Immunic Therapeutics

Developing Selective Oral Therapies in Immunology

NASDAQ: IMUX | October 2025

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, availability and terms of necessary financing, 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, regulations and tariffs; 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, 2024, 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.

CLINICAL-STAGE BIOPHARMACEUTICAL COMPANY (NASDAQ: IMUX)

Dedicated to improving the lives of patients with chronic inflammatory and autoimmune diseases

Innovative pipeline:
First-in-class oral drugs with unique modes of actions for multiple sclerosis and gastrointestinal diseases

Positive MS phase 2 data sets:
Underline neuroprotective effect of Nurr1 activation by vidofludimus calcium

Large commercial opportunity:
$3-7 billion peak sales potential for vidofludimus calcium in MS

Experienced leadership team:
Successfully developed and commercialized multiple medicines

Financials:
Cash balance of $55.3 million as of June 30, 2025

Immunic THERAPEUTICS

Leadership Team

Company is Led by an Experienced Management Team

Daniel Vitt, PhD
Chief Executive Officer

Jason Tardio, MBA
President & Chief Operating Officer

Andreas Muehler, MD, MBA
Chief Medical Officer

Hella Kohlhof, PhD
Chief Scientific Officer

Glenn Whaley, CPA
Chief Financial Officer

Patrick Walsh
Chief Business Officer

Inderpal Singh
General Counsel

Werner Gladdines
Chief Development Officer

Duane Nash, MD, JD, MBA
Executive Chairman

Immunic THERAPEUTICS

Advanced Clinical Pipeline

Well Differentiated Programs in Various Phases of Clinical Development

Program	Preclinical	Phase 1	Phase 2	Phase 3	Key Program Updates
Vidofludimus Calcium (IMU-838)*	Relapsing Multiple Sclerosis (RMS) – ENSURE-1 and ENSURE-2 Trials Progressive Multiple Sclerosis (PMS) – CALLIPER Trial Ulcerative Colitis (UC) – CALDOSE-1 Trial				✓ Phase 2 EMPhASIS trial in RRMS successfully completed, significantly reduced brain lesions, encouraging results in reducing disability worsening ✓ Interim analysis of ENSURE program completed, IDMC recommendation to continue trials as planned, both ENSURE trials fully enrolled in May 2025 ✓ CALLIPER trial successfully completed, substantial reductions in disability worsening ✓ Phase 2 CALDOSE-1 trial in UC completed, effective in 50 weeks maintenance phase ▪ Top-line data for both ENSURE trials expected by end of 2026
IMU-856	Celiac Disease and other Gastrointestinal Disorders				✓ Phase 1/1b trial in healthy volunteers and celiac disease completed, first proof-of-concept in celiac disease ✓ Dose-dependent increase of endogenous GLP-1 in post hoc analysis of phase 1b trial in celiac disease ▪ Further clinical testing in preparation
IMU-381	Gastrointestinal Diseases				

■ Ongoing ■ Completed ■ In preparation or planned

RRMS: relapsing-remitting multiple sclerosis; IDMC: Independent Data Monitoring Committee; GLP-1: glucagon-like peptide-1
*Additional investigator-sponsored phase 2 RAPID_REVIVE trial of vidofludimus calcium in post COVID syndrome ongoing, sponsoredby University Hospital Frankfurt

Immunic THERAPEUTICS

Vidofludimus Calcium in Multiple Sclerosis (MS)

Targeted to Elevate the Standard of Care for the Full Spectrum of Multiple Sclerosis Patients

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

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

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

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

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

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

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

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

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

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

1.0
No disability, minimal signs of MS

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

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

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

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

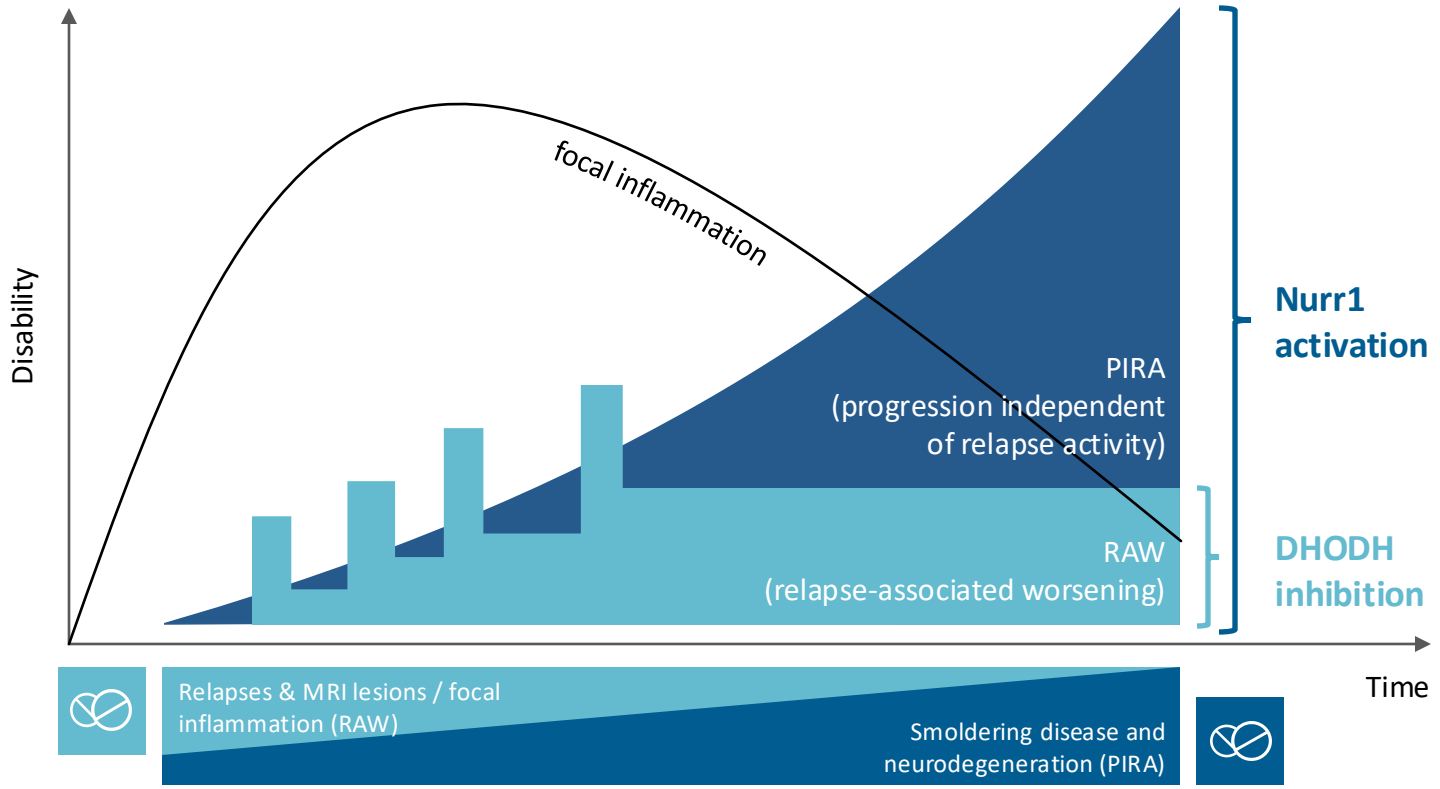
9.0
Confined to bed, can still communicate and eat

10
Death by MS

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

Immunic THERAPEUTICS

“Invisible” Disability Progression Over Time Requires a Neuroprotective 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; MS: multiple sclerosis

One stage model of MS[1]:

- All patients exhibit **progressive components from disease onset**
- Can be overlapped by relapsing components in the early phases

To address this, new treatments should:

- Have a significant impact on relapses and focal MRI activity
- Reduce RAW
- Tackle processes responsible for smoldering MS/PIRA

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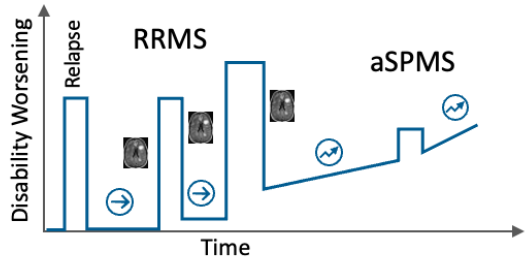
Vidofludimus Calcium Has the Potential to be the First and Only Oral DMT Approved for Both Relapsing and Progressive MS

Relapsing MS (RMS)

Relapsing MS

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

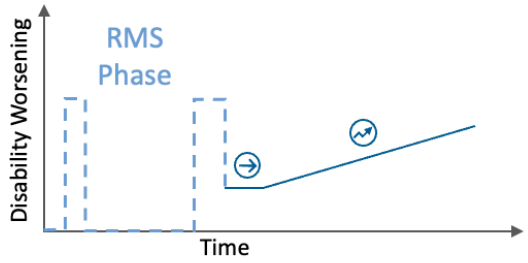


~900,000 patients diagnosed

Progressive MS (PMS)

Non-Active SPMS

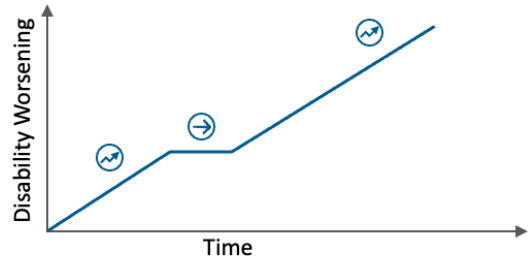
Relapses have stopped, but disability progression continues



~175,000 patients diagnosed

Primary Progressive MS

Disability worsening without relapses from the start



~120,000 patients diagnosed

DHODH Inhibition

Nurr1 Activation

Relapses and focal inflammation (RAW)

Smoldering disease and neurodegeneration (PIRA)

DMT: disease-modifying therapy; MS: multiple sclerosis; RRMS: relapsing-remitting MS; SPMS: secondary progressive MS; aSPMS: active SPMS; MRI: magnetic resonance imaging; DHODH: dihydroorotate dehydrogenase; Nurr1: nuclear receptor-related 1; RAW: relapse-associated worsening; PIRA: progression independent of relapse activity

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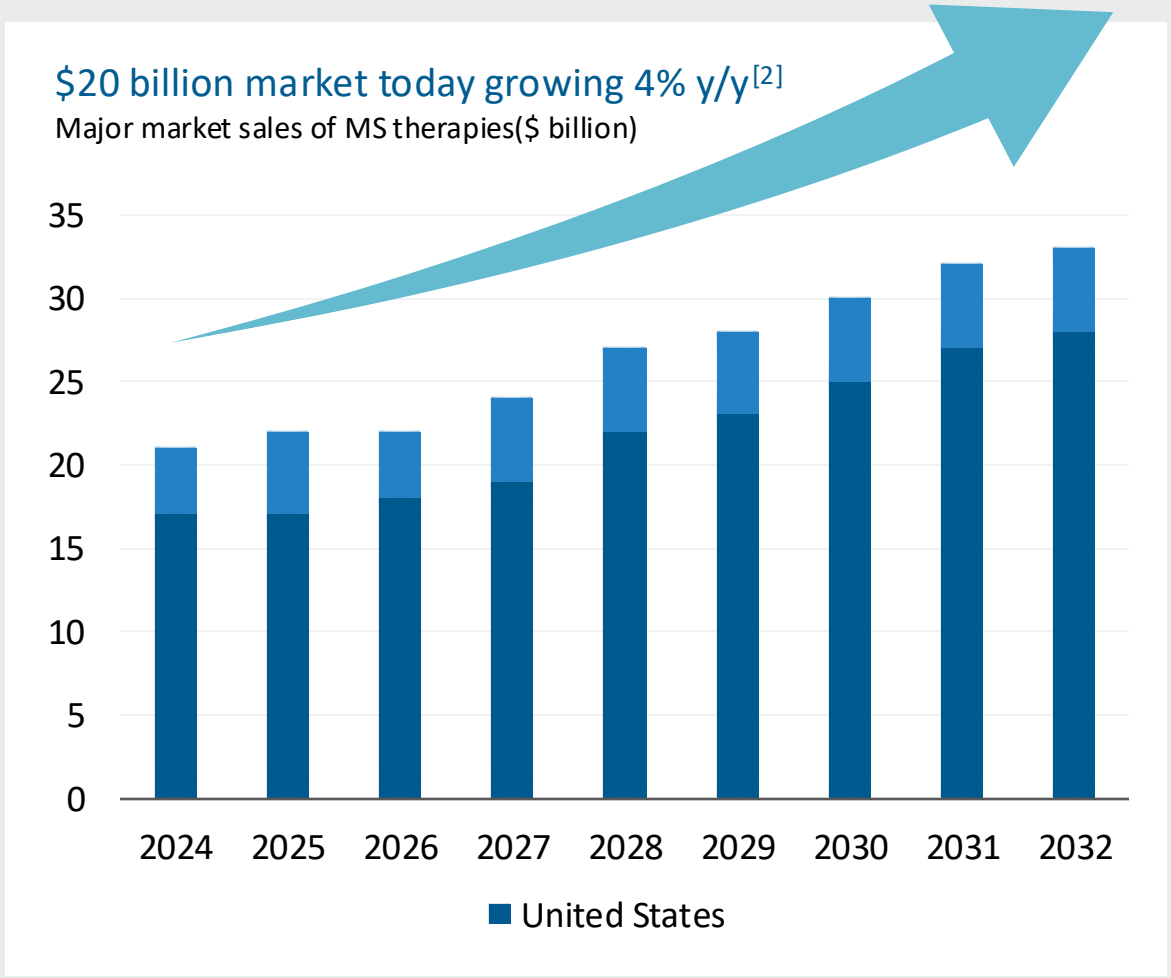
A Large and Growing Global Market Where Multiple Blockbusters Coexist

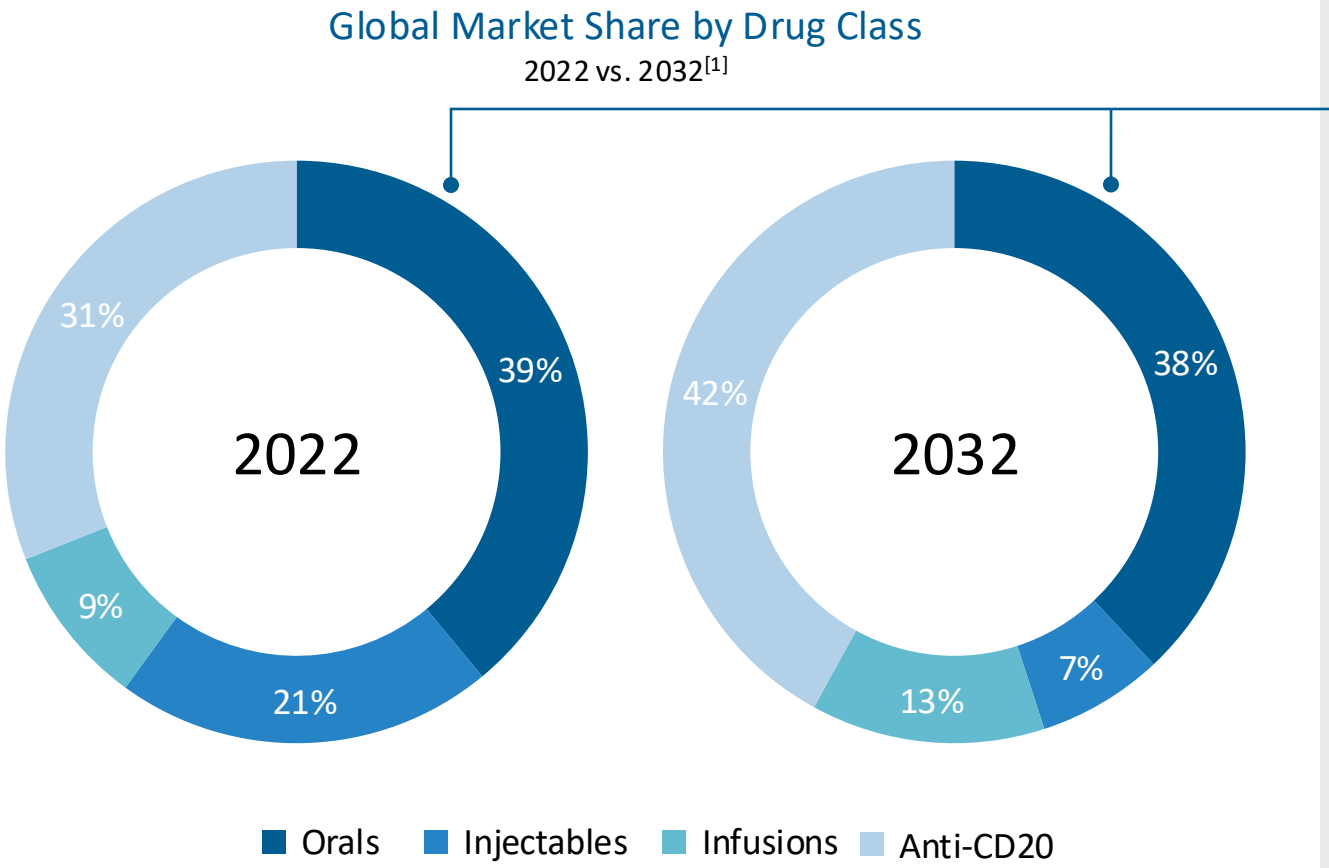
Many brands are generating in excess of $1 billion in global annual sales in 2024[1]

Ocrevus®	$7.6 billion
Kesimpta®	$3.2 billion
Tysabri®	$1.7 billion
Tecfidera® & Vumerity®	$1.6 billion
Mavenclad®	$1.15 billion
Avonex® & Plegridy®	$968 million
Rebif®	$626 million
Gilenya®	$552 million
Aubagio®	$379 million
Briumvi®	$310 million



[1] Company public filings [2] Sales numbers in G7 countries (US, UK, Canada, Japan, Germany, France, Italy) in USD billion; Multiple Sclerosis Landscape and Forecast by Decision Resources Group Part of Clarivate

