Immunic Therapeutics

Developing Selective Oral Therapies in Immunology

NASDAQ: IMUX | October 2023

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.

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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.

Immunic THERAPEUTICS

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

Glenn Whaley
CFO

Inderpal Singh
General Counsel

Duane Nash, MD, JD, MBA
Executive Chairman

Renowned International Board of Directors

Duane Nash, MD, JD, MBA
Executive Chairman

Daniel Vitt, PhD
CEO & President

Barclay A. Phillips
Lead Independent Director

Tamar Howson, CFA
Independent Director

Joerg Neermann, PhD
Independent Director

Richard Rudick, MD
Independent Director

Maria Törnsén
Independent Director

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Advanced Clinical Pipeline

Well Differentiated Programs in Various Phases of Clinical Development

Program	Preclinical	Phase 1	Phase 2	Phase 3	Key Milestones
Vidofludimus Calcium (IMU-838)	Relapsing Multiple Sclerosis (RMS) – ENSURE Trials Progressive Multiple Sclerosis (PMS) – CALLIPER Trial Ulcerative Colitis (UC) – CALDOSE-1 Trial				▪ Interim analysis of CALLIPER trial in PMS planned after half of the patients completed 24 weeks of treatment, estimated for fall 2023 ▪ CALLIPER trial estimated to readout in April 2025 ▪ Interim analysis of first ENSURE trial in RMS planned after approximately half of the events occurred, estimated for late 2024 ▪ ENSURE-1 trial estimated to readout end of 2025, ENSURE-2 soon thereafter
IMU-856	Celiac Disease				
IMU-381	Gastrointestinal Diseases				

■ Completed or ongoing ■ In preparation or planned

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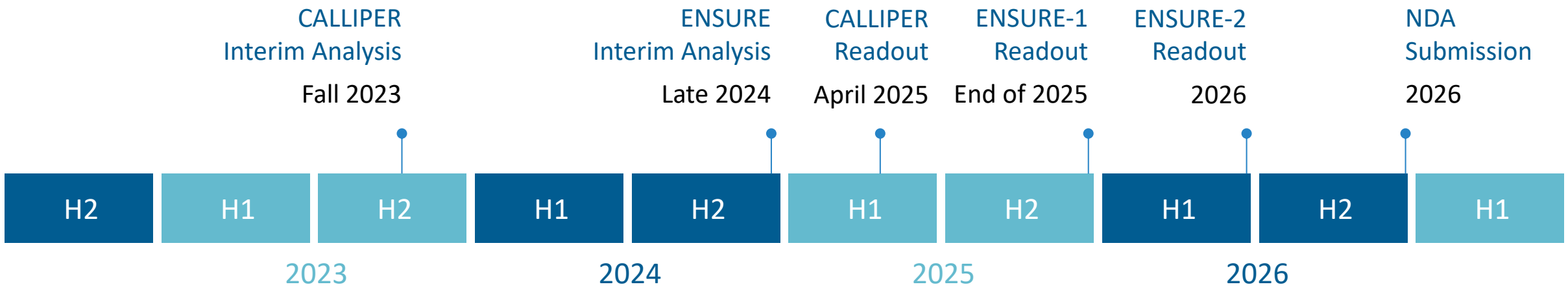
Straightforward Path Towards Potential Approval



RMS ENSURE-1 – Phase 3

RMS ENSURE-2 – Phase 3

PMS CALLIPER – Phase 2

PMS Phase 3

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.

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Vidofludimus Calcium in Multiple Sclerosis (MS)

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

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

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

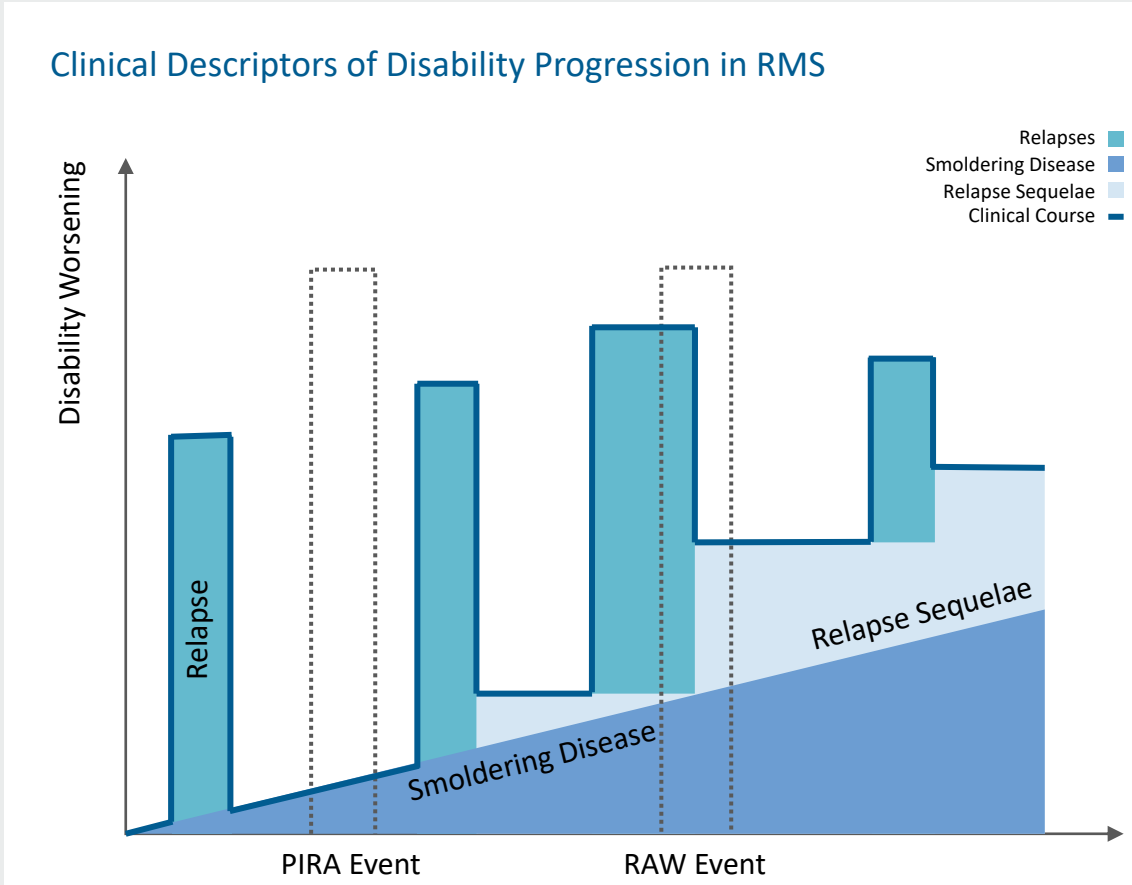
Therapeutic Goal: Preventing Disability Worsening

- 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

MS Patients Worsen in Disability Over Time

- Relapse-associated worsening (RAW) and progression independent of relapse activity (PIRA) both contribute to disability worsening in RMS and PMS patients
- Long time belief that, in RMS, disability originates more or less exclusively from RAW
- 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”



Adapted from Kretzschmar A., Symposium „Every Journey Begins with a Single Step: Visualizing the Chronic Nature of MS”, MSVirtual2020 / 8th Joint ACTRIMS-ECTRIMS Meeting
RMS: relapsing multiple sclerosis; PMS: progressive multiple sclerosis; PIRA: progression independent of relapse activity; RAW: relapse-associated worsening

Vidofludimus Calcium Addresses Multiple Drivers of Neurodegeneration in MS Patients

1 Anti-Inflammatory Effects

- Selectively targets hyperactive immune cells
- Reduces MRI lesions
- Reduces relapses
- Mechanism already shown to reduce brain atrophy
- Addressing RAW

2 Anti-Viral Effects

- Established, broad-spectrum antiviral activity
- EBV linked to MS
- Potent anti-EBV activity
- Potential to suppress EBV-related T cells

3 Direct Neuroprotective Effects

- Impact on validated neuroprotective target
- Impact on serum neurofilament light chain
- Encouraging clinical signals from phase 2 trial on change in EDSS
- Potential to target PIRA

Vidofludimus calcium can target various aspects of ‘smoldering’ MS

MRI: magnetic resonance imaging; RAW: relapse-associated worsening; PIRA: progression independent of relapse activity; EDSS: Expanded Disability Status Scale; EBV: Epstein-Barr virus

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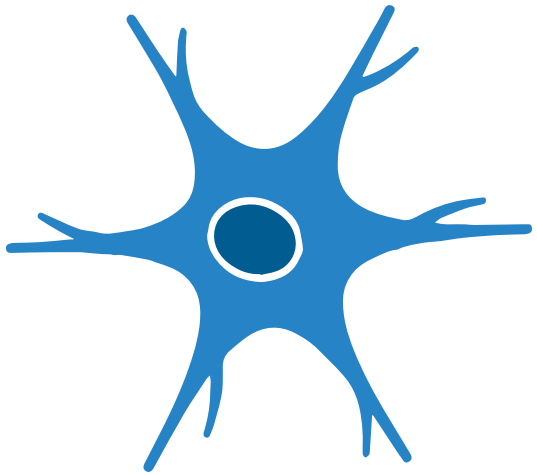
Vidofludimus Calcium Addresses Smoldering Neurodegeneration

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

Nurr1 Activator

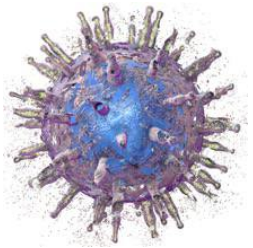
- Protecting neurons from cell death
- Continuous effect independent from focal inflammation



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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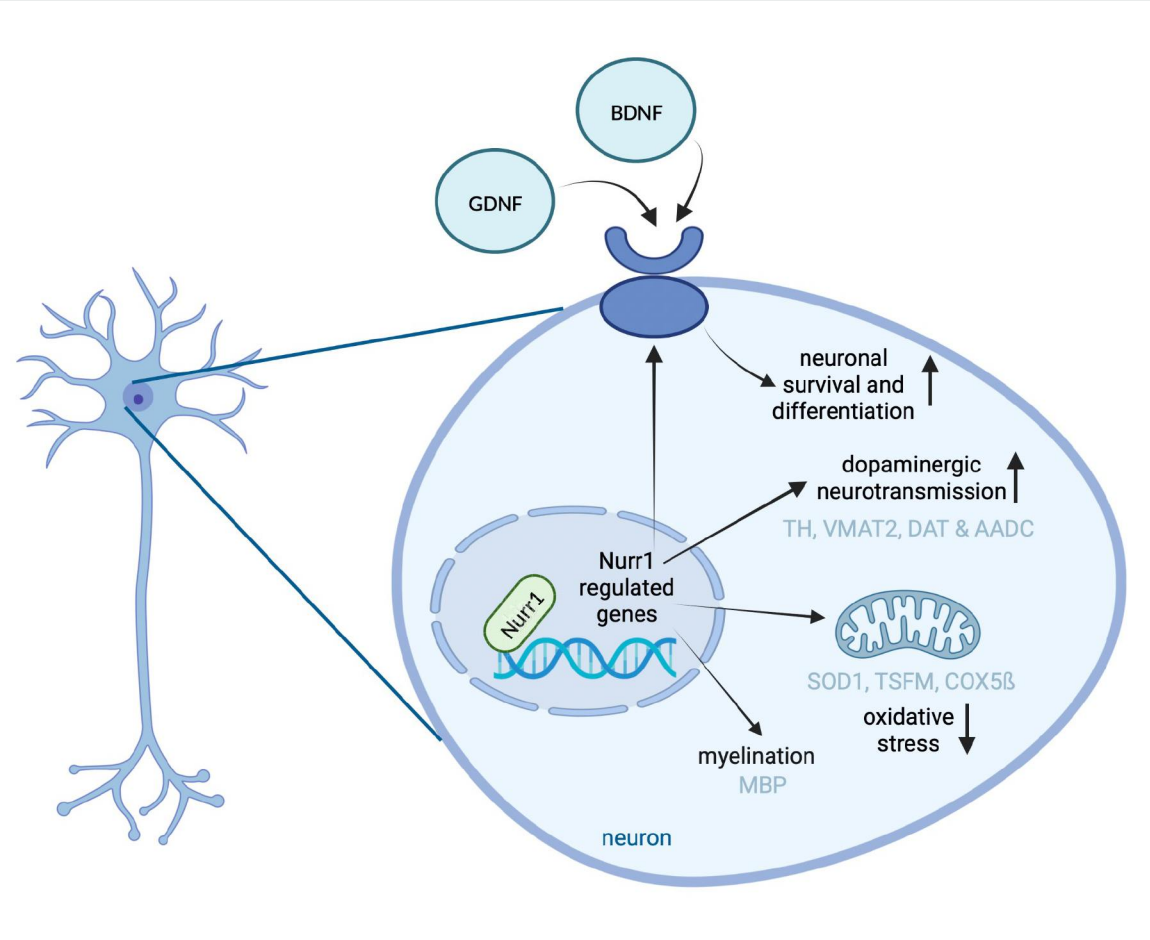
Nurr1 Is a Nuclear Receptor Involved in Neuroprotection



