Immunic Therapeutics

Positive Data from Phase 2 CALLIPER Trial of Vidofludimus Calcium in Progressive Multiple Sclerosis

NASDAQ: IMUX | April 30, 2025

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Positive Data from Phase 2 CALLIPER Trial of Vidofludimus Calcium in Progressive Multiple Sclerosis

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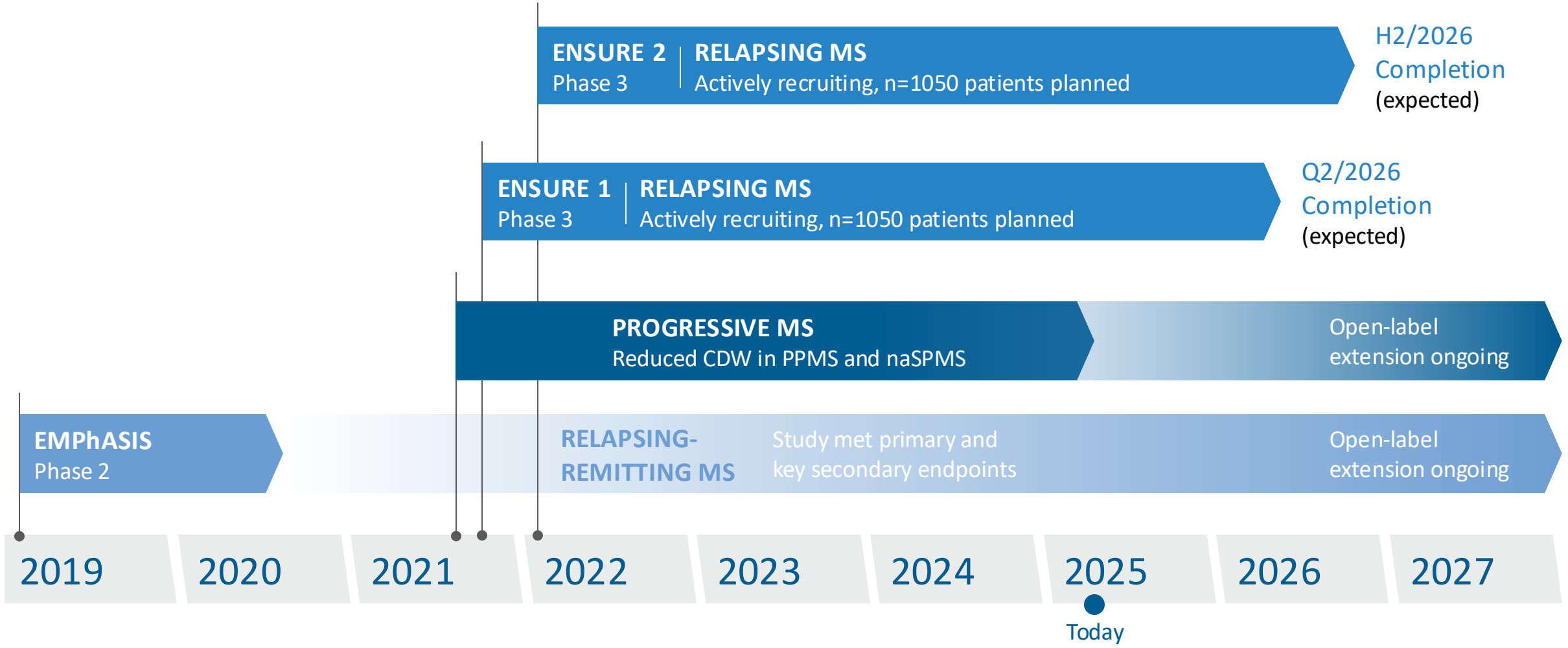
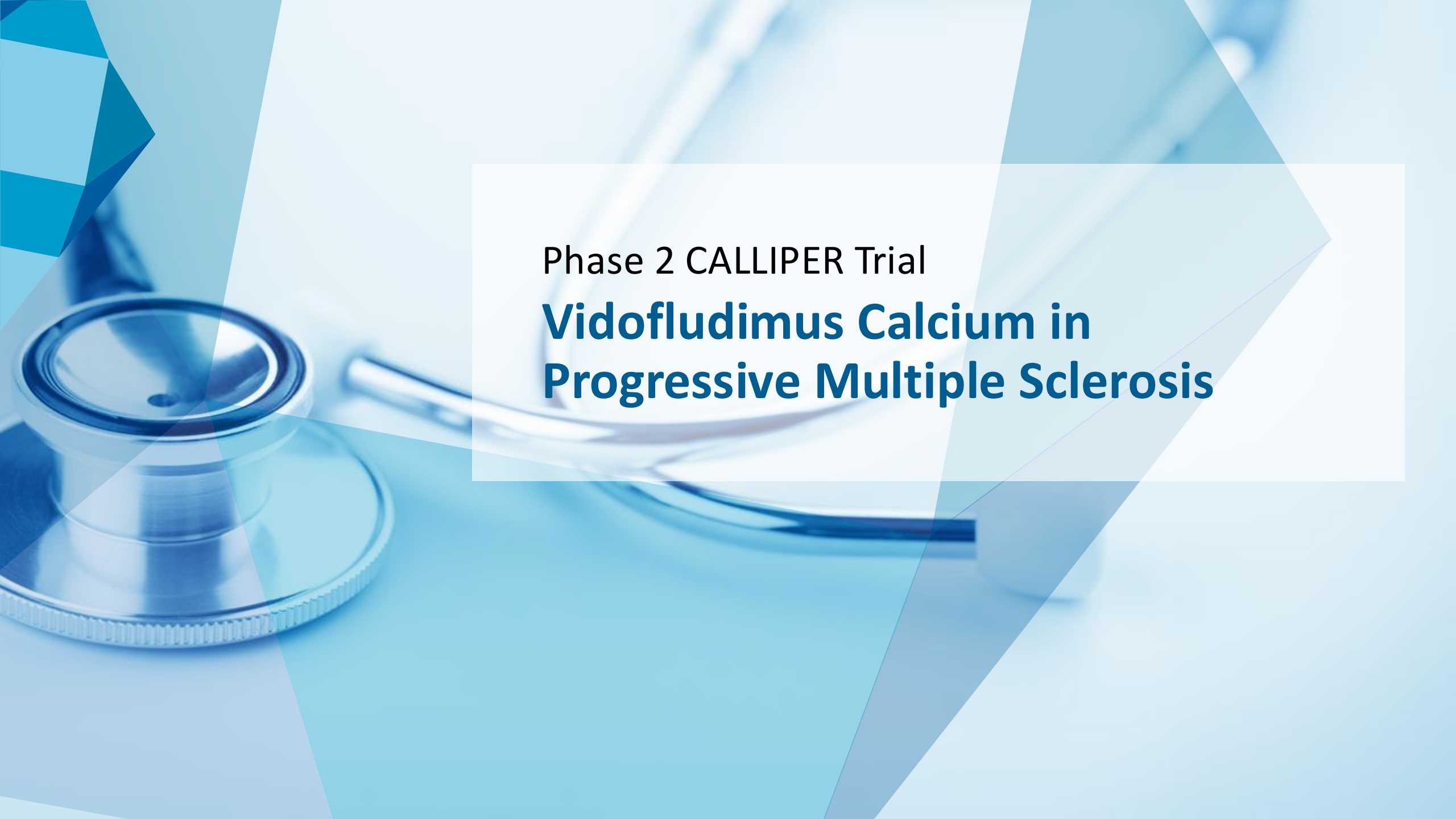
Vidofludimus Calcium: Clinical Trials Overview in Multiple Sclerosis (MS)



CDW: confirmed disability worsening; PPMS: primary progressive multiple sclerosis; naSPMS: non-active secondary progressive multiple sclerosis



Phase 2 CALLIPER Trial

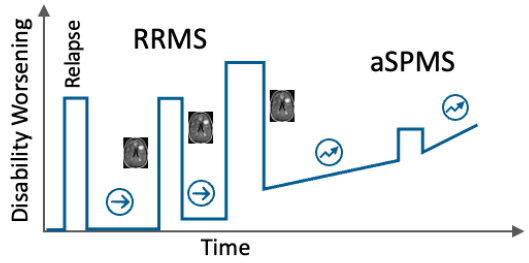
Vidofludimus Calcium in Progressive Multiple Sclerosis

