Immunic Therapeutics

Developing Selective Oral Drugs in Immunology

NASDAQ: IMUX | March 9-10, 2021 | H.C. Wainwright Global Life Sciences Conference

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 plans to develop and commercialize its product candidates, including IMU-838, IMU-935 and IMU-856; the timing of initiation of Immunic's planned clinical trials; the potential for IMU-838 to safely and effectively target and treat relapsing-remitting multiple sclerosis or infections associated with coronavirus disease 2019 (COVID-19); the impact of future preclinical and clinical data on IMU-838 and the Company's other product candidates; the availability or efficacy of Immunic's potential treatment options that may be supported by trial data discussed herein; expectations regarding potential market size; the timing of the availability of data from Immunic's clinical trials; the timing of any planned investigational new drug application or new drug application; Immunic's plans to research, develop and commercialize its current and future product candidates; 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; 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 identify additional products or product candidates with significant commercial potential; developments and projections relating to Immunic's competitors and industry; the impact of government laws and regulations; Immunic's ability to protect its intellectual property position; 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 the other risks set forth in the company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020, filed with the 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 Vision

We are developing new therapies with best-in-class potential for the treatment of chronic inflammatory and autoimmune diseases.

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Development Pipeline

Program	Indication	Target	Preclinical	Phase 1	Phase 2	Phase 3
IMU-838	Multiple Sclerosis	DHODH	■	■	■	■
	Ulcerative Colitis	DHODH	■	■	■	
	Crohn's Disease	DHODH	■	■		
	Primary Sclerosing Cholangitis	DHODH	■	■	■	Investigator-Sponsored Trial performed at Mayo Clinic / NIH
	COVID-19*	DHODH	■	■	■	■
IMU-935	Psoriasis	RORγt	■	■		
	Guillain-Barré Syndrome	RORγt	■	■		
IMU-856	Gastrointestinal Diseases	Intestinal Barrier Function	■	■		

■ Completed or ongoing ■ In preparation or planned

* Additional investigator-sponsored phase 2 clinical trial of IMU-838 in combination with oseltamivir in patients with moderate-to-severe COVID-19 ongoing in collaboration with the University Hospitals Coventry and Warwickshire NHS Trust, UK

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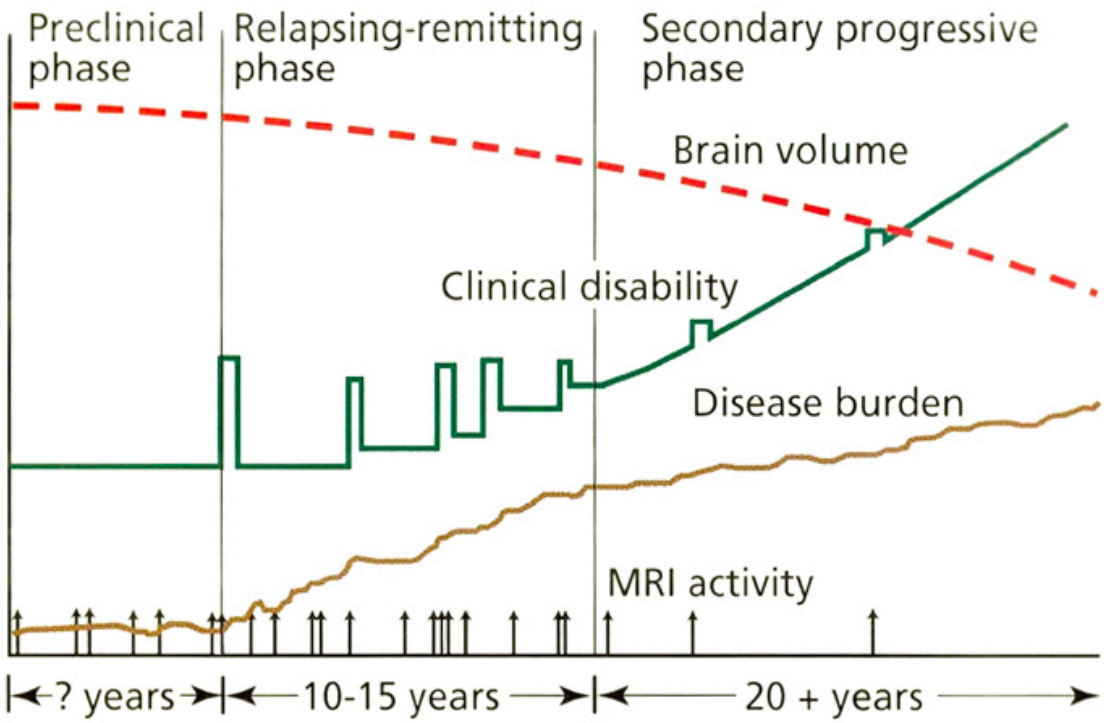
High Unmet Medical Need

Targeting Multiple Sclerosis (MS)

Treatment Compliance and Persistence are Important Considerations for Life-Long Diseases such as MS

MS Disease Course[1]



Nonadherence or Nonpersistence of MS Treatments Can Lead to Greater Risk for Negative Clinical Outcomes[2]

- Real-life 12-months discontinuation rates of MS treatments

	USA[3]	Canada[4]
Fingolimod	26%	24%
Dimethyl fumarate	44%	30%
Teriflunomide	50%	25%
Natalizumab	N/A	29%

For a life-long disease, patients require easy, convenient and safe therapies that allow them to avoid treatment interruptions.

