Immunic Therapeutics

Developing Selective Oral Therapies in Immunology

NASDAQ: IMUX | April 2024

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; 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.

Our Mission

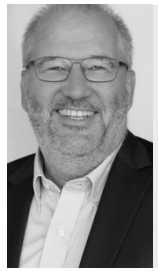
We are developing a pipeline of next-generation selective oral therapies focused on offering patients with chronic inflammatory and autoimmune diseases new and clinically meaningful treatment options.

Leadership Team

Company is Led by an Experienced Management Team

Daniel Vitt, PhD
CEO & President

Hella Kohlhof, PhD
CSO



Andreas Muehler, MD, MBA
CMO

Patrick Walsh
CBO

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Executive Chairman

Renowned International Board of Directors

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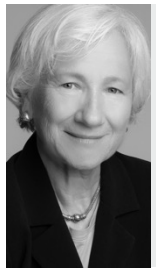
CEO & President

Barclay A. Phillips
Lead Independent Director



Tamar Howson, CFA
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Independent Director

Immunic THERAPEUTICS

Advanced Clinical Pipeline

Well Differentiated Programs in Various Phases of Clinical Development

Program	Preclinical	Phase 1	Phase 2	Phase 3
Vidofludimus Calcium (IMU-838)	Relapsing Multiple Sclerosis (RMS) – ENSURE Trials			
	Progressive Multiple Sclerosis (PMS) – CALLIPER Trial			
	Ulcerative Colitis (UC) – CALDOSE-1 Trial			
IMU-856	Celiac Disease			
IMU-381	Gastrointestinal Diseases			

■ Completed or ongoing ■ In preparation or planned

Immunic THERAPEUTICS

Vidofludimus Calcium in Multiple Sclerosis (MS)

Targeted to Elevate the Standard of Care With a Holistic Solution for the Full Spectrum of MS Patients

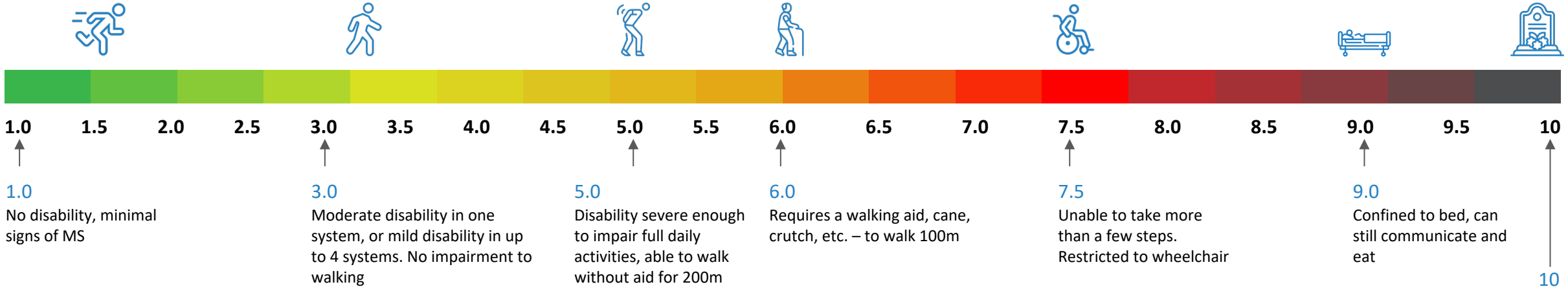
MS is a Lifelong Neurodegenerative Disease

Lifelong Disease Requiring Decades of Therapy

- ~2.8 million people affected worldwide (~1M in US)[1]
- Often diagnosed in younger adults (3:1 women:men)
- Epidemiologic study showed a clear association between EBV infection and occurrence of MS; 32-fold increased risk in EBV-infected patients[2]

Therapeutic Goal: Preventing Disability Worsening

- Key unmet need prevention or slowing of long-term disability worsening
- Historical focus has been on prevention of relapses via broad immunosuppression



[1] MS International Federation (2020): Atlas of MS, https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms; Illustration adapted from: VOX, https://futurism.com/reversal-of-multiple-sclerosis-via-risky-stem-cell-treatment-confirmed, and Multiple Sclerosis Trust, https://www.mstrust.org.uk/; [2] Bjornevik K. et al., Science. 10.1126/science.abj8222; PML: progressive multifocal leukoencephalopathy; M: million; Source: mistrust.org.uk

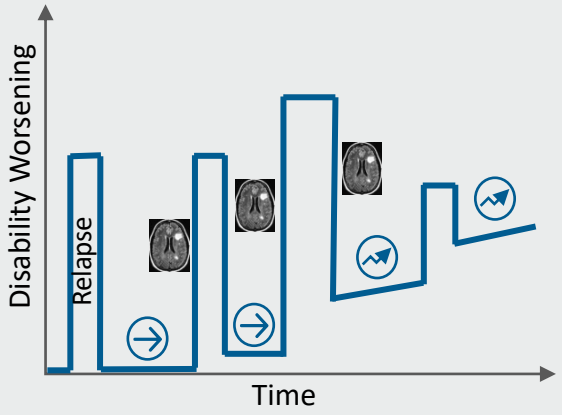
Disability Worsens Over Time in All Forms of MS

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

Relapsing Forms of MS (RMS)

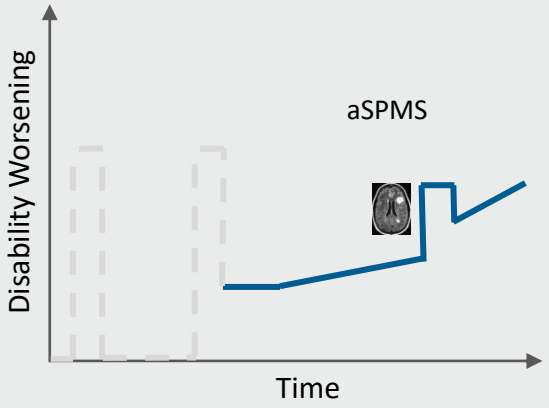
RRMS

- Relapses and MRI lesions dominate clinical course



Active SPMS

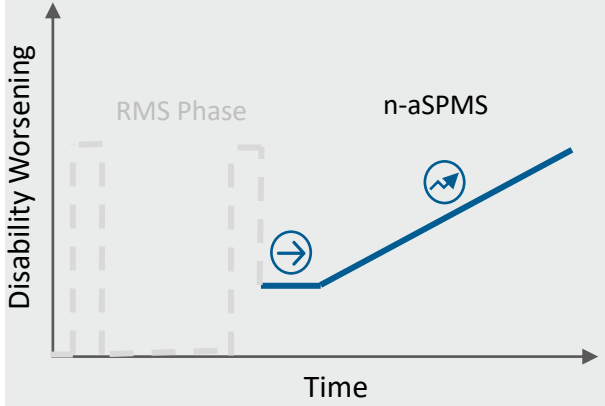
- Fewer relapses and lesions with continuous disability progression



Progressive Forms of MS (PMS)

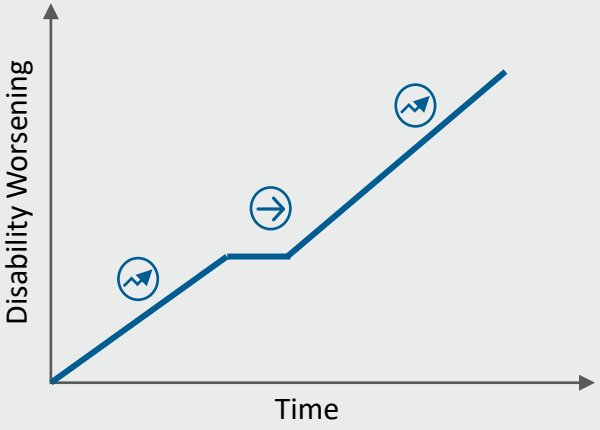
Non-Active SPMS

- Relapses have stopped, but disability progression continues



PPMS

- Disability worsening without relapses from the start



Relapses & MRI lesions / focal inflammation (RAW)

Smoldering disease and progression independent of relapse activity (PIRA)*

Adapted from Kretzschmar A., MSVirtual2020; *Lublin FD, et al. Brain. 2022 Sep 14;145(9):3147-3161

MS: multiple sclerosis; MRI: magnetic resonance imaging; RAW: relapse-associated worsening; PIRA: progression independent of relapse activity; RRMS: relapsing-remitting MS; SPMS: secondary progressive MS; PPMS: primary progressive MS; a: active; n-a: non-active

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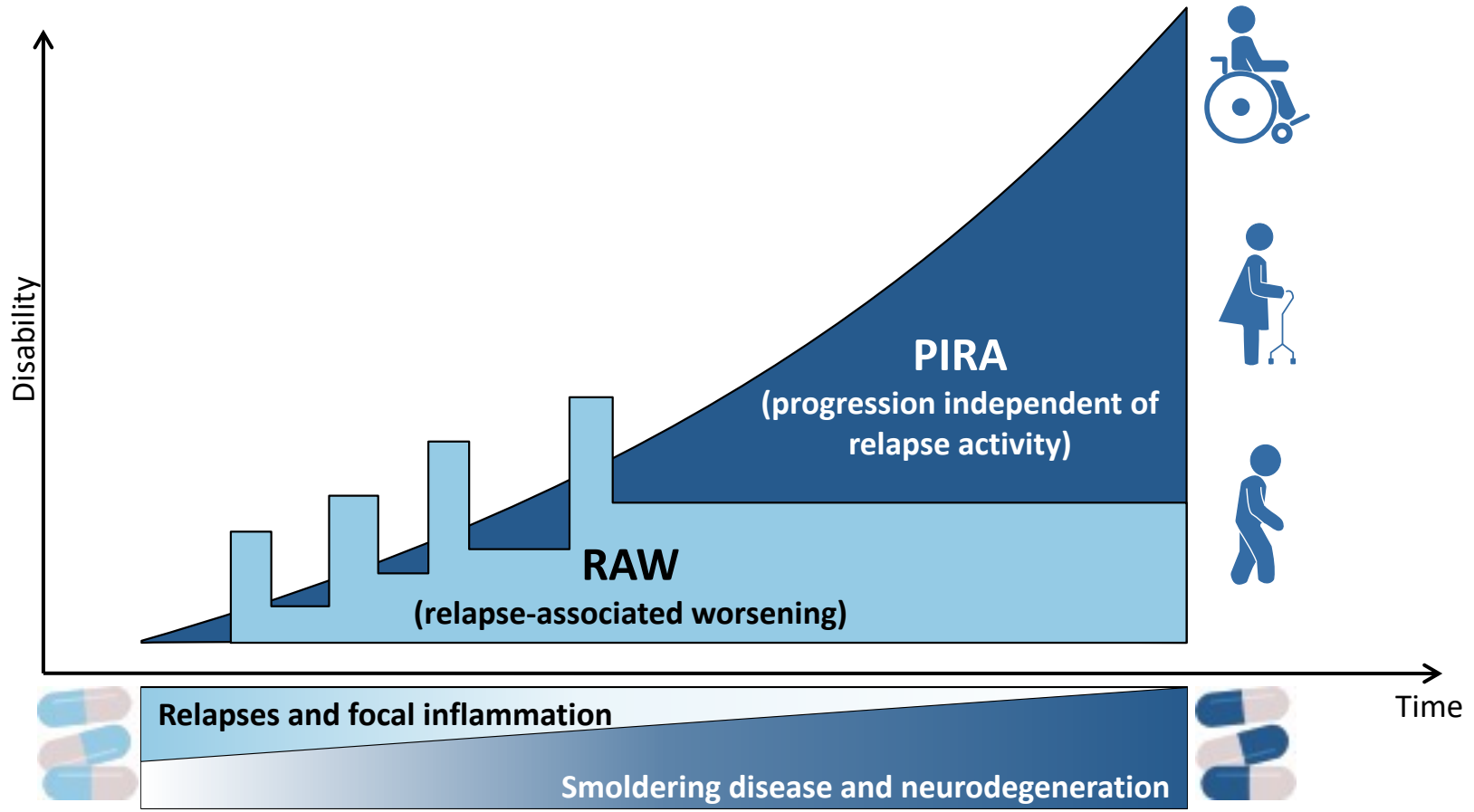
Underlying “Invisible Disability Accumulation” Contributes to Multiple Sclerosis Progression Over Time



Newer data shows that half of the disability accumulation in relapsing MS comes from PIRA and is contributed to the underlying “invisible disability accumulation” or “smoldering disease”[1]

Graphic adapted from Kretzschmar A., Symposium „Every Journey Begins with a Single Step: Visualizing the Chronic Nature of MS”, MSVirtual2020 / 8th Joint ACTRIMS-ECTRIMS Meeting

[1] Lublin FD, et al. Brain. 2022 Sep 14;145(9):3147-3161; Müller J, et al. JAMA Neurol. 2023;80(11):1232–1245

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Vidofludimus Calcium Aimed to Go Above and Beyond Current Care to Comprehensively Address Patients' Needs

Targeted to Elevate the Standard of Care With a Holistic Solution for MS Patients

Uniquely matched to the multi-faceted neurodegeneration of smoldering and active MS

- Neuroprotective effects
- Anti-inflammatory effects
- Anti-viral effects

Seeks to provide unrivaled safety, tolerability & convenience

- Targeted to set the new standard for patient preference, exceeding all options including glatiramer acetate

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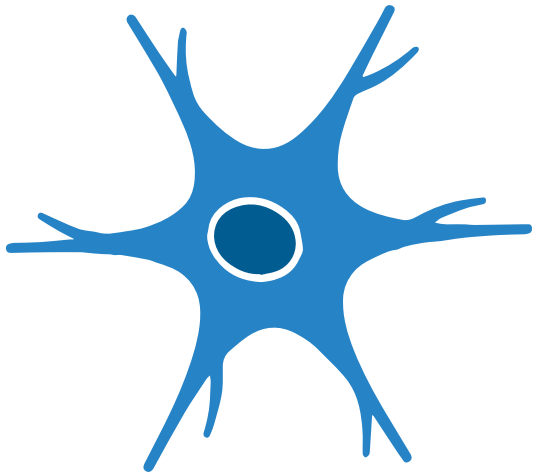
Vidofludimus Calcium Addresses Smoldering Neurodegeneration

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

Nurr1 Activator

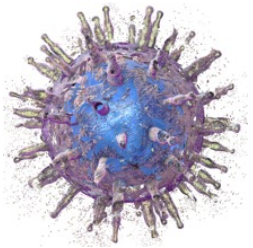
- Protecting neurons from cell death
- Continuous effect independent from focal inflammation



DHODH Inhibitor

- Selective anti-inflammatory effect reduces focal inflammation
- Antiviral effect prevents 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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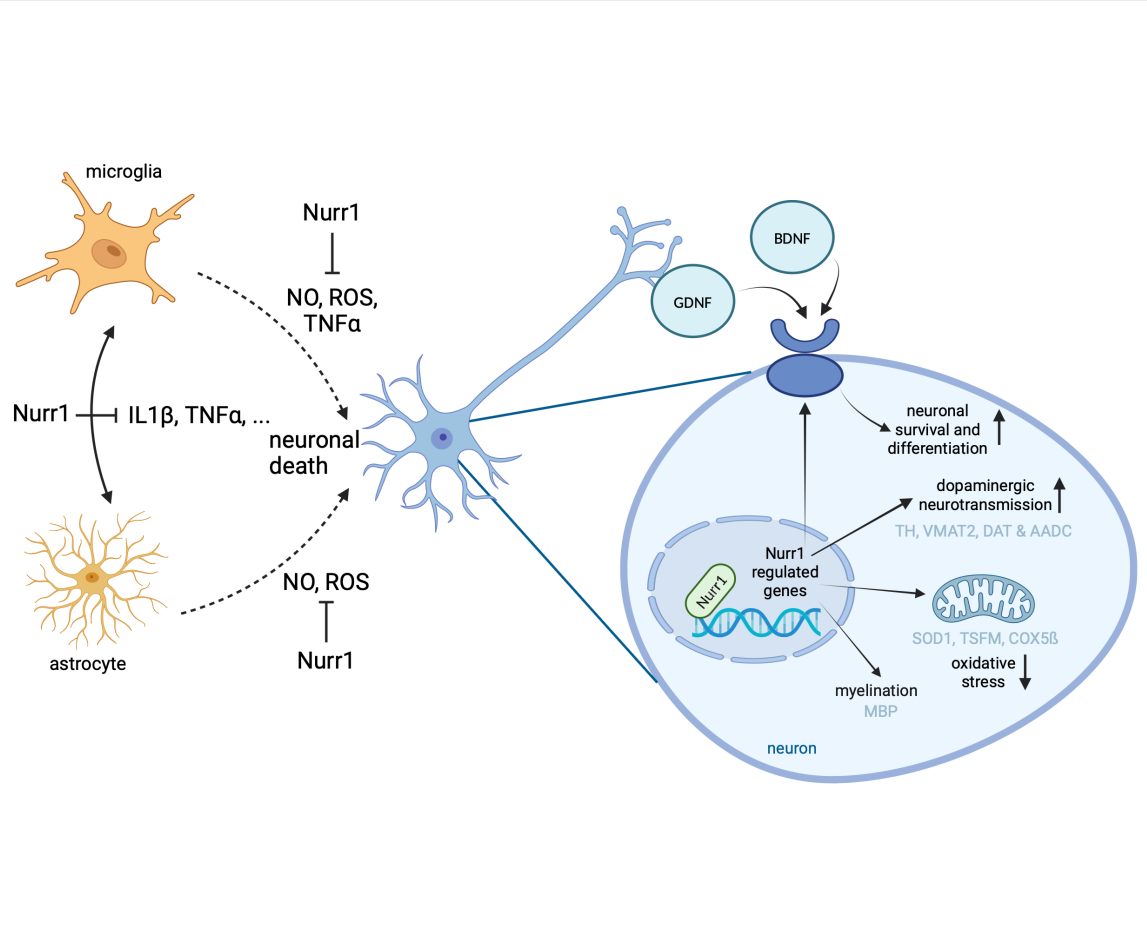
Nurr1 Is a Nuclear Receptor Involved in Neuroprotection