Vidofludimus Calcium Has the Potential to be the First and Only Oral DMT Approved for Both Relapsing and Progressive MS

Relapsing MS (RMS)

Relapsing MS

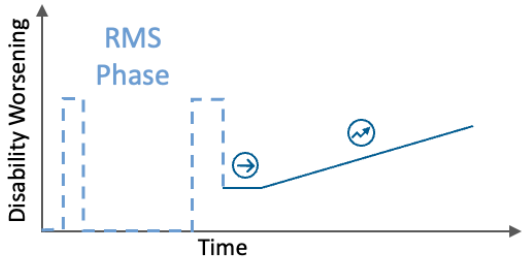
- Relapses and MRI lesions dominate clinical course (RRMS)
- Fewer relapses and lesions with continuous disability progression (aSPMS)



~900,000 patients diagnosed

Progressive MS (PMS)

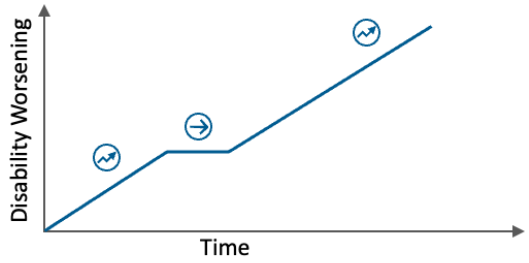
Relapses have stopped, but disability progression continues



~175,000 patients diagnosed

Primary Progressive MS

Disability worsening without relapses from the start



~120,000 patients diagnosed

DHODH Inhibition

Nurr1 Activation

Relapses and focal inflammation

Smoldering disease and neurodegeneration

DMT: disease-modifying therapy; MS: multiple sclerosis; RRMS: relapsing-remitting MS; SPMS: secondary progressive MS; aSPMS: active SPMS; MRI: magnetic resonance imaging; Nurr1: nuclear receptor-related 1; DHODH: dihydroorotate dehydrogenase

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Regardless of the Subtype, the Outcome of Every Patient Journey in Multiple Sclerosis Is Physical and/or Cognitive Disability

1.0
No disability, minimal signs of MS

3.0
Moderate disability in one system, or mild disability in up to four systems. No impairment to walking

5.0
Disability severe enough to impair full daily activities, able to walk without aid for 200m

6.0
Requires a walking aid, cane, crutch, etc. – to walk 100m

7.5
Unable to take more than a few steps. Restricted to wheelchair

9.0
Confined to bed, can still communicate and eat

10
Death by MS

While over 15 anti-inflammatory treatments exist for relapsing multiple sclerosis, <u>there is no therapy available that</u> directly impacts the neurodegeneration driving disability progression

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Why Did Immunic Conduct the Exploratory CALLIPER Trial in Patients With Progressive Multiple Sclerosis?

Objectives of the Exploratory Phase 2 CALLIPER Trial

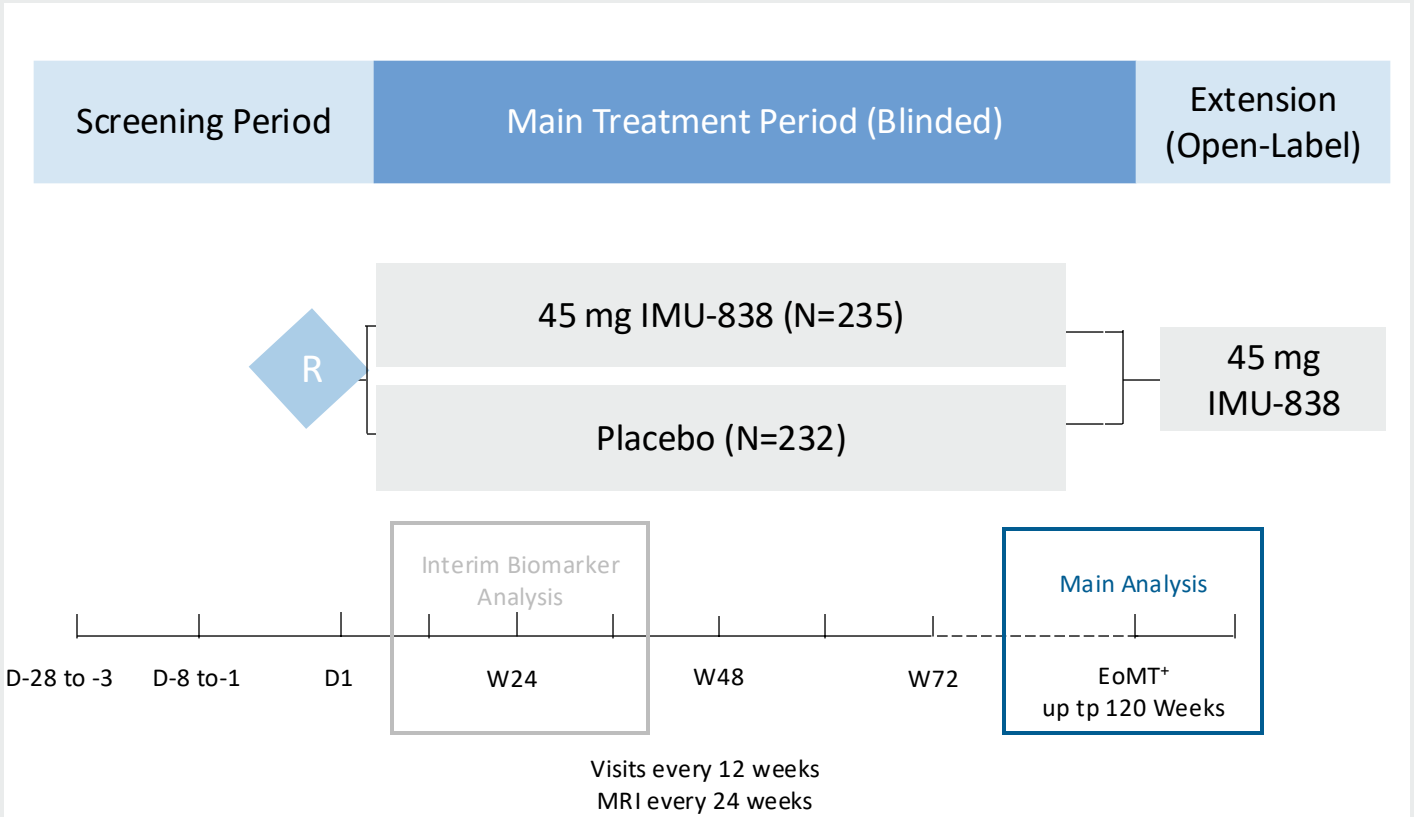
Scientific: Does vidofludimus calcium show signs of direct neuroprotection in multiple sclerosis via its mechanism of Nurr1 activation?

Clinical: Can vidofludimus calcium make a clinically meaningful impact in progressive multiple sclerosis patients?

- Can it reduce disability worsening?
- Are other clinical datapoints impacted?
- Is the safety and tolerability profile favorable as in previous studies?

Commercial: Which progressive multiple sclerosis indications should be further pursued with vidofludimus calcium in confirmatory trials?