[1] Adapted from Fox RJ, Cohen JA: Multiple sclerosis: the importance of early recognition and treatment. Cleve Clin J of Med, 2001; 68:157–70
[2] Tan H, et al. Impact of adherence to disease-modifying therapies on clinical and economic outcomes among patients with multiple sclerosis. Adv Ther. 2011;28(1):51-61
[3] Johnson et al., J Manag Care Spec Pharm. 2017;23(8):844-52
[4] Duquette P, Yeung M, Mouallif S, Nakhaipour HR, Haddad P, Schecter R 2019 PLoS ONE 14(1): e0210417. https://doi.org/10.1371/journal.pone.0210417

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Despite Many Therapies Approved (and Nearing Approval) for Relapsing Forms of MS, There Remains Ample Opportunity for a …

- Safe
- Oral
- Well-Tolerated
- Robust Anti-Inflammatory, with
- Neuroprotective Properties Beyond What Would be Expected by Reducing Inflammation.

EMPhASIS: Phase 2 Study Overview in RRMS
NCT03846219

Coordinating Investigator

Robert Fox (Cleveland Clinic)

Included Patient Population: RRMS With Relevant Disease Activity

- Male or female (18 ≥ age ≤ 55)
- RRMS diagnosis (Revised McDonald criteria 2017)
- Evidence of disease activity based on relapse and MRI criteria
- Baseline EDSS: 0 ≥ EDSS ≤ 4.0
- Performed in Central and Eastern Europe

Blinded Treatment Period

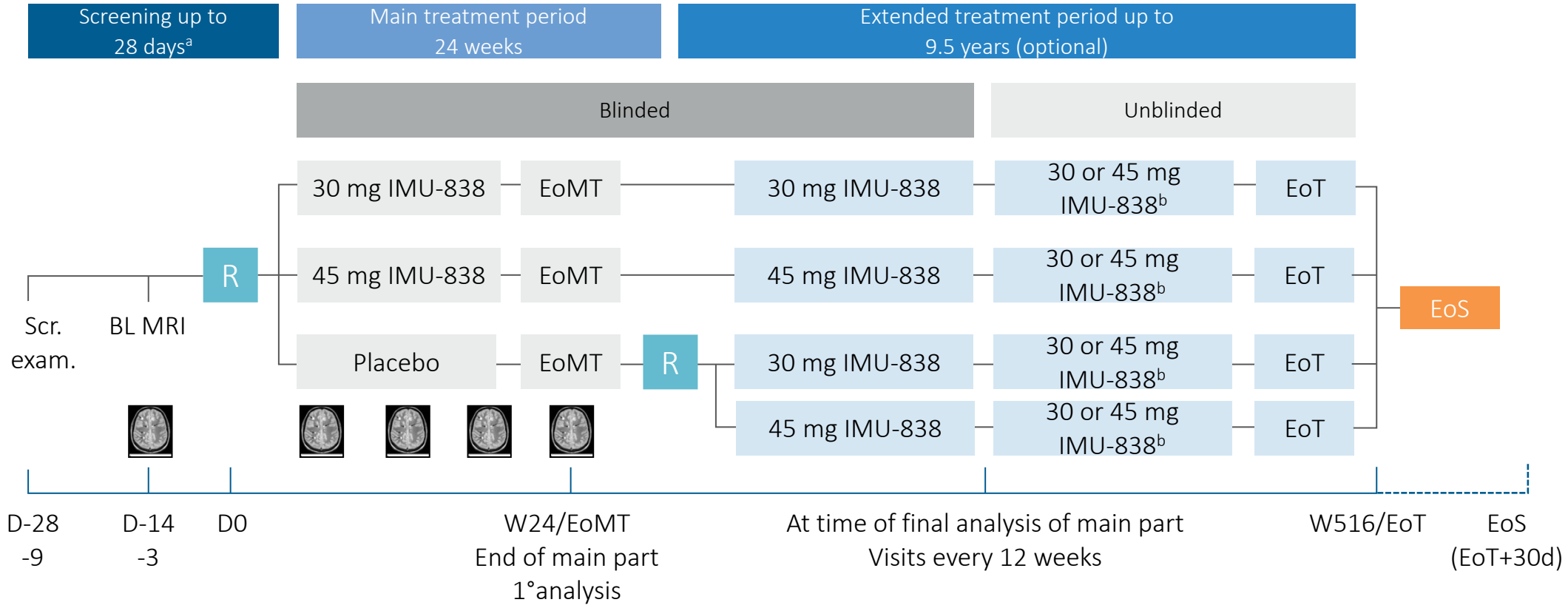
- Parallel group design with placebo control
- Overall blinded treatment period of 24 weeks
- MRI every six weeks

