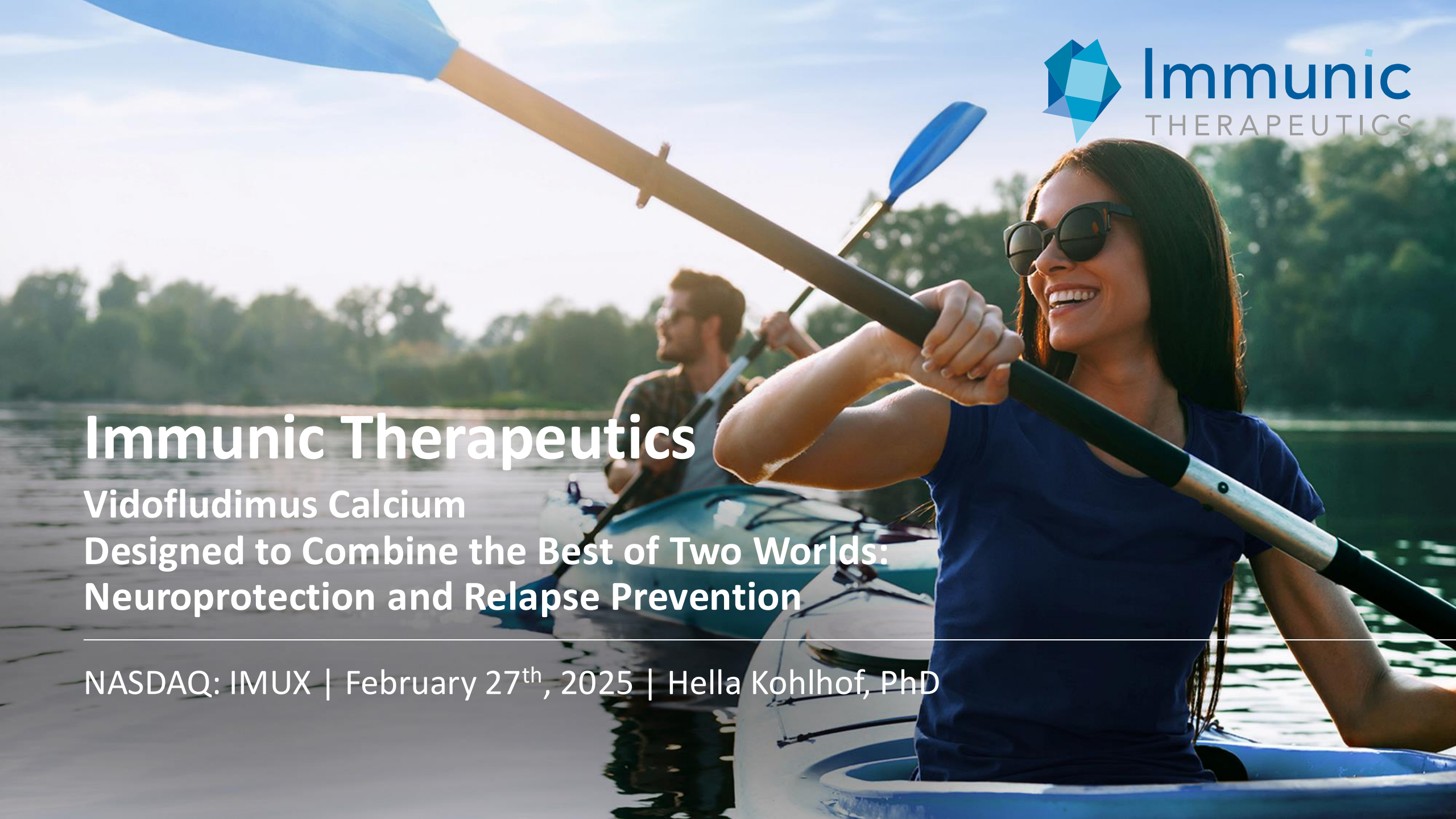


Immunic Therapeutics

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

NASDAQ: IMUX | February 27th, 2025 | Hella Kohlhof, PhD

Cautionary Note Regarding Forward-Looking Statements

This presentation contains “forward-looking statements” that involve substantial risks and uncertainties for purposes of the safe harbor within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These include statements regarding management’s intentions, plans, beliefs, expectations or forecasts for the future, and, therefore, you are cautioned not to place undue reliance on them. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. Immunic undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise, except to the extent required by law. We use words such as “anticipates,” “believes,” “plans,” “expects,” “projects,” “future,” “intends,” “may,” “will,” “should,” “could,” “estimates,” “predicts,” “potential,” “continue,” “guidance,” and similar expressions to identify these forward-looking statements that are intended to be covered by the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995.

Such forward-looking statements are based on our expectations and involve risks and uncertainties; consequently, actual results may differ materially from those expressed or implied in the statements due to a number of factors, including, but not limited to, risks relating to strategy, future operations, future financial position, future revenue, projected expenses, prospects, plans and objectives of management. Risks and uncertainties that may cause actual results to differ materially from those expressed or implied in any forward-looking statement include, but are not limited to: Immunic’s development programs and the targeted diseases; the potential for Immunic’s development programs to safely and effectively target and treat the diseases mentioned herein; preclinical and clinical data for Immunic’s development programs; the impact of future preclinical and clinical data on Immunic’s product candidates; the timing of the availability of data from Immunic’s clinical trials; the availability or efficacy of Immunic’s potential treatment options that may be supported by trial data discussed herein; the timing of current and future clinical trials and anticipated clinical milestones; Immunic’s ability to protect its intellectual property position; Immunic’s plans to research, develop and commercialize its current and future product candidates; the timing of any planned investigational new drug application or new drug application; the development and commercial potential of any product candidates of the company; expectations regarding potential market size; developments and projections relating to Immunic’s competitors and industry; the clinical utility, potential benefits and market acceptance of Immunic’s product candidates; Immunic’s commercialization, marketing and manufacturing capabilities and strategy; Immunic’s ability to successfully collaborate with existing collaborators or enter into new collaboration agreements, and to fulfill its obligations under any such collaboration agreements; Immunic’s ability to identify additional products or product candidates with significant commercial potential; the impact of government laws and regulations; the COVID-19 pandemic; impacts of the conflicts in Ukraine – Russia and the Middle East; Immunic’s listing on The Nasdaq Global Select Market; expectations regarding the capitalization, resources and ownership structure of the company; the executive and board structure of the company; Immunic’s estimates regarding future revenue, expenses, capital requirements and need for additional financing, including the ability to satisfy the minimum average price and trading volume conditions required to receive funding in tranche 2 and 3 of the January 2024 private placement; the nature, strategy and focus of the company and further updates with respect thereto; and the other risks set forth in the company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2023, filed with the U.S. Securities and Exchange Commission.

Forward-looking statements included in this presentation are based on information available to Immunic as of the date of this presentation. Immunic does not undertake any obligation to update such forward-looking statements except as required by applicable law.

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: Achieves **best-in-class benefit / risk profile** by combining **strong efficacy** with **safety**, **tolerability**, and **once-daily** convenience

---

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

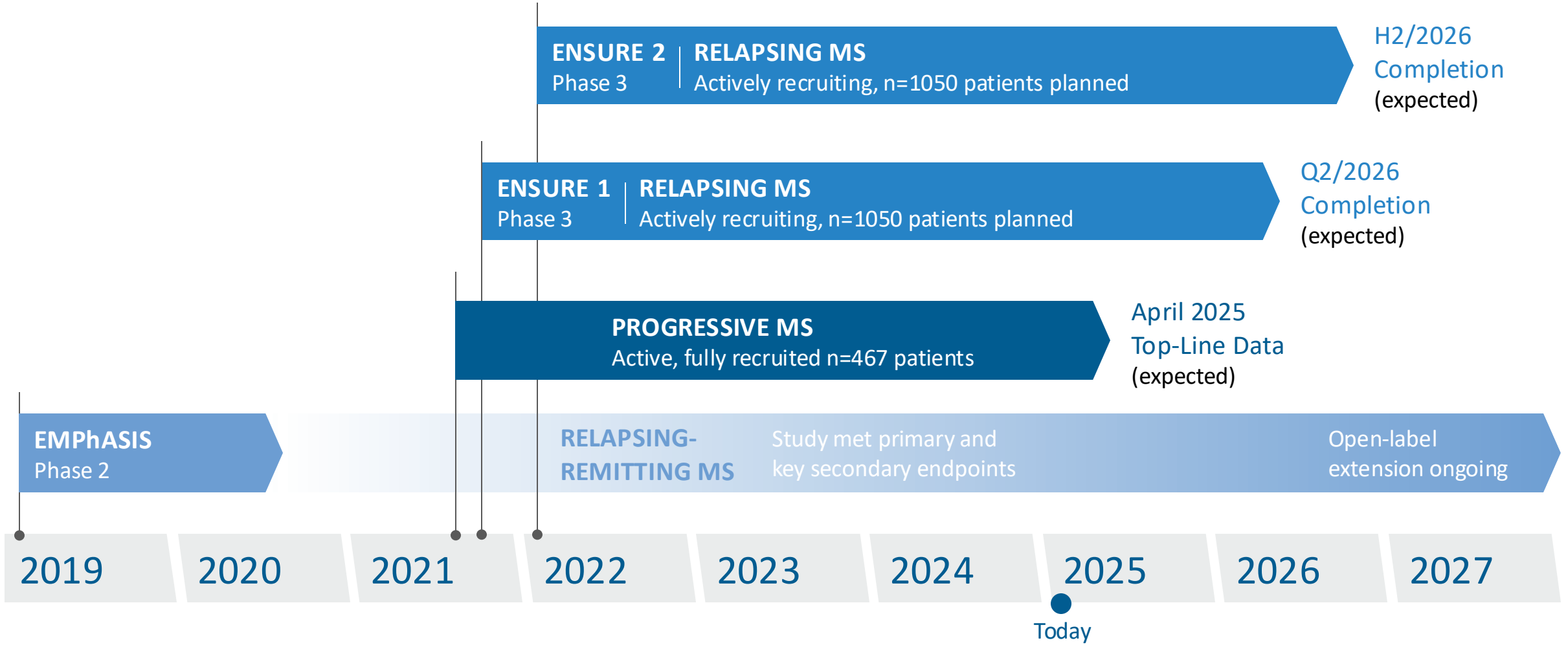
No anticipated black box warnings or serious infection risk (e.g., PML, malignancies, etc.)