CALLIPER: Phase 2 Clinical Trial in Progressive Multiple Sclerosis
NCT05054140

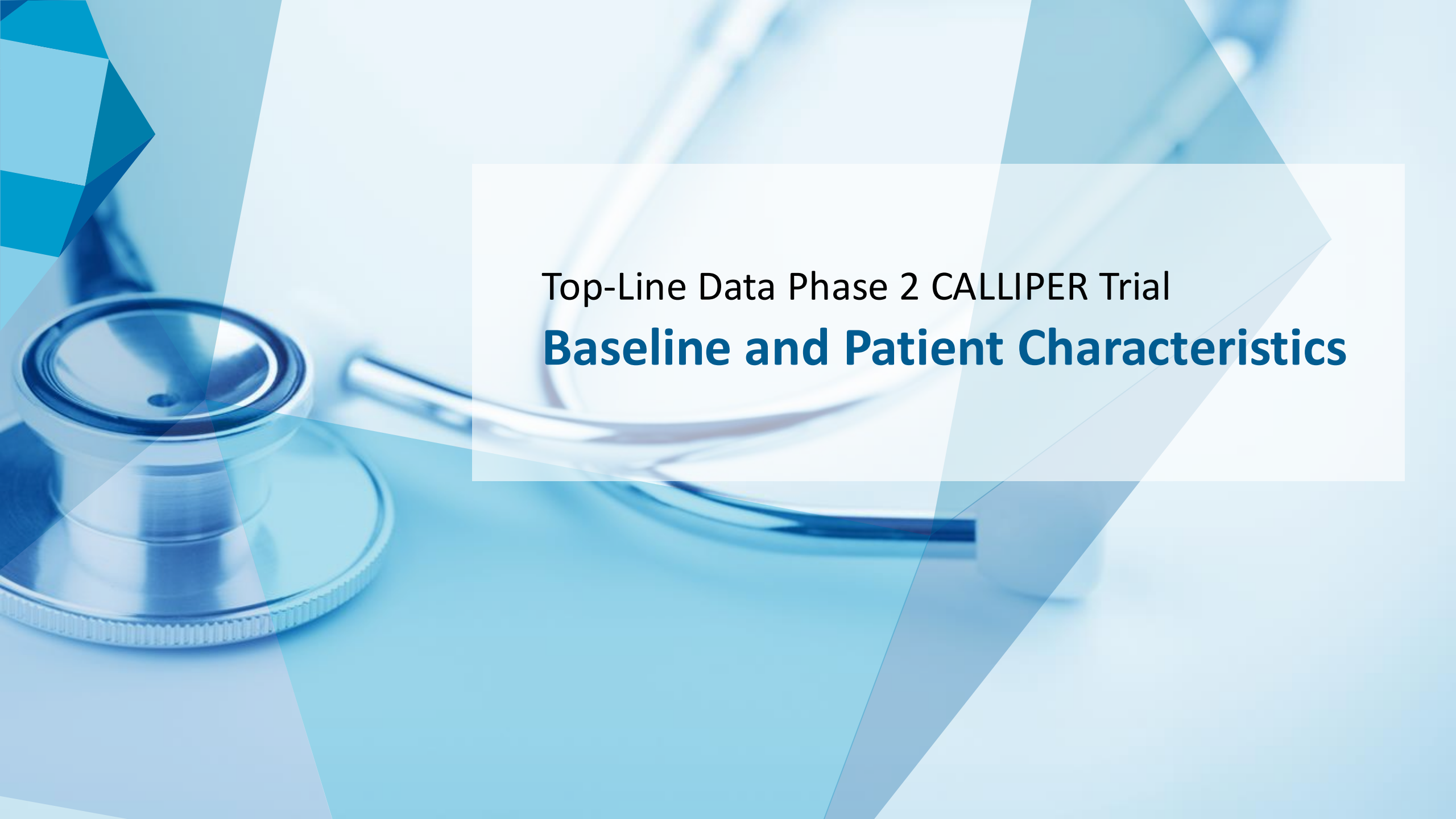


Coordinating Investigator: Robert J. Fox, M.D., Cleveland Clinic

Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase 2 Trial

- 467 adult patients, aged 18 to 65 years, enrolled at more than 70 sites in North America, Western, Central and Eastern Europe
  - PPMS or SPMS diagnosis (revised McDonald criteria 2017)
  - EDSS score at screening between 3.0 to 6.5
  - No relapse in last 24 months before randomization
  - Evidence of disability progression
- Randomization to 45 mg vidofludimus calcium or placebo QD
- Blinded main treatment period up to 120 weeks
- Optional, approximately 8-year, open-label extension period

EoMT: end of main treatment period, either at Week 120 or when last enrolled patient reached Week 72
R: randomization; D: day; W: week; EoMT: end of main treatment period; MRI: magnetic resonance imaging; PPMS: primary progressive multiple sclerosis; SPMS: secondary progressive multiple sclerosis; EDSS: Expanded Disability Status Scale; QD: quaque die = once-daily



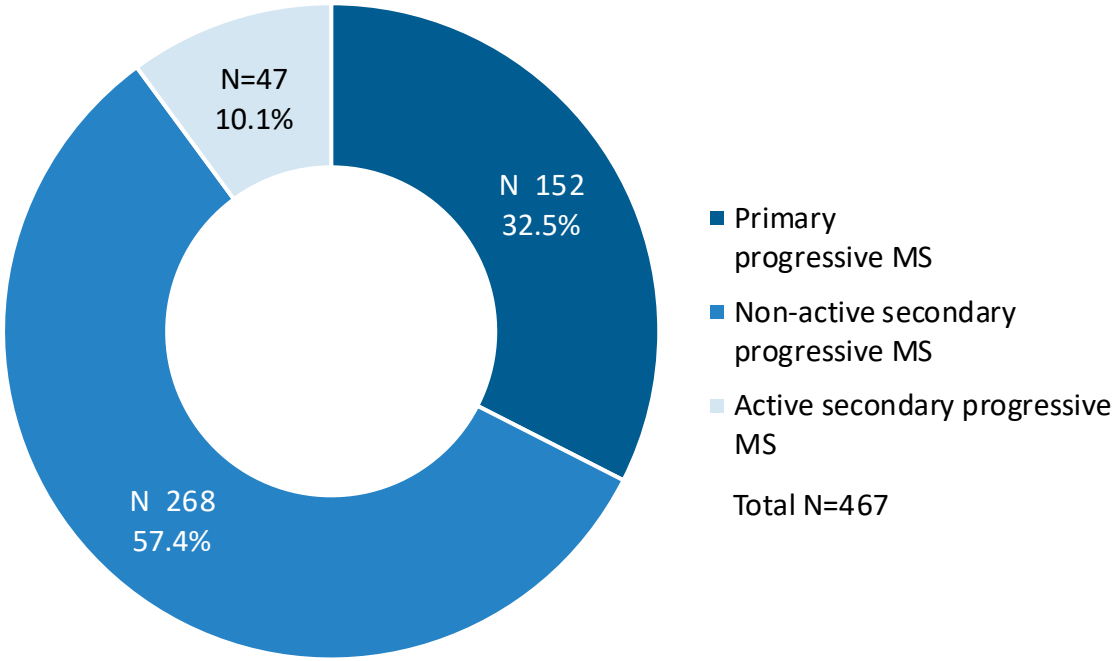
Top-Line Data Phase 2 CALLIPER Trial

Baseline and Patient Characteristics

CALLIPER: Patient Demographics and Baseline Characteristics

Total Study Population of 467 Enrolled Patients

Progressive Disease Subtypes



Baseline Characteristics

Baseline Patient Characteristics	Total (N=467)
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)	25.0 [15.8 – 46.6]
SDMT [points], median (min-max)	35.0 [0-180]
EDSS at Visit 1, median (min-max)	5.5 [2.5-6.5]
MS relapses during last 24 months, median (min-max)	0.0 [0-0]
Gd+ lesions at baseline MRI (%)	16.3%

Baseline characteristics initially assessed by the investigators when patients entered screening based on history. These data summarize the disease subtype as assessed by the investigator at the time of randomization. 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

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Top-Line Data Phase 2 CALLIPER Trial

Clinical Endpoints

Vidofludimus Calcium Showed Substantial Reduction of 24wCDW-EDSS Events

Vidofludimus Calcium Reduced Relative Risk of 24wCDW in Overall Study Population and Subtypes Compared to Placebo

Proportion of Patients With 24wCDW Events	Overall CALLIPER Patient Population (N=467)	PPMS (N=152)	naSPMS (N=268)
Vidofludimus Calcium	16.2%	19.5%	14.1%
Placebo	20.3%	28.0%	16.5%
Relative Risk Ratio for 24wCDW	0.80	0.70	0.85
Relative Risk Reduction for 24wCDW	**20%**	**30%**	**15%**

Based on intent-to-treat population (ITT), patients are analyzed as randomized; 24wCDW: 24-week confirmed disability worsening; naSPMS: non-active secondary progressive multiple sclerosis; PPMS: primary progressive multiple sclerosis
24-week confirmed disability worsening based on EDSS scale (24wCDW), total of 85 events in the intent-to-treat population of CALLIPER trial
Data displayed for the reduction of risk of occurrence of 24wCDW events, percentages refer to the rate of 24wCDW in each of the treatment arms per disease subtype. Disease subtype as per investigator diagnosis at screening.

