# Immunic Therapeutics

## Developing Selective Oral Therapies in Immunology

NASDAQ: IMUX | May 15, 2023 | Bio€quity Europe 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.

# 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<br>Progressive Multiple Sclerosis (PMS) – CALLIPER Trial<br>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 H2/2023<br>▪ CALLIPER trial estimated to readout end of 2024<br>▪ Interim analysis of first ENSURE trial in RMS planned after approximately half of the events occurred, estimated for late 2024<br>▪ 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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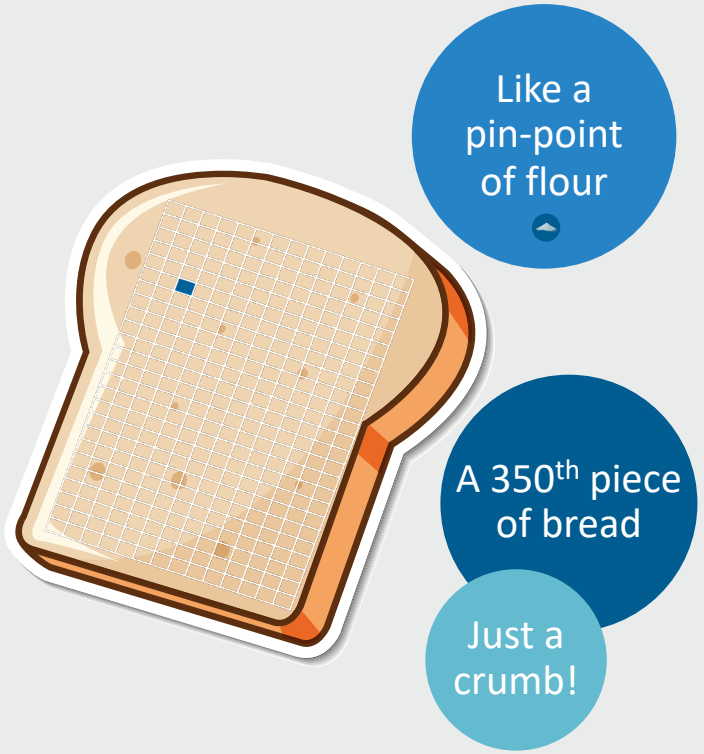
IMU-856

# Restoring a Healthy Gut by Renewal of the Gut Wall

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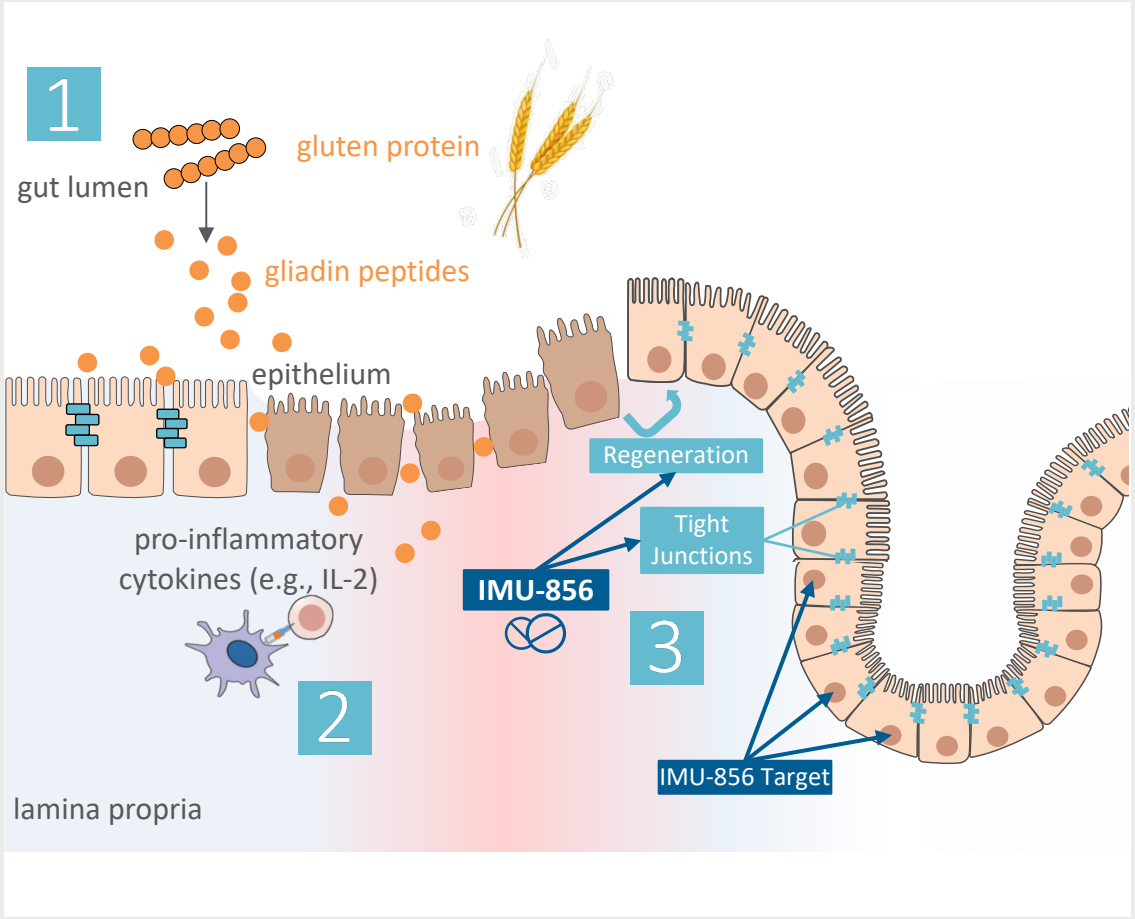
# First Proof-of-Concept for Gastrointestinal Disorders in Celiac Disease