Extended Treatment Period

- Up to 9.5 years
- Extension study to observe long-term safety

EDSS: Expanded Disability Status Scale; MRI: magnetic resonance imaging

EMPhASIS: Phase 2 Trial Design in RRMS



Key study endpoints: to evaluate the **cumulative number of new combined unique active lesions up to week 24**

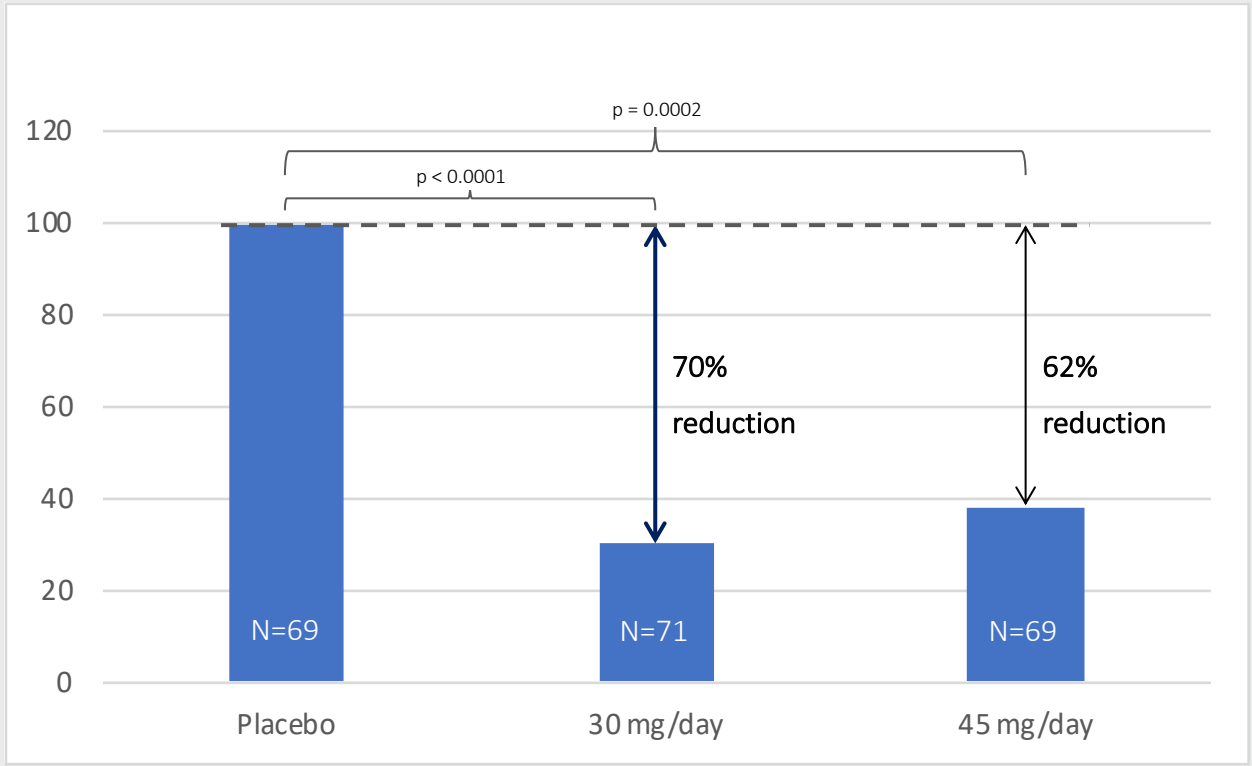
- **Primary endpoint: 45 mg IMU-838 vs. placebo**
- **Key secondary endpoint: 30 mg IMU-838 vs. placebo**

a) Can be interrupted/extended, if the baseline MRI must be repeated due to poor quality (to be done as soon as possible). If results of the central MRI assessment are not available in time for randomization, the screening period can be extended by up to 7 days, if needed.
b) After unblinding of the main treatment period, the investigator can decide with the patient if and at which dose the treatment will be continued.
BL: baseline; exam.: examination; D: day; EoMT: end of main treatment; EoS: end of trial; EoT: end of treatment; MRI: magnetic resonance imaging; R: randomization; Scr.: screening; W: week

Phase 2 EMPhASIS Trial of IMU-838 in RRMS

Efficacy

Study Met Primary and Key Secondary Endpoints



Suppression of CUA MRI Lesions
IMU-838 versus Placebo over 24 weeks

Robust efficacy demonstrated for both investigated doses of IMU-838 with high statistical significance.