Oral DMTs Will Continue to Play a Big Role as Important Treatment Options



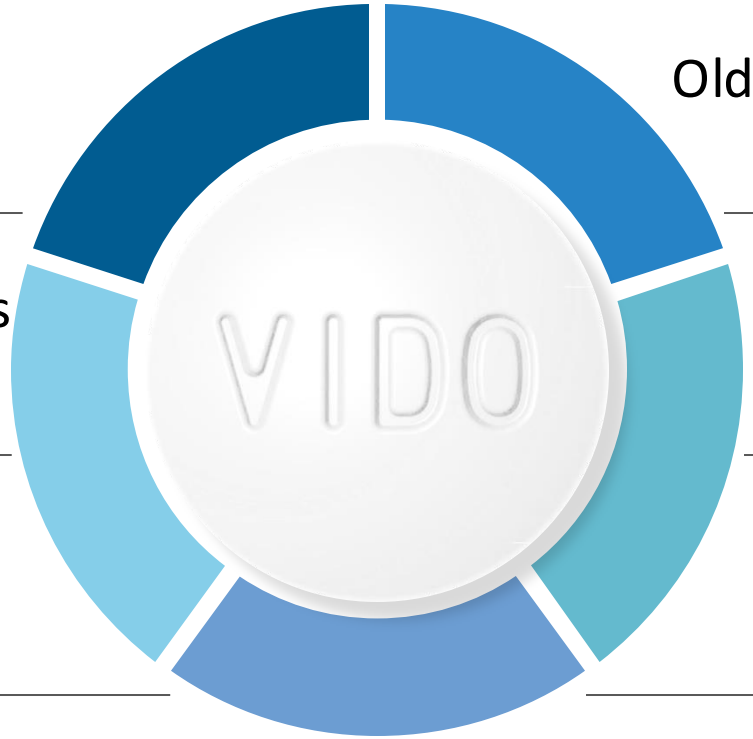
While anti-CD20 class of therapies continues to grow, oral class still expected to capture over 1/3 of the global market

- 42% of patients prefer oral medicines[2]
- Early-line reliance on injectable therapies will continue to wane as the market shifts to using oral therapies earlier
- 15% of patients with PPMS and 25% of patients with non-active SPMS received oral treatments (off label)[3]

[1] Sales numbers in G7 countries (US, UK, Canada, Japan, Germany, France, Italy) in USD billion; 2024 Multiple Sclerosis Landscape and Forecast by Decision Resources Group Part of Clarivate. [2] Jonker MF, et al. Med Decis Making. 2020 Feb;40(2):198-211 [3] Watson C, et al. Neurol Ther. 2023 Dec;12(6):1961-1979 / DMT: disease-modifying therapy; CD20: B lymphocyte cell-surface molecule; SPMS: secondary progressive MS; PPMS: primary progressive MS

Multiple MS Patient Segments Could Benefit from Vidofludimus Calcium

- Newly diagnosed patients
- Patients switching therapies due to progression
- Patients switching off anti-CD20 therapies due to safety concerns



- Older patients where immuno-suppression is a concern
- Untreated patients
- Patients with progressive disease (naSPMS & PPMS)

MS: multiple sclerosis; naSPMS: non-active secondary progressive MS; PPMS: primary progressive MS

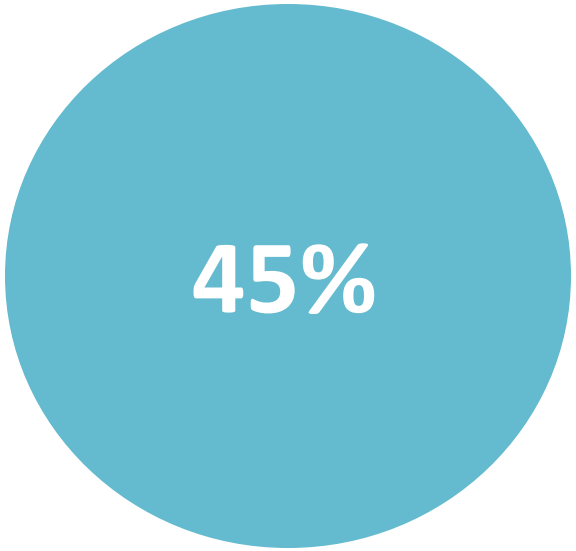
Vidofludimus Calcium: Derisked Near-Term Opportunity With $3-7 Billion Peak Potential

	RMS	naSPMS	PPMS
Indication	RMS	naSPMS	PPMS
Status	Phase 3	Phase 3-ready	Phase 3-ready
Clinical Evidence	78% reduction of new Gd+ lesions (Phase 2)	19% reduction of 24-week CDW (Phase 2)	31% reduction of 24-week CDW (Phase 2)
Eligible Population	**~900K**	**~175K**	**~120K**
Patients Treated	**~525K**	**~65K**	**~54K**
Potential Peak Sales	**$1-2B**	**$1-2B**	**$2-3B**

Patient and market size numbers sourced via internal Immunic analysis and 2024 Multiple Sclerosis Landscape and Forecast report by Decision Resources Group Part of Clarivate
RMS: relapsing MS; naSPMS: non-active secondary progressive MS; PPMS: primary progressive MS; Gd+: gadolinium-enhancing; CDW: confirmed disability worsening; K: thousand; B: billion

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

diagnosed PPMS patients in the US & EU5



of diagnosed PPMS patients are currently on a DMT

in PPMS sales for the only approved product

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

PPMS: primary progressive multiple sclerosis; DMT: disease-modifying therapy; K: thousand; B: billion / Patient and market size numbers sourced via internal Immunic analysis and 2024 Multiple Sclerosis Landscape and Forecast report by Decision Resources Group Part of Clarivate; EU5 countries: France, Germany, Italy, Spain, and United Kingdom; TD Cowen Therapeutic Categories Outlook Comprehensive Study – Multiple Sclerosis October 2024

Vidofludimus Calcium in Multiple Sclerosis (MS)

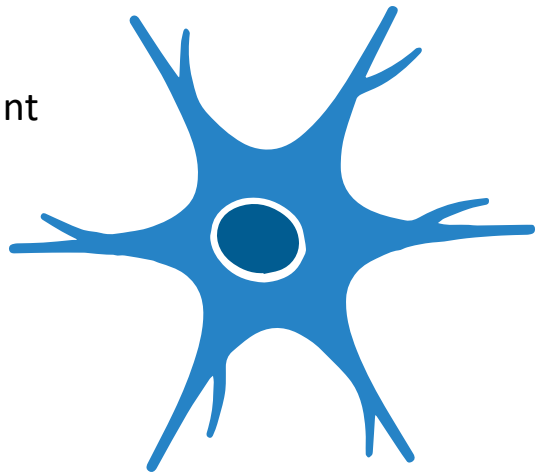
First-in-Class, Potent Nurr1 Activator and Selective DHODH Inhibitor

Vidofludimus Calcium Addresses Smoldering Neurodegeneration

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

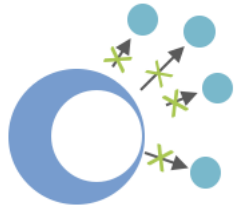
First-in-Class Nurr1 Activator

- 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

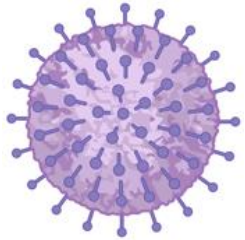


Selective DHODH Inhibitor

- 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

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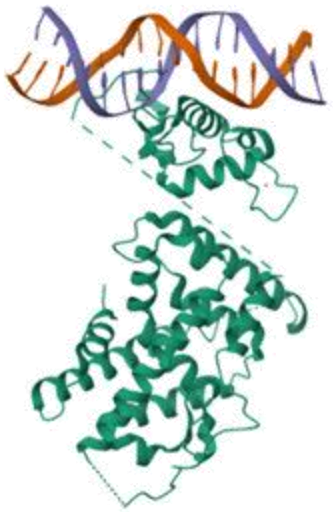
Vidofludimus Calcium Activates Nurr1, Shown to Increase Neuronal Survival

Nurr1 Binding

Nurr1 is a transcription factor binding to DNA[1]

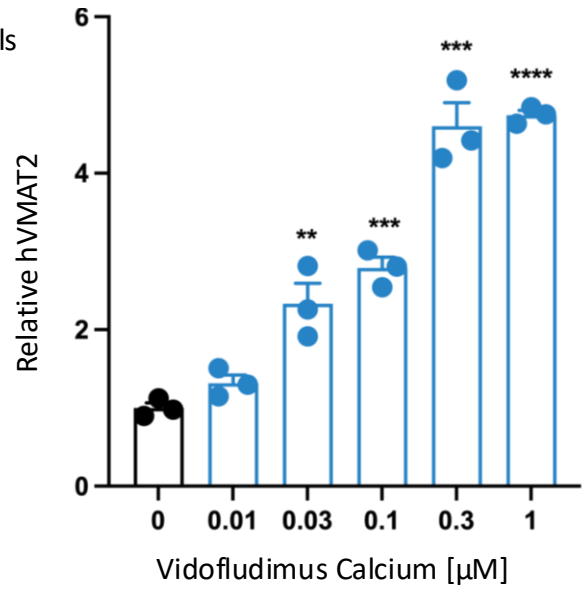
Vidofludimus calcium binds to and strongly activates Nurr1 activity with nM values



Gene Expression Regulation

Vidofludimus calcium induces a > 2-fold induction of target gene expression of VMAT2 at 30 nM concentration[2]

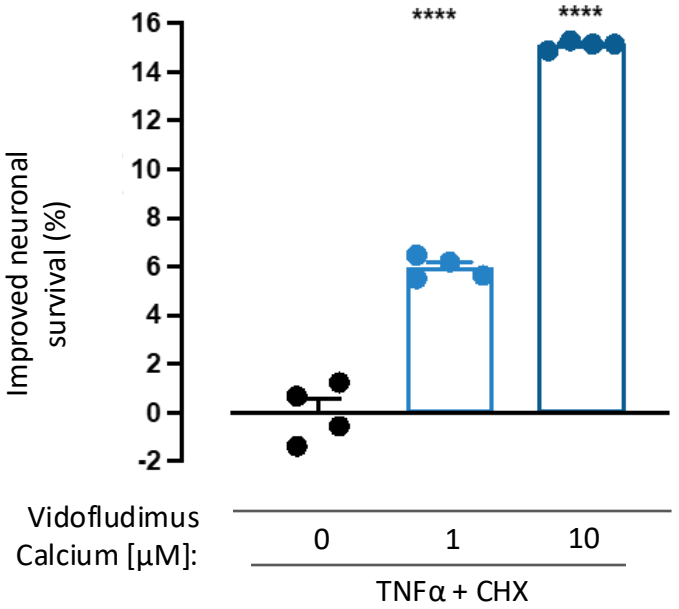
Human microglia cells (HMC3)



Improves Neuronal Survival

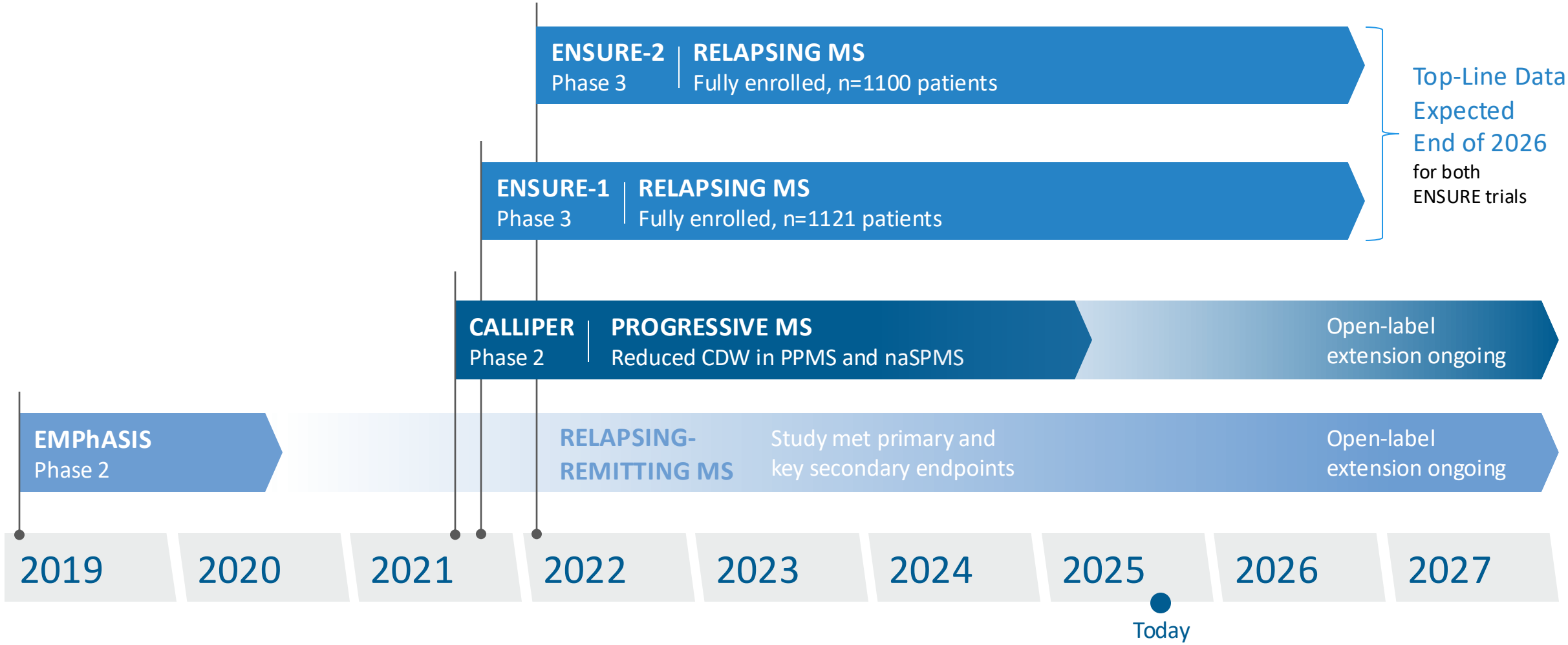
Vidofludimus calcium improves neuronal survival via Nurr1 activation[3]

N2A cells



[1] Vietor et al., Journal of Medicinal Chemistry 2023 66 (9), 6391-6402 The related research project was funded by the German Federal Ministry of Education and Research under the grant number 03INT607AA; Structure: Zhao, M. et.al. (2022) Proc Natl Acad Sci USA 119; [2] Sun, Zuoming. City of Hope. 2023, unpublished [3] Unpublished data: Sun lab, City of Hope, Duarte; 2023 / Nurr1: nuclear receptor-related 1; DNA: deoxyribonucleic acid; VMAT2: vesicular monoamine transporter 2; DMSO: dimethyl sulfoxide; TNF: tumor necrosis factor

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



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

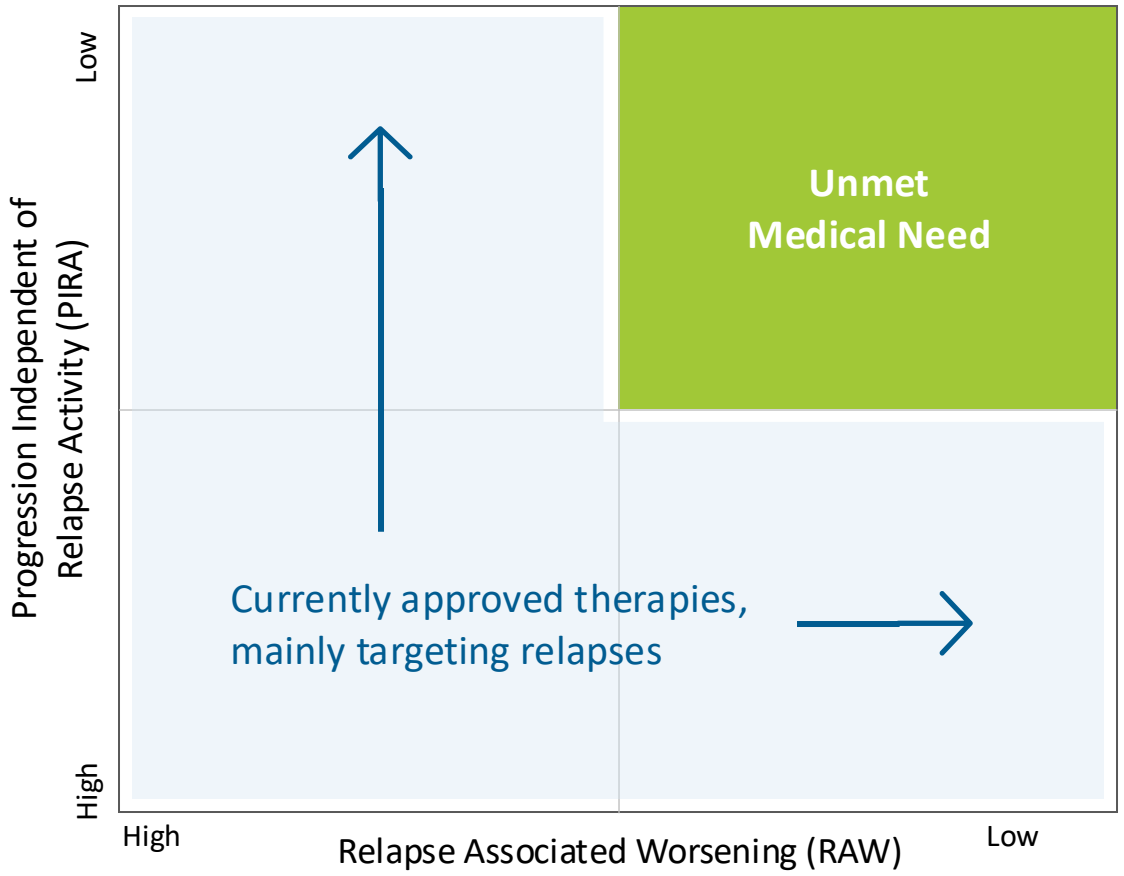
Vidofludimus Calcium in Multiple Sclerosis (MS)

Development in Relapsing Multiple Sclerosis (RMS)

Vidofludimus Calcium Could be the First Treatment Option for Relapsing MS Fulfilling the Current Unmet Needs of Patients

