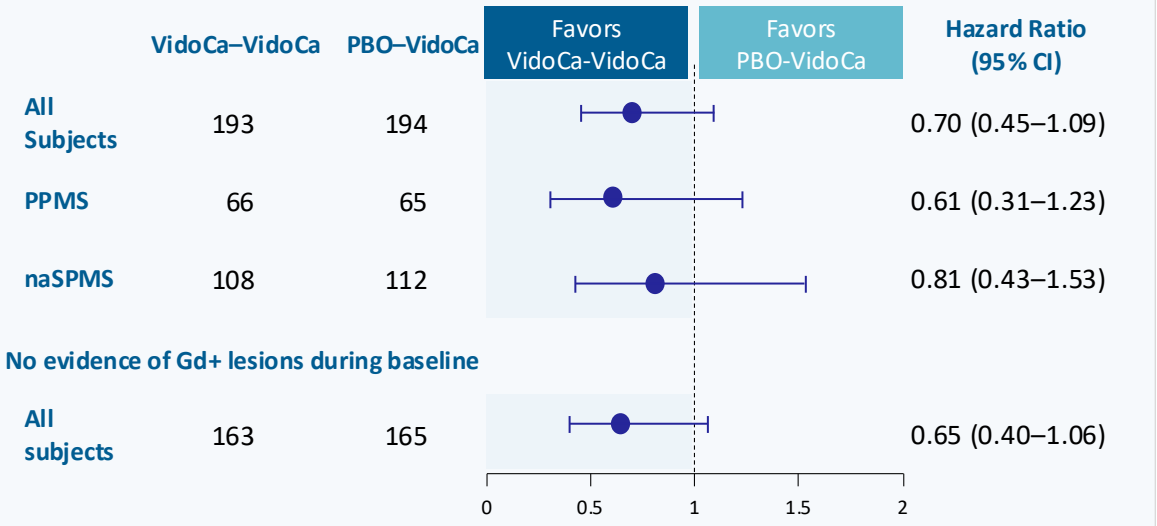
Number of patients included: baseline 418 (VidoCa 209, placebo 209), W24 411 (VidoCa 204, placebo 207), W48 401 (VidoCa 200, placebo 201), W72 360 (VidoCa 183, placebo 177), W96 196 (VidoCa 103, placebo 93). Mixed model for repeated measures (MMRM) estimates are adjusted for stratification factors used at baseline randomization. 2-sided *p* value is presented. / Sciacca, et al. Poster presented at: ACTRIMS Forum 2026. Poster P130 / MRI: magnetic resonance imaging; SEL: slowly expanding lesions; VidoCa: vidofludimus calcium

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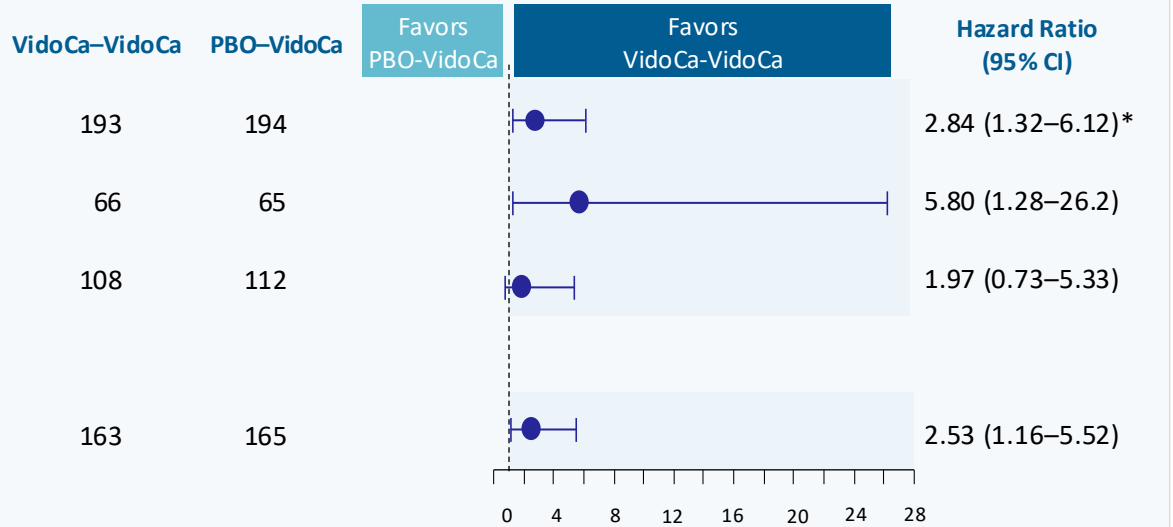
CALLIPER: Favorable Trends Across Exploratory Disability Outcomes Maintained Into Open-Label Extension

Exploratory 24-Week CDW and CDI Outcomes by Subgroup Through OLE Cut-off

24wCDW – OLE ITT



24wCDI– OLE ITT

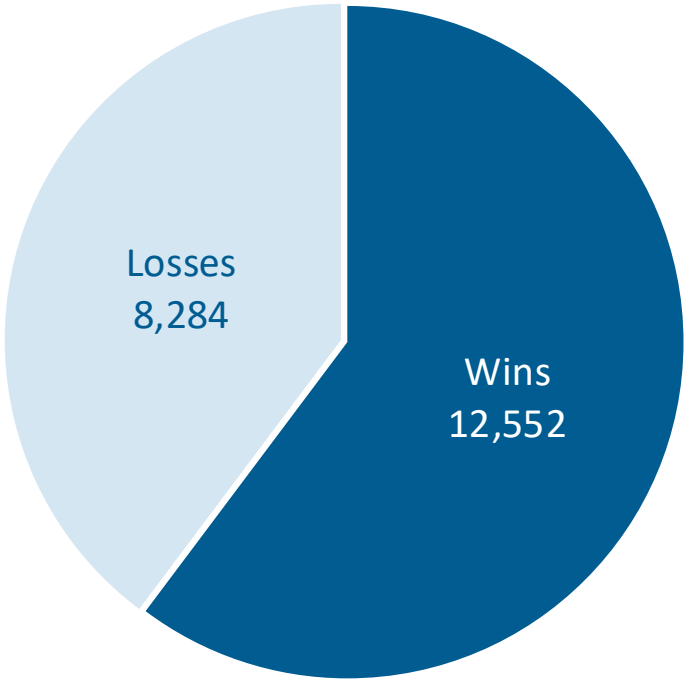


Favorable disability trends on CDW and CDI seen in the MT were sustained in the OLE, with a nominally significant effect in CDI seen in participants in the vidofludimus calcium-vidofludimus calcium arm compared to the PBO-VidoCa arm (all subjects, *p=0.0075).