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Comparison CALLIPER Versus ORATORIO Trials in PPMS Population

	ORATORIO* (N=732)	CALLIPER (N=152)
Mean Age (Years)	44.6	47.4
Female (N,%)	361 (49.3%)	93 (61.1%)
EDSS - Mean	4.7	4.9
EDSS - Median	4.5	4.5
Gd+ Lesions at Baseline MRI (N,%)	26.6%	17.8%
Relative Risk Reduction of 24wCDW, Active Over Placebo	**25%**	**30%**

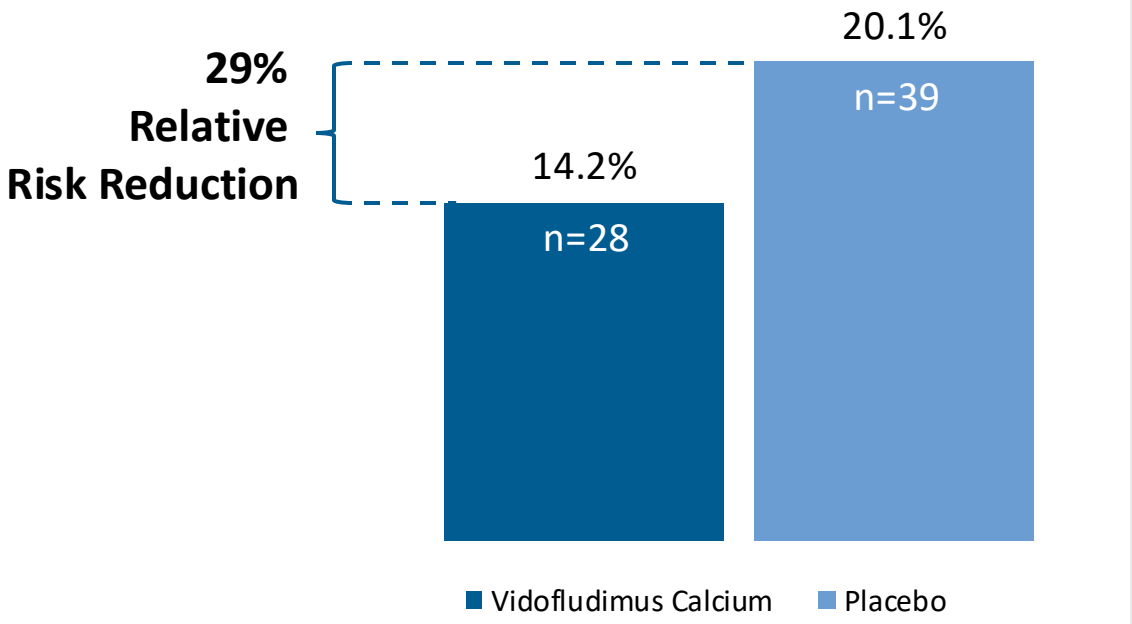
* Clinical Review Report: Ocrelizumab (Ocrevus): (Hoffmann-La Roche Limited): Indication: Management of adult patients with early primary progressive multiple sclerosis as defined by disease duration and level of disability, in conjunction with imaging features characteristic of inflammatory activity [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2018 May. Results. Available from: https://www.ncbi.nlm.nih.gov/books/NBK533357/

PPMS: primary progressive multiple sclerosis; EDSS: Expanded Disability Status Scale; Gd+: gadolinium-enhancing lesions found on T1-weighted MRI images; MRI: magnetic resonance imaging; 24wCDW: 24-week confirmed disability worsening

Vidofludimus Calcium Reduced Relative Risk of 24wCDW Events in Patients Without Gd+ Lesions at Baseline

Proportion and number of patients without Gd+ lesions at baseline with 24wCDW EDSS in vidofludimus calcium group (N=197) compared to placebo (N=194)

% of patients with 24wCDW of the total number in the respective treatment group



Reduction of 24wCDW Events by 29% in Patients With Highest Need

- 391 of 467 patients had no Gd+ lesions at baseline
- In this group, vidofludimus calcium reduced 24wCDW events by 29%, with relative risk ratio of RR=0.71
- **Precisely the patients who were largely shown to not benefit from current anti-inflammatory therapies**
- **Underlines neuroprotective effect of Nurr1 activation by vidofludimus calcium**

24wCDW: 24-week confirmed disability worsening; Gd+: gadolinium-enhancing; EDSS: Expanded Disability Status Scale; Nurr1: nuclear receptor-related 1

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CALLIPER successfully demonstrated the neuroprotective potential of vidofludimus calcium in PMS patients

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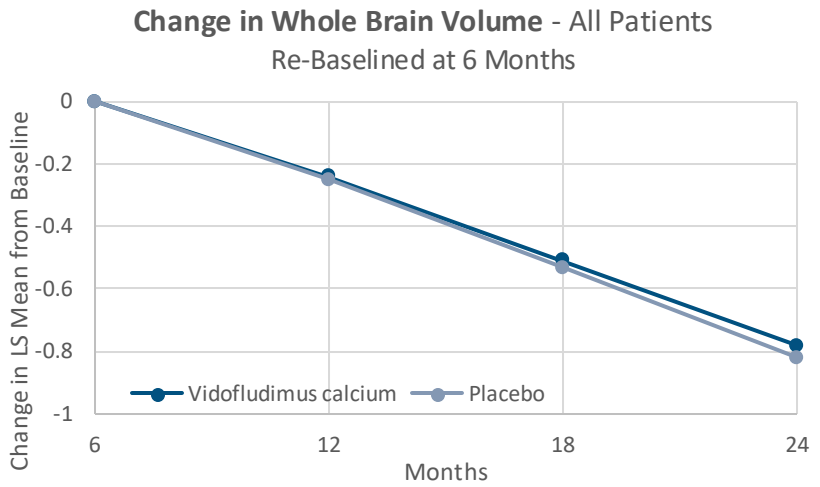
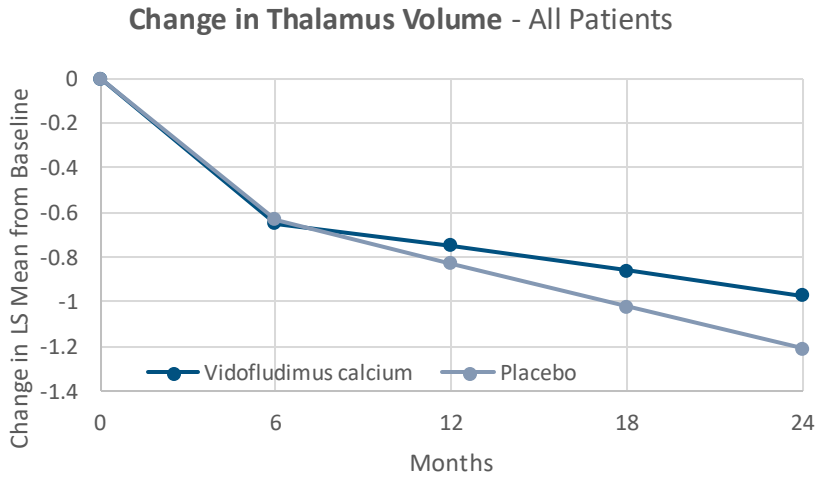
Clinically meaningful risk reduction of confirmed disability worsening of 20% in overall PMS population and even more prominent 30% reduction in PPMS population

Top-Line Data Phase 2 CALLIPER Trial

Magnetic Resonance Imaging (MRI) Endpoints

Brain Atrophy Endpoints Consistently Demonstrated Beneficial Effect of Vidofludimus Calcium Compared to Placebo