Nurr1 activation mediates neuronal survival

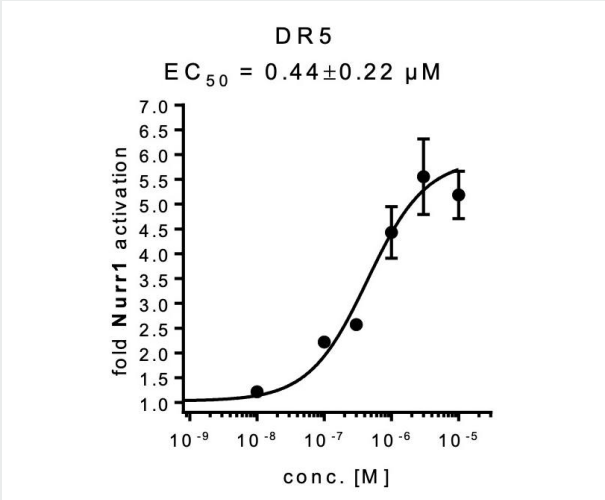
Nurr1 activation increases dopaminergic neurotransmission

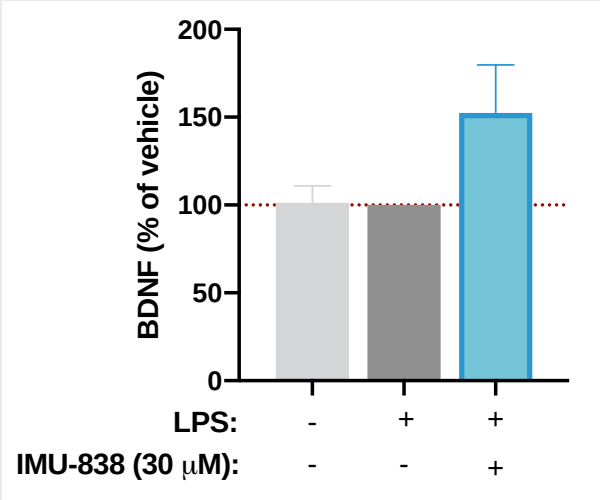
Nurr1 activation in motor neurons may halt neurodegeneration and disability progression

Vietor et al., Journal of Medicinal Chemistry 2023 66 (9), 6391-6402; Schiro et al., 2022, Frontiers in Neurology, adapted from Willems, 2022, J med chem
Nurr1: nuclear receptor related 1; GDNF: glial cell line-derived neurotrophic factor; BDNF: brain-derived neurotrophic factor

Vidofludimus Calcium Binds to and Strongly Activates Nurr1

- Vidofludimus calcium induces a 5-fold activation, with an EC_{50} of 440 nM concentration
- Nurr1 is a transcription factor binding to DNA
- Vidofludimus calcium enhances production of the Nurr1 target BDNF, positively impacting neuronal survival and myelination





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

Vietor et al., Journal of Medicinal Chemistry 2023 66 (9), 6391-6402; Structure: Zhao, M. et.al. (2022) Proc Natl Acad Sci USA 119; Nurr1: nuclear receptor related 1; DNA: deoxyribonucleic acid; BDNF: brain-derived neurotrophic factor

The related research project was funded by the German Federal Ministry of Education and Research under the grant number 03INT607AA.

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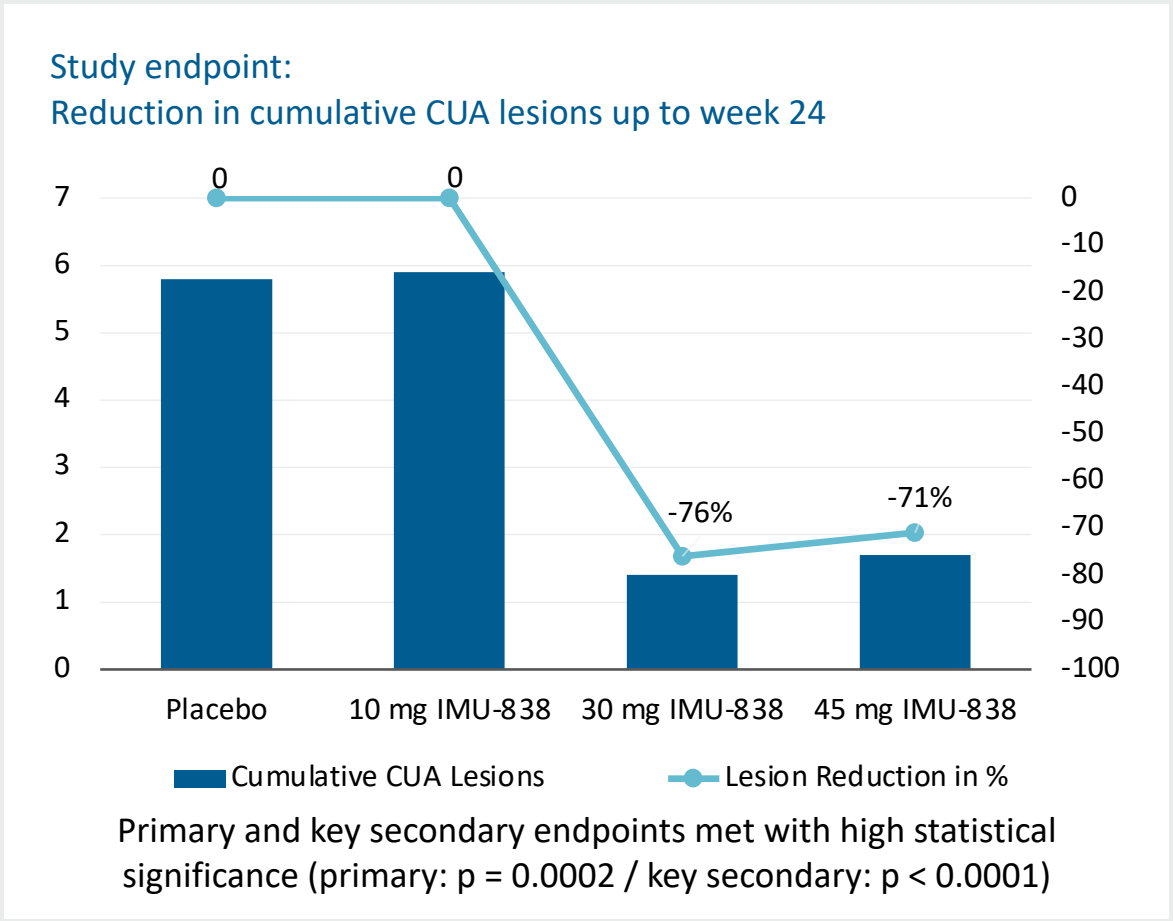
EMPhASIS Trial: Strong Reduction of MRI Lesion Activity

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



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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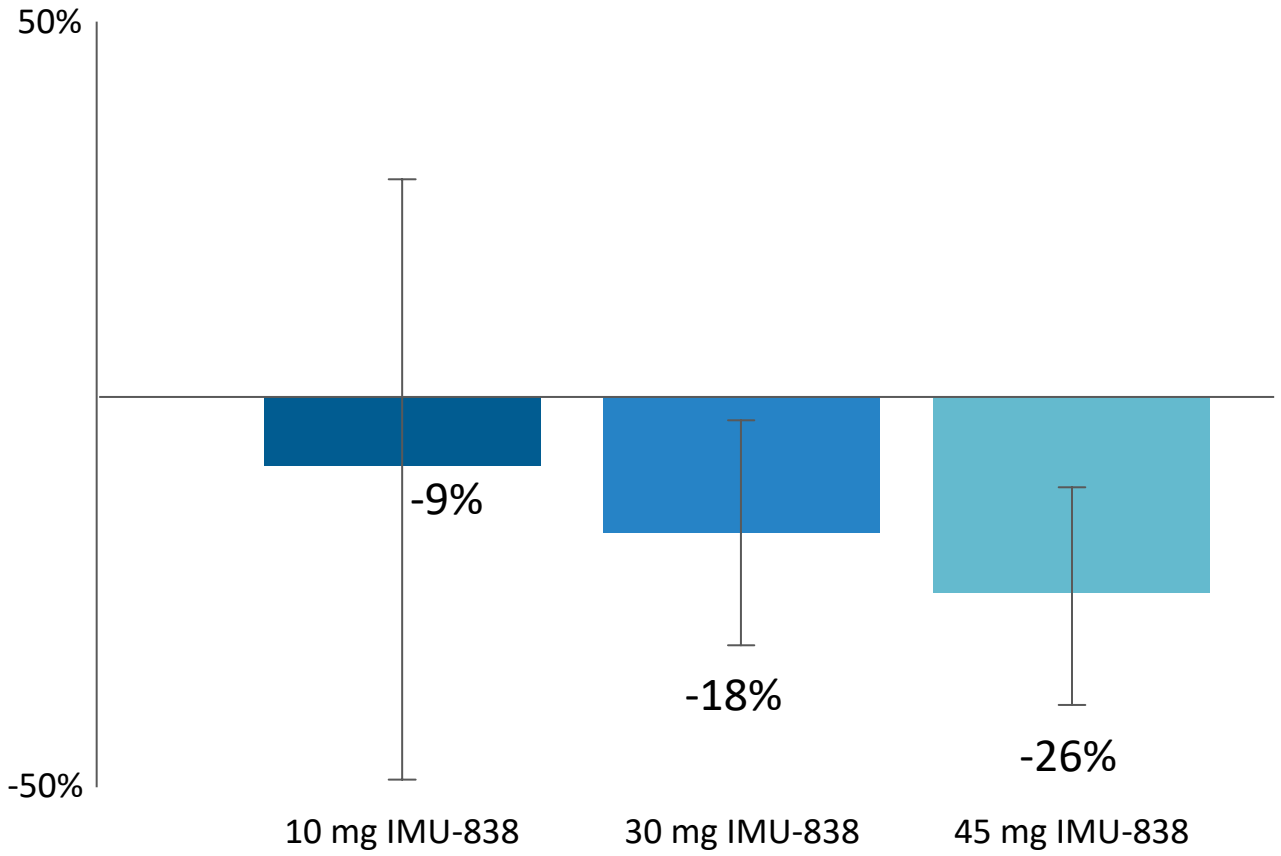
EMPhASIS Trial: Reduction of Serum NfL Concentrations Observed

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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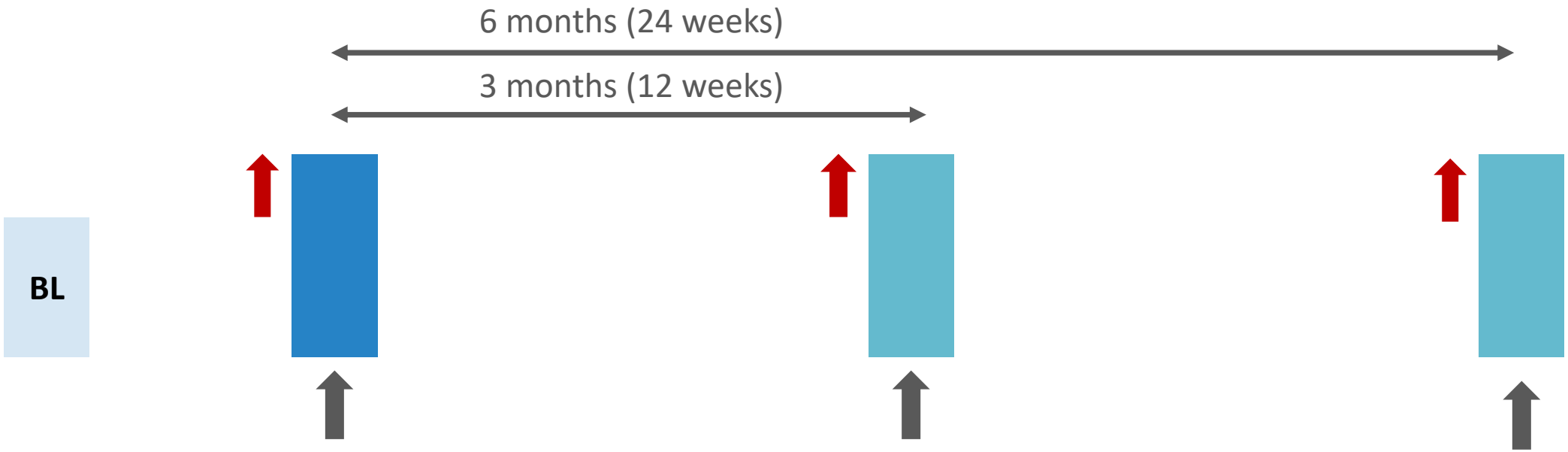
EMPhASIS Trial: Measurement of Confirmed Disability Worsening (CDW) Events



"Trigger Event"

Increase in 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

"Confirmation Event"

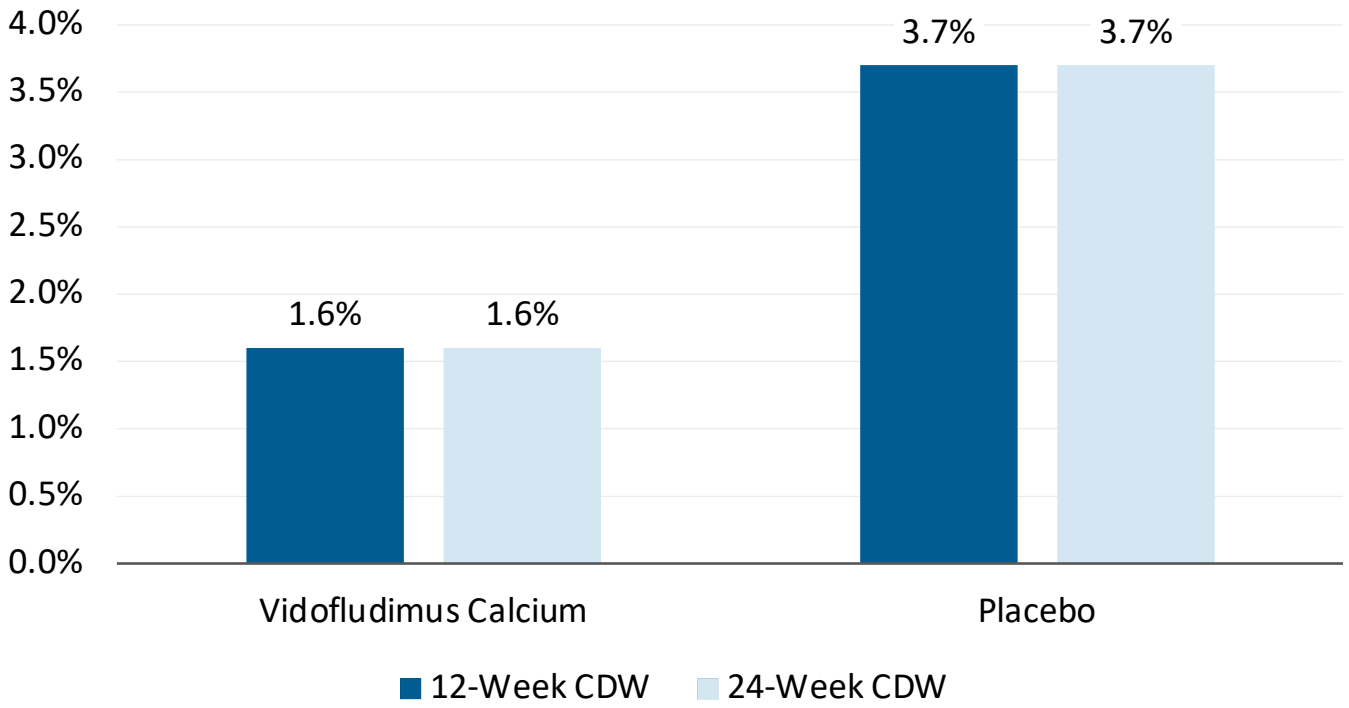
At the confirmation event and each assessment between trigger and possible confirmation event, EDSS must be at least as high as at the trigger event.