## 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

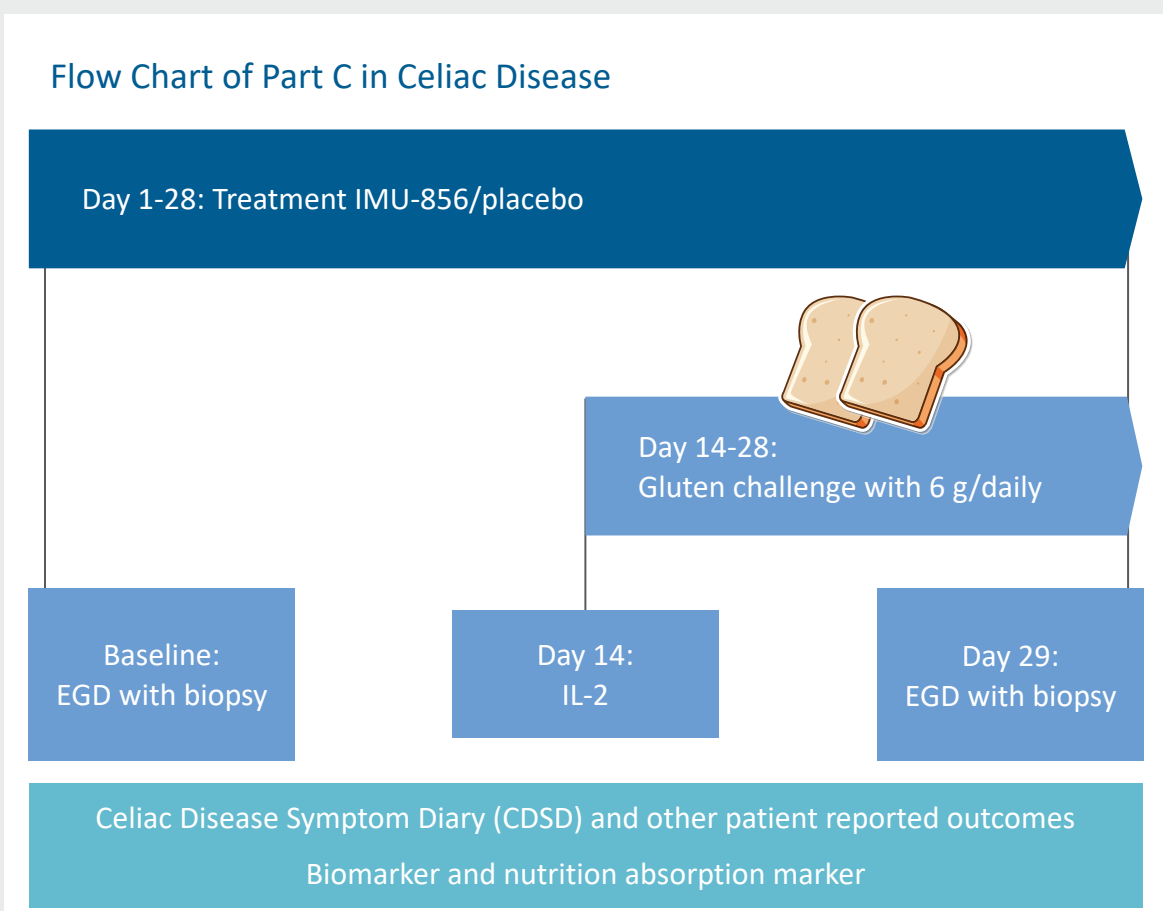
Picture: self-drawn; [1] Caio et al. BMC Medicine (2019) 17:142
HLA: human leukocyte antigen; TG2: tissue transglutaminase 2; CD: cluster of differentiation; IL: interleukin