Goals for New Relapsing Multiple Sclerosis Treatments

- Developing a new therapy offering:
  - Neuroprotection and effect on progression independent of relapse activity (PIRA)
  - Excellent safety and tolerability
  - Easy to use, convenient oral administration without complex screening requirements
- Developing a new therapy for newly diagnosed patients and as an excellent switch opportunity



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

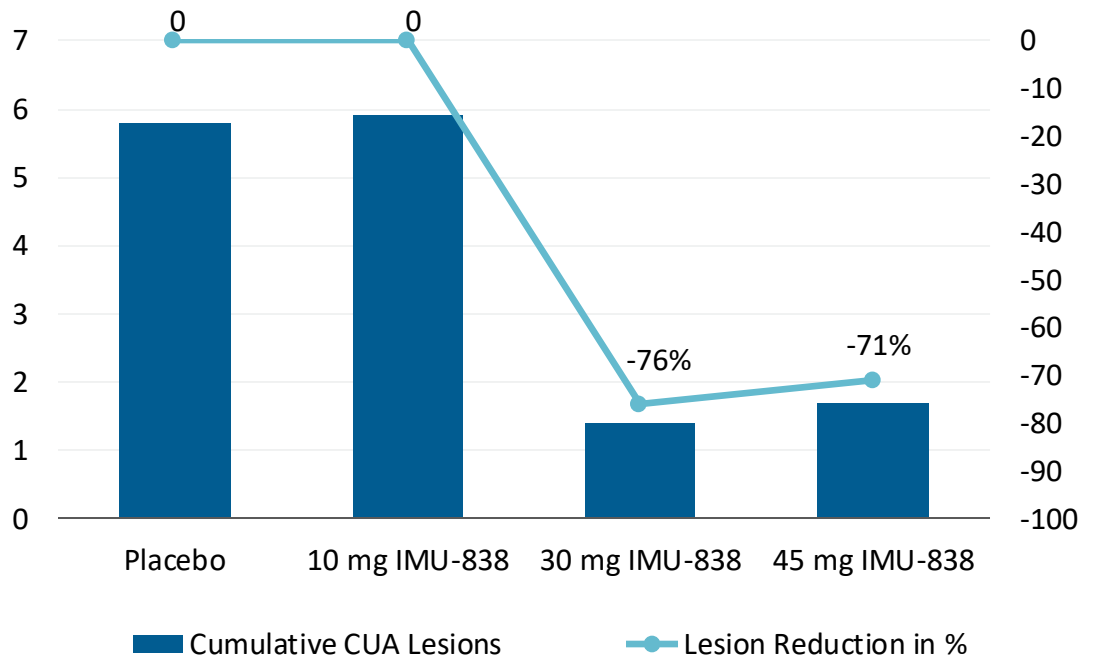
- Randomized 268 patients in 36 centers across four European countries
- Vidofludimus calcium showed strong activity in relapsing-remitting MS population
  - Primary and key secondary endpoints met with high statistical significance: strong reduction of MRI lesion activity
  - Reduced serum NfL concentrations
  - 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

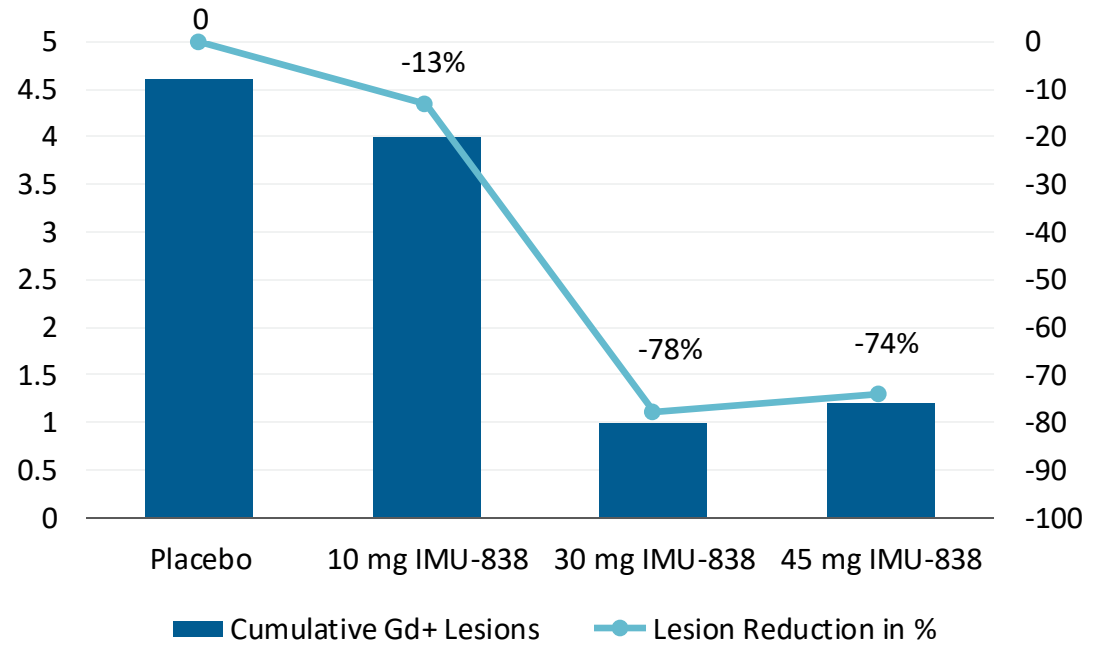
EMPhASIS: Strong Reduction of MRI Lesion Activity

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

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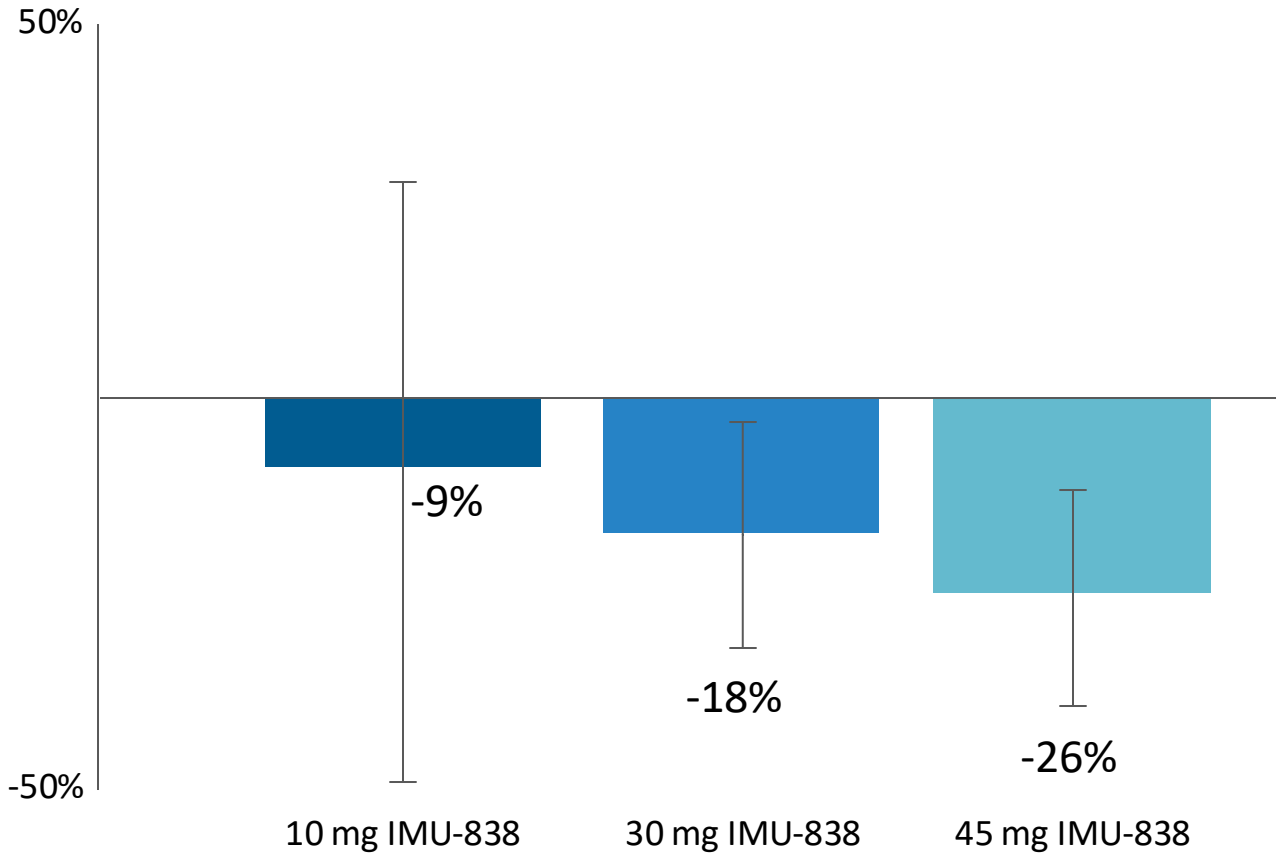
EMPhASIS: Reduction of Serum NfL Concentrations Observed

Versus Placebo After 24 Weeks, Pooled Cohorts 1 & 2



Vidofludimus calcium showed remarkable reduction in NfL levels in all active doses tested compared with placebo

- Clear dose-response relationship in NfL reduction
- Higher doses expected to show stronger neuroprotective effects

Displayed are median values of differences between percentage change of serum neurofilament light chain concentration (Hodges-Lehmann estimation), treatment vs. placebo
Data shows 10 mg versus placebo for Cohort 2 and 30/45 mg versus placebo for Cohort 1; NfL: neurofilament light chain

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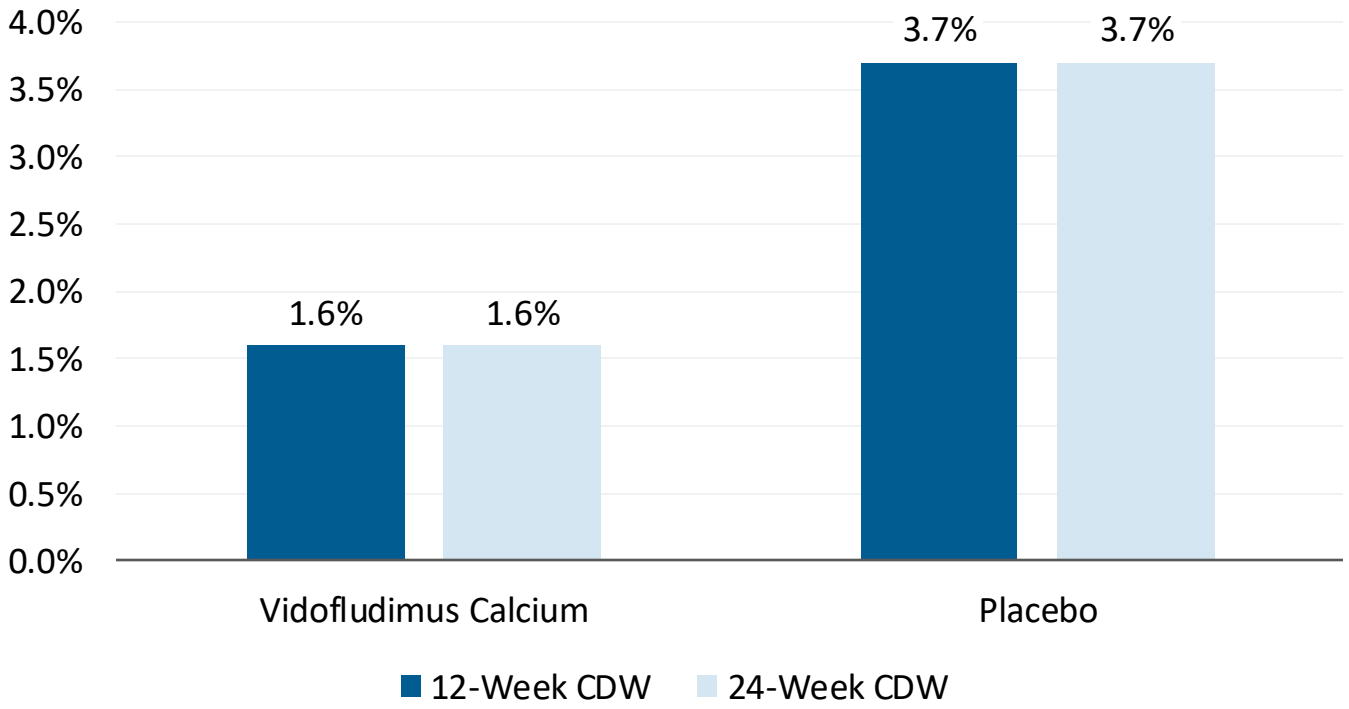
EMPhASIS: Reduced Confirmed Disability Worsening Events

End of 24-Week Blinded Treatment Period

CDW Events at the End of the 24-Week Blinded Treatment Period



CDW: confirmed disability worsening; EDSS: Expanded Disability Status Scale
Only disability worsenings with a trigger point during the 24-wek blinded treatment period are considered. The EDSS increases during the blinded treatment phase were subsequently confirmed during open-label extension phase of the trial. Patients at risk in this analysis are 187 for vidofludimus calcium (pooling 10, 30 and 45 mg data) and 81 for placebo. The trigger event is an EDSS progression defined as an increase in the EDSS compared to Baseline of at least 1.5 points if Baseline EDSS = 0, of at least 1.0 points if Baseline EDSS of 1-5, or of at least 0.5 points if Baseline EDSS ≥ 5.5
12-week CDW: The confirmation event is at least 77 days after the trigger event. At the confirmation event and each assessment between trigger and possible confirmation event, EDSS must be at least as high as at the trigger event.
24-week CDW is are defined analogously, the only difference being the time interval between trigger event and confirmation visit, which is at least 161 days.
Full analysis set pooled cohorts 1&2 (N10 = 47, N30 = 71, N45 = 69, NPBO C1 = 69, NPBO C2 = 12)

- Signal in preventing 12-week and 24-week confirmed disability worsening events as compared to placebo
- Confirmatory data will be obtained in phase 3 ENSURE clinical program

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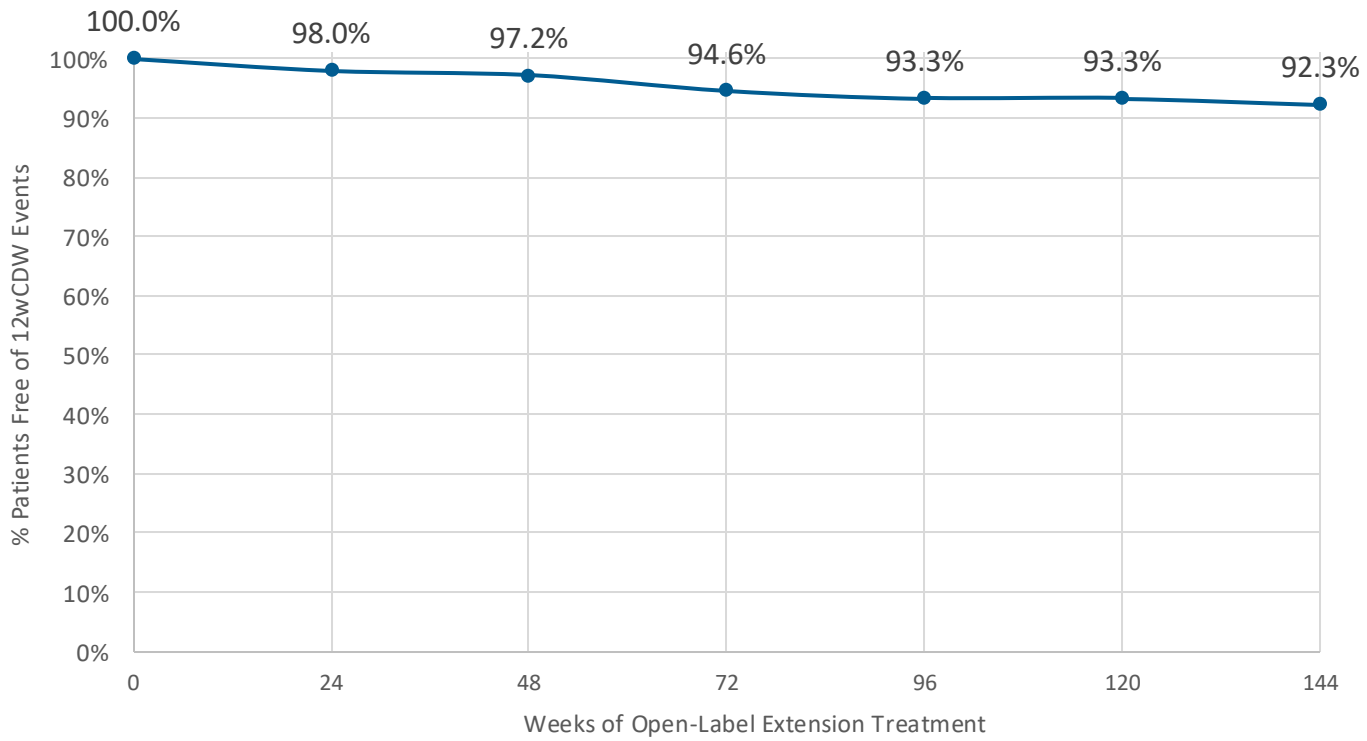
EMPhASIS: Low Rates of Confirmed Disability Worsening Events

Open-Label Extension Period, 196 Patients Reaching 144 Weeks of Treatment

Proportion of patients free of 12-week confirmed disability worsening after up to 144 weeks of open-label extension vidofludimus calcium treatment



- At week 144, 92.3 % of patients remained free of 12-week CDW
- 29 CDW events confirmed at 12 weeks following trigger event through week 144
- Of these, 13 events (44.8%) defined as relapse-associated worsening (RAW), while only 4 (13.8%) as progression independent of relapse activity (PIRA)
- Low discontinuation rate with 196 out of 254 patients reaching 144 weeks of OLE treatment
- More than 180 patients still in the OLE phase of the EMPhASIS trial*
- Vidofludimus calcium continued to demonstrate favorable safety and tolerability profile

CDW: confirmed disability worsening; OLE: open-label extension; * as of January 2025