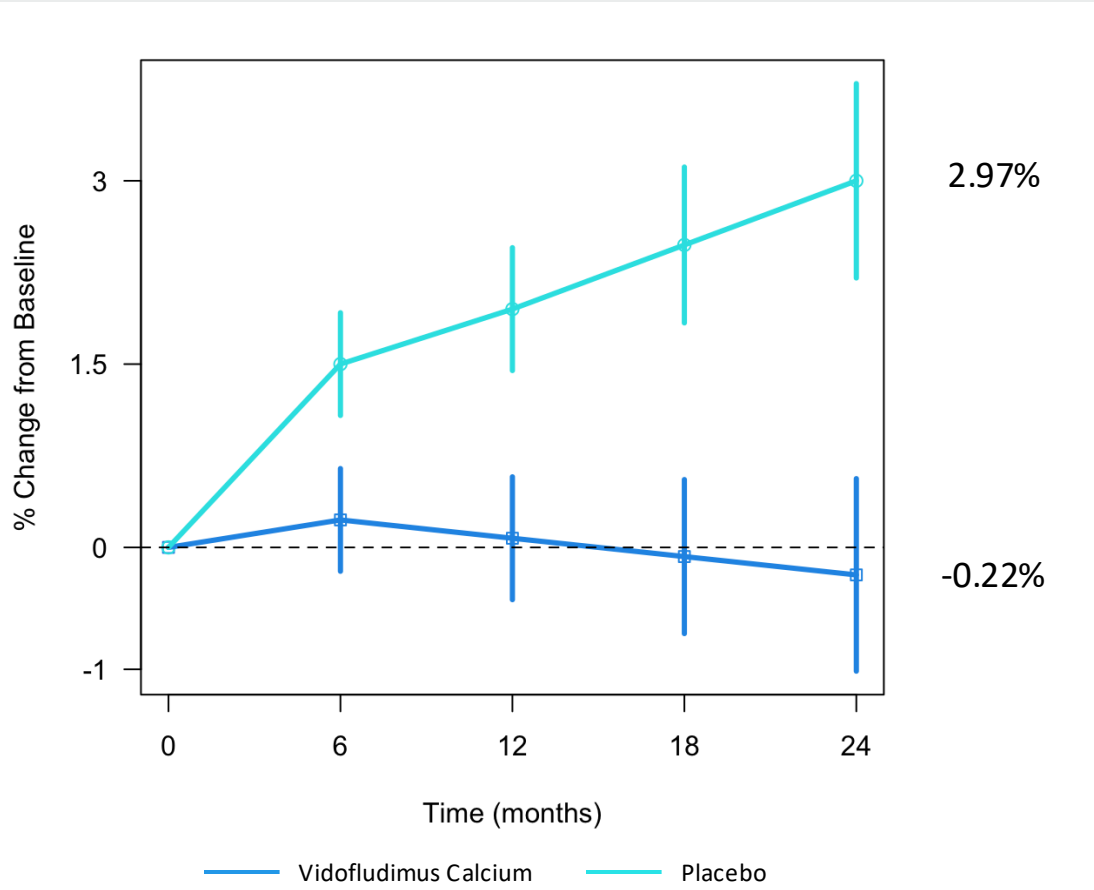




- Modest benefit on exploratory primary MRI endpoint: decreased annualized rate of whole brain atrophy: 5% improvement of vidofludimus calcium compared to placebo at 24 months
- Substantially reduced annualized rate of thalamic brain volume loss by 20% in patients with PMS compared to placebo at 24 months
  - Change in thalamus volume is more sensitive MRI atrophy measure in PMS[1,2,3]
  - Thalamic atrophy is prevalent in PMS[4,5] and data have shown strong associations between thalamic atrophy and clinical disability progression[6]

[1] Moccia M et al., Multiple Sclerosis JournalVolume 23, Issue 12, October 2017 [2] Azevedo CJ et al., Ann Neurol. 2018 Feb;83(2):223-234 [3] Azevedo CJ et al., Ann Neurol 2018 Jan 12; [e-pub] [4] Cao Y et al., Neuropsychol Rev 2021 [5] Mesaros S et al., AJNR Am J Neuroradiol 2011;32:1016–1020 [6] Schoonheim MM et al., Mult Scler 2021:13524585211008743
MRI: magnetic resonance imaging; LS: least square; PBVC = percent brain volume change (using the Siena method); intent-to-treat population (all patients are analyzed as randomized)
For the calculation of least square means, patients with a valid baseline MRI are considered. Missing values are calculated based on the analysis set. Estimates are obtained from a random intercept, random slope mixed model, accounting for treatment effect and stratified by the randomization strata (disease type and baseline EDSS score). Convergence and positive estimated G matrix was achieved with an Autoregressive Order One (AR(1)) covariance matrix. The annualized rate of PBVC is the population slope within treatment group as change from baseline. The effect estimate of the treatment difference is equivalent to the difference between annualized rates. For the primary estimand, data collected up to 30 days after the onset date of a post-baseline relapse or between the start and 30 days after the end of any rescue medication intake were set to missing. Data after treatment discontinuation was included in the analysis.

Vidofludimus Calcium Substantially Lowered Volume of New/Enlarging T2 Lesions Compared to Placebo



- Change of T2 lesion volume (cm^3) gets steadily worse compared to baseline in placebo patients while remaining stable in vidofludimus calcium patients
- Volume change different between arms at every time point in the study

	Percent Change
Vidofludimus Calcium	-0.22%
Placebo	+2.97%
Benefit Vidofludimus Calcium Over Placebo at Month 24	3.19%

T2 lesion load: volume of lesions on T2-weighted magnetic resonance images; intent-to-treat population (all patients are analyzed as randomized)
Estimates obtained from a random intercept, random slope mixed model, accounting for treatment effect and stratified by the randomization strata (disease type and baseline EDSS score). The population slope within treatment group as change from baseline. For the primary estimand, data collected up to 30 days after the onset date of a post-baseline relapse or between the start and 30 days after the end of any rescue medication intake were set to missing. Data after treatment discontinuation was included in the analysis.

Top-Line Data Phase 2 CALLIPER Trial

Safety and Tolerability

Top-Line Data Confirmed Favorable Safety and Tolerability Profile of Vidofludimus Calcium Observed in Previous Clinical Trials

Number of Patients With Any TEAE and SAE

	Vidofludimus Calcium N=235	Placebo N=233
Any TEAE, n(%)	163 (69.4)	159 (68.5)
Any SAE n(%)	19 (8.1)	15 (6.5)

- No new safety signals identified
- Occurrence of TEAEs and SAEs with similar frequency in both treatment arms

Five Most Common TEAE Events

	Vidofludimus Calcium	Placebo	Total
Urinary tract infection	161	152	313
Upper respiratory infection	57	49	106
Headache	16	42	58
Back pain	11	24	35
Fall	15	17	32

Most Common SAE Events (all SAE with total incidence >1)

	Vidofludimus Calcium	Placebo	Total
Pyelonephritis	1	1	2
Femoral neck fracture	0	2	2
Femur fracture	0	2	2
Vertigo	2	0	2

TEAE: treatment-emergent adverse event; SAE: serious adverse event

Safety Population contains any patient who received at least 1 dose of study drug, Vidofludimus calcium (N=235), Placebo (N=232), Total (N=467). All other SAE not listed had only single occurrences in the CALLIPER trial.

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Top-Line Data Phase 2 CALLIPER Trial