EDSS: Expanded Disability Status Scale; BL: baseline (for example pre-study or at the beginning of a certain study phase)

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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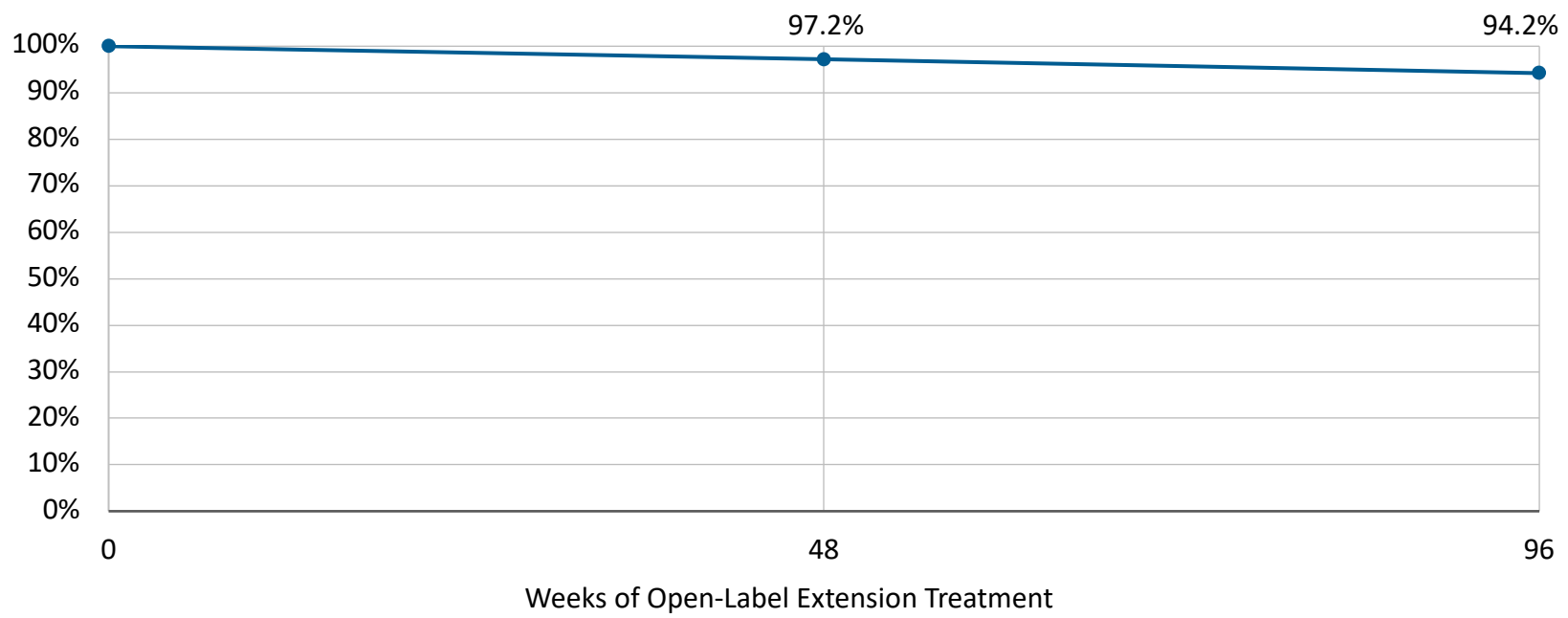
EMPhASIS Trial: Interim Analysis Regarding 12-Week CDW Events

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



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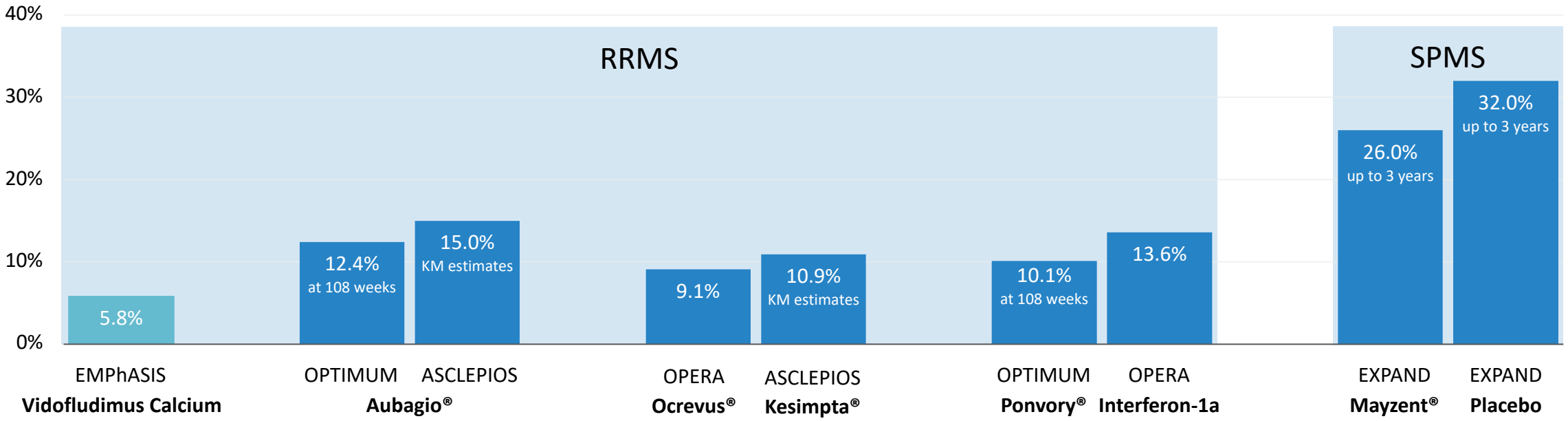
12-Week Confirmed Disease Worsening after 2 Years (96 Weeks)

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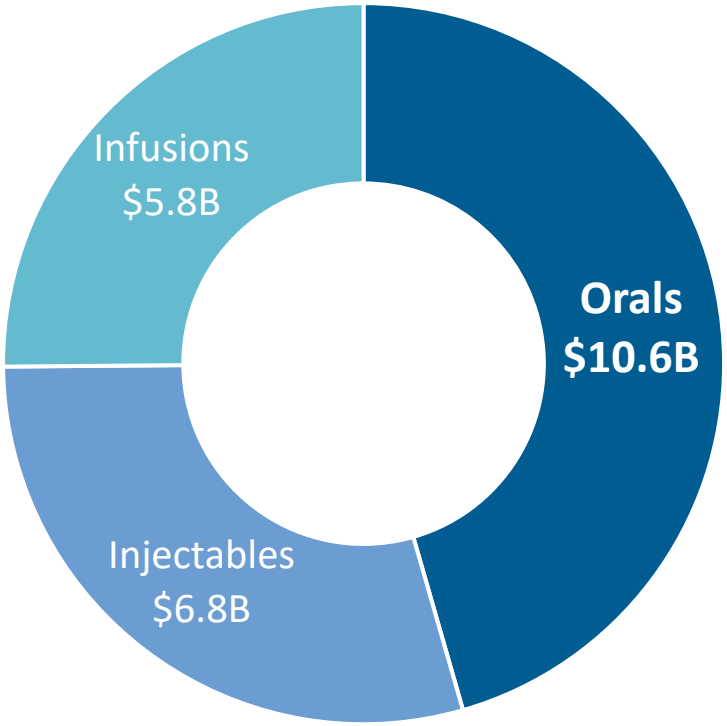
The Global MS Market Exceeds $23B in Annual Sales, With $1B+ Contributions from Multiple Brands

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

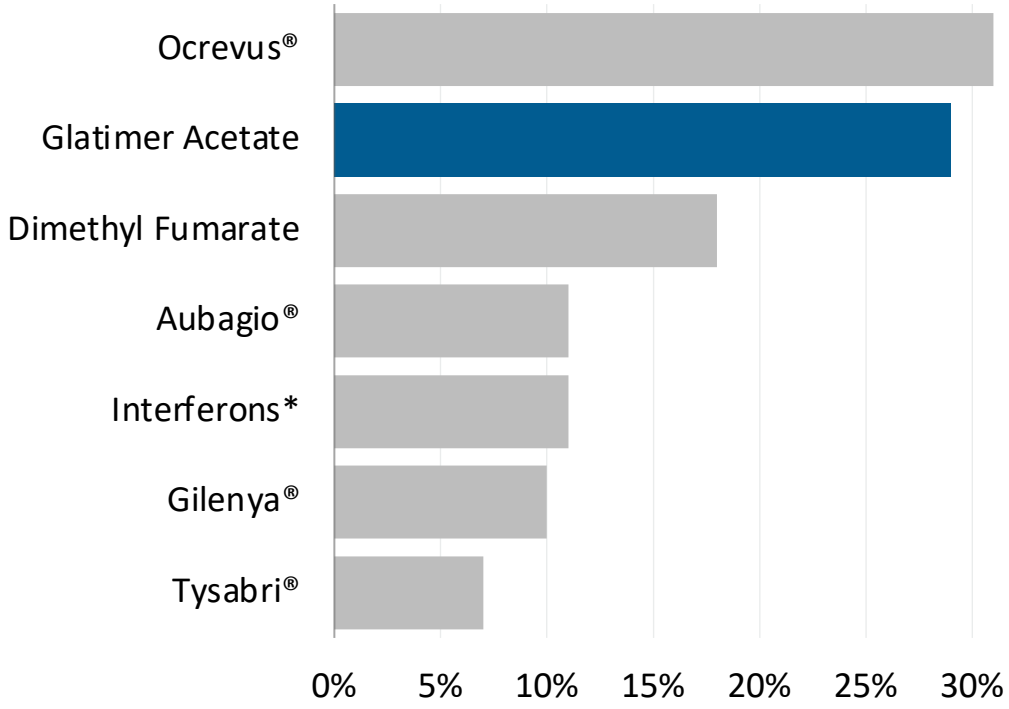
* Sales numbers in G7 countries (US, UK, Canada, Japan, Germany, France, Italy) in USD billion; S1P: sphingosine-1-phosphate
Source: Multiple Sclerosis Landscape and Forecast by Decision Resources Group Part of Clarivate

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]

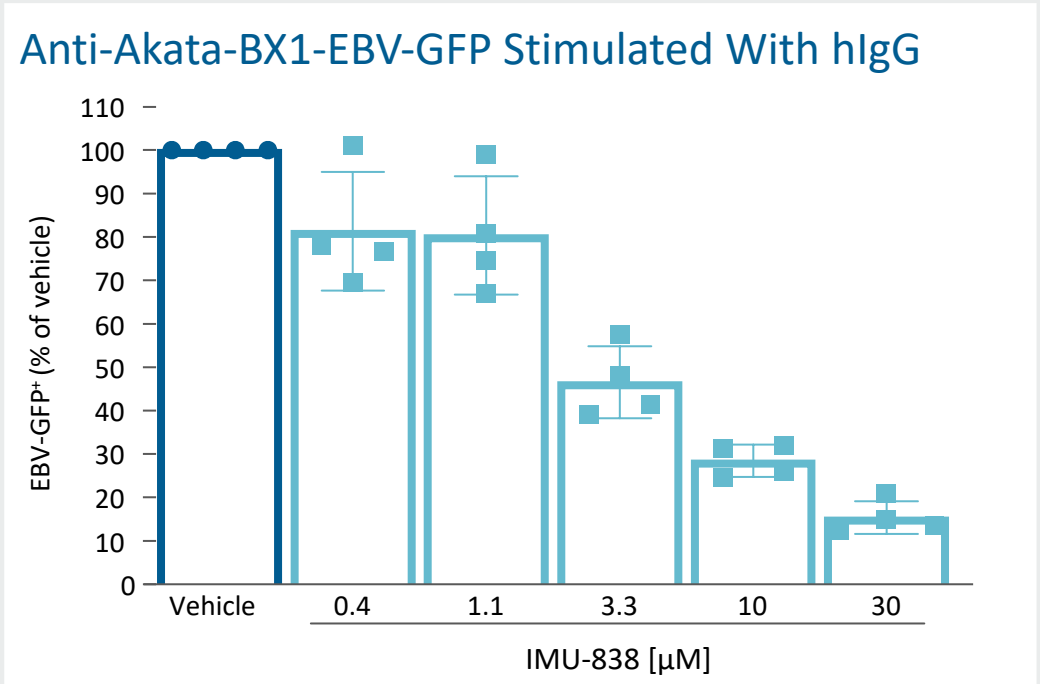
Evidence Supporting Commercial Potential