If approved, peak sales potential for vidofludimus calcium of $2-6 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

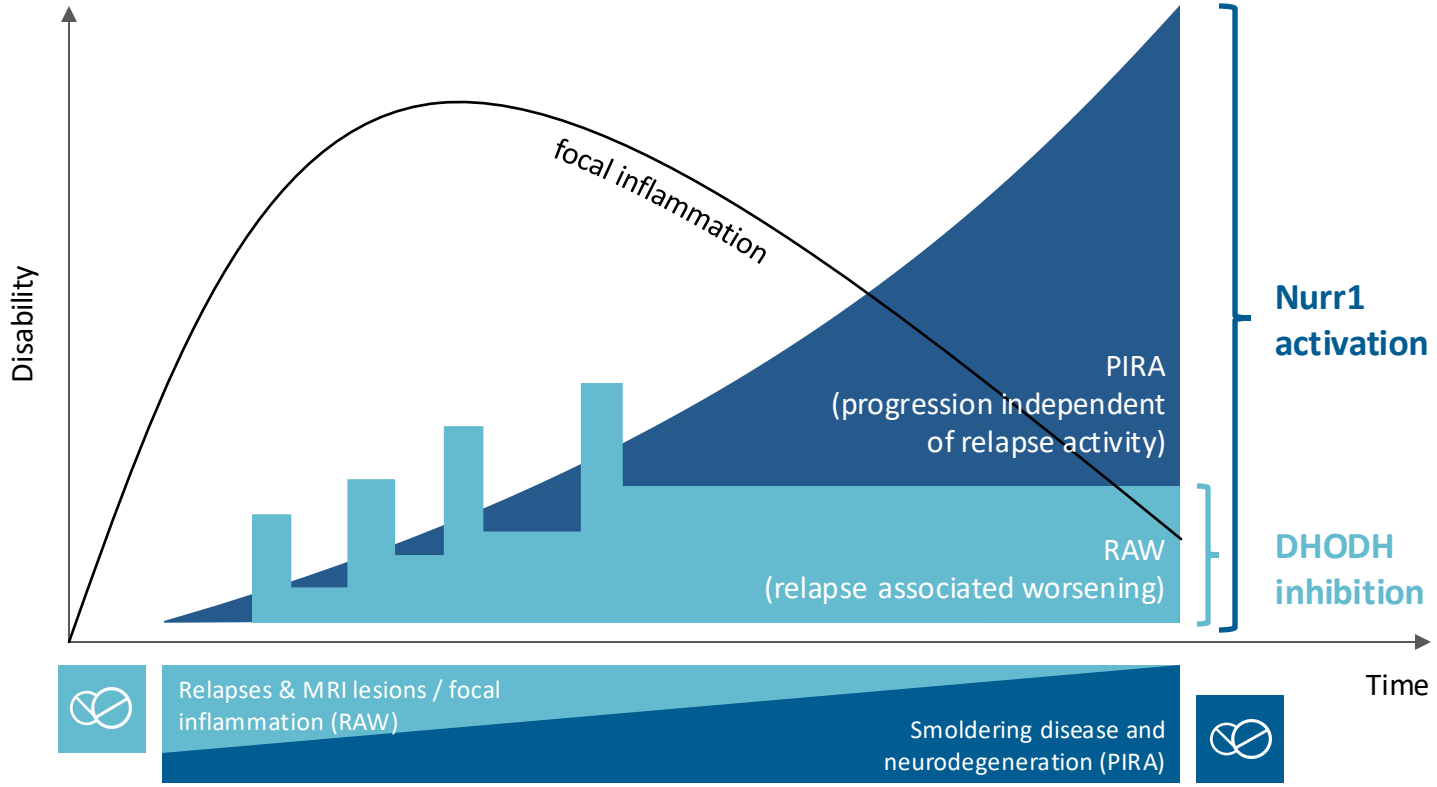
Immunic THERAPEUTICS

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



Immunic THERAPEUTICS

Underlying “Invisible Disability Accumulation” Contributes to Disability Progression Over Time Requiring a Dual Mode of Action Approach



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 [1] Scalfari A. Mult Scler. 2021 Jun;27(7):1002-1004 / MRI: magnetic resonance imaging; Nurr1: nuclear receptor-related 1; DHODH: dihydroorotate dehydrogenase; DMT: disease modifying therapy; MS: multiple sclerosis

These observations challenge the dichotomy between relapsing and progressive disease, supporting a one stage disorder model of MS, where all patients exhibit a **progressive course from the disease onset**, which can be overlapped by relapses.[1]

The ideal DMT agent will have a significant impact on relapses and focal MRI activity to reduce RAW but also halts the putative processes responsible for smoldering MS/PIRA.

Vidofludimus Calcium in Multiple Sclerosis (MS)

Development in Relapsing Multiple Sclerosis (RMS)

EMPhASIS: Completed Phase 2 Trial in Relapsing-Remitting MS
NCT03846219

Coordinating Investigator

Robert J. Fox, M.D.
Cleveland Clinic

Double-Blind, Placebo-Controlled, Randomized, Parallel-Group Trial

- Blinded main treatment period of 24 weeks
- Cohort 1: 30 and 45 mg or placebo QD
- Cohort 2: 10 mg or placebo QD
- Extended treatment period of up to 9.5 years ongoing to observe long-term safety is ongoing

Trial Met Key Efficacy and Safety Endpoints

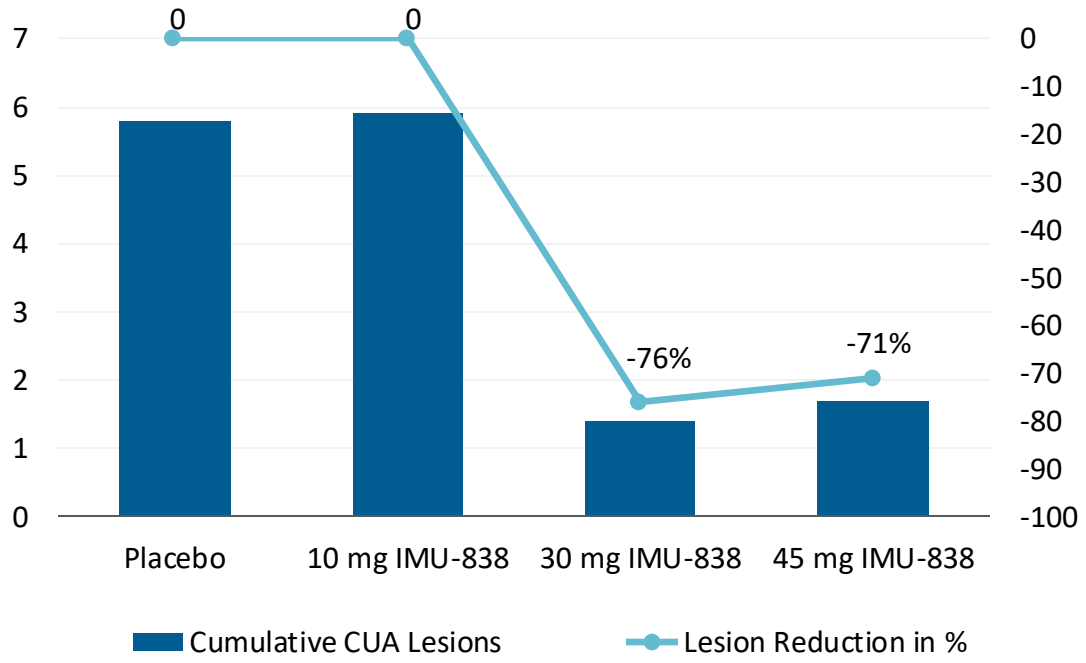
- Randomized **268** patients in 36 centers across four European countries
- Vidofludimus calcium showed strong activity in relapsing-remitting MS population
  - **Primary** and **key secondary endpoints met** with high statistical **significance**: strong reduction of **MRI** lesion activity
  - Reduced serum **NfL** concentrations
  - Signal in preventing confirmed **disability worsening**
- Vidofludimus calcium's **safety profile** was similar to placebo
  - No general safety signals observed
  - Low discontinuation rates, considerably lower than placebo

MS: multiple sclerosis; QD: quaque die = once-daily; MRI: magnetic resonance imaging; NfL: neurofilament light chain

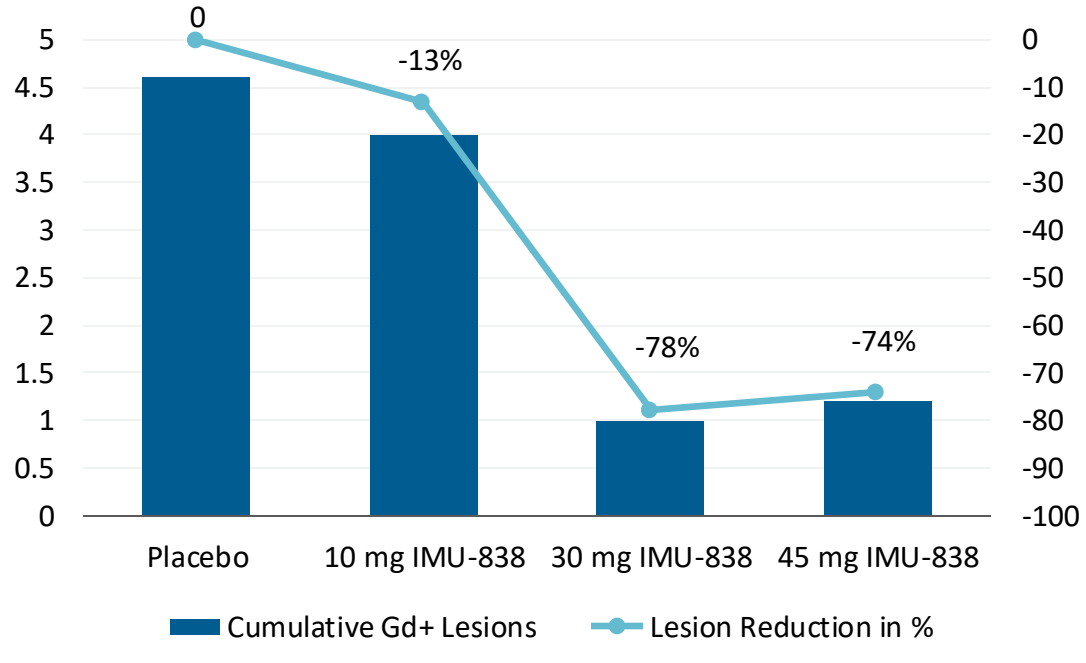
EMPhASIS: Strong Reduction of MRI Lesion Activity

Primary Endpoint Hit With High Statistical Significance, Pooled Cohorts 1 & 2

Reduction in Cumulative CUA Lesions up to Week 24



Reduction in Gd+ Lesions up to Week 24



Primary and key secondary endpoints of cumulative number of new CUA lesions up to week 24 met with high statistical significance