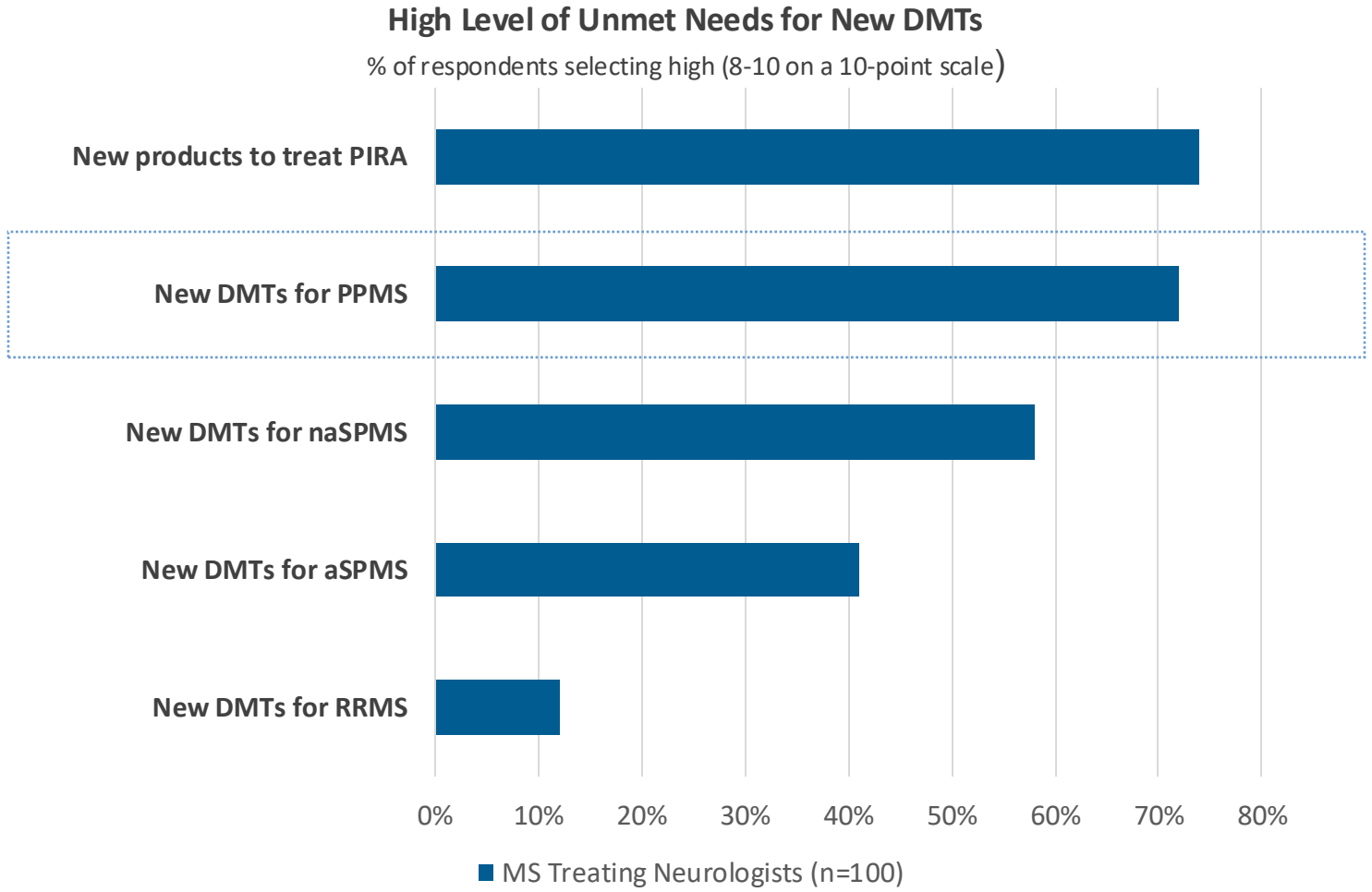
Commercial Background

Huge Unmet Medical Need Exists in PPMS, An Underdiagnosed and Tougher to Treat Patient Population

- PPMS, which affects **10-15% of people diagnosed with MS**, is characterized by a steady worsening of neurological function from the beginning of the disease, without distinct relapses or periods of remission
- Compared with RMS, PPMS 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**
- **~120,000 patients diagnosed** (US & EU5), of which only ~54,000 (45%) are currently treated by disease-modifying therapies
- **Underdiagnosed and undertreated**, due to lack of safe, effective and convenient treatments (only one approved therapy)

PPMS: primary progressive multiple sclerosis; RMS: relapsing multiple sclerosis / Gross HJ, Watson C. Neuropsychiatr Dis Treat. 2017;13:1349–1357; National Multiple Sclerosis Society website: https://www.nationalmssociety.org/understanding-ms/what-is-ms/types-of-ms/primary-progressive-ms; Patient numbers sourced via internal Immunic analysis and 2024 Multiple Sclerosis Landscape and Forecast report by Decision Resources Group Part of Clarivate; EU5 countries: France, Germany, Italy, Spain, and United Kingdom

Even With an Approved Therapy, Neurologists Still Identify New DMTs to Treat PPMS as an Area of High Unmet Need in MS



"We need a safe and effective oral treatment for PPMS."

"Always room for improved efficacy, particularly for primary 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."

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

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Currently Approved Therapy Does Not Address PPMS Patient Needs

Non-immunosuppressant mode of action:

- B-cell depletion significantly reduces the body's immune response, making patients more susceptible to various infections, including opportunistic ones. This is a major concern, particularly in PPMS where the disease course is progressive and immune system function is already potentially compromised.
- Vaccine responses are significantly blunted in patients on B-cell depleting therapies, adding to concerns with an age-dependent decreased immune response.

Convenience:

- Patients with PPMS may experience difficulties with mobility and fatigue, making it hard to travel to and from infusion appointments.

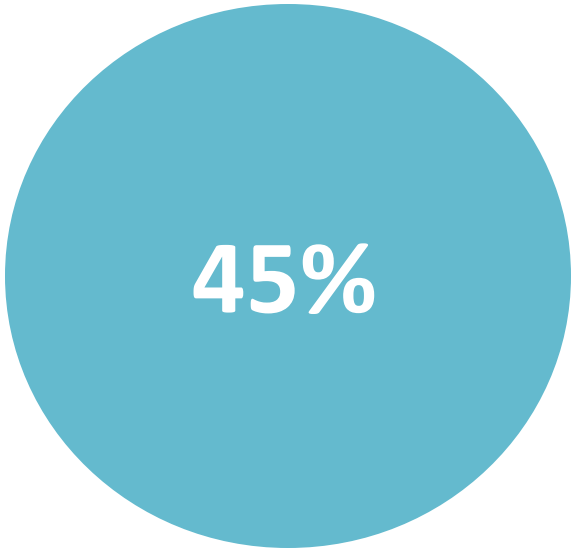
Lack of complex monitoring:

- Safety monitoring for anti-CD20 therapy involves regular monitoring of immunoglobulin levels, vigilance for infusion reactions, and ongoing surveillance for potential opportunistic infections, particularly those associated with hypogammaglobulinemia. Routine laboratory monitoring includes CBC, CD19 count, IgG, IgM and HCG in women of childbearing age.

PPMS: primary progressive multiple sclerosis / Garg H, Bush S, Gappmaier E. Int J MS Care. 2016 Mar-Apr;18(2):71-7; Safety Monitoring of Disease-Modifying Therapies in Multiple Sclerosis: https://practicalneurology.com/diseases-diagnoses/ms-immune-disorders/safety-monitoring-of-disease-modifying-therapies-in-multiple-sclerosis/32085/#:~:text=Anti%2DCD20%20therapies%20require%20baseline%20CBC%20with%20differential,planning%20because%20of%20prolonged%20intervals%20between%20dosing

Global Market for PPMS Treatment Estimated to Be $6+ Billion But Less Than Half of All Diagnosed Patients Are Treated Today

diagnosed PPMS patients in the US & EU5



of diagnosed PPMS patients are currently on a DMT

in PPMS sales for the only approved product

Total global market for PPMS estimated to be $6B+ and expected to grow with the approval and increased availability of new medicines

PPMS: primary progressive multiple sclerosis; DMT: disease-modifying therapy; K: thousand; B: billion / 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; EU5 countries: France, Germany, Italy, Spain, and United Kingdom; TD Cowen Therapeutic Categories Outlook Comprehensive Study – Multiple Sclerosis October 2024

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Vidofludimus Calcium: Derisked Near-Term Opportunity With $3-7 Billion Peak Potential

	RMS	naSPMS	PPMS
Indication			
Status	Phase 3	Phase 3-ready	Phase 3-ready
Clinical Evidence	76% reduction in new Gd+ lesions (Phase 2)	15% relative risk reduction in 24-week CDW (Phase 2)	30% relative risk reduction in 24-week CDW (Phase 2)
Eligible Population	**~900K**	**~175K**	**~120K**
Next Milestones	Phase 3 completion expected **2026**	End of phase 2 meeting with regulators **TBD**	End of phase 2 meeting with regulators **TBD**
Potential Peak Sales	**$1-2B**	**$1-2B**	**$2-3B**

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
RMS: relapsing MS; naSPMS: non-active secondary progressive MS; PPMS: primary progressive MS; Gd+: gadolinium-enhancing; CDW: confirmed disability worsening; K: thousand; B: billion

Vidofludimus Calcium Has the Potential to Transform the Oral Multiple Sclerosis DMT Market

Designed to Combine the Best of Two Worlds: Neuroprotection and Relapse Prevention

First-in-class, dual mode of action approach designed to address the **full spectrum of disease:**

- Nurr1 activation provides **direct neuroprotective effects**
- DHODH inhibition is associated with **anti-inflammatory effects**

Oral DMT category: Aims for **best-in-class benefit / risk profile** by combining **strong efficacy** with **safety**, **tolerability**, and **once-daily** convenience

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No first-dose or on-treatment monitoring makes it an **easy start or switch to therapy**

No anticipated black box warnings or serious infection risk (e.g., PML, malignancies, etc.)