# 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




EGD: esophagogastroduodenoscopy; IL: interleukin



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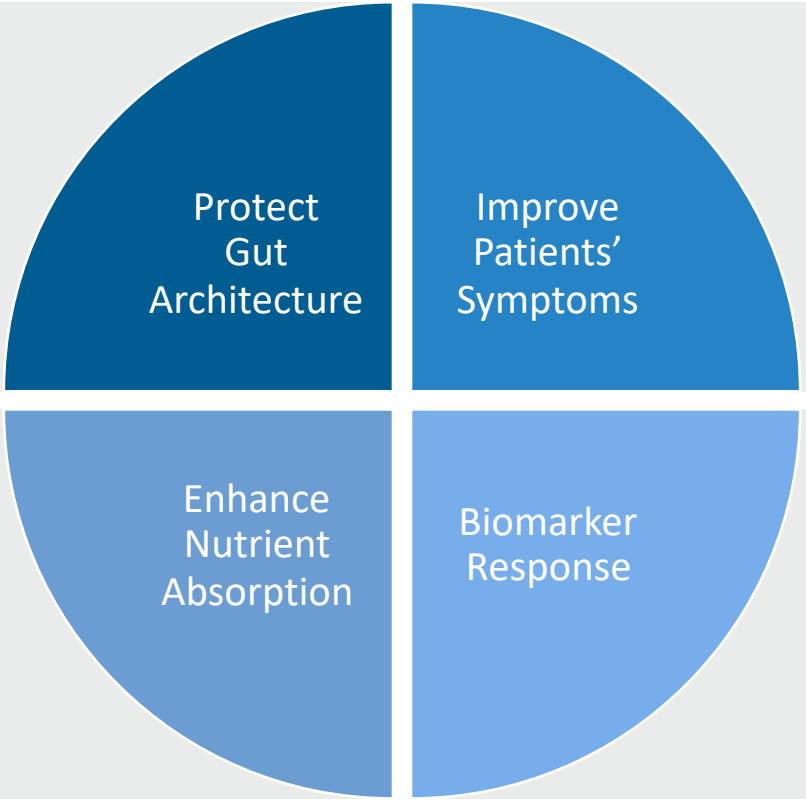
# IMU-856 Shows Positive Effects in Main Four Dimensions of Clinical Outcome in Celiac Disease Patients

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




IMU-856 reduces/reverses gluten-induced symptoms reported by patients

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

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

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



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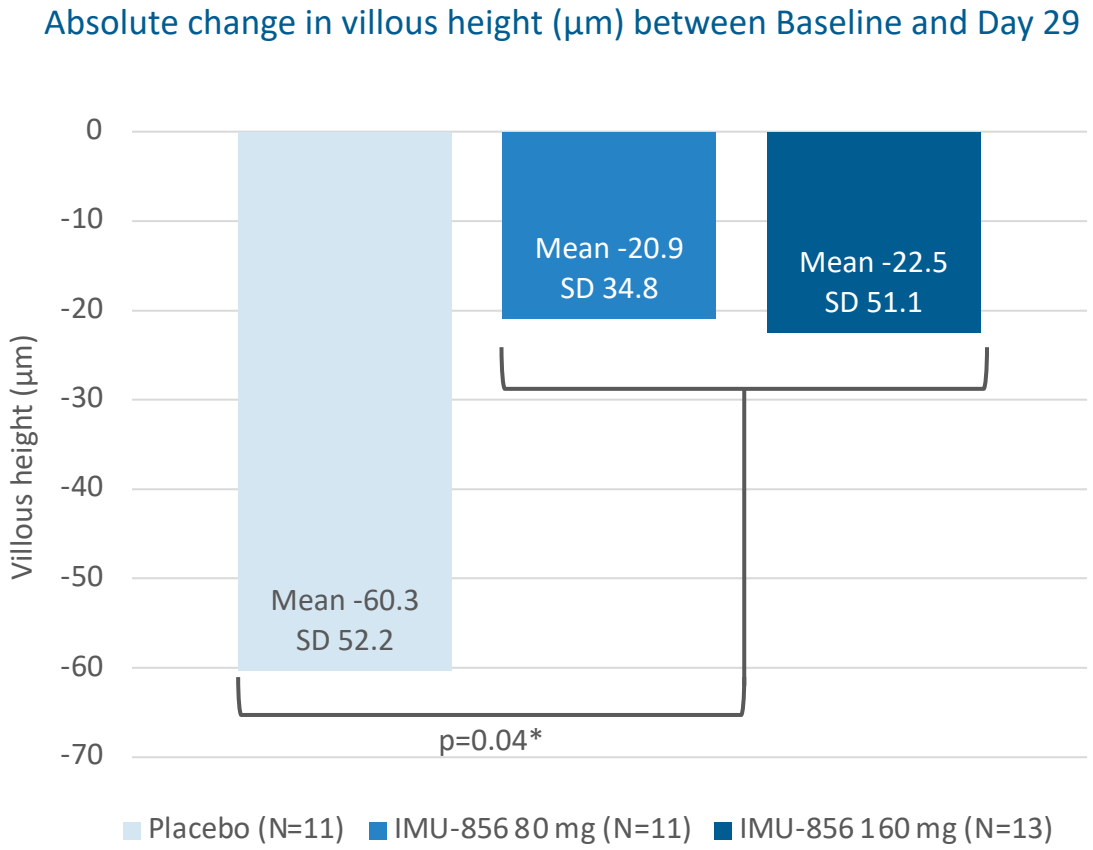
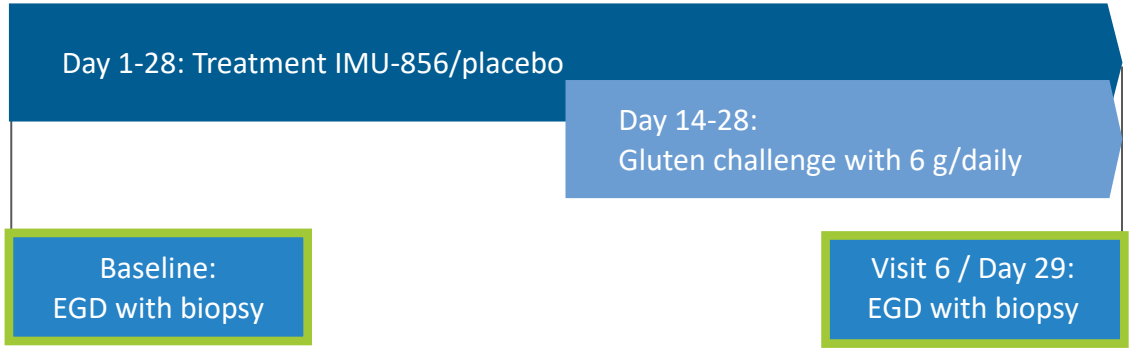
# IMU-856 Protects Villous Height as Compared to Placebo