(primary 45 mg vs. placebo: p = 0.0002 / key secondary 30 mg vs. placebo: p < 0.0001)

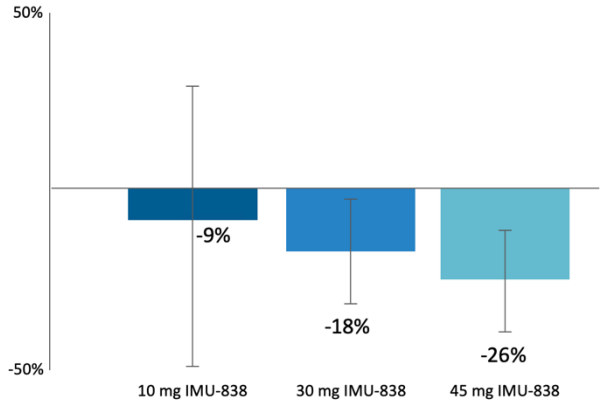
As Cohort 2 only allowed MRI machines of 1.5T, pooled data of Cohorts 1 & 2 only include patients that were evaluated at MRI field strength of 1.5 Tesla. Modified full analysis set C1/C2 (N10 = 47, N30 = 65, N45 = 66, NPBO C1 = 59, NPBO C2 = 12)
Data displayed are as adjusted mean values. Estimates are 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 / RRMS: relapsing-remitting multiple sclerosis; MRI: magnetic resonance imaging; CUA: cumulative unique active, Gd+: gadolinium-enhancing

Immunic THERAPEUTICS

Phase 2 EMPhASIS Trial Outcomes Drove Excitement for Further Investigation of Potential Neuroprotective Properties

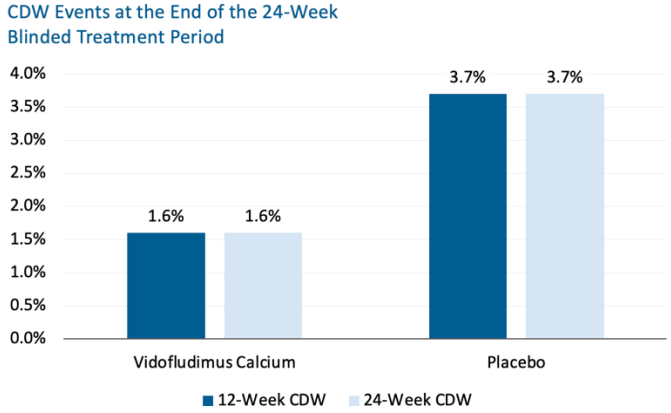
In the phase 2 EMPhASIS trial in RRMS, the following observations provided the rationale for testing vidofludimus calcium as a possible neuroprotective therapy in PMS:

Dose-dependent reduction of the biomarker serum neurofilament light chain (NfL)



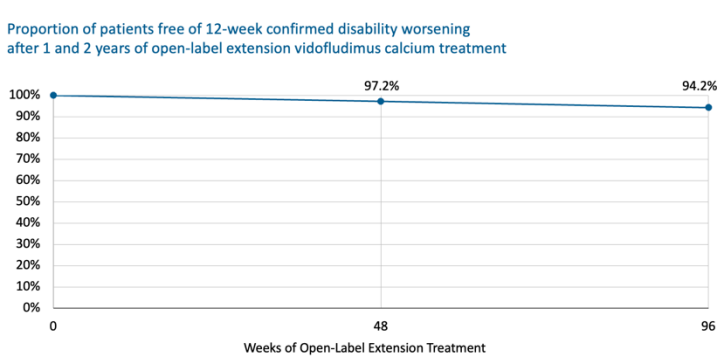
EMPhASIS: vidofludimus calcium showed a remarkable reduction in NfL levels after 24 weeks in all active doses tested compared with placebo

Substantial numerical reduction of confirmed disability worsening (CDW) favoring vidofludimus calcium



EMPhASIS: vidofludimus calcium showed a signal in preventing 12-week and 24-week CDW events as compared to placebo

Low rates of confirmed disability worsening events (<6% of patients) in 2-year open-label treatment



EMPhASIS: only a few patients on continuous treatment with vidofludimus calcium develop 12-week CDW events over a 2-year time frame

MS: multiple sclerosis; PMS: progressive MS; RRMS: relapsing-remitting MS

Immunic THERAPEUTICS

ENSURE: Ongoing Pivotal Phase 3 Trials in Relapsing MS
NCT05134441 & NCT05201638

Coordinating Investigator

Robert J. Fox, M.D.
Cleveland Clinic

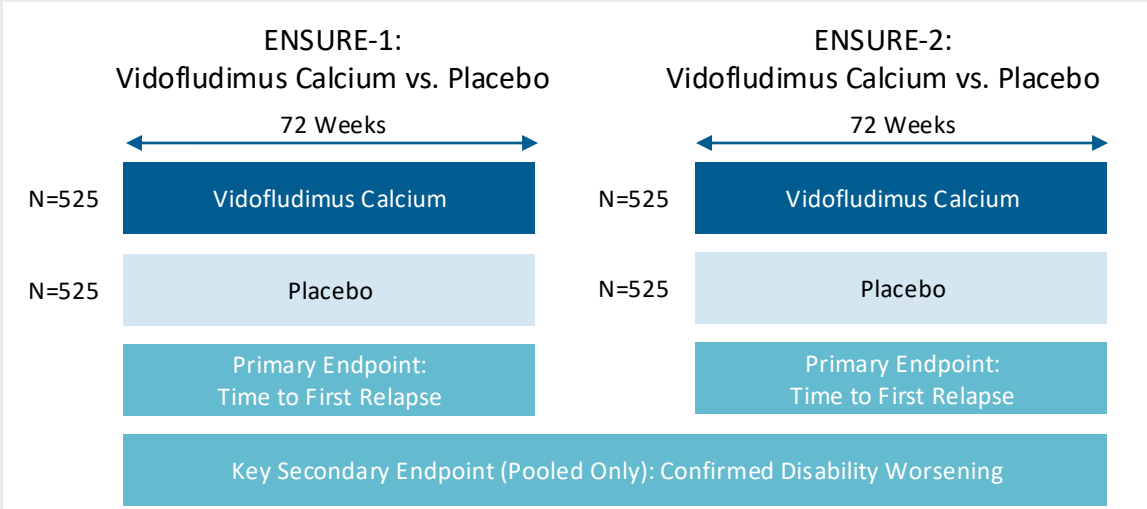
Included Patient Population: Relapsing Forms of MS

- Adult patients aged 18 to 55 years
- Established diagnosis of MS (revised McDonald criteria 2017)
- Confirmed relapsing MS (1996 Lublin criteria[1])
- Active disease as defined by Lublin 2014
- EDSS score at screening between 0 to 5.5

[1] Lublin FD, et al. Neurology. 2014;83(3):278-286
MS: multiple sclerosis; EDSS: Expanded Disability Status Scale; QD: quaque die = once-daily

Two Multicenter, Randomized, Double-Blind Phase 3 Trials

- Approximately 1,050 patients in each trial
- More than 100 sites in the United States, Latin America, Central and Eastern Europe, and India in each trial
- Randomization to 30 mg vidofludimus calcium or placebo QD
- Completion ENSURE-1 expected in Q2/2026, ENSURE-2 in H2/2026



ENSURE: Positive Outcome of Interim Futility Analysis

- Unblinded Independent Data Monitoring Committee (IDMC) confirmed predetermined **futility criteria have not been met**
- IDMC recommended **continuing trial without changes**, including **no need for a potential upsizing**
- Based on a pre-specified assessment after approximately half of the planned first relapse events occurred in the double-blind treatment periods
- Based on a conditional power analysis by an unblinded IDMC
- Immunic has remained blinded and has not seen any of the data available to the IDMC to make their recommendations

Vidofludimus Calcium in Multiple Sclerosis (MS)

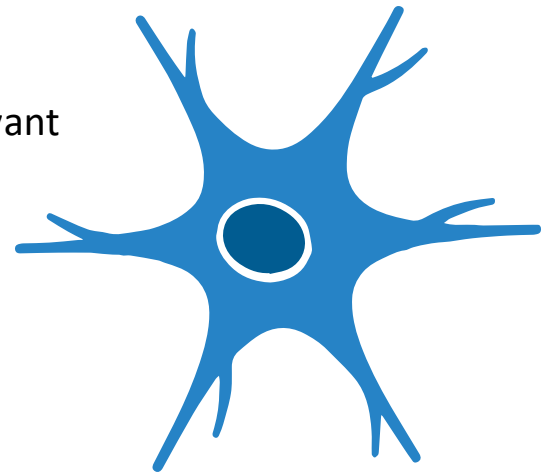
First-in-Class, Potent Nurr1 Activator and Selective DHODH Inhibitor

Vidofludimus Calcium Addresses Smoldering Neurodegeneration

First-in-Class Nurr1 Activator, Targeting Improvement of Physical and Mental Ability of Multiple Sclerosis Patients

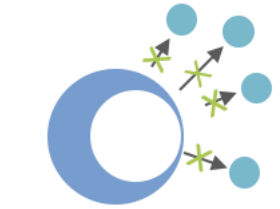
Nurr1 Activator

- Direct and indirect **neuroprotective** effects
- Involved in protecting relevant neurons from cell death
- Known effects reducing activation of microglia and astrocytes
- Effect independent from focal inflammation

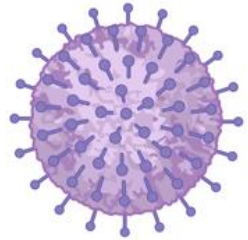


DHODH Inhibitor

- Selectively targets hyperactive immune cells
- Selective **anti-inflammatory** effects, reducing focal inflammation, magnetic resonance imaging lesions and relapses
- Broad-spectrum **antiviral** effects prevent reactivation of EBV and could stop cross reactive immune responses



