Immunic THERAPEUTICS

# Relapsing Multiple Sclerosis R&D Day

**September 9, 2026**
**Virtual**

**NASDAQ: IMUX**

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# Virtual Relapsing 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

**Amit Bar-Or, MD, FRCPC**
Department of Neurology, Perelman School of Medicine, University of Pennsylvania

**Stephen Krieger, MD, FAAN**
Department of Neurology, Icahn School of Medicine, The Mount Sinai Hospital

## Moderator

**Jessica Breu**
Vice President Investor Relations and Communications

# Vidofludimus Calcium – Unique Potential to Transform the MS Treatment Landscape

## Agenda Virtual Relapsing Multiple Sclerosis R&D Day

| | | |
|---|---|---|
| 11:00 - 11:05 | **Welcome and Introduction** | Erik Lundgren<br>Chief Executive Officer |
| 11:05 - 11:20 | **Expert Talk: Multiple Sclerosis: Targeting Novel Mechanisms to Address Unmet Clinical Needs** | Amit Bar-Or, MD, FRCPC<br>Department of Neurology, Perelman School of Medicine, University of Pennsylvania |
| 11:20 - 11:35 | **Vidofludimus Calcium's Dual Mode of Action: Benefits Beyond Traditional Anti-Inflammatory Treatment** | Hella Kohlhof, PhD<br>Co-Founder & Chief Scientific Officer |
| 11:35 - 11:45 | **Ongoing Phase 3 ENSURE Program of Vidofludimus Calcium in Relapsing Multiple Sclerosis** | Michael A. Panzara, MD, MPH<br>Chief Medical Officer |
| 11:45 - 12:00 | **Expert Talk: The Unmet Need in Relapsing Multiple Sclerosis Has Changed** | Stephen Krieger, MD, FAAN<br>Department of Neurology, Icahn School of Medicine, The Mount Sinai Hospital |
| 12:00 - 12:15 | **Positioning and Commercial Opportunity for Vidofludimus Calcium in Relapsing Multiple Sclerosis** | Jason Tardio<br>President & Chief Operating Officer |
| 12:15 - 12:20 | **Outlook: Upcoming Milestones for Vidofludimus Calcium in Multiple Sclerosis** | Erik Lundgren<br>Chief Executive Officer |
| 12:20 - 12:30 | **Q&A Session** | |

# 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**

# 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<br>ENSURE-1 |  | Both trials fully enrolled | Top-line data for both trials expected by end of 2026 |
| **Vidofludimus Calcium** (IMU-838) | Relapsing MS<br>ENSURE-2 |  | Both trials fully enrolled | Top-line data for both trials expected by end of 2026 |
| **Vidofludimus Calcium** (IMU-838) | Progressive MS<br>Phase 3 |  | In preparation | Initiation of Phase 3 program expected later in 2026 |
| **Vidofludimus Calcium** (IMU-838) | Relapsing-Remitting MS<br>EMPhASIS |  | Trial met primary and key secondary endpoints<br>OLE ongoing | Additional OLE data expected |
| **Vidofludimus Calcium** (IMU-838) | Progressive MS<br>CALLIPER |  | Numerically reduced CDW, signals for CDI*<br>OLE ongoing | Additional OLE data expected |
| **IMU-381** | Neurologic Diseases<br>Nurr1 Platform |  | Candidate screening | Lead candidate identification |

* 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

# Vidofludimus Calcium Has the Potential to Transform the MS Market

## Substantial Opportunities: MS Remains a Large and Growing Market

### BLOCKBUSTER POTENTIAL

MS has produced **11 distinct billion-dollar products over the last 25 years**, making it one of the most commercially successful specialty pharmaceutical markets in neurology.

The global MS market continues to grow and is estimated to exceed **$30 billion annually** by the early 2030s.[1]

### Attractive Market Dynamics

- Multiple blockbuster therapies can **successfully coexist**, reflecting the large patient population, heterogenous disease presentation, and evolving unmet needs.
- The MS market is **not a winner-take-all market** and switching is common, expected, and often necessary throughout a patient's disease journey.

### Innovation Drives

- **Novel mechanisms of action** are urgently needed, particularly to address the neurodegenerative aspect of the disease.
- New entrants offering **improved efficacy, safety, or tolerability** are capturing share despite competition from incumbent products.

1. Sales numbers in G7 countries (U.S., UK, Canada, Japan, Germany, France, Italy) in USD billion; Multiple Sclerosis Landscape and Forecast by Decision Resources Group Part of Clarivate

MS: multiple sclerosis

# Expert Talk: Amit Bar-Or, MD, FRCPC

Department of Neurology, Perelman School of Medicine,
University of Pennsylvania

# Vidofludimus Calcium's Dual Mode of Action: Benefits Beyond Traditional Anti-Inflammatory Treatment

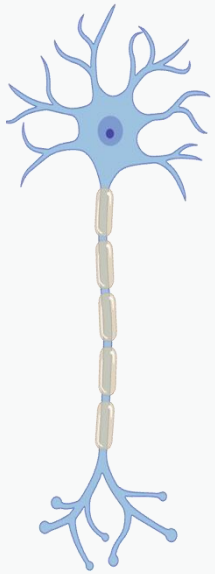
Hella Kohlhof, PhD I Co-Founder & Chief Scientific Officer

# Vidofludimus Calcium: A Unique Dual Mechanism Approach to MS

Potentially the Only Oral MS Drug Addressing Both PIRA and RAW Simultaneously

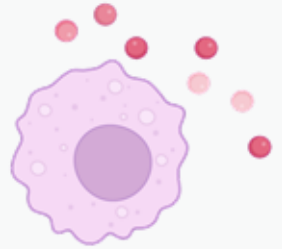
## Direct Nurr1 Activator

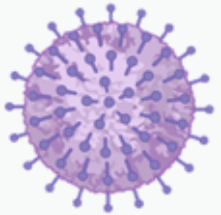
- Modulates gene expression directly in neurons, mediating neuroprotection and neuronal survival
- Reduces neurotoxicity of microglia and astrocytes, indirectly supporting neuronal survival
- Targeting neurodegeneration beyond focal inflammation



## Selective DHODH Inhibitor

- Selectively targets metabolically hyperactive T and B lymphocytes
- Reduces focal inflammation, MRI lesions, and relapses
- Prevents reactivation of EBV





PIRA: progression independent of relapse activity; RAW: relapse-associated worsening; Nurr1: nuclear receptor related 1; DHODH: dihydroorotate dehydrogenase; MRI: magnetic resonance imaging; EBV: Epstein-Barr virus

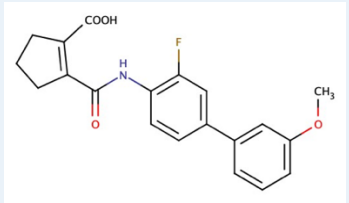
# Vidofludimus Calcium is a Selective DHODH Inhibitor

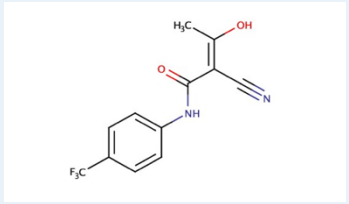
## Selectively inhibits DHODH

| | DHODH IC50 in nM | | |
|---|---|---|---|
| | **Human** | **Murine** | **Rat** |
| **Vidofludimus** | 240 | 5100 | 1000 |
| **Teriflunomide** | 1700 | 300 | 4 |

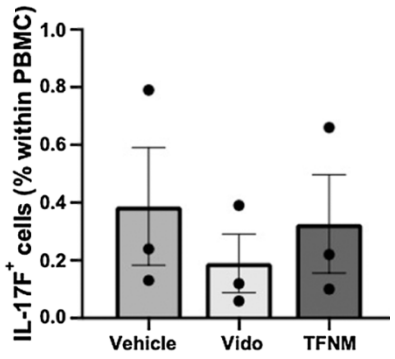
**Vidofludimus** does **not inhibit kinases** in a panel of 94 human kinases

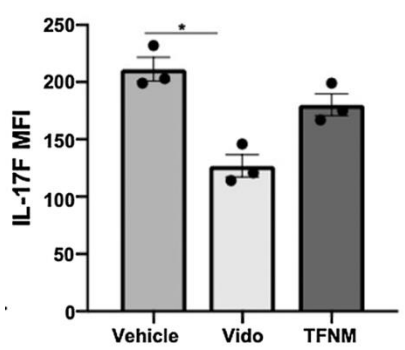
Whereas teriflunomide targets PIM, Aurora A, PDGFR, **EGFR***



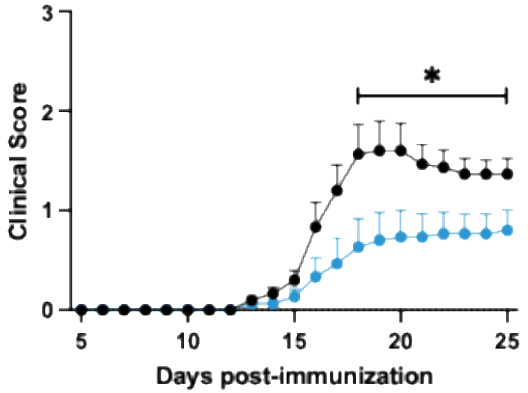




## Reduces hyperactive/high affinity immune cells, due to restriction of pyrimidines




## Reduces disease score in an inflammation driven EAE model

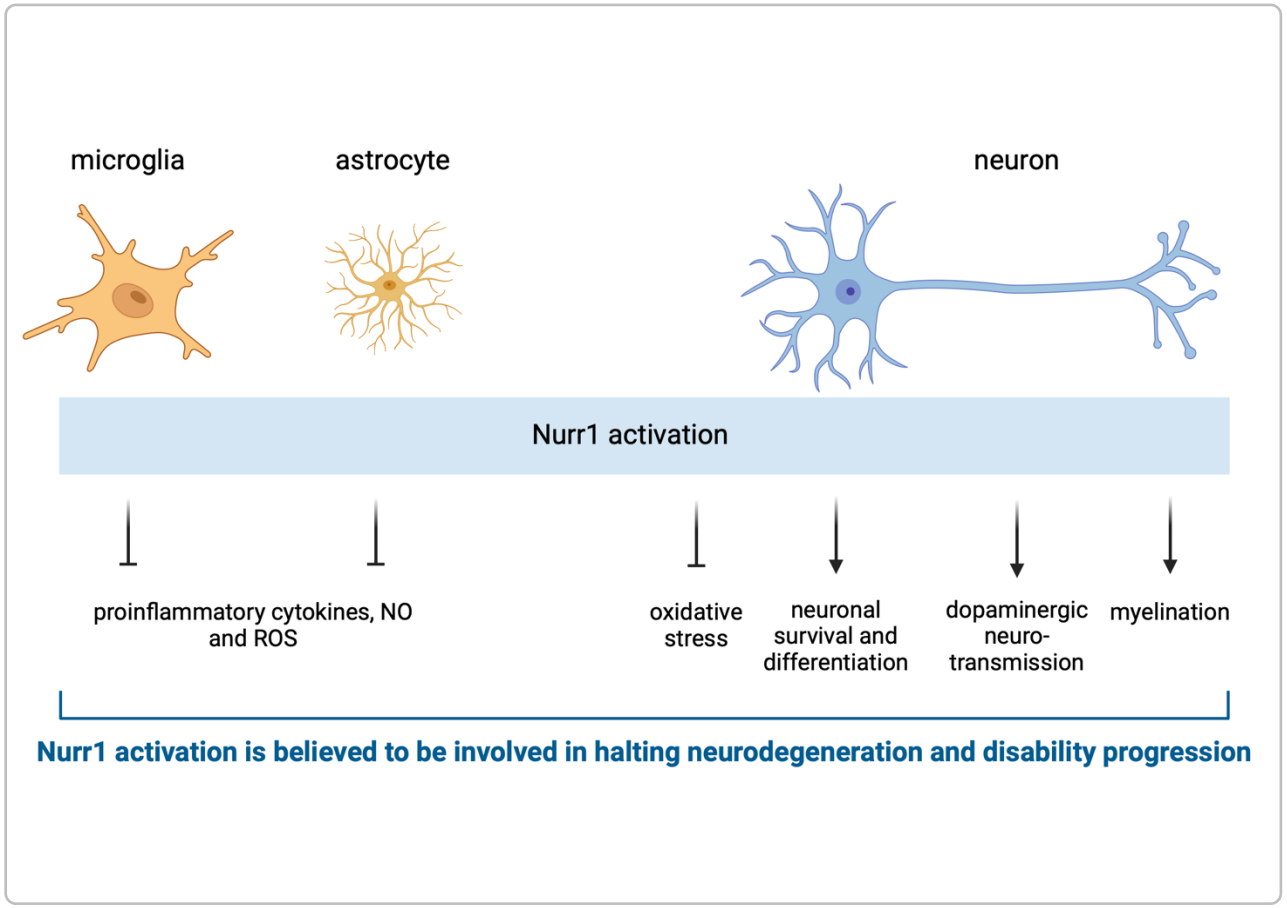



**Vehicle**

**Vido 150 mg/kg**

* at teriflunomide 7 mg trough levels 60 uM; EGFR inhibition is known to be related to skin disorders, diarrhea, liver enzyme elevations (Orlowski et al., 2016); IL-17 assay: vidofludimus 10 uM; teriflunomide 100 uM
DHODH: dihydroorotate dehydrogenase; EAE: experimental autoimmune encephalomyelitis

# … and a Potent Nurr1 Activator – Relevant in MS Biology and Neuroprotection




- Nurr1 regulates neuronal survival, oxidative stress responses, and neuroinflammatory signaling.[1]
- Reduced Nurr1 expression in RRMS is associated with higher relapse rate and EDSS.[2]
- Nurr1 expression normalizes during pregnancy, coinciding with reduced MS disease activity.[3]
- In postmortem MS motor cortex, higher Nurr1 expression is associated with greater neuronal preservation.[4]

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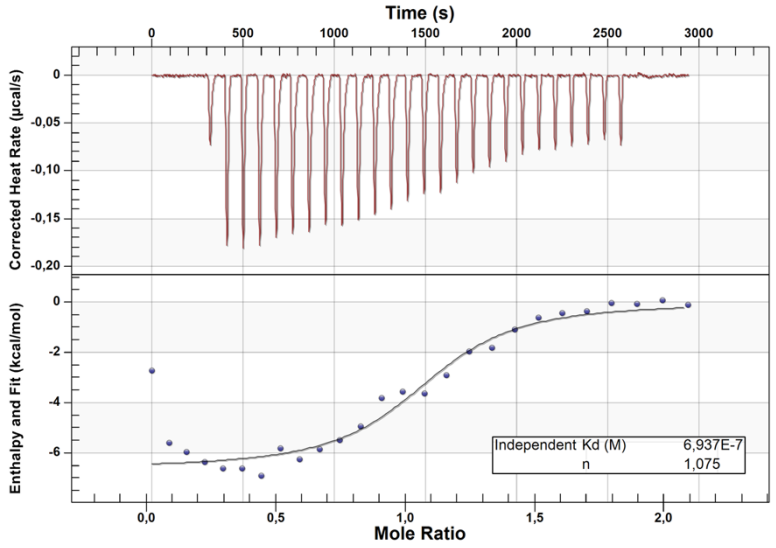
Adapted from Willems S et al. 2022. J Med Chem. created in BioRender.com; [1]Jeon et al. 2019. Aging Dis. [2]Montarolo et al. 2019. Int J Mol Sci. [3]Gilli et al. 2010. PLoS One. [4]Pansieri et al. 2023. Brain Commun
Nurr1: nuclear receptor-related 1; NO: nitric oxide; ROS: reactive oxygen species; RRMS: relapsing-remitting multiple sclerosis; EDSS: Expanded Disability Status Scale

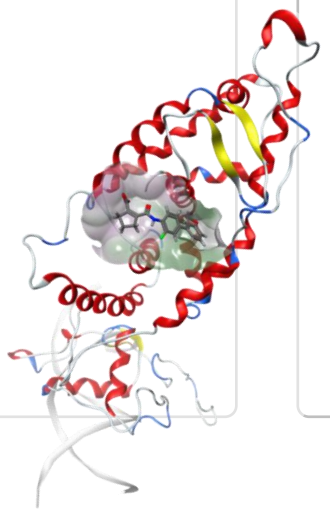
# Vidofludimus Calcium Directly Binds to Nurr1