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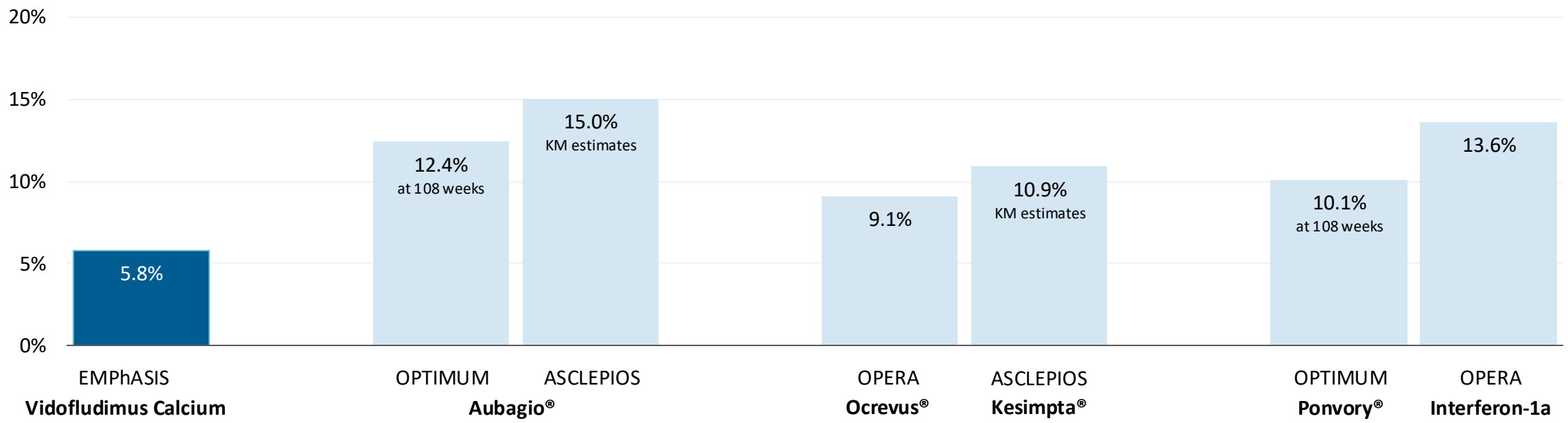
EMPhASIS: 12-Week Confirmed Disease Worsening After 2 Years

Interim Analysis Open-Label Extension Period Compared to Select Historical Trials

RRMS patients with 12-week (3-months) confirmed disability worsening after 2 Years (96 Weeks) (% of patients at risk)



The trigger event is any EDSS progression during the open-label extension (OLE) period defined as an increase in the EDSS compared to start of the OLE period (Baseline) of at least 1.5 points if Baseline EDSS = 0, of at least 1.0 points if Baseline EDSS of 1-5, or of at least 0.5 points if Baseline EDSS ≥ 5.5. Patients with RRMS at risk in this EMPhASIS analysis are 158 at 96 weeks. Data cut-off was Oct 16, 2022. This includes all patients randomized to either placebo or any dose of vidofludimus calcium during the 24-week blinded treatment period and then continued with open-label treatment with either 30 mg or 45 mg vidofludimus calcium. Survival rates and times estimated by the Kaplan-Meier method. 95% CI for rates based on Greenwood's formula.; 12-week CDW: The confirmation event is at least 77 days after the trigger event. At the confirmation event and each assessment between trigger and possible confirmation event, EDSS must be at least as high as at the trigger event.; 24-week CDW is are defined analogously, the only difference being the time interval between trigger event and confirmation visit, which is at least 161 days.; KM: graphical estimates from published Kaplan-Meier curves; EDSS: Expanded Disability Status Scale; RRMS: relapsing-remitting multiple sclerosis. All trials performed in RRMS. Vidofludimus Calcium: Immunic data; OPTIMUM: Kappos et al. 2021; ASCLEPIOS: Hauser et al. 2020; OPERA: Hauser et al. 2017

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Vidofludimus Calcium: Unrivaled Safety and Tolerability Profile Observed in Multiple Clinical Trials

- Safety profile similar to placebo: no general safety signals observed in clinical trials so far
- No increased rates of diarrhea, neutropenia, or alopecia
- No increased rates of infections and infestations or hematology values
- Drug exposure tested in approximately 2,700 human subjects and patients, to date, with data available up to 5.5 years
- Low rates of adverse events
- No signals for hepatotoxicity or elevations of liver enzymes and no Hy's law cases observed to date

Vidofludimus Calcium's Safety Profile to Date is Unique

	PML risk	Increased number of infections	Vaccination limitations	Gastrointestinal toxicities, incl. diarrhea	Cardiovascular risks, incl. blood pressure	Lymphopenia	Neutropenia	Risk of liver injury	Increased risk of cancer	Macular edema
Vidofludimus Calcium	●	●	●	●	●	●	●	●	●	●

● Favorable profile

PML: progressive multifocal leukoencephalopathy

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EMPhASIS: Vidofludimus Calcium Well-Tolerated With Adverse Events Similar to Placebo

Safety & 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 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%
Series adverse events	**1%**	**3%**	**0%**
Treatment discontinuation for any reason	**7%**	**3%**	**6%**
Treatment-emergent adverse events leading to treatment discontinuation	**4%**	**0%**	**3%**

The observed adverse events were generally mild in nature.

There were very few adverse events with medium and high incidence rate.

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EMPhASIS: Patients Feel Well-Treated With Vidofludimus Calcium

Reflected in **Low Discontinuation Rates** for Vidofludimus Calcium-Treated RRMS Patients, Considerably Lower Than Placebo*

	Vidofludimus Calcium	Glatiramer Acetate [1]	Aubagio® [2]	Tecfidera® [3]	Gilenya® [4]	Zeposia® [5]
Administration	Oral	Injectable	Oral	Oral	Oral	Oral
Daily Dose	30 mg QD	20 mg QD	14 mg QD	240 mg TID	1.25 mg QD	1 mg QD
Treatment Period	24 weeks	9 months	36 weeks	24 weeks	6 months	24 weeks
Active Treatment	**2.8%**	**5.9%**	**19.3%**	**15.6%**	**5.4%**	**2.3%**
Placebo	**7.2%**	**5.8%**	**6.6%**	**9.2%**	**6.5%**	**3.4%**

*The table summarizes the data on treatment/study discontinuation rates of the commercial dose in phase 2 trials of RRMS drugs. If the commercial dose was not included in the phase 2 trials, the dose closest to the commercial dose was shown. This high-level comparison is provided for illustrative purposes only, is based on publicly available data and does not purport to be a comprehensive comparison or depiction of the other trials. Larger data sets than presented in this presentation are publicly available for certain of the compounds included on this slide. Please note that these results are taken from placebo-controlled trials, and these medications have not been tested in head-to-head assessments.

[1] Comi et al. Ann Neurol. 2001;49(3):290-297 [2] O'Connor et al. Neurology. 2006;66(6):894-900 [3] Kappos et al. Lancet. 2008;372(9648):1463-1472 [4] Kappos et al. N Engl J Med. 2006;355(11):1124-1140 [5] Cohen JA, Arnold DL, Comi G, et al. Lancet Neurol. 2016;15(4):373-381; QD: quaque die = once-daily; TID: ter in die = three times daily; RRMS: relapsing-remitting multiple sclerosis

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

Coordinating Investigator

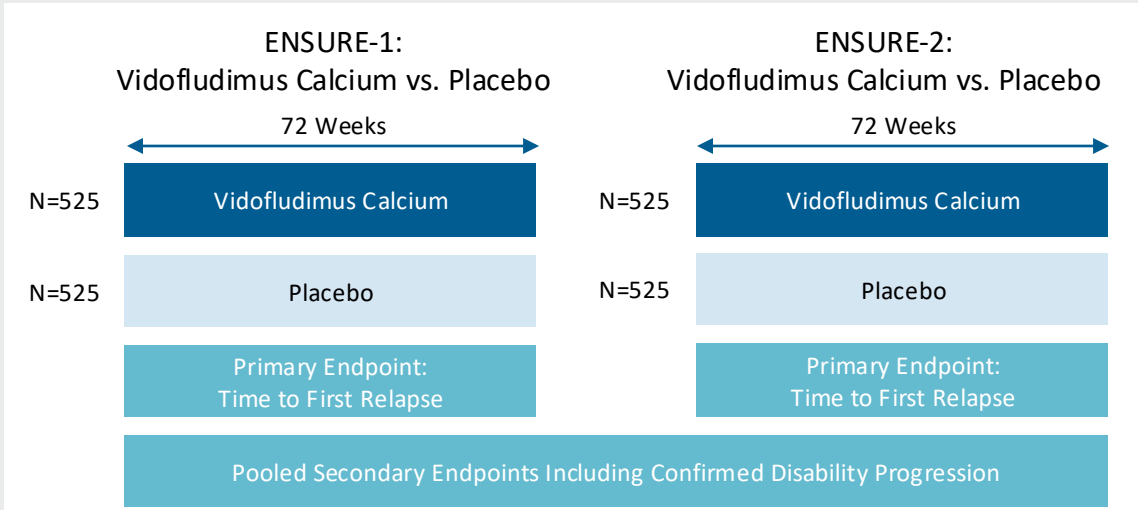
Robert J. Fox, M.D.
Cleveland Clinic

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

Two Multicenter, Randomized, Double-Blind Phase 3 Trials

- More than 100 sites in 15 countries in each trial, including the United States, India, Middle East and North Africa, Latin America, Central and Eastern Europe
- Randomization to 30 mg vidofludimus calcium or placebo QD
- Positive interim analysis: Unblinded IDMC recommended continuing trial without changes, including no need for a potential upsizing
- Enrollment completed: 1,121 patients in ENSURE-1; 1,100 patients in ENSURE-2
- Top-line data for both ENSURE trials expected by end of 2026



[1] Lublin FD, et al. Neurology. 2014;83(3):278-286
MS: multiple sclerosis; EDSS: Expanded Disability Status Scale; QD: quaque die = once-daily
IDMC: Independent Data Monitoring Committee; N: number of patients

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Vidofludimus Calcium in Multiple Sclerosis (MS)

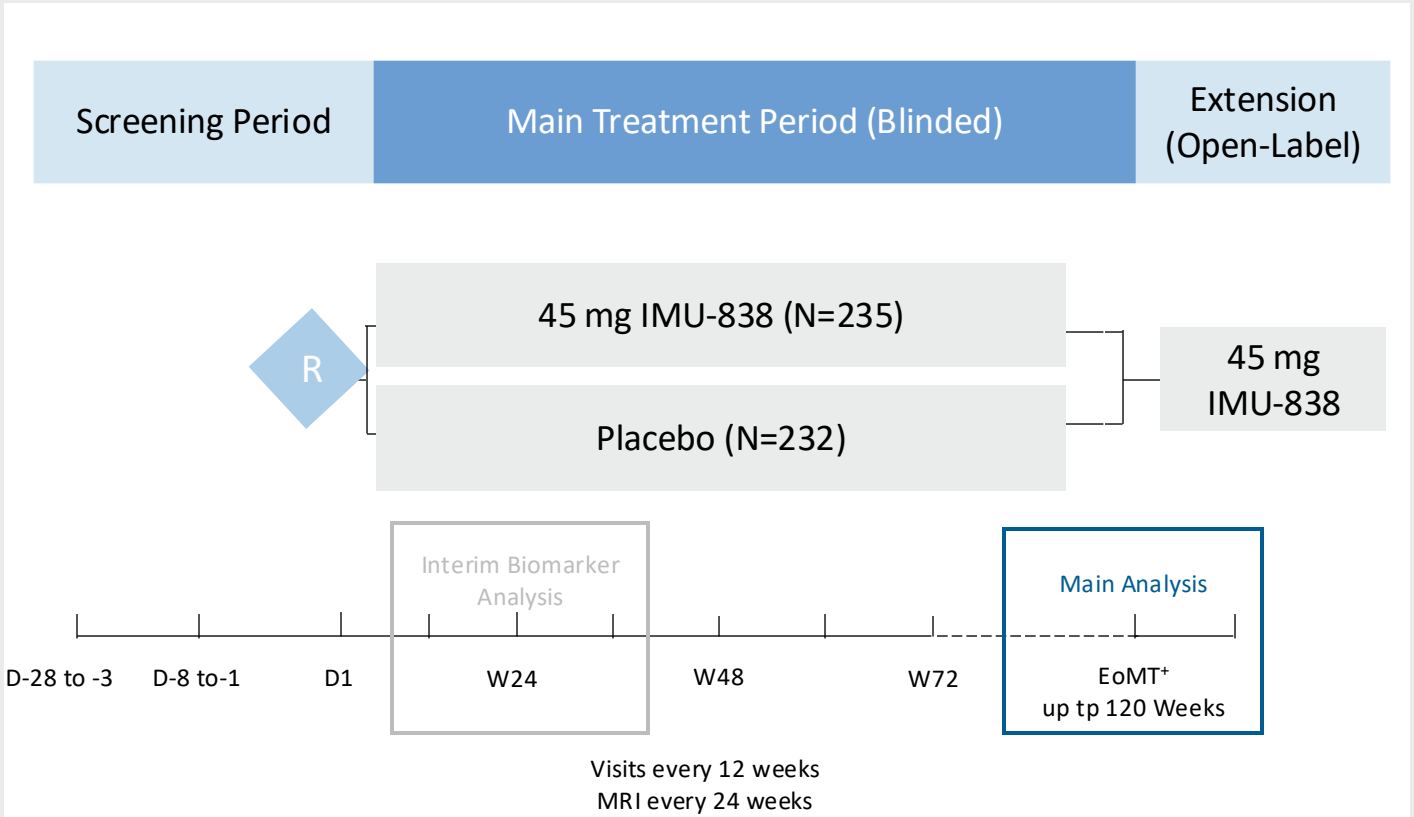
Development in Progressive Multiple Sclerosis (PMS)

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

- PPMS, which affects **10-15% of people diagnosed with MS**, is characterized by a steady worsening of neurological function from the beginning of the disease, without distinct relapses or periods of remission
- Compared with RMS, PPMS is clinically associated with **greater symptom severity** and **functional impairment, higher rates of unemployment** and **hospitalization, greater economic burden,** and a more **substantial impact on health-related quality of life**
- **~120,000 patients diagnosed** (US & EU5), of which only ~54,000 (45%) are currently treated by disease-modifying therapies
- **Underdiagnosed and undertreated**, due to lack of safe, effective and convenient treatments (only one approved therapy)

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

CALLIPER: Phase 2 Clinical Trial in Progressive Multiple Sclerosis
NCT05054140



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

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

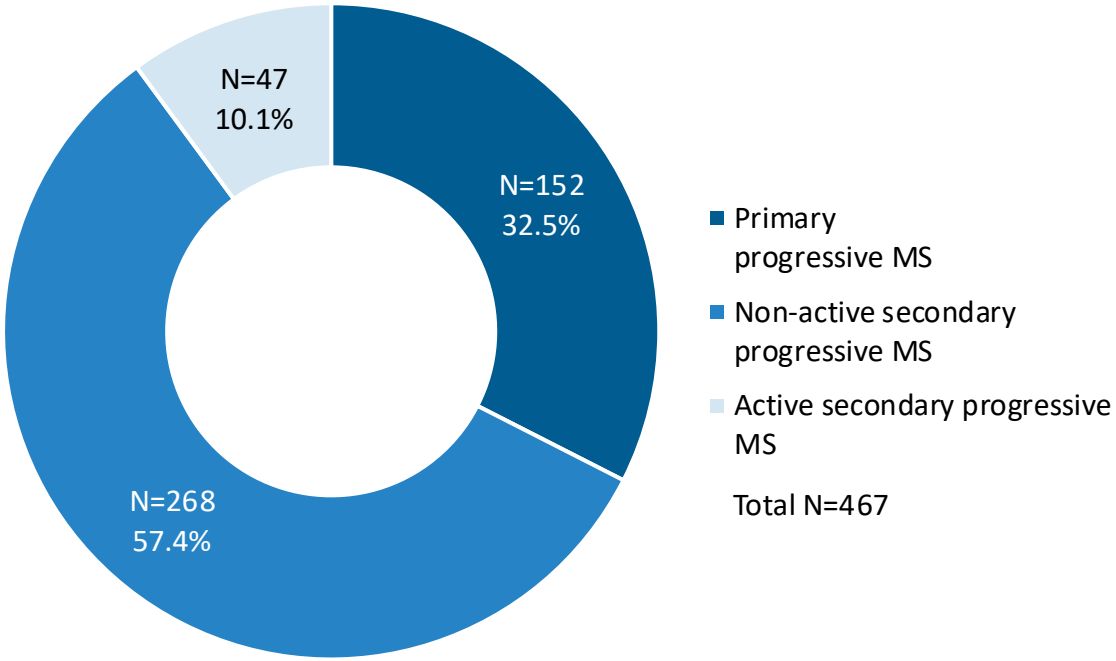
- 467 adult patients, aged 18 to 65 years, enrolled at more than 70 sites in North America, Western, Central and Eastern Europe
  - PPMS or SPMS diagnosis (revised McDonald criteria 2017)
  - EDSS score at screening between 3.0 to 6.5
  - No relapse in last 24 months before randomization
  - Evidence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

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

CALLIPER: Patient Demographics and Baseline Characteristics

Total Study Population of 467 Enrolled Patients

Progressive Disease Subtypes



Baseline Characteristics

Baseline Patient Characteristics	Total (N=467)
Age [years], median (min-max)	51.0 (21-65)
Gender (n and % female)	302 (64.7%)
Race (n and % White)	460 (98.7%)
BMI [kg/m^2], median (min-max)	24.85 [14.0 - 46.6]
SDMT [points], median (min-max)	40 [8-80]
EDSS at Visit 1, median (min-max)	5.5 [2.5-6.5]
MS relapses during last 24 months, median (min-max)	0.0 [0-1]
Gd+ lesions at baseline MRI (%)	16.3%
Treatment duration, median	589 days