- 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 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 2b 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.

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-viral effects
- Anti-inflammatory 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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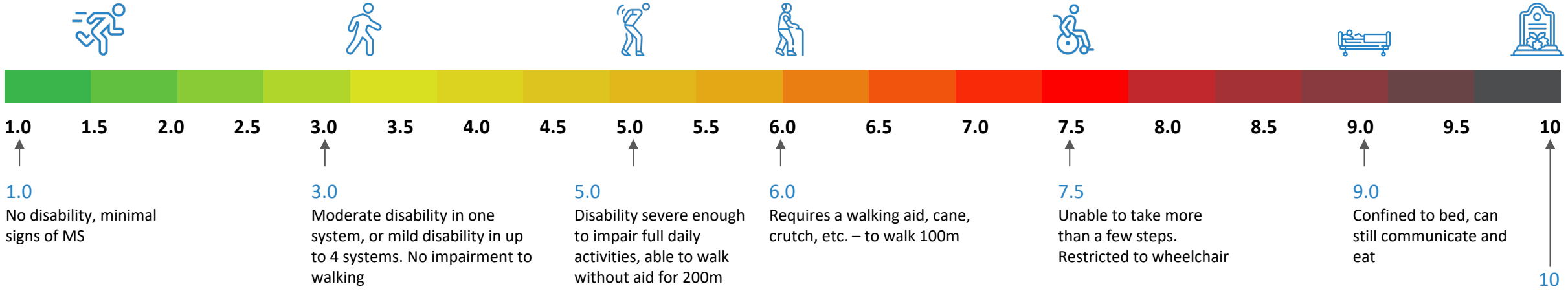
# MS is a Lifelong Neurodegenerative Disease