## ITC

### ISOTHERMAL TITRATION CALORIMETRY

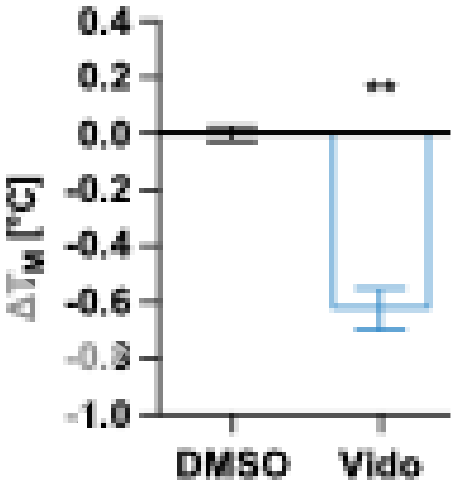



Vidofludimus Calcium → Binding signal detected



## DSF

### DIFFERENTIAL SCANNING FLUORIMETRY




$\Delta T_M$ (melting temperature) shifts indicate ligand-Nurr1 interaction

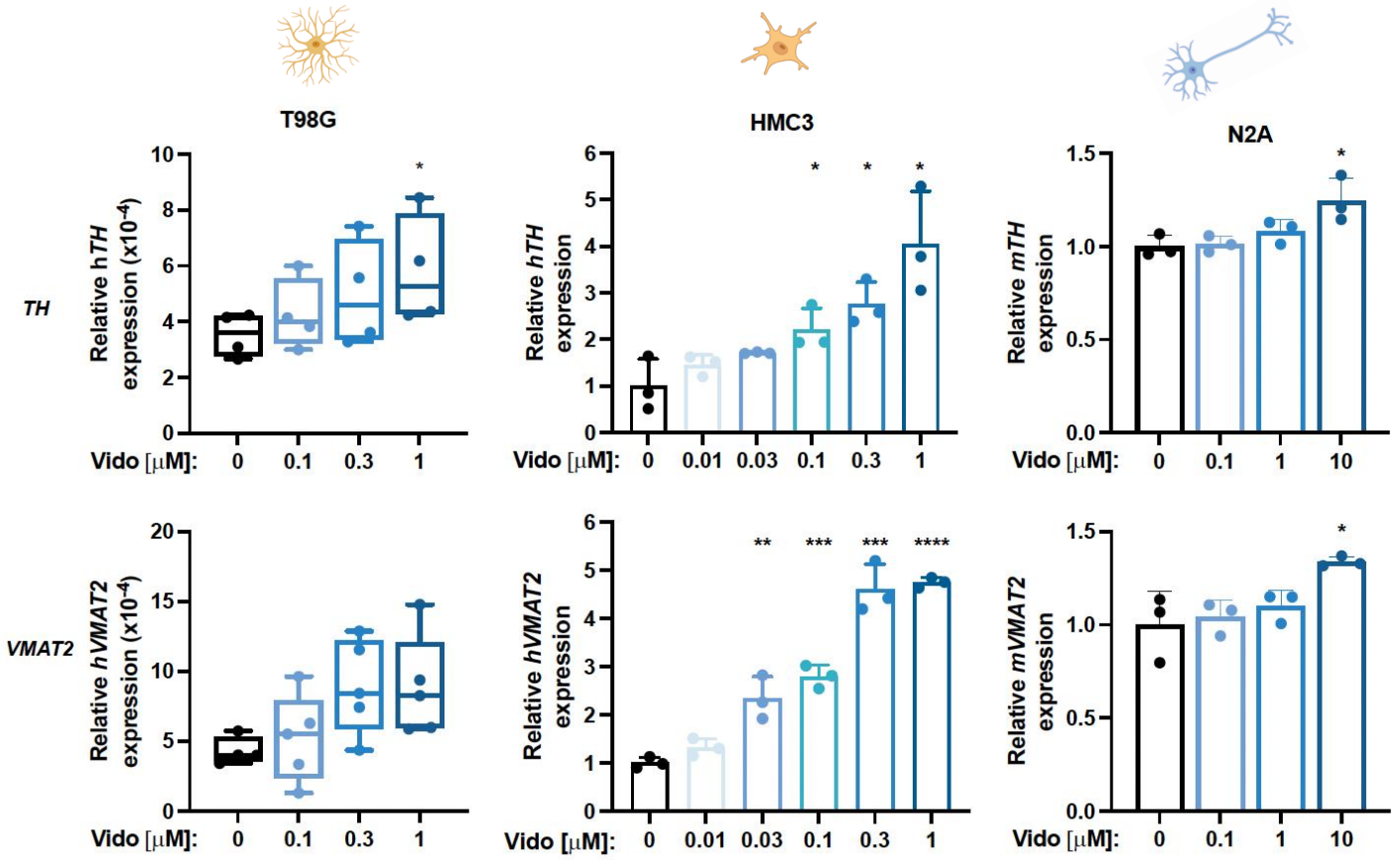
Vidofludimus calcium induces a $\Delta T_M$ shift

Performed at LMU, Munich, Daniel Merk

Nurr1: nuclear receptor-related 1; ΔTM : change in protein melting temperature

# Nurr1-Associated Gene Expression by Vidofludimus Calcium

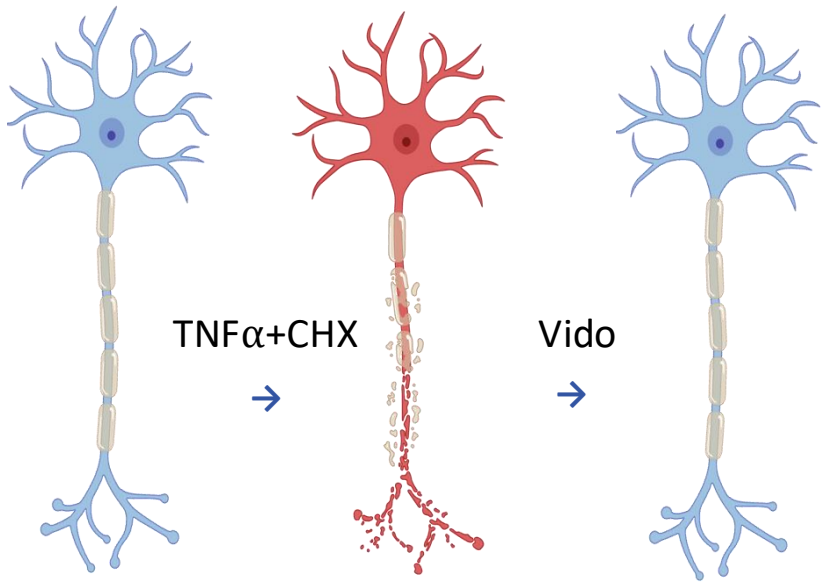
Vidofludimus calcium increased expression of selected Nurr1-regulated genes involved in neuronal function in different cell types.

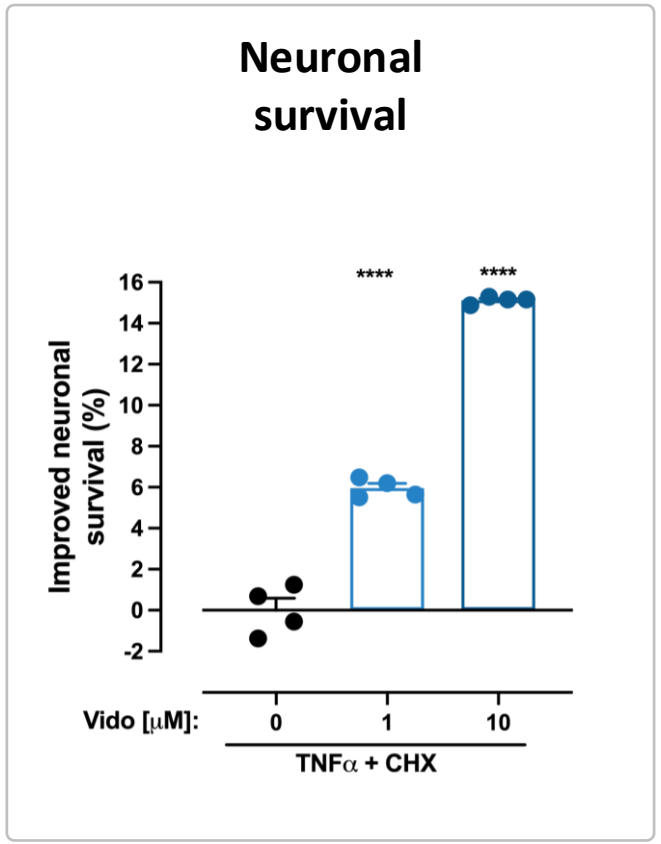


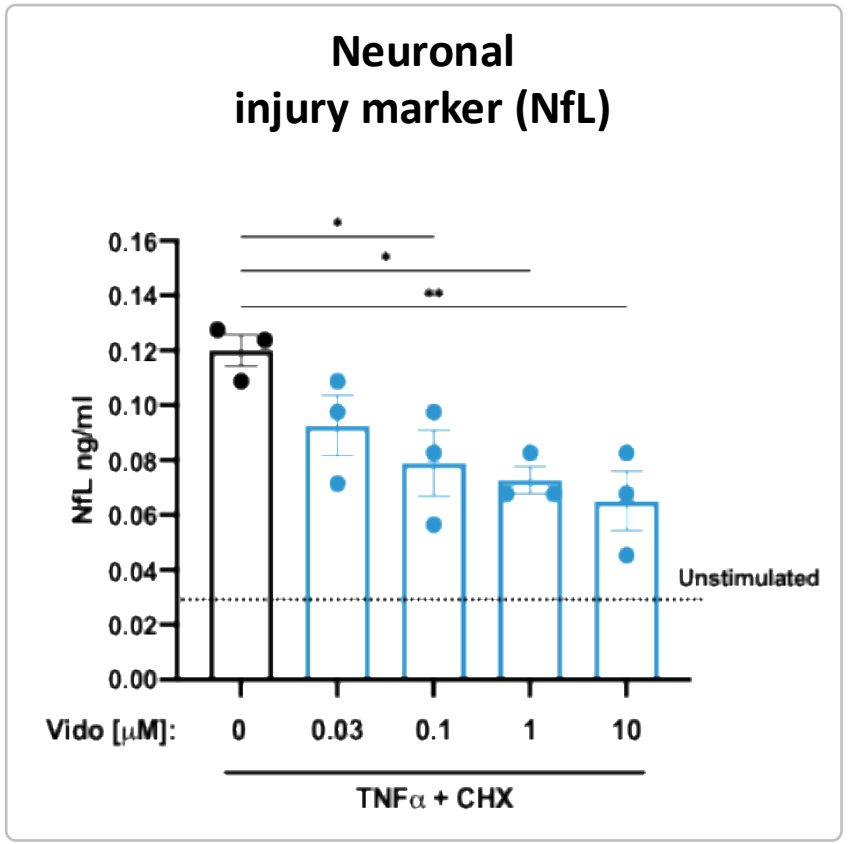

Performed at LMU, Munich, Daniel Merk and City of Hope, USA, Zuoming Sun

Nurr1: nuclear receptor-related 1; TH: tyrosine hydroxylase; VMAT2: vesicular monoamine transporter 2; T98G: human astrocyte-like glial tumor cells; HMC3: human microglial cell line; N2A: murine neuronal model

# Vidofludimus Calcium Improved Neuronal Survival and Reduced Injury Under Apoptotic Stress (TNFα+CHX Model)



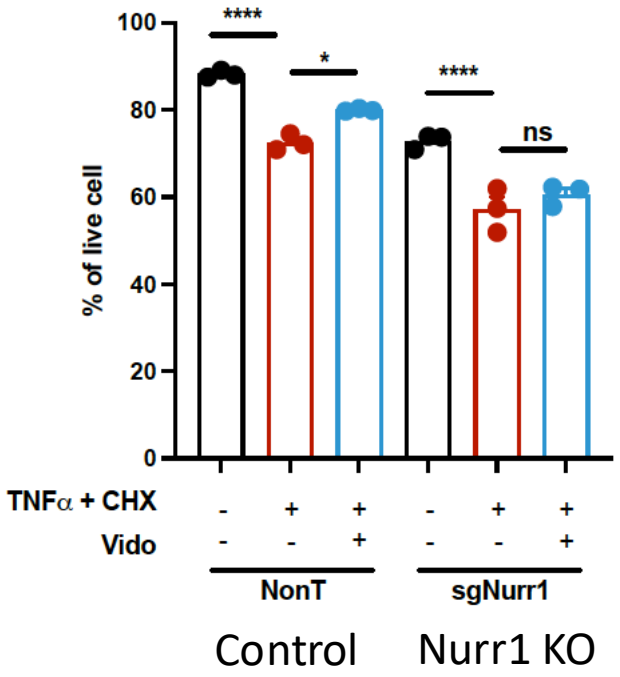

Vidofludimus calcium was associated with improved neuronal survival and reduced NfL release under apoptotic stress in N2A cells.

Performed at City of Hope, USA, Zuoming Sun

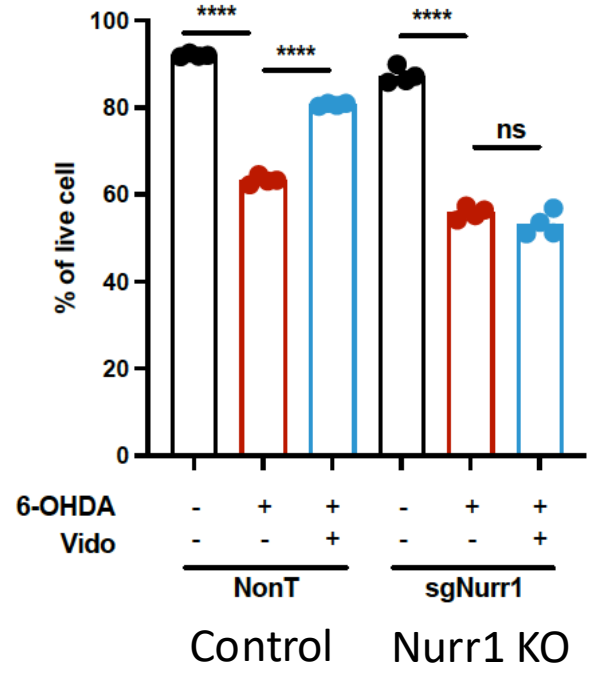
TNF: tumor necrosis factor; CHX: cycloheximide; SH-SY5Y: human neuroblastoma line; NfL: neurofilament light chain