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

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

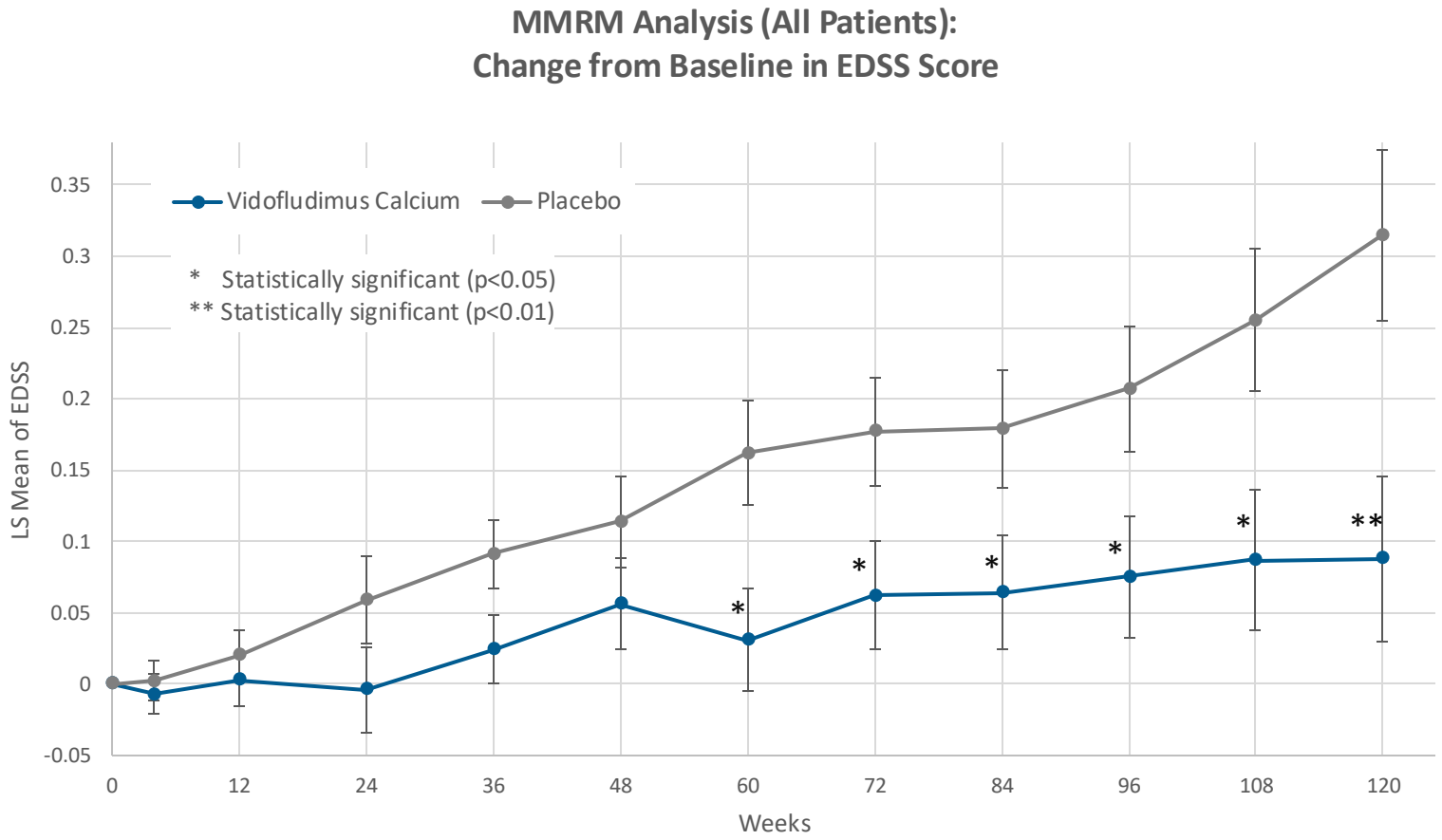
Clinically meaningful risk reduction of confirmed disability worsening of 24% in overall PMS population and even more prominent 31% reduction in PPMS population

CALLIPER: Vidofludimus Calcium Reduced **Time to 24wCDW** in Overall Study Population and All Subtypes Compared to Placebo

	Overall CALLIPER Patient Population (N=467)	**PPMS** (N=152)	**naSPMS** (N=268)	**aSPMS** (N=47)
HR (Kaplan Meier)	0.762	0.687	0.808	0.644
95 % CI	[0.479; 1.210]	[0.330; 1.430]	[0.418, 1.564]	[0.143, 2.892]
p-value	0.249	0.315	0.527	0.566
Risk Reduction of tt24wCDW	**23.8%**	**31.3%**	**19.2%**	**33.6%**

24wCDW: 24-week confirmed disability worsening; tt: time to; PPMS: primary progressive multiple sclerosis; naSPMS: non-active secondary progressive multiple sclerosis; aSPMS: active secondary progressive multiple sclerosis; HR: hazard ratio; CI: confidence interval / Intent-to-treat population (ITT); patients analyzed as randomized; disease subtype as per diagnosis at screening; presented is 24wCDW with applied imputation for participants who discontinued the double-blind main treatment period due to disease progression and who already achieved 12-week CDW confirmation; 24wCDW is defined as patients with worsening in EDSS sustained over at least 22 weeks (154 days)

CALLIPER: Vidofludimus Calcium Significantly Reduced EDSS Increase from Baseline Compared to Placebo



- Patients treated with vidofludimus calcium showed only minimal worsening of EDSS LS mean from baseline
- Placebo treated cohort showed steady increase in LS mean of EDSS
- Difference significant starting at week 60

EDSS: expanded disability status scale; MMRM: mixed models for repeated measure; LS: least square

MMRMs analysis: For the calculation of LS means based on the MMRM, patients with baseline and at least one-post baseline visit are considered. Missing values are calculated based on the analysis set. Estimates are adjusted for stratification factors used at baseline randomization (disease type and baseline EDSS value). 2-sided p-value is presented. Error bars show the standard error of the LS Mean. Data are based on group level analysis for overall CALLIPER population, total N= 467, vidofludimus calcium N=235, placebo N=232

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Comparison CALLIPER Versus ORATORIO Trials in PPMS Population

	ORATORIO* (N=732)	CALLIPER (N=152)
Mean Age (Years)	44.6	47.4
Female (N,%)	361 (49.3%)	93 (61.1%)
EDSS - Mean	4.7	4.9
EDSS - Median	4.5	4.5
Gd+ Lesions at Baseline MRI (N,%)	26.6%	17.8%
Relative Risk Reduction of Time to 24wCDW Active Over Placebo	**25%**	**31%**

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

PPMS: primary progressive multiple sclerosis; EDSS: Expanded Disability Status Scale; Gd+: gadolinium-enhancing lesions found on T1-weighted MRI images; MRI: magnetic resonance imaging; tt24wCDW: time to 24-week confirmed disability worsening; N: number of patients evaluated

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Hazard Ratio Analysis 3-Months Confirmed Disability Worsening Phase 3 Ocrelizumab ORATORIO Study

Reduction of 12-week confirmed disability events seems to be largely driven by patients with active disease (MRI lesions) and young age (labeled as “early PPMS with signs of active disease”)

	Hazard Ratio 12-Week CDW
Patient age ≤ 45 years and Gd+ lesions at baseline	0.52
Overall study outcome (all patients)	0.76
Patients without Gd+ lesions during study	**0.84**
Patient age >45 years	0.91
Patient age >45 years and without Gd+ lesions during study	0.93

EMA Medical Reviewer Comment:

During the scientific assessment the Applicant modified the indication to 'early PPMS', and better reflect the results of the performed trial. Younger age was correlated with more MRI activity. It seems that younger patients with T1 Gd-enhancing lesions at baseline have a better treatment effect. This supports an indication in early PPMS early with imaging features characteristic of inflammatory disease.

EMA Clinical Review

PPMS: primary progressive multiple sclerosis; MRI: magnetic resonance imaging; CDW: confirmed disability worsening; Gd+: gadolinium-enhancing

CALLIPER: Vidofludimus Calcium Substantially Reduced 24wCDW in Patients Without Gd+ Lesions at Baseline

Time to 24wCDW With No Evidence of Gd+ Lesions at Baseline

Group	Number of Patients	HR	95 % CI	p-value	RRR tt24wCDW
All Patients	391	0.663	[0.394, 1.115]	0.121	**33.7%**
PPMS	125	0.656	[0.294; 1.464]	0.303	**34.4%**
naSPMS	250	0.702	[0.346, 1.422]	0.326	**29.8%**

- Precisely the patients who were largely shown to **not benefit from current anti-inflammatory therapies**
- These **clinical effects underlines neuroprotective effect** of Nurr1 activation by vidofludimus calcium

24wCDW: 24-week confirmed disability worsening based on the EDSS (expanded disability status scale) score; tt: time to; Gd+: gadolinium-enhancing; HR: hazard ratio; CI: confidence interval; RRR: relative risk reduction; disease subtype as per diagnosis at screening visit 1
24wCDW is defined as patients with worsening in EDSS sustained for at least 22 weeks (154 days) given the visit window +-7 days. Confirmed disability progression event status was imputed for participants who completed the trial, met the criteria for confirmed disability progression sustained for at least 12 weeks, and continued to meet the criteria for disability progression according to the EDSS score through the final trial assessment but did not reach the 24-week confirmation visit. Total of 73 events for 24wCDW based on EDSS, 70 events observed and 3 events imputed after 12-week confirmation before end of study (performed as sensitivity analysis).

CALLIPER: Vidofludimus Calcium Demonstrated Statistically Significant 24-Week Confirmed Disability Improvement

24wCDI Events	Vidofludimus Calcium	Placebo	Hazard Ratio [95% CI] p-value
CALLIPER Overall Population	19/235 (8.1%)	8/232 (3.4%)	**2.441** [1.068; 5.581] **0.034***
PPMS	8/77 (10.4%)	3/75 (4.0%)	**2.823** [0.747;10.672] 0.126
naSPMS	9/135 (6.7%)	5/133 (3.8%)	**1.813** [0.607; 5.414] 0.286

- Patients treated with vidofludimus calcium showed approximately 2-fold increase in 24wCDI event numbers over placebo
- Consistent effects across subtypes, with clearest signal in PPMS subtype

MS: multiple sclerosis; PPMS: primary progressive MS, naSPMS: non-active secondary progressive MS; aSPMS: active secondary progressive MS; nrSPMS: non-relapsing secondary progressive MS; 24wCDI: 24-week confirmed disability improvement; 6mCDI: 6-months confirmed disability improvement; EDSS: Expanded Disability Status Scale / Disability improvement in the CALLIPER study is defined as an increase of the EDSS score compared to BL of at least 1.0 point for patients with a BL EDSS score ≤5.5 or an increase of ≥0.5 point if EDSS at entry is >5.5. The event is counted as 24wCDI if the improvement is sustained over at least 24 week.

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

Number of Patients With Any TEAE and SAE

N (%) of Patients	Vidofludimus Calcium N=235	Placebo N=232
Any TEAE, n(%)	163 (69.4%)	159 (68.5%)
Any SAE, n(%)	19 (8.1%)	15 (6.5%)

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

Five Most Common TEAE Events

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

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

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

TEAE: treatment-emergent adverse event; SAE: serious adverse event; N: number of patients; n: number of events
Safety Population contains any patient who received at least one dose of study drug, vidofludimus calcium (N=235), placebo (N=232), total (N=467). All other SAE not listed had only single occurrences in the CALLIPER trial.

CALLIPER: Liver Enzyme Elevations

No Evidence of Increased Rates of Liver Enzyme Elevations

Elevations of Alanine Aminotransferase (ALT)

	Vidofludimus Calcium (n=235)	Placebo (n=232)
ALT>3xULN	7 (3.0%)	6 (2.6%)
ALT>5xULN	2 (0.9%)	4 (1.7%)
ALT>10xULN	1 (0.4%)	4 (1.7%)
ALT>20xULN	1 (0.4%)	1 (0.4%)
Hy's Law Cases	0	0

Elevations of Aspartate Aminotransferase (AST)

	Vidofludimus Calcium (n=235)	Placebo (n=232)
AST>3xULN	5 (2.2%)	5 (2.2%)
AST>5xULN	1 (0.4%)	5 (2.2%)
AST>10xULN	1 (0.4%)	1 (0.4%)
AST>20xULN	1 (0.4%)	1 (0.4%)
Hy's Law Cases	0	0

ULN: upper limit of normal reference range

Tables depict number of patients with any increase fulfilling the criteria at any point during the double-blind treatment (main treatment period). Hy's Lase cases are defined as liver enzyme elevation of greater than 3xULN with concurrent elevation of serum total bilirubin greater than 2xULN.

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

- Clinically meaningful risk reduction of 24wCDW by 24% in overall study population; even more prominent 31% reduction in high unmet need population of PPMS
- Remarkable 34% reduction of 24wCDW in patients without baseline inflammatory lesions in overall study population
- Confirmed favorable safety and tolerability observed in previous clinical trials; no new safety signals identified
- As of April 2025, more than 375 patients continue to be treated in open-label extension phase of CALLIPER trial
- Underlines Nurr1 activation as new mode of action for preventing neurodegeneration in MS and substantiates impact on disability accumulation by both PIRA and RAW
- Further de-risks ongoing phase 3 ENSURE program with potential to offer relapsing MS patients an oral, safe and neuroprotective treatment early in the disease

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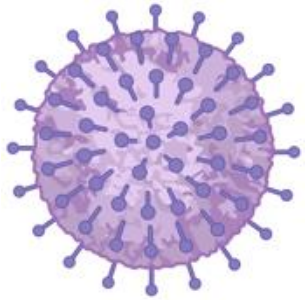
Vidofludimus Calcium: DHODH Inhibition Provides Broad-Spectrum Antiviral Activity Against Different Pathogenic Viruses

Inhibits Epstein-Barr Virus (EBV) Replication and Reactivation

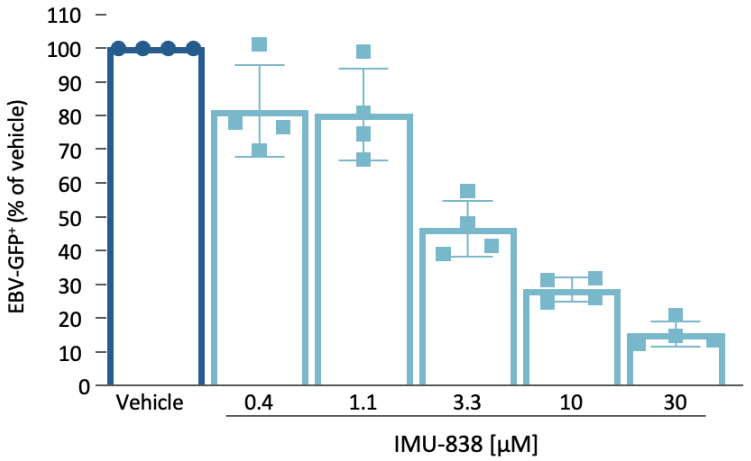
By targeting the host cell metabolism, vidofludimus calcium has shown to be active against different RNA and DNA viruses *in vitro*

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



Showed Dose-Dependent Inhibition of EBV Reactivation

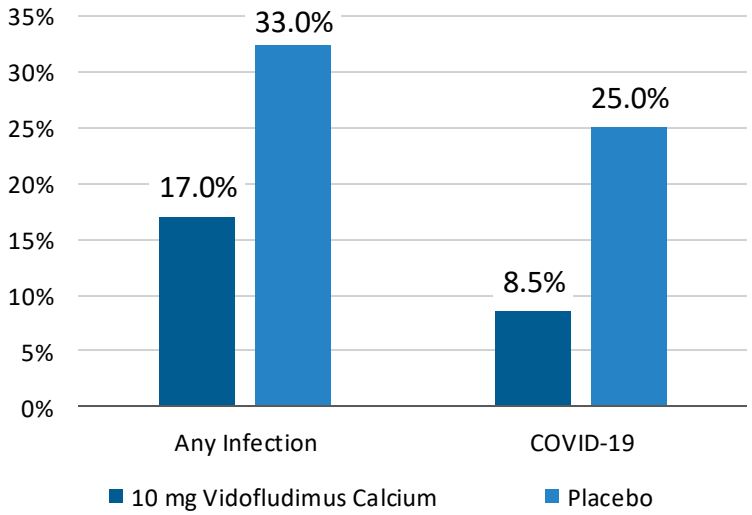
Anti-Akata-BX1-EBV-GFP stimulated with hIgG



Decreased Number of Opportunistic SARS-CoV-2 Infections

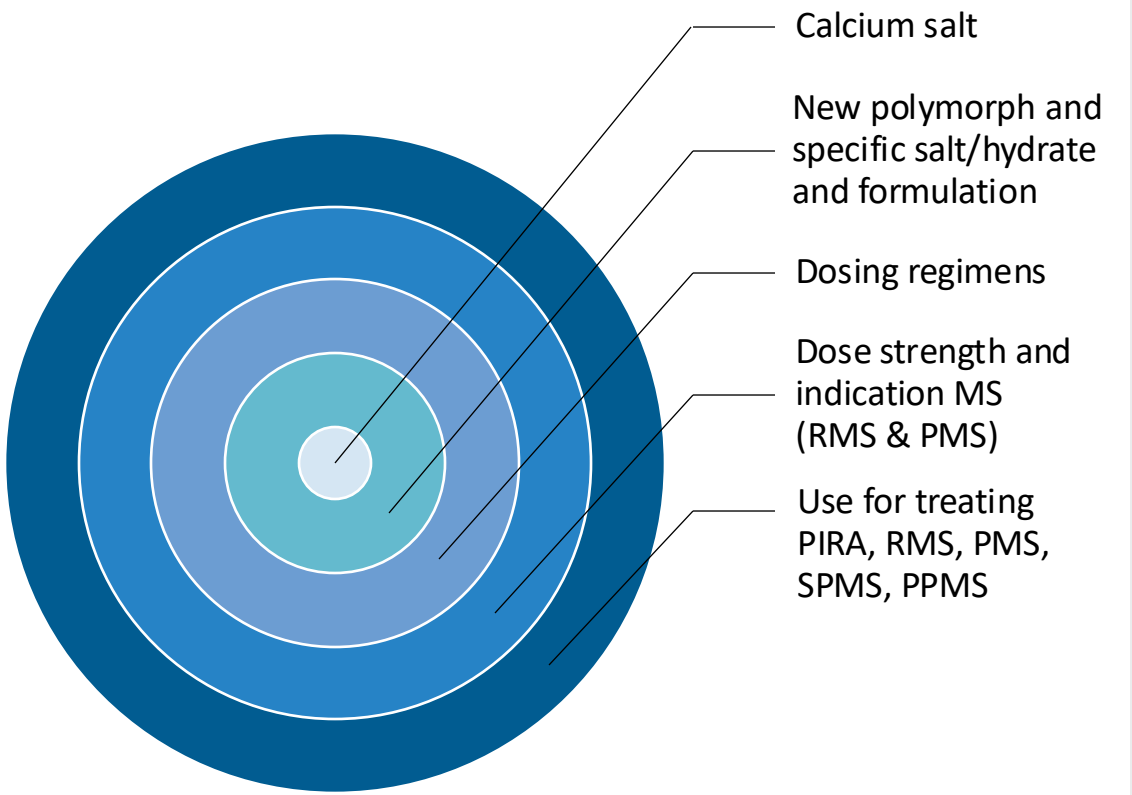
Vidofludimus calcium showed interesting hints for clinical anti-SARS-CoV-2 activity in the phase 2 EMPhASIS trial in RRMS