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

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

Showed Concentration-Dependent Anti-EBV Activity



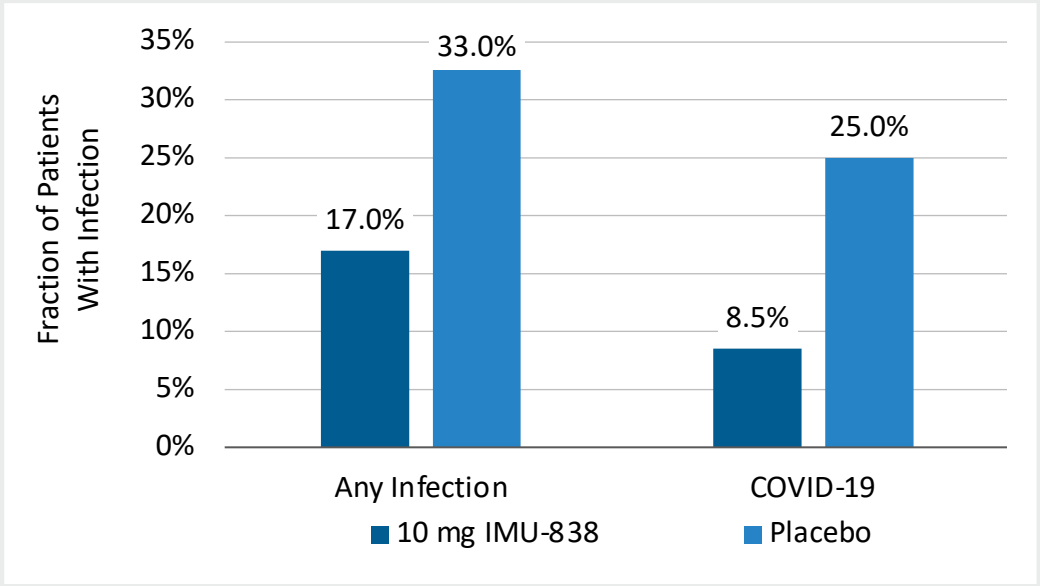
Inhibits Epstein-Barr Virus (EBV) Replication and Reactivation

- 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 1,400 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%**	**2.2%**
Placebo	**7.2%**	**5.8%**	**6.6%**	**9.2%**	**6.5%**	**3.3%**

*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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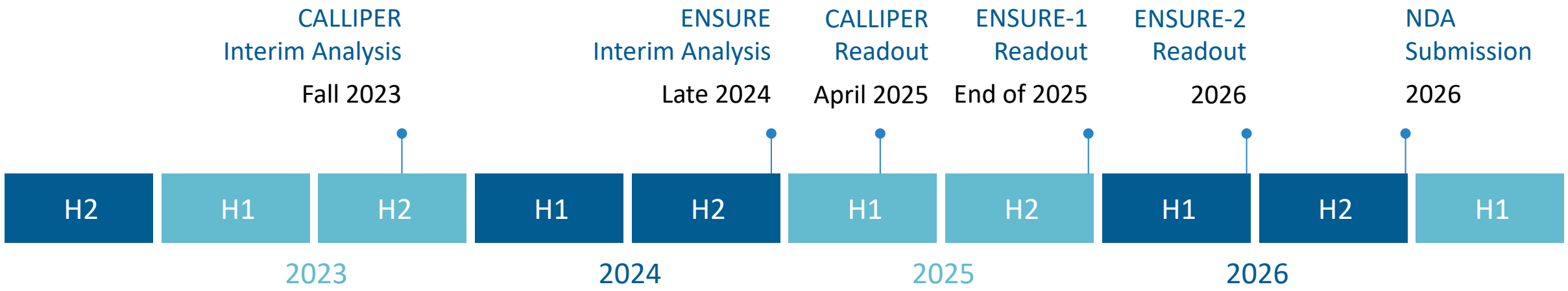
Straightforward Path Towards Potential Approval



RMS ENSURE-1 – Phase 3

RMS ENSURE-2 – Phase 3

PMS CALLIPER – Phase 2

PMS Phase 3

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.

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

Coordinating Investigator

Robert J. Fox, M.D.
Cleveland Clinic

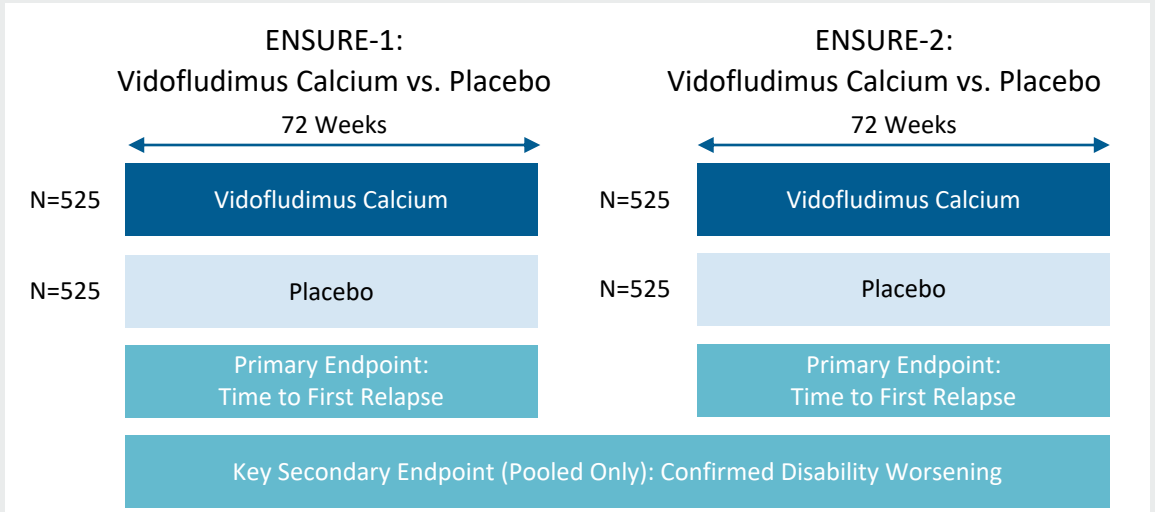
Included Patient Population: Relapsing Forms of MS

- 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



CALLIPER Trial: Ongoing Phase 2 Trial Intended to Complement the Phase 3 Program in RMS

Coordinating Investigator

Robert J. Fox, M.D.
Cleveland Clinic

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

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

- 467 patients enrolled at more than 70 sites in North America, Western, Central and Eastern Europe
- Randomization to 45 mg vidofludimus calcium or placebo QD
- Primary endpoint: annualized rate of percent brain volume change up to 120 weeks

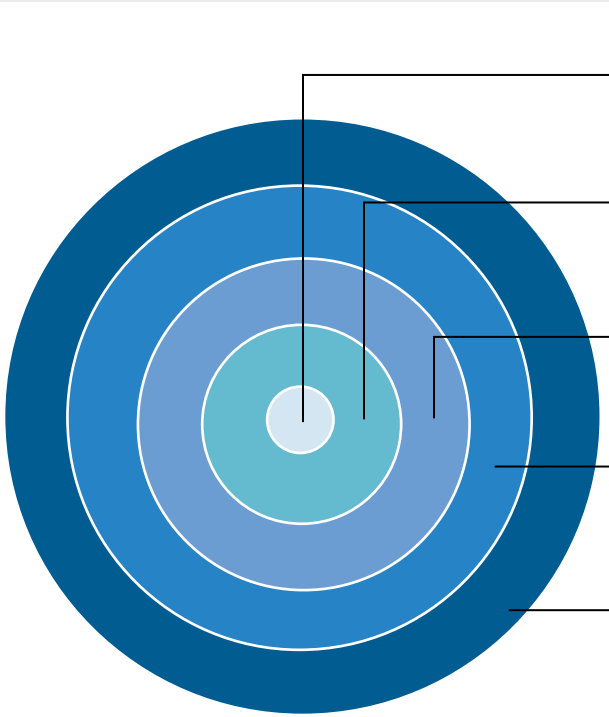
Treatment Schedule

- Blinded 120-week main treatment period
- Optional, approximately 8-year, open-label extension period
- Interim analysis of serum neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) planned after approximately half of the patients have completed 24-weeks of treatment

* NCT05054140
PPMS: primary progressive multiple sclerosis; SPMS: secondary progressive multiple sclerosis; EDSS: Expanded Disability Status Scale; QD: quaque die = once-daily

Vidofludimus Calcium: Intellectual Property Position

Immunic has created a multilayered approach to exclusivity:



- Patent on calcium salt forms of vidofludimus calcium, granted in the United States, Europe and other key markets – could be valid up to 2036 if PTE is applied
- Patent filed on the dosing regimen protecting the applied dosing scheme used in the clinical trials – granted in Japan already – would expire in 2038, if granted
- New patent filed in 2018 on the specific polymorph of vidofludimus calcium used in current studies – expires in 2039, if granted
- New patent application filed in the US protecting the dose strength of vidofludimus calcium in patients with MS – would be valid until 2041, if granted
- Further patent application planned for the use in specific diseases and patient subsets which would protect vidofludimus calcium in relevant diseases until 2044
- Another level of protection can be expected by data exclusivity in the United States and in Europe based on vidofludimus calcium's classification as a New Chemical Entity (NCE)

IP: intellectual property; PTE: Patent Term Extension (US only)

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 1,400 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**

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

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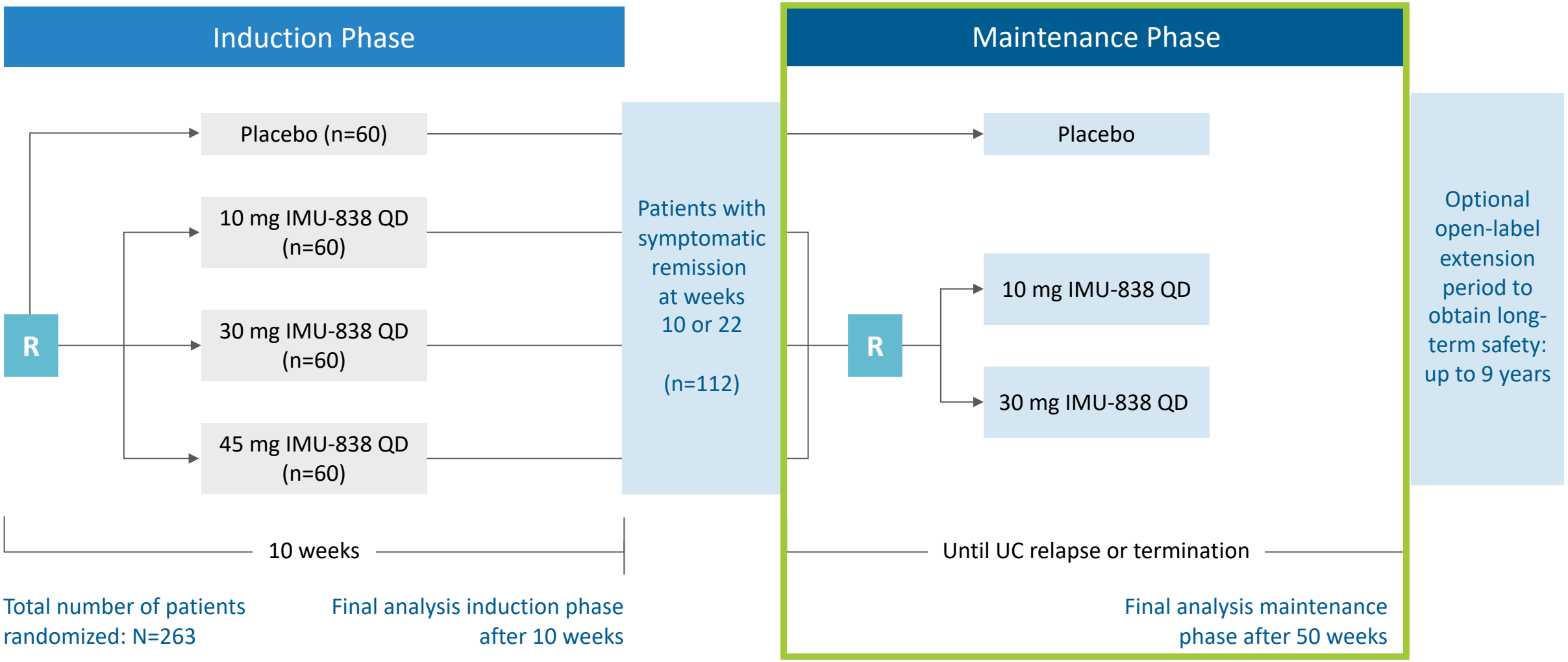
Vidofludimus Calcium in Ulcerative Colitis (UC)