# Vidofludimus-Associated Improved Neuronal Survival Requires Nurr1

**TNFα+CHX**



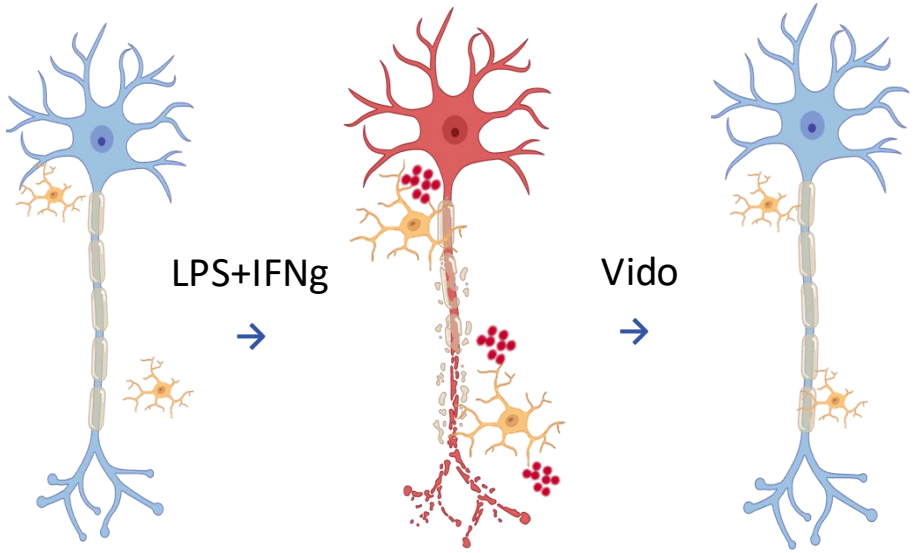

**6-OHDA**

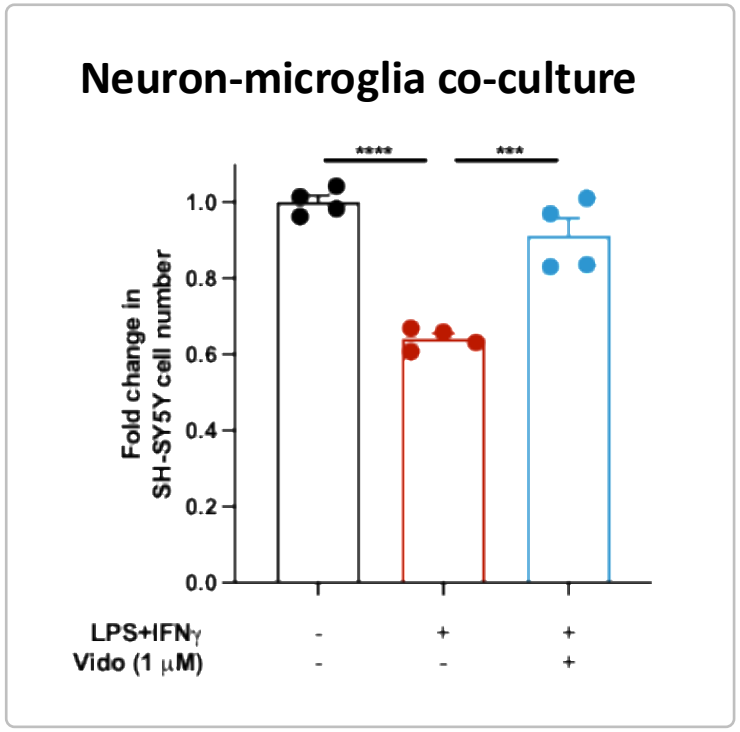


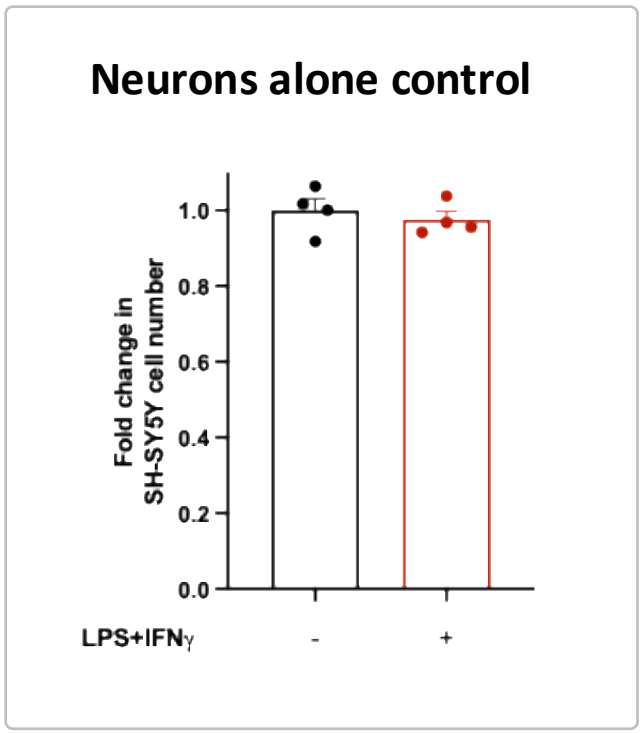

CRISPR-mediated Nurr1 knockout abolished the neuronal survival benefit of vidofludimus calcium under different models of apoptosis in SH-SY5Y line.

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

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




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

Performed at City of Hope, USA, Zuoming Sun

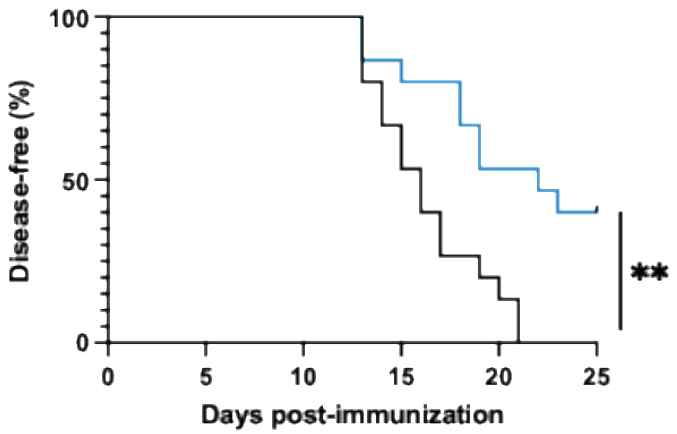
LPS: lipopolysaccharide; IFN: interferon; SH-SY5Y: human neuroblastoma line

# Vidofludimus Calcium Reduced Disease Severity in EAE

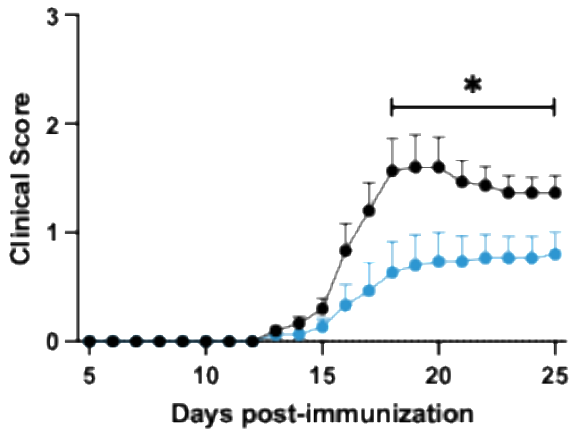
**Vehicle**

**Vido 150 mg/kg**

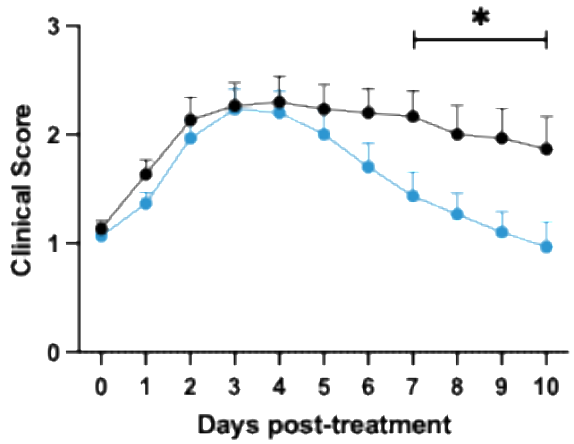
## Prophylactic




## Prophylactic




## Therapeutic



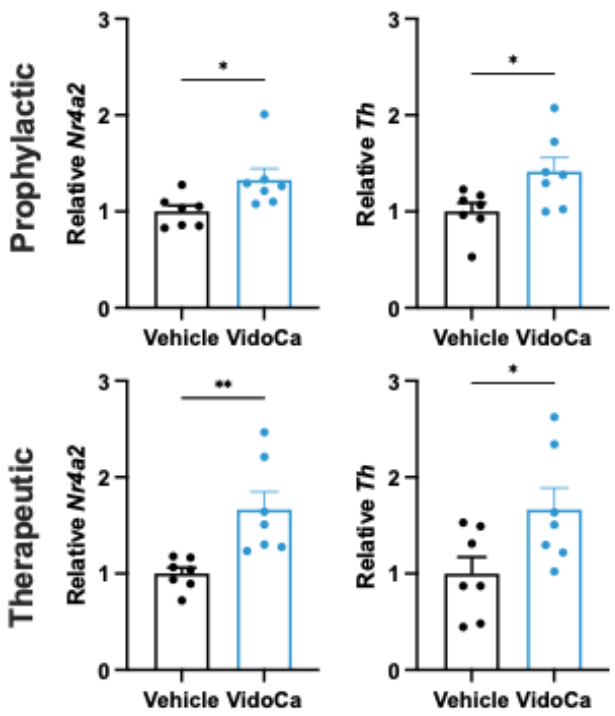

Vidofludimus calcium reduced clinical disease severity in both prophylactic and therapeutic EAE models.

Performed at City of Hope, USA, Zuoming Sun

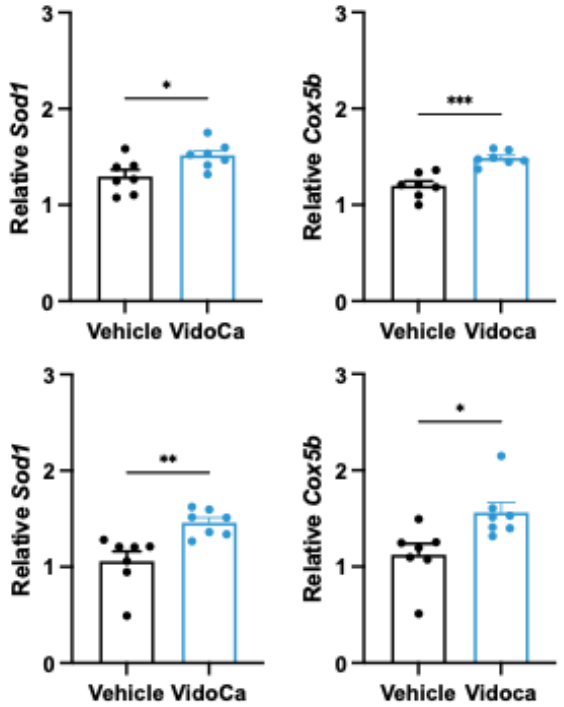
EAE: experimental autoimmune encephalomyelitis

# Vidofludimus Calcium Modulated Nurr1-Related Gene Expression in CNS

## BRAIN




## SPINAL CORD




**Vehicle**

**Vido 150 mg/kg**

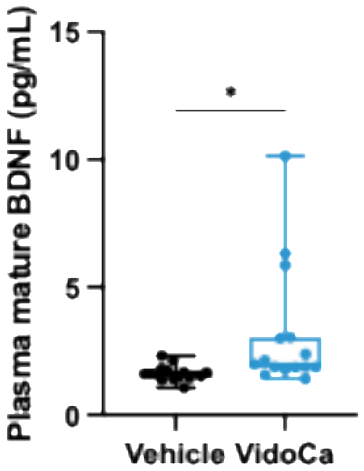
Vidofludimus calcium treatment was associated with modulation of Nurr1-related gene expression in CNS tissue, in both prophylactic and therapeutic EAE settings.

Performed at City of Hope, USA, Zuoming Sun / Nurr1: nuclear receptor-related 1; CNS: central nervous system; Nr4a2: nuclear receptor 4A2, TH: tyrosine hydroxylase; SOD1: superoxide dismutase 1; Cox5b: cytochrome c oxidase subunit 5B; EAE: experimental autoimmune encephalomyelitis

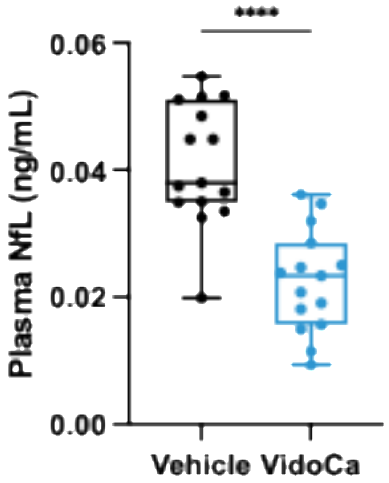
# Vidofludimus Calcium Modulated Neurotrophic and Neuroaxonal Markers in EAE

**Vehicle**
**Vido 150 mg/kg**

## BDNF




## NFL



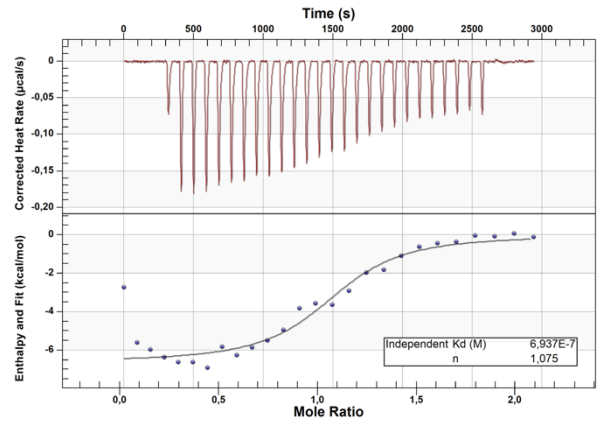

Vidofludimus calcium treatment was associated with increased plasma BDNF and reduced NfL levels in both prophylactic and therapeutic settings.*

Performed at City of Hope, USA, Zuoming Sun * Data from therapeutic study are shown. Similar results were found in the prophylactic setting.
EAE: experimental autoimmune encephalomyelitis; BDNF: brain-derived neurotrophic factor; NfL: neurofilament light chain