CUA MRI Lesions: combined unique active magnetic resonance imaging lesions. Sum of the number of all new Gadolinium-enhancing lesions on T1-weighted MRI and the number of all new or substantially enlarged lesions on T2-weighted MRI (non-enhancing on T1-weighted MRI), avoiding double counting.
Estimates are adjusted for baseline volume of T2 lesions, MRI field strength (1.5 or 3.0 Tesla), and baseline number of Gadolinium-enhancing lesions (0, >=1) using a generalized linear model with a negative binomial distribution and a logarithmic link function. Log transformation of time from first IMP dose to date of last MRI assessment is used as offset term.

Study Results 1: Robust Efficacy

The **Robust MRI Lesion Suppression of IMU-838** Compares Favorably to Other First-Line and Oral Base Medications Commercially Available in RRMS.*

	IMU-838	IMU-838	Glatiramer acetate[1]	Teriflunomide[2]	Dimethyl fumarate[3]	Fingolimod[4]	Siponimod[5]
Administration	Oral	Oral	Injectable	Oral	Oral	Oral	Oral
Daily Dose	45 mg QD	30 mg QD	20 mg QD	14 mg QD	240 mg TID	1.25 mg QD	2 mg QD
MRI Endpoint	Cumulative CUA lesions	Cumulative CUA lesions	Cumulative Gd lesions	Mean CUA lesions/scan	Cumulative Gd lesions	Cumulative Gd lesions	Cumulative CUA lesions
Treatment Duration	24 weeks	24 weeks	9 months	36 weeks	24 weeks	6 months	3 months
Suppression of MRI Activity	**62%**	**70%**	**29%**	**61%**	**69%**	**43%**	**70%**

*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.

QD: quaque die = once-daily; TID: ter in die = three times daily; CUA: combined unique active; MRI: magnetic resonance imaging; Gd: Gadolinium

[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] Selmaj et al. Lancet Neurol. 2013;12(8):756-767

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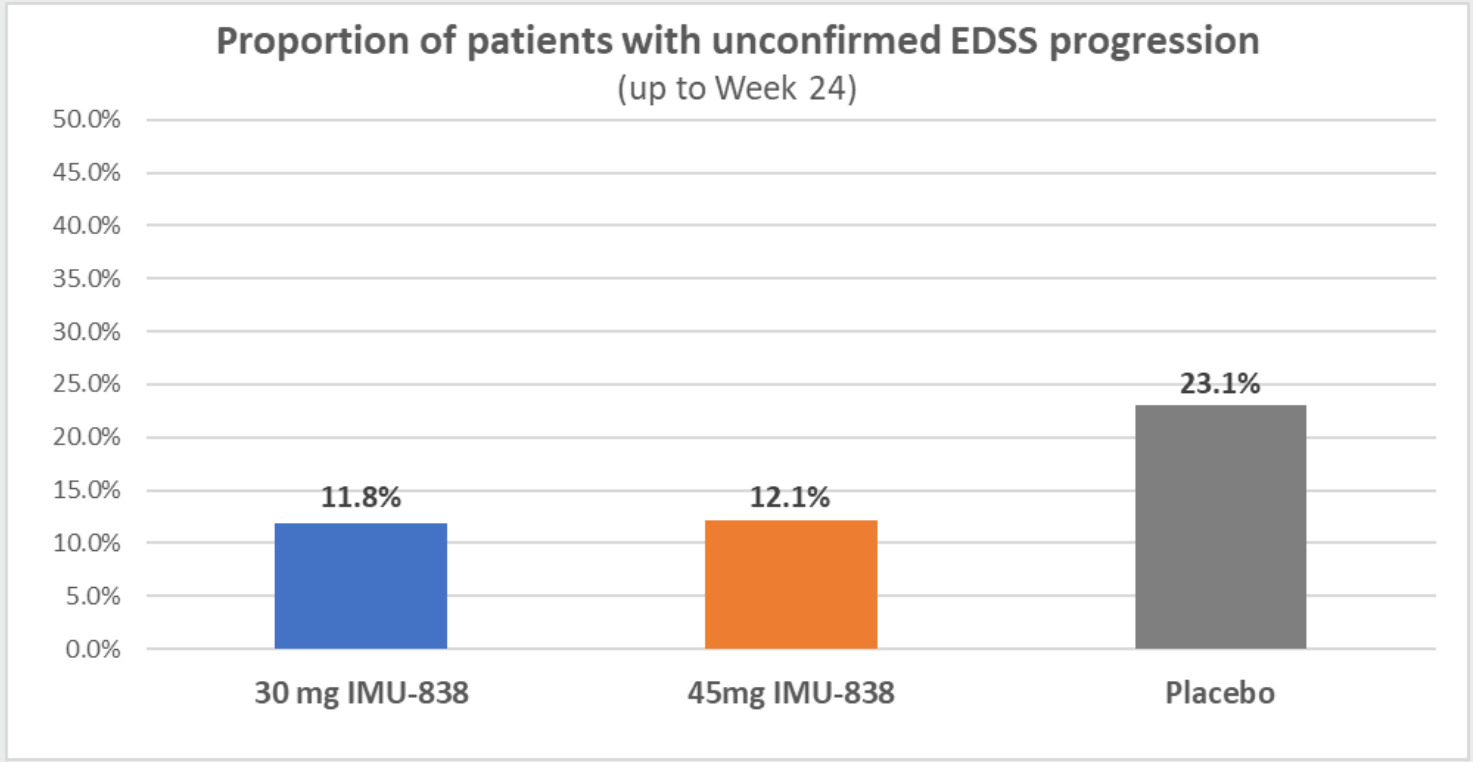
Unconfirmed Disability Progression up to Week 24



Despite the study's relatively small sample size and short duration of blinded treatment (24 weeks), a positive signal on unconfirmed disability was detected.