CALDOSE-1: Final Week 50 Maintenance Phase Data

CALDOSE-1: Phase 2 Trial Design in UC

NCT03341962



Total number of patients randomized: N=263

Final analysis induction phase after 10 weeks

Final analysis maintenance phase after 50 weeks

R: randomization; QD: quaque die = once-daily

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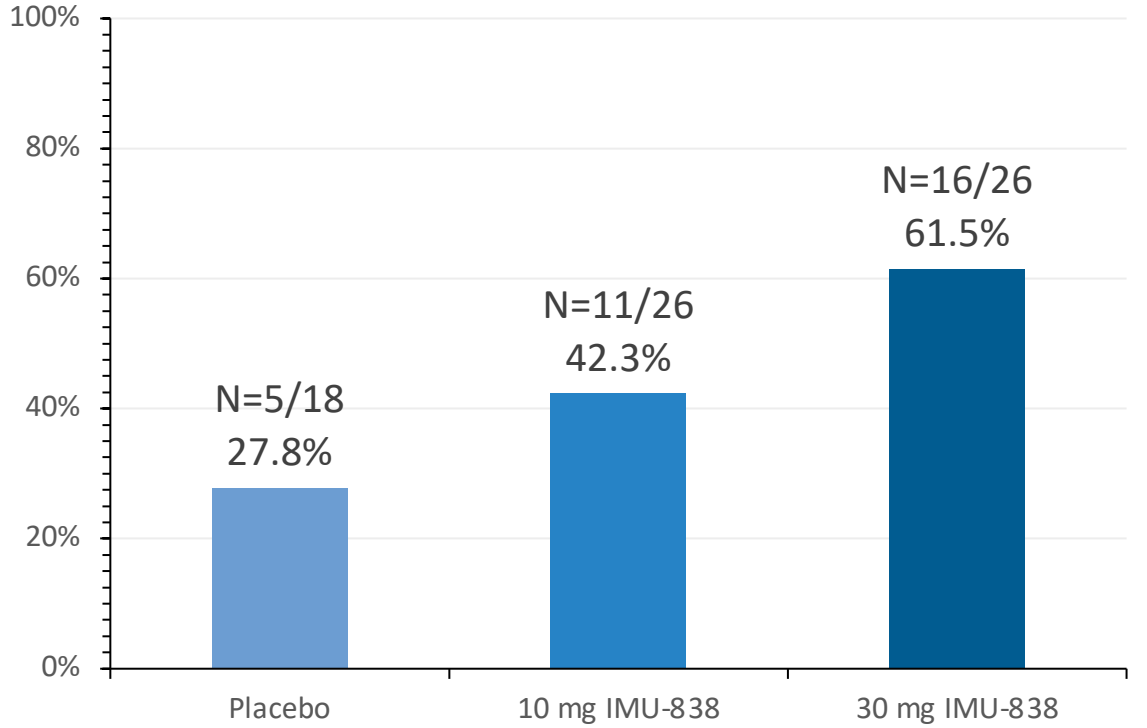
Dose-Linear Increase in Clinical Remission at Week 50 For Vidofludimus Calcium as Compared to Placebo

Clinical Remission at Week 50

Full Analysis Set$_{MP}$ (N_{PBO} = 27, N_{10} = 45, N_{30} = 40)

Data Set: (n-evaluable/n-total of group)	Placebo (N=18/21)	10 mg IMU-838 (N=26/35)	30 mg IMU-838 (N=26/29)
Number of patients with clinical remission	5	11	16
Clinical remission rate	**27.8%**	**42.3%**	**61.5%**

Clinical Remission at Week 50

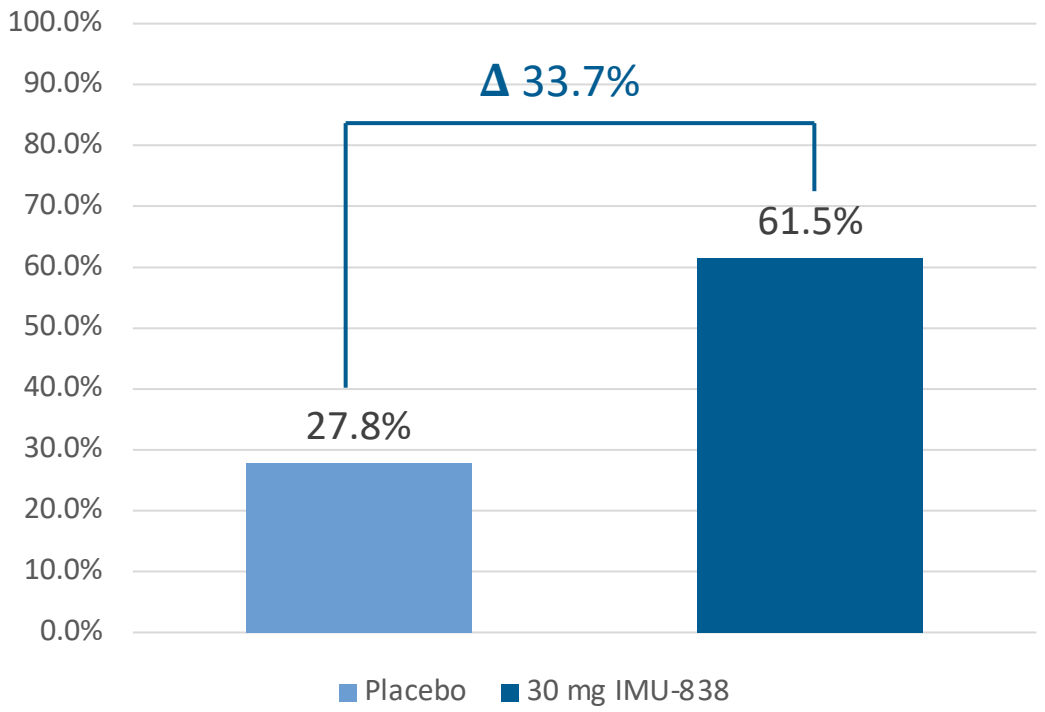


Clinical remission: composite of patient-reported symptomatic remission (stool frequency Mayo subscore of 0 or 1, rectal bleeding Mayo score of 0) and modified Mayo endoscopy subscore of 0 or 1; PBO: placebo
Full Analysis Set MP: all patients randomized into maintenance phase.

Exploratory Statistical Analysis of Clinical Remission

Statistically Significant Difference in Favor of 30 mg Vidofludimus Calcium Versus Placebo

Clinical Remission at Week 50



30 mg of vidofludimus calcium found to be statistically superior to achieve clinical remission during maintenance treatment at week 50 as compared to placebo

Planned treatment	Clinical remission at week 50	Number of patients (N)	Proportion of patients (%)	Statistical output (t-test)
30 mg IMU-838	Yes	16	61.5%	p-value (two-sided) **p=0.0358** odds ratio (30 mg IMU-838 / placebo) 4.1600
	No	10	38.5%	
Placebo	Yes	5	27.8%	
	No	13	72.8%	

Clinical remission: composite of patient-reported symptomatic remission (stool frequency Mayo subscore of 0 or 1, rectal bleeding Mayo score of 0) and modified Mayo endoscopy subscore of 0 or 1
Full Analysis Set of Maintenance Phase (N10 = 45, N30 = 40, NPBO = 27), Post-Hoc Unplanned Analysis: Two-sided Pearson's chi-square test (significance level alpha=0.05) for achieving clinical remission at week 50 between 30 mg IMU-838 and placebo

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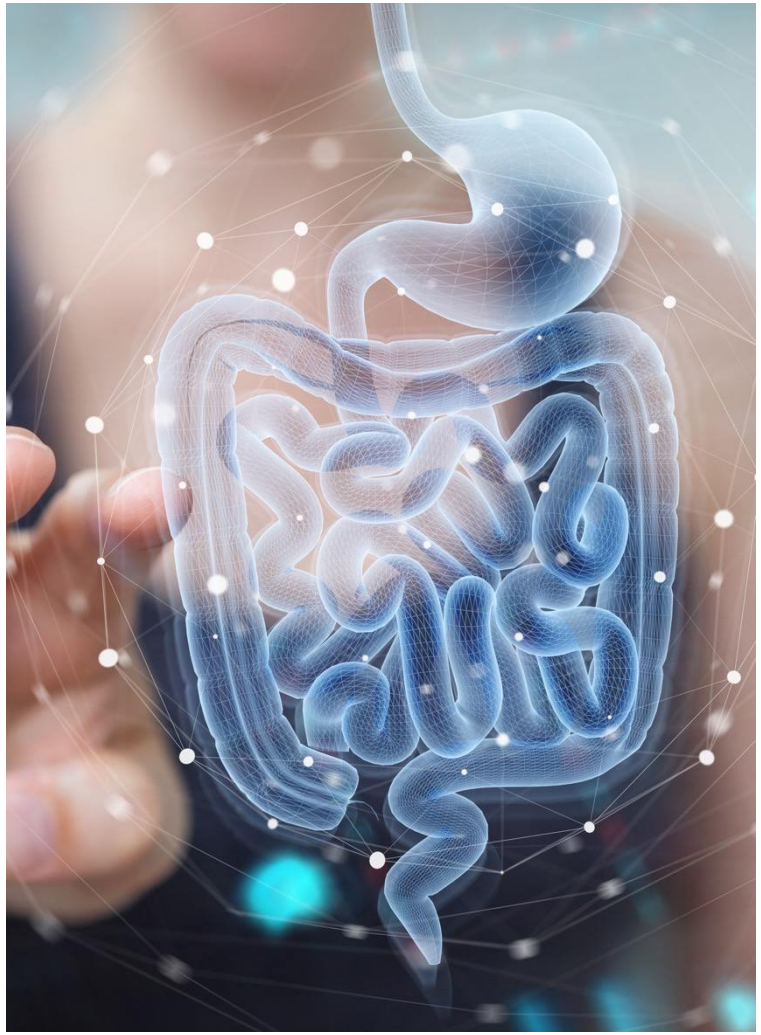
Maintenance Phase CALDOSE-1 Trial: Summary

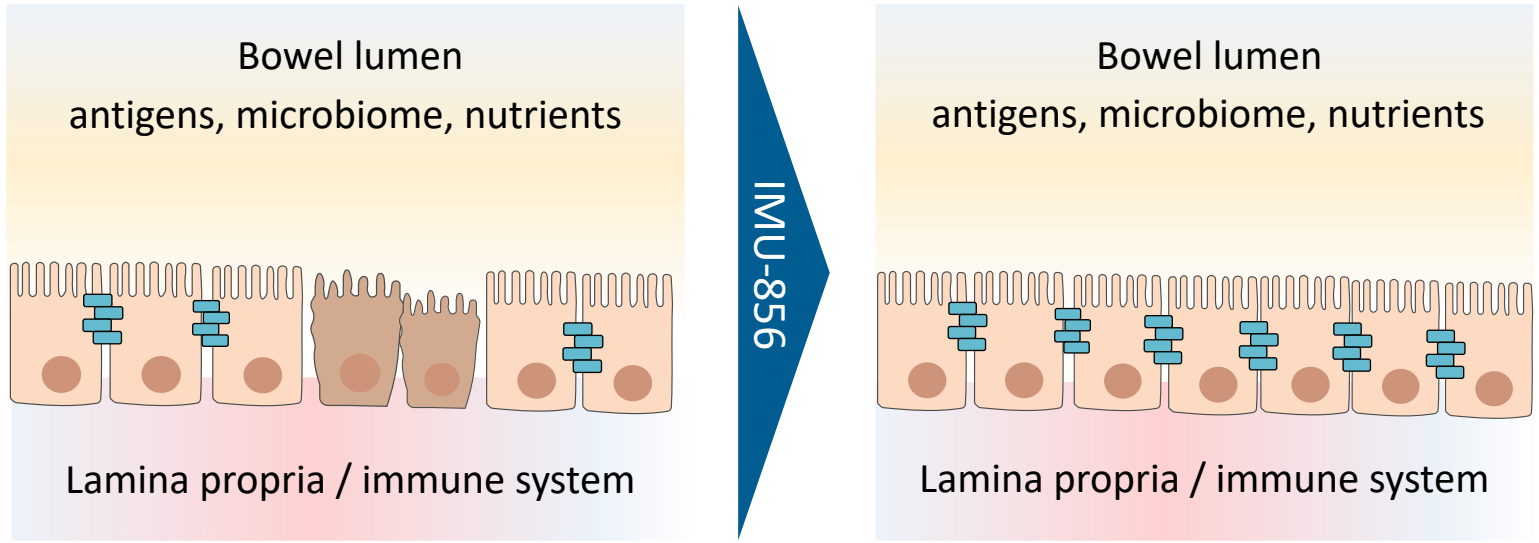


- Maintenance phase results confirm that vidofludimus calcium provides a benefit regarding clinical remission, as compared to placebo, in UC patients without concurrent use of corticosteroids.
- At week 50, the dose of 30 mg vidofludimus calcium once-daily demonstrated a statistically significant higher proportion of patients (p=0.0358) achieving clinical remission versus placebo (exploratory analysis).
- Vidofludimus calcium also demonstrated a trend to provide benefits versus placebo in other endpoints, including endoscopic healing, microscopic healing and steroid-free clinical remission.
- For most efficacy endpoints, a dose-linear response was observed for 10 mg and 30 mg vidofludimus calcium.
- Overall, the safety and tolerability profile of vidofludimus calcium in UC patients is comparable to placebo and in line with prior data sets in other patient populations.