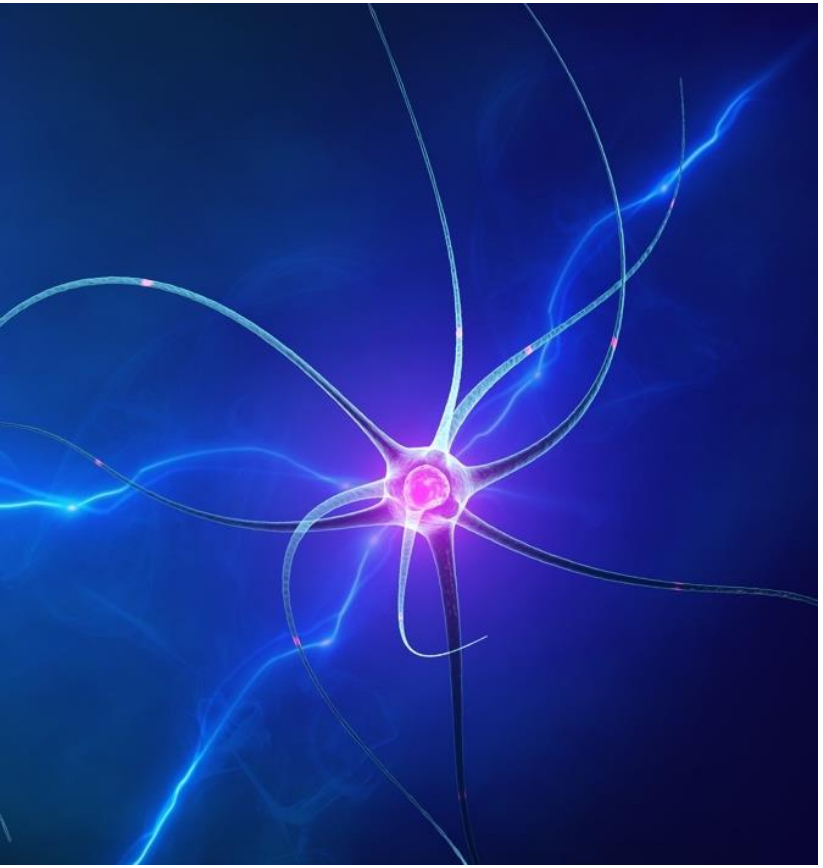
Blocking of Th17/Th1 cytokines



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

Role of Nurr1 in MS: Nurr1 is Downregulated in MS Patients

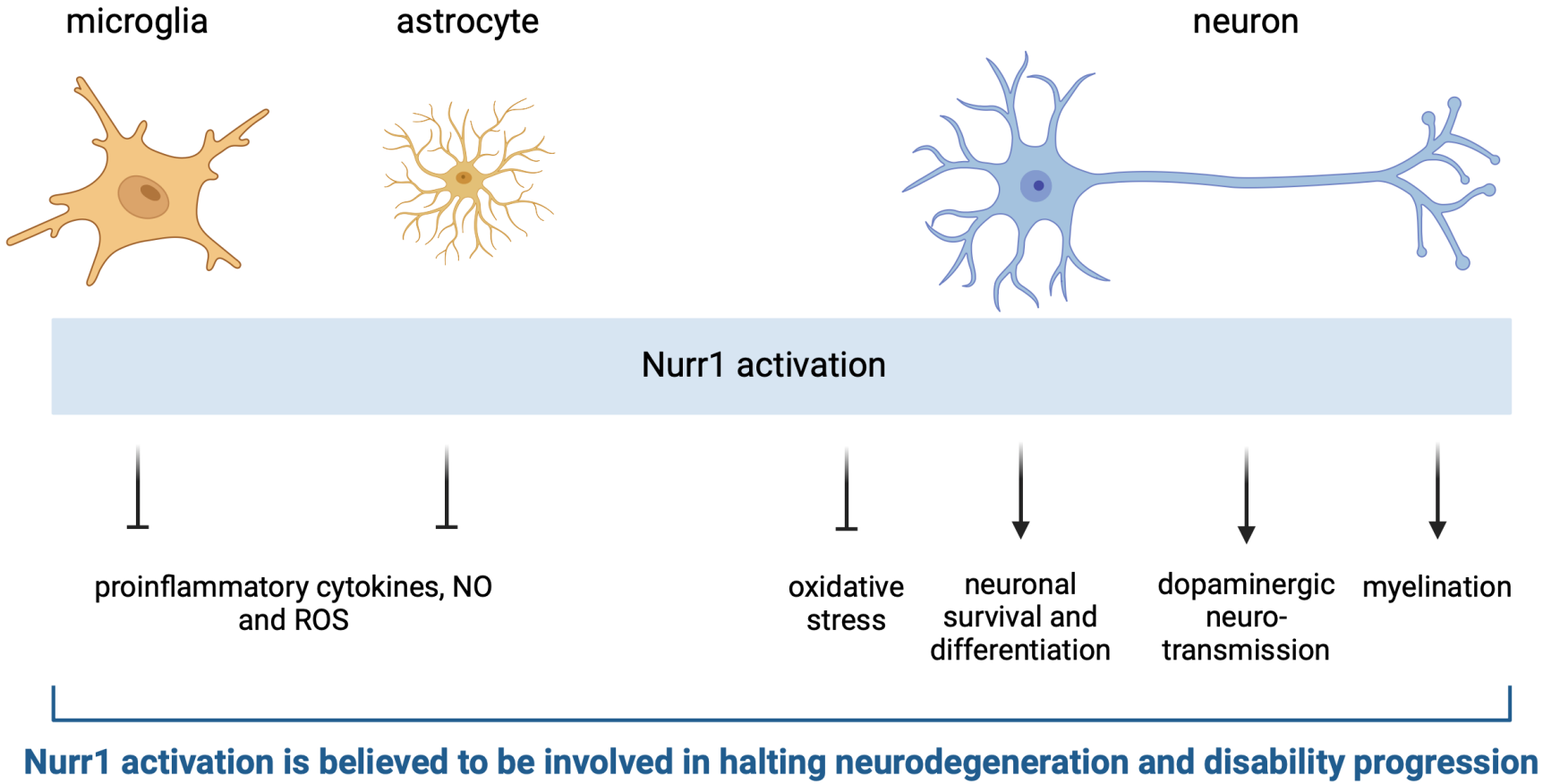
Nurr1 Is a Nuclear Receptor Involved in Neuroprotection



- Nurr1 activation delays the onset of the MS and counteracts inflammation in EAE animal models of MS.[1]
- In untreated patients with relapsing-remitting MS, Nurr1 was significantly downregulated compared to healthy controls.[2]
- Nurr1 gene expression level negatively correlates with the aggressiveness of the pathology and clinical parameters of MS, e.g., relapse rate and EDSS, in which more aggressive forms of the disease were characterized by lower levels of the Nurr1 transcript.[3]
- In brain tissue from people with progressive MS, higher levels of Nurr1 are associated with less nerve loss.[4]

[1] Montarolo et al., Inflamm. Res. 2015, 64, 841–844 [2] Gilli et al., PLoS ONE 2010, 5, e8692 [3] Gilli et al., Arch. Neurol. 2011, 68, 1–10 [4] Pansieri et al., Brain Commun. 2023 Mar 17;5(2):fcad072 / MS: multiple sclerosis; Nurr1: nuclear receptor-related 1; EAE: experimental autoimmune encephalomyelitis; EDSS: Expanded Disability Status Scale

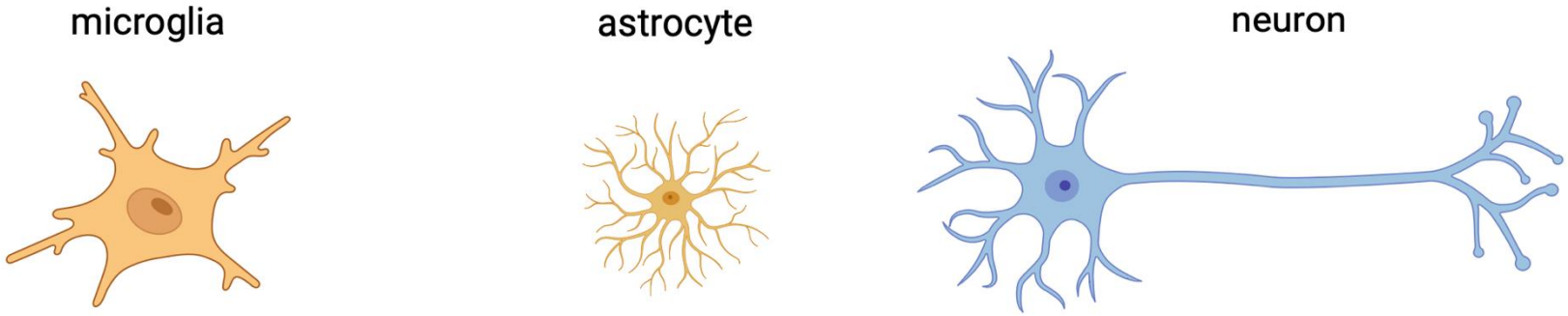
Nurr1 Is a Nuclear Receptor Involved in Neuroprotection



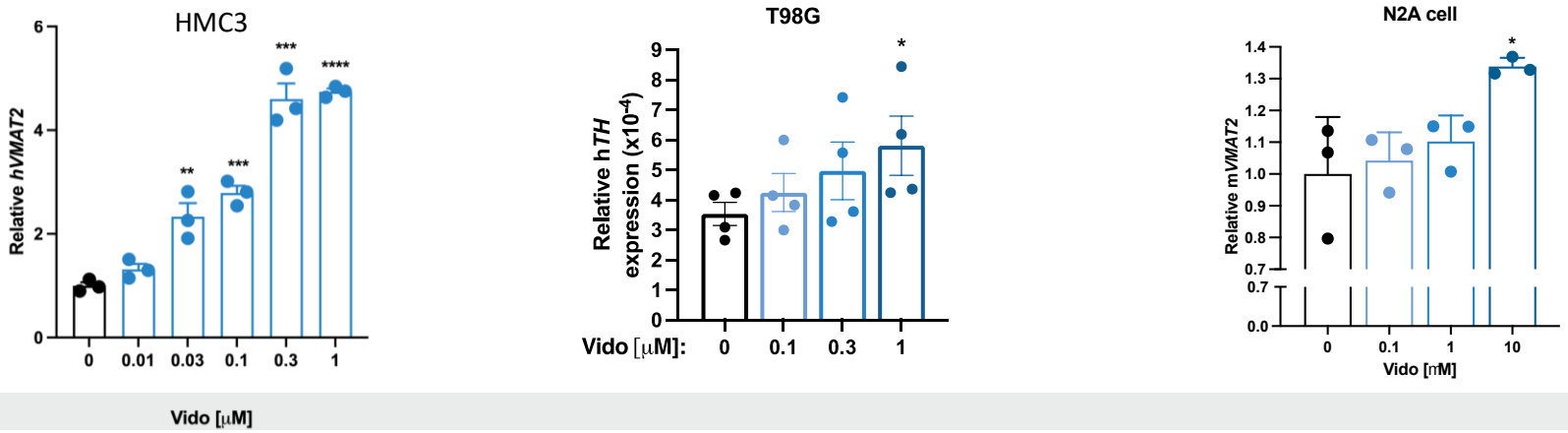
Vietor et al., Journal of Medicinal Chemistry 2023 66 (9), 6391-6402; Schiro et al., 2022, Frontiers in Neurology, adapted from Willems S, Merk D. J Med Chem. 2022;65(14):9548-9563; illustrations created in BioRender.com
Nurr1: nuclear receptor-related 1; NO: nitric oxide; ROS: reactive oxygen species