# Is Every DHODH Inhibitor a Nurr1 Agonist? – NO!

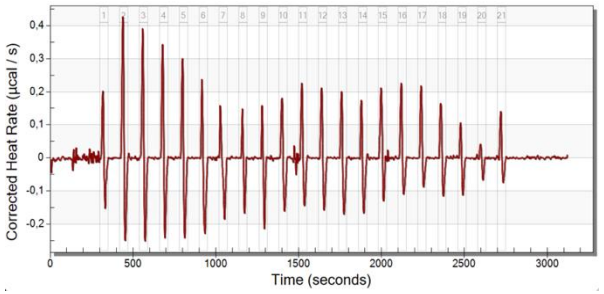
## ITC

### ISOTHERMAL TITRATION CALORIMETRY




**Vidofludimus Calcium**

→ Binding signal detected

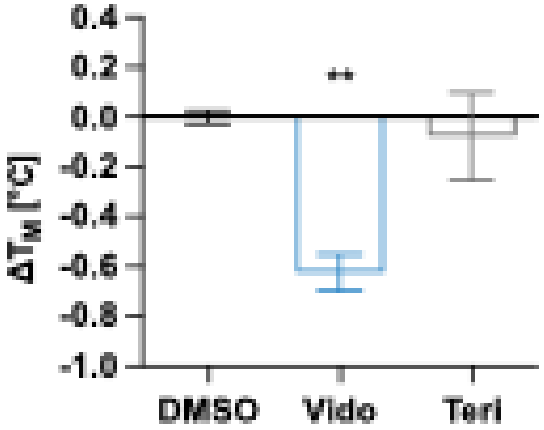



**Teriflunomide**

→ No measurable binding

## DSF

### DIFFERENTIAL SCANNING FLUORIMETRY

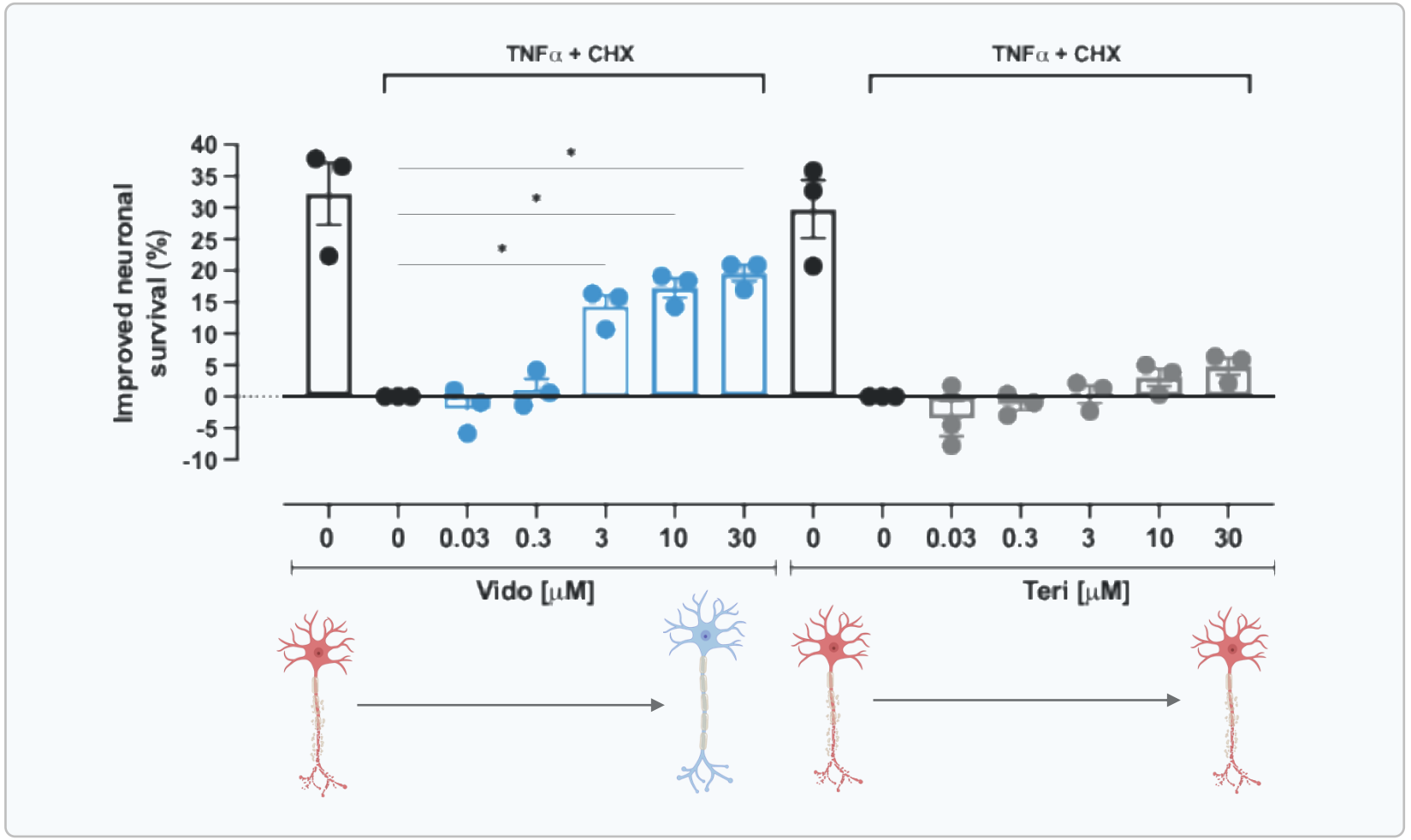



$\Delta T_M$ (melting temperature) shifts indicate ligand-Nurr1 interaction

Vidofludimus calcium induces a $\Delta T_M$ 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

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




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

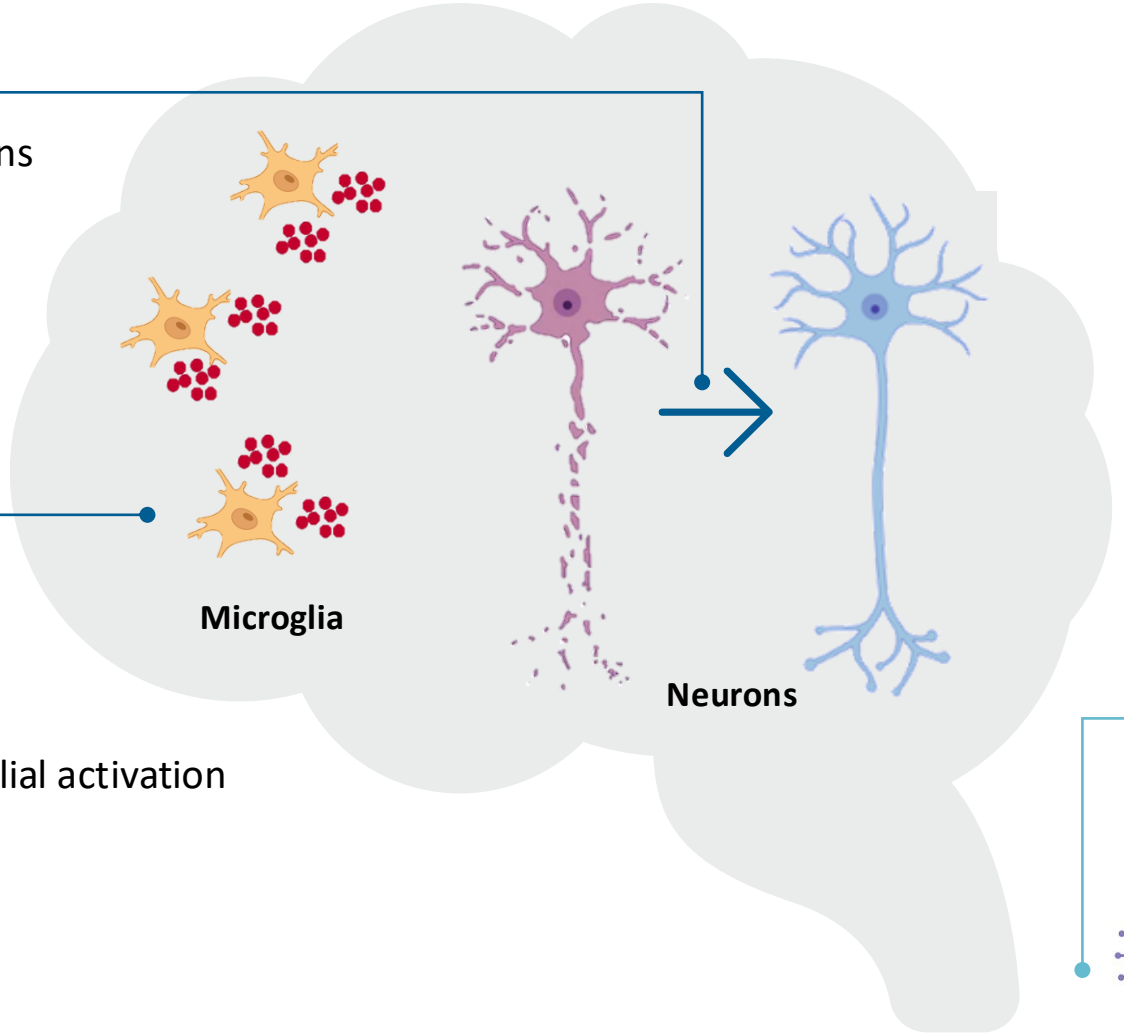
Performed at City of Hope, USA, Zuoming Sun
TNF: tumor necrosis factor; CHX: cycloheximide

# Vidofludimus Calcium: Nurr1 Activation and Selective DHODH Inhibition

Improving survival of neurons

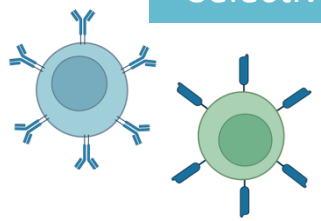
Direct Nurr1 Activation

Reducing neurotoxic microglial activation



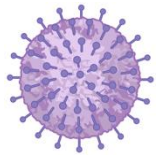

Targeting metabolically active T & B cells

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

# Ongoing Phase 3 ENSURE Program of Vidofludimus Calcium in Relapsing MS

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

# Vidofludimus Calcium in Relapsing MS: Even with 20+ Approved DMTs, Significant Unmet Needs Exist

## Relapsing MS

**~400K** Diagnosed Patients in the U.S.[1,2]

- High unmet needs remain despite numerous approved therapies, particularly for preventing disability progression or improving symptoms.
- Physicians continue to seek differentiated oral therapies with a favorable profile of benefit/risk and convenience.
- Even with a multitude of options, ~30-35% of diagnosed patients are currently not treated with a DMT.[1,2]
- MS treatment is dynamic, with physicians routinely switching therapies based upon profile, changing needs over patient journey.

"I was disappointed when I was told I was now too old to continue with any of these drugs, and I now feel lost."

"Fatigue and cognitive issues are my greatest struggle I have a cousin with MS who has more mobility issues and isn't able to leave her house. While our two versions of MS look different to the outside world, there's a huge weight that we both carry. I'm here to fight for us both."

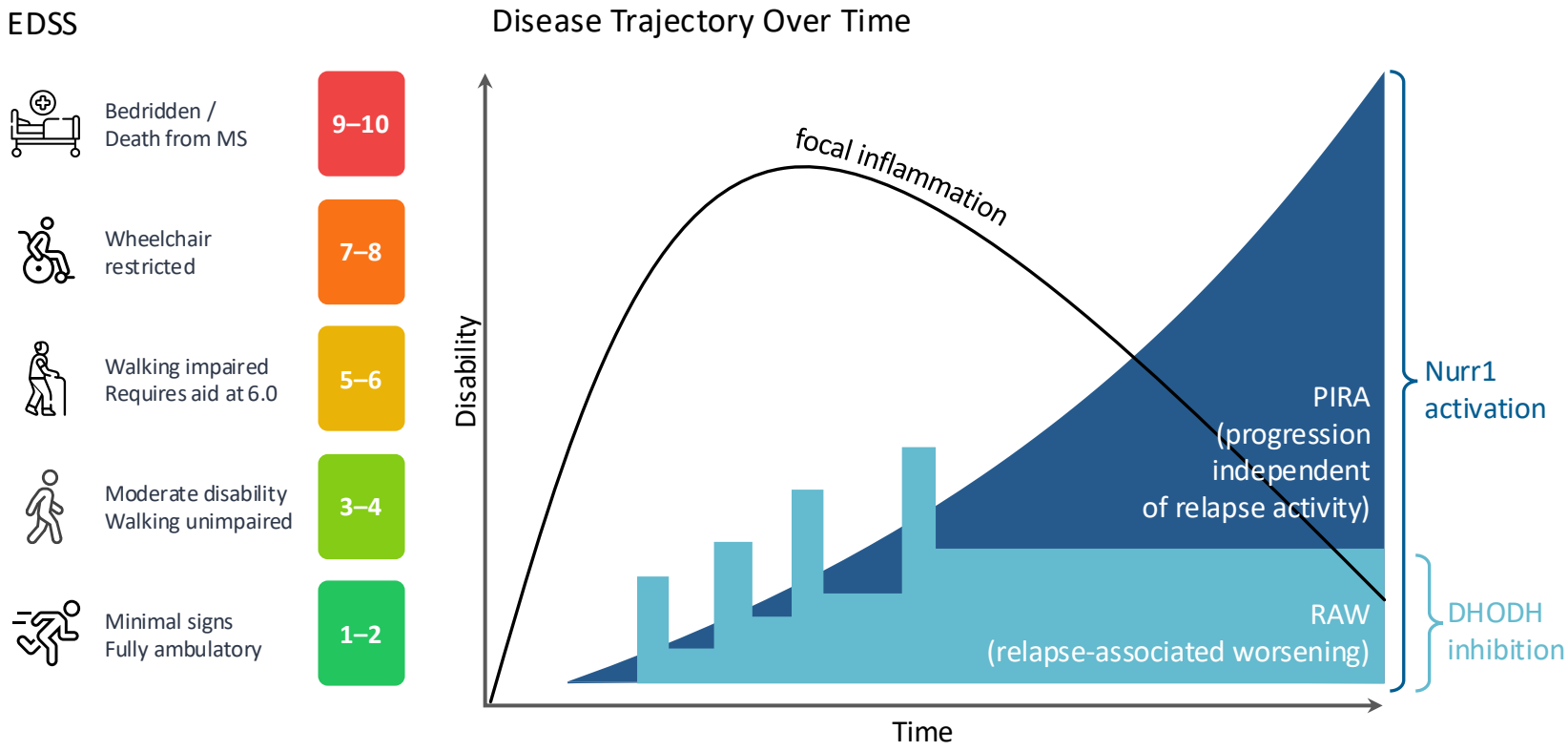
"At 69, my focus is on whether it's time to stop. Some sources say that the MS has quieted at this age, but I'm afraid to stop if the drug is still working."

"The shift from a predictable twice-a-day pill to a DMT that requires pretreatment protocols and travel to an infusion site has changed my life this year. After being mostly symptom-free since I was diagnosed, I've not felt good since the day of my first infusion."


1. Multiple Sclerosis Disease Landscape and Forecast Research Report by Decision Resources Group Part of Clarivate; 2. Immunic analysis; Quotes and image: National MS Society Voice of the Patient Report 2026
MS: multiple sclerosis; DMT: disease-modifying therapy; NDA: New Drug Application; IDMC: Independent Data Monitoring Committee

# Current DMTs Target Inflammation, None Stop/Reverse Disability Accumulation

## 20+ Therapies Exist for Relapsing MS, None Adequately Address the Neurodegeneration Driving Progression




**Progression Independent of Relapse Activity (PIRA):** Neurodegeneration accumulates continuously, even in patients with no relapses and inactive MRIs, driving long-term disability and impacting quality of life.

**Relapse-Associated Worsening (RAW):** Inflammatory attacks drive acute MRI lesions and episodic disability worsening. 20+ approved disease-modifying therapies potentially address this component.

Future MS therapies should address both acute inflammatory activity and the mechanisms driving progression, while maintaining favorable safety and tolerability profiles to facilitate long-term use.

Graphic adapted from Kretzschmar A., Symposium MSVirtual2020 / 8th Joint ACTRIMS-ECTRIMS Meeting and REVIEW article, Front. Immunol., 29 November 2023, Sec. Multiple Sclerosis and Neuroimmunology, Volume 14 – 2023 / MS: multiple sclerosis; DMT: disease-modifying therapy; EDSS: Expanded Disability Status Scale; Nurr1: nuclear receptor-related-1; DHODH: dihydroorotate dehydrogenase; MRI: magnetic resonance imaging

# EMPhASIS: Strong Efficacy, Durable Long-Term Benefit, and Favorable Safety and Tolerability in Relapsing-Remitting MS

## Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase 2 Clinical Trial (NCT03846219)

268 patients in 36 centers across four European countries

Double-blind treatment period of 24 weeks

- Cohort 1: 30 mg and 45 mg vidofludimus calcium or placebo QD
- Cohort 2: 10 mg vidofludimus calcium or placebo QD

**Key Inclusion Criteria:**

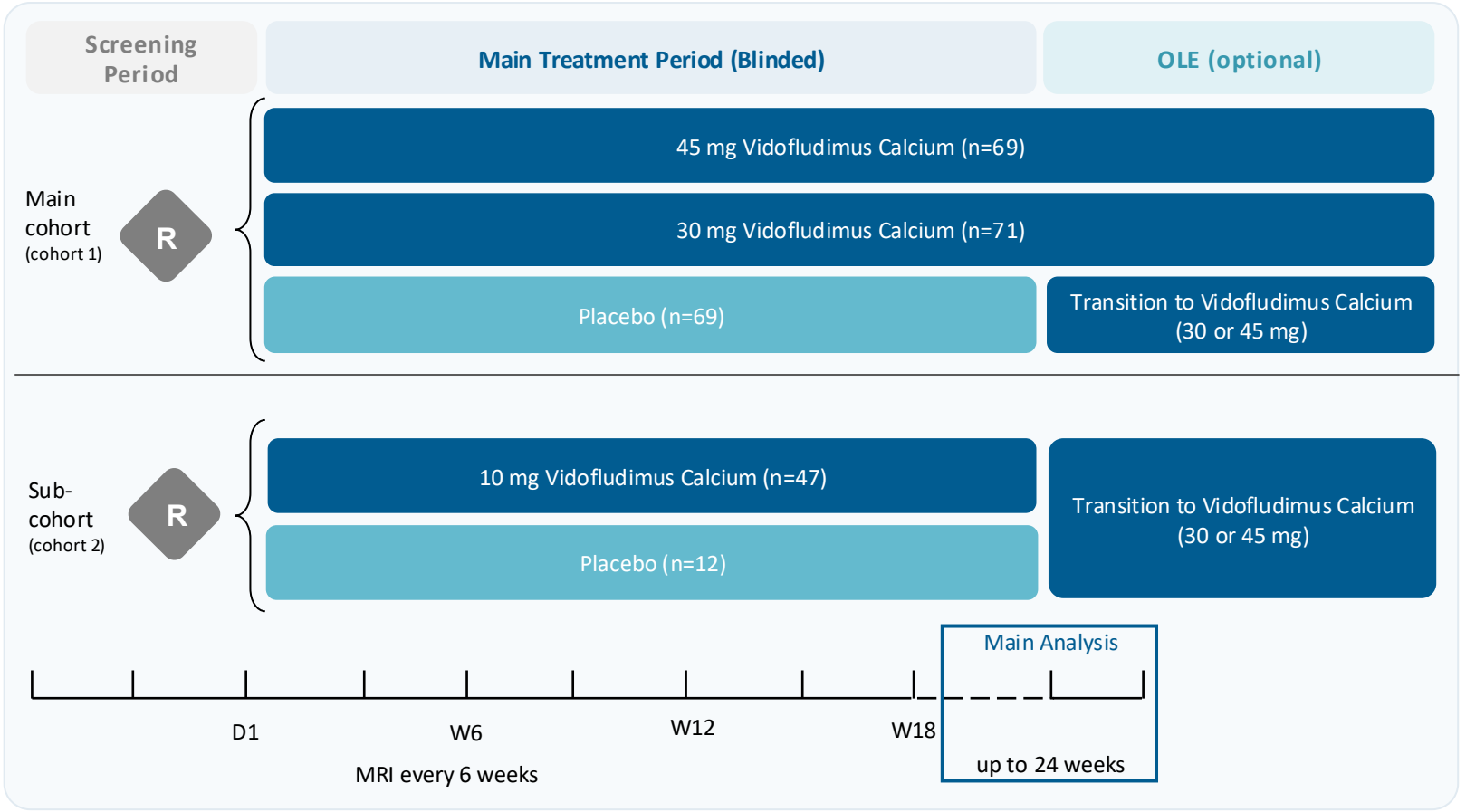
- Patients aged 18 to 65 years (inclusive)
- RRMS according to revised McDonald criteria (2017)
- EDSS score between 0 and 4.0 at screening