- Nurr1 activation mediates neuronal survival
- Nurr1 activation prevents microglia/ astrocyte-driven neurotoxicity in the brain
- Nurr1 activation in motor neurons may halt neurodegeneration and disability progression

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

Nurr1: nuclear receptor related 1; IL: interleukin; TNF: tumor necrosis factor; NO: nitric oxide; ROS: reactive oxygen species; GDNF: glial cell line-derived neurotrophic factor; BDNF: brain-derived neurotrophic factor

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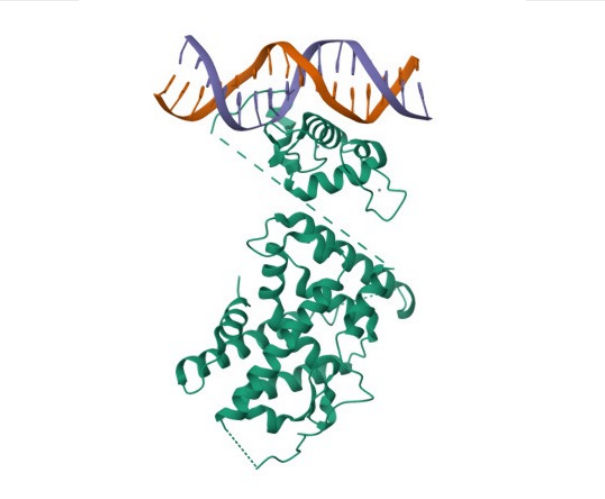
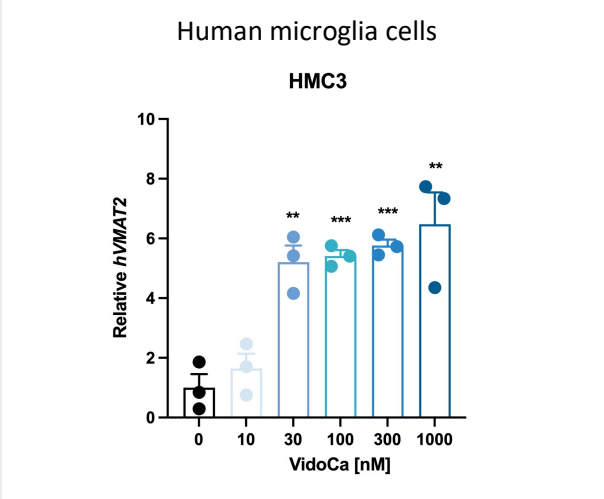
Vidofludimus Calcium Binds to and Strongly Activates Nurr1

Nurr1 is a transcription factor binding to DNA[1]



Vidofludimus calcium induces a 5-fold induction of target gene expression of VMAT2 at 30 nM concentration[2]



Vidofludimus Calcium → binds and activates → **Nurr1** → activates → **Neuronal Survival**

[1] Vietor et al., Journal of Medicinal Chemistry 2023 66 (9), 6391-6402; Structure: Zhao, M. et.al. (2022) Proc Natl Acad Sci USA 119; The related research project was funded by the German Federal Ministry of Education and Research under the grant number 03INT607AA.
[2] Sun, Zuoming. City of Hope. 2023, unpublished / Nurr1: nuclear receptor related 1; DNA: deoxyribonucleic acid; VMAT2: vesicular monoamine transporter 2; HMC3: human microglial cell line

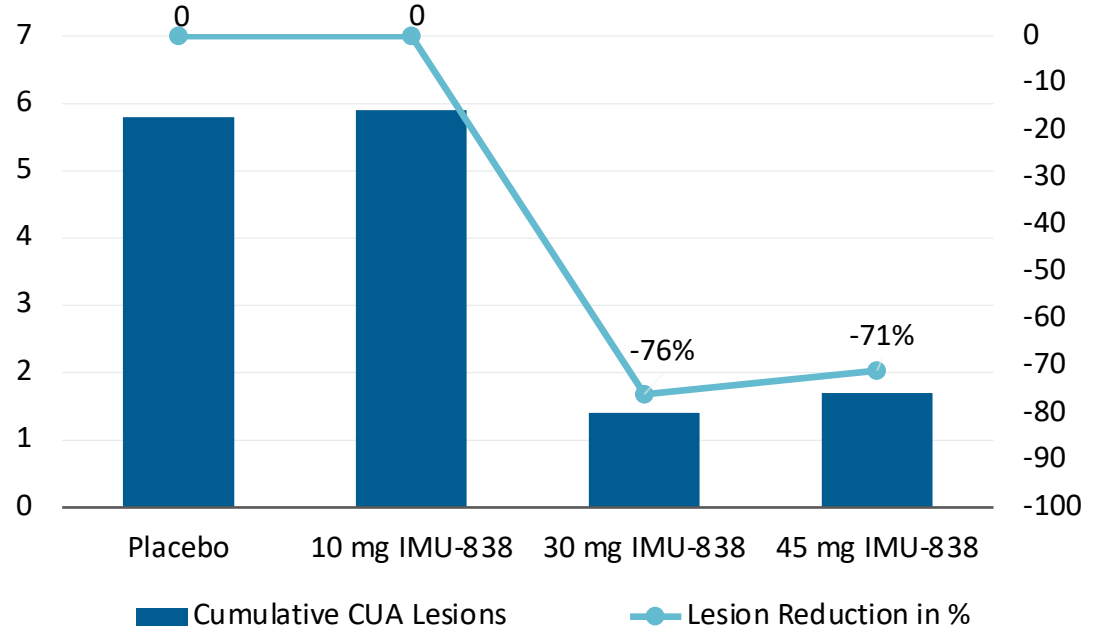
EMPhASIS Trial: Strong Reduction of MRI Lesion Activity

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

Vidofludimus Calcium Showed Strong Activity on Primary Study Endpoint in Phase 2 EMPhASIS Trial

- Double-blind, placebo-controlled, randomized, parallel-group phase 2 trial in RRMS
- Blinded main treatment period of 24 weeks
- Randomized 268 patients in 36 centers across four European countries
- Cohort 1: 30 and 45 mg or placebo
- Cohort 2: 10 mg or placebo
- Extended treatment period of up to 9.5 years to observe long-term safety is ongoing

Study endpoint:
Reduction in cumulative CUA lesions up to week 24



Primary and key secondary endpoints met with high statistical significance (primary: p = 0.0002 / key secondary: 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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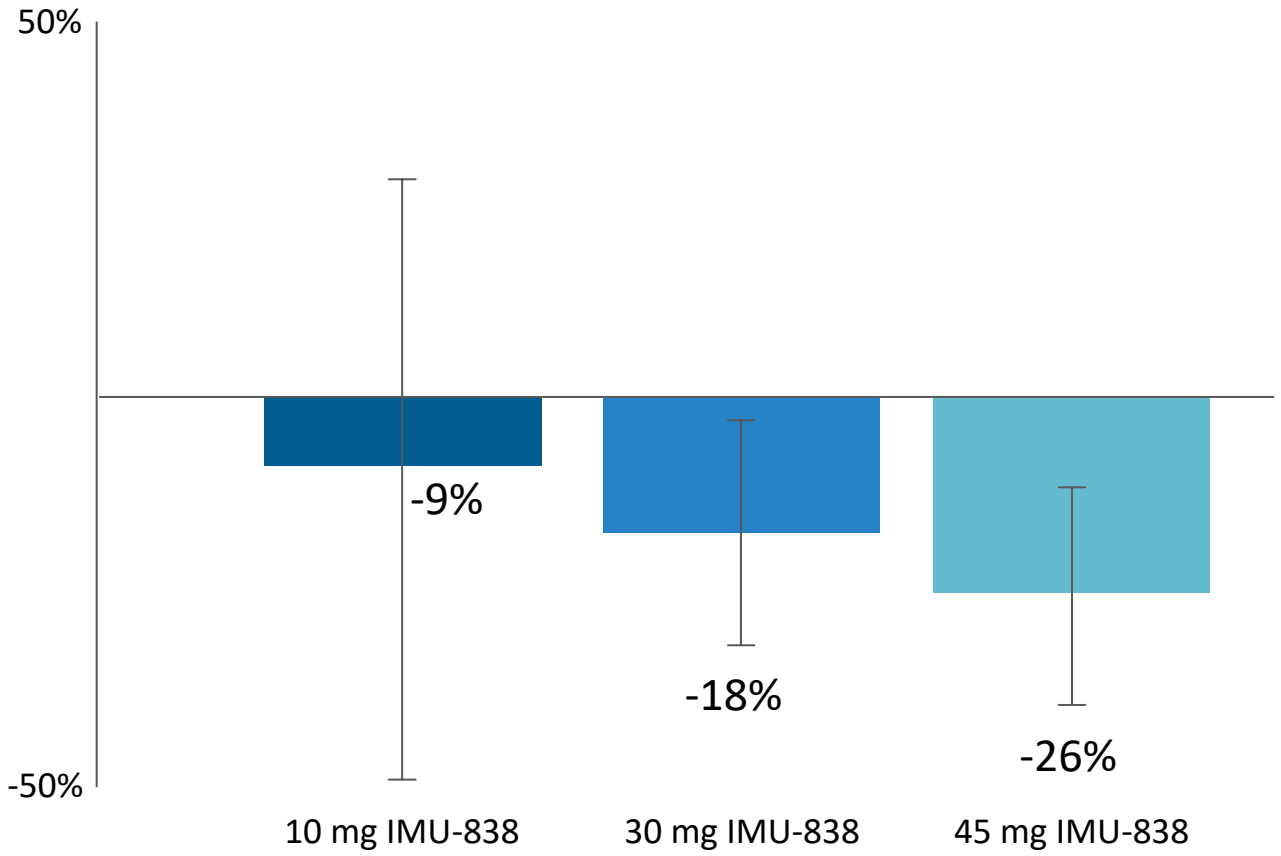
EMPhASIS Trial: Reduction of Serum NfL Concentrations Observed

Versus Placebo After 24 Weeks, Pooled Cohorts 1 & 2



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

- The relative change of serum NfL versus placebo is proportional to vidofludimus calcium dose.
- Higher doses are 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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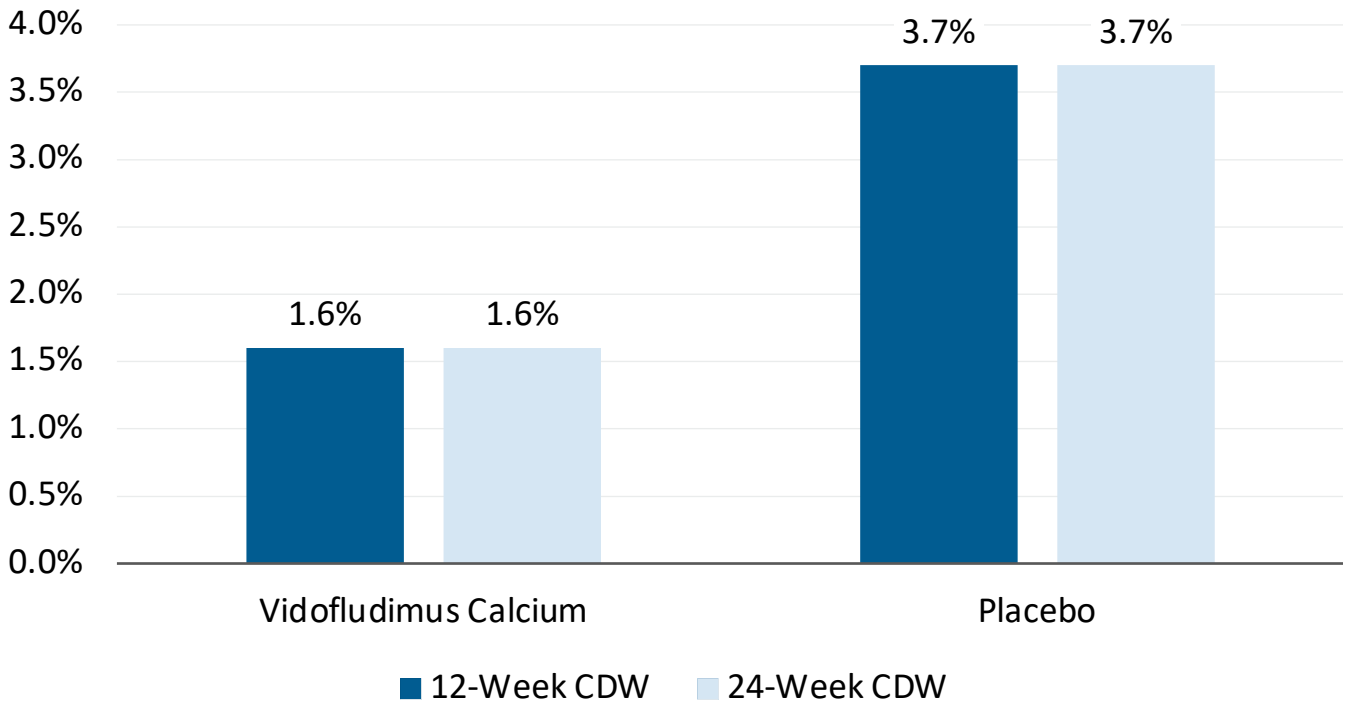
EMPhASIS Trial: Confirmed Disability Worsening Events

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)

Data confirms a signal in preventing 12-week and 24-week confirmed disability worsening events as compared to placebo. Confirmatory data will be obtained in the phase 3 ENSURE clinical program.