- 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

Several Layers of Patents Protecting Vidofludimus Calcium



Eight Independent Patent Families Protecting Vidofludimus Calcium

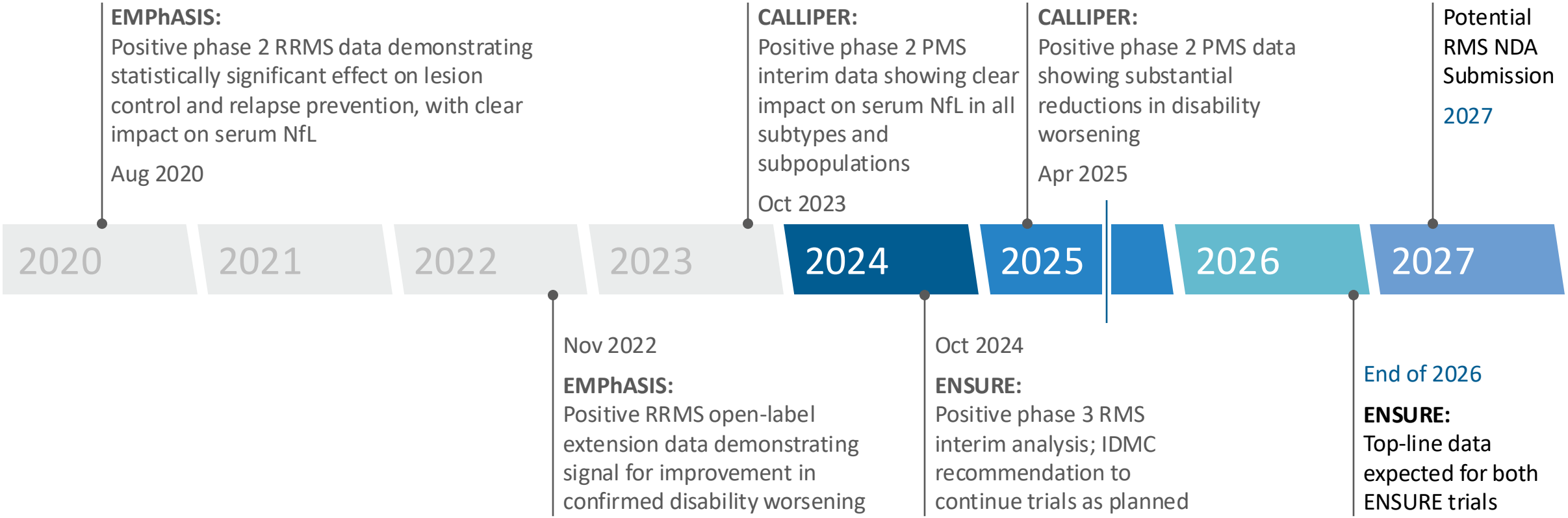
- IP for superior calcium salt and specific polymorph of the drug product
  - Additional patent directed to specific polymorph matching the only polymorph in the drug product granted in the US and other jurisdictions
- Broad IP for all salts directed to dosing regimens, covers all label-relevant dosing schemes, granted in the US and Japan
- Dose strengths subject of another granted patent in the US
- Use of vidofludimus for treating PIRA as well as other neurodegenerative diseases, also including biomarker-based subgroups, filed in 2023
- Another level of protection expected by data exclusivity based on vidofludimus calcium's classification as New Chemical Entity (NCE)

Patent portfolio expected to provide exclusivity into 2041 in the US, unless extended further

IP: intellectual property; MS: multiple sclerosis; RMS: relapsing MS; PMS: progressive MS; SPMS: secondary progressive MS; PPMS: primary progressive MS; PIRA: progression independent of relapse activity

Vidofludimus Calcium in Multiple Sclerosis

Consistent and Differentiated Results to Date Support Straightforward Path Towards Potential Regulatory Approvals



Although we currently believe that each of these goals is achievable, they are each dependent on numerous factors, most of which are not under our direct control and can be difficult to predict. We plan to periodically review this assessment and provide updates of material changes as appropriate. / MS: multiple sclerosis; RRMS: relapsing-remitting MS; RMS: relapsing MS; PMS: progressive MS; NfL: neurofilament light chain

Immunic THERAPEUTICS

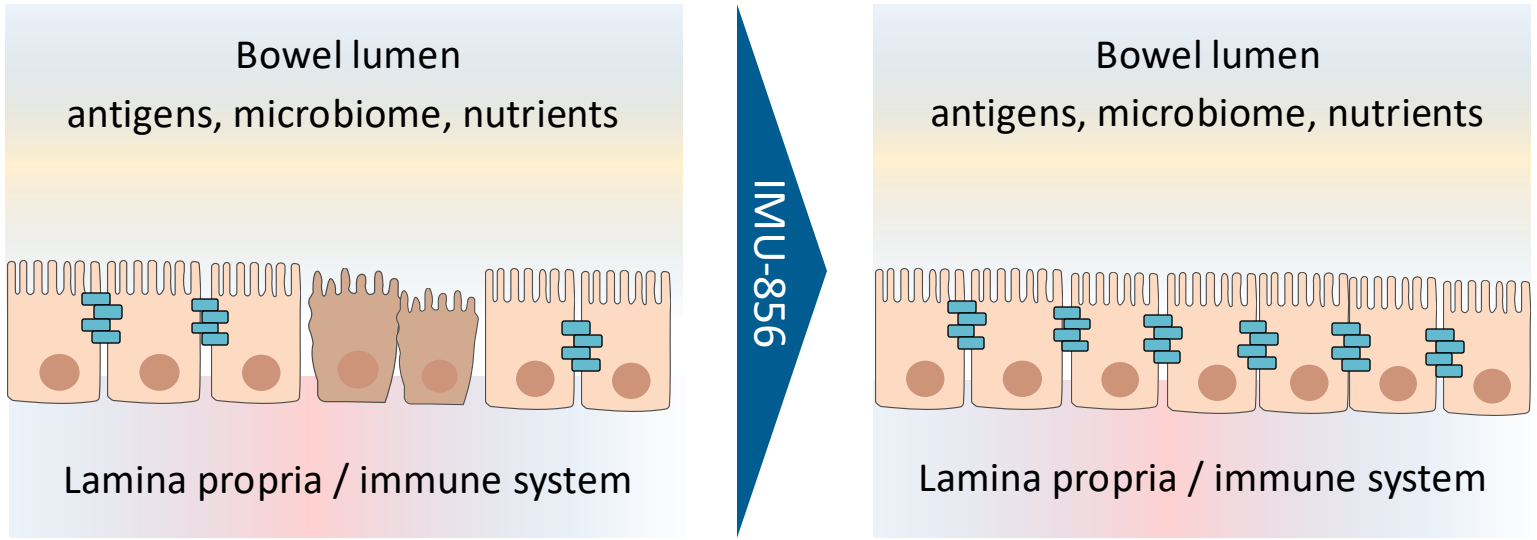
IMU-856

Restoring a Healthy Gut through Renewal of the Bowel Wall

IMU-856 Targets Physiological Intestinal Epithelial Regeneration and Restoration of Gut Cell Function

- Innovative oral therapeutic approach potentially applicable to a broad range of gastrointestinal disorders
- Targets physiological intestinal epithelial regeneration, including gut hormon-producing cells
- Designed to strengthen gut wall integrity and function without immunosuppression

Once-Daily, Oral IMU-856 Aims to Regenerate the Gut Wall and Barrier Function by a New Innovative Targeted Mechanism



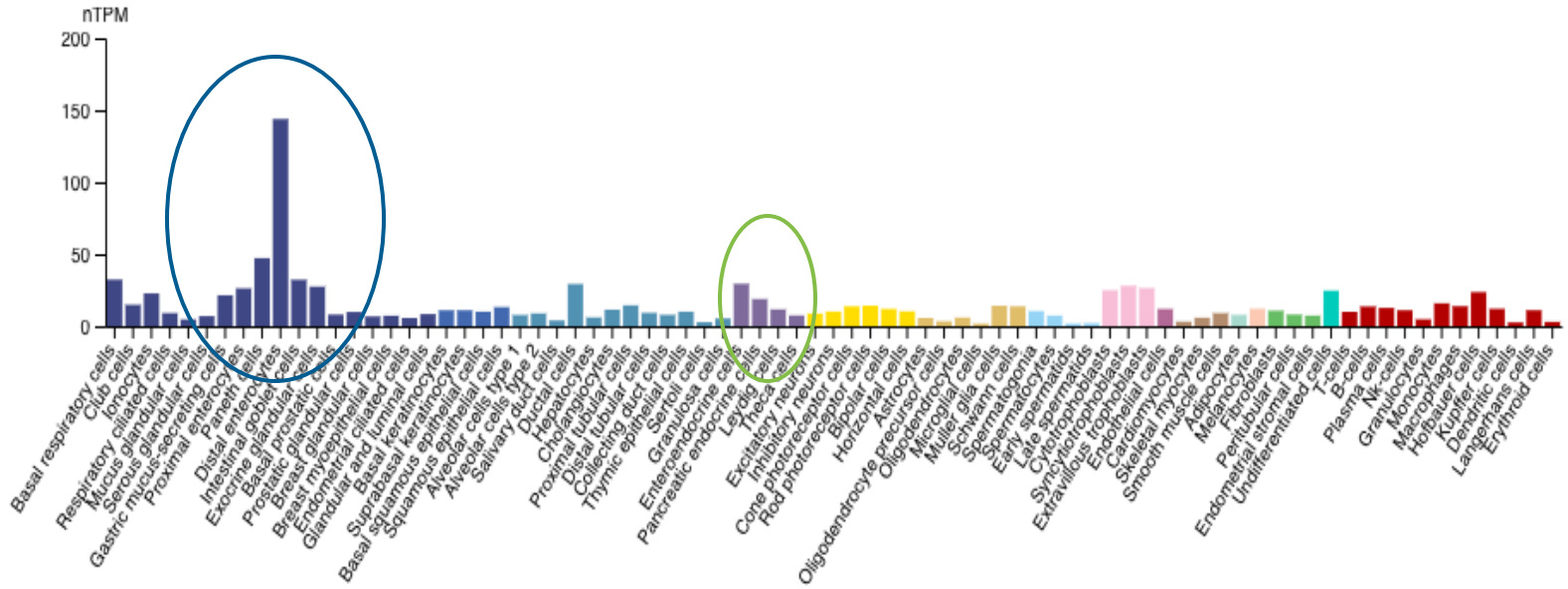
IMU-856:

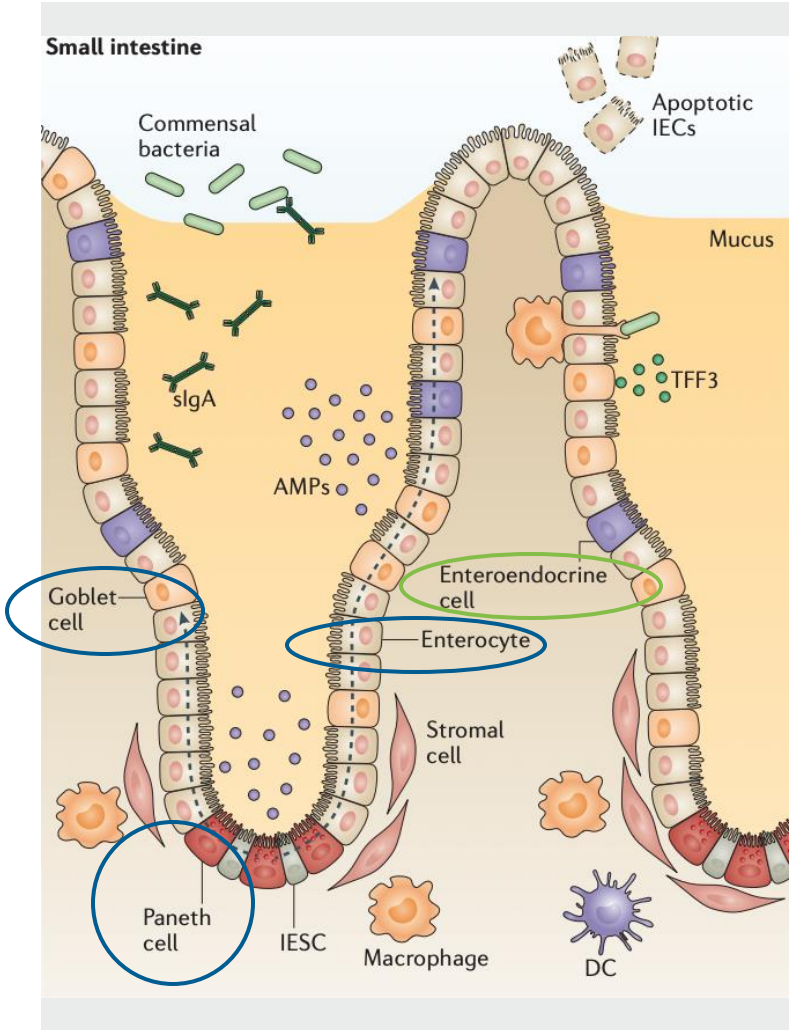
- First-in-class modulator of sirtuin 6 (SIRT6), targets physiological intestinal epithelial regeneration and restoration of barrier function
- Provides protection and enhances transport of nutrients
- This new approach avoids immunosuppression

Immunic THERAPEUTICS

SIRT6 Target Is Highly Expressed in Gut Epithelial Cells

Highest mRNA Expressions in Paneth Cells, Enterocytes, Goblet Cells and Enteroendocrine Cells such as L-Cells





Left: https://www.proteinatlas.org/ / Right: Peterson, L., Artis, D. Nat Rev Immunol 14, 141–153 (2014)
SIRT: sirtuin; mRNA: messenger ribonucleic acid; nTPM: normalized transcript per million

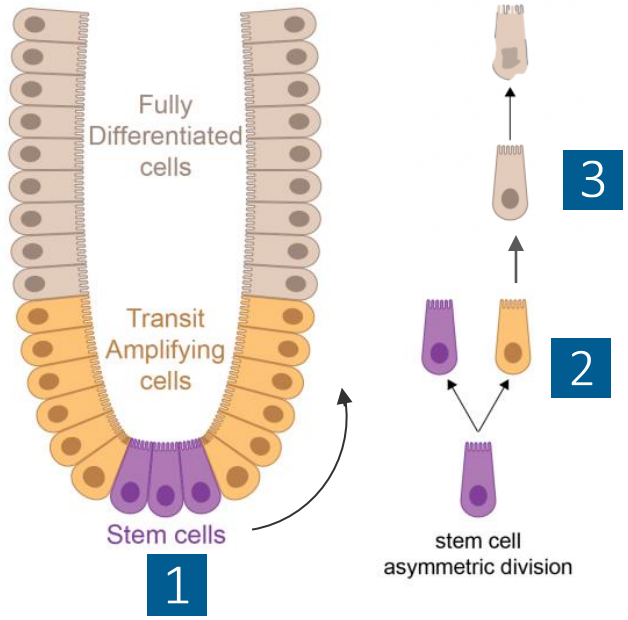
IMU-856 Enhances the Natural Regenerative Process in the Gut

Gut wall renewal is a normal physiological process

1. Regeneration begins in the crypts, where intestinal stem cells are located
2. Stem cells undergo asymmetric division thereby producing fully differentiated epithelial gut cells and renewing intestinal stem cells
3. These new epithelial cells are renewing the lining of crypts and villi to maintain healthy gut and proper intestinal barrier

→ IMU-856 is an epigenetic regulator which enhances this natural tissue renewal phenotype

Asymmetric cell division renews stem cells and regenerates the gut wall



Adapted from Mamis K et al., Proc. R. Soc. B. 290:20231020 (2023)

IMU-856: Additional Pharmacological Effect

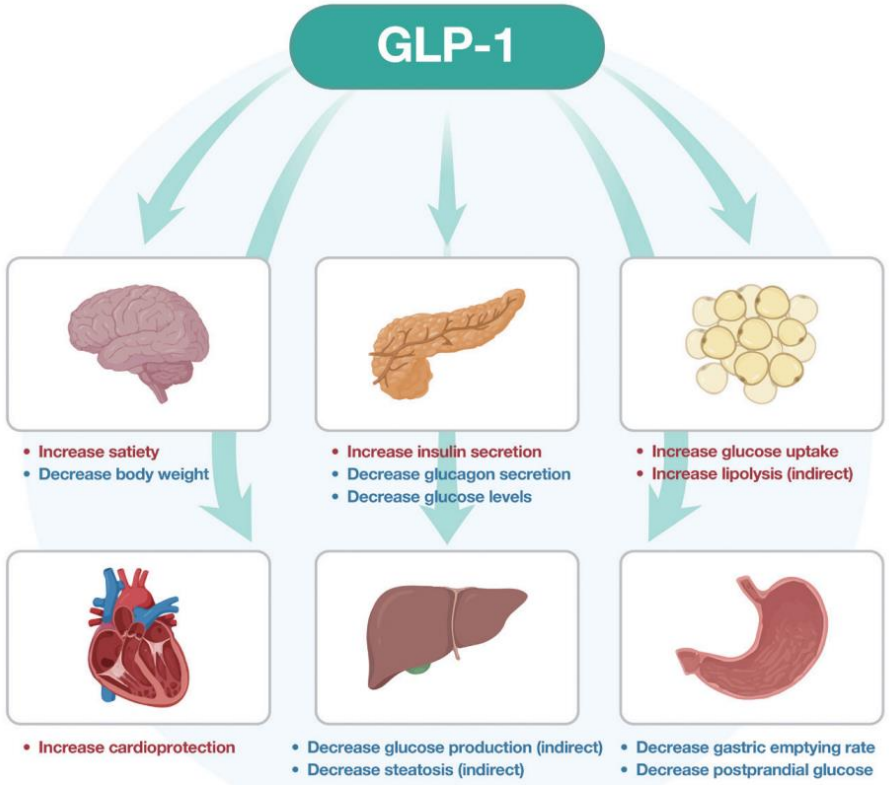
Dose-Dependent Increase of GLP-1 in Patients