Fox R, et al. Poster presentation: ECTRIMS 2026; 21-23 October 2026; Toronto. P0387 / MS: multiple sclerosis; PPMS: primary progressive MS; naSPMS: non-active secondary progressive MS; 24wCDW: 24-week confirmed disability worsening; 24wCDI: 24-week confirmed disability improvement; OLE: open-label extension; ITT: intent-to-treat; VidoCa: vidofludimus calcium; PBO: placebo; CI: confidence interval; Gd+: gadolinium-enhancing

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Net Clinical Benefit: Vidofludimus Calcium Treated Patients Were 1.5x More Likely to Have a Beneficial Disability Outcome



Total Pairs	Wins	Losses	Ties	Win %	Loss %	Tie %	Win Ratio
54520	12552	8284	33684	23.02%	15.19%	61.78%	1.51

WIN RATIO

$$WR = \frac{12{,}552 \text{ (wins)}}{8{,}284 \text{ (losses)}} = 1.51$$

Nominal p=0.042

In 54,520 pairs of patients, treatment with vidofludimus calcium resulted in more wins on CDW and/or CDI as compared to the placebo arm, suggesting more favorable outcomes on disability after vidofludimus calcium treatment.

WR: win ratio; CDW: confirmed disability worsening; CDI: confirmed disability improvement

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CALLIPER: Favorable Safety and Tolerability Profile Through Week 120

Five Most Common TEAEs	Placebo (n=232)	45 mg Vidofludimus Calcium (n=235)
Urinary tract infection	36 (15.5)	39 (16.6)
Headache	16 (6.9)	10 (4.3)
Back pain	17 (7.4)	9 (3.8)
Fall	11 (4.7)	9 (3.8)
Upper respiratory infection	11 (4.7)	15 (6.4)

ALT Laboratory Findings

Threshold	Placebo (n=232)	45 mg Vidofludimus Calcium (n=235)
ALT >3×ULN	6 (2.6%)	7 (3.0%)
ALT >5×ULN	4 (1.7%)	2 (0.9%)
ALT >10×ULN	4 (1.7%)	1 (0.4%)

AST Laboratory Findings

Threshold	Placebo (n=232)	45 mg Vidofludimus Calcium (n=235)
AST >3×ULN	5 (2.2%)	5 (2.2%)
AST >5×ULN	5 (2.2%)	1 (0.4%)
AST >10×ULN	1 (0.4%)	1 (0.4%)

- No new safety signals observed during main treatment period through 120 weeks
- Comparable rates of TEAEs (69.4% vs. 68.5%) and SAEs (8.1% vs. 6.5%) for vidofludimus calcium versus placebo
- No Hy's Law cases observed
- Overall, 45 mg vidofludimus calcium showed a similar safety and tolerability profile versus placebo

Hy's Law cases are defined as liver enzyme elevation of greater than 3xULN with concurrent elevation of serum total bilirubin greater than 2xULN.
Fox R, et al. Oral presentation: ECTRIMS 2025; 24-26 September 2025; Barcelona, Spain. #O024
ALT: alanine aminotransferase; AST: aspartate aminotransferase; TEAE: treatment-emergent adverse event; SAE: serious adverse event; ULN: upper limit of normal reference range

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CALLIPER: Low Treatment Discontinuations Through Week 120

	Treatment Discontinuations	
	Placebo	45mg Vidofludimus Calcium
Treatment period	120 weeks	120 weeks
Discontinuation due to progression	39 (16.8)	27 (11.5)
Discontinuation for other reasons	38 (16.4)	41 (17.5)
Entered open-label extension	194	193

- 82.8% (387/467) of trial participants elected to enter the open-label extension.
- During the main treatment period, which extended to 120 weeks, participants had the option to switch to 45 mg of vidofludimus calcium from placebo (or continue vidofludimus calcium if in the treatment arm) on or after week 72 and continue into the open-label extension.

Immunic THERAPEUTICS

Data on file, unpublished data

PROTECT-MS

Multicenter, Randomized, Double-blind, Placebo-controlled, Phase 3 Trial to Evaluate Efficacy, Safety, and Tolerability of IMU-838 (Vidofludimus Calcium) in Participants with Progressive Multiple Sclerosis

PROTECT-MS Study Population

PROTECT-MS will evaluate the spectrum of progressive MS by enrolling people with non-active **SPMS** and **PPMS**

Key Inclusion Criteria:

- \+ Age 18-65
- \+ Non-active SPMS or PPMS
- \+ No disease activity (relapses or new MRI lesions) in the prior 2 years
- \+ Disability progression documented in the prior year
- \+ EDSS 3.0-6.5
- \+ Appropriate washout from other disease modifying therapies (at least 6 months for anti-CD20 therapy)

- – No exclusions due to drug-drug interactions or use of antiplatelet/anticoagulant treatment

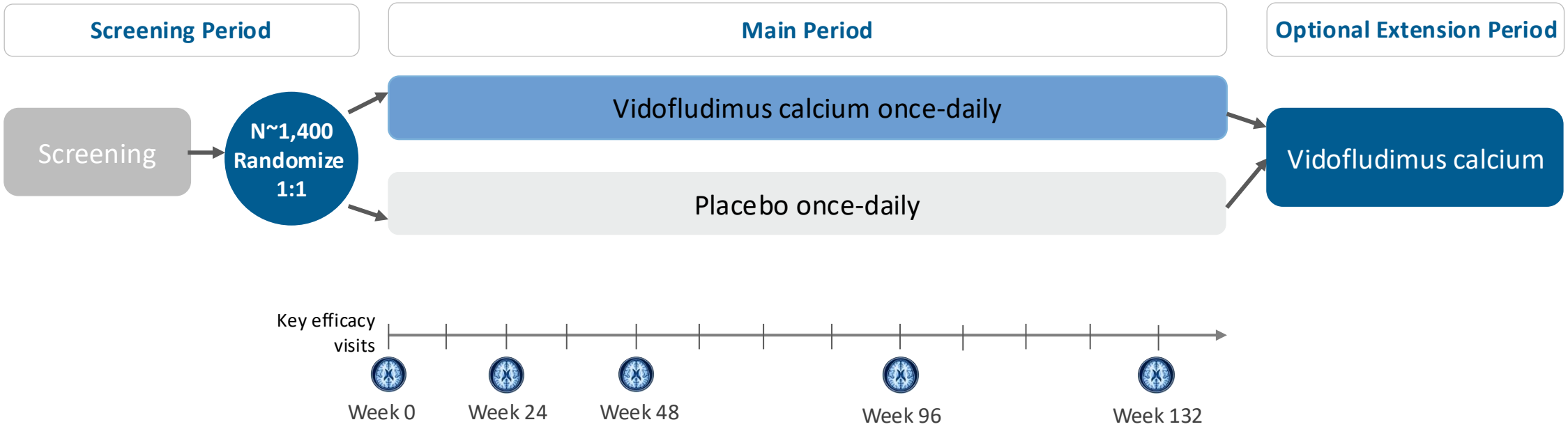
Immunic THERAPEUTICS

Study design is not final and is subject to change.
MS: multiple sclerosis; SPMS: secondary progressive MS; PPMS: primary progressive MS; MRI: magnetic resonance imaging; EDSS: Expanded Disability Status Scale