## 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

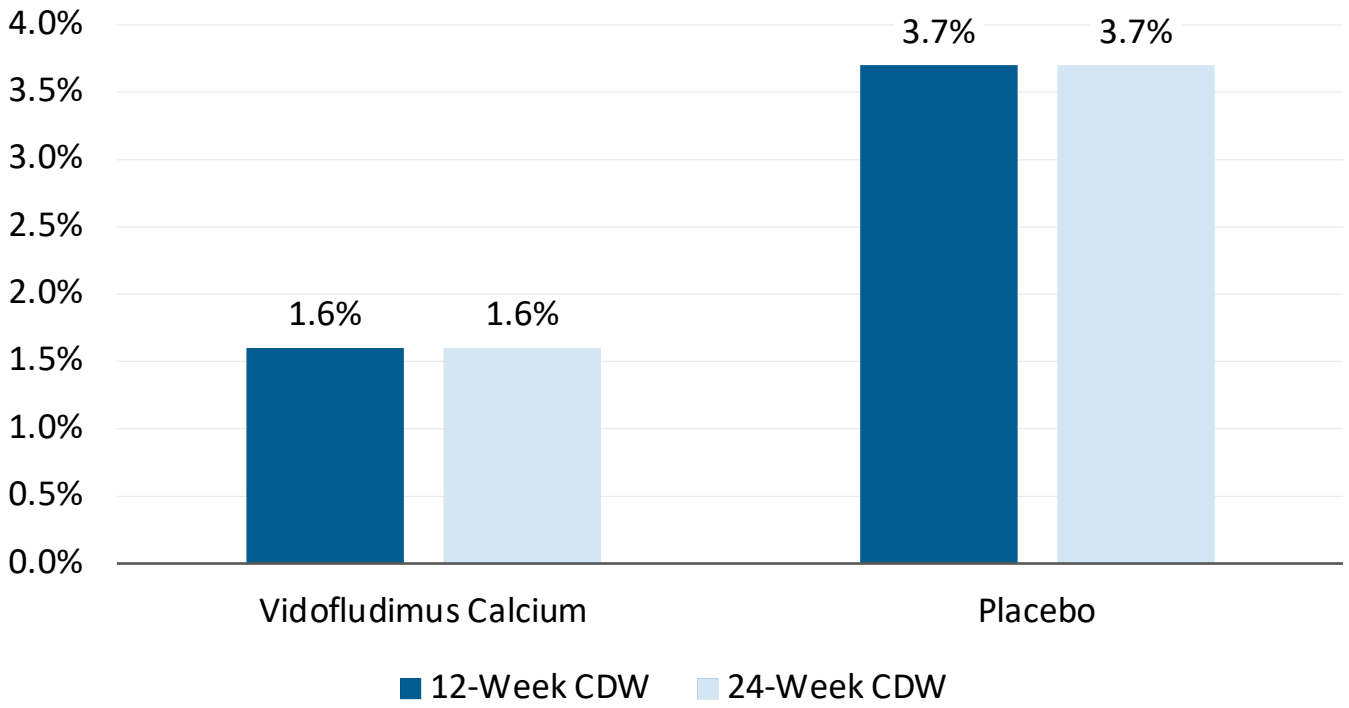



[1] MS International Federation (2020): Atlas of MS, https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms; Illustration adapted from: VOX, https://futurism.com/reversal-of-multiple-sclerosis-via-risky-stem-cell-treatment-confirmed, and Multiple Sclerosis Trust, https://www.mstrust.org.uk/;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

# 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 confirm 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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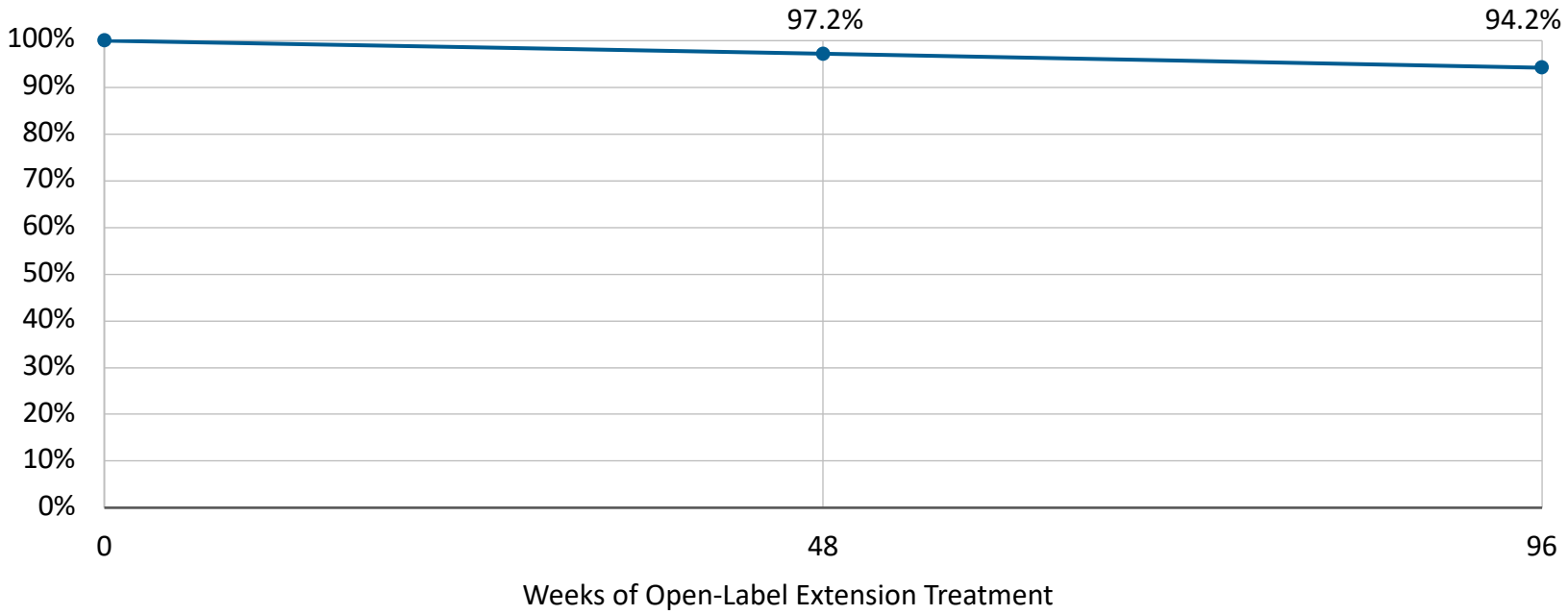
# EMPhASIS Trial: Interim Analysis Regarding 12-Week CDW Events