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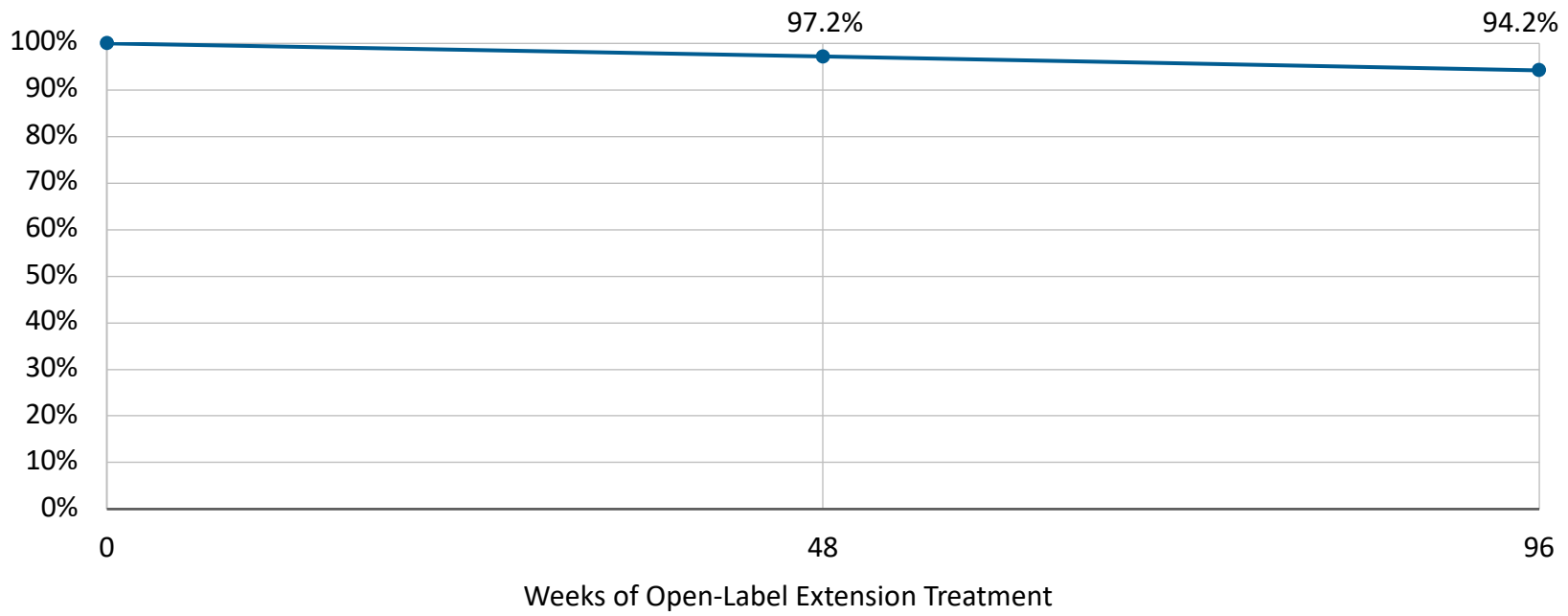
EMPhASIS Trial: Interim Analysis Regarding 12-Week CDW Events

Patients Free of 12-Week CDW After 1 and 2 Years of OLE Vidofludimus Calcium Treatment

Proportion of Patients Free From
12-Week Confirmed Disability Worsening



Data confirms that only a few patients on continuous treatment with vidofludimus calcium develop 12-week confirmed CDW events over a 2-year time frame.

CDW: confirmed disability worsening; EDSS: Expanded Disability Status Scale; Only disability worsenings compared to start of extended treatment are considered. Patients at risk in this analysis are 223 at 48 weeks and 158 for 96 weeks. This includes all patients randomized to either placebo or any dose of vidofludimus calcium. After 24 week of blinded treatment, all patients 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.; 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.

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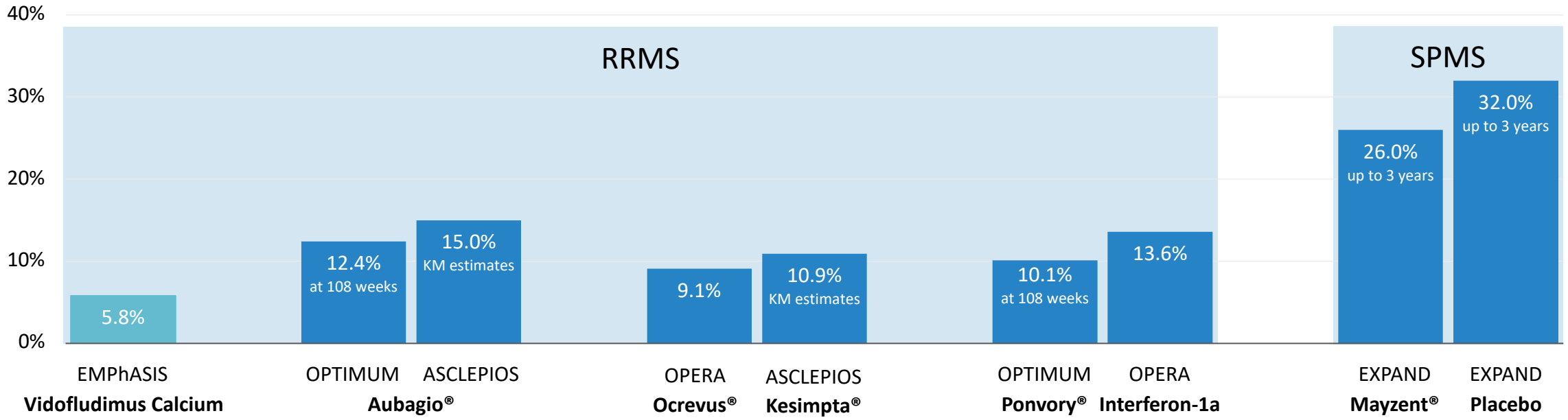
12-Week Confirmed Disease Worsening after 2 Years (96 Weeks)

EMPhASIS Data from OLE Interim Analysis 2022 Compared to Select Historical Trials

Patients With 12-Week/3-Months Confirmed Disability Worsening (% 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; SPMS: secondary progressive multiple sclerosis. All trials performed in relapsing-remitting Multiple Sclerosis. Except EXPAND trial was performed in patients with active and non-active secondary progressive MS (SPMS).; Vidofludimus Calcium: Immunic data; OPTIMUM: Kappos et al. 2021; ASCLEPIOS: Hauser et al. 2020; EXPAND: Kappos et al. 2018; ULTIMATE: Steinman et al. 2022; OPERA: Hauser et al. 2017

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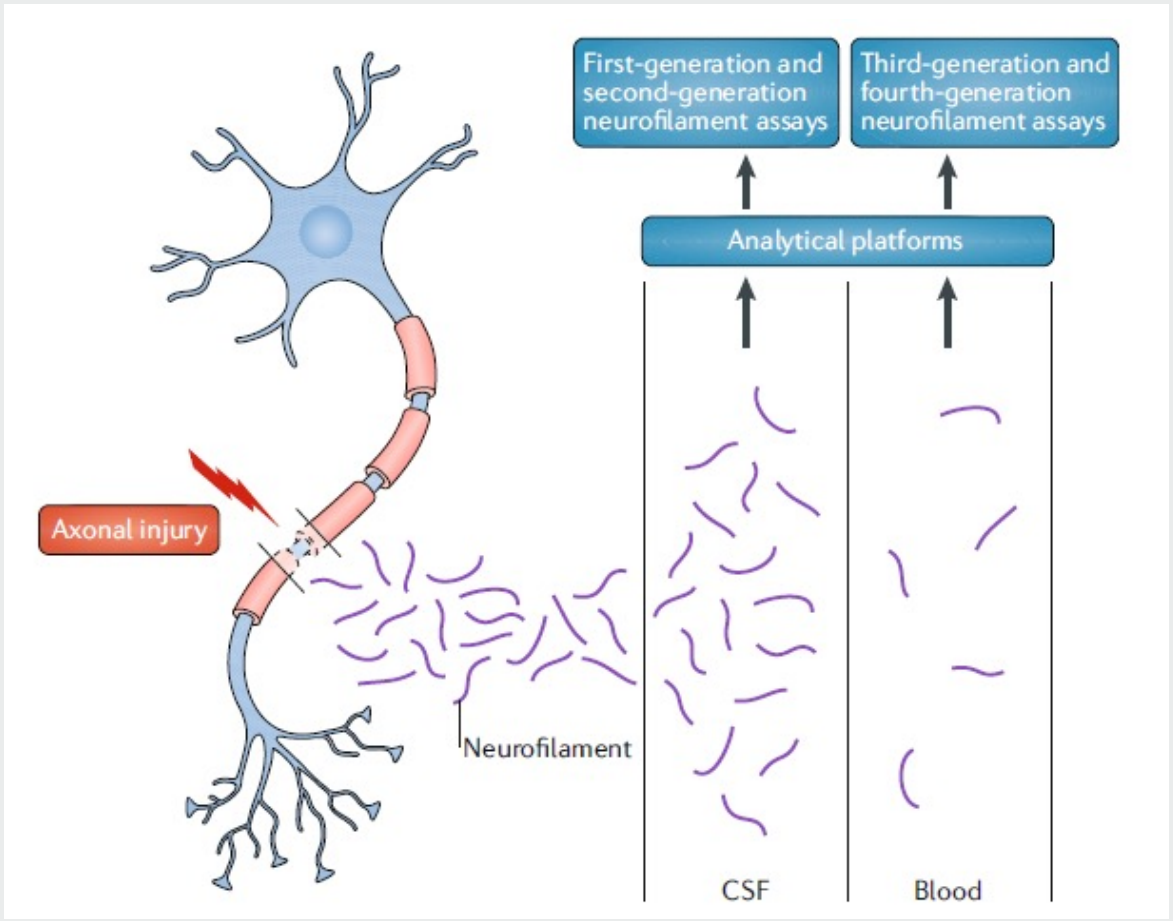
Neurofilaments Are Neuronal Proteins Released Upon Axonal Injury Measurable in Blood

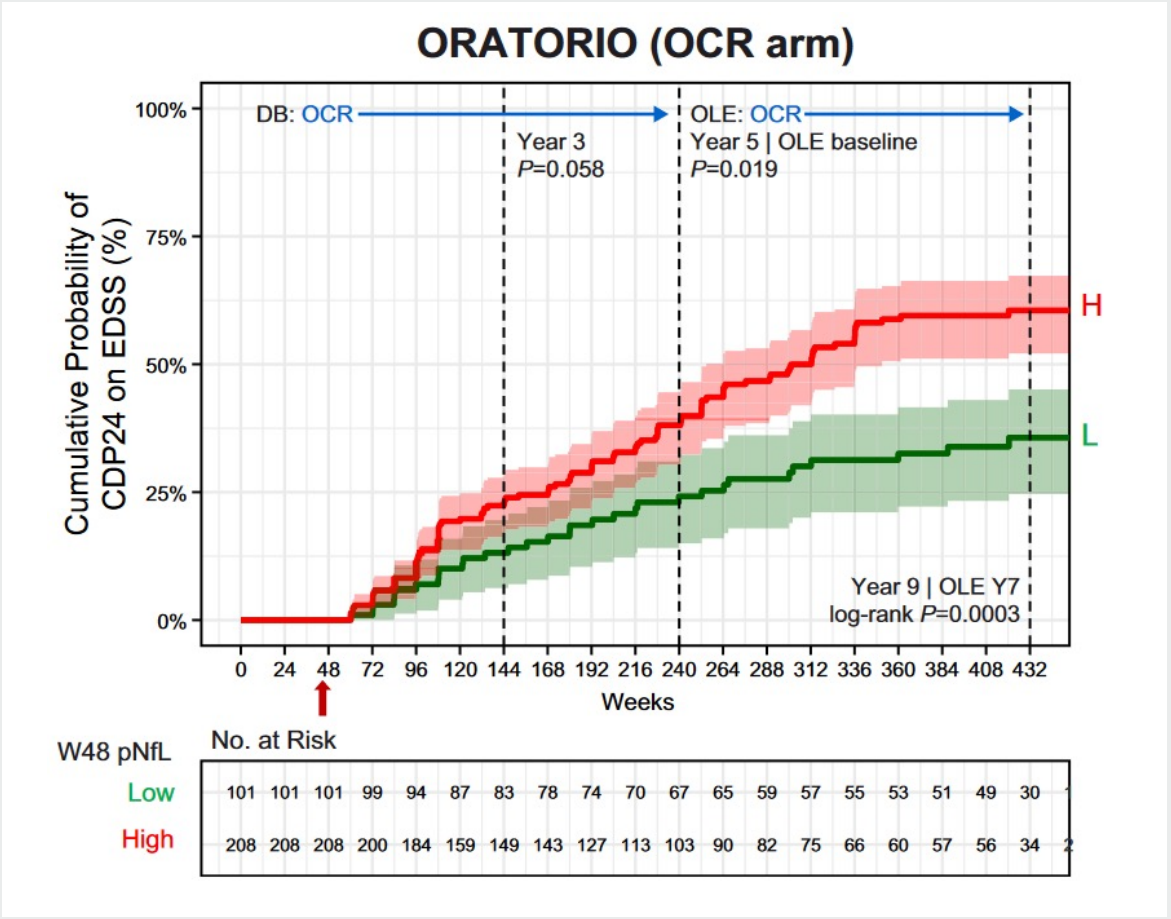
Cross-Disease Neurologic Biomarker for Neurodegenerative Diseases

- Neurofilaments are highly specific neuronal proteins that, upon neuroaxonal injury, are degraded into peptides, shed to the cerebrospinal fluid (CSF), and are eventually measurable in the peripheral blood[1]
- NfL elevations can be detected preceding CDW in non-relapse PMS patients[2]
- Time-to-event analysis confirmed association between NfL levels and future disability outcome within approximately 1-2 years[2]



[1] Kuhle J. et al., Mult Scler. 2013;19(12):1597-1603; Kuhle J. et al., Neurology. 2019;92(10):e1007-e1015; Gaiottino J. et al., PLoS One. 2013;8(9):e75091; Morris JR, Lasek RJ, J Cell Biol. 1982 Jan;92(1):192-8; Fuchs E, Cleveland DW, Science. 1998;279(5350):514-519; Bridel C. et al., JAMA Neurol. 2019;76(9):1035-1048 [2] Abdelhak A. et al. JAMA Neurol. 2023;80(12):1317–1325 / Right: Khalil M. et al., Nat Rev Neurol 14, 577–589 (2018) / NfL: neurofilament light; CDW: confirmed disability worsening; PMS: progressive multiple sclerosis

PPMS Patients Treated with Ocrelizumab That Achieved Lower Levels of NfL Had a Lower Risk for Future Disability



Ocrelizumab ORATORIO Study in PPMS as Historical Comparison

- Blood NfL levels re-baselined at Week 48, an optimized cut-off was created between high (H) and low (L) NfL levels
- Patients then followed in continuing double-blind and/or OLE treatment with ocrelizumab, monitored for 24-week CDP over 8 years

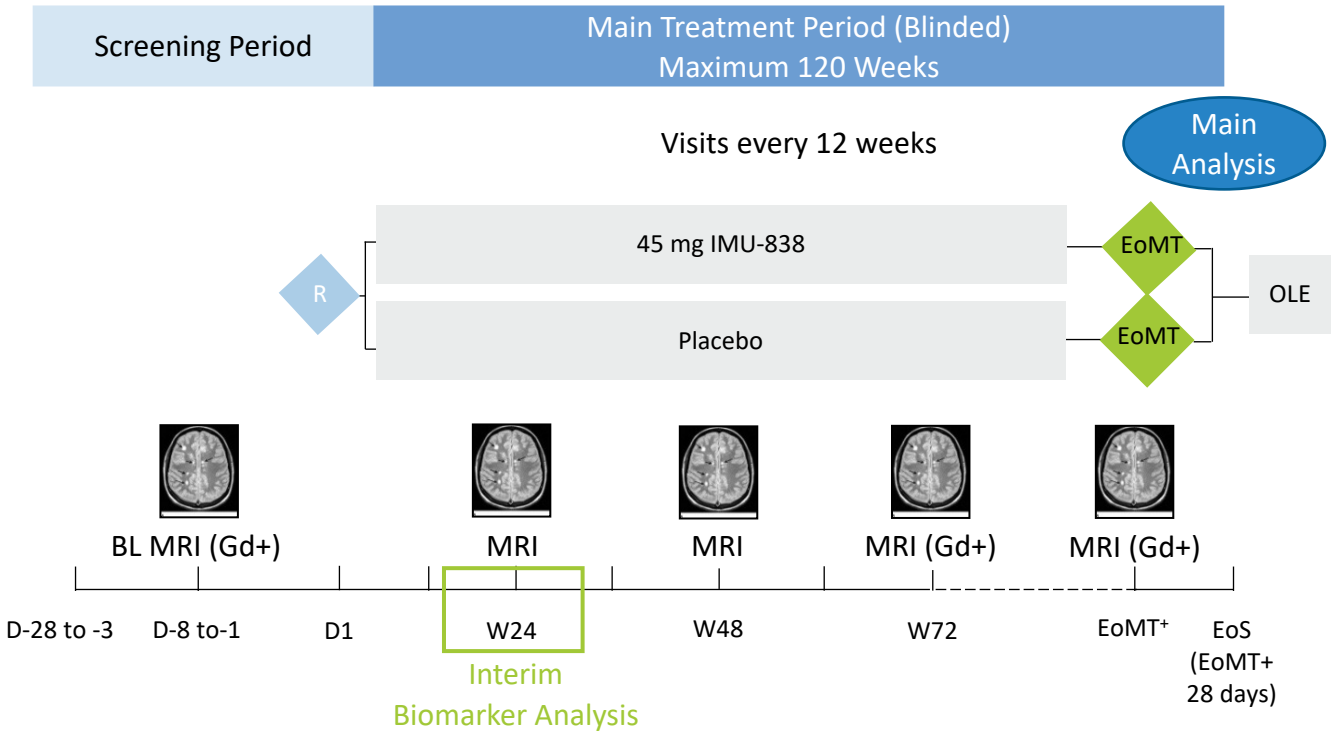
Findings:

- Relationship found between Week 48 blood NfL and risk for subsequent 24-week CDP in PPMS patients
- **Patients with low NfL levels have a lower risk of future disability worsening**

Bar-Or A. et al., EBioMedicine. 2023 Jul;93:104662

PPMS: primary progressive multiple sclerosis; OCR: ocrelizumab; DB: double-blind; OLE: open-label extension; EDSS: Expanded Disability Status Scale; H: high; L: low; pNfL: plasma neurofilament light; sNfL: serum neurofilament light; CDP: confirmed disability progression

CALLIPER: Ongoing Phase 2 Clinical Trial in Progressive Multiple Sclerosis (PMS)



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

- Coordinating Investigator: Robert J. Fox, M.D., Cleveland Clinic
- 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
- Blinded 120-week main treatment period
- Optional, approximately 8-year, open-label extension period

Included Patient Population: Progressive Forms of MS

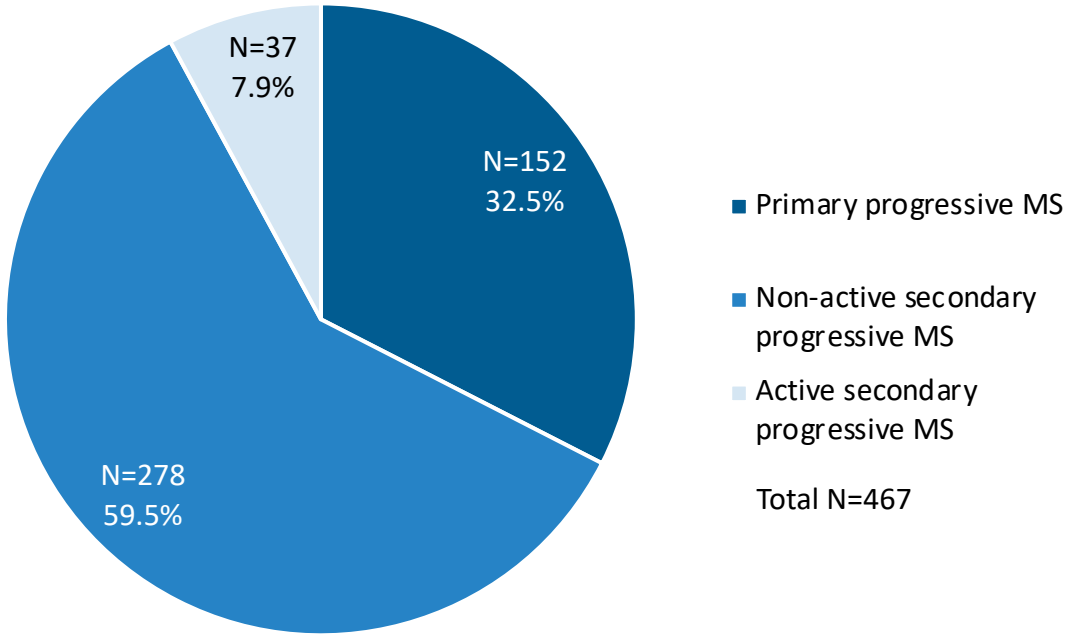
- Adult patients aged 18 to 65 years
- PPMS or SPMS diagnosis (Revised McDonald criteria 2017)
- EDSS score at screening between 3.0 to 6.5
- No evidence of relapse in last 24 months before randomization
- Evidence of disability progression

*NCT05054140 +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; 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

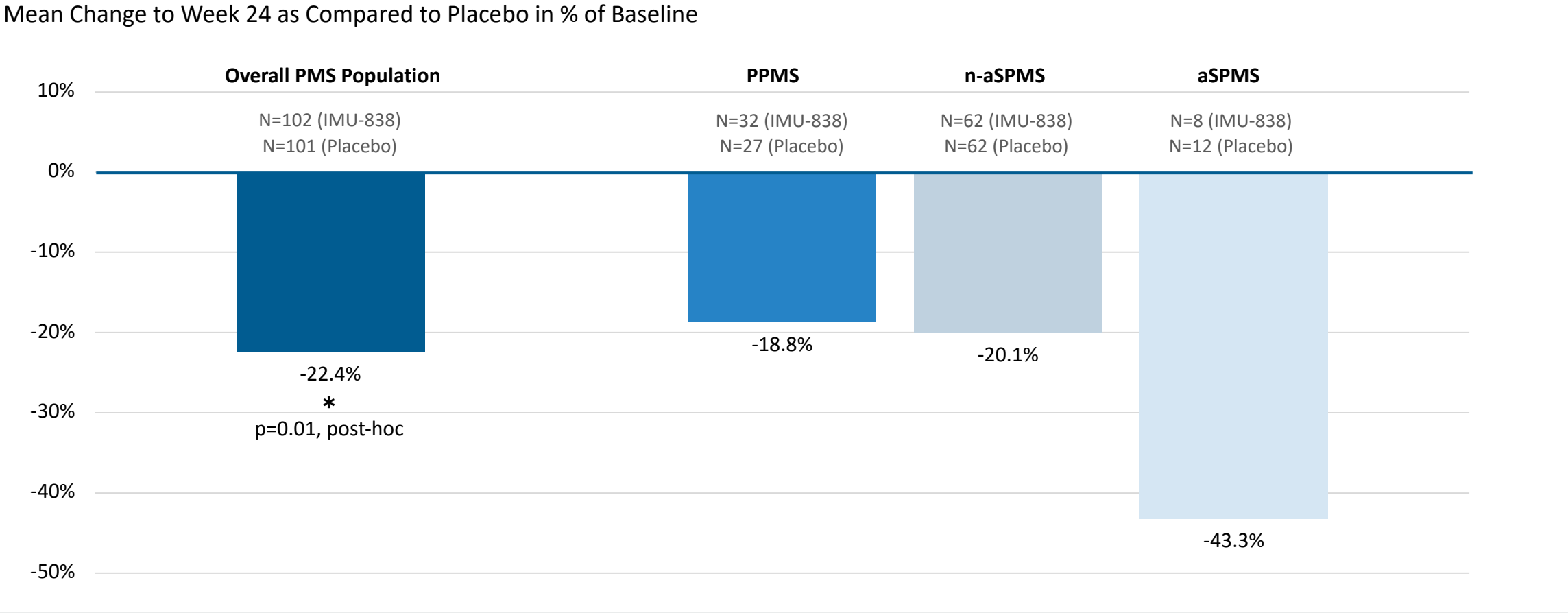


Baseline Characteristics

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)	25.0 [15.8 – 46.6]
SDMT [points], median (min-max)	35.0 [0-180]
EDSS at Visit 1, median (min-max)	5.5 [2.5-6.5]
MS relapses during last 24 months, median (min-max)	0.0 [0-1]

Disease subtype information are used as diagnosis entered by investigator at study entry
BMI: body mass index; SDMT: Symbol Digit Modalities Test; EDSS: Expanded Disability Status Scale

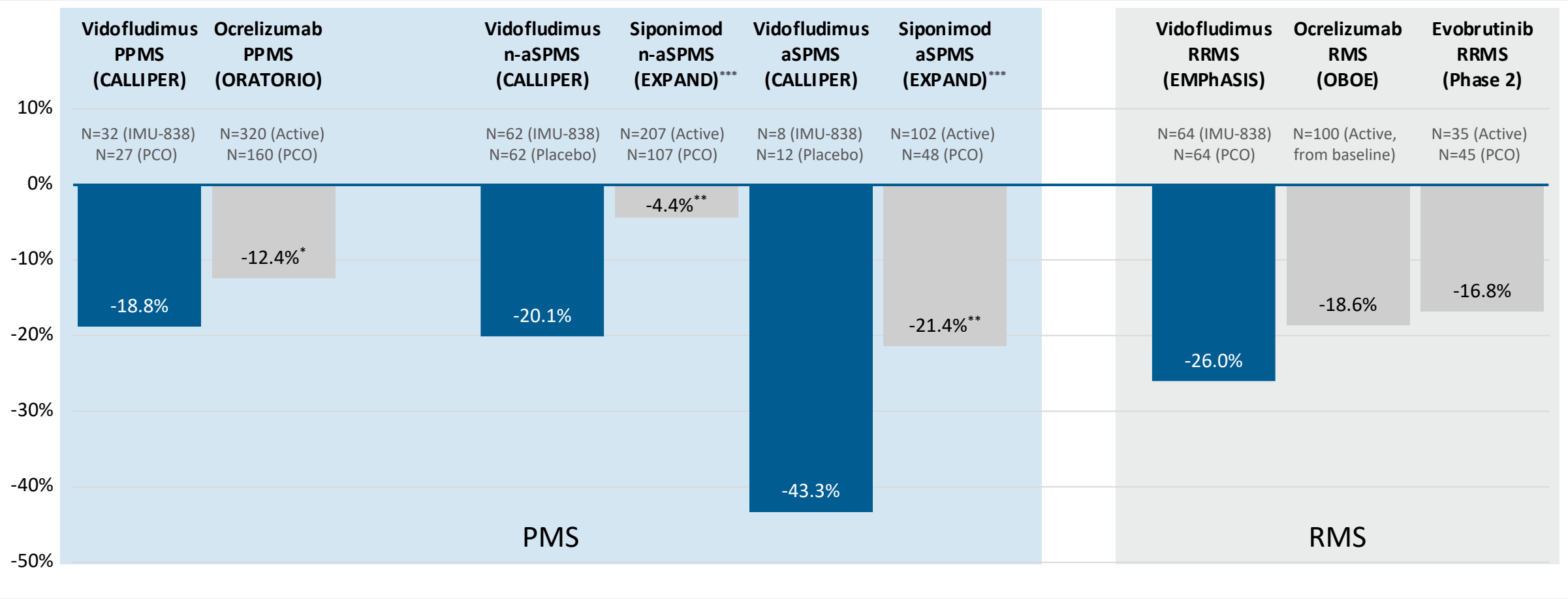
Improvements in Serum NfL for Vidofludimus Calcium Consistent Throughout the Overall PMS Population and All Subtypes



Standard deviation for change from baseline in % of baseline: CALLIPER week 24: IMU-838 35.7%, PPMS: IMU-838 7.1%, n-aSPMS: 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 n-aSPMS designation as per diagnosis by clinical investigator at study entry
RRMS: relapsing-remitting multiple sclerosis; PPMS: primary progressive multiple sclerosis; SPMS: secondary progressive multiple sclerosis; n-a: non-active; a: active

NfL Reduction Compares Favorably with Other MS Therapies

CALLIPER Interim Data Compared to Select Historical Trials



CALLIPER: N = Number of patients in the 45 mg IMU-838 groups, only patients with both baseline and week 24 values considered for change from baseline analysis, arithmetic mean value for group averages; includes all randomized patients with available NfL data at interim analysis
Standard deviation for change from baseline in % of baseline: CALLIPER week 24: IMU-838 35.7%; 95% Hodges-Lehmann confidence bound EMPhASIS week 24 for 45mg IMU-838: lower boundary -41.0%, upper boundary -12.0%
ORATORIO: Bar-Or A. et al., EBioMedicine. 2023 Jul;93:104662; EXPAND: Leppert D., et al., Neurology. 2022 May 24;98(21):e2120-e2131; OBOE: Cross A. et al., Neurology Apr 2019, 92 (15 Supplement) S56.008; evobrutinib: Kuhle J. et al., AAN 2021 Virtual Congress
*plasma NfL levels; ** 12-month data, geometric mean; *** Displayed are data for subpopulation without relapses (n-aSPMS) and with relapses (aSPMS); PCO: placebo; PPMS: primary progressive multiple sclerosis; SPMS: secondary progressive multiple sclerosis; RRMS: relapsing-remitting multiple sclerosis; RMS: relapsing multiple sclerosis; n-a: non-active; a: active

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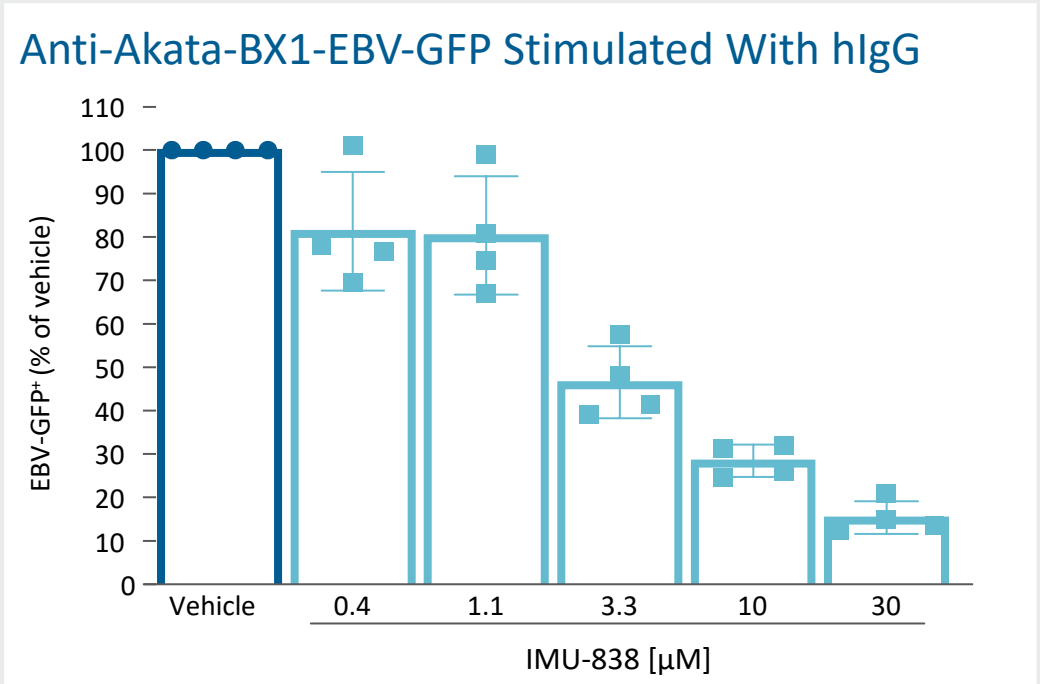
Positive Interim Biomarker Data of Vidofludimus Calcium in Progressive Multiple Sclerosis (PMS)

- 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; brain volume data of the full 467 patients expected in April of 2025
- Results of this interim analysis may inform the ability to potentially reduce PIRA events in the ongoing phase 3 ENSURE program in RMS

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

Showed Concentration-Dependent Anti-EBV Activity



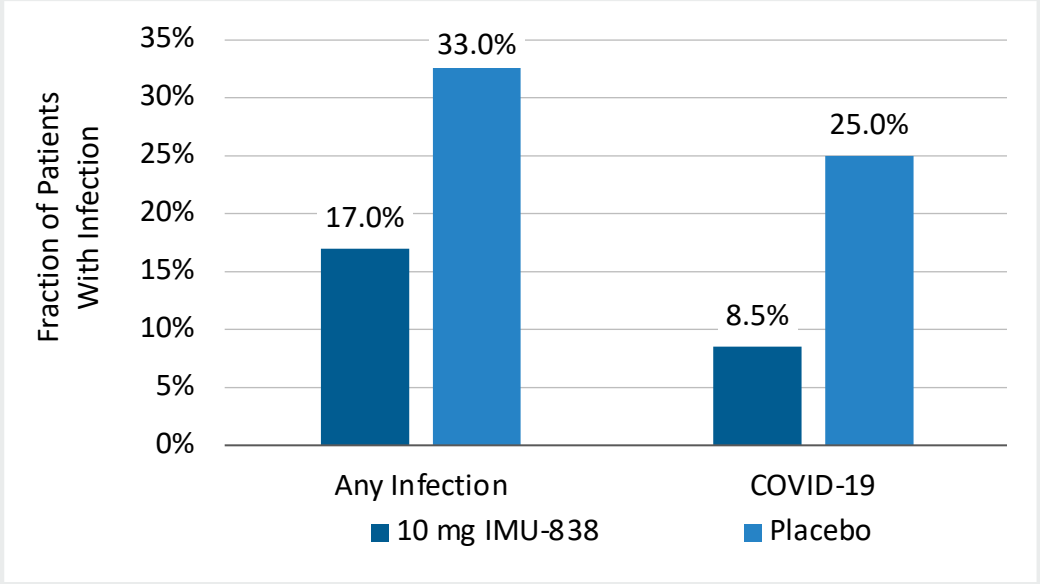
Inhibits Epstein-Barr Virus (EBV) Replication and Reactivation