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PROTECT-MS Study Design

Key Objective:
To determine if vidofludimus calcium impacts disability progression in people with progressive MS



- Stratify randomization by progressive MS subtype and EDSS
- Study visits are every 3 months
- Primary analysis will occur when the required number of disability events have occurred; duration of study participation is variable
- Interim analyses will assess for futility, adapt the sample size, and potentially enable early stopping due to efficacy

Immunic THERAPEUTICS

Study design is not final and is subject to change.
MS: multiple sclerosis; EDSS: Expanded Disability Status Scale

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PROTECT-MS Study Endpoints

Primary Endpoint: Time to 24-Week Confirmed Disability Worsening (CDW) or 9HPT

Secondary and Exploratory Endpoints

Disability	Imaging	PROs
Confirmed disability improvement (CDI)	Slowly expanding lesions (SEL)	Quality of life
Net clinical benefit (impact on CDW & CDI)	Paramagnetic rim lesions (PRL)	Walking
9HPT	Brain & thalamic volume	Fatigue
T25FWT	Number and volume of new/enlarging T2 lesions	Treatment satisfaction
SDMT		Employment
Stride velocity (via wearable)		Caregiver burden

Standard Safety Assessments Will Be Performed

Immunic THERAPEUTICS

Study design is not final and is subject to change. / MS: multiple sclerosis; CDW: confirmed disability worsening; CDI: confirmed disability improvement; 9HPT: 9-Hole Peg Test; T25FWT: Timed 25-foot Walk Test; SDMT: Symbol Digit Modalities Test; PROs: Patient-Reported Outcomes

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Vidofludimus Calcium in Progressive MS: Treatment Paradigm Changing Potential

Strong Imaging and Exploratory Disability Phase 2 Efficacy Signals*

Favorable and Consistent Safety Profile at 45 mg Dose

Positive Phase 2 Signals in Non-Active Patients Supporting Nurr1-Linked Biology

› Initiation of Phase 3 clinical trial in progressive MS ongoing, with first-patient-enrolled expected in H1/2027

Immunic THERAPEUTICS

* Primary percent brain volume change endpoint not met
MS: multiple sclerosis; Nurr1: nuclear receptor-related-1

Commercial Opportunity for Vidofludimus Calcium in Progressive MS

Jason Tardio I President & Chief Operating Officer

The Significant Unmet Need in Progressive MS Creates a Compelling Opportunity for Differentiated Therapies

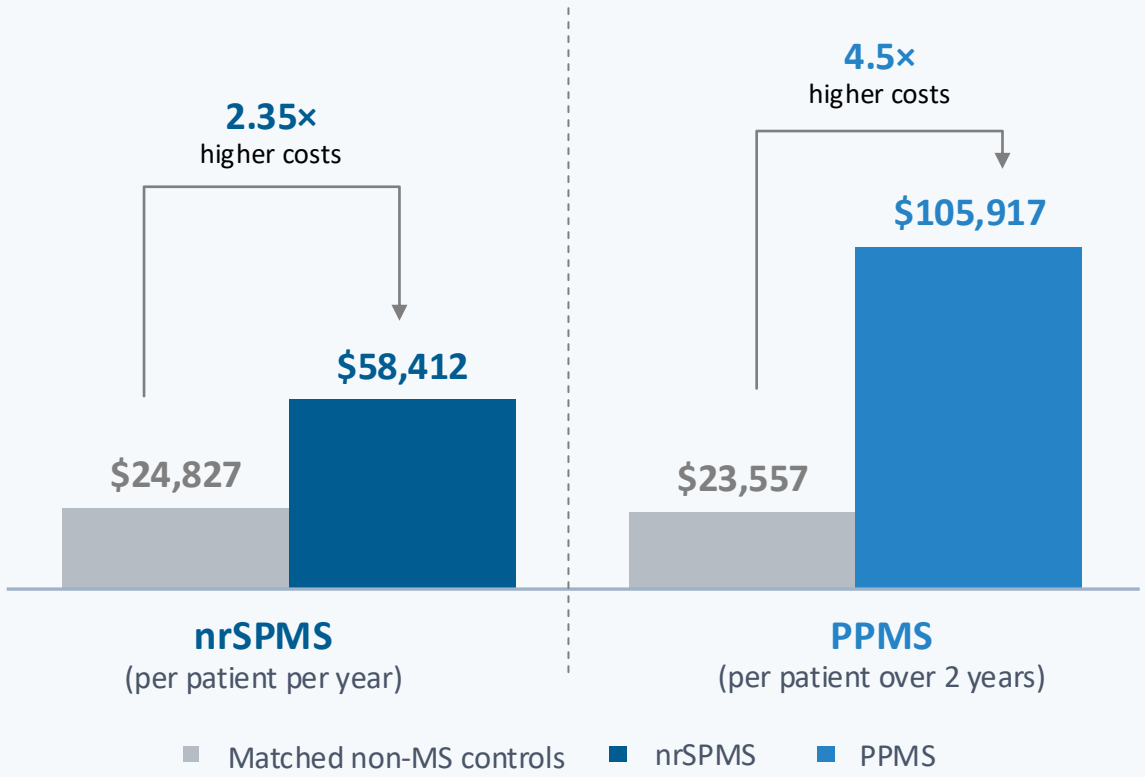
Substantial Unmet Need	Progressive MS (SPMS and PPMS) affects ~25% of people diagnosed with MS [1] and remains a major area of unmet need, with irreversible disability accumulation, high patient and caregiver burden, and significant economic impact.
Inadequate Current Options	Available therapies provide only modest benefit and face important limitations, including limited efficacy in non-active disease, long-term safety and tolerability concerns, and regulatory restrictions.
Clear Stakeholder Demand	Neurologists consistently identify progressive MS as the most important area for new, effective and safe treatment options.
An Evolving Landscape	A number of emerging therapies (e.g., BTK inhibitors) are targeting progression, but each faces meaningful efficacy, safety and regulatory challenges, reinforcing the opportunity for differentiated approaches.
A Meaningful Opportunity	There is a compelling opportunity in a multi-billion-dollar market to deliver a therapy that meaningfully slows disability progression with a favorable long-term safety and tolerability profile, particularly for older and more vulnerable patients.