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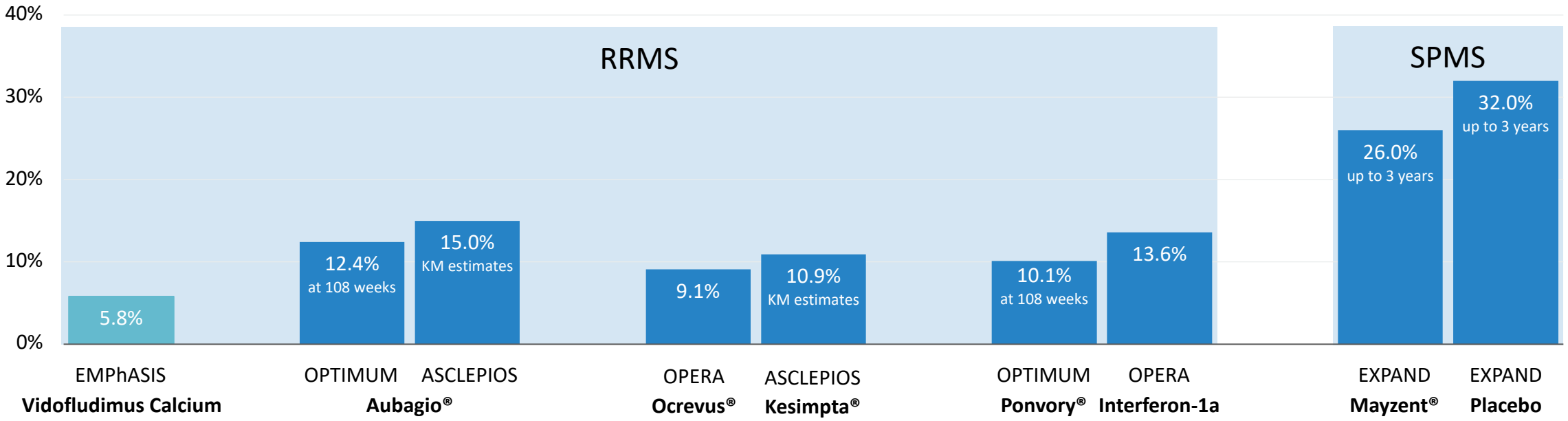
# 12-Week Confirmed Disease Worsening after 2 Years (96 Weeks)

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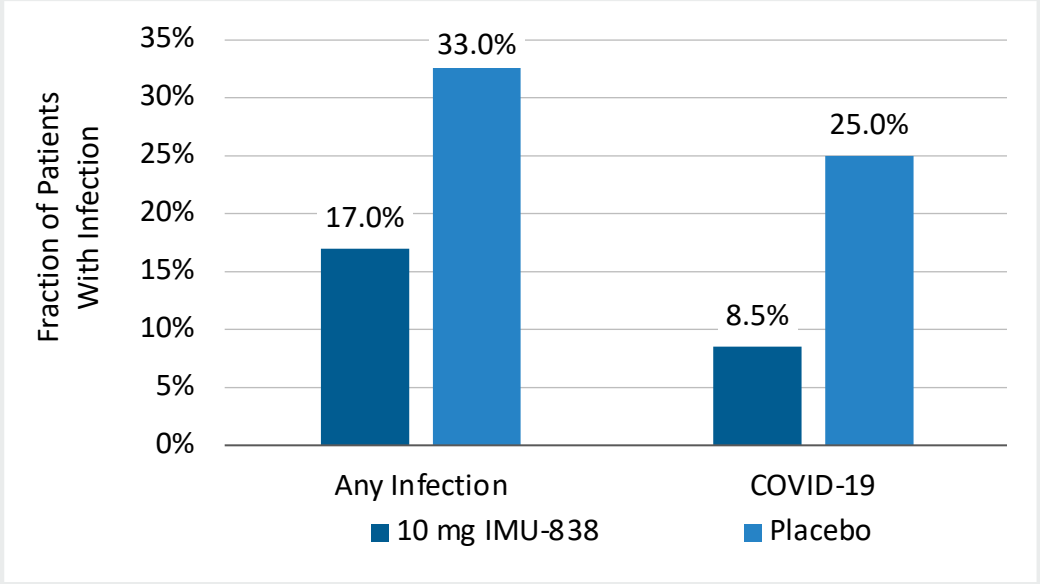
# Vidofludimus Calcium Showed Interesting Hints for Clinical Anti-SARS-CoV-2 Activity and Maintaining Humoral Response