IMU-856

Restoring a Healthy Gut by Renewal of the Gut Wall

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



IMU-856:

- First-in-class epigenetic modulator of sirtuin 6 (SIRT6), aimed to regenerate gut wall and restore barrier function
- Provides protection and enhances transport of nutrients
- This new approach prevents immunosuppression

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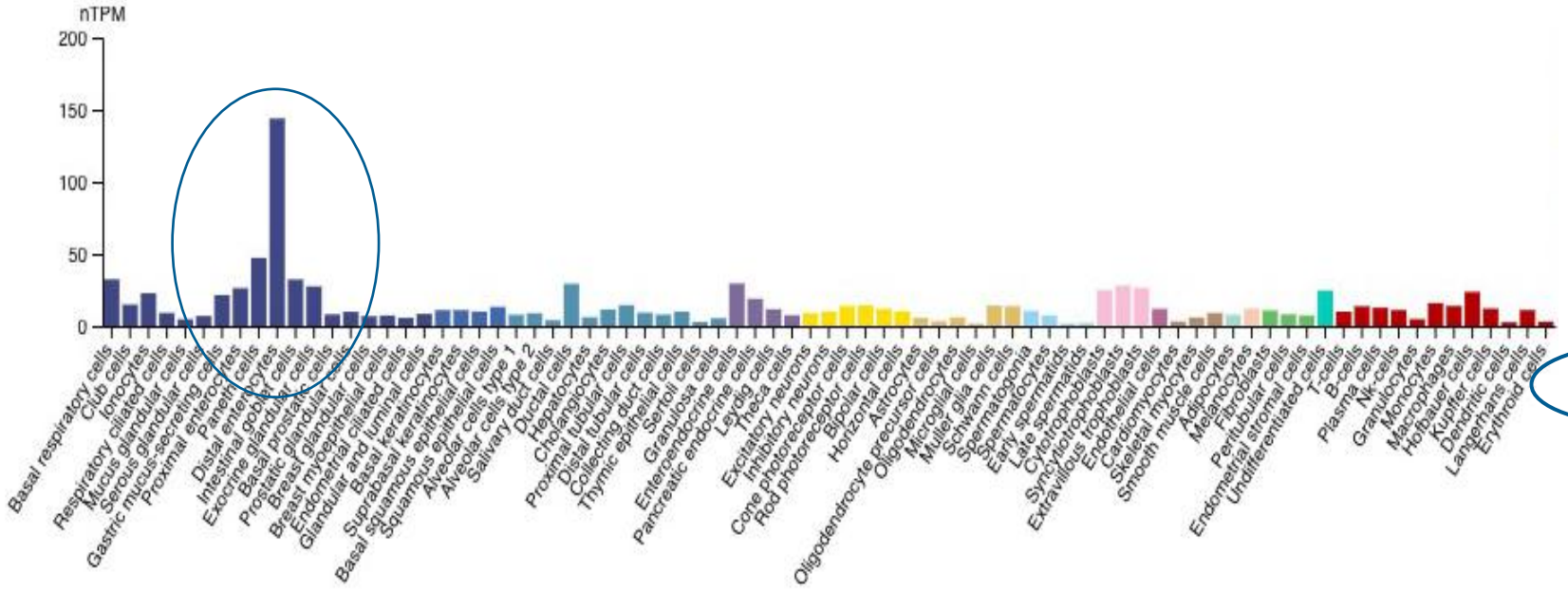
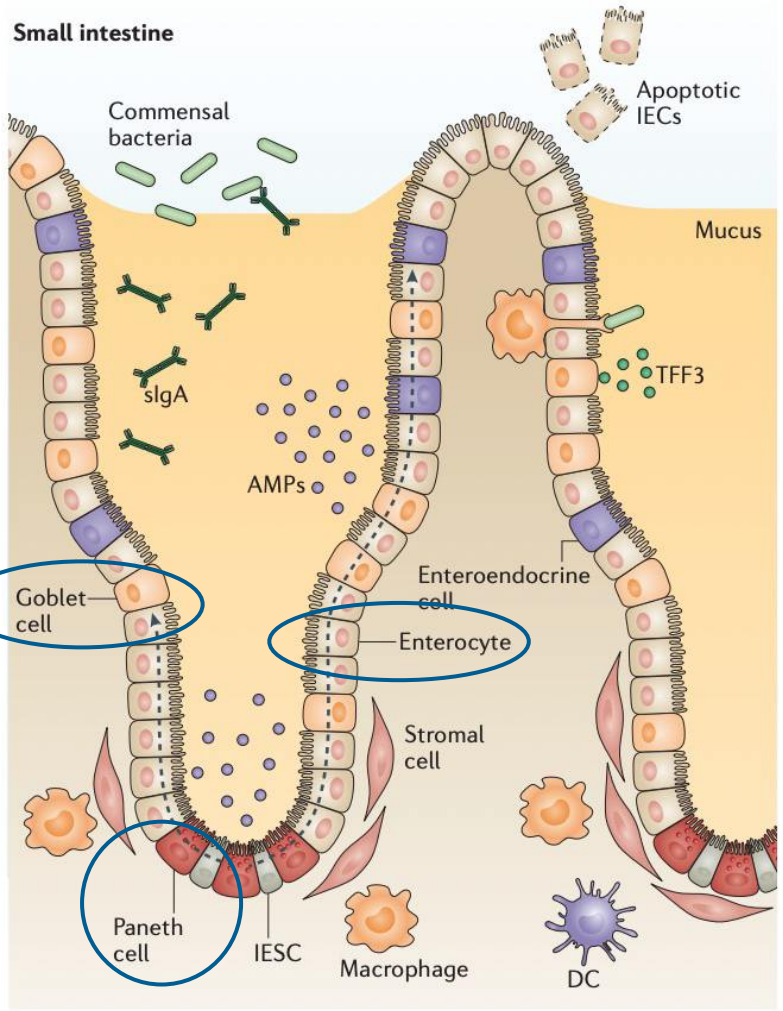
SIRT6 Is Mainly Expressed in Gut Epithelial Cells – Highest in Paneth Cells, Enterocytes and Goblet Cells





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

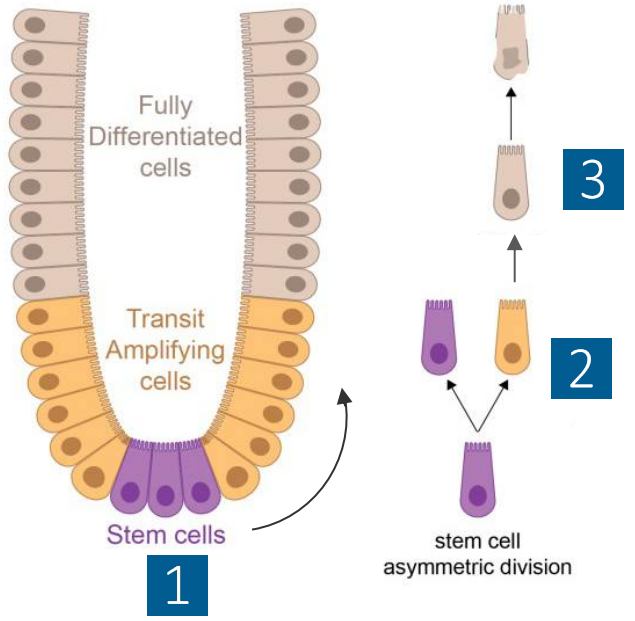
IMU-856 Enhances the Natural Regenerative Process in the Gut

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

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IMU-856 Could Elevate the Standard-of-Care Across Multiple Gastrointestinal Diseases With Histologic Damage

Celiac Disease
>2 million patients in US

- Major unmet need, with no drug treatment options available

Crohn's Disease
~1 million patients in US

- No effective oral treatment options available

Ulcerative Colitis
~1 million patients in US

- Good alternative to existing immunosuppressive therapies

Combination Therapy in Multiple GI Diseases
Multi-million patients in US

- Potential for complementary / synergistic effects across multiple, serious gastrointestinal diseases

Clinical phase 2 preparations in process

Significant upside opportunity (pipeline in a pill)

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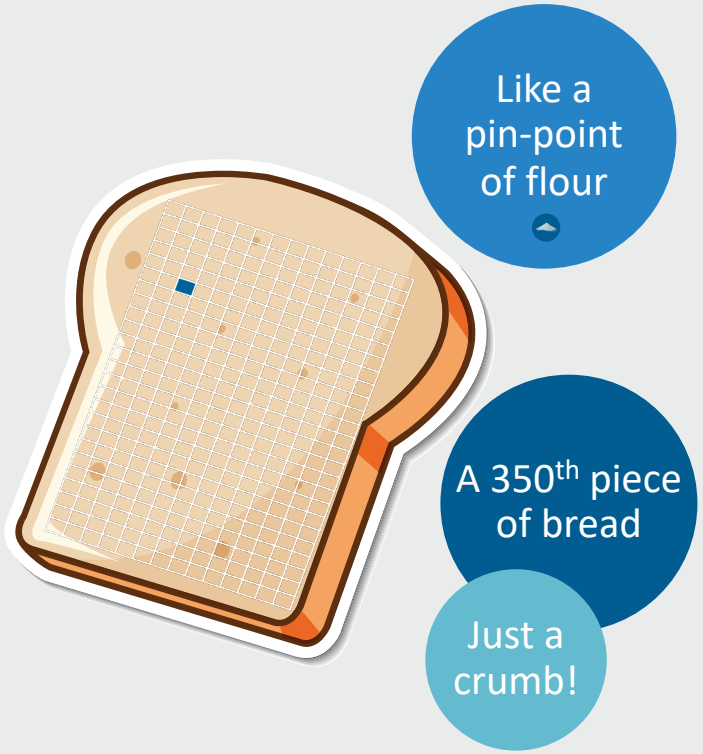
Celiac Disease Currently Has No Adequate Treatment Options

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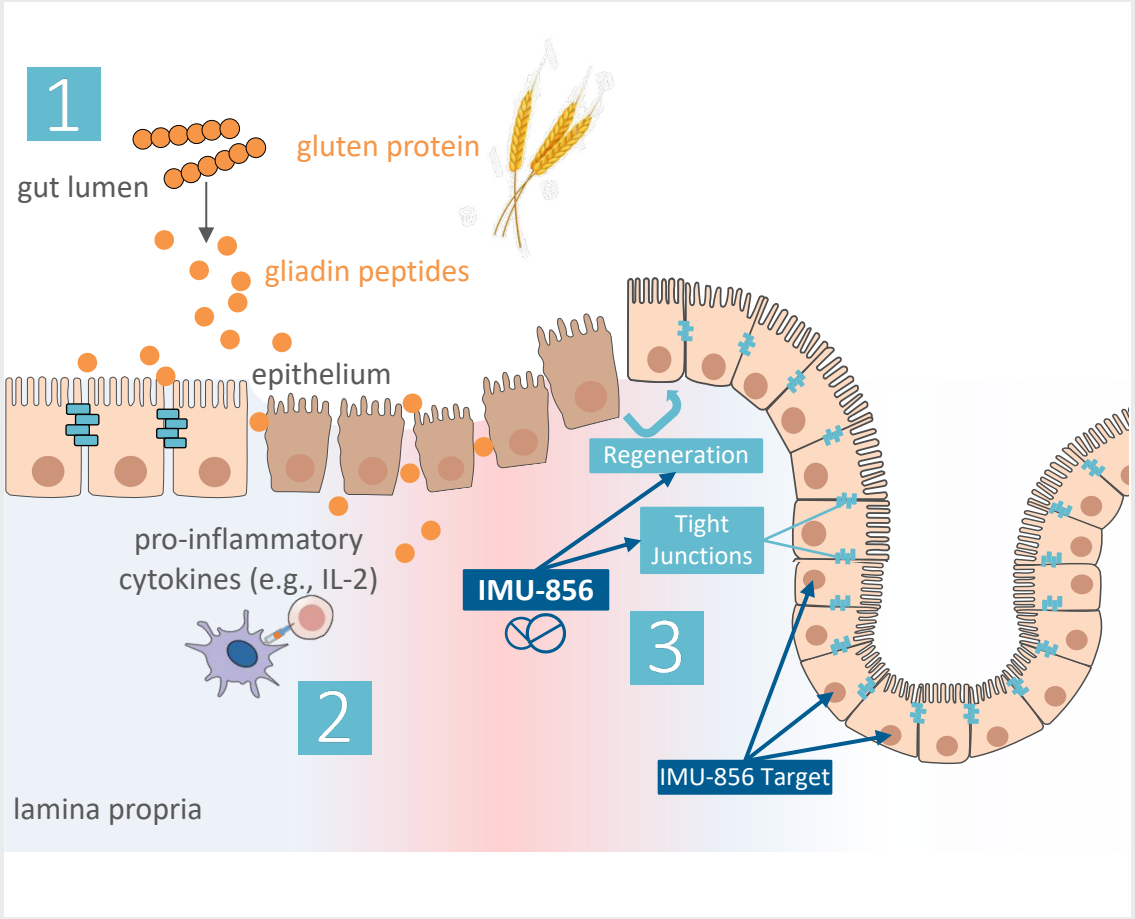
First Proof-of-Concept for Gastrointestinal Disorders in Celiac Disease