**Primary Endpoint:**

- Cumulative number of CUA MRI lesions on 45 mg dose versus placebo

**Secondary Endpoints Include:**

- Cumulative number of CUA MRI lesions on 30 mg, new Gd+ lesions



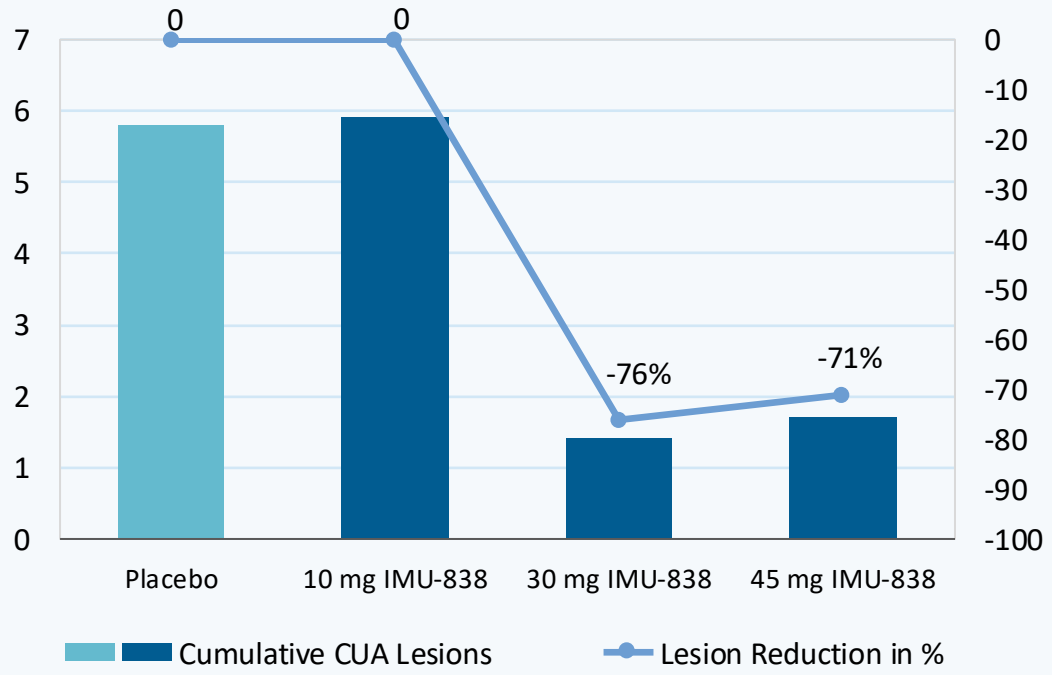

Fox RJ, et al. Ann Clin Transl Neurol. 2022;9(7):977-987; Fox RJ, et al. Neurol Neuroimmunol Neuroinflamm. 2024;11(3):e200208; ClinicalTrials.gov NCT03846219

MS: multiple sclerosis; RRMS: relapsing-remitting MS; QD: quaque die = once-daily; EDSS: Expanded Disability Status Scale; CUA: combined unique active; MRI: magnetic resonance imaging; Gd+: gadolinium-enhancing; OLE: open-label extension; R: randomization; D: day; W: week

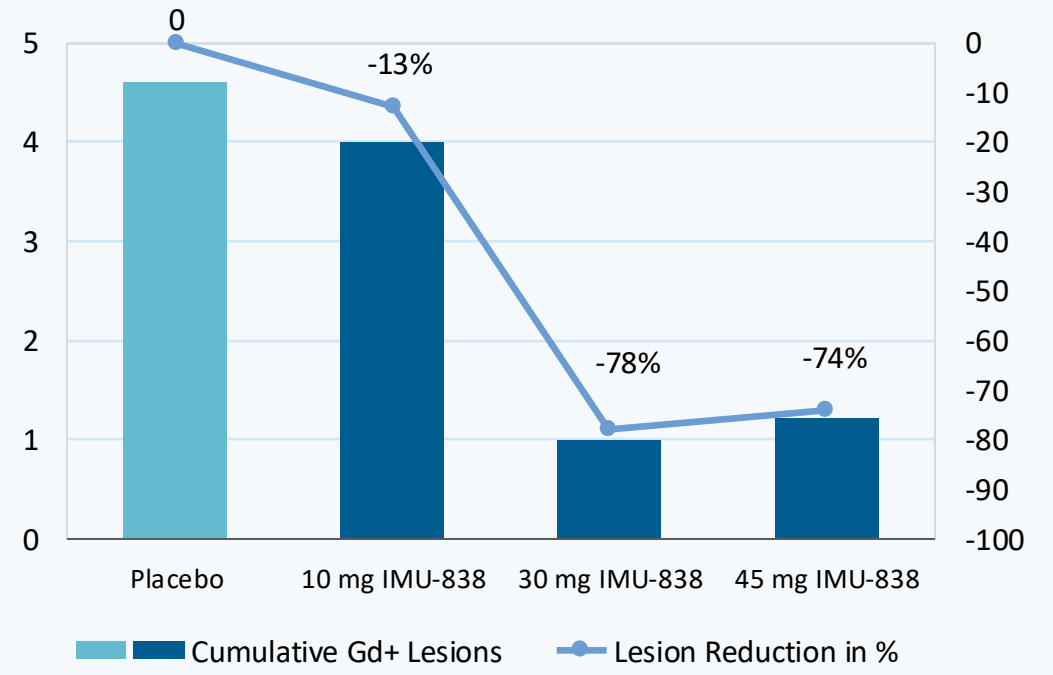
# Robust Reduction in MRI Lesion Activity Over 24 Weeks

Primary and Key Secondary Endpoints Both Highly Statistically Significant, Pooled Cohorts 1&2

## Reduction in CUA Lesions up to Week 24



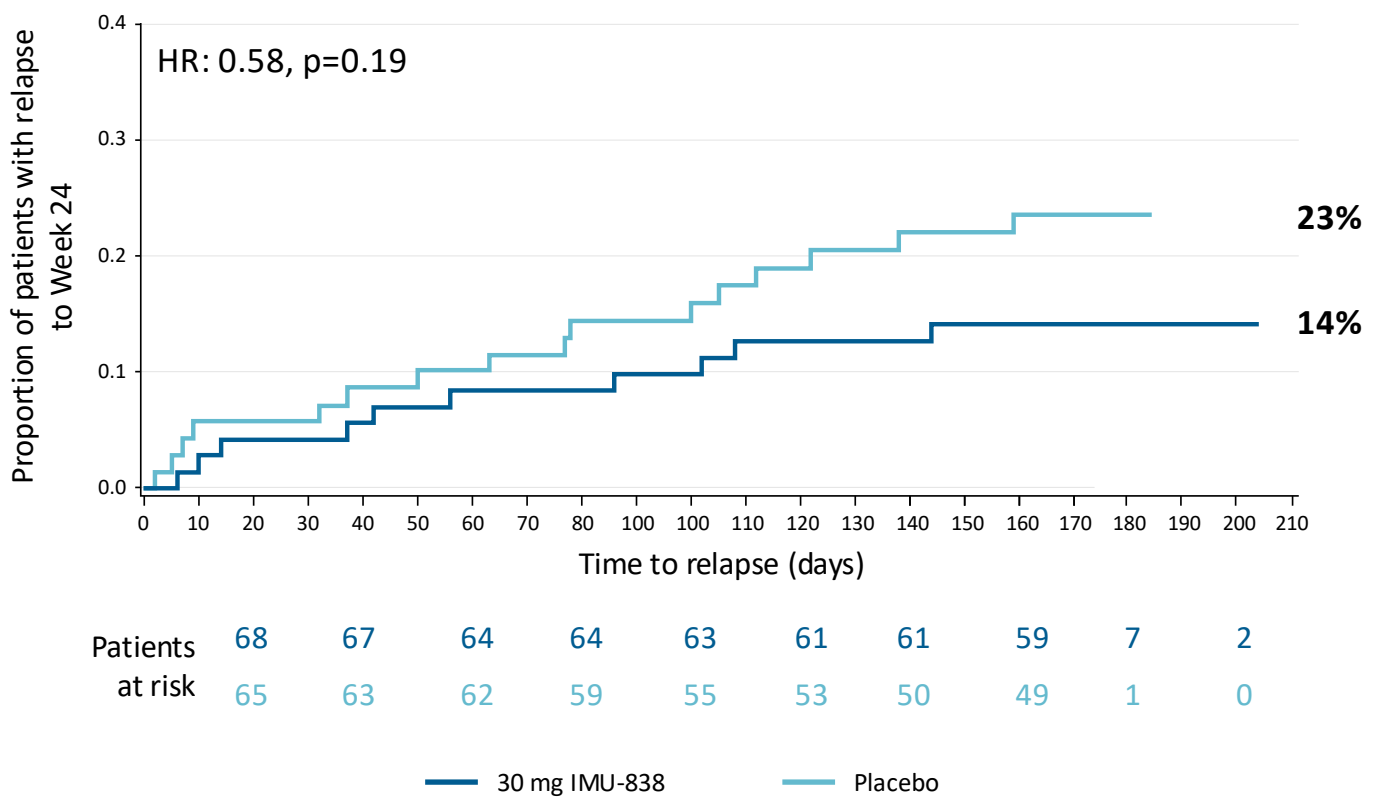

## Reduction in Gd+ Lesions up to Week 24




**Statistically significant effects on the primary and key secondary endpoints of new CUA lesions**
(primary 45 mg versus placebo: p=0.0002 / key secondary 30 mg versus placebo: p<0.0001)

As Cohort 2 only allowed MRI machines of 1.5T, pooled data of Cohorts 1&2 only include patients that were evaluated at MRI field strength of 1.5 Tesla. Modified full analysis set C1/C2 (N10=47, N30=65, N45=66, NPBO C1=59, NPBO C2=12). Data displayed are as adjusted mean values. Estimates are adjusted for baseline volume of T2 lesions and baseline number of Gd+ lesions (0, >=1) using a generalized linear model with a negative binomial distribution and a logarithmic link function. Log transformation of time from first investigational medicinal product (IMP) dose to date of last MRI assessment with non-missing values is used as offset term. / MRI: magnetic resonance imaging; CUA: cumulative unique active, Gd+: gadolinium-enhancing

# Encouraging Trend on Risk of Relapse, Despite Study Size and Duration




Relative risk of relapse reduced by 42% (HR: 0.58, p=0.19) in 30 mg group vs. placebo

Apparent onset of effect within 6-8 weeks, increasing over time

Regulatory alignment and precedent[1] for the time to first relapse primary endpoint in relapsing MS

1. Reference: Tecfidera® label

MS: multiple sclerosis; HR: hazard ratio

# Favorable Safety and Tolerability Profile with Similar Incidence to Placebo

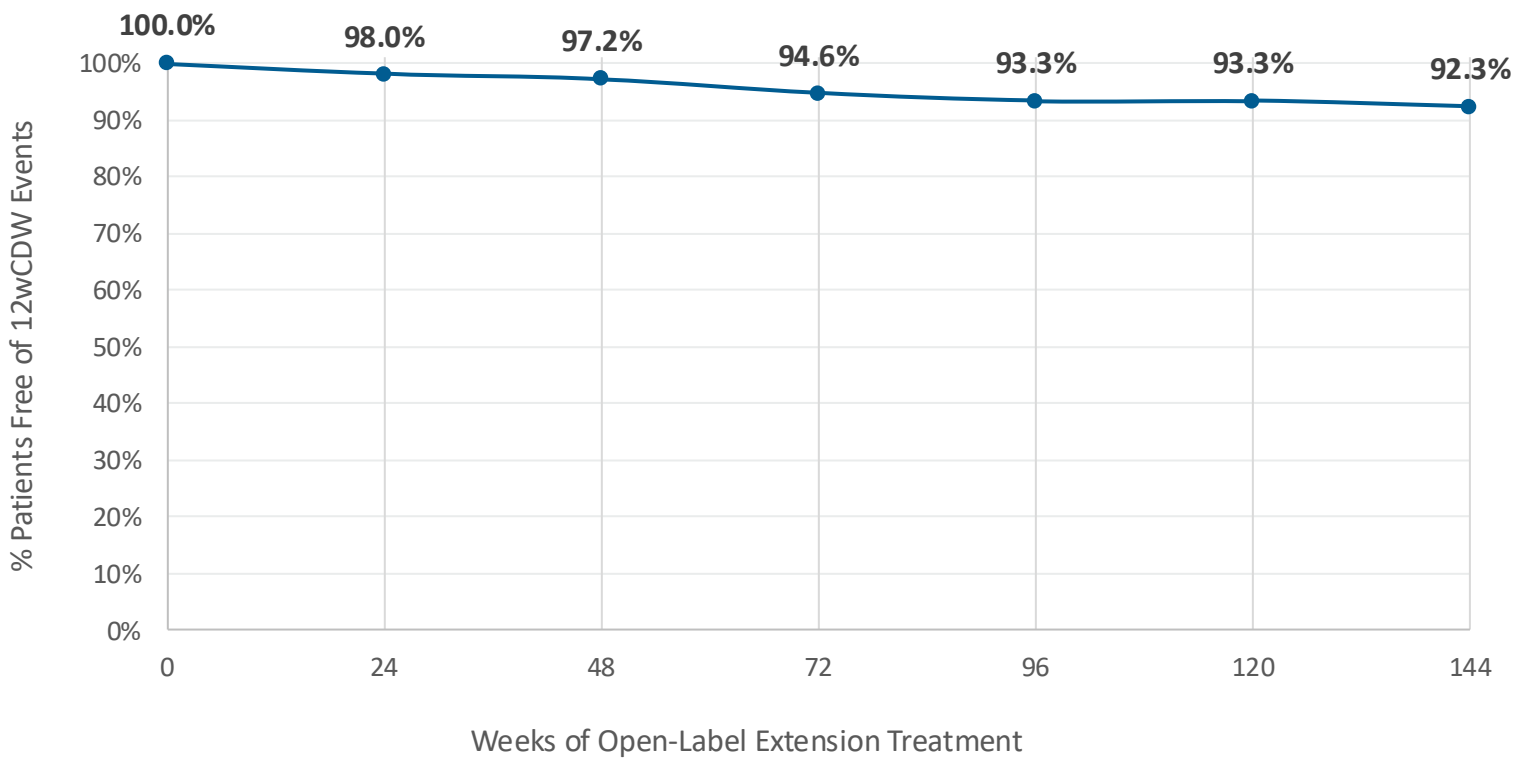
| Safety and Tolerability Endpoints | Placebo | Vidofludimus Calcium 30 mg | Vidofludimus Calcium 45 mg |
|---|---|---|---|
| **Any treatment-emergent adverse event** | **44%** | **45%** | **41%** |
| **Treatment-emergent adverse events occurring in >5% of total patients by preferred term** | | | |
| Headache | 6% | 4% | 6% |
| Nasopharyngitis | 4% | 4% | 7% |
| **Treatment-emergent adverse events occurring in 2%-5% of total patients by preferred term** | | | |
| Upper respiratory tract infection | 4% | 3% | 0% |
| Viral respiratory tract infection | 4% | 0% | 3% |
| **Treatment-emergent adverse events occurring in >1 to <2% of total patients by preferred term** | | | |
| Back pain | 3% | 1% | 0% |
| ALT (alanine aminotransferase) increase | 3% | 1% | 0% |
| Influenza | 3% | 0% | 1% |
| Liver enzymes elevated | 1% | 1% | 3% |
| Nausea | 1% | 1% | 3% |
| Bronchitis | 1% | 0% | 3% |
| Alopecia | 0% | 4% | 1% |
| Fatigue | 0% | 3% | 3% |
| Rash | 0% | 3% | 3% |
| Cystitis | 0% | 1% | 4% |
| **Treatment-emergent adverse events by severity** | | | |
| Mild | 33% | 41% | 30% |
| Moderate | 12% | 16% | 23% |
| Severe | 1% | 0% | 0% |
| **Serious adverse events** | **1%** | **3%** | **0%** |
| **Treatment discontinuation for any reason** | **7%** | **3%** | **6%** |
| **Treatment-emergent adverse events leading to treatment discontinuation** | **4%** | **0%** | **3%** |

### Key Safety Observations:

- No signal for liver injury
- No indications of immune or bone marrow suppression
- No clear signals of gastrointestinal effects or hair loss
- Half-life of 30 hours allows for ease of treatment changes, discontinuations
- Part of a safety database of over 3,500 participants exposed to vidofludimus across completed and ongoing studies with maximum exposure >6.5 years

Three patients experienced 4 serious adverse events in the vidofludimus calcium 30 mg (n=2) and the placebo group (n=1). They were considered unrelated to treatment: hydronephrosis and ureterolithiasis (vidofludimus calcium 30 mg), open fracture (vidofludimus calcium 30 mg), and squamous cell carcinoma of the cervix (placebo).