Nurr1 Is a Nuclear Receptor Involved in Neuroprotection

Nurr1 is expressed in different cells relevant for neuroprotection



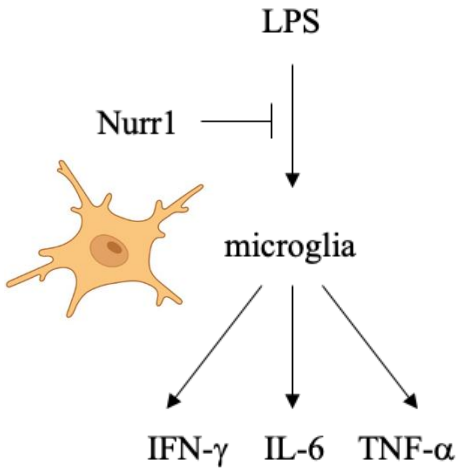
Nurr1 activation by vidofludimus calcium leads to induction of primary target genes in these cells

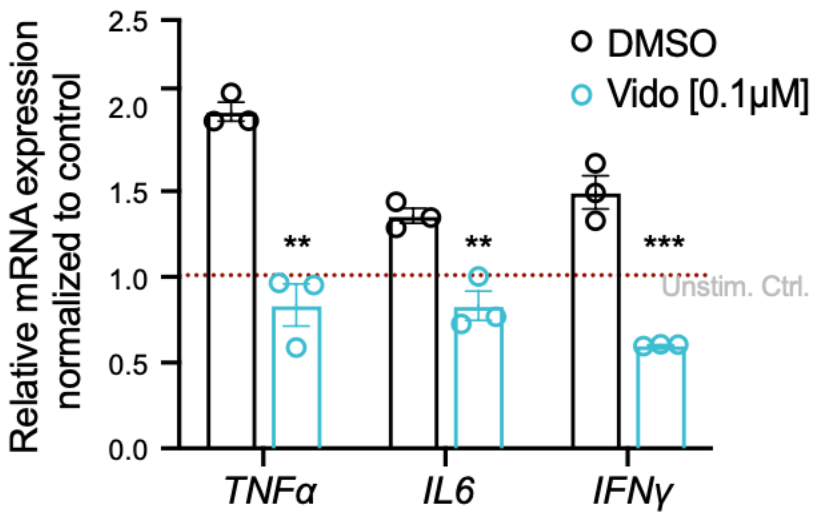


Unpublished gene expression data from Sun Lab, CoH, USA and Merk Lab, LMU, Germany; illustrations created in BioRender.com
Nurr1: nuclear receptor-related 1; NO: nitric oxide; ROS: reactive oxygen species

Vidofludimus Calcium Reduces Microglia Activation

- Nurr1 can prevent antigen-induced activation of microglia and subsequent production of pro-inflammatory cytokines in the brain. In our experiment, vidofludimus calcium (#1260) attenuated LPS-stimulated IL-6, TNFα and IFNγ production in human HMC3 microglial cells at low doses of 100 nM.



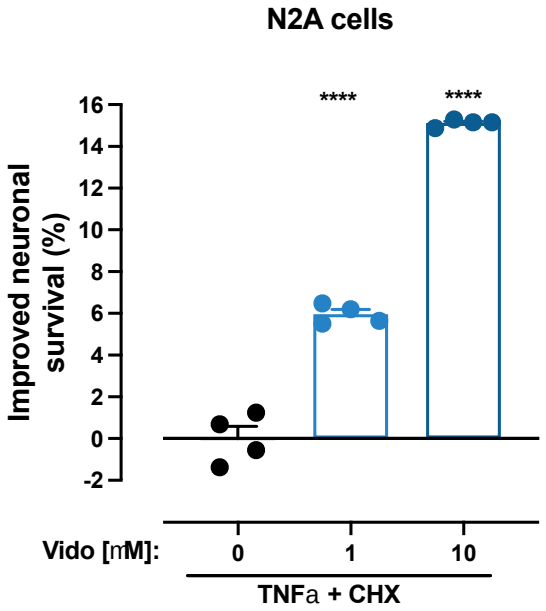


Unpublished data: Sun lab, City of Hope, Duarte; 2023; illustration created in BioRender.com

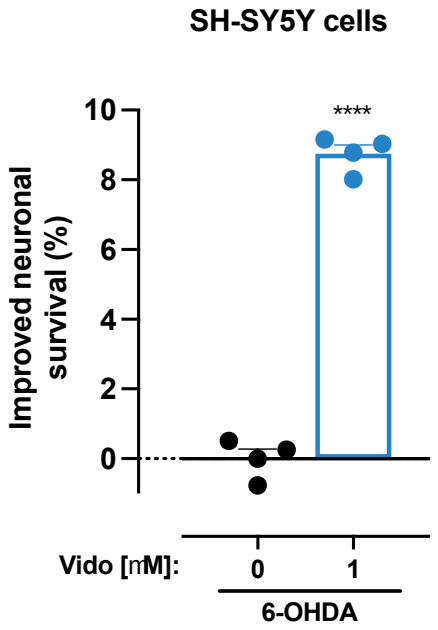
Vidofludimus Calcium Improves Neuronal Survival

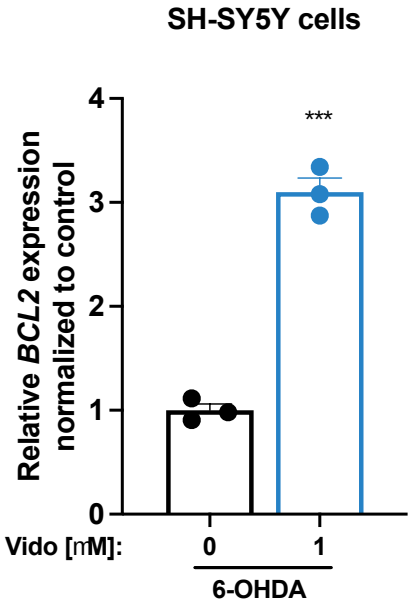
Protective Effects Already Present at 1 µM Concentrations in Human and Murine Cell Systems

- Vidofludimus calcium dose dependently improves survival of murine neuronal cells after apoptosis induction by TNFα+CHX



- Vidofludimus calcium improves neuronal survival after apoptosis induction by the neurotoxic agent 6-OHDA via up-regulation of pro-survival gene BCL2



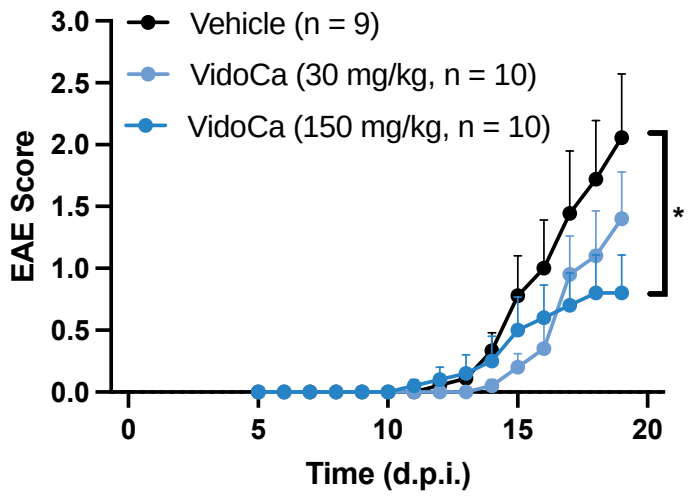


Vidofludimus calcium prevents/ameliorates apoptosis induction in neuronal cells via Nurr1 activation

Unpublished data: Sun lab, City of Hope, Duarte; 2023

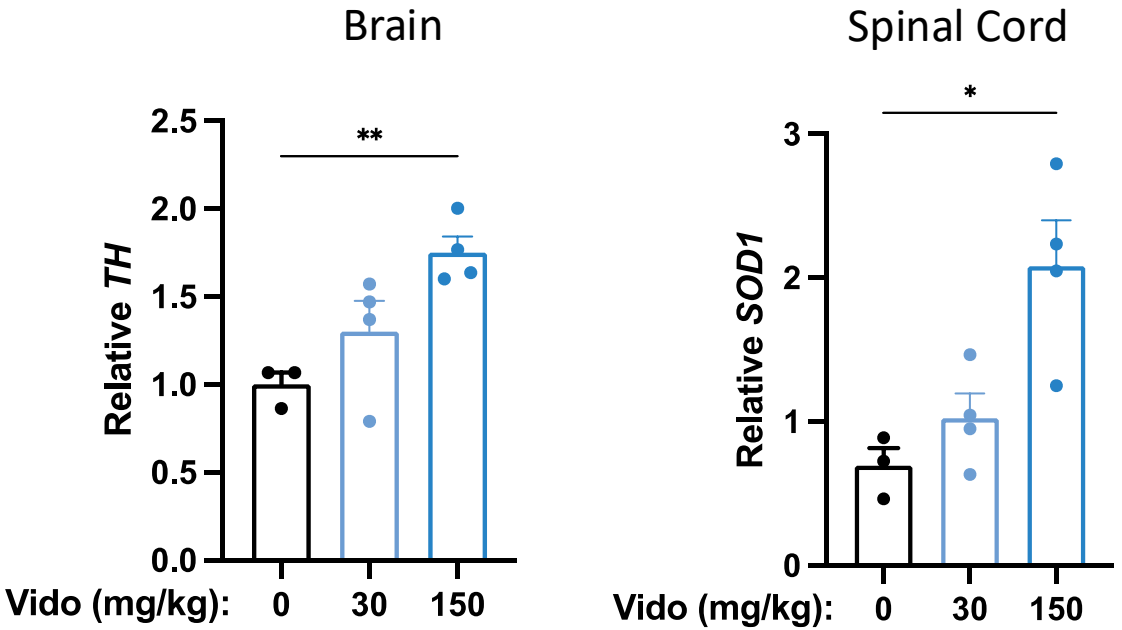
High Dose of Vidofludimus Calcium Demonstrated Activity in Murine EAE Model 1/2