Intestinal Production of GLP-1 Mediates Effects on Body Weight

GLP-1: Glucagon-Like Peptide-1

- Peptide hormone generated through enzymatic breakdown of proglucagon
- Endocrine hormone, secreted by **enteroendocrine L-cells** located in the distal jejunum, ileum, and colon in response to **nutrient ingestion** and neuroendocrine stimulation
- Typical physiological **increase** in GLP-1 levels in healthy humans **after a meal is 2-3 times**
- GLP-1 increase leads to slow gut motility, lower food intake, increase satiety and induce insulin secretion

Main Physiologic Effects of GLP-1

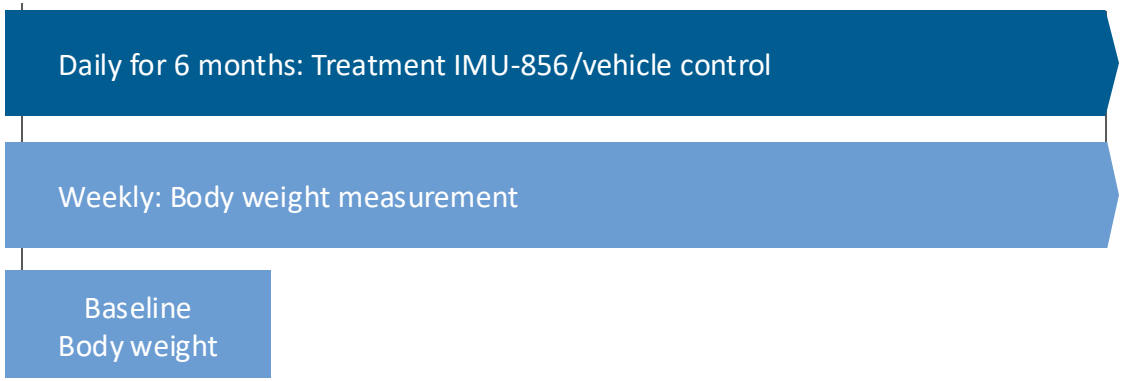


Left: Review Zheng, Z., Zong, Y., Ma, Y. et al. Sig Transduct Target Ther 9, 234 (2024); right: Jakubowska A, Roux CWL, Viljoen A. Endocrinol Metab (Seoul). 2024 Feb;39(1):12-22

IMU-856: Effects on Body Weight in Preclinical Experiment and on Blood GLP-1 Levels in Celiac Disease Clinical Trial

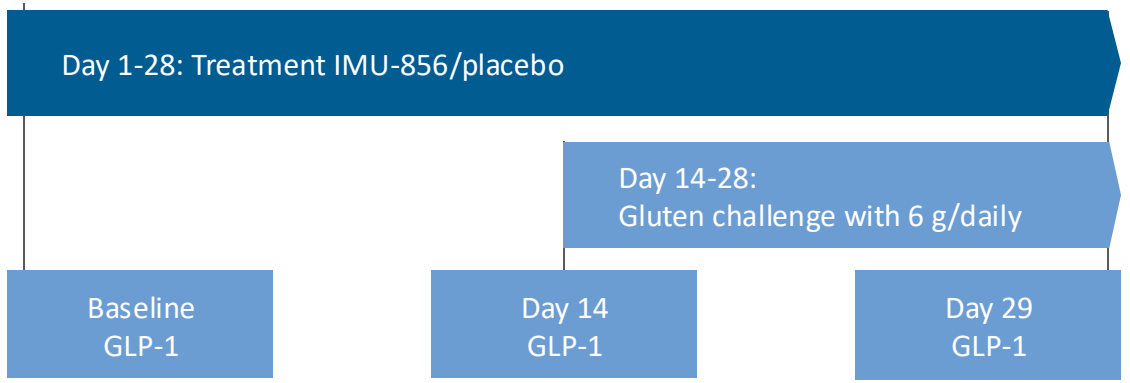
6-Months *In Vivo* Study

- Regulated GLP study[1] to support clinical development
- Daily oral treatment of rats[2] for 6 months
- Dosing: 0 (vehicle), 10, 25, 75 mg/kg/day of IMU-856
- Weekly body weight measurement



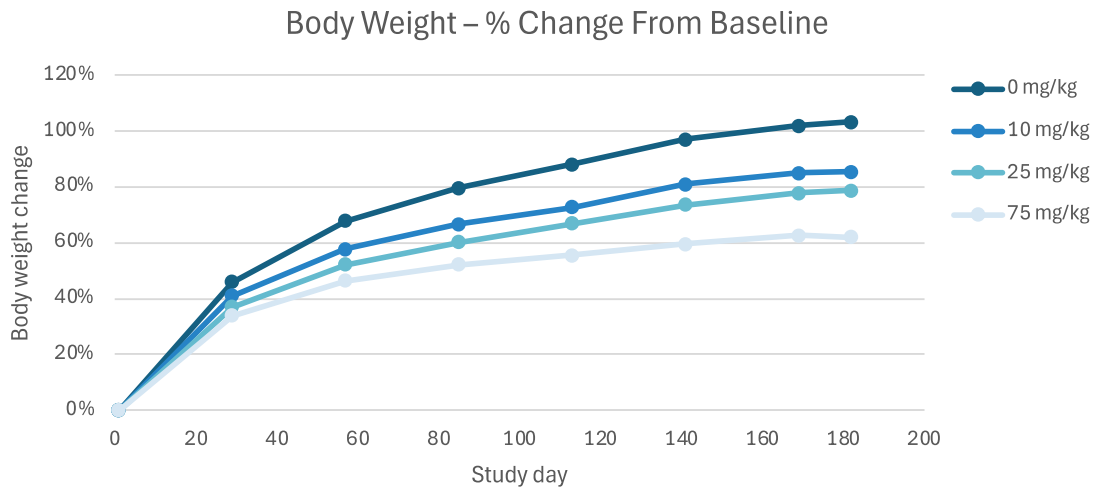
Phase 1b Clinical Trial of IMU-856

- Designed to explore effects of gluten challenge in a celiac disease patient population
- Total of 43 patients enrolled (IMU-856: N=29)
- Dosing: 80 and 160 mg QD of IMU-856, or placebo
- Double-blind treatment period of 28 days, 13 days without and 15 days with 6 g daily gluten challenge
- Patients measured post hoc for plasma GLP-1 concentrations



[1] according to ICH M3(R2) [2] Wistar Han rats / GLP-1: glucagon-like peptide-1; GLP: Good Laboratory Practice; QD: quaque die = once-daily; ICH: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

In a 6-Months *In Vivo* Study, IMU-856 Dose-Dependently Reduced Weight Gain



Reduction of weight gain in % compared to vehicle control

10 mg/kg	-18 %
25 mg/kg	-23 %
75 mg/kg	-40 %

- Dose-dependent effect on body weight gain
- Linked to reduced food consumption
- Effect in both males and females
- No effect on general health condition

IMU-856 reduced body weight gain in a dose-dependent fashion up to -40 % compared to vehicle control

Reduced body weight gain observed in 6-month toxicology study. Rats were 7-8 weeks old at study start and were expected to gain weight over the course of the study. Data show less weight gain in IMU-856 treated animals in connection with reduced food consumption.

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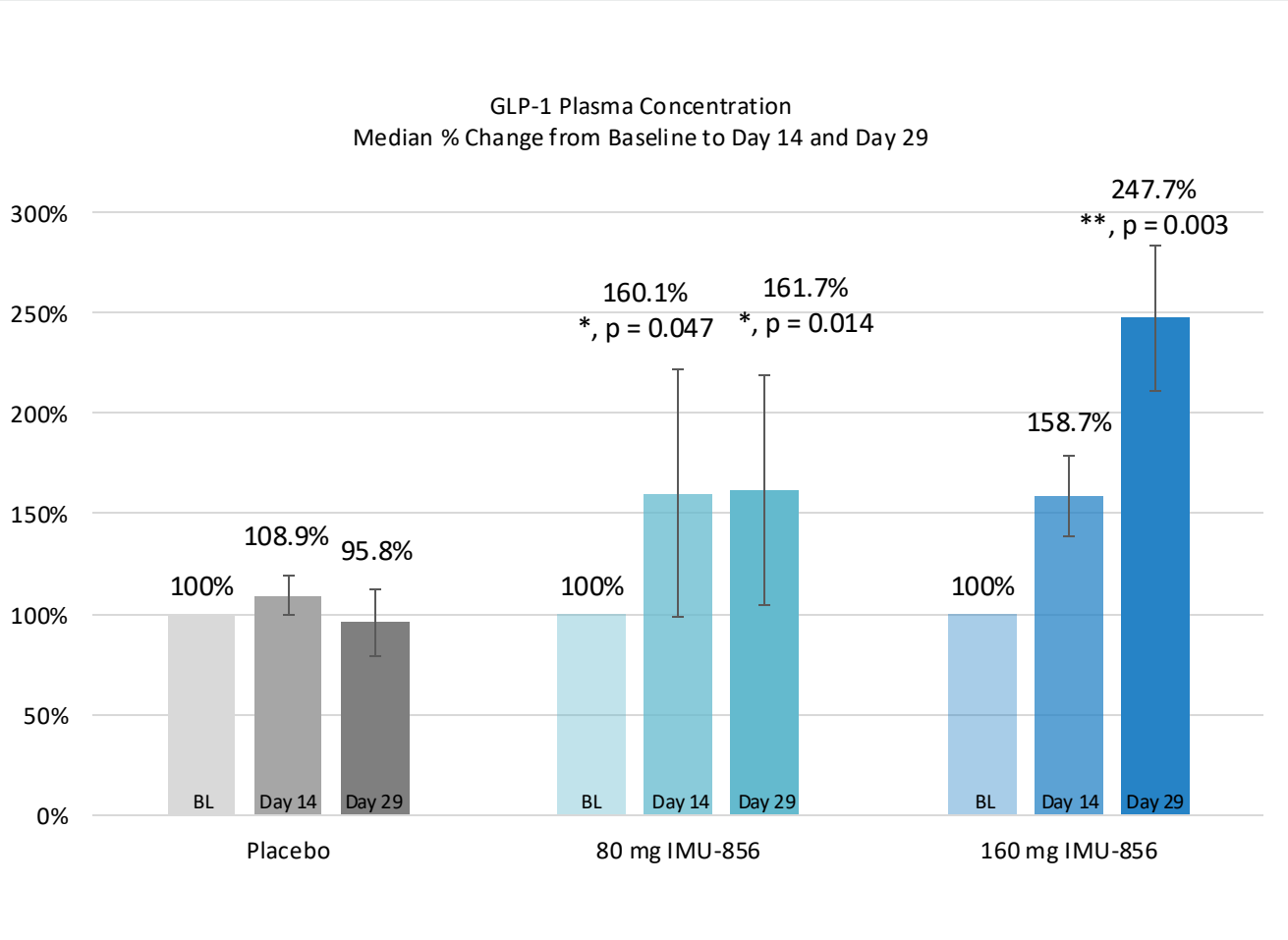
Confirmation of Effects as Part of Phase 1b Clinical Trial: IMU-856 Dose-Dependently Increased GLP-1 in Celiac Disease **Patients**



28-day phase 1b clinical trial of IMU-856 in celiac disease

- Patients measured for plasma GLP-1 concentrations: N=11 (placebo), N=13 (80 mg IMU-856), N=13 (160 mg IMU-856)
- Baseline: Day 1, N=37 over all arms
- Day 14: before start of challenge, N=36
- Day 29: after last treatment on Day 28, N=32
- Morning baseline levels under fasting conditions

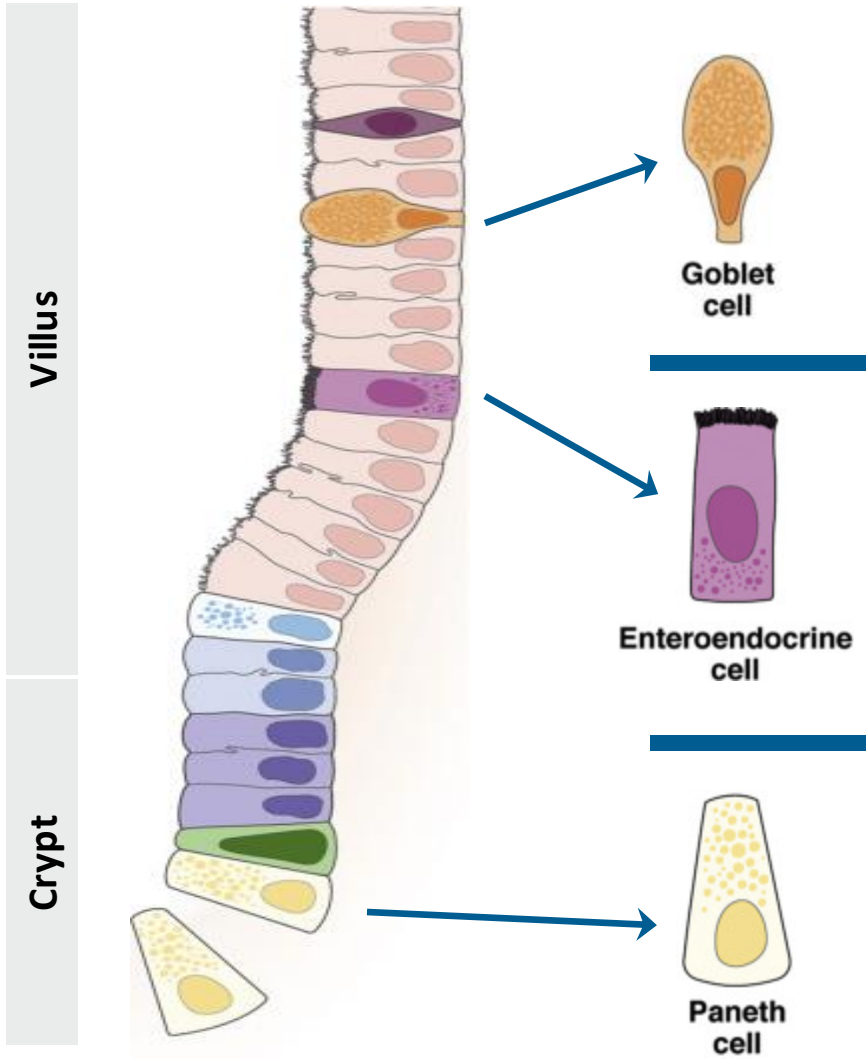
- **Dose-dependent increase of endogenous GLP-1 levels of up to 2.5 times versus placebo control**
- **Typical physiological increase in GLP-1 levels in healthy humans after a meal is also 2-3 times**

Statistics: two-sided Mann-Whitney U, treatment vs. placebo at Day 14 and Day 29 / GLP-1: glucagon-like peptide-1; BL: baseline

Immunic THERAPEUTICS

Main Secretory Epithelial Cells of the Small Intestine and Colon Epithelium

All Have Been Shown to Express SIRT6 Target



Produce and release a protective mucus layer, with the main component of this mucus being a protein called mucin

Secret gastrointestinal hormones: such as gastric inhibitory peptide (GIP), glucagon-like peptides (GLP-1 and GLP-2), cholecystokinin (CCK), ghrelin, neurotensin, serotonin (5-hydroxy-tryptamine or 5-HT), and peptide YY (PYY)

Secrete antimicrobial peptides and proteins, most notably defensins

Meyer AR, Brown ME, McGrath PS, Dempsey PJ. Cell Mol Gastroenterol Hepatol. 2022;13(3):843-856 / SIRT: sirtuin

IMU-856: A Novel Mechanism Offering Potential to Go Beyond Existing GLP-1, GLP-2, GIP Mimetics

SIRT6 Targeting Approach
IMU-856

- **Functional improvement** of enteroendocrine and other epithelial cells through increasing physiologic cell regeneration in gut wall
- Secretion of the **physiological GLP-1** protein and possible increase of secretion of **multiple incretins** (currently being investigated)
- Improvement of gut barrier and functionality in general
- **Oral** administration, small molecule

Incretin Mimetics
GLP-1, GLP-2, GIP

- Providing **synthetic peptides** that mimic the natural hormones secreted by enteroendocrine cells
- Targets **one or two target incretins** only (at this point)
- **Injectable**, peptide

SIRT: sirtuin; GLP: glucagon-like peptide; GIP: glucose-dependent insulin-tropic polypeptide

Obesity Market Expected to Reach More Than $170 Billion Globally by 2031[1]

Unmet Needs Still Exist to Address This Growing Medical Challenge

- Obesity and overweight are among the fastest growing and most prevalent chronic human conditions in the world affecting ~2.5 billion adults worldwide[2]
- The economic impact of obesity and overweight in the United States is estimated to be $706 billion, increasing to $2.6 trillion by 2060[3]
- GLP-1 receptor agonist class has revolutionized obesity treatment but there are still **unmet needs for novel mode of actions**, **oral administration**, increased tolerability and greater efficacy
- Current drugs in development are mainly peptidomimetics – with challenges in oral administration

[1] GlobalData Pharma DECODED, Feb. 11th 2025 "Obesity: Seven-Market Drug Forecast and Market Analysis – Update" [2] https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight#:~:text=In%202022%2C%202.5%20billion%20adults%20aged%2018%20years%20and%20older,1990%20to%2020%25%20in%202022
[3] https://data.worldobesity.org/economic-impact-new/countries/US.pdf

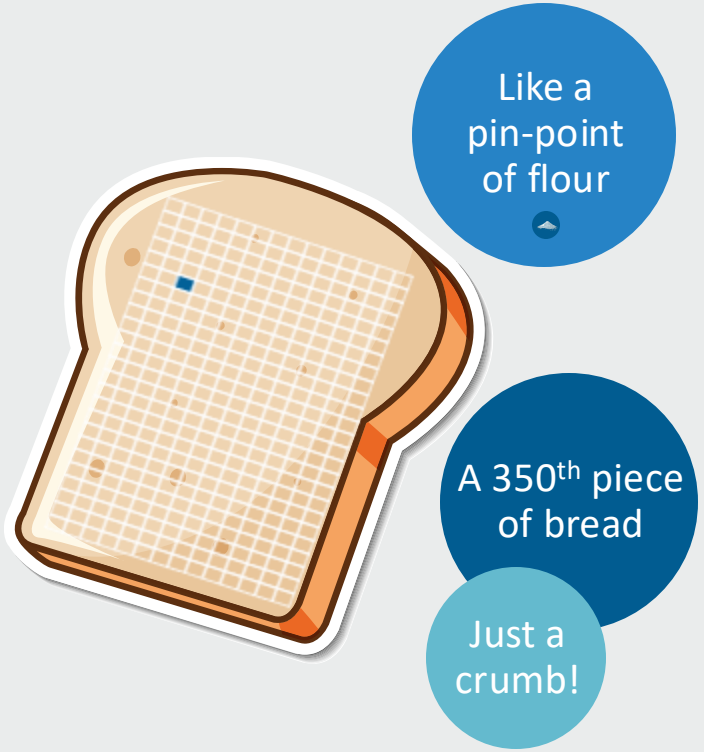
IMU-856 in Celiac Disease

Demonstrated Clinical Proof-of-Concept in a Phase 1b Clinical Trial

Celiac Disease Currently Has No Adequate Treatment Options

- Two million patients diagnosed with celiac disease in the US; more than one million more undiagnosed[1,2]
- Most studies report between **24% and 47%**[3-8] of patients with signs and symptoms of ongoing active celiac disease (OACD) **despite a gluten-free diet,** most likely due to continuous (inadvertent) gluten exposure
- **Only established therapeutic option is a life-long strict adherence to a gluten-free diet**[9], which involves complete avoidance of proteins from wheat, barley, and rye
- Gluten challenge is an accepted concept for clinical trials in celiac disease

10 mg of gluten is the total limit for all foods combined for the entire day.