## 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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# Vidofludimus Calcium's Safety Profile to Date is Unique

| | Vidofludimus Calcium [1] | Aubagio® [2] | Ocrevus® [3] | Tecfidera® [4] | Mavenclad® [5] | Gilenya® [6] | Mayzent® [7] | Zeposia® [8] |
|---|---|---|---|---|---|---|---|---|
| PML risk | ● | ● | ● | ● | ● | ● | ● | ● |
| Increased number of infections | ● | ● | ● | ● | ● | ● | ● | ● |
| Vaccination limitations | ● | ● | ● | ● | ● | ● | ● | ● |
| Gastrointestinal toxicities, incl. diarrhea | ● | ● | ● | ● | ● | ● | ● | ● |
| Cardiovascular risks, incl. blood pressure | ● | ● | ● | ● | ● | ● | ● | ● |
| Lymphopenia | ● | ● | ● | ● | ● | ● | ● | ● |
| Neutropenia | ● | ● | ● | ● | ● | ● | ● | ● |
| Risk of liver injury | ● | ! | ● | ● | ● | ● | ● | ● |
| Rebound effect | ○ | ● | ● | ● | ● | ● | ● | ● |
| Increased risk of cancer | ● | ● | ● | ● | ! | ● | ● | ● |
| Macular edema | ● | ● | ● | ● | ● | ● | ● | ● |

● Favorable Profile ● Clinical Concern / Risk ● Substantial Risk ! Black Box Warning ○ No data available

This classification is based on Immunic's assumptions according to clinical trial results regarding likelihood and severity of risk as well as FDA labels of the drugs displayed: [1] https://imux.com/immunic-inc-publishes-full-unblinded-clinical-data-from-phase-2-emphasis-trial-of-imu-838-in-patients-with-relapsing-remitting-multiple-sclerosis-and-announces-poster-presentation-at-the-msvirtual20/ [2] O'Connor et al., 2011 NEJM [3] oiajfoij. Hauser et al. 2017., NEJM, Montalban et al. 2017, NEJM [4] Gold et al., 2012 NEJM, Fox et al., 2012 NEJM [5] Giovannoni et al., 2010 NEJM [6] Kappos et al., 2010 NEJM, Cohen et al., 2010 NEJM [7] Kappos et al 2018 Lancet [8] Comi et al., 2020 Lancet, Cohen et al., 2020 Lancet



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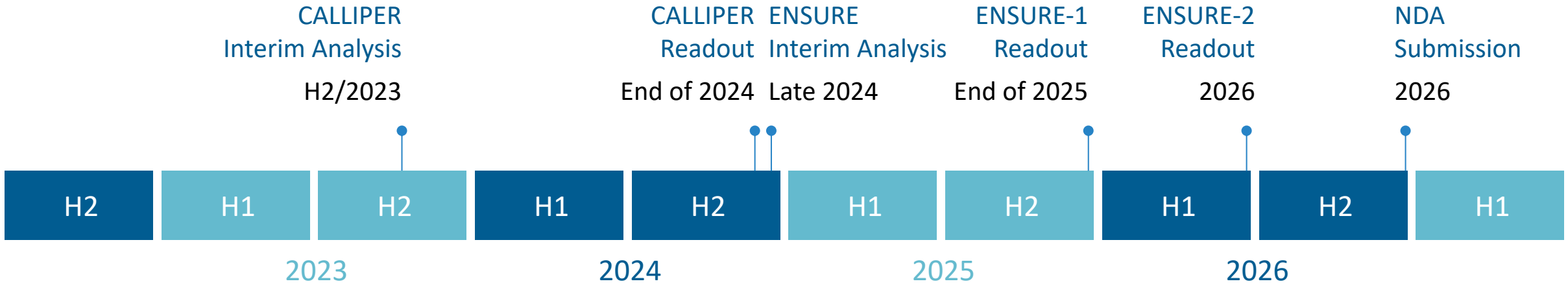
# Straightforward Path Towards Potential Approval