Developing new DMTs for progressive MS continues to represent one of the biggest remaining unmet needs in MS

1. Patient and market size numbers sourced via internal Immunic analysis and 2024 Multiple Sclerosis Landscape and Forecast report by Decision Resources Group Part of Clarivate; 2. 2024 Multiple Sclerosis Landscape and Forecast report by Decision Resources Group Part of Clarivate. Total market size was determined by the number of diagnosed cases multiplied by current net pricing for DMTs in each region.
MS: multiple sclerosis; SPMS: secondary progressive MS; PPMS: primary progressive MS; DMT: disease-modifying therapy

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Progressive MS Places a Substantial Economic Burden on Patients, Families and the Healthcare System



Worsening disability in nrSPMS and PPMS drives higher healthcare utilization, greater need for supportive care and long-term services, and increased indirect costs such as loss of productivity and informal caregiving.

Key Drivers of Economic Impact in Progressive MS

Healthcare utilization
More frequent hospitalizations, physician visits, rehabilitation and long-term care.

Medical and supportive care
Use of mobility equipment, home modifications and assistive services.

Loss of productivity
Reduced employment, presenteeism and premature retirement.

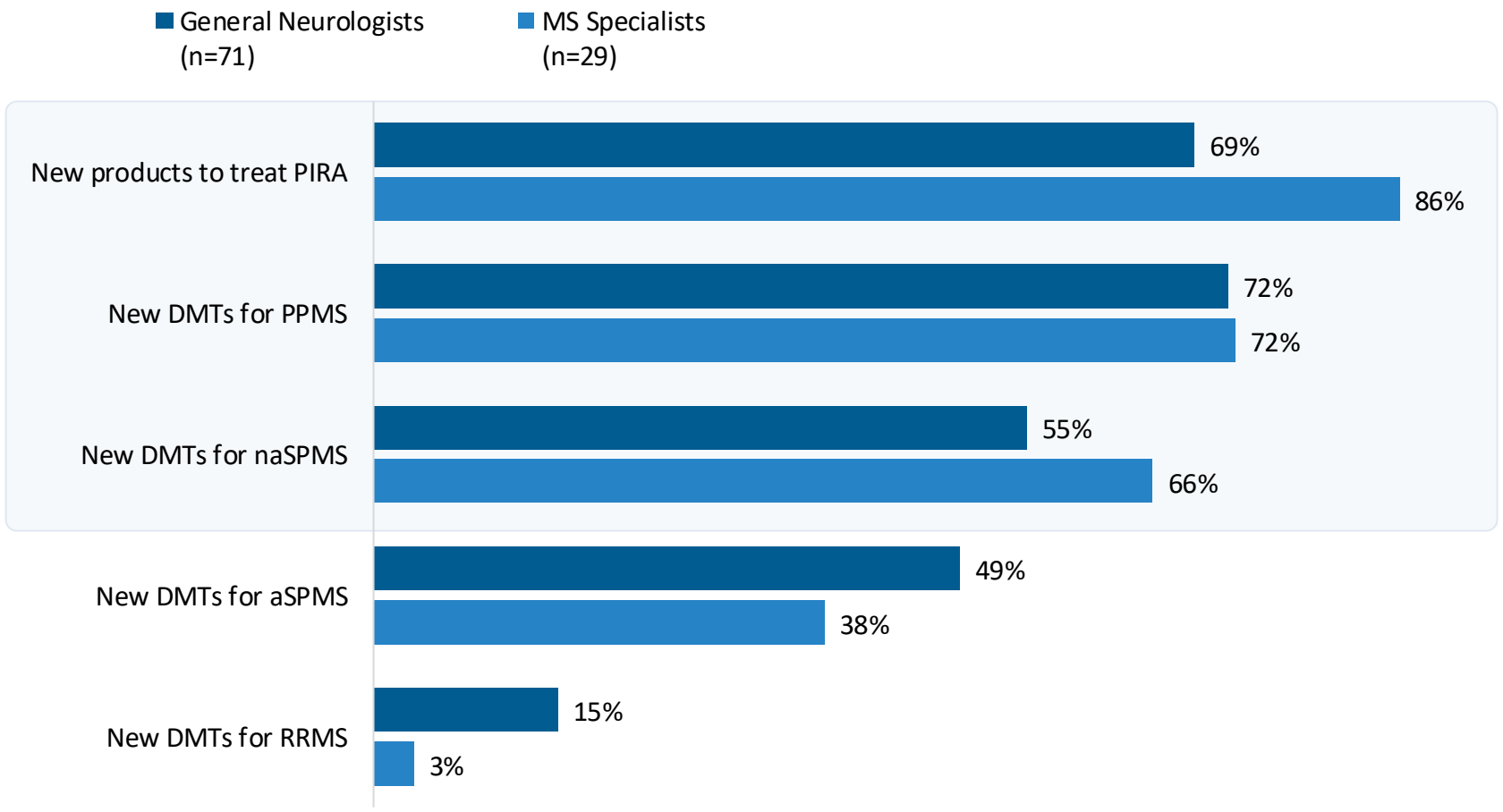
Informal caregiving
Significant time and out-of-pocket costs for family and caregivers.

Increasing costs with disability
Economic burden rises substantially as disability accumulates.

1. Greene N, et al. Neurology. 2024;102(7 Suppl 1):3573; 2. Understanding the Burden of Illness in People with Primary Progressive Multiple Sclerosis in the United States: A Matched-Cohort Study. Research poster. 2025; 3. Chataway J, et al. Curr Med Res Opin. 2021;37(6):995–1004; 4. Oreja-Guevara C, et al. BMC Health Serv Res. 2025;25:525
MS: multiple sclerosis; SPMS: secondary progressive MS; PPMS: primary progressive MS; nr: non-relapsing

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Neurologists Highlight the Critical Need for New Disease-Modifying Therapies in Progressive MS