If approved, peak sales potential for vidofludimus calcium of $3-7 billion[1]

DMT: disease-modifying therapy; Nurr1: nuclear receptor-related 1; DHODH: dihydroorotate dehydrogenase; PML: progressive multifocal leukoencephalopathy [1] Based on Immunic internal market research

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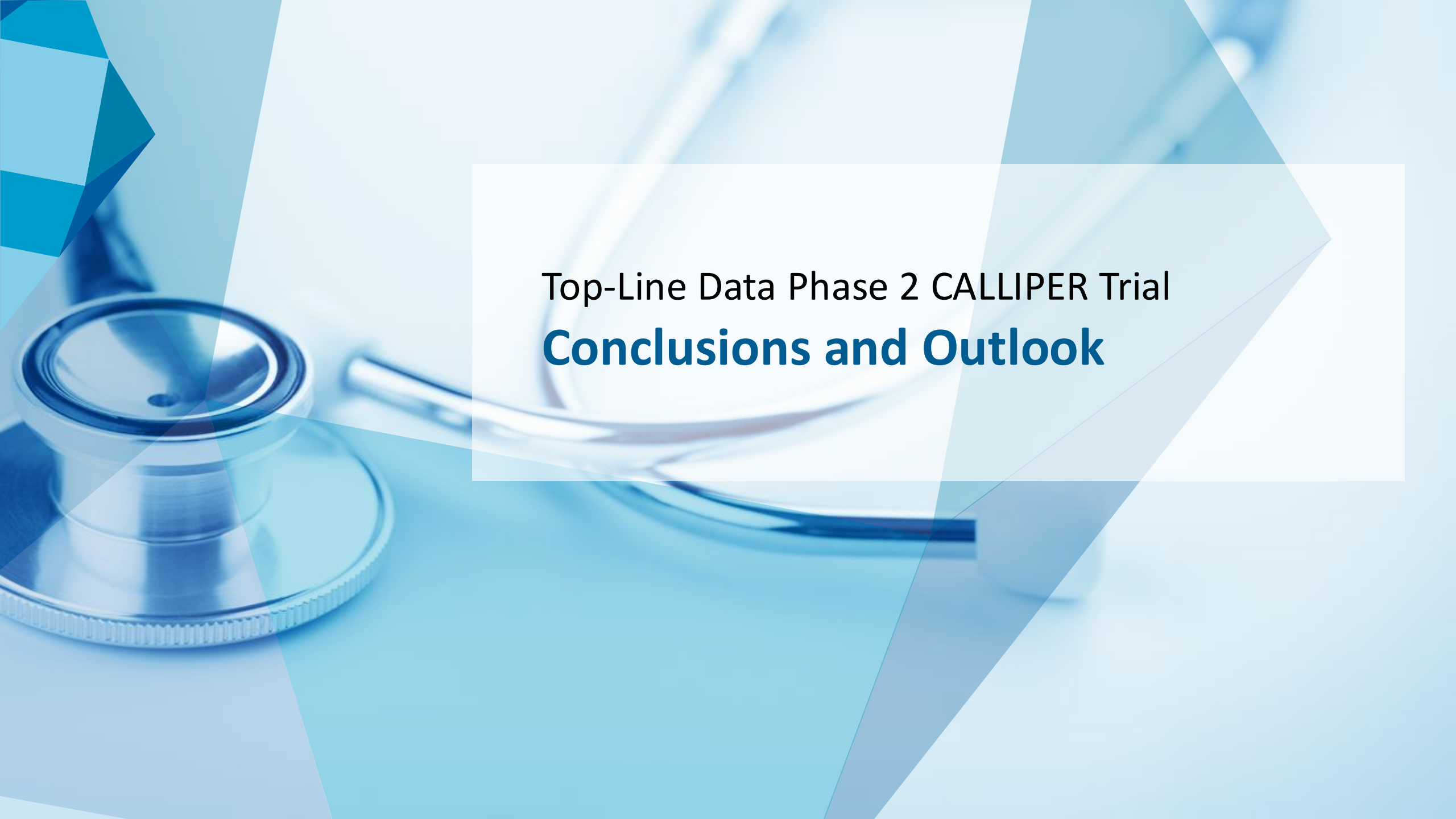

Top-Line Data Phase 2 CALLIPER Trial

Conclusions and Outlook

“We are delighted about the phase 2 CALLIPER results showing that vidofludimus calcium outperformed historic trials in PPMS regarding numerical reduction of disability progression events.”

CALLIPER Data Paves Way for Potential Registrational Study in PPMS

Data Impressively Confirms Main Objectives of this Exploratory Phase 2 Clinical Trial

- Achieved unprecedented proof of concept, in particular, regarding the key medical and future phase 3 endpoint of confirmed disability progression – not only for primary progressive multiple sclerosis but also for non-active secondary progressive multiple sclerosis
- Vidofludimus calcium addresses a $6+ billion market in PPMS, alone, where currently only one therapy is approved
- Results to be discussed with healthcare authorities to determine appropriate next steps for vidofludimus calcium in progressive multiple sclerosis, including potential application for breakthrough designation

Market size numbers sourced via internal Immunic analysis

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Top-Line Data Phase 2 CALLIPER Trial

Q&A Session

Top-Line Data Phase 2 CALLIPER Trial

Summary

Positive Data from Phase 2 CALLIPER Trial of Vidofludimus Calcium in Progressive Multiple Sclerosis

- Reduced relative risk of 24wCDW by 20% in overall study population; even more prominent 30% reduction in high unmet need population of PPMS
- Remarkable 29% reduction of disability worsening in patients without baseline inflammatory lesions in overall study population
- Confirmed favorable safety and tolerability observed in previous clinical trials; no new safety signals identified
- As of April 2025, more than 375 patients continue to be treated in open-label extension phase of CALLIPER trial
- Underlines Nurr1 activation as new mode of action for preventing neurodegeneration in MS and substantiates impact on disability accumulation by both PIRA and RAW
- Further de-risks ongoing phase 3 ENSURE program with potential to offer relapsing MS patients an oral, safe and neuroprotective treatment early in the disease

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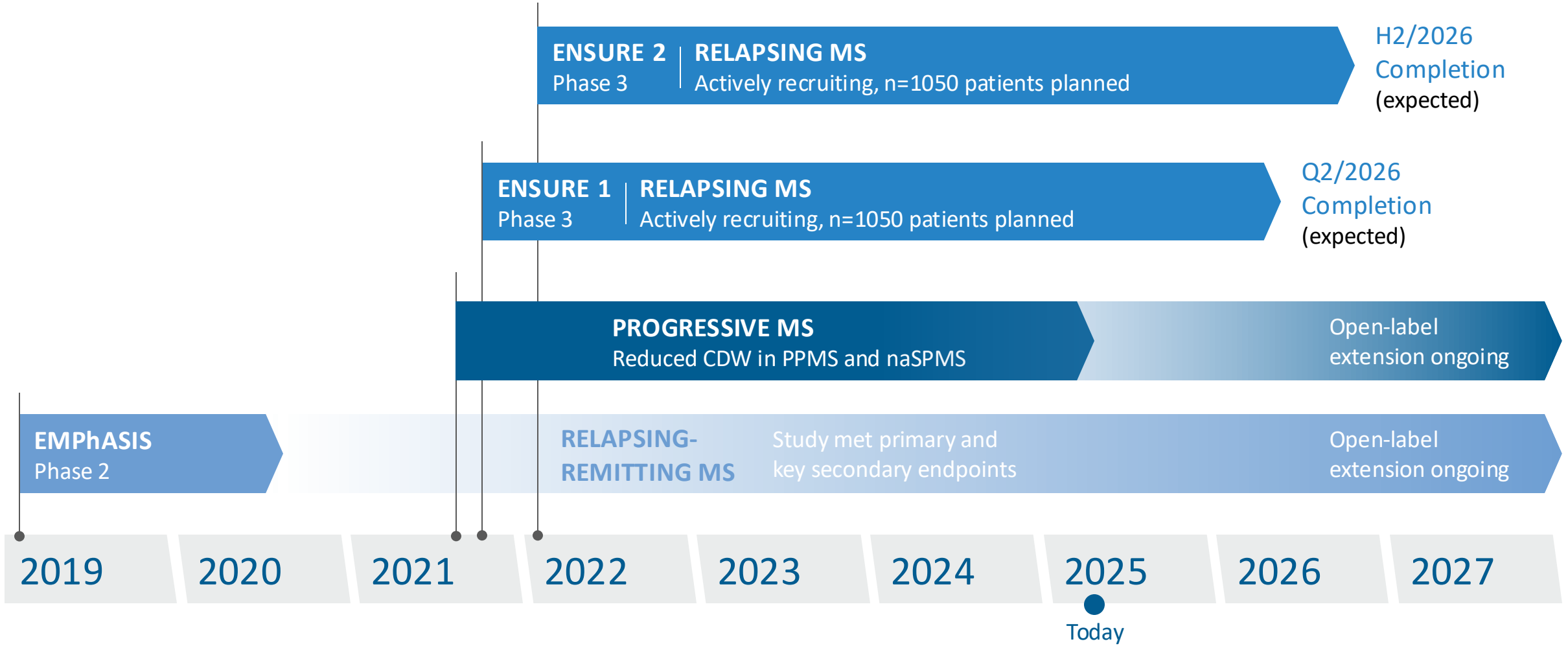
Vidofludimus Calcium: Clinical Trials Overview in Multiple Sclerosis (MS)



CDW: confirmed disability worsening; PPMS: primary progressive multiple sclerosis; naSPMS: non-active secondary progressive multiple sclerosis

Thank You!