EDSS progression is defined as an increase of the EDSS score compared to baseline of at least 1.0 point for patients with a baseline EDSS score of 1 to 4.0 or of at least 1.5 points for patients with a baseline EDSS score of 0. There is no confirmation of EDSS progression in this trial due to its short duration.
Patients with missing assessments at week 24 without a progression at any time are set to missing.

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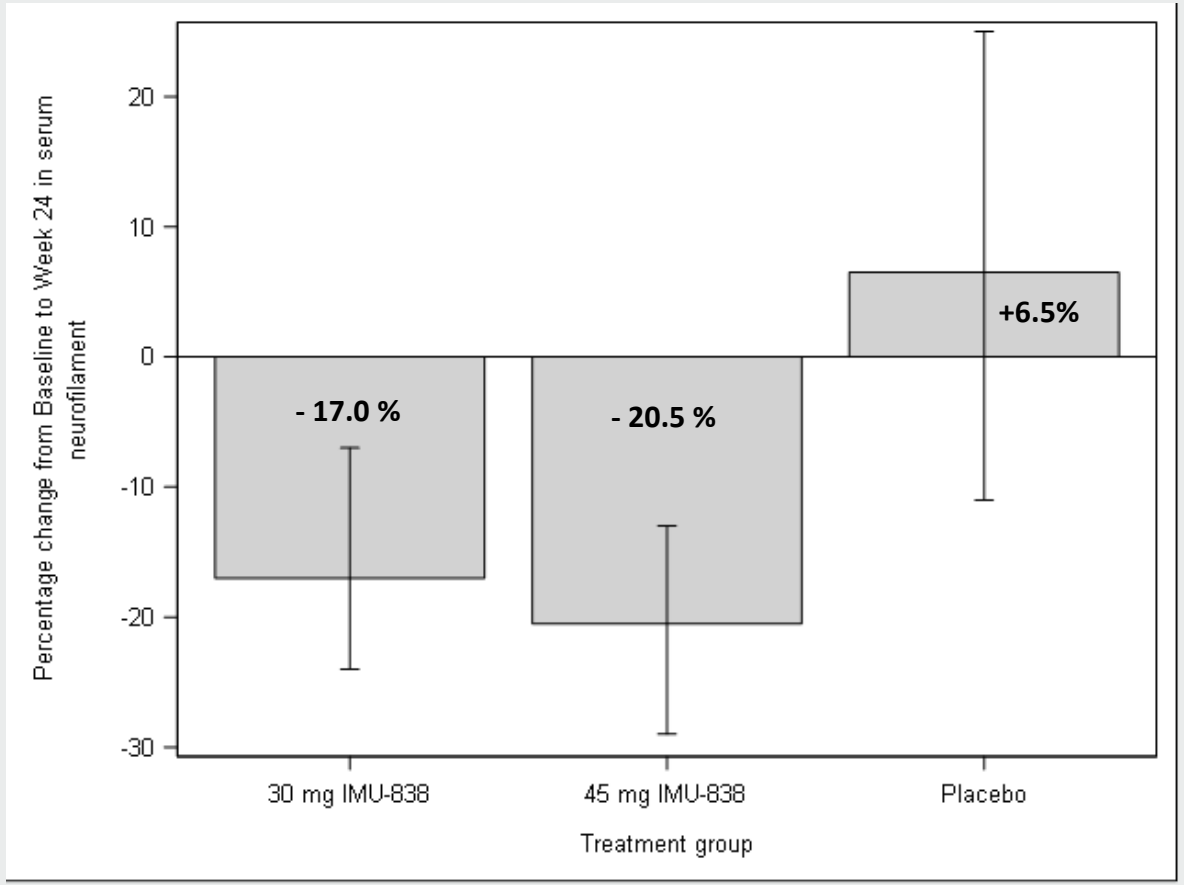
Neurofilament Light Chain in Serum

Biomarker for Axonal Damage



Robust decrease in serum neurofilament light chain provides evidence of potential neuroprotective activity for IMU-838.