How much is 10 mg of gluten?

[1] Singh et al., Clinical Gastroenterology and Hepatology 2018;16:823–836 [2] Choung et al., Mayo Clin Proc. 2016 Dec 5:S0025-6196(16)30634-6 [3] Lebwohl et al., Aliment Pharmacol Ther. 2014 March ; 39(5): 488–495 [4] Lanzini et al., Aliment Pharmacol Ther. 2009; 29(12):1299–308 [5] Ciacci et al., Digestion. 2002; 66(3):178–85 [6] Selby et al., Scand J Gastroenterol. 1999; 34(9):909–14 [7] Rubio-Tapia et al., Am J Gastroenterol. 2010; 105(6):1412–20 [8] Sharkey et al., Aliment Pharmacol Ther. 2013; 38(10):1278–91 [9]: https://nationalceliac.org/celiac-disease-questions/understanding-gluten-levels/ (text and picture)

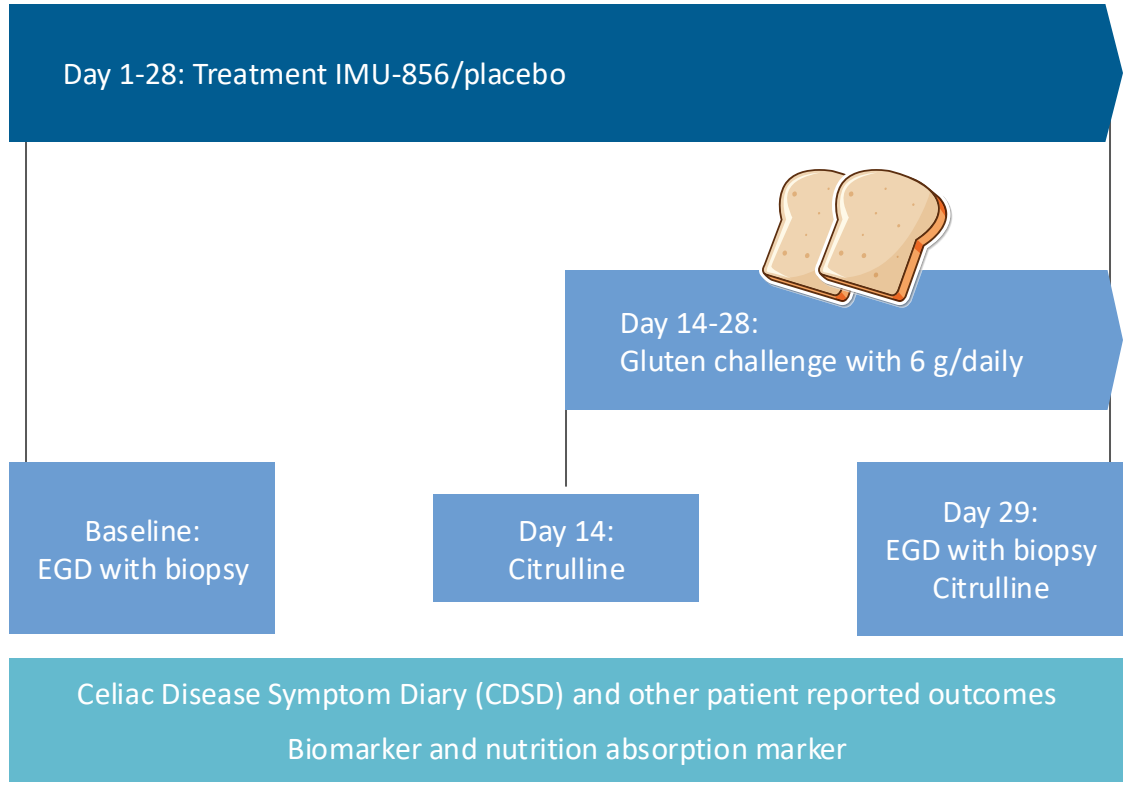
Immunic THERAPEUTICS

IMU-856 Demonstrated Clinical Proof-of-Concept in a Phase 1b Clinical Trial in Celiac Disease

Proof-of-Concept Study Designed as a Gluten Challenge Trial

- **Celiac disease used as disease model to provide clinical proof-of-activity of IMU-856 in a 28-day trial setting**
- Designed to explore effects of gluten challenge in a celiac disease patient population
- Dosing: 80 and 160 mg QD of IMU-856, or placebo
- 43 patients enrolled (IMU-856: N=29)
- Assessed safety, tolerability, pharmacokinetics, and pharmacodynamics of IMU-856
- Proof-of-concept: measured histological changes, blood biomarkers of epithelial mass, nutrient uptake and disease-related symptoms

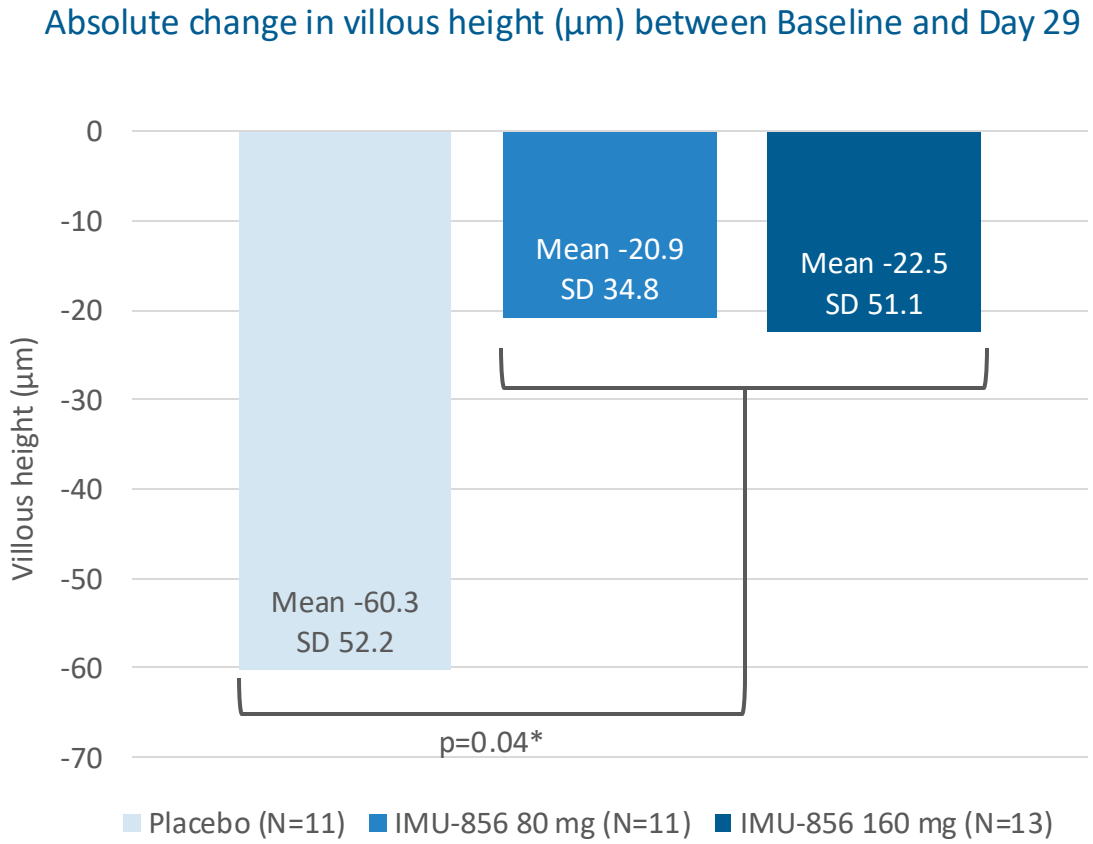
Flow Chart of Phase 1b Clinical Trial in Celiac Disease

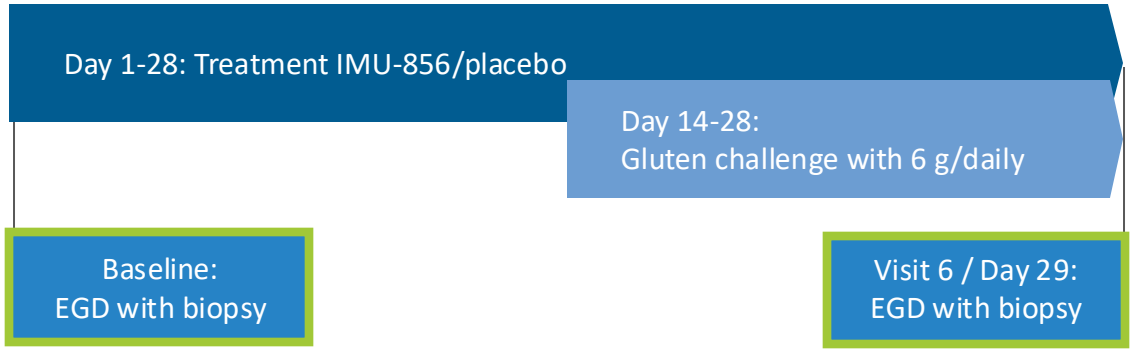


QD: quaque die = once-daily; EGD: esophagogastroduodenoscopy

Immunic THERAPEUTICS

IMU-856 Protected Against Gluten-Induced Decrease in Villous Height as Compared to Placebo



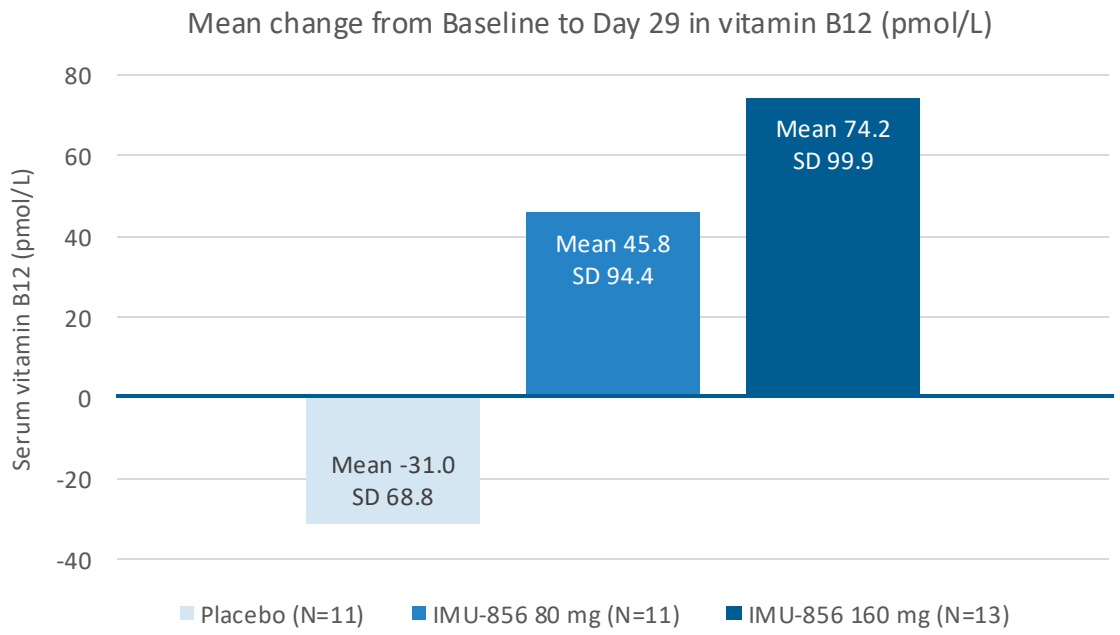


- Substantial protection for IMU-856 treatment groups as compared to placebo
- Reached statistical significance* for this objective readout which is known to be relevant to influence future medical complications of celiac disease
- Assessed by central pathology laboratory and blinded pathology reader

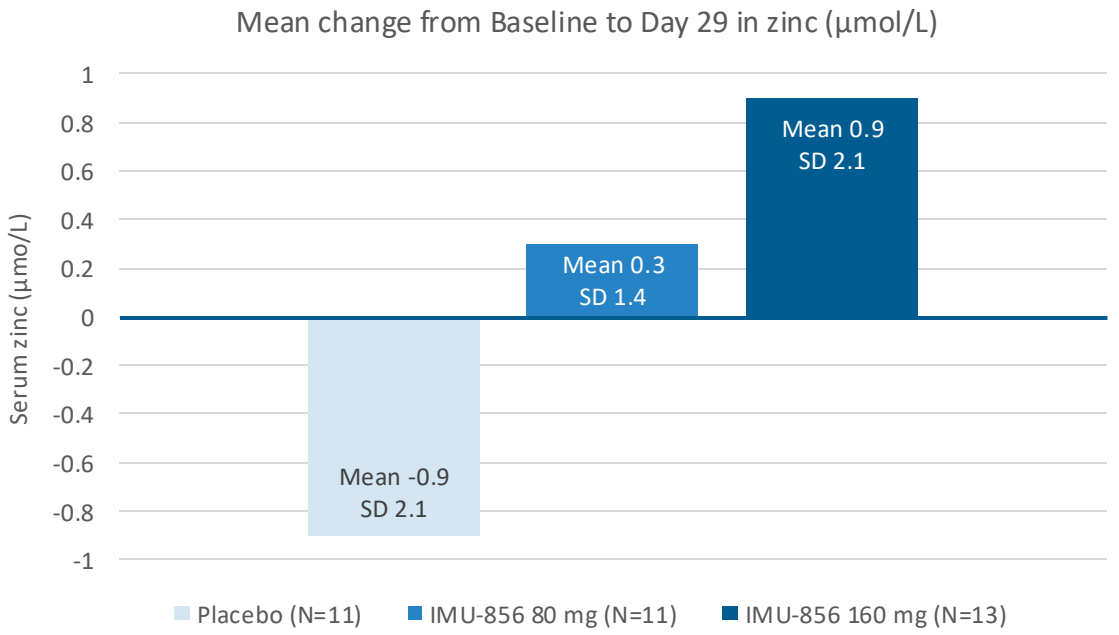
* Wilcoxon Two-Sample Test comparison between pooled IMU-856 groups and placebo, performed as post-hoc exploratory statistical analysis
Disease Analysis Set: N=35/43 included in histology analysis set. 8 patients not included in this analysis due to early termination. Gluten Challenge for 15 days with 6 g daily. Central pathology laboratory: Jilab Inc. Tampere, Finland
EGD: esophagogastroduodenoscopy; SD: standard deviation

IMU-856 Improved Uptake of Actively Transported Essential Nutrients Vitamin B12 and Zinc

Vitamin B12



Zinc



SD: standard deviation

Immunic Therapeutics

Summary

Summary: Vidofludimus Calcium Is a Derisked Near-Term Opportunity

Innovative clinical pipeline: First-in-class oral drugs with unique modes of actions for multiple sclerosis and gastrointestinal diseases in various phases of clinical development

Relapsing MS opportunity is meaningful and de-risked:

- Oral category going to remain a large portion of overall MS market; peak sales potential for vidofludimus calcium of $1-2 billion
- Currently available oral therapies have limitations in benefit/risk profile; there is need for improvement
- Vidofludimus calcium has the potential to address these shortcomings and transform the oral MS DMT market
- ENSURE program: Two identical phase 3 clinical trials, designed to achieve potential regulatory approval of vidofludimus calcium in relapsing MS in a low-risk study design; top-line data for both ENSURE trials expected by end of 2026

Progressive MS provides tremendous upside opportunity:

- High unmet medical need market: No approved therapies for non-active SPMS; one approved therapy for PPMS (infusion)
- Peak sales potential for vidofludimus calcium of $3-5 billion across respective indications
- Phase 2 CALLIPER trial successfully demonstrated neuroprotective potential of vidofludimus calcium in progressive MS patients
- Results to be discussed with healthcare authorities to determine appropriate next steps

Financials:

Cash position: $55.3 million (as of June 30, 2025), shares outstanding: 98,650,590 (as of July 31, 2025)

Thank You!

Jessica Breu

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