- Viruses rely on the host cell‘s infrastructure for replication
- Inhibition of DHODH by vidofludimus calcium leads to a depletion of pyrimidine nucleotides that are needed for the
  - Production of viral RNA and DNA (virus genome)
  - And Production of viral proteins (via mRNA)
- By targeting the host cell metabolism, vidofludimus calcium has shown to be active against different RNA and DNA viruses *in vitro* including strong anti-EBV activity

Left: Marschall et al., Poster ECTRIMS 2021 / Right: Eur J Clin Invest. 2020;50:e13366
EBV: Epstein-Barr virus; IgG: immunoglobulin G; (m)RNA: (messenger) ribonucleic acid; DNA: deoxyribonucleic acid

Vidofludimus Calcium Showed Interesting Hints for Clinical Anti-SARS-CoV-2 Activity and Maintaining Humoral Response

Treatment Corresponds with Decreased Number of Opportunistic SARS-CoV-2 Infections



Phase 2 EMPhASIS Trial in RRMS

Number of reported COVID-19 cases in Cohort 2

Treatment Does Not Interfere With Antibody Development During SARS-CoV-2 Infection

	Day 6		Day 14		Day 28	
	IgA	IgG	IgA	IgG	IgA	IgG
Placebo	84%	88%	94%	94%	97%	99%
Vidofludimus Calcium	86%	93%	97%	97%	95%	100%

Phase 2 CALVID-1 Trial in COVID-19

Proportion of patients with anti-SARS-CoV-2 IgA or IgG antibodies

COVID-19: coronavirus disease 2019; SARS-CoV-2: severe acute respiratory syndrome coronavirus; RRMS: relapsing-remitting multiple sclerosis; QD: quaque die = once-daily; IgA: immunoglobulin A; IgG: immunoglobulin G

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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 more than 1,800 human subjects and patients, to date
- Low rates of adverse events
- No signals for hepatotoxicity or elevations of liver enzymes and no Hy's law cases observed

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 Trial: 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

Immunic THERAPEUTICS

Straightforward Approval Strategy in Multiple Sclerosis

Enables Clear Demonstration of Effect on Smoldering MS

Phase 3 ENSURE Program in RMS[1]

- Two identical pivotal trials in RMS patients
- Goal: Low risk clinical program for regulatory approval of vidofludimus calcium
- Dosage: 30 mg vidofludimus calcium QD

Phase 2 CALLIPER Trial in PMS[2]

- Phase 2 trial in PMS patients
- Goal: Demonstrate vidofludimus calcium's potential for neuroprotective activity in a non-relapse setting
- Dosage: 45 mg vidofludimus calcium QD

Intended to Provide a Straightforward Path Towards Potential Regulatory Approval:

- Immunic believes that the phase 3 ENSURE program provides a straight-forward path towards regulatory approval of vidofludimus calcium in RMS.
- CALLIPER is designed to corroborate vidofludimus calcium's neuroprotective potential to support the drug's unique profile.

[1] ClinicalTrials.gov: NCT05134441 & NCT05201638; [2] ClinicalTrials.gov: NCT05054140
RMS: relapsing multiple sclerosis; PMS: progressive multiple sclerosis; QD: quaque die = once-daily

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ENSURE Program: Ongoing Pivotal Phase 3 Trials in RMS
NCT05134441 & NCT05201638

Coordinating Investigator

Robert J. Fox, M.D.
Cleveland Clinic

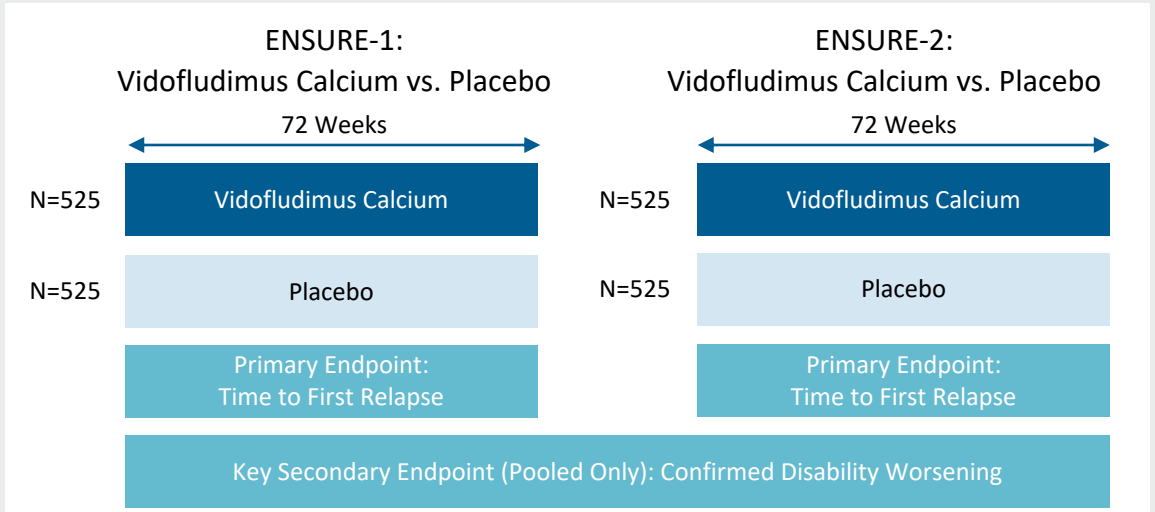
Included Patient Population: Relapsing Forms of MS

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

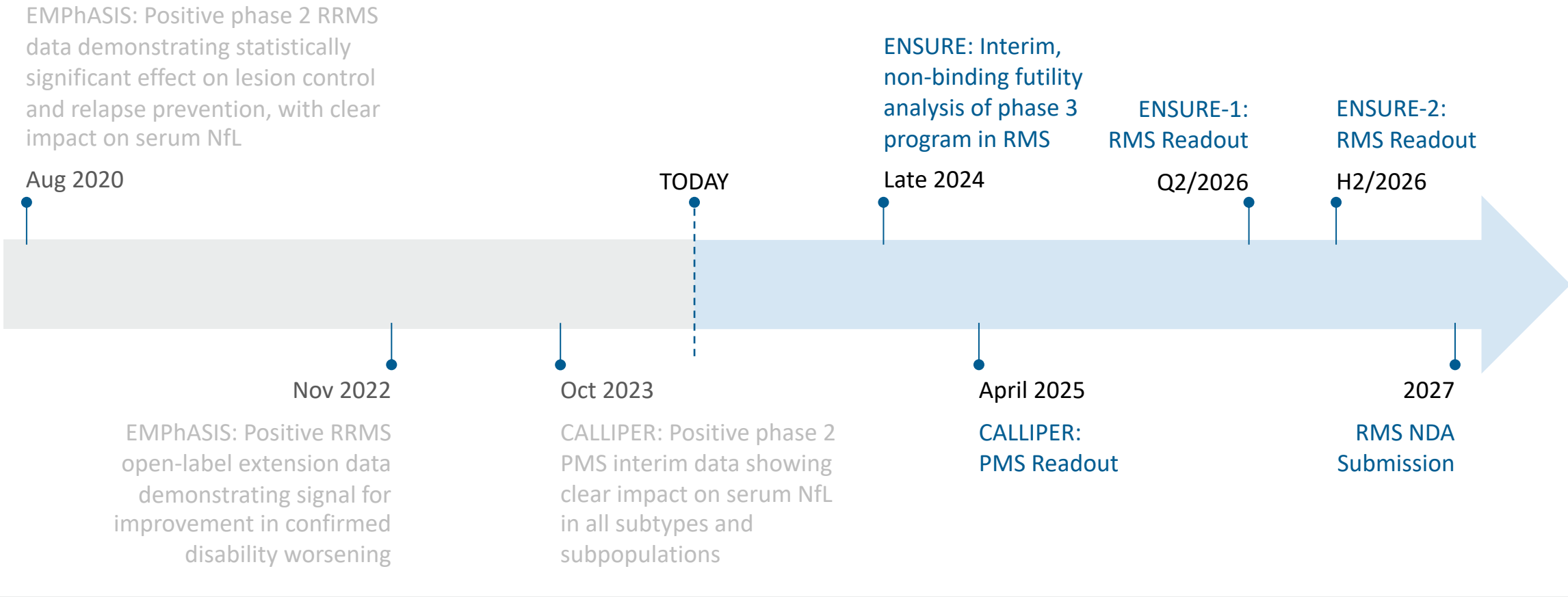
Lublin FD, et al. Neurology. 2014;83(3):278-286
EDSS: Expanded Disability Status Scale; QD: quaque die = once-daily

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



Vidofludimus Calcium in MS: Consistent and Differentiated Results to Date Support Straightforward Path Towards Potential Regulatory Approvals

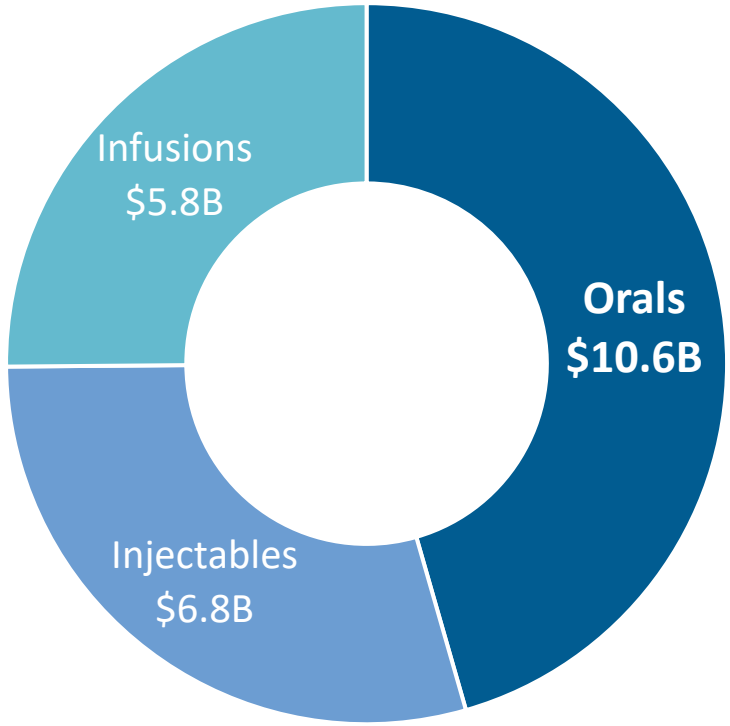


Although we currently believe that each of these goals is achievable, they are each dependent on numerous factors, most of which are not under our direct control and can be difficult to predict. We plan to periodically review this assessment and provide updates of material changes as appropriate. / MS: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

Immunic THERAPEUTICS

The Global MS Market Exceeds $23B in Annual Sales, With $1B+ Contributions from Multiple Brands

Oral Drugs Represent Most Significant Share of Total Sales in Major Territories (2020)



Most brands are generating in excess of $1 billion in global annual sales in 2022, with most sales coming from the U.S.

- Ocrevus® – $6.3 billion
- Aubagio® – $2.1 billion
- Gilenya® – $2.0 billion
- Tysabri® – $2.0 billion
- Tecfidera® & Vumerity® – $1.9 billion
- Avonex® & Plegridy® – $1.3 billion
- Kesimpta® – $1.1 billion
- Rebif® – $933 million

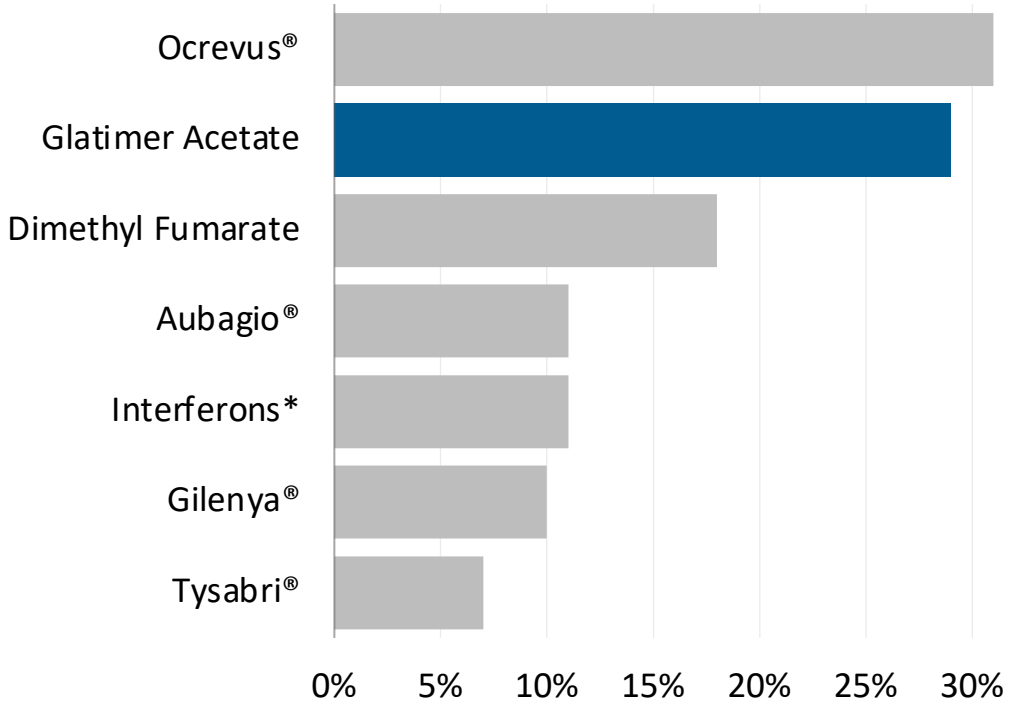
* Sales numbers in G7 countries (US, UK, Canada, Japan, Germany, France, Italy) in USD billion; S1P: sphingosine-1-phosphate
Source: Multiple Sclerosis Landscape and Forecast by Decision Resources Group Part of Clarivate

Claims Analysis Evidences That Significant Proportion of the MS Patient Population Prioritizes Safety Over Efficacy

- Despite only 34% prevention of relapses at two years, glatiramer acetate is the second most commonly used DMT
- Patient choice of other options comes with harmful tradeoffs:
  - Loss of immunity, B cells
  - PML risk, infections, cancer
  - High adverse event rates
  - Monitoring requirements
  - Tolerability challenges

Claims Analysis Over Most Recent Three Years

Percent of Patients Exposed to Each DMT



Patient treatment exposure data based on proprietary research performed in partnership with Trinity Partners & utilizing Komodo Health claims data analysis, 2022. All % of patients without relapses at 2 years provided per product labels. *Interferons share of patients treated includes combined Avonex® and Rebif®-treated patients. DMT: disease modifying therapy, PML: progressive multifocal leukoencephalopathy

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The Unmet Needs in MS Encompasses Multiple Patient Segments

725,000 US diagnosed MS patients[1]
Multiple opportunities to address unmet needs of patients

Market Opportunity

$10 B

$1 B

Risk intolerant patients

Raise efficacy standard for established segment

- ~30% of treated patients still choosing glatiramer acetate (worst efficacy of all DMTs)[2]

Patients who need alternatives

MoA to match MS pathophysiology

- Numerous shortcomings exist with existing DMTs for 30% of patients[2]
- Treatment switches common

Patients with progressive disease

Address disability progression

- Biomarker impact rivals Ocrevus® (only DMT with label for primary progressive patients)
- Disability progression remains largest unmet need