# Open-Label Extension Phase: High Retention Rate with 92.3% of Patients CDW-Free at 144 Weeks




- At week 144, 92.3% of patients remained free of 12-week CDW, with 92.7% free of 24-week CDW
- Low discontinuation rate with 196 out of 254 patients reaching 144 weeks of OLE treatment and >170 patients still in the OLE phase*
- Apparent favorable safety and tolerability profile continues

Stable low progression rate through 144 weeks consistent with sustained effects potentially through immunomodulatory and neuroprotective pathways

187 patients evaluated up to Week 144 and included in this CDW analysis; * as of May 2026
CDW: confirmed disability worsening; OLE: open-label extension

# ENSURE Phase 3: Two Fully Enrolled Pivotal Trials Designed to Confirm Immunomodulatory Effects Specifically Through Relapse Reduction

## Randomized, Double-Blind, Placebo-Controlled Trials (NCT05134441 & NCT05201638)

- More than 100 sites in 15 countries
- Approx. 1,100 relapsing MS patients randomized 1:1 in each trial (total N=2,221)

## Endpoints

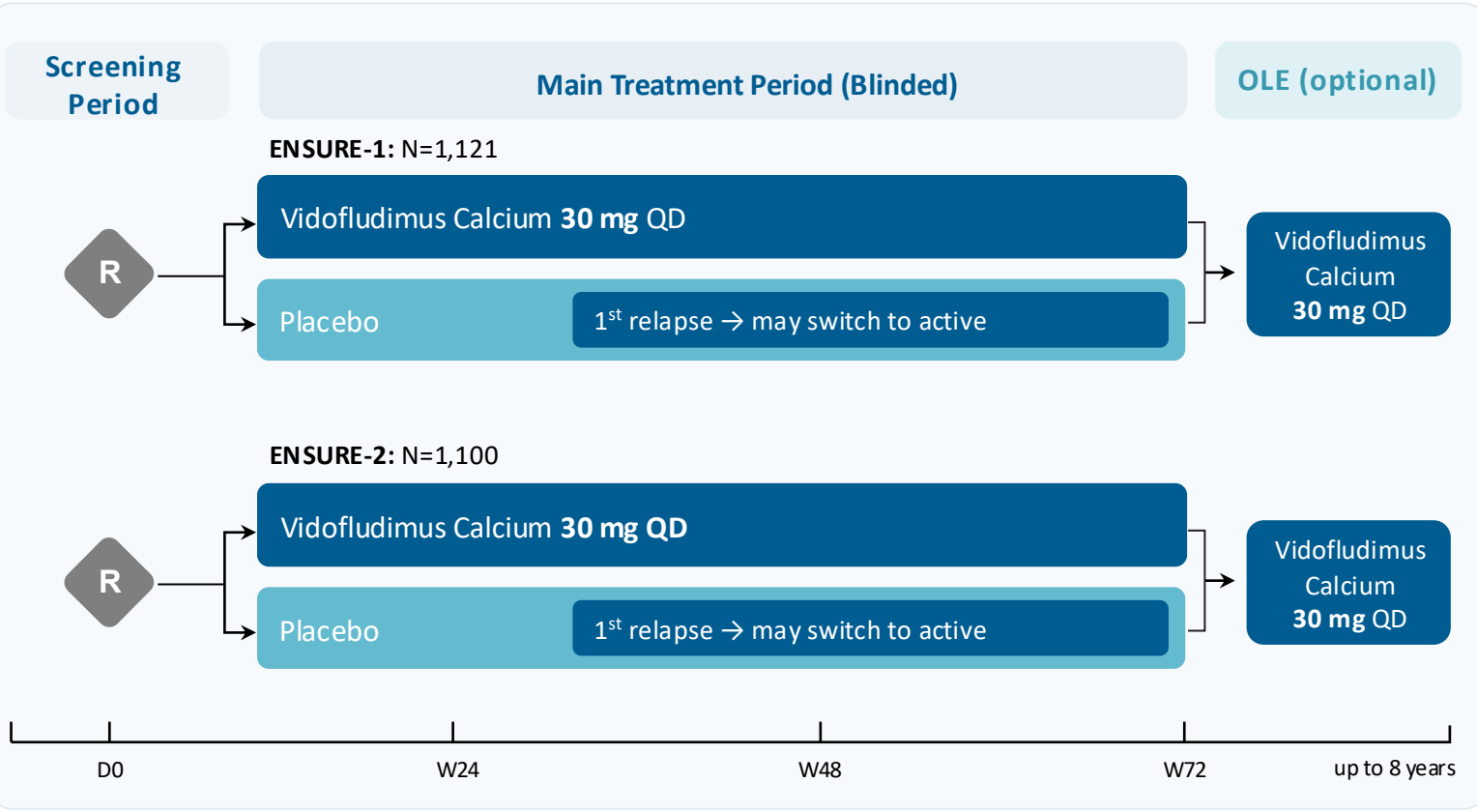
**Primary:**

- Time to first relapse (i.e., relative risk reduction)

**Key Secondary Include:**

- New and/or enlarging T2 MRI lesions, Gd+ T1 MRI lesions, ARR, time to CDI (pooled), time to CDW (pooled)

Rescue with active treatment post-relapse included to assure patient safety, however, rescue further reduces likelihood of seeing effects on disability endpoints




**Top-line data expected by end of 2026**

- A positive readout of the ENSURE trials would pave the way for U.S. NDA submission
- Regulatory alignment and precedent[1] for the time to first relapse primary endpoint in relapsing MS
- Positive interim analysis in October 2024: Unblinded IDMC recommended continuing trial without changes, including no need sample-size expansion

1. Reference: Tecfidera® label / MS: multiple sclerosis; MRI: magnetic resonance imaging; Gd+: gadolinium-enhancing; ARR: annualized relapse rate; CDI; confirmed disability improvement; CDW: confirmed disability worsening; OLE: open-label extension; QD: quaque die = once-daily; R: randomization; D: day; W: week; NDA: New Drug Application; IDMC: Independent Data Monitoring Committee

# Countries and Inclusion/Exclusion Criteria of ENSURE Selected to Enable Recruitment of Early, Active Patient Population Into Placebo Controlled Trials

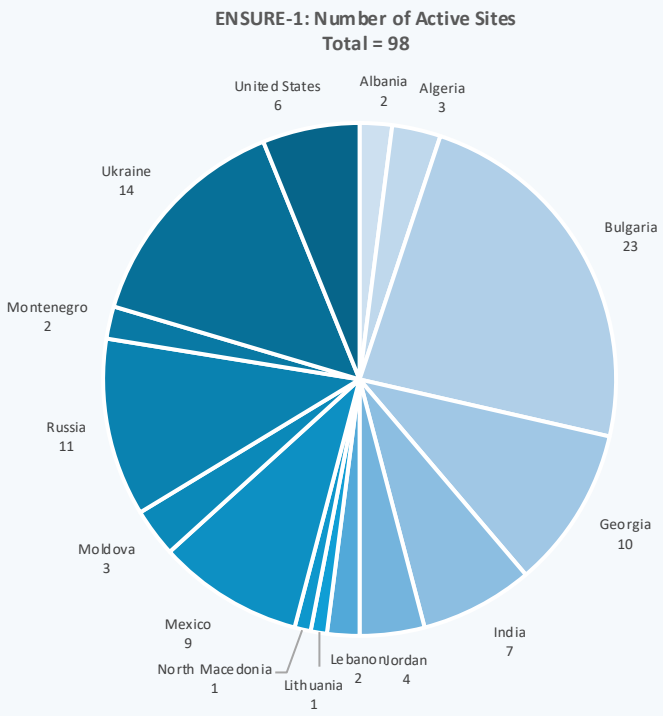
## Key Inclusion Criteria

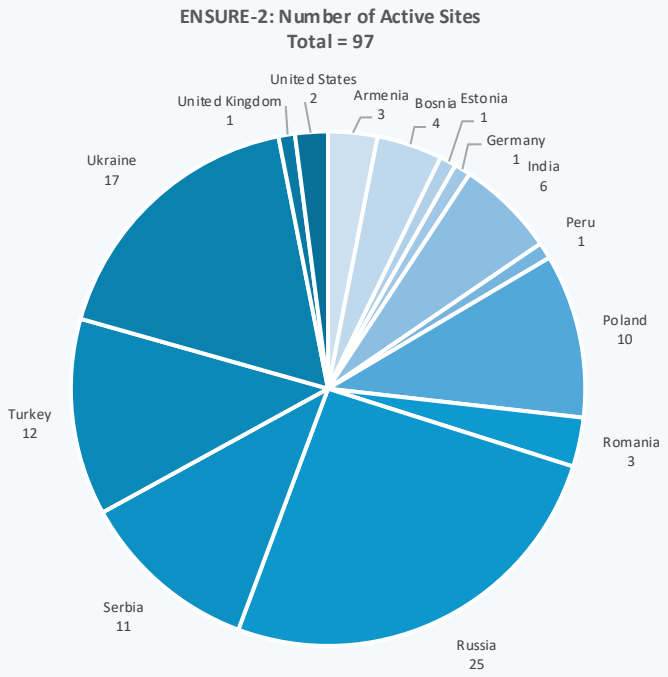
- Patients aged 18 to 55 years
- Diagnosis of relapsing MS[1,2]
- Active disease as defined by Lublin 2014[3]
- EDSS score at screening between 0 to 5.5

## Key Exclusion Criteria

- Patients with non-active SPMS and PPMS
- Concomitant use of MS treatments or prior use without adequate washout
- History of liver or renal impairment
- Clinically significant medical illness or laboratory abnormalities

## Distribution of Clinical Trial Sites[4]




1. Revised McDonald criteria 2017: Thompson AJ, et al. Lancet Neurol. 2018;17(2):162-173; 2. Confirmed relapsing MS as defined by 1996 Lublin criteria: Lublin FD, Reingold SC. Neurology. 1996;46(4):907-911; 3. Active disease as defined by Lublin 2014: Lublin FD, Eur Neurol. 2014;72 Suppl 1:1-5; 4. Internal data as of September 2026 / MS: multiple sclerosis; SPMS: secondary progressive MS; PPMS: primary progressive MS; EDSS: Expanded Disability Status Scale

# Recruited Patients in ENSURE Similar to Population Recruited into EMPhASIS

Total of 2,221 Enrolled Patients, Nearly 50% Received Prior MS Treatment

## ENSURE Baseline Patient Characteristics[1]

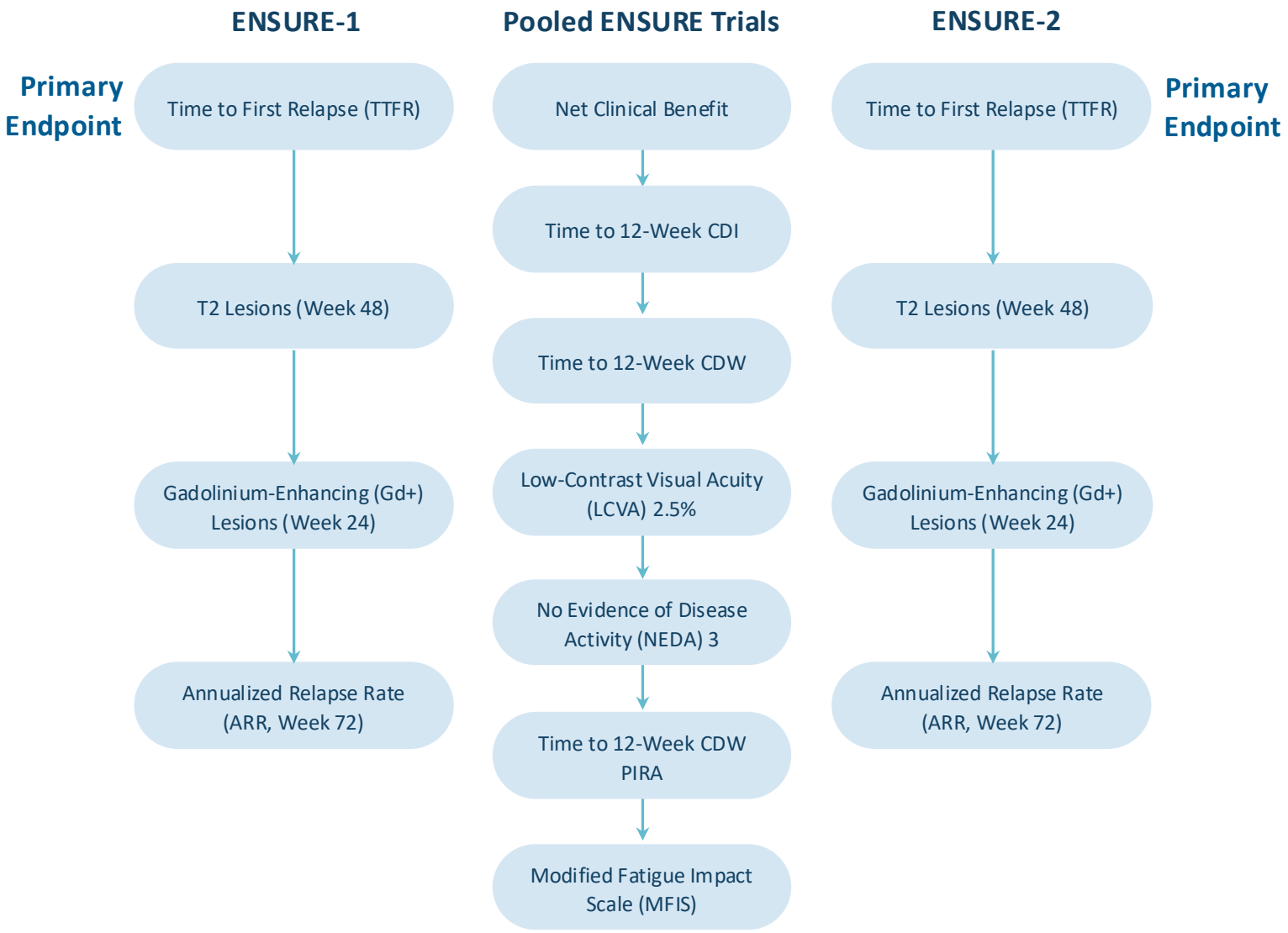
| | ENSURE-1 (N=1,121) | ENSURE-2 (N=1,100) |
|---|---|---|
| Mean age (SD), years | 37.9 (9.28) | 37.6 (9.25) |
| Female | 65.2% | 67.9% |
| Male | 34.8% | 32.1% |
| Baseline EDSS <=2.5 | 43.3% | 54.5% |
| Baseline EDSS >2.5 | 56.7% | 45.5% |
| Received prior treatment | 46.4% | 48.9% |
| Disease subtypes at baseline | RRMS: 96.7%<br>aSPMS: 3.2% | RRMS: 96.6%<br>aSPMS: 3.3% |

## EMPhASIS Baseline Patient Characteristics

| | EMPhASIS (N=249)[2] |
|---|---|
| Mean age (SD), years | 36.9 (8.9) |
| Female | 66.7% |
| Male | 33.3% |
| Baseline EDSS <=2.5 | 52.2% |
| Baseline EDSS >2.5 | 47.8% |
| Received prior treatment | 59.8% |

1. Internal data as of February 2026; 2. As Cohort 2 only allowed MRI machines of 1.5T, pooled data of Cohorts 1&2 only include patients that were evaluated at MRI field strength of 1.5T.
MS: multiple sclerosis; RRMS: relapsing-remitting MS; aSPMS: active secondary progressive MS; EDSS: Expanded Disability Status Scale; SD: standard deviation

# Primary and Secondary Endpoints Selected to Ensure Robust Assessment of Clinical and Imaging Outcomes Meaningful to People with MS




> "I hope to see different kinds of MS drugs: ones that stop the progression, ones that restore lost function, and ones that address the underlying pathology of the disease. These developments would not only bring relief, but also real hope for the future."