Dose dependent reduction of clinical score in EAE mouse model



Primary Nurr1 target genes are regulated in brain and spinal cord

- TH – brain Tyrosine Hydroxylase
- SOD – spinal cord protects against ROS

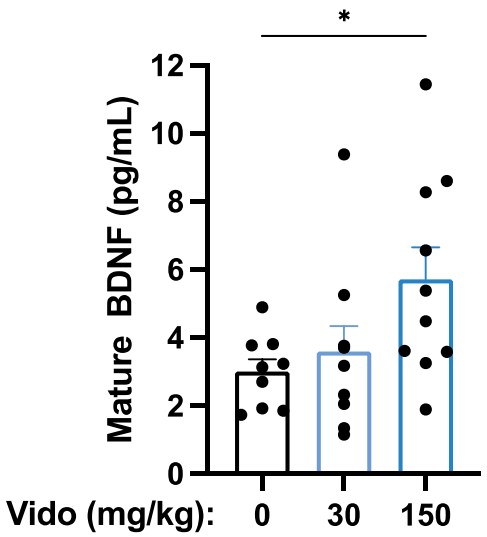


Mouse EAE model performed at City of Hope, 2024

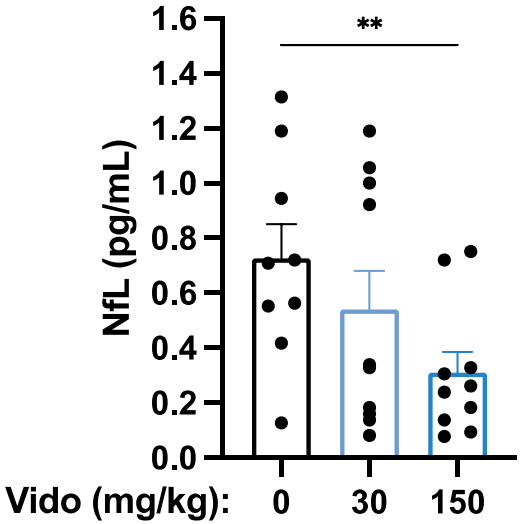
Vidofludimus Calcium Induces Nurr1 Effects *In Vivo,* EAE Model 2/2

Brain-derived neurotrophic factor (**BDNF**) plays an important role in neuronal survival and growth and is is a direct target of Nurr1

Vidofludimus calcium induces mature BDNF secretion in plasma of treated animals



Neurofilament light chain (**NfL**) is a neuronal protein associated with neurodegeneration and neuroaxonal damage. Inline with the activity in clinical score and gene regulation, we see a significant reduction of NfL plasma levels in treated mice

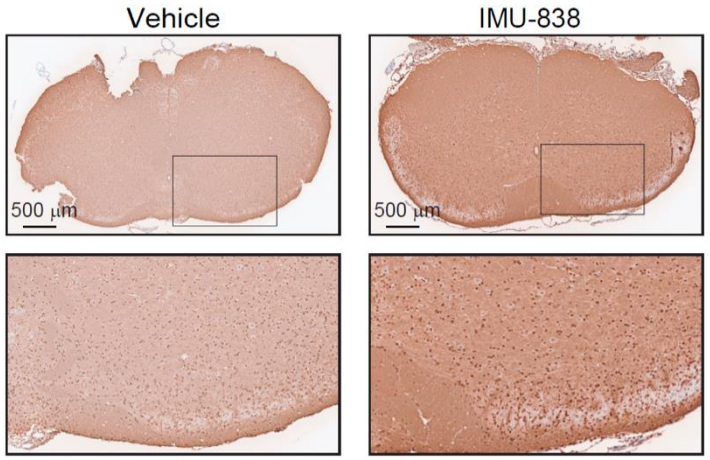


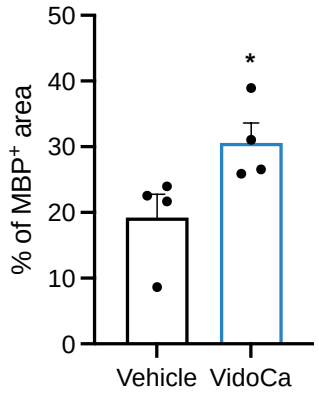
Sun Lab, City of Hope, Duarte; unpublished data

Activity of Vidofludimus Calcium in Murine EAE Model is Supported by Histological Improvement in Spinal Cord

- Improving myelination status

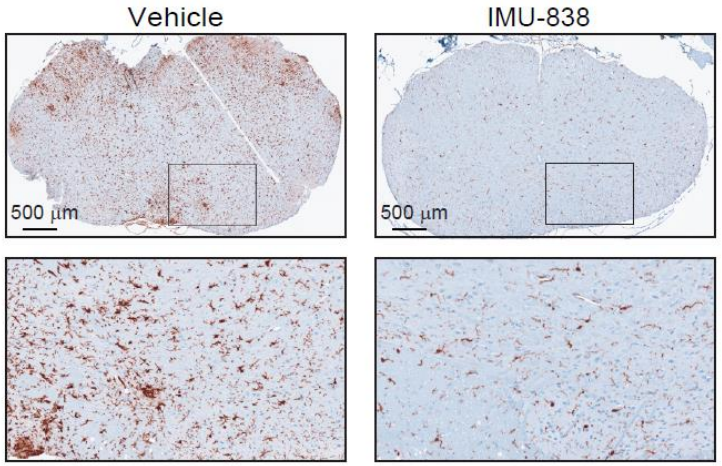
Spinal cord, MBP staining
(MBP: a structure protein of myelin)

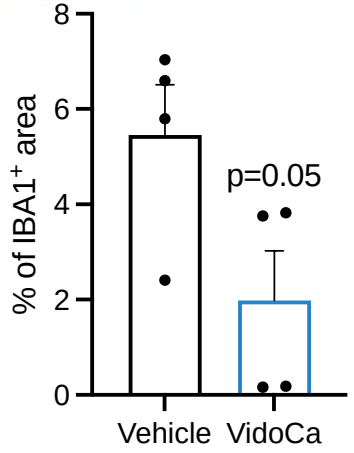




- Reducing microglia activation

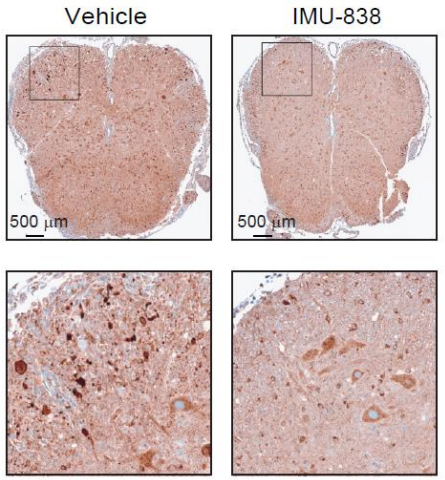
Spinal cord, IBA1 staining
(IBA1: microglia activation marker)

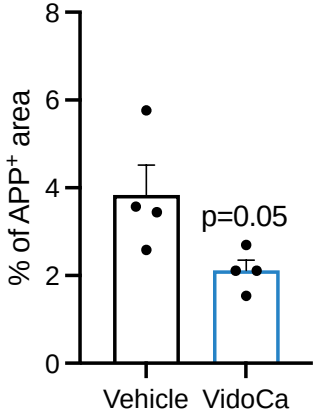




- Reducing axonal injury

Spinal cord, APP staining
(APP: axonal injury marker)



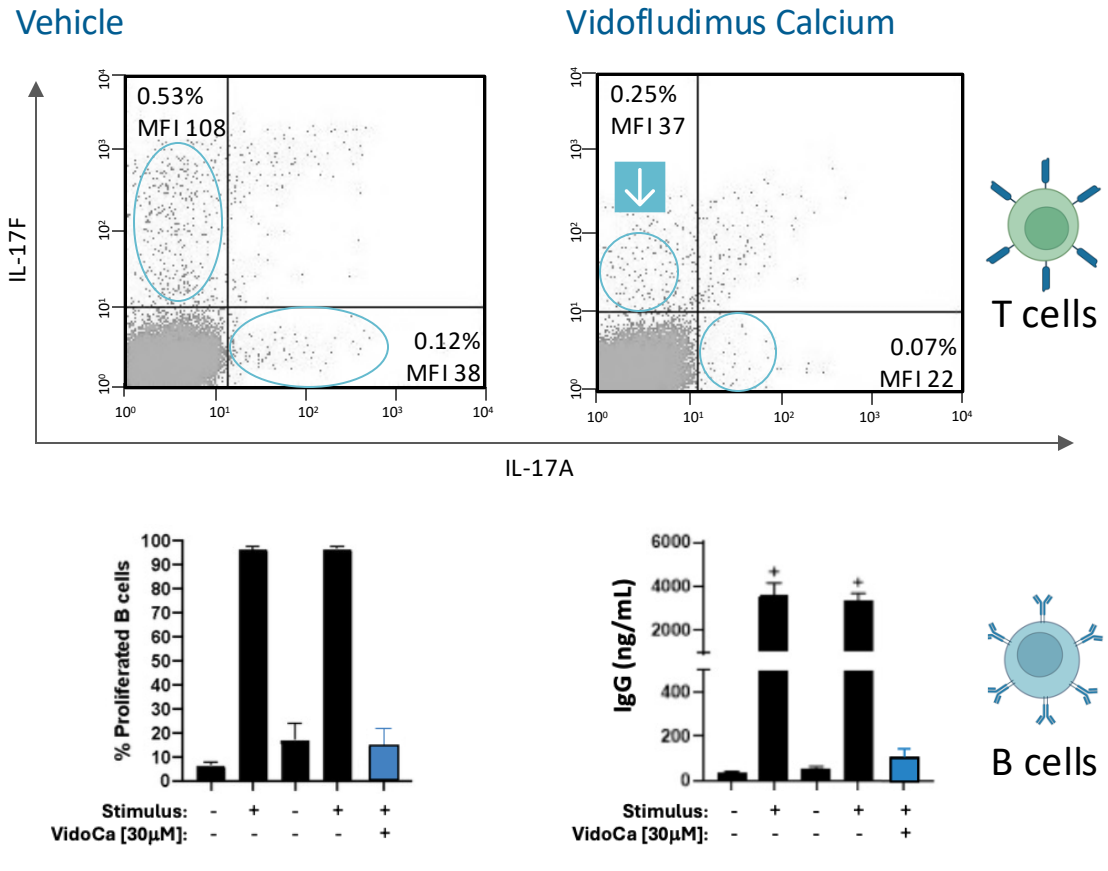


Mouse EAE model performed at City of Hope, 2024

Vidofludimus Calcium Specifically Targets Highly Metabolically Activated Immune Cells – Acting on Focal Inflammation in MS