> *We need a safe and effective oral treatment for progressive MS.*

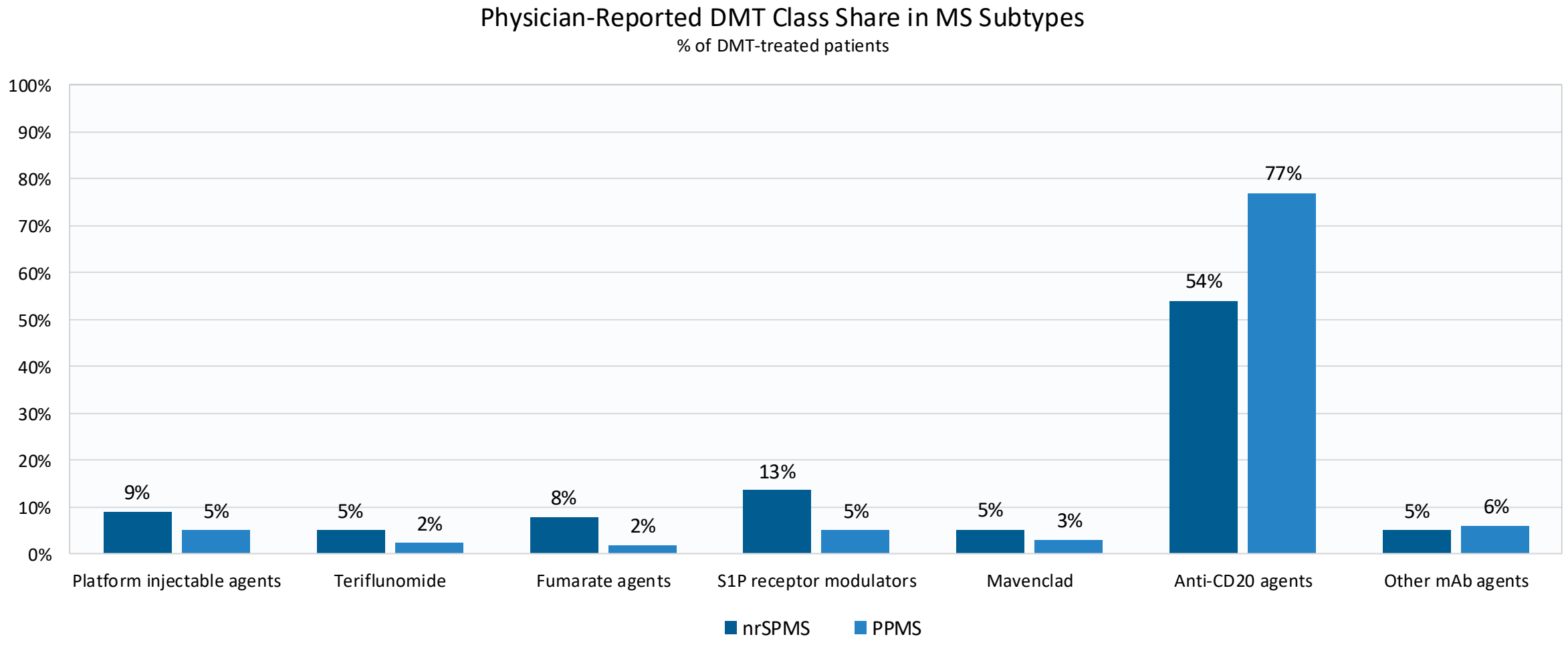
> *Always room for improved efficacy, particularly for progressive MS without safety/tolerability concerns.*

> *I would say that treatment of progressive MS is the biggest challenge. I don't think there are any good treatments for secondary or primary progressive MS*

Spherix Global Insights Realtime Dynamic Multiple Sclerosis report Q3 2024 / MS: multiple sclerosis; SPMS: secondary progressive MS; PPMS: primary progressive MS; RRMS: relapsing-remitting MS; na: non-active; a: active; PIRA: progression independent of relapse activity; DMT: disease-modifying therapy

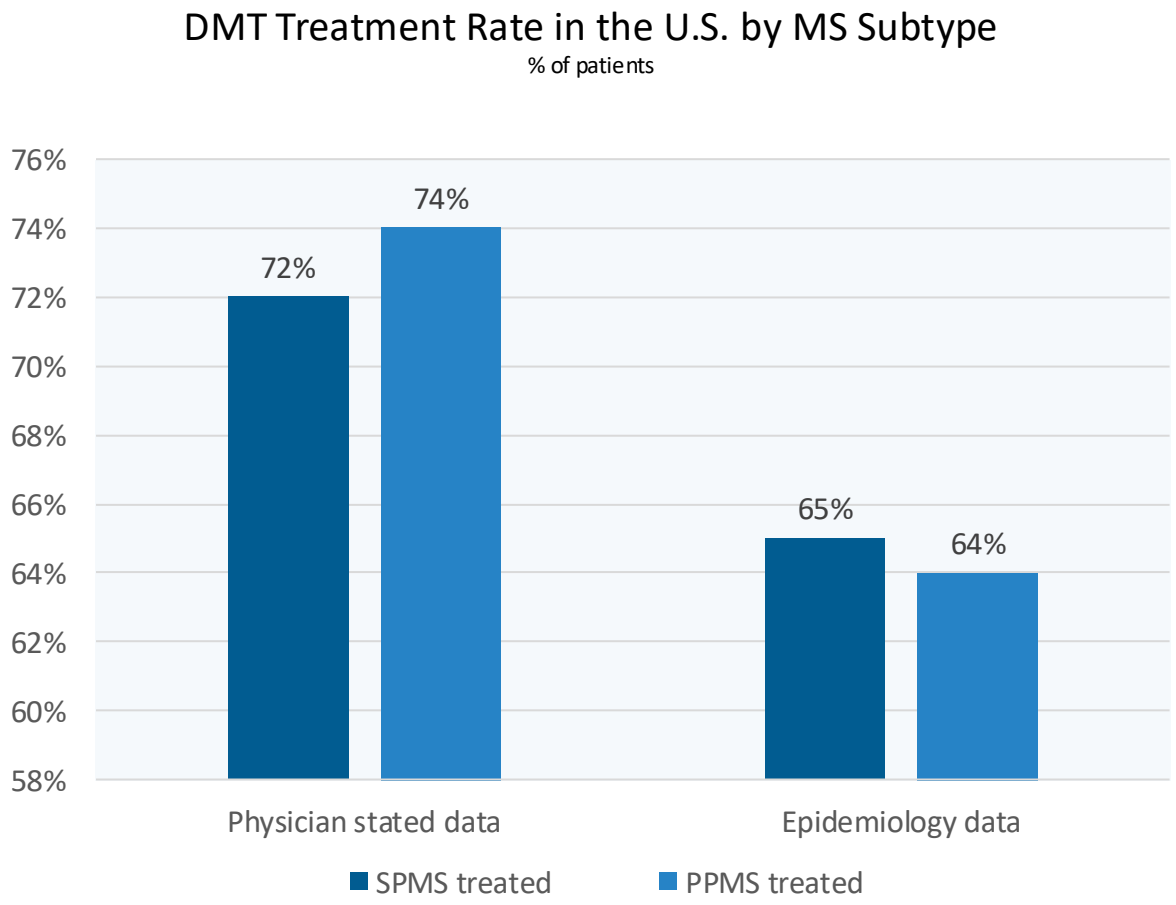
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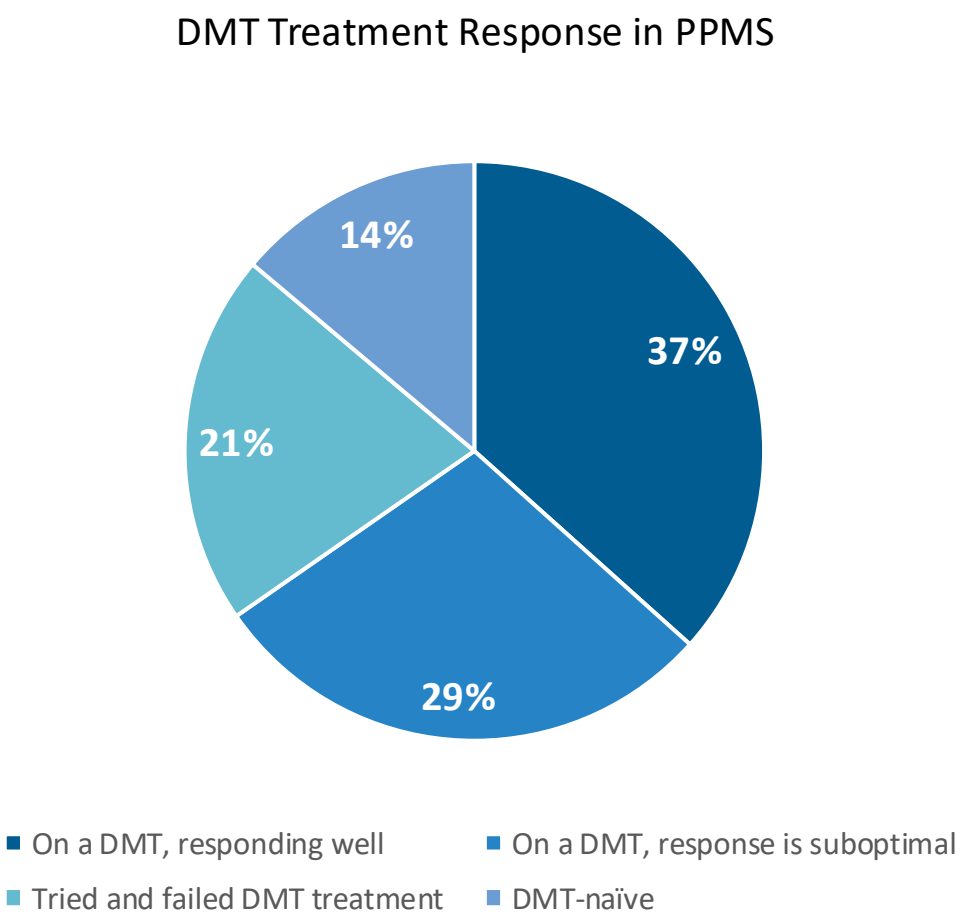
Anti-CD20 Therapies Dominate Progressive MS Treatment, Highlighting the Need for Alternative Therapeutic Options