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Top-Line Data Phase 2 CALLIPER Trial

Back-up

Large Proportion of Patients With Non-Active Disease as Compared to Historical Studies

	CALLIPER PPMS	ORATORIO PPMS***	CALLIPER naSPMS	EXPAND a/naSPMS**	HERCULES nrSPMS*
Gd+ at Screening	17.8%	22.4%	6.8%	21%	12.6%
On-Study Relapses	3.3% (5/152)	16%	7.1% (19/268)	19%	Not reported
Relapses Within 24 Months Prior to Study Entry	0%	0%	0%	64%	0%

PMS: progressive multiple sclerosis; PPMS: primary PMS; naSPMS: non-active secondary PMS; aSPMS: active secondary PMS; nrSPMS: non-relapsing secondary PMS; Gd+: gadolinium-enhancing
*Fox RJ., Bar-Or A., Traboulsee A. et al., Presented at: 2024 ECTRIMS; September 18-20; Copenhagen, Denmark. Abstract 4027 **Kappos L. et al., EXPAND Clinical Investigators. Lancet. 2018 Mar 31;391(10127):1263-1273 ***Clinical Review Report: Ocrelizumab (Ocrevus): (Hoffmann-La Roche Limited): Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2018 May. Results. Available from: https://www.ncbi.nlm.nih.gov/books/NBK533357/

Comparison of Patient Characteristics for CALLIPER Trial Versus ORATORIO Trial in the PPMS Population

	ORATORIO*		CALLIPER	
	Ocrelizimab	Placebo	Vidofludimus Calcium	Placebo
	(N=488)	(N=244)	(N=77)	(N=75)
Mean Age (Years)	44.7	44.4	47.3	45.3
Female (N,%)	237 (48.6%)	124 (50.8%)	51 (66.2%)	42 (56.0%)
EDSS - Mean	4.7	4.7	4.9	4.9
EDSS - Median	4.5	4.5	4.5	4.5
Gd+ Lesions at Baseline MRI (N,%)	27.5%	24.7%	**15.6%**	**20.0%**

* Clinical Review Report: Ocrelizumab (Ocrevus): (Hoffmann-La Roche Limited): Indication: Management of adult patients with early primary progressive multiple sclerosis as defined by disease duration and level of disability, in conjunction with imaging features characteristic of inflammatory activity [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2018 May. Results. Available from: https://www.ncbi.nlm.nih.gov/books/NBK533357/

PPMS: primary progressive multiple sclerosis; VidoCa: vidofludimus calcium; EDSS: Expanded Disability Status Scale; Gd+: gadolinium-enhancing lesions found on T1-weighted MRI images; MRI: magnetic resonance imaging

Comparison Patient Characteristics for CALLIPER Trial Versus Other Studies in the Non-Active/Non-Relapsing SPMS Population

	HERCULES 3*		CALLIPER	
	Tolebrutinib	Placebo	Vidofludimus Calcium	Placebo
	(N=754)	(N=377)	(N=135)	(N=133)
Mean Age (Years)	48.9	48.9	51.3	50.9
Female (N,%)	454 (60.2%)	242 (64.2%)	85 (63.0%)	93 (69.9%)
EDSS - Mean	5.49	5.59	5.35	5.35
EDSS - Median	6.0	6.0	6.0	6.0
Gd+ Lesions at Baseline MRI (%)	12.5%	13.1%	**7.4%**	**6.0%**

* Fox R.J., Bar-Or A., Traboulsee A. et al., Presented at: 2024 ECTRIMS; September 18-20; Copenhagen, Denmark. Abstract 4027

SPMS: secondary progressive multiple sclerosis; VidoCa: vidofludimus calcium; EDSS: Expanded Disability Status Scale; Gd+: gadolinium-enhancing lesions found on T1-weighted MRI images; MRI: magnetic resonance imaging

Vidofludimus Calcium Reduced Relative Risk of 24wCDW in Overall Study Population and Subtypes Compared to Placebo

Proportion of Patients With 24wCDW Events	Overall CALLIPER Patient Population	PPMS	naSPMS
Vidofludimus Calcium	16.2% (38/235)	19.5% (15/77)	14.1% (19/135)
Placebo	20.3% (47/232)	28.0% (21/75)	16.5% (22/133)
Relative Risk Ratio for 24wCDW	0.80	0.70	0.85
Relative Risk Reduction for 24wCDW	**20%**	**30%**	**15%**

Based on intent-to-treat population (ITT), patients are analyzed as randomized; 24wCDW: 24-week confirmed disability worsening; naSPMS: non-active secondary progressive multiple sclerosis; PPMS: primary progressive multiple sclerosis
24-week confirmed disability worsening based on EDSS scale (24wCDW), total of 85 events in the intent-to-treat population of CALLIPER trial
Data displayed for the reduction of risk of occurrence of 24wCDW events, percentages refer to the rate of 24wCDW in each of the treatment arms per disease subtype. Disease subtype as per investigator diagnosis at screening.

Relative Risk Reduction of 24wCDW Events Shows Similar Performance in Various Non-Active Patient Subpopulations

Proportion of Patients With 24wCDW Events	Overall CALLIPER Patient Population	Non-Active Disease	No Gd+ Lesions at Baseline	Non-Relapsing Population
Vidofludimus Calcium	16.2% (38/235)	12.1% (15/124)	14.2% (28/197)	14.4% (32/222)
Placebo	20.3% (47/232)	16.2% (18/111)	20.1% (39/194)	17.4% (38/218)
Relative Risk Ratio for 24wCDW	**0.80**	**0.75**	**0.71**	**0.83**
Relative Risk Reduction for 24wCDW	**20%**	**27%**	**29%**	**17%**

Provides Further Evidence for the Potential Neuroprotective Effects of Vidofludimus Calcium

Based on intent-to-treat population (ITT), patients are analyzed as randomized; 24wCDW: 24-week confirmed disability worsening; naSPMS: non-active secondary progressive multiple sclerosis; PPMS: primary progressive multiple sclerosis
24-week confirmed disability worsening based on EDSS scale (24wCDW), total of 85 events in the intent-to-treat population of CALLIPER trial. Data displayed for the reduction of risk of occurrence of 24wCDW events, percentages refer to the rate of 24wCDW in each of the treatment arms per disease subtype. Disease subtype as per investigator diagnosis at screening. Non-active disease: no study relapses, no Gd+ lesions at baseline or during study, no new or enlarging T2 lesions during study. No Gd+ lesions at baseline: in addition to no relapses in 24 months prior to study entry (as required by inclusion criteria). Non-relapsing population: no on-study relapses, in addition to no relapses in 24 months prior to study entry (as required by inclusion criteria)

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Vidofludimus Calcium Reduces Gadolinium-Enhancing Lesions During Study Period

Number of Patients with Gd+ Lesions	Overall CALLIPER Study Population	PPMS	a/naSPMS
Vidofludimus Calcium	6.4%	5.2%	7.0%
Placebo	10.8%	12.0%	10.2%
Relative Risk Ratio	0.59	0.43	0.69
Relative Risk Reduction	**41%**	**57%**	**31%**

ITT = intent-to-treat analysis set; Gd+ = gadolinium-enhancing (in magnetic resonance imaging examinations); PPMS = primary progressive multiple sclerosis; SPMS = secondary progressive multiple sclerosis; a: active; na: non-active; N = total number of patients in the treatment group and analysis set; n = number of patients in the corresponding category and treatment group
Percentages for subcategories of Disease Type are calculated based on total number of patients in the corresponding disease type and treatment group. Disease subtypes are based on investigator diagnosis at screening visit.