Untreated patients

Increase treatment rate

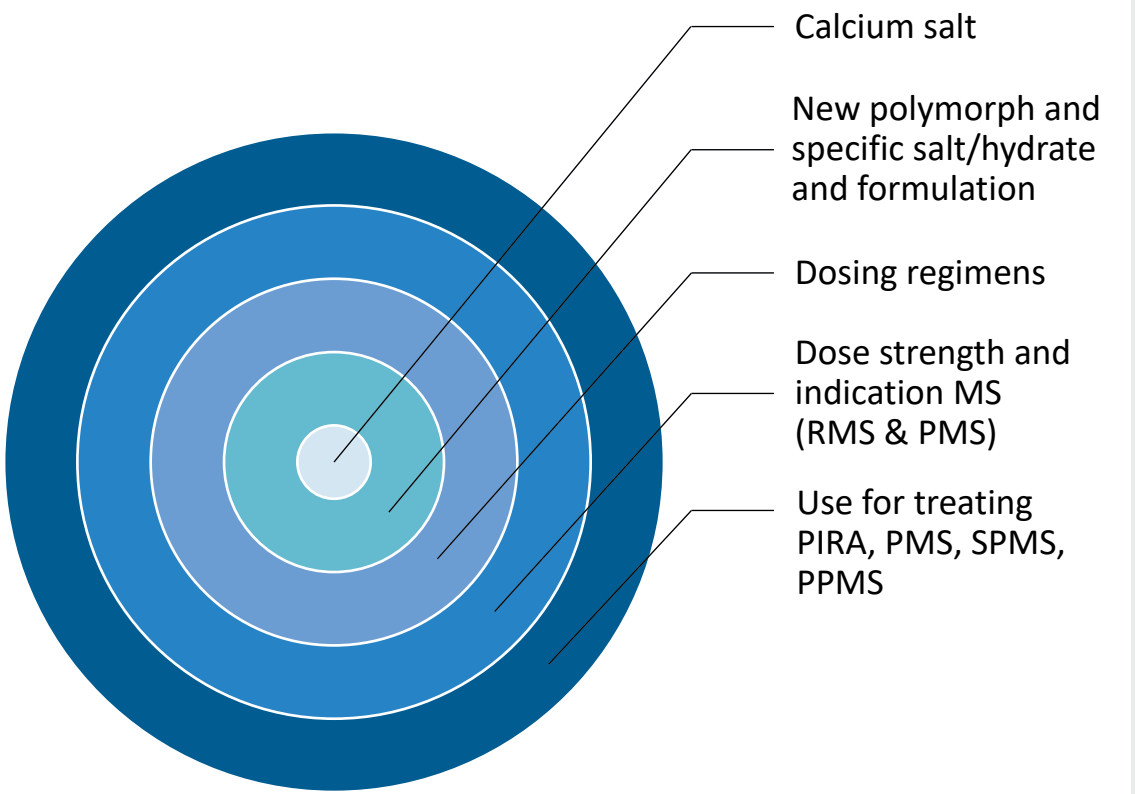
- ~50% of patients with MS do not receive DMT treatment[2,3]

Evidence Supporting Commercial Potential

Completed phase 2 trial (EMPhASIS) & ongoing phase 3 program (ENSURE)	Progressive MS trial (CALLIPER)	Full data package

[1] Company estimates leveraging Briggs, F. B., & Hill, E. (2019). Multiple Sclerosis Journal & Wallin, M. T., Culpepper, W. J., Campbell, J. D., Nelson, L. M., Langer-Gould, A., Marrie, R. A., & Buka, S. L. (2019). Neurology, 92(10), e1029-e1040
[2] Proprietary research performed in 2022 in partnership with Trinity Partners and utilizing Komodo Health claims data analysis [3] Fox RJ, Cosenza C, Cripps L, Ford P, Mercer M, Natarajan S, Salter A, Tyry T, Cofield SS. Neurology. 2019 Apr 2;92(14):e1634-e1642
DMT: disease modifying therapy; MoA: mode of action; B: billion

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 allowed 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 PMS and 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 Targeted to Elevate the Standard of Care With a Holistic Solution for the Full Spectrum of MS Patients

Phase 3 program of vidofludimus calcium in RMS ongoing based on **excellent clinical data** package

→

- Strong effect on all relevant endpoints in 268 RRMS patients, including anti-inflammatory and neuroprotective effects
- Unrivaled safety, to date, with over 1,800 individuals treated

Third-party data clearly highlights the unmet need of **preventing disability progression**, with relapse-independent disease progression being dominant even in early RRMS

→

- The understanding of MS has evolved, with evidence showing a smoldering disease that is connected to Epstein-Barr virus and subsequent inflammation & neurodegeneration

Vidofludimus calcium selectively manages all three components needed to **quell smoldering MS**

→

- Neuroprotective effects
- Anti-inflammatory effects
- Anti-viral effects

Large market opportunity exists for a therapy that can holistically and sustainably address patients' needs

→

- Even current market leaders only optimize for one feature
- Current treatment options have serious tolerability downsides

RMS: relapsing multiple sclerosis; RRMS: relapsing-remitting multiple sclerosis

Immunic THERAPEUTICS

IMU-856

Restoring a Healthy Gut through Renewal of the Bowel Wall

IMU-856 Could Be the Perfect New Solution for Treating Gastrointestinal Disorders Without Harming the Immune System

- Innovative oral therapeutic approach applicable to a broad range of gastrointestinal disorders
- Targets physiological intestinal epithelial regeneration
- Achieves gut wall healing without immunosuppression

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IMU-856 Uniquely Suited for Potential Use in a Broad Spectrum of Serious Gastrointestinal Diseases

Demonstrated clinical proof-of-concept: Positive effects shown in a phase 1b clinical trial on **gastrointestinal architecture and function** applicable to multiple diseases with histological damage

Celiac Disease
>2 million patients[1]

- High unmet medical need, currently no approved drugs
- Phase 2 trial to demonstrate histological and functional improvement in patients with ongoing active celiac disease

Inflammatory Bowel Disease
>1 million patients[2]

- Potential synergies in combination with IL-23 or anti-integrin treatments to break efficacy ceiling

Short Bowel Syndrome
High-value orphan indication

- High unmet medical need indication with large commercial potential
- Potential for rapid assessment in a small study

[1] https://www.niddk.nih.gov/health-information/digestive-diseases/celiac-disease/definition-facts [2] Lewis JD, et al. Gastroenterology. 2023;165(5):1197-1205.e2

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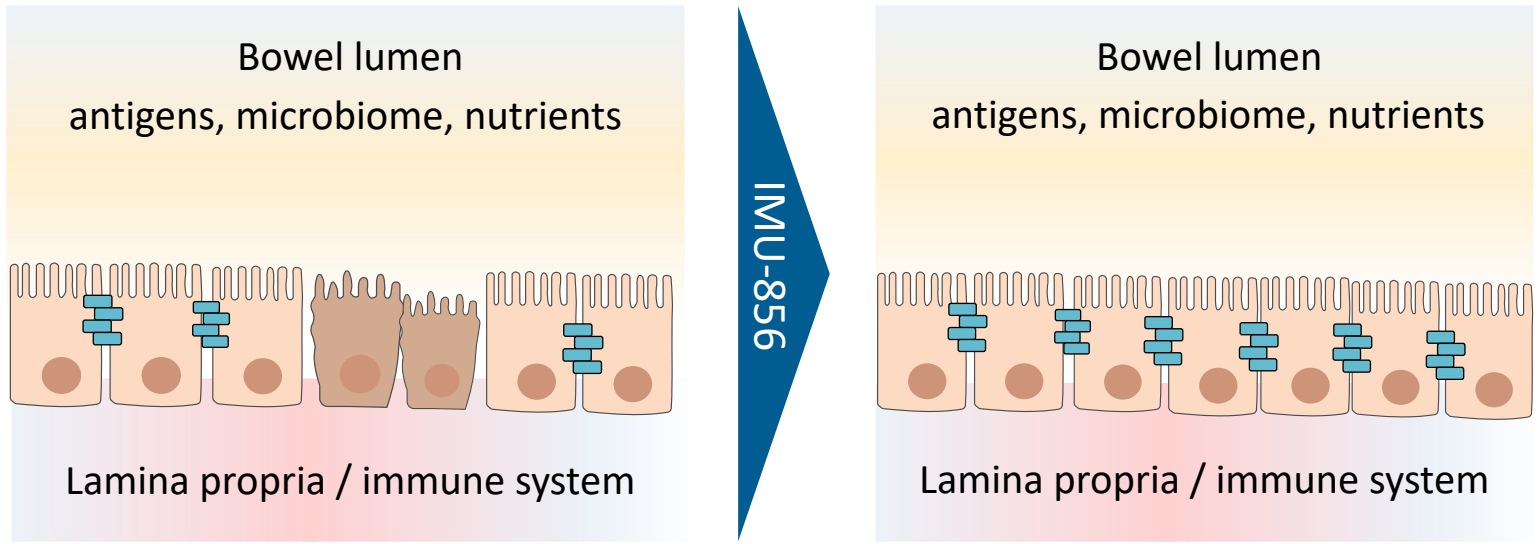
Once-Daily, Oral IMU-856 Aims to Regenerate the Gut Wall and Barrier Function by a New Innovative Targeted Mechanism



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

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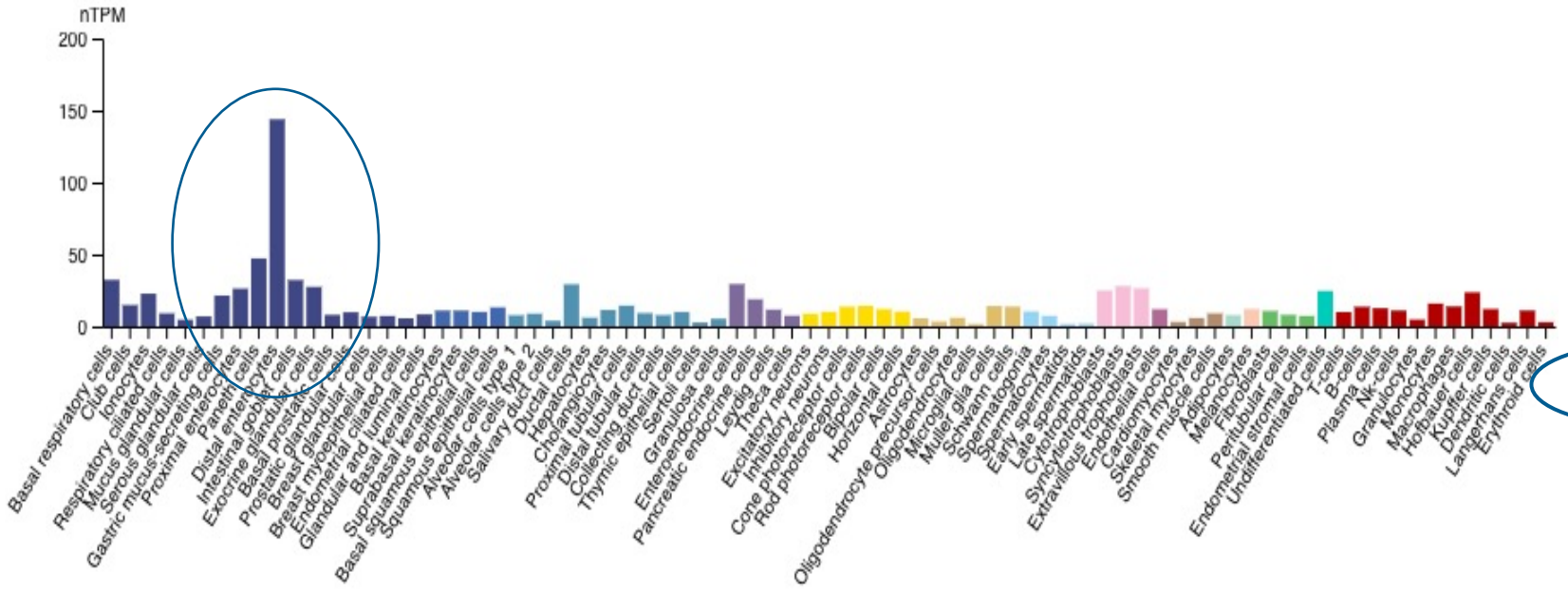
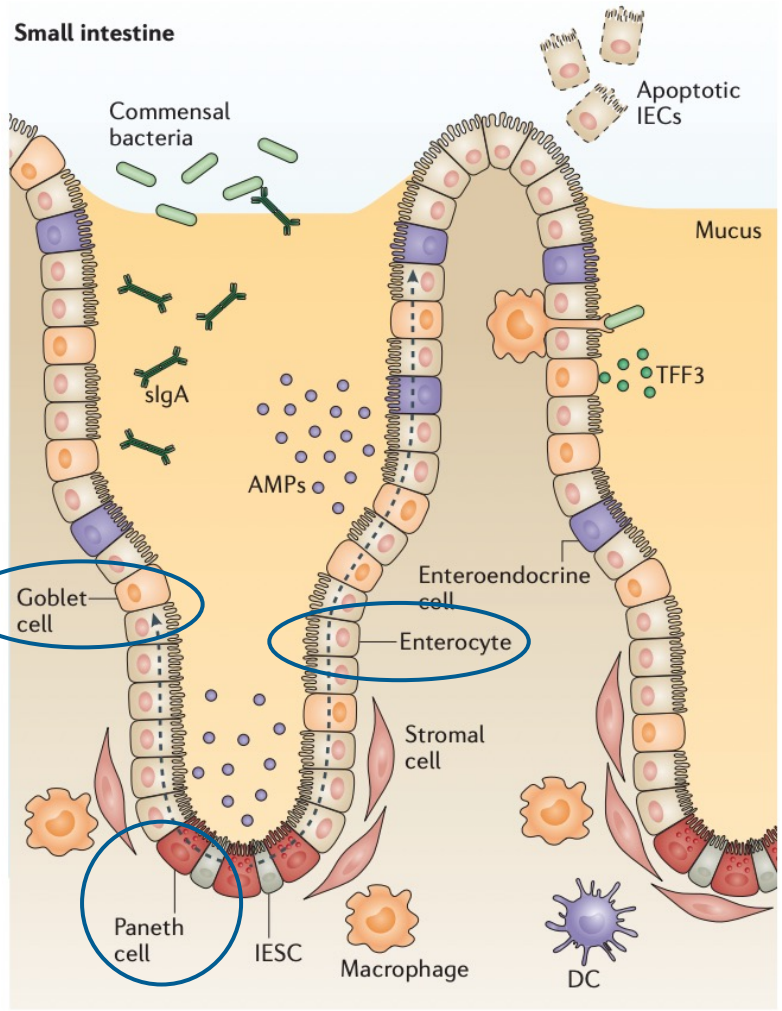
SIRT6 Target Is Selectively Expressed in Gut Epithelial Cells

Highest mRNA Expressions in Paneth Cells, Enterocytes and Goblet Cells





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

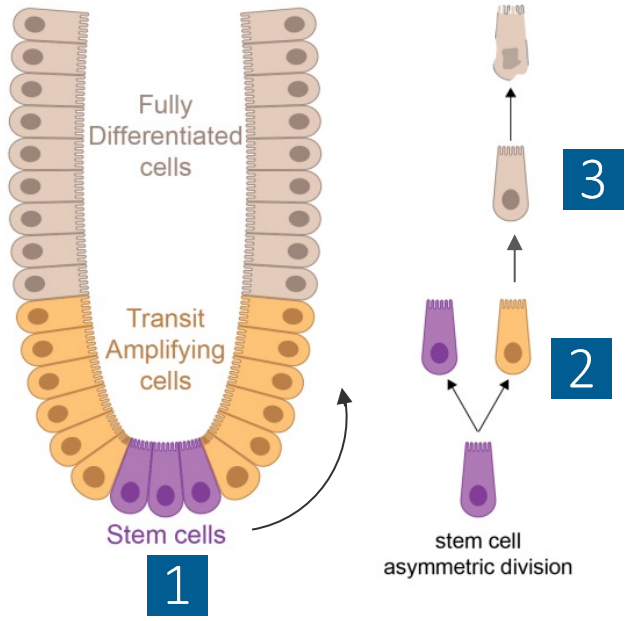
IMU-856 Enhances the Natural Regenerative Process in the Gut

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

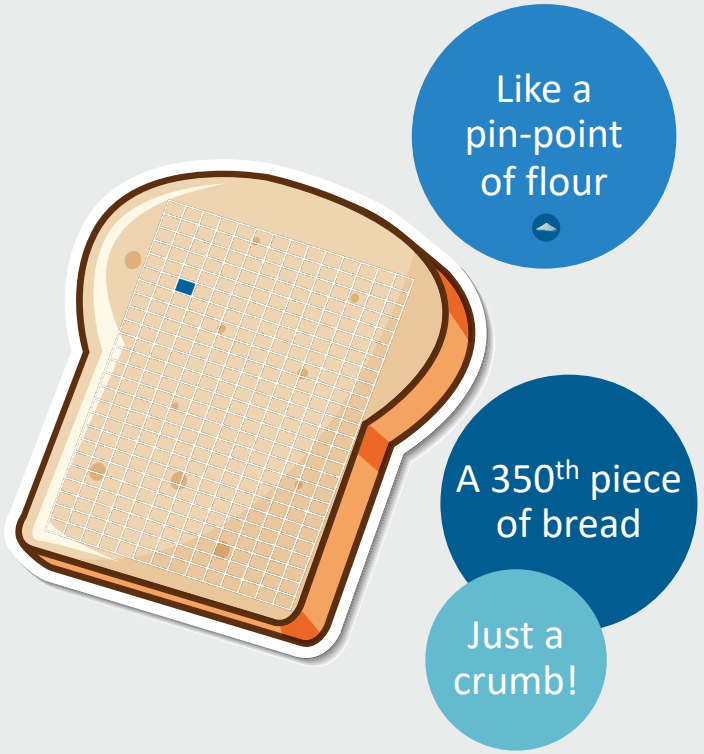


Adapted from Mamis et al., 2023, cbioRxiv

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)