Spherix Global Insights Realtime Dynamic Multiple Sclerosis report 2026. For your MS patients with the below subtypes currently treated with DMTs, what is your current share? (n=98, 60 General/Other Neurologists and 38 MS Specialists) / MS: multiple sclerosis; SPMS: secondary progressive MS; PPMS: primary progressive MS; nr: non-relapsing; DMT: disease-modifying therapy; mAb: monoclonal antibody

Despite High DMT Utilization, Progressive MS Patients Are Not Achieving Optimal Treatment Outcomes, With Only 37% Responding Well

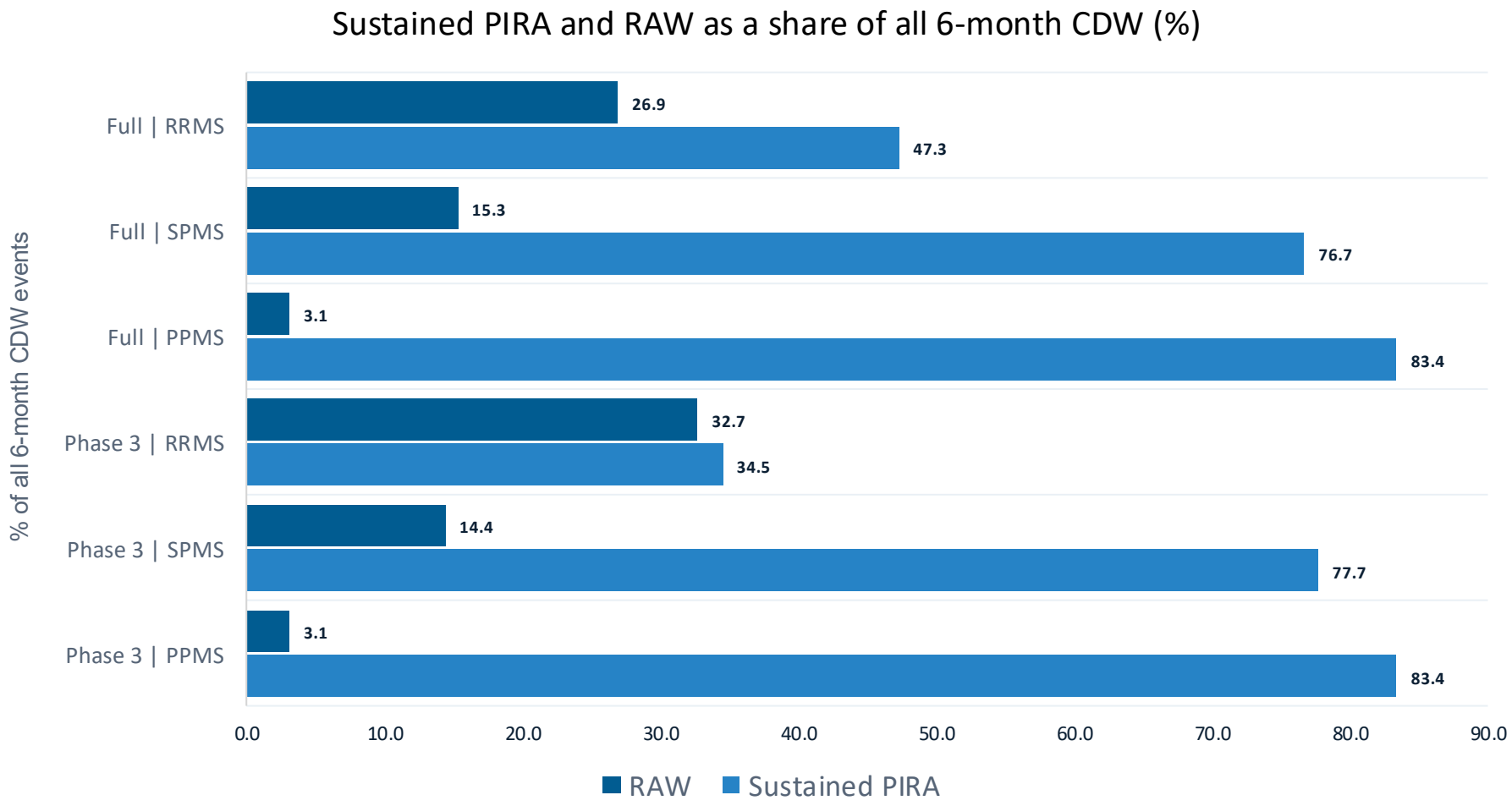




Immunic THERAPEUTICS

Spherix Global Insights Realtime Dynamic Multiple Sclerosis report 2026 (n=98, 60 General/Other Neurologists and 38 MS Specialists). Response rate data is for patients with PPMS.
MS: multiple sclerosis; SPMS: secondary progressive MS; PPMS: primary progressive MS; DMT: disease-modifying therapy