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

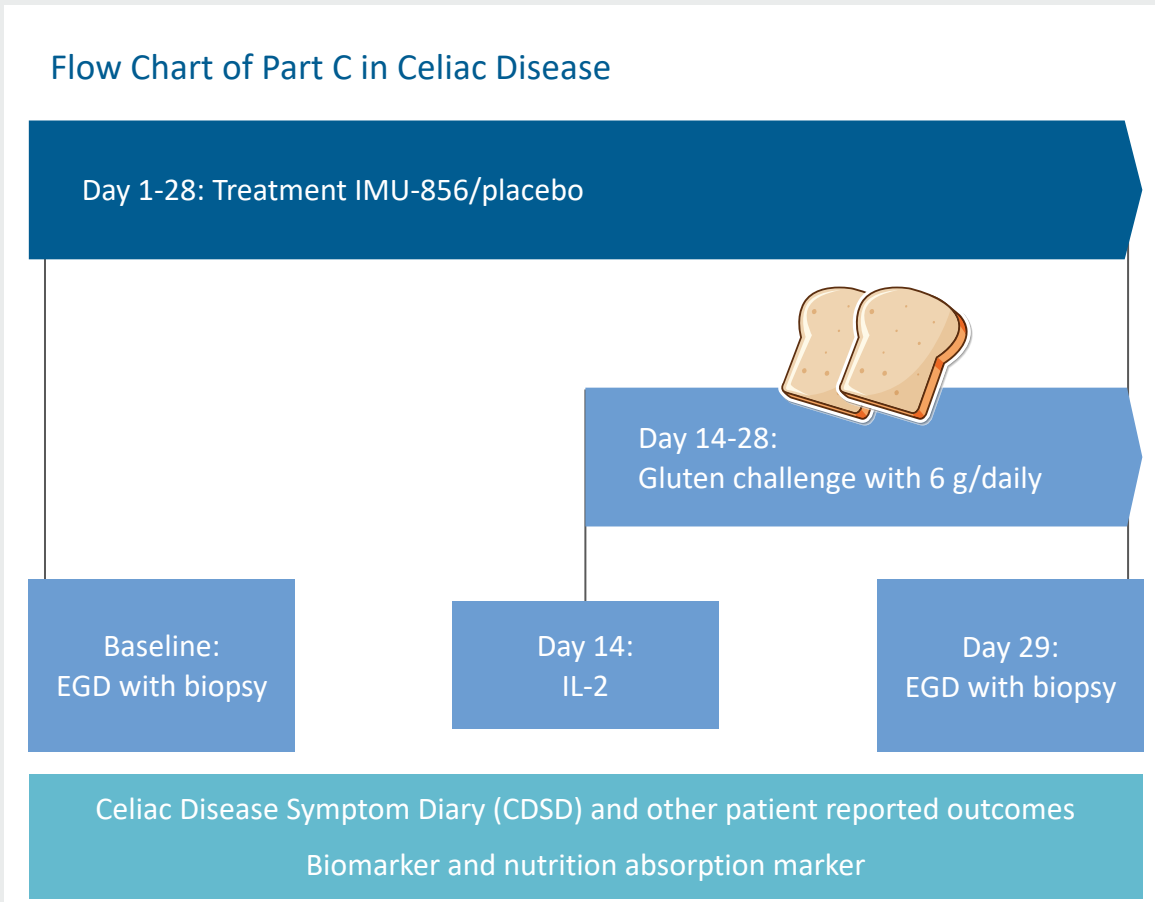
Picture: self-drawn; [1] Caio et al. BMC Medicine (2019) 17:142
HLA: human leukocyte antigen; TG2: tissue transglutaminase 2; CD: cluster of differentiation; IL: interleukin

Phase 1b Clinical Trial of IMU-856 in Celiac Disease

Designed as a Gluten Challenge Trial

Proof-of-Concept Study

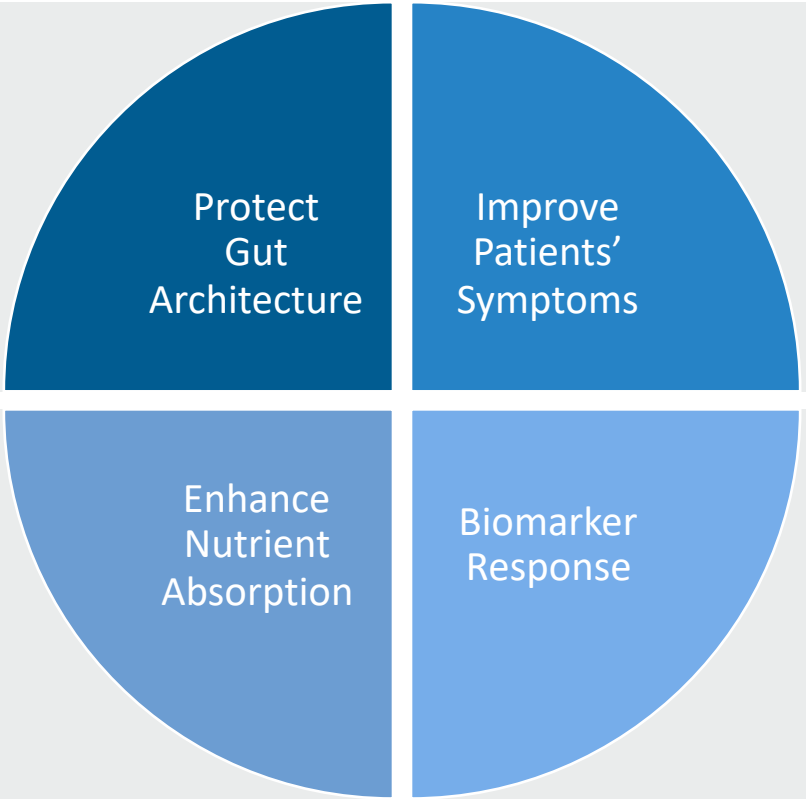
- Part C planned to include a well-controlled celiac disease patient population
- Dosing: 80 and 160 mg QD of IMU-856
- 43 patients enrolled
- Performed at sites in Australia and New Zealand
- Designed to assess safety, tolerability and pharmacokinetics of IMU-856
- Measured histologic changes, blood biomarkers, nutrient uptake and disease-related symptoms



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

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

IMU-856 effectively reduced 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

IMU-856 dampened gluten-induced immune activation, as measured by IL-2, and showed positive impact on citrulline

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

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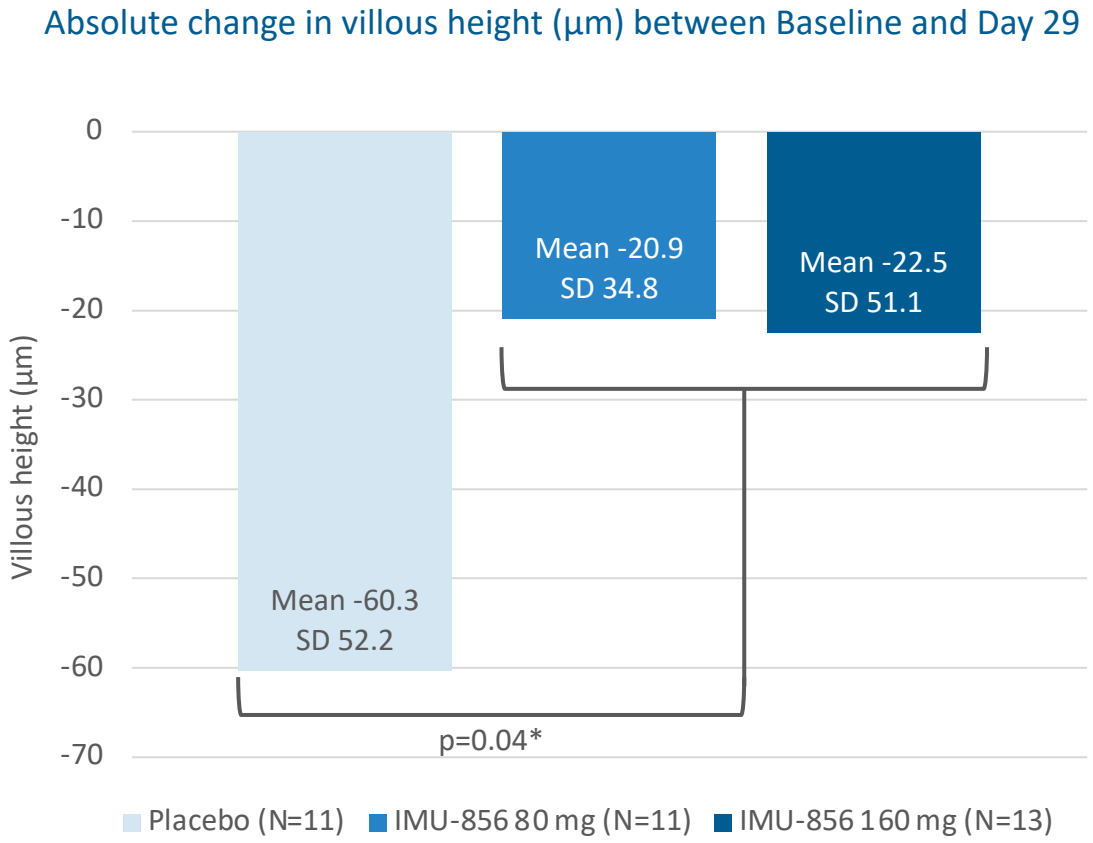
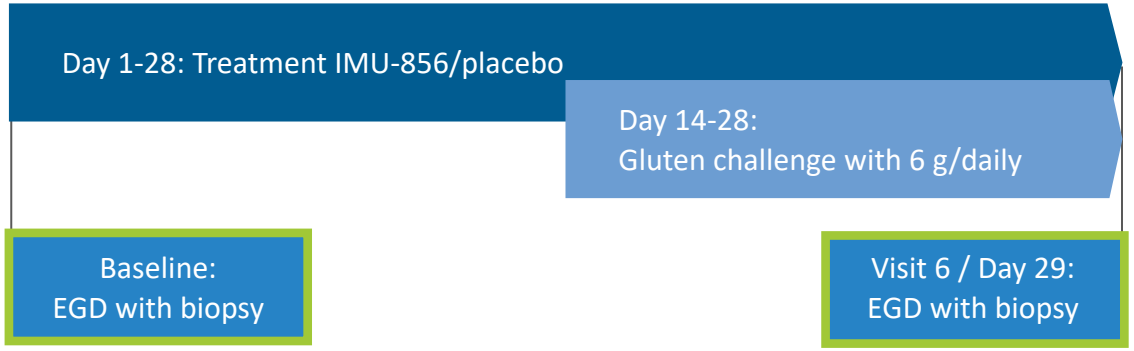
IMU-856 Protected Villous Height as Compared to Placebo



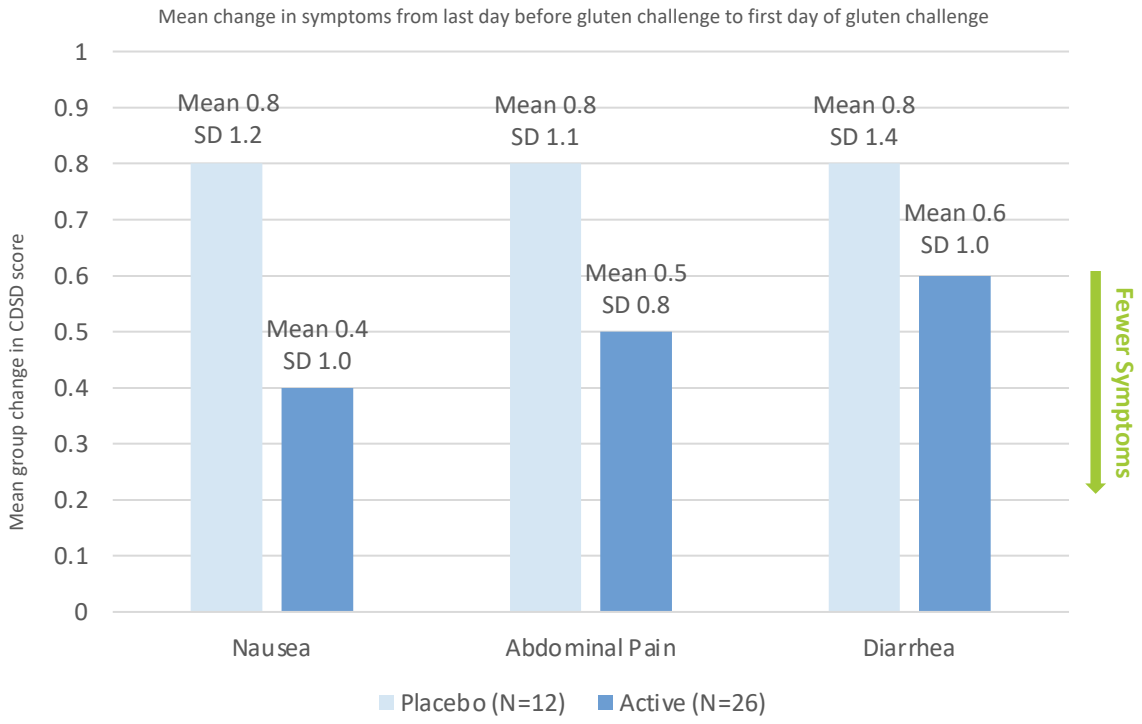


- Substantial protection for IMU-856 treatment groups as compared to placebo
- Reached statistical significance* for this objective readout which is known to be relevant to influence future medical complications of celiac disease
- Assessed by central pathology laboratory and blinded pathology reader