Quantification of neurofilament light polypeptide (NEFL) by an electrochemiluminescent immunoassay (ECLIA) in blood serum samples

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Phase 2 EMPhASIS Trial of IMU-838 in RRMS

Safety

Study Results 2: Low Discontinuation Rates

Low Discontinuation Rates for IMU-838 Treated RRMS Patients, Considerably Lower Than Placebo, Indicate an Overall Encouraging Tolerance Profile While Providing a Sense of Efficacy to Patients.*

	IMU-838	IMU-838	Glatiramer acetate[1]	Teriflunomide[2]	Dimethyl fumarate[3]	Fingolimod[4]	Siponimod[5]
Administration	Oral	Oral	Injectable	Oral	Oral	Oral	Oral
Daily Dose	45 mg QD	30 mg QD	20 mg QD	14 mg QD	240 mg TID	1.25 mg QD	2 mg QD
Treatment Period	24 weeks	24 weeks	9 months	36 weeks	24 weeks	6 months	3 months
Active Treatment	**5.8%**	**2.8%**	**5.9%**	**19.3%**	**15.6%**	**5.4%**	**14.3%**
Placebo	**7.2%**	**7.2%**	**5.8%**	**6.6%**	**9.2%**	**6.5%**	**8.9%**

*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.

QD: quaque die = once-daily; TID: ter in die = three times daily

[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] Selmaj et al. Lancet Neurol. 2013;12(8):756-767

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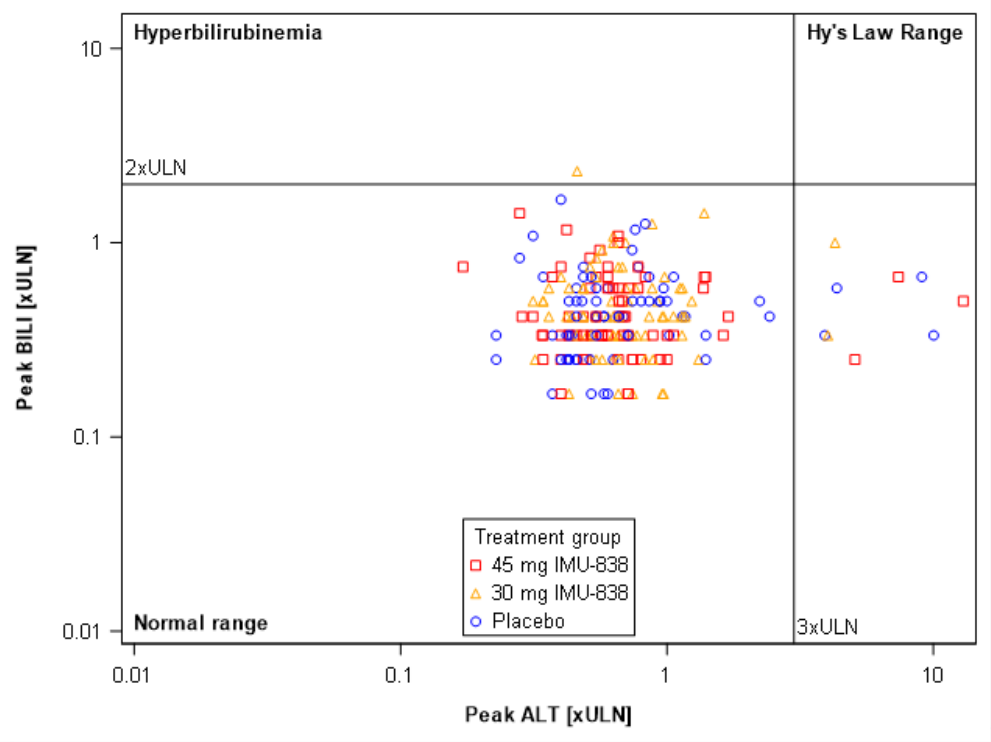
Absence of Hepatotoxicity Signals

Hy's Law Assessment for Drug-Induced Liver Injury

Absence of Hepatotoxicity Signals and Other Relevant Adverse Events Leading to Discontinuations Differentiates Against Other Available Oral RRMS Medications.

Hy's Law Assessment (ALT)



Liver Enzyme Elevations

	IMU-838 (30 mg and 45 mg pooled)	Placebo
Number of Patients	140	69
ALT or AST >5xULN	2.9% (4)	2.9% (2)
ALT or AST >10xULN	0.7% (1)	1.4% (1)
ALT or AST >15xULN	0.0% (0)	0.0% (0)

No signal for hepatoxicity has been observed anywhere in the entire IMU-838 development program, including in the EMPhASIS trial.

ALT: alanine aminotransferase; AST: aspartate aminotransferase; ULN: upper limit of normal; BILI: bilirubin

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IMU-838 in RRMS: Further Development Plan

Completion of Phase 2 Data Set

- Double-blind Cohort 2 sub-trial ongoing to obtain exploratory data on expanded dose response of IMU-838:
  - Cohort of approx. 60 patients receiving 10 mg/day of IMU-838 or placebo for 24 weeks
  - Expected to provide additional data to address any potential regulatory requests in the context of the design of a phase 3 program
  - Unblinded interim analysis of selected MRI data planned after all Cohort 2 patients completed week 12 MRI assessments
    - This interim data is currently expected to be available at the end of March or in early April 2021

Preparation of a Phase 3 Program

- Formal phase 3 feasibility activities already ongoing
- Formal end-of-phase 2 meeting requests to regulatory authorities planned to be submitted around the end of Q1/2021
- Details on the design of the envisaged phase 3 program planned to be announced after the end-of-phase 2 meetings, whose outcome is expected to be available in or about May 2021
- Phase 3 program expected to start in H2/2021

MRI: magnetic resonance imaging

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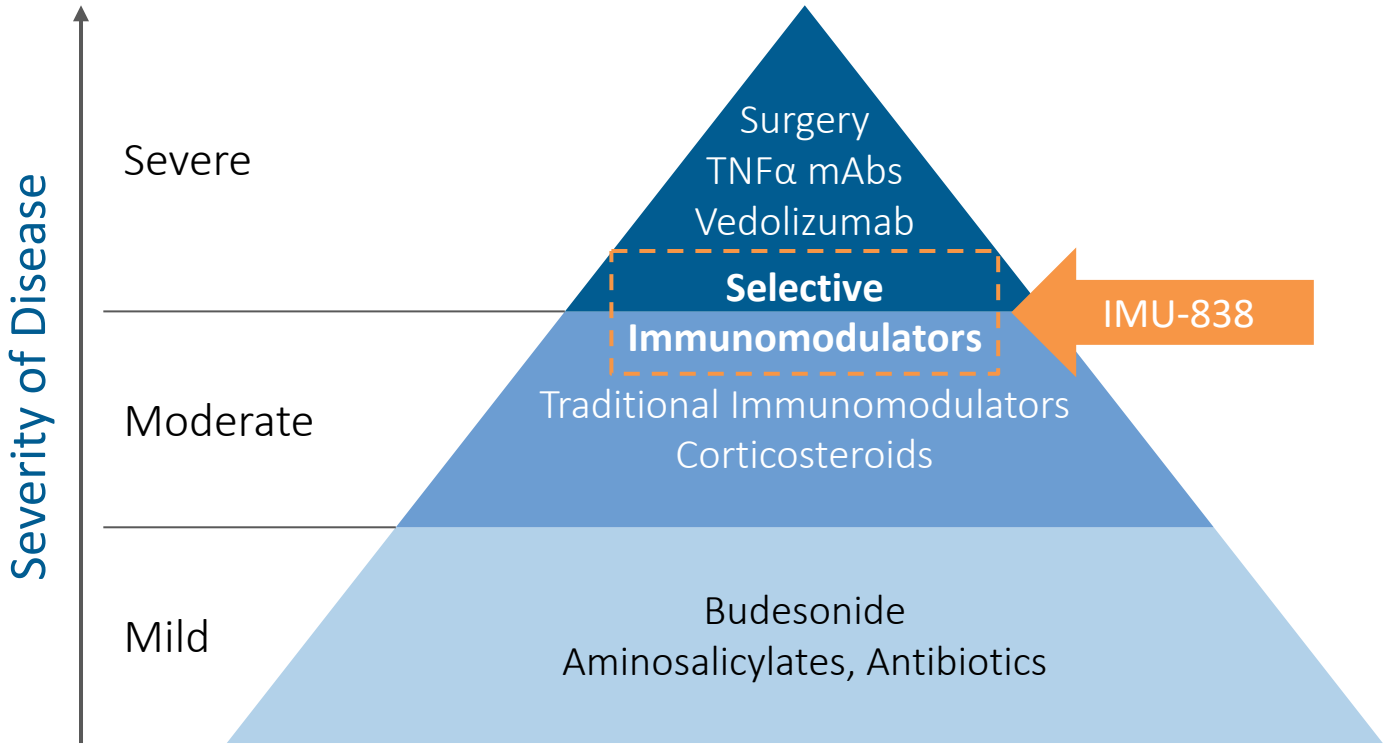
IMU-838 in Inflammatory Bowel Disease (IBD)

New Oral Treatment Option with Promising Safety Profile

IBD: Therapeutic Pyramid



Current Solutions Have Limitations

- Substantial side effects due to long-term use includes increased rate of cancer risk and virus reactivation of currently used immunosuppressants[1] [2] [3]
- Antibodies lose activity over time[4]

[1] Present, Daniel H., et al. Annals of internal medicine 1989; 111.8: 641-649 [2] Dayharsh, Gerald A., et al. Gastroenterology 2002; 122.1: 72-77
[3] Winthrop, Kevin L., et al. Arthritis & rheumatology 2014; 66.10: 2675-2684 [4] Roda, Giulia, et al. Clinical and translational gastroenterology 2017; 7.1: e135
TNF: tumor necrosis factor; mAb: monoclonal antibody

CALDOSE-1: Clinical Phase 2 in UC Ongoing
NCT03341962

Coordinating Investigator:
Dr. Geert d'Haens
(AMC Amsterdam)

Active IND in the United States

Overall Number of Patients:
240

Currently More Than 100 Active Sites in 14 Countries:
USA, Western, Central and Eastern Europe

Interim Analysis Established Potentially Broad Effective Dose Range:

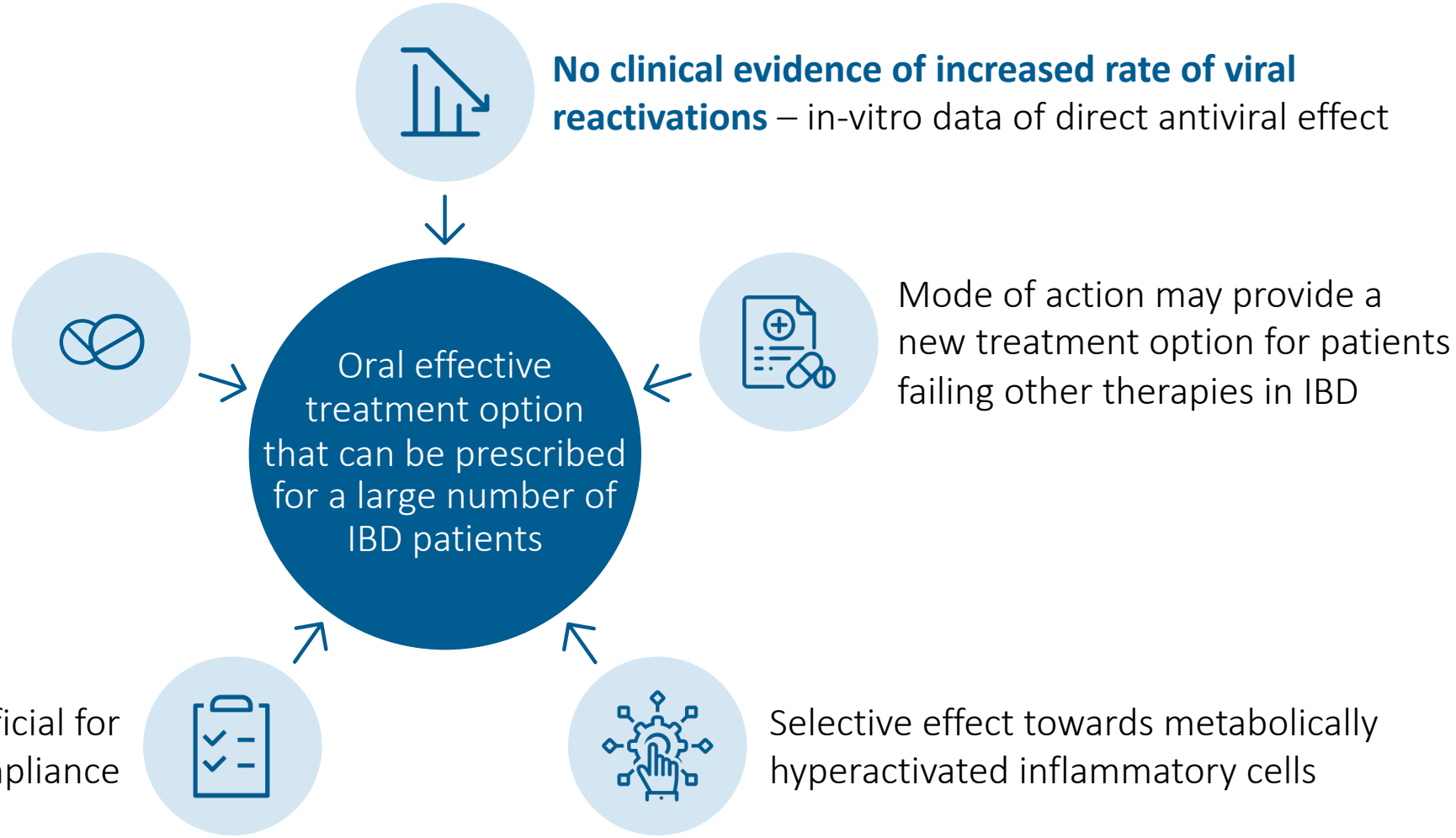
- Performed by an unblinded data review committee in August 2019
- Analysis based on all available clinical, endoscopic, biomarker, PD, and safety data
- No intolerable dose identified
- No safety signal observed

Primary Endpoint:
Proportion of patients with symptomatic remission and endoscopic healing at week 10

Timelines:
Study started in April 2018
Recruitment expected to be completed end of 2021
Currently estimated to deliver top-line data in H1/2022

IND: investigational new drug

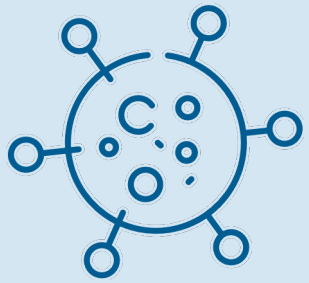
IMU-838: Key Strengths That Address Limitation of Existing Therapies in IBD