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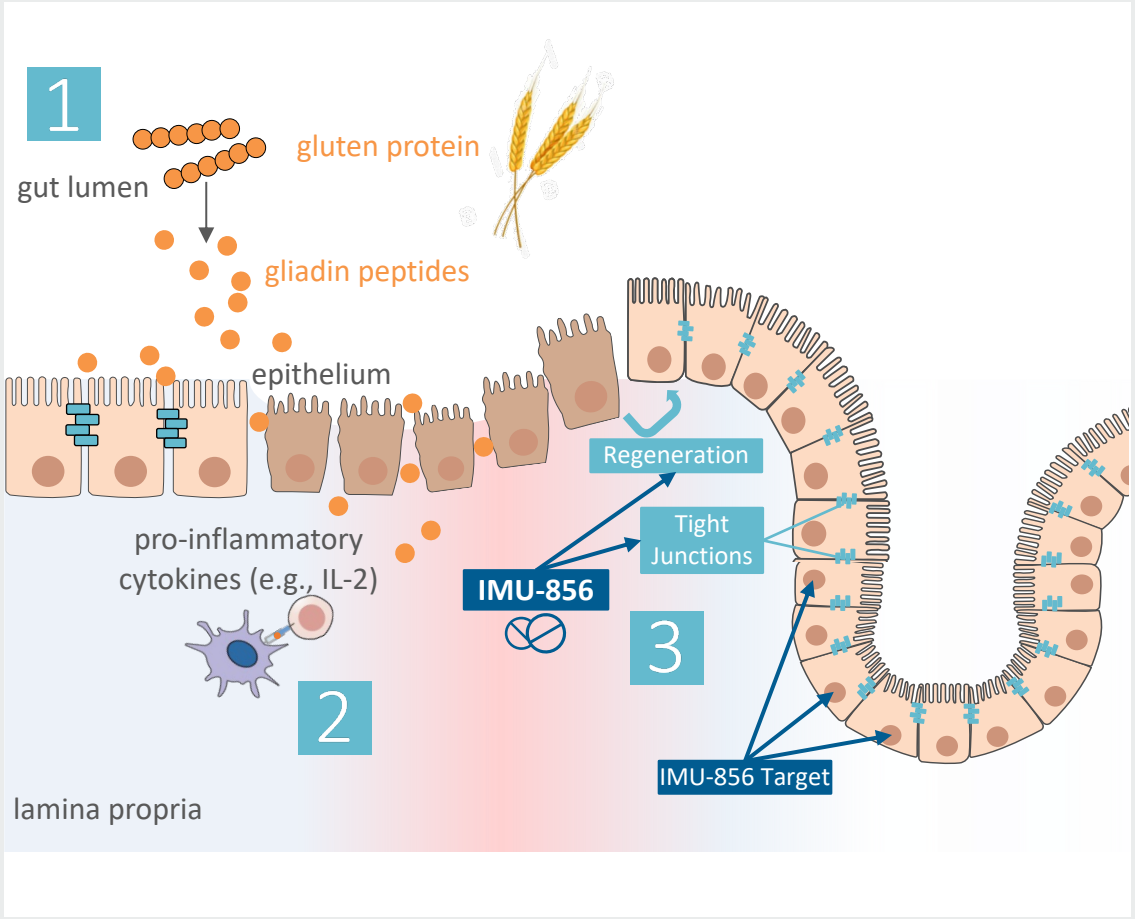
First Proof-of-Concept for Gastrointestinal Disorders in Celiac Disease

Celiac Disease is a Serious Life-Long Disease



Celiac disease is a **multifactorial, complex autoimmune disease** caused by an immune reaction against a degradation product of gluten and is strongly associated with **specific HLA class II gene variants** (HLA-DQ2 and -DQ8)[1]

1
- Gluten is degraded into **gliadin peptides** which are taken up by the bowel epithelium (trans- or paracellular)

2
- In patients with a specific HLA protein (DQ2 and DQ8) composition, deaminated gliadin (by TG2) is recognized by CD4+ T cells and can trigger an immune response which leads upon continued gliadin uptake to
  - **Increased intestinal permeability**
  - **Epithelial and mucosal damage** with negative changes of the gut architecture, including villous atrophy leading to malabsorption of nutrients

3
- Hypothesis for IMU-856's mode of action:
  - Restores villous architecture by triggering regenerative processes of the epithelial lining
  - Improves intestinal barrier function

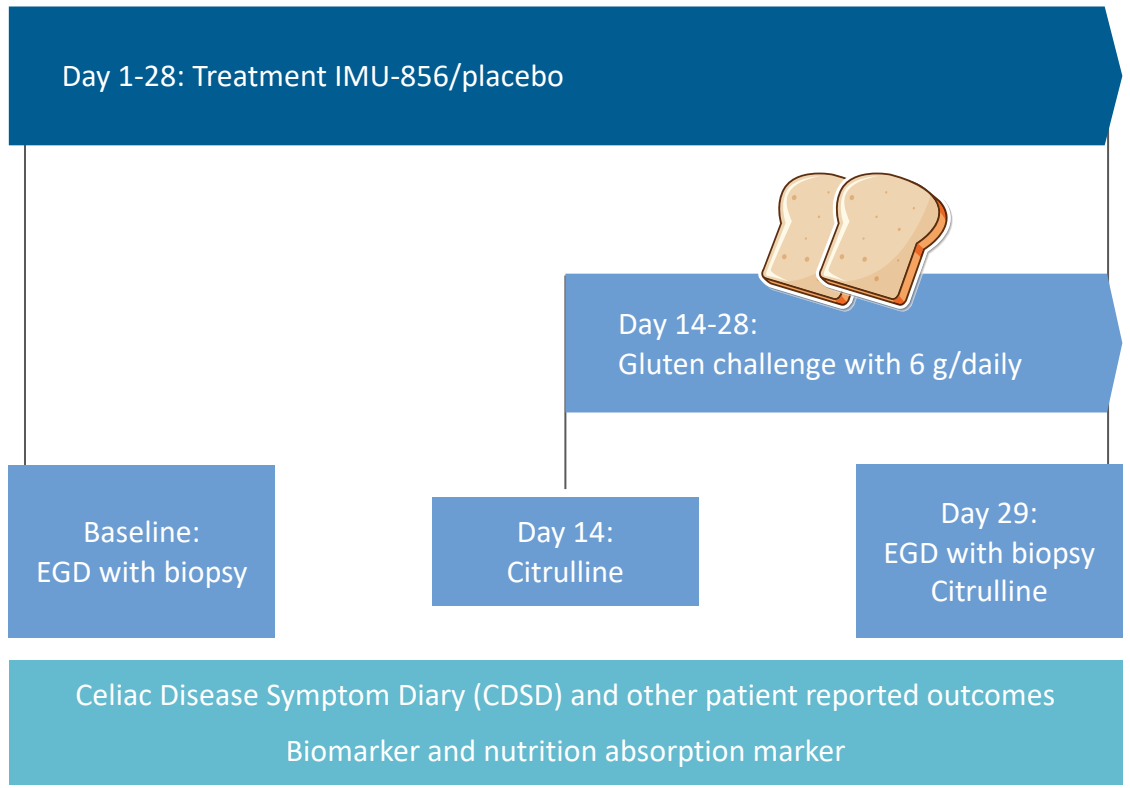
Picture: self-drawn; [1] Caio et al. BMC Medicine (2019) 17:142
HLA: human leukocyte antigen; TG2: tissue transglutaminase 2; CD: cluster of differentiation; IL: interleukin

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

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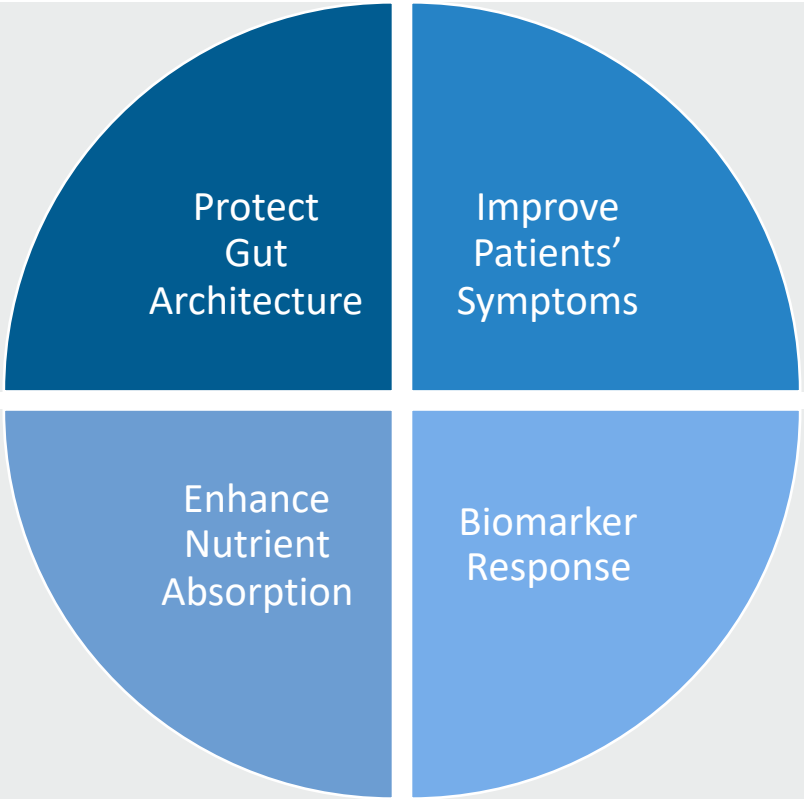
IMU-856 Showed Positive Effects in Four Main Dimensions of Clinical Outcome in Celiac Disease Patients

IMU-856 effectively protected against gluten-induced intestinal damage, as measured by villous height



IMU-856 reduced/reversed gluten-induced symptoms reported by patients

IMU-856 restored villi absorptive function resulting in improved uptake of nutrients such as vitamin B12 and zinc

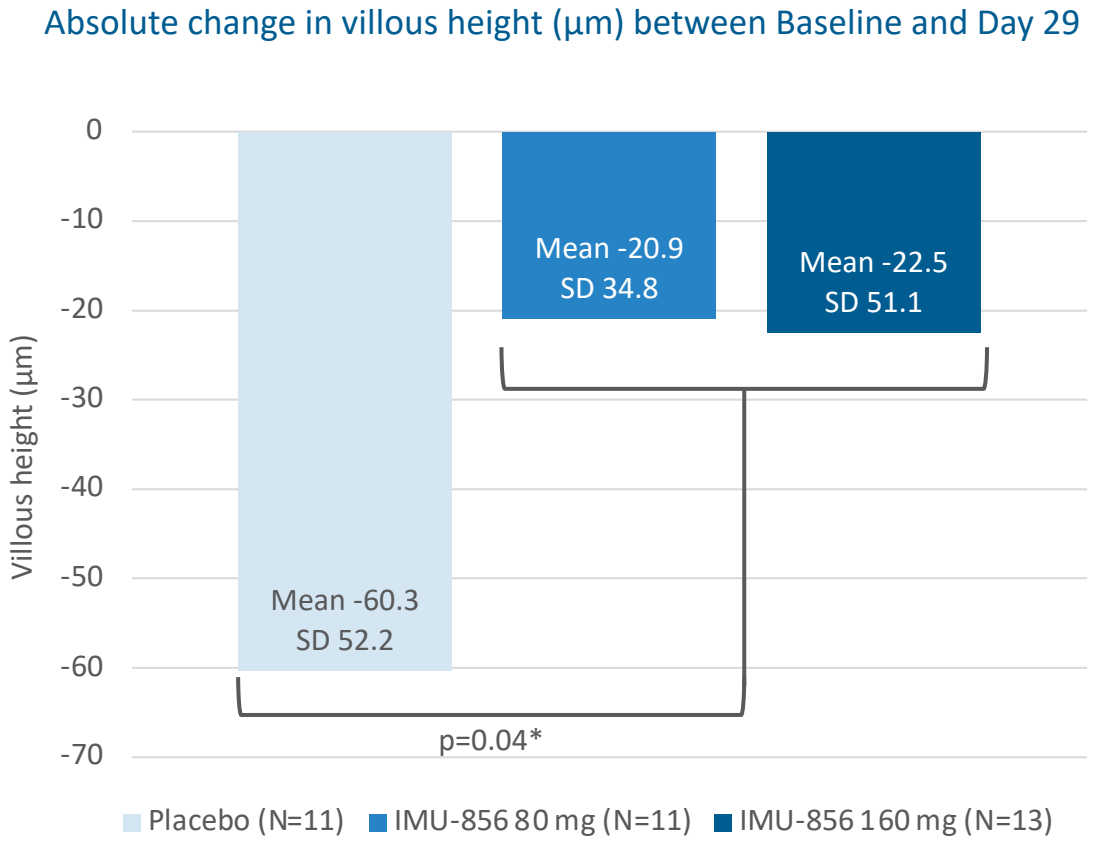
IMU-856 improved blood biomarker such as citrulline levels

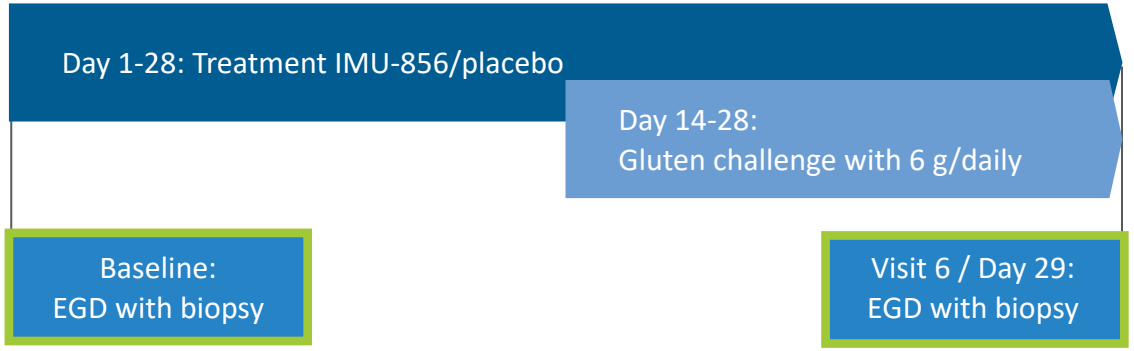
All these effects achieved without any known or observed suppression of the immune system