Hyperactive/High-Affinity Immune Cells are Specifically Dependent on **DHODH**

- High metabolic turnover in high-affinity/strongly activated immune cells
- High amounts of nucleotides for **mRNA** synthesis (up to 100-fold higher nucleotide demand for RNA synthesis than for DNA synthesis)
- T cells: Reduction of high producers of IL-17A & F
- B cells: Reduction of strongly activated B cells
  - Proliferation
  - Production of IgG



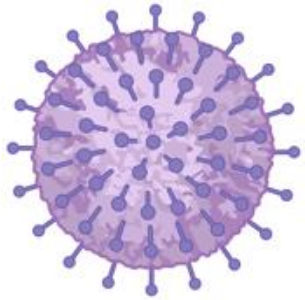
Klotz et al., Science Translational Medicine, 11, Mai 2019; Muehler et al., Multiple Sclerosis and Related Disorders 43 (2020) 102; Unpublished data Immunic (B cells activation with CpG-ODN+sCD40L+anti-IL21)

Vidofludimus Calcium: DHODH Inhibition Provides Broad-Spectrum Antiviral Activity Against Different Pathogenic Viruses

Inhibits Epstein-Barr Virus (EBV) Replication and Reactivation

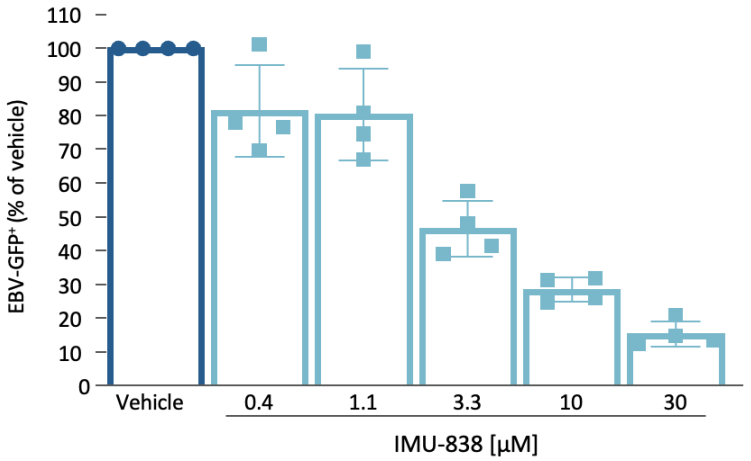
By targeting the host cell metabolism, vidofludimus calcium has shown to be active against different RNA and DNA viruses *in vitro*

- Shows antiviral activity with EC_{50} values in single digit µM range
- Including strong anti-EBV activity



Showed Dose-Dependent Inhibition of EBV Reactivation

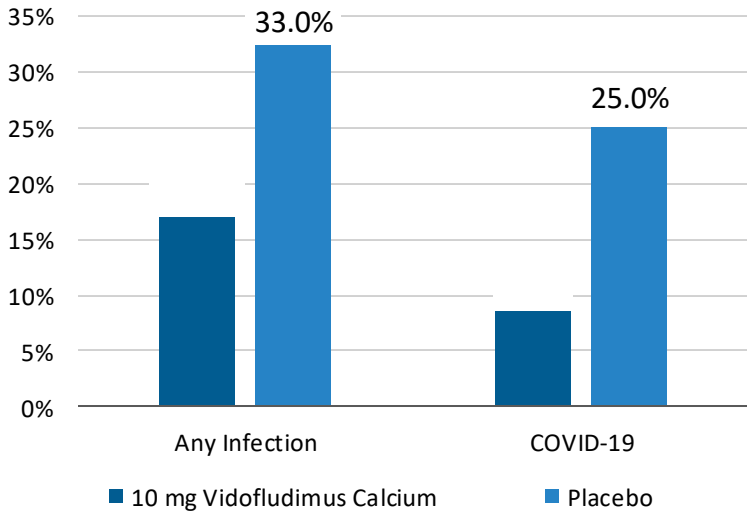
Anti-Akata-BX1-EBV-GFP stimulated with hIgG



Decreased Number of Opportunistic SARS-CoV-2 Infections

Vidofludimus calcium showed interesting hints for clinical anti-SARS-CoV-2 activity in the phase 2 EMPhASIS trial in RRMS

- Number of reported COVID-19 cases Cohort 2:



Left: Eur J Clin Invest. 2020;50:e13366 / middle: Marschall et al., Poster ECTRIMS 2021 / right: Immunic data; DHODH: dihydroorotate dehydrogenase; RNA: ribonucleic acid; DNA: deoxyribonucleic acid; EC50: half-maximal effective concentration; EBV: Epstein-Barr virus; hIgG: human immunoglobulin G; SARS-CoV-2: severe acute respiratory syndrome coronavirus; COVID-19: coronavirus disease 2019; RRMS: relapsing-remitting multiple sclerosis

Vidofludimus Calcium: General Effects on MS Disease Processes

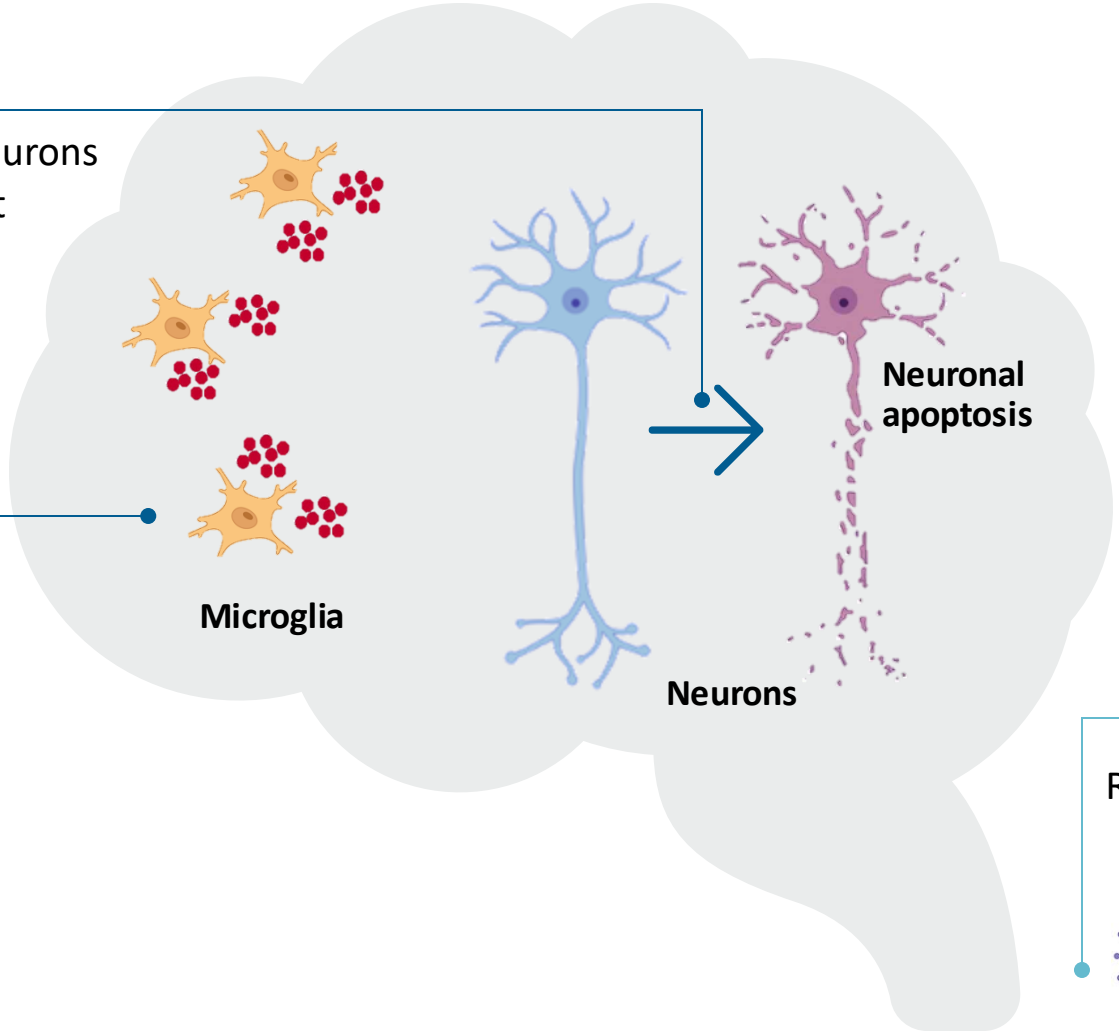
1

Improving the survival of neurons in a neurotoxic environment

Nurr1 Activation

2

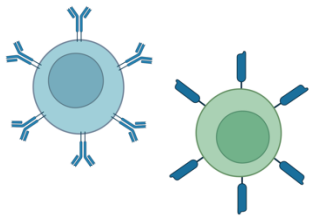
Reducing the activation of microglia (which are a source of a neurotoxic environment)



3

Targeting metabolically active immune cells involved in MS

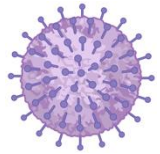
DHODH Inhibition



B & T cells

4

Reducing smoldering disease by blocking the constant trigger of immune cells via inhibition of EBV reactivation