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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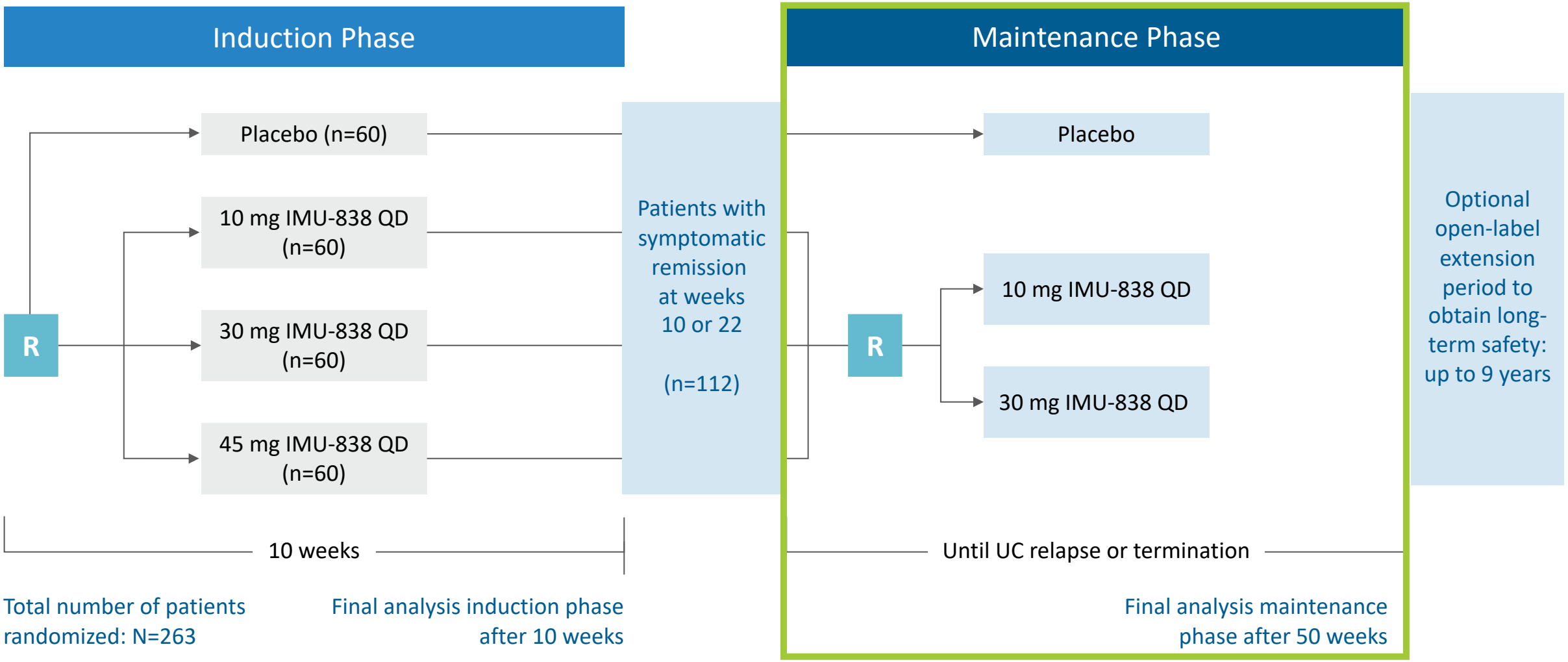
Vidofludimus Calcium in Ulcerative Colitis (UC)

# 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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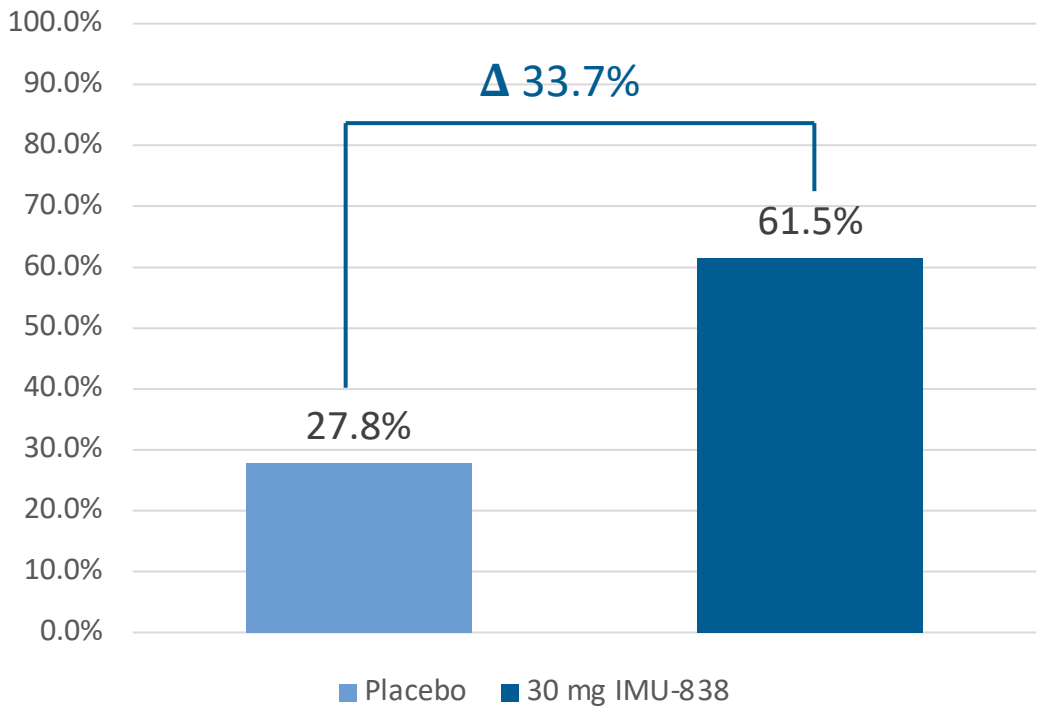
# Exploratory Statistical Analysis of Clinical Remission

## 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**<br><br>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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# 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 2b testing

### Cash runway into Q4/2024

Cash position: USD 97.1 million (as of Mar 31, 2023)

Shares outstanding: 44,403,838 (as of May 2, 2023)



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# Thank You!


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