IMU-856 was observed to be safe and well-tolerated in this trial

Immunic THERAPEUTICS

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



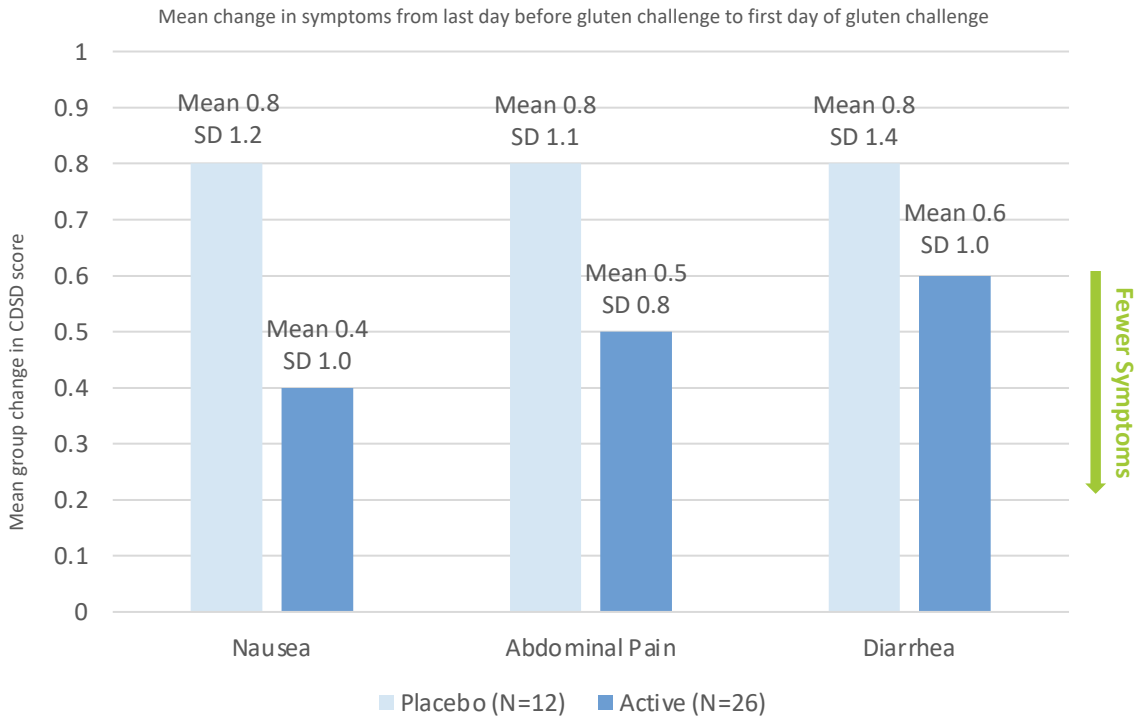


- Substantial protection for IMU-856 treatment groups as compared to placebo
- Reached statistical significance* for this objective readout which is known to be relevant to influence future medical complications of celiac disease
- Assessed by central pathology laboratory and blinded pathology reader

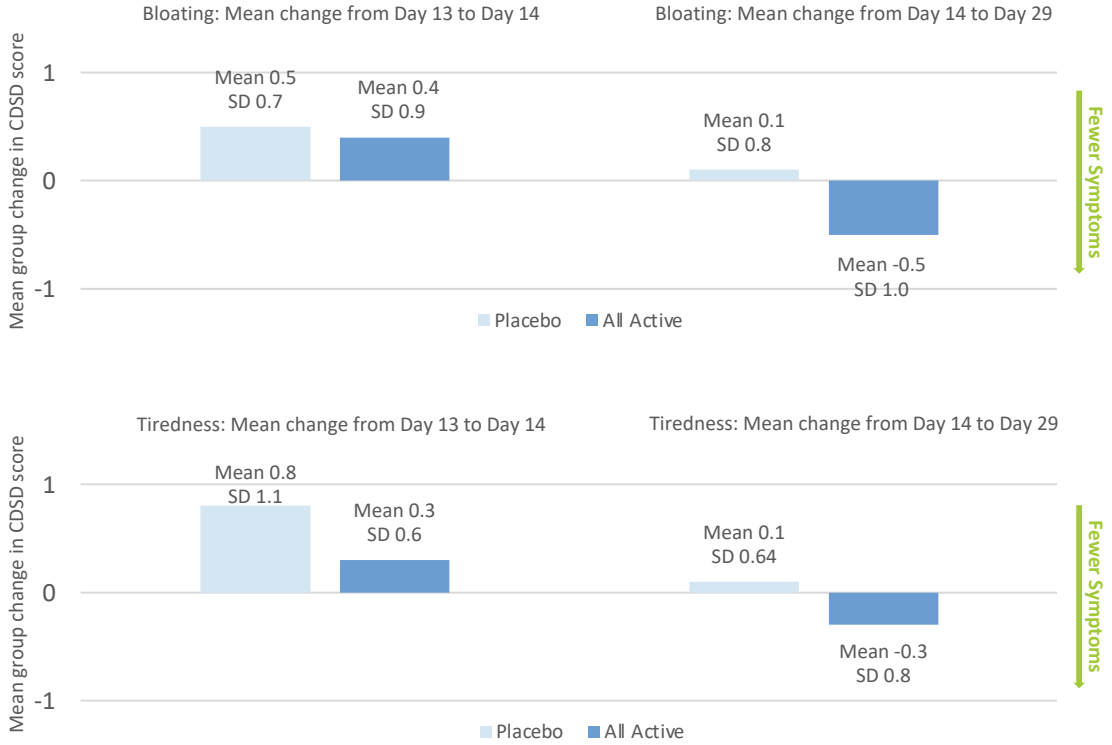
* Wilcoxon Two-Sample Test comparison between pooled IMU-856 groups and placebo, performed as post-hoc exploratory statistical analysis
Disease Analysis Set: N=35/43 included in histology analysis set. 8 patients not included in this analysis due to early termination. Gluten Challenge for 15 days with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

IMU-856 Suppressed Acute and Chronic Symptoms After Gluten Challenge

IMU-856 Treated Patients Had Fewer Symptoms After First Day of Gluten Challenge Than Placebo Patients (on Day 14)



IMU-856 Treated Patients Recovered From Bloating and Tiredness Symptoms on Continued Treatment During Gluten Challenge



Assessed via Celiac Disease Symptom Diary (CDSD); Day 13: Last day before Gluten Challenge. Day 14: First Day of Gluten Challenge. Day 29: First Day after Completion of Gluten Challenge
Fewer symptoms includes either less patients with symptoms or less severity of symptoms; SD: standard deviation

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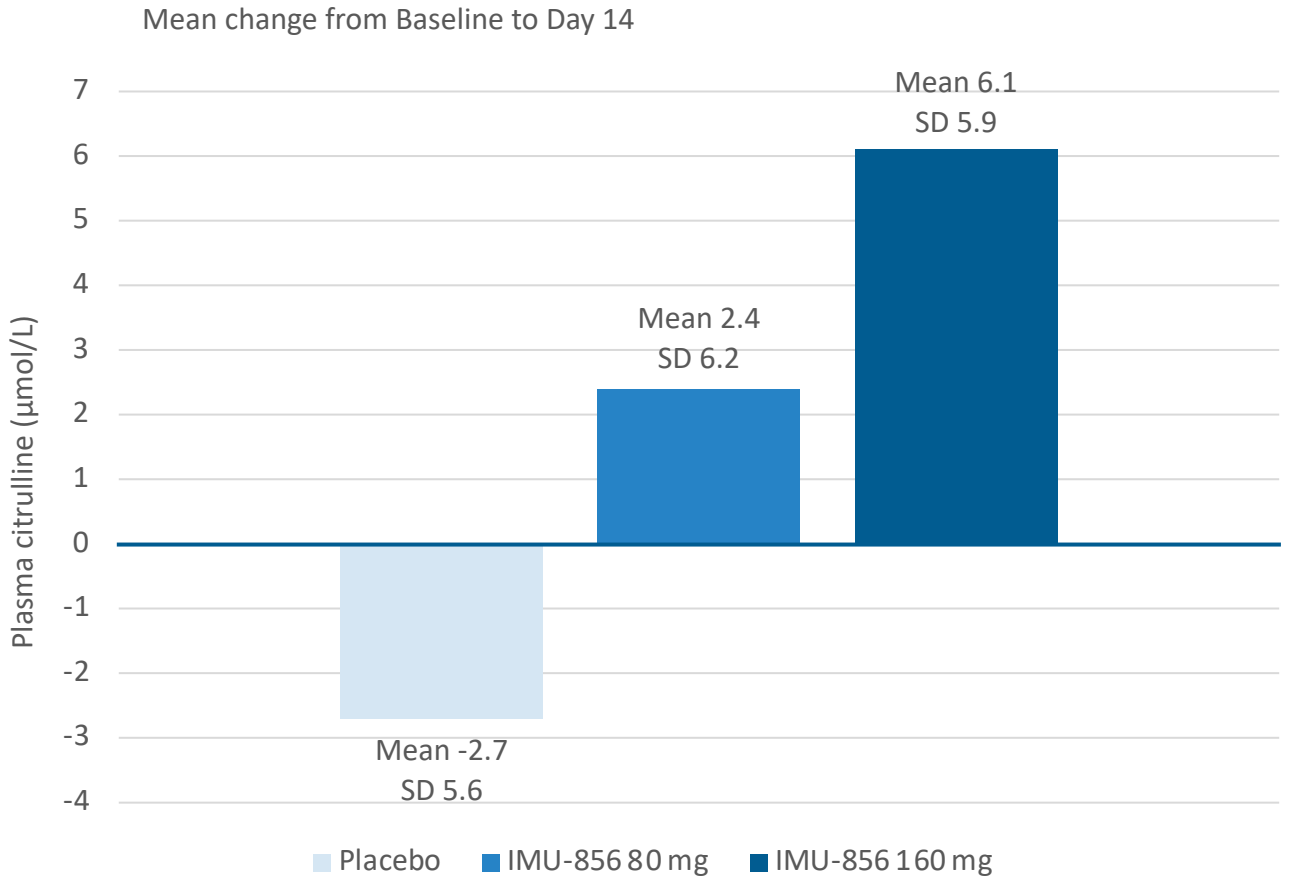
IMU-856 Showed Signal for Improved Citrulline Levels

Biomarker Reflecting the Overall Mass and Function of Enterocytes



Plasma citrulline levels are known to be related to intestinal epithelial mass and function[1]

- Citrulline levels increase with improvement of enteropathy[2]
- IMU-856 increased citrulline levels dose proportionally (despite gluten challenge), whereas being reduced in placebo patients

[1] Singh et al., J. Clin. Med. 2019, 8, 885; doi:10.3390/jcm8060885 [2] Fragkos et al., United Eur. Gastroenterol. J. 2018, 6, 181–191 &/ Number of Patients: Placebo: N=13 for Mean Change Baseline to Day 14, N=11 for Mean Change Baseline to Day 29; IMU-856 80 mg: N=14 for Mean Change Baseline to Day 14, N=11 for Mean Change Baseline to Day 29; IMU-856 160 mg: N=13 for Mean Change Baseline to Day 14, N=13 for Mean Change Baseline to Day 29; SD: standard deviation

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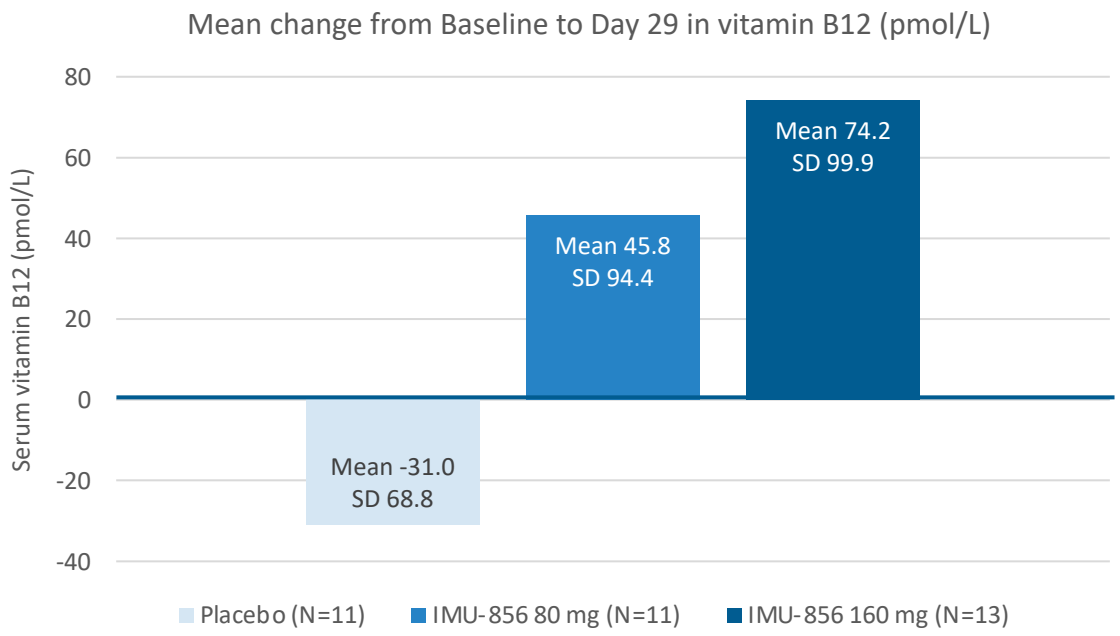
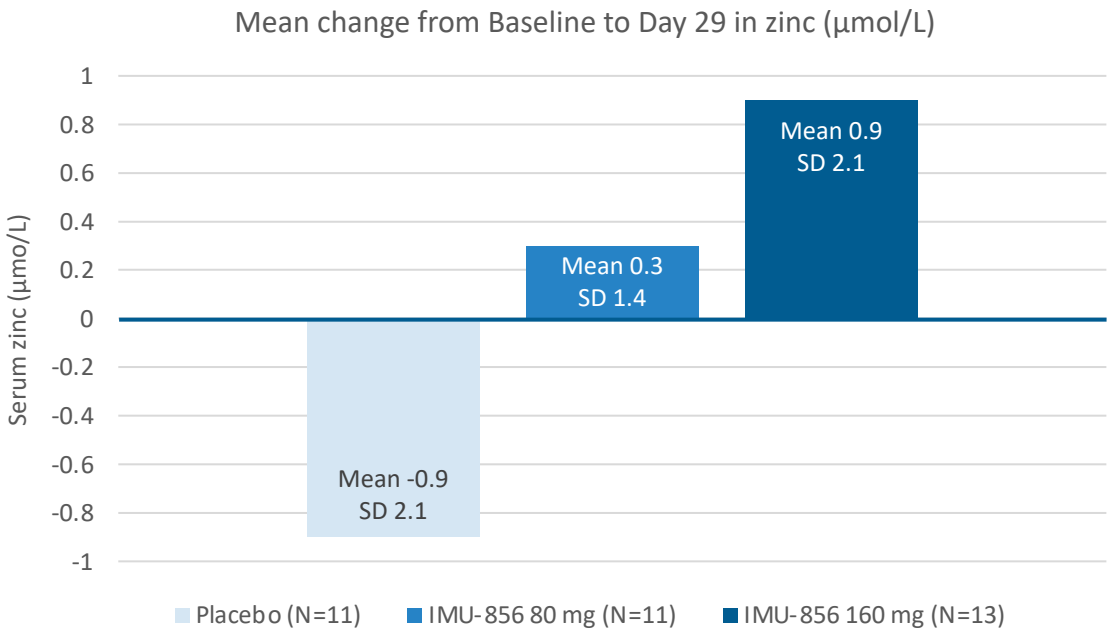
IMU-856 Treatment Resulted in Enhanced Uptake of Actively Transported Essential Nutrients Vitamin B12 and Zinc

Vitamin B12



Zinc



SD: standard deviation

IMU-856 Could Become a Game Changer for the Treatment of Gastrointestinal Disorders

- IMU-856 is poised to be a **potential paradigm shift** in how to treat gastrointestinal diseases.
- Dozens of endpoints were investigated in this proof-of-concept trial and all demonstrated that **IMU-856 has a beneficial effect** in the treated celiac disease patients.
- IMU-856 was shown to be **safe and well-tolerated** in this trial.
- Immunic is **preparing clinical phase 2 testing** of IMU-856 in ongoing active celiac disease.
- IMU-856 has the potential for broad development where renewal of the gut wall is important; **multiple indications** are under evaluation.

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Immunic Therapeutics

Summary

Summary: Advanced Pipeline of Next-Generation Oral Therapies

Advanced clinical pipeline:

well-differentiated investigational medicines in various phases of clinical development

RMS phase 3 program of vidofludimus calcium ongoing

intended to provide a straightforward path towards regulatory approval

PMS phase 2 trial of vidofludimus calcium ongoing

designed to corroborate vidofludimus calcium's neuroprotective potential

Vidofludimus calcium active in UC:

maintenance therapy in moderate-to-severe UC patients showed significant benefit in clinical remission

IMU-856 for intestinal barrier function:

demonstrated clinical proof-of-concept in phase 1b trial in celiac disease; in preparations for phase 2 testing

Cash runway into Q3/2025

Cash position: USD 46.7 million (as of Dec 31, 2023) plus up to USD 240 million raised in January 2024

Summary: Several Clinical Value Inflection Points Ahead

IMU-838 in PMS	▪ Readout phase 2 CALLIPER trial estimated for April 2025
IMU-838 in RMS	▪ Interim futility analysis phase 3 ENSURE program estimated for late 2024 ▪ Readout first phase 3 ENSURE trial estimated for Q2/2026, second in H2/2026
IMU-856	▪ Phase 2 clinical trial in preparation ▪ Applicable to a multitude of gastrointestinal disorders

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Thank You!

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