> "My biggest concern is continued progression that will further limit my life. I can no longer drive due to vision issues. What happens if my spouse is no longer around to drive when needed?"

> "I've been on the same DMT for 11 years and I'm fortunate that it seems to be preventing relapses. I'm taking it to keep me from getting sicker, yet it's making me more fatigued, I get hot flashes at least a few times a week, and experience other side effects. These medications that should be helping us shouldn't be making us more uncomfortable in our day-to-day lives."

> "Fatigue is something I constantly have, but when all the other symptoms start to trip me up, fatigue is always there to make it that much worse."

CDI: confirmed disability improvement; CDW: confirmed disability worsening; PIRA: progression independent of relapse activity

# Vidofludimus Calcium in Relapsing MS: Targeted NDA Submission Driven by Near-Term Pivotal Readouts

**Robust Phase 2 EMPhASIS Results on Inflammatory Endpoints**

**Phase 3 ENSURE Development Largely De-Risked**

**Clear Path to Regulatory Submission Upon Positive Outcome**

- Fully enrolled Phase 3 ENSURE-1 and ENSURE-2 trials with top-line data expected by year-end 2026
- NDA submission in the U.S. targeted for mid-2027, followed by potential U.S. regulatory approval in 2028
- Regulatory alignment and precedent[1] for the time to first relapse primary endpoint in relapsing MS

1. Reference: Tecfidera® label

MS: multiple sclerosis; NDA: New Drug Application

# Expert Talk: Stephen Krieger, MD, FAAN

Department of Neurology, Icahn School of Medicine,
The Mount Sinai Hospital

# Positioning and Commercial Opportunity for Vidofludimus Calcium in Relapsing MS

Jason Tardio I President & Chief Operating Officer

# Even With 20+ Approved Therapies, Significant Unmet Needs Remain in Relapsing MS

## PIRA[1,2]

- PIRA begins early in relapsing MS and becomes an increasingly important driver of disability over time
- PIRA is the dominant driver of disability accumulation as MS progresses, based on an analysis of ~35,000 clinical trial participants
- PIRA persists despite strong relapse control: ~90% of confirmed disability accumulation in pooled trial of an anti-CD20 was attributable to PIRA

## Better Safety[3,4]

- Many DMTs carry meaningful safety trade-offs, including serious infections, malignancy concerns and laboratory abnormalities
- Long-term anti-CD20 therapy can increase immune-related risks, including hypogammaglobulinemia and infections
- Safety becomes increasingly important with age as immunosenescence and comorbidities shift the benefit-risk equation

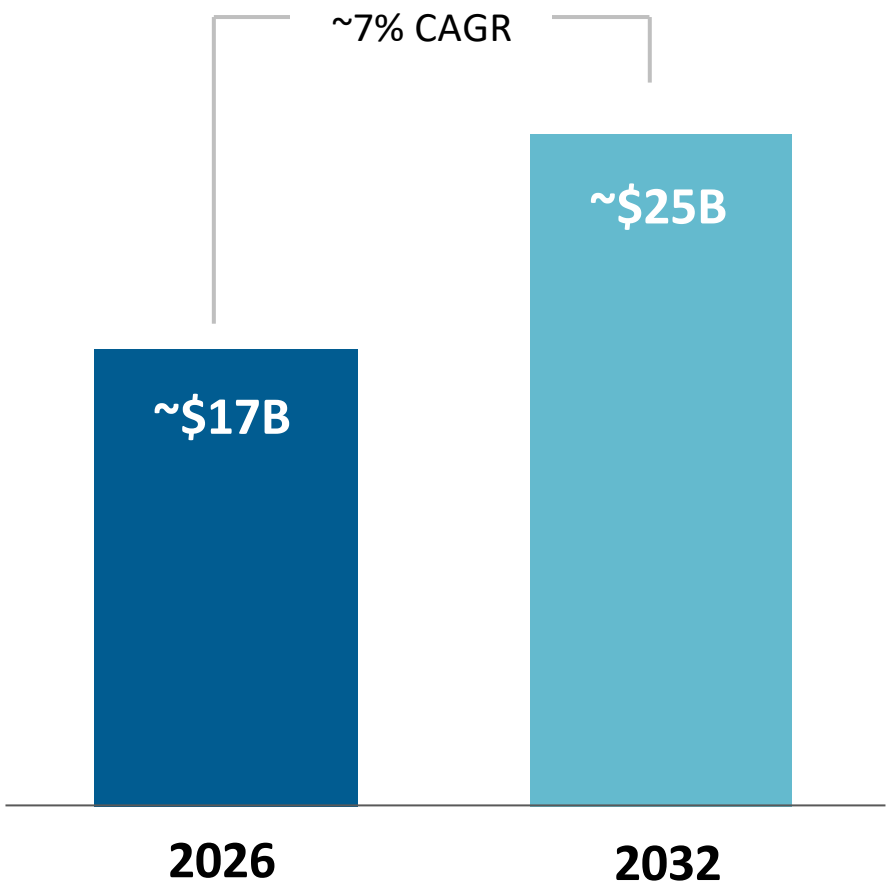
## Improved Tolerability[3,5,6]

- Tolerability is a top patient priority when selecting an MS therapy
- Side effects are a major driver of discontinuation: 46.9% of fingolimod and 67.8% of dimethyl fumarate discontinuations in one real-world study
- Poor tolerability can undermine persistence, making switching necessary even when a therapy is effective

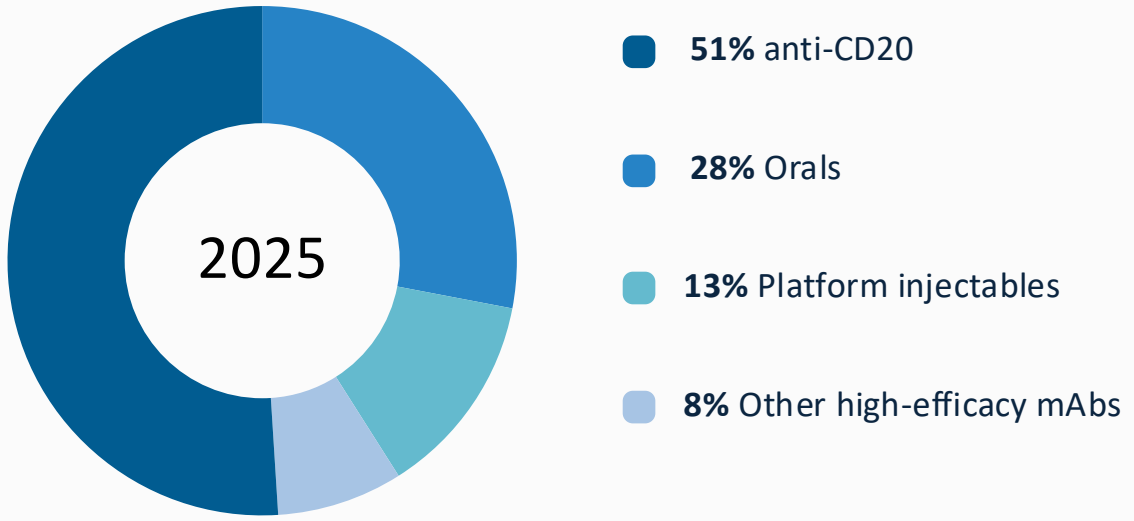


1. Lublin FD, et al. Brain. 2022;145:3147-3161; 2. Kappos L, et al. JAMA Neurol. 2020;77:1132-1140; 3. Rae-Grant A, et al. Neurology. 2018;90:777-788; 4. Elgenidy A, et al. Front Neurol. 2024;15:1380654; 5. Kremer IEH, et al. Mult Scler Relat Disord. 2020;39:101929; 6. Wicks P, et al. BMC Res Notes. 2016;9:434 / MS: multiple sclerosis; PIRA: progression independent of relapse activity; DMT: disease-modifying therapy

# The U.S. Relapsing MS Market is Large, Continues to Grow, and Oral DMTs Remain a Sizable Class




**Total U.S. Relapsing MS Patient Share by Class[2]**




Sales numbers in G7 countries (U.S., UK, Canada, Japan, Germany, France, Italy) in USD billion; Multiple Sclerosis Landscape and Forecast by Decision Resources Group Part of Clarivate; 1. Company public filings; 2. IQVIA TRx market share - IQVIA SMART / MS: multiple sclerosis; DMT: disease-modifying therapy; CAGR: compound annual growth rate; mAbs: monoclonal antibodies

# Not a Winner Take All Market: Dynamic with ~90K U.S. Patients Making a Treatment Decision Each Year, with Another ~125K Currently Untreated

## THE RELAPSING MS PATIENT JOURNEY CREATES MULTIPLE TREATMENT DECISION POINTS

**01**
**INITIATE**
Newly diagnosed or first DMT

**02**
**SWITCH**
Breakthrough disease or inadequate response[2,3]

**03**
**SWITCH**
Tolerability, safety or convenience[2,3]

**04**
**EVOLVE**
De-escalation / older age[4]

**Switching is a feature of MS care**[2,3,4]

No single DMT optimizes every attribute for every patient at every stage; treatment priorities can change over decades

**Opportunity for vidofludimus calcium to compete for the right patient at multiple points across the relapsing MS journey**

**~45K** relapsing MS patients **initiate therapy** each year[1]

**~45K** prescriptions for patients **switching therapy** each year[1]

**~125K** diagnosed relapsing MS patients **currently untreated**[1]

1. Decision Resources Group (DRG), part of Clarivate. U.S. Multiple Sclerosis Market Assessment, 2026; 2. Kalincik T, et al. Front Neurol. 2021;12:647811; 3. Rae-Grant A, et al. Neurology. 2018;90:777-788;
4. Dersch RS, et al. Neurol Neuroimmunol Neuroinflamm. 2026;13(5):e200621 / MS: multiple sclerosis; DMT: disease-modifying therapy

# MS Treatment Is Highly Personalized for Each Patient and Influenced by Both Patient Preference and MS Treatment Philosophies by HCPs

## Personalized by Patient Characteristics[1,2]

- **Disease Severity**
- **Age / Immunity Status**
- **Preferred Route of Administration**
- **Risk Tolerance**

## MS Treaters Are Highly Heterogeneous with Diverse Treatment Philosophies and Prescribing Behaviors[1,2]

### Specialty

General neurologists, MS specialists, APPs

### Treatment Approach

Escalation vs induction paradigm

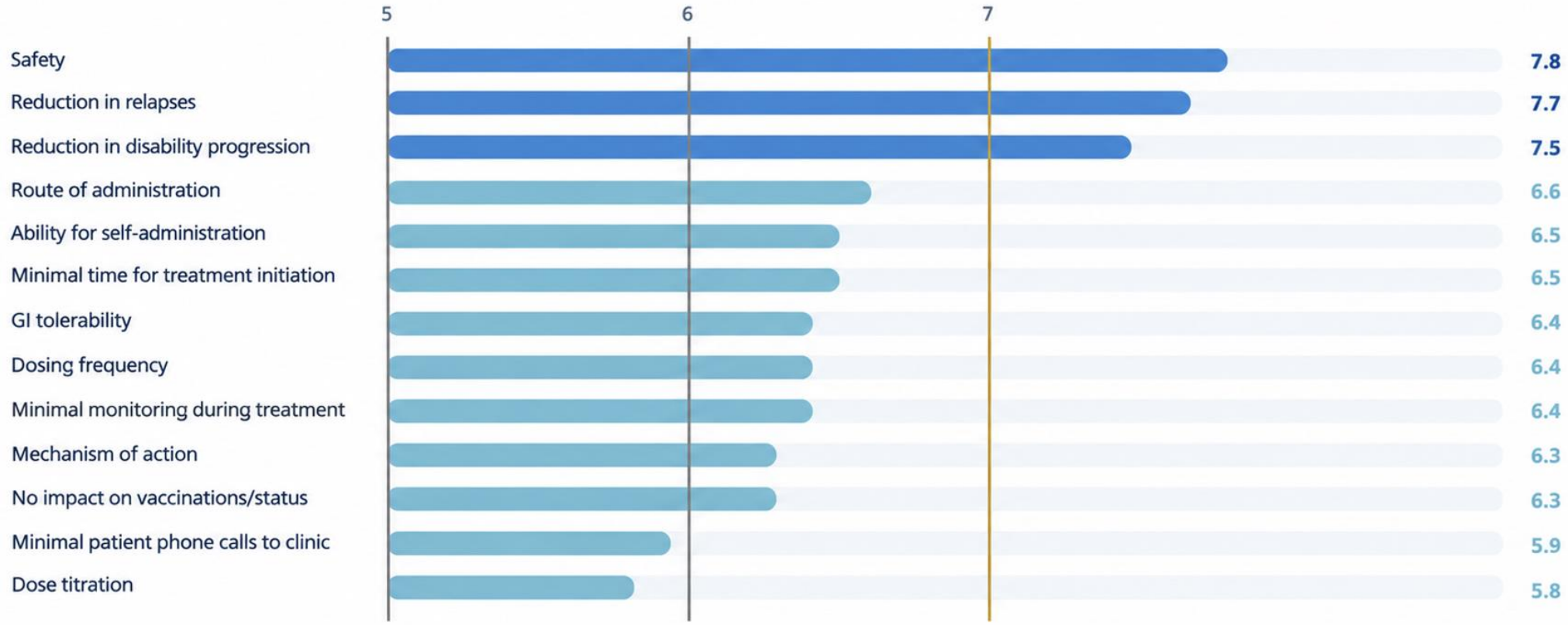
### Practice Setting

Accounts vs. community

**Vidofludimus Calcium may help to meet individual patient needs and diverse the MS prescribing community to tailor the engagement strategy and activate stakeholders.**

1. Syneos Health Analysis: 2026 Market Landscape Assessment for Vidofludimus Calcium in Multiple Sclerosis; 2. ZS Associates Market Research
MS: multiple sclerosis; HCP: Health Care Professional; APP: Advanced Practice Provider