~80% of Confirmed Disability Worsening in Progressive MS Occurs Independent of Relapses, Underscoring the Need for Therapies Targeting Neurodegeneration



Lublin FD, et al. Brain. 2022;145(9):3147-3161. doi:10.1093 / MS: multiple sclerosis; RRMS: relapsing-remitting MS; SPMS: secondary progressive MS; PPMS: primary progressive MS; PIRA: progression independent of relapse activity; RAW: relapse-associated worsening; CDW: confirmed disability worsening

Vidofludimus Calcium Combines Potential Neuroprotective Effects Via Nurr1 Activation With Anti-Inflammatory Effects of Selective DHODH Inhibition

Safety

Potentially reduces key safety concerns associated with currently marketed DMTs, including hepatotoxicity, serious infections, and lymphopenia

Tolerability

Favorable tolerability profile to date, with low AE-related discontinuation rates and without prominent GI, flushing or alopecia-related tolerability issues seen with some marketed DMTs



Neuroprotection/Anti-inflammation

Combines neuroprotective effects through Nurr1 activation with anti-inflammatory effects by selectively inhibiting DHODH

Oral Convenience

Oral administration simplifies treatment for patients, HCPs and offices while supporting long-term adherence

Vidofludimus Calcium's differentiation will be driven by the totality of evidence across its dual mode of action, efficacy, safety, tolerability, and convenience profile

HCP: Health Care Professional; DMT: disease-modifying therapy; AE: adverse event; GI: gastrointestinal; Nurr1: nuclear receptor related 1; DHODH: dihydroorotate dehydrogenase

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Vidofludimus Calcium Offers a Differentiated Approach in the Progressive MS Pipeline

Phase 3 Progressive MS Pipeline

COMPANY	PROGRAM	MOA	ROA	PPMS	SPMS
Immunic THERAPEUTICS	**Vidofludimus Calcium**	**Nurr1 activator / Selective DHODH inhibitor**	**Oral QD**	**PPMS**	**naSPMS**
Zenas BioPharma	Orelabrutinib	BTKi	Oral QD	PPMS	naSPMS
Roche	Fenebrutinib	BTKi	Oral BID	PPMS (NDA under review)	N/A
NOVARTIS	Remibrutinib	BTKi	Oral BID	N/A	nrSPMS
sanofi	Frexalimab	CD40L	IV Q4W SC Q4W	N/A	nrSPMS

MS: multiple sclerosis; SPMS: secondary progressive MS; PPMS: primary progressive MS; na: non-active; nr: non-relapsing; MoA: mode of action; RoA: route of administration; QD: quaque die = once-daily; BID: bis in die = twice-daily; IV: intravenous; SC: subcutaneous; NDA: New Drug Application

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Current and Emerging Progressive MS Therapies Face Important Efficacy, Safety and Regulatory Challenges

Ocrevus® (ocrelizumab)[1]
PPMS

Efficacy

Modest effect in a representative progressive MS population: Benefit may be limited in older, less inflammatory patients

Safety

Long-term immunosuppression concerns: sustained B-cell depletion associated with serious infections and declining immunoglobulins, particularly in older patients with comorbidities

Regulatory

More restrictive European label: Limited to early PPMS (based on disease duration, disability level, and imaging activity)

Fenebrutinib[2]
PPMS

Efficacy

Uncertain incremental efficacy over Ocrevus®: noninferior, but not superior, to Ocrevus® in Phase 3

Safety

Emerging safety concerns: higher liver enzyme elevations (13.3% vs. 2.9% with Ocrevus®) and a numerical imbalance in deaths (7 vs. 1), assessed as unrelated to treatment

Regulatory

Potential limitations for long-term use: liver monitoring requirements, twice-daily dosing, and uncertainty regarding long-term safety, particularly in older patients with comorbidities

Tolebrutinib[3]
nrSPMS

Efficacy

Unresolved benefit-risk profile: Statistically significant relative reduction in six-month confirmed disability progression vs. placebo in Phase 3, but with significant safety and regulatory challenges

Safety

Serious hepatotoxicity concerns: drug-induced liver injury, including a reported fatality, prompting intensive liver function monitoring

Regulatory

Restricted European approval and uncertain U.S. outlook: Approved in Europe under a restricted label (adult patients with SPMS without relapses in the last 2 years), with liver safety monitoring requirements; unresolved concerns regarding severe liver injury could limit broader clinical adoption

Immunic THERAPEUTICS

1. Montalban X, et al. N Engl J Med. 2017;376:209–220. ORATORIO study; CADTH Clinical Review Report, 2018; 2. Roche/Genentech. FENtrepid Phase 3 results. February 7, 2026; 3. Fox RJ, et al. N Engl J Med. 2025; FDA Complete Response Letter, NDA 219624, December 23, 2025 / MS: multiple sclerosis; SPMS: secondary progressive MS; PPMS: primary progressive MS; nr: non-relapsing

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Progressive MS Represents a Multi-Billion-Dollar Global Market Opportunity With Significant Growth Potential

United States	Europe/UK
~175K diagnosed cases of SPMS and PPMS	~165K diagnosed cases of SPMS and PPMS
~115K SPMS and PPMS patients receiving DMTs	~58K SPMS and PPMS patients receiving DMTs
Current SPMS and PPMS commercial opportunity in the U.S. estimated to be between $8B - 13B	Current SPMS and PPMS commercial opportunity in Europe/UK estimated to be between $1.5 - $5B

Total global market for progressive MS is large and expected to grow with the approval and increased availability of new medicines

Immunic THERAPEUTICS

Patient numbers sourced via internal Immunic analysis and the 2024 Multiple Sclerosis Landscape and Forecast report by Decision Resources Group Part of Clarivate. Total market size was determined by the number of diagnosed cases multiplied by current net pricing for DMTs in each region. / MS: multiple sclerosis; SPMS: secondary progressive MS; PPMS: primary progressive MS; DMT: disease-modifying therapy