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

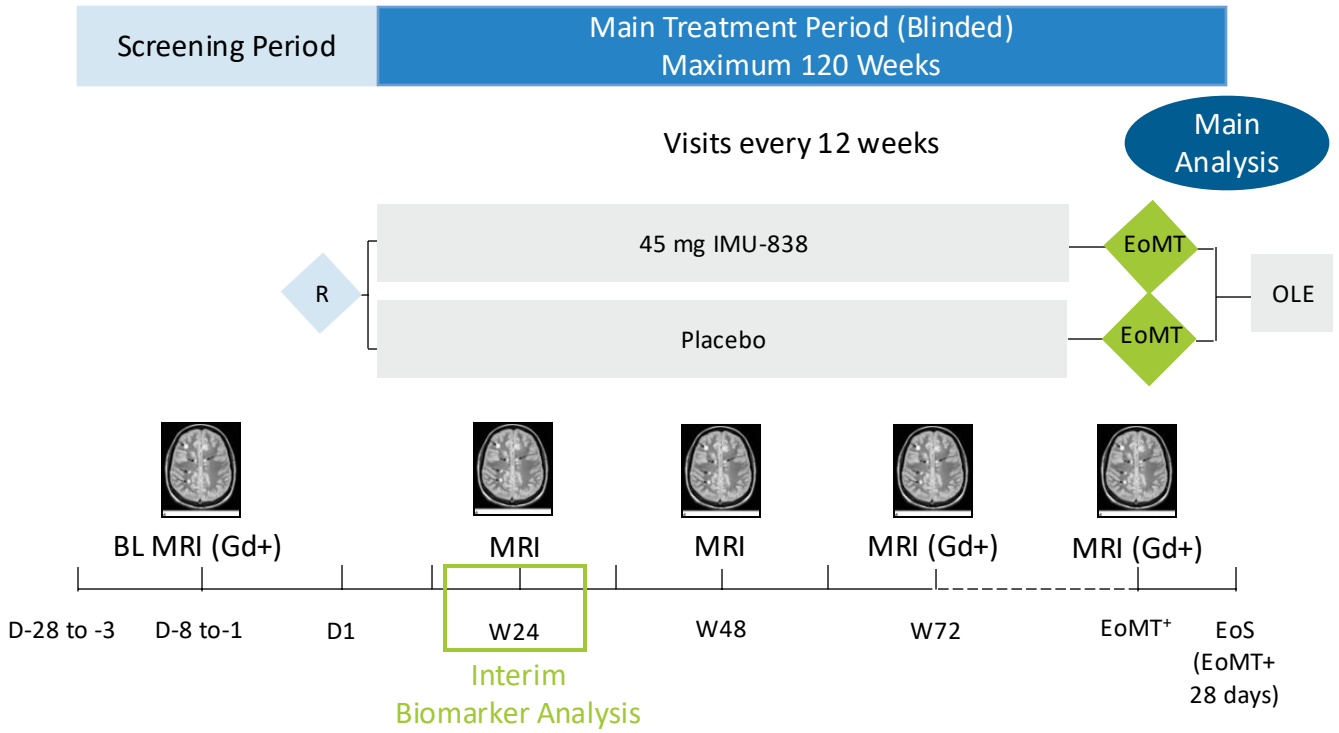
Immunic THERAPEUTICS

Vidofludimus Calcium in Multiple Sclerosis (MS)

Development in Progressive Multiple Sclerosis (PMS)

CALLIPER: Ongoing Phase 2 Clinical Trial in Progressive MS

NCT05054140



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

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

- 467 patients enrolled at more than 70 sites in North America, Western, Central and Eastern Europe
- Randomization to 45 mg vidofludimus calcium or placebo QD
- Primary endpoint: annualized rate of percent brain volume change up to 120 weeks
- Key secondary endpoint: time to 24-week confirmed composite disability progression based on EDSS, timed 25-foot walk and 9-hole peg test
- Blinded main treatment period up to 120 weeks
- Optional, approximately 8-year, open-label extension period

Included Patient Population: Progressive Forms of MS

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

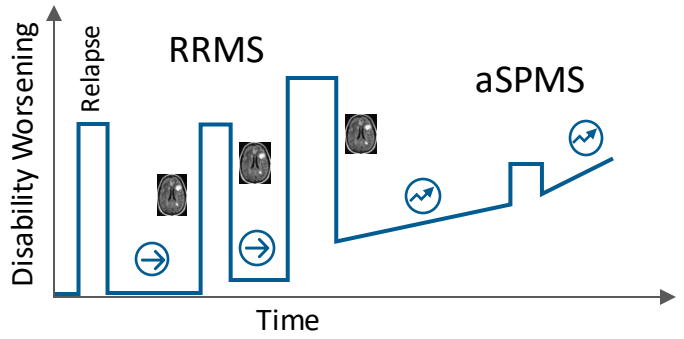
+EoMT: at W120 or when last enrolled patient reaches W72
BL: baseline; D: day; EoMT: end of main treatment period; EoS: end of study; MRI: magnetic resonance imaging; Gd+: gadolinium-enhancing; OLE: open-label extension; R: randomization; W: week; QD: quaque die = once-daily; EDSS: Expanded Disability Status Scale; PPMS: primary progressive multiple sclerosis; SPMS: secondary progressive multiple sclerosis

There Are Three Distinct MS Indications

The Different Indications Have Different Paths and Drivers of the Disability Progression

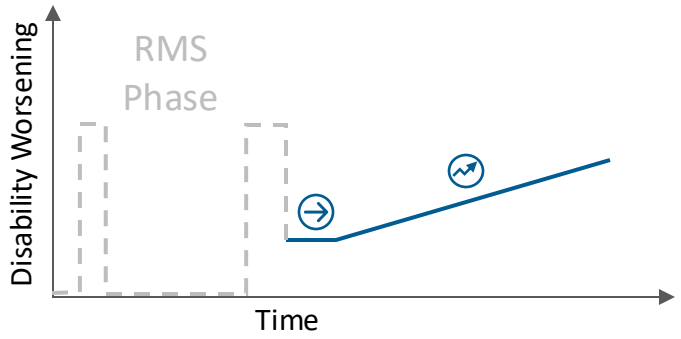
Relapsing MS

- Includes relapsing-remitting MS and active secondary progressive MS
- Relapses and MRI lesions dominate clinical course, disability progression already present
- Current drugs mainly address relapses and relapse-associated disability worsening



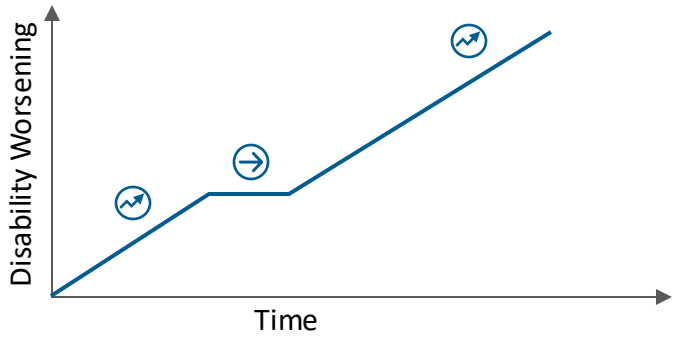
Non-Active SPMS

- Relapses have stopped, but disability progression continues
- No therapies approved, to date



Primary Progressive MS

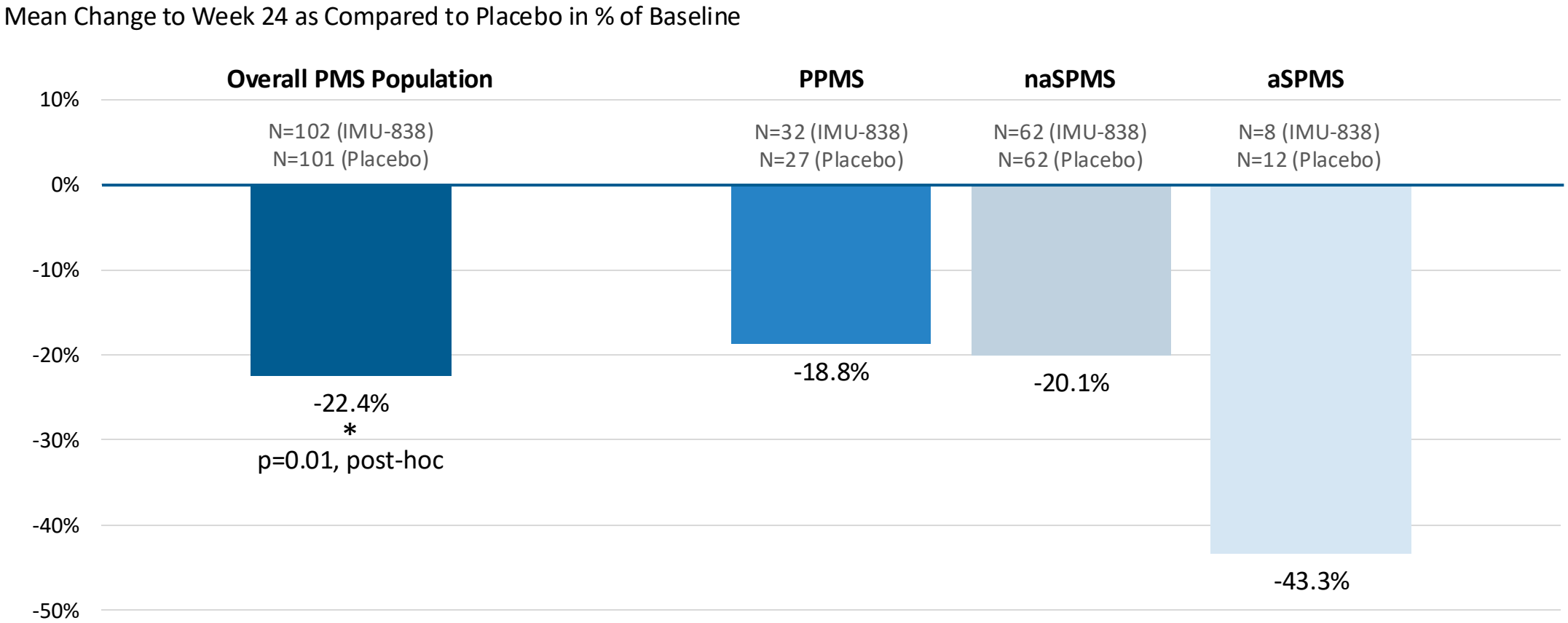
- Disability worsening without relapses from the start without predominance of relapses
- Only one drug approved, so far



Adapted from Kretzschmar A., MSVirtual2020; *Lublin FD, et al. Brain. 2022 Sep 14;145(9):3147-3161
MS: multiple sclerosis; MRI: magnetic resonance imaging; RRMS: relapsing-remitting MS; SPMS: secondary progressive MS; aSPMS: active SPMS

Immunic THERAPEUTICS

CALLIPER Interim Data: Improvements in Serum NfL for Vidofludimus Calcium Consistent Throughout the Overall PMS Population and All Subtypes



Standard deviation for change from baseline in % of baseline: CALLIPER week 24: IMU-838 35.7%, PPMS: IMU-838 7.1%, naSPMS: IMU-838 14.7%, aSPMS: IMU-838 10.3%, 95% Hodges-Lehmann confidence bound EMPhASIS week 24 for 45mg IMU-838: lower boundary -41.0%, upper boundary -12.0%, includes all randomized patients with available neurofilament data at interim analysis, arithmetic mean value for group averages; aSPMS and naSPMS designation as per diagnosis by clinical investigator at study entry

Positive Interim Biomarker Data of Vidofludimus Calcium in Progressive Multiple Sclerosis

- Biomarker evidence that vidofludimus calcium's activity extends beyond the previously observed anti inflammatory effects, thereby further reinforcing its neuroprotective potential
- Vidofludimus calcium aiming to address high unmet medical need in non active SPMS where no relevant treatments are available in the US
- Overall CALLIPER trial ongoing; top line data of the full 467 patients expected in April 2025
- Results of this interim analysis may inform the ability to potentially reduce PIRA events in the ongoing phase 3 ENSURE program in RMS

Thank You!

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Chief Scientific Officer

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www.imux.com