# HCPs Weigh the Overall Benefit-Risk Profile When Selecting DMTs, with Safety the Most Important Product Attribute

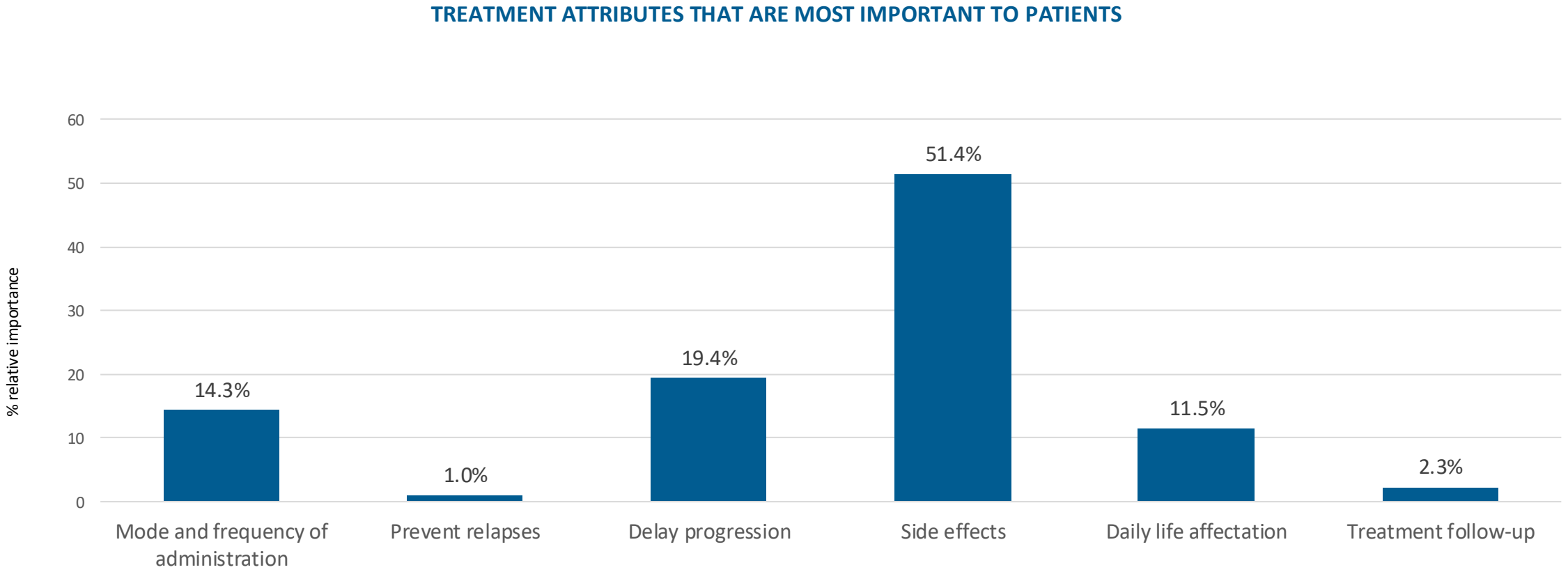



Direct assessment of product attribute importance by HCPs rating on a 9-point scale

Bandari D, et al., J Med Econ. 2023 Jan-Dec;26(1):1507-1518

HCP: Health Care Professional; DMT: disease-modifying therapy; GI: gastrointestinal

# Patients Also Weigh the Overall Benefit-Risk Profile, with Side Effects as the Top Driver of Selection




García-Domínguez JM, Muñoz D, Comellas M, Gonzalbo I, Lizán L, Polanco Sánchez C. Patient Prefer Adherence. 2016;10:1945–1956

# Vidofludimus Calcium Is Targeted to Deliver the Optimal Balance of the Treatment Attributes That Matter Most to Patients and HCPs

## 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

# Vidofludimus Calcium Could Address Several Large, Underserved Relapsing MS Patient Segments

## Treated Relapsing MS Patients

- **A favorable risk-benefit profile is a key driver of treatment preference** among patients and HCPs
- **3 key patient segments remain underserved by current therapies** with high monitoring burden or tolerability limitations
- Vidofludimus calcium is well positioned to address these unmet needs as **a more tolerable, lower-burden treatment option**

## Addressable Patient Segments for Vidofludimus Calcium

**Patients who Prefer Oral DMTs**

Patients seeking convenience, flexibility and avoidance of infusion or injection burden

**Patients sequencing from anti-CD20s**

Patients discontinuing an anti-CD20 due to cumulative safety or tolerability concerns

**Older Individuals with relapsing MS**

Older patients with more comorbidities and a shifting risk-benefit profile

## Size of Opportunity

**~100K relapsing MS patients** are currently treated with oral DMTs[1]

**~40K relapsing MS patients** switch away from anti-CD20s[1]

**~22K relapsing MS patients** discontinue from anti-CD20s[1,2]

**~185K relapsing MS patients** currently treated are aged 55+[1]

1. Estimates based on data from claims analysis representing a snapshot of the total U.S. relapsing MS population; 2. Discontinuation defined as no further treatment claims for 360 days following the last observed prescription activity / MS: multiple sclerosis; HCP: Health Care Professional; DMT: disease-modifying therapy

# Vidofludimus Calcium May Offer an Effective, Safe and Well-Tolerated Oral Option That Can Support Adherence and Long-Term Disease Management

**~25%**

of relapsing MS patients **start on an oral DMT**

**~100K** relapsing MS patients are currently treated with an oral DMT

**~30%**

of relapsing MS patients starting on an oral DMT will **discontinue within one year**[2,3]

An **effective, safe and well-tolerated treatment could support adherence and long-term disease management** particularly for patients with needle aversion, busy lifestyles or limited access to infusion centers

**Vidofludimus calcium has the opportunity to play across the oral market for patients who prefer oral therapies, including within-class switchers and patients discontinuing initial oral DMT.**

Immunic THERAPEUTICS

1. Size of oral market estimated based on 2025 annual sales for Oral DMTs and accounting for 60% market share from generics based on claims data analysis; 2. Estimates based on claims data representing a snapshot of the U.S. relapsing MS population; 3. Discontinuation defined as no further treatment claims for 360 days following the last observed prescription activity / MS: multiple sclerosis; DMT: disease-modifying therapy

# Vidofludimus Calcium May Offer a Non-Immunosuppressant DMT for Anti-CD20 Patients Who Cannot Tolerate Anti-CD20 or Need to Sequence Away

**~15%**

of anti-CD20 patients **use extended interval dosing**[1]

~33K of relapsing MS patients are currently using alternative dosing schedules to reduce infection risk

**~18%**

of anti-CD20 patients **switch away** from an anti-CD20[1]

~40K patients switch away from anti-CD20s annually

**~15%**

of anti-CD20 patients will **discontinue within one year**[1,2]

~22K patients discontinue from anti-CD20s

Anti-CD20s are widely used in relapsing MS patients but can be associated with high infection risk

Patients require follow-on therapies maintaining disease control without compromising immune function

Patients discontinuing anti-CD20s may restart treatment if a lower-burden option is available for durable disease control

**Vidofludimus calcium offers a potentially safe and effective follow-on option that preserves disease control without further compromising immune defense.**

Immunic THERAPEUTICS

1. Estimates based on claims data representing a snapshot of the U.S. relapsing MS population; 2. Discontinuation defined as no further treatment claims for 360 days following the last observed prescription activity; 3. Assumes ~ 10% anticipated use of VC in this patient segment based on preliminary qualitative U.S. neurologist interviews / MS: multiple sclerosis; DMT: disease-modifying therapy

# Vidofludimus Calcium May Offer a Differentiated Option for Older Relapsing MS Patients as Age-Related Safety Considerations Reshape Treatment Priorities

**~47%**

of relapsing MS patients are aged 55+

~185K of currently treated relapsing MS patients are aged >55+[1]

**~15%**

of relapsing MS patients aged 55+ are on teriflunomide

**In older relapsing MS patients, immunosenescence and comorbidities can increase infection risk** and reduce the suitability of prolonged high-efficacy immunosuppressive treatment

Although inflammatory activity may decline with age, **incomplete relapse recovery can drive cumulative disability, reinforcing the need for ongoing disease control**

A therapy that **maintains disease control while limiting broad immunosuppression could provide a safety net** for older clinically stable patients

**Vidofludimus calcium provides a lower-burden treatment option for older, clinically stable relapsing MS patients who remain vulnerable to disability progression and still require relapse protection.**

Immunic THERAPEUTICS

1. Based on claims data analysis that includes calculation applying a lower treatment rate in the 55+ population; 2. Assumes ~ 15% anticipated use of VC in this patient segment based on 12 preliminary qualitative U.S. neurologist interviews / MS: multiple sclerosis

# Key Takeaways: Vidofludimus Calcium Has the Potential to Address Significant Opportunities in Relapsing MS

**1**

### LARGE AND GROWING MARKET

The U.S. relapsing MS market is ~$17B today and projected to reach ~$25B by 2032, with oral DMTs remaining a significant treatment class

**2**

### NOT A WINNER-TAKE-ALL MARKET

Patients initiate, switch and evolve therapy throughout their disease journey, creating multiple opportunities for a differentiated new therapy to compete

**3**

### SIGNIFICANT UNMET NEED REMAINS

Despite 20+ approved therapies, important unmet needs persist—particularly PIRA/disability progression, better safety and improved tolerability

**4**

### BENEFIT-RISK DRIVES CHOICE

Treatment decisions are not based on efficacy alone: safety is the highest-rated attribute for HCPs, while side effects are the leading consideration for patients

**5**

### DIFFERENTIATED VIDOFLUDIMUS CALCIUM PROFILE

Vidofludimus calcium combines Nurr1-mediated neuroprotective effects and DHODH-mediated anti-inflammatory effects with oral convenience and a potentially favorable safety/tolerability profile

**6**

### MULTIPLE PATHS TO ADOPTION

Potential opportunity spans patients who prefer oral DMTs, patients sequencing from anti-CD20 therapy, and older relapsing MS patients whose benefit-risk priorities evolve with age

**If approved for relapsing MS, vidofludimus calcium could capture meaningful sales in the $17B+ U.S. market**

Immunic THERAPEUTICS

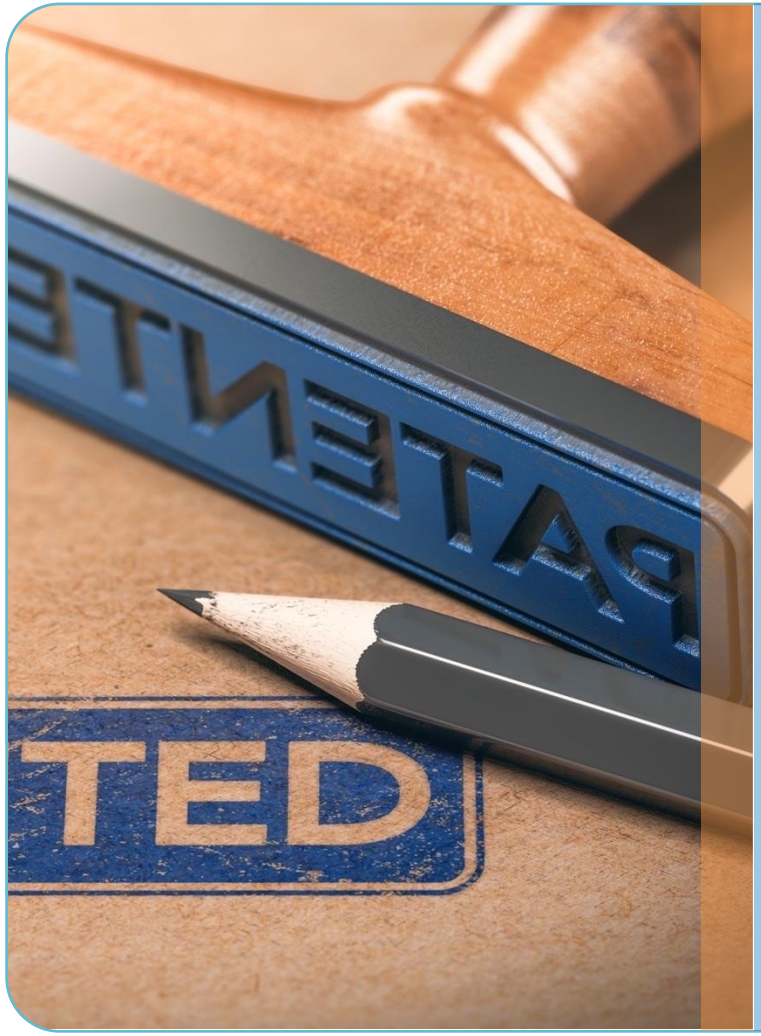
Sales numbers in G7 countries (U.S., UK, Canada, Japan, Germany, France, Italy) in USD billion; Multiple Sclerosis Landscape and Forecast by Decision Resources Group Part of Clarivate; Company public filings; IQVIA TRx market share - IQVIA SMART; Kalincik T, et al. Front Neurol. 2021;12:647811; Rae-Grant A, et al. Neurology. 2018;90:777-788; Dersch RS, et al. Neurol Neuroimmunol Neuroinflamm. 2026;13(5):e200062; Lublin FD, et al. Brain. 2022;145:3147-3161; Kappos L, et al. JAMA Neurol. 2020;77:1132-1140; Rae-Grant A, et al. Neurology. 2018;90:777-788; Elgenidy A, et al. Front Neurol. 2024;15:1380654; Kremer IEH, et al. Mult Scler Relat Disord. 2020;39:101929; Wicks P, et al. BMC Res Notes. 2016;9:434; Bandari D, et al., J Med Econ. 2023 Jan-Dec;26(1):1507-1518; Garcia-Domínguez JM, Muñoz D, Comellas M, Gonzalbo I, Lizán L, Polanco Sánchez C. Patient Prefer Adherence. 2016;10:1945–1956 / MS: multiple sclerosis; DMT: disease-modifying therapy; PIRA: progression independent of relapse activity; Nurr1: nuclear receptor related 1; DHODH: dihydroorotate dehydrogenase; HCP: Health Care Professional

# Outlook: Upcoming Milestones for Vidofludimus Calcium in MS

Erik Lundgren | Chief Executive Officer

# Multi-Layered Intellectual Property (IP) Strategy Approach

Exclusivity for Vidofludimus Expected up to **2044** in the US



**Multi-layered IP strategy** approach with 10 independent patent families to effectively protect vidofludimus (free acid and salts) with **Orange Book listable patents up to 2044** in the US, or even beyond

Main IP value driver is a smart two-fold approach to protect vidofludimus via **composition-of-matter** patents on the one hand and **indication** as well as **method-of-treatment** patents on the other hand, supplemented by additional layers of protection such as **dose strength and formulation** patents

Two main pillars are:

- **Calcium salt and calcium polymorph patent** covering the stable, crystalline polymorphic form, which is the only polymorph in the developed drug product
- Broad **dosing regimens patent** directed to the safety and label relevant dosing regimen of **vidofludimus in all (salt) forms;** this titration scheme was part of every safety testing and therefore this regimens patent cannot be avoided

# Value Creation Roadmap

Multiple Catalysts Through 2030

| | 2H 2026 | 2027 | 2028 |
|---|---|---|---|
| **Relapsing MS**<br>ENSURE-1 and ENSURE-2 | Top-line data expected by end of 2026 | Targeted relapsing MS NDA submission in mid-2027 | Potential relapsing MS U.S. regulatory approval in 2028 |
| **Progressive MS**<br>CALLIPER and Phase 3 Trial | Progressive MS Phase 3 initiation expected later in 2026 | | |

MS: multiple sclerosis; NDA: New Drug Application

# Building a Leading MS Company: A Phased Commercial Strategy

U.S. Relapsing MS Opportunity to Build a Profitable, Fully Integrated Commercial Organization Serves as Platform for Long-Term Global Leadership in MS

### 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 (long-term market estimated up to $12B[1]) reinforcing Immunic's position as a leading global MS company

NASDAQ: IMUX – leadership team with proven track record in MS drug development and commercialization – intellectual property protection expected up to 2044 in the U.S. – funding expected into late 2027

1. Immunic estimate based on reported prevalence and assumed future pricing of DMTs for progressive MS

MS: multiple sclerosis; DMT: disease-modifying therapy

Sneak Preview:

# **Virtual Progressive MS R&D Day**

November 5, 2026

12:30 pm ET

# Q&A Session

# Thank you!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