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Success Across Relapsing and Progressive MS Phase 3 Studies Could Position Vidofludimus Calcium as the Only DMT Indicated For All MS Subtypes

Relapsing MS (Inflammatory Disease Activity)

Progressive MS (Disability Accumulation)

CIS
(clinically isolated syndrome)

First clinical episode suggestive of MS

→

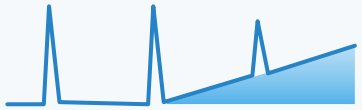
RRMS
(relapsing-remitting MS)



Distinct relapses with recovery between episodes

→

aSPMS
(active secondary progressive MS)



Progression of disability with ongoing relapse activity

→

naSPMS
(non-active secondary progressive MS)



Progressive disability with little or no relapse activity

→

PPMS
(primary progressive MS)



Progressive disability from disease onset (without relapses)

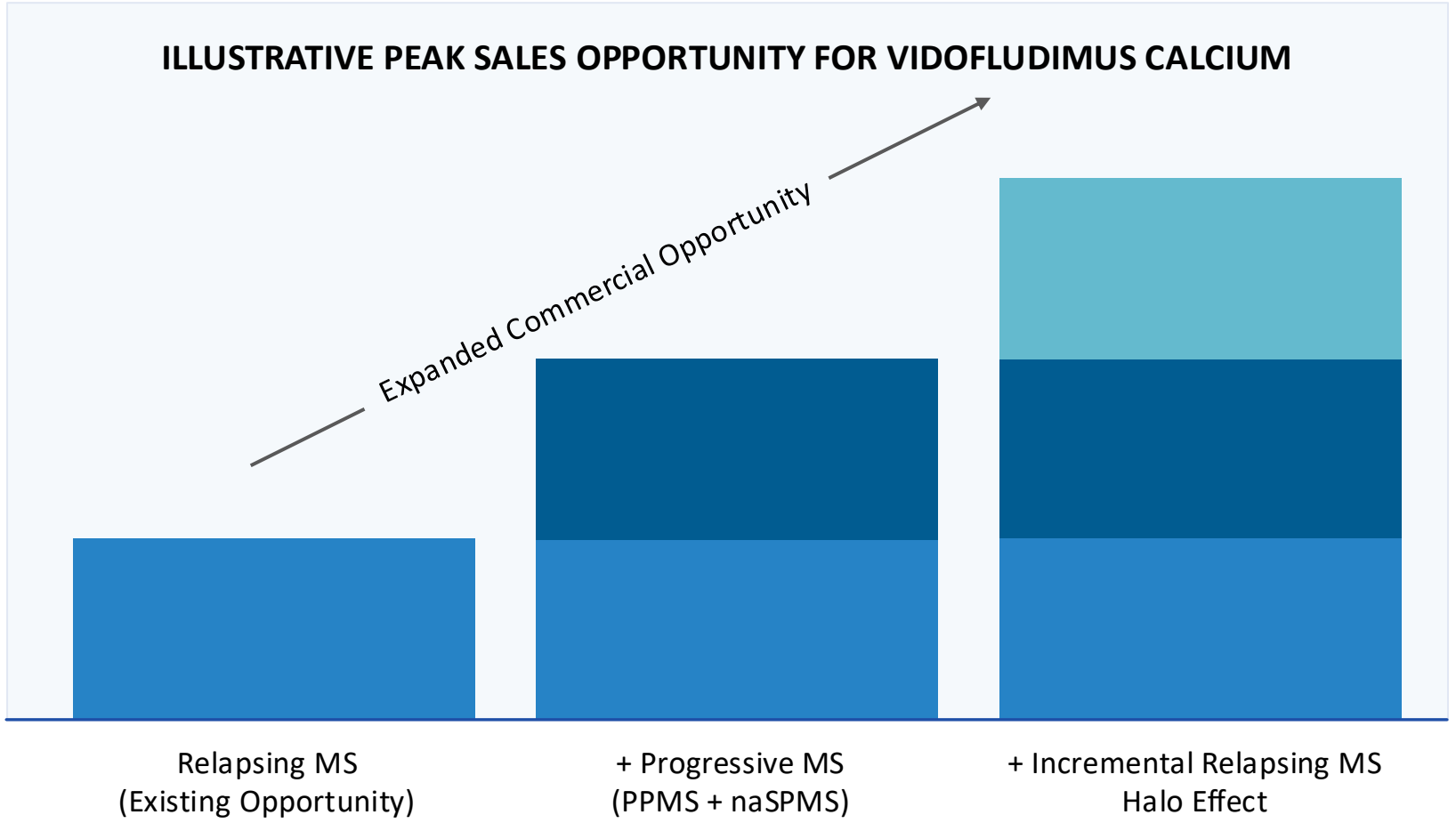
Vidofludimus Calcium
Potential to address the full spectrum of MS (CIS, RRMS, aSPMS, naSPMS and PPMS)

Demonstrating benefit across both relapsing and progressive MS could accelerate uptake in the larger relapsing MS population pushing peak sales for vidofludimus calcium to multi-blockbuster status

MS: multiple sclerosis; CIS: clinically isolated syndrome; RRMS: relapsing-remitting MS; SPMS: secondary progressive MS; PPMS: primary progressive MS; a: active; na: non-active; DMT: disease-modifying therapy

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A Phase 3 Win in Progressive MS Could Also Significantly Expand Vidofludimus Calcium's Peak Sales Potential in Relapsing MS



Potential halo effect in relapsing MS
(e.g., greater physician confidence, earlier use)

Progressive MS
(PPMS + naSPMS)

Relapsing MS
(RRMS + aSPMS)

Illustrative only. Not a forecast. Actual peak sales will depend on clinical results, regulatory approvals, pricing, market access and other factors.
MS: multiple sclerosis; RRMS: relapsing-remitting MS; SPMS: secondary progressive MS; PPMS: primary progressive MS; na: non-active; a: active; DMT: disease-modifying therapy

Outlook: Upcoming Milestones for Vidofludimus Calcium in MS

Erik Lundgren | Chief Executive Officer

Value Creation Roadmap

Multiple Catalysts Through 2030

	2H 2026	2027	2028
Relapsing MS ENSURE-1 and ENSURE-2	Top-line data expected in December 2026	Targeted relapsing MS NDA submission in mid-2027	Potential relapsing MS U.S. regulatory approval in 2028
Progressive MS CALLIPER and Phase 3 Trial	Initiation of Phase 3 trial ongoing	First-patient-enrolled in Phase 3 trial expected in H1/2027	

MS: multiple sclerosis; NDA: New Drug Application

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Q&A Session

Thank you!



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