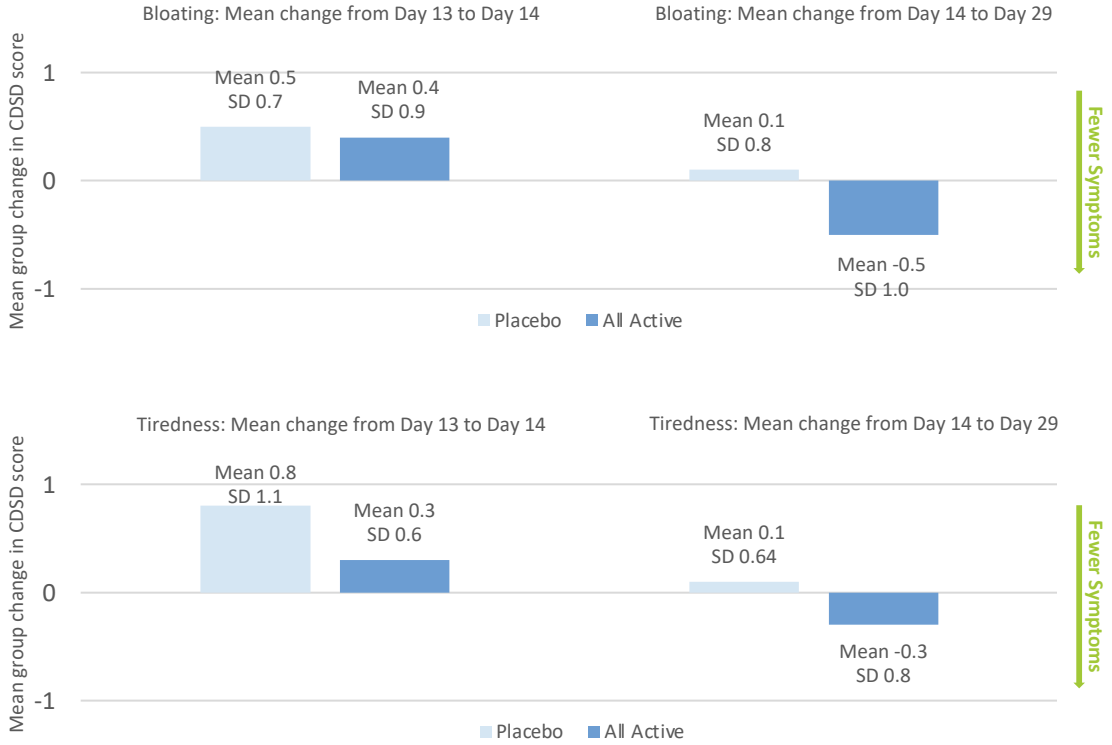
* Wilcoxon Two-Sample Test comparison between pooled IMU-856 groups and placebo, performed as post-hoc exploratory statistical analysis
Disease Analysis Set: N=35/43 included in histology analysis set. 8 patients not included in this analysis due to early termination. Gluten Challenge for 15 days with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

IMU-856 Surpressed 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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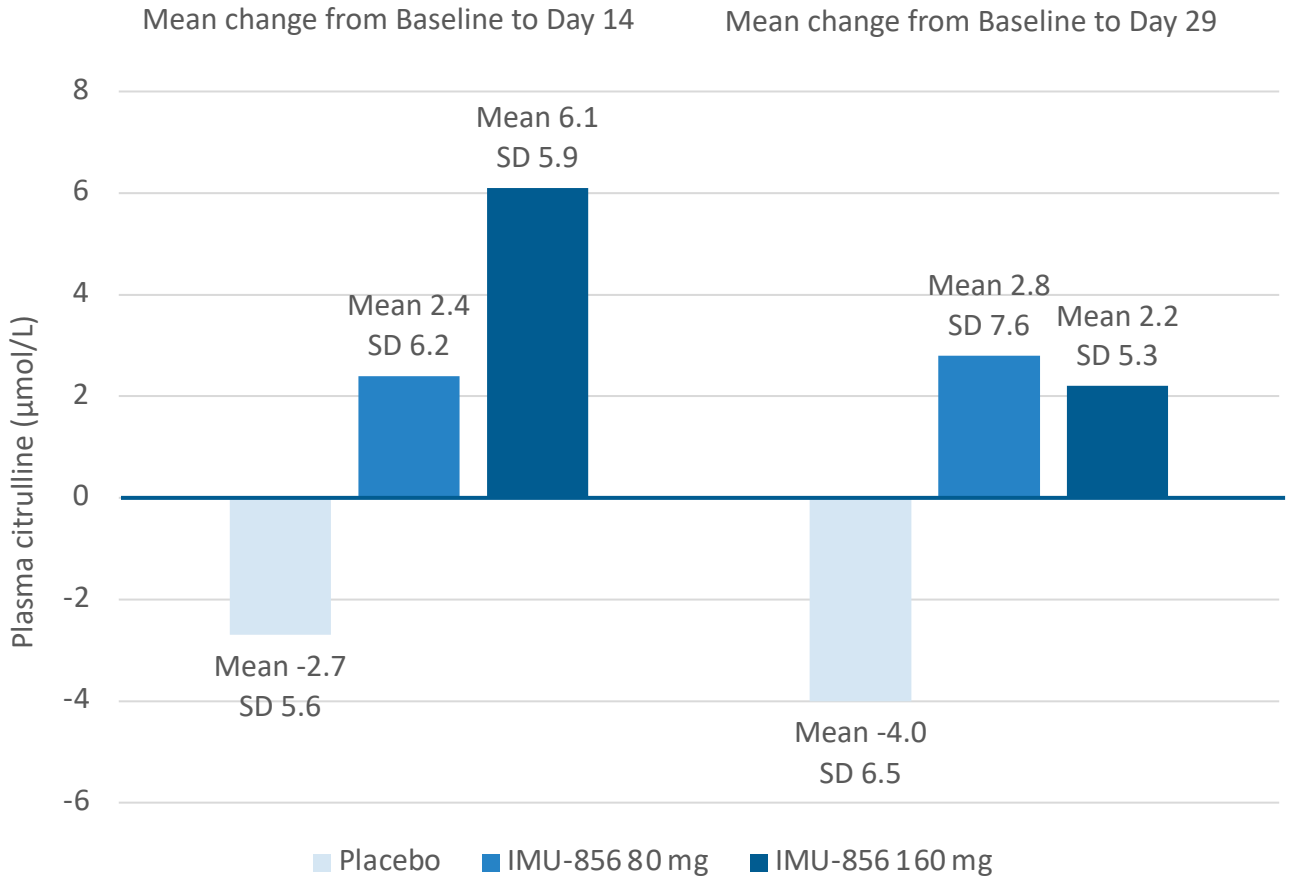
IMU-856 Showed Signal for Improving Citrulline

Biomarker Reflecting the Health Status and Function of Enterocytes



Citrulline is a non-essential amino acid that is mainly produced by the enterocyte and, hence, the level of citrulline in plasma can represent the mass and metabolic function of the enterocytes[1]

Plasma citrulline levels are known to be related to villous atrophy

- Citrulline levels increase with gluten-free diet and with improvement of enteropathy[2]
- IMU-856 increased citrulline levels dose proportionally, whereas being reduced in placebo treated celiac disease 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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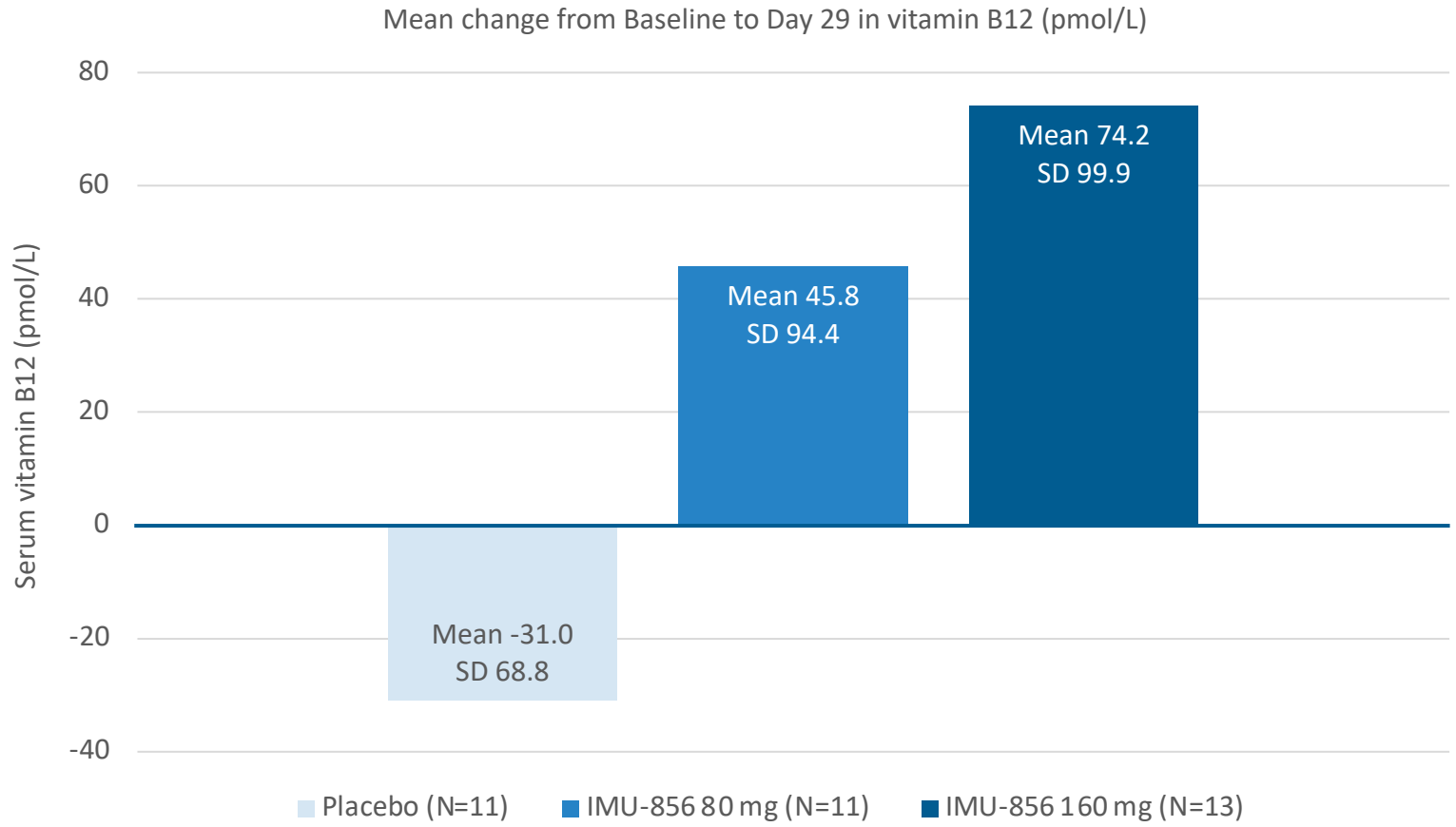
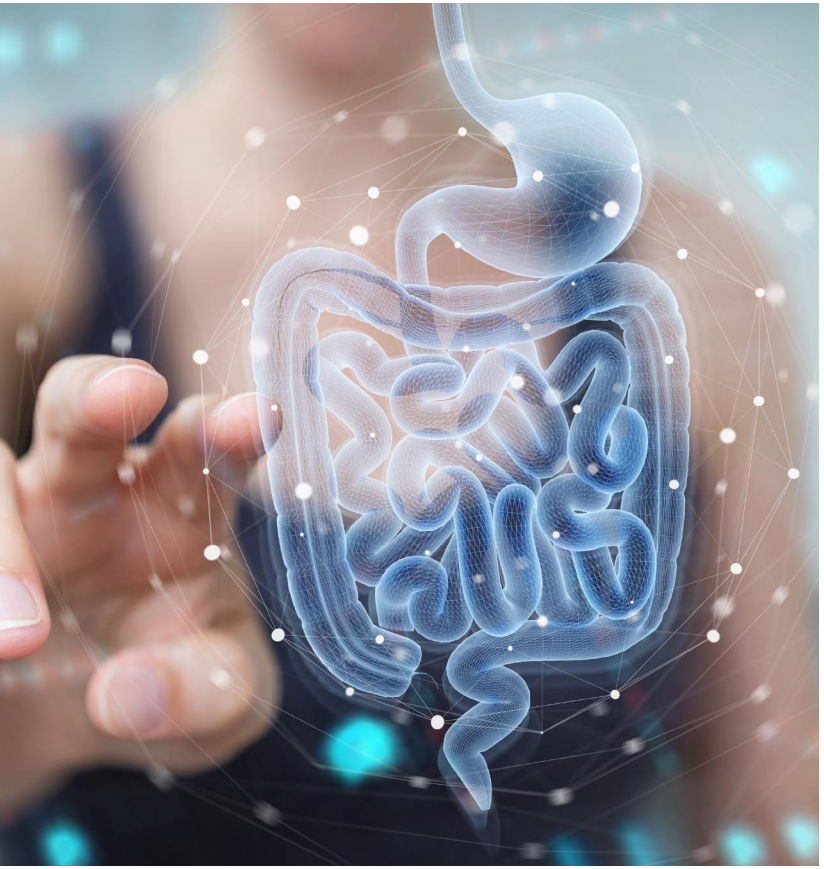
IMU-856 Showed Enhanced Uptake of Vitamin B12



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 small exploratory 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.

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 Q4/2024

Cash position: USD 77.3 million (as of Jun 30, 2023)

Shares outstanding: 44,595,383 (as of Jul 28, 2023)

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Summary: Several Clinical Value Inflection Points Expected

IMU-838 in PMS	▪ Interim analysis phase 2 CALLIPER trial estimated for fall 2023 ▪ Readout phase 2 CALLIPER trial estimated for April 2025
IMU-838 in RMS	▪ Interim analysis phase 3 ENSURE program estimated for late 2024 ▪ Readout of first phase 3 ENSURE trial estimated for end of 2025
IMU-856	▪ Phase 2 clinical trial in preparation ▪ Also applicable for other gastrointestinal disorders

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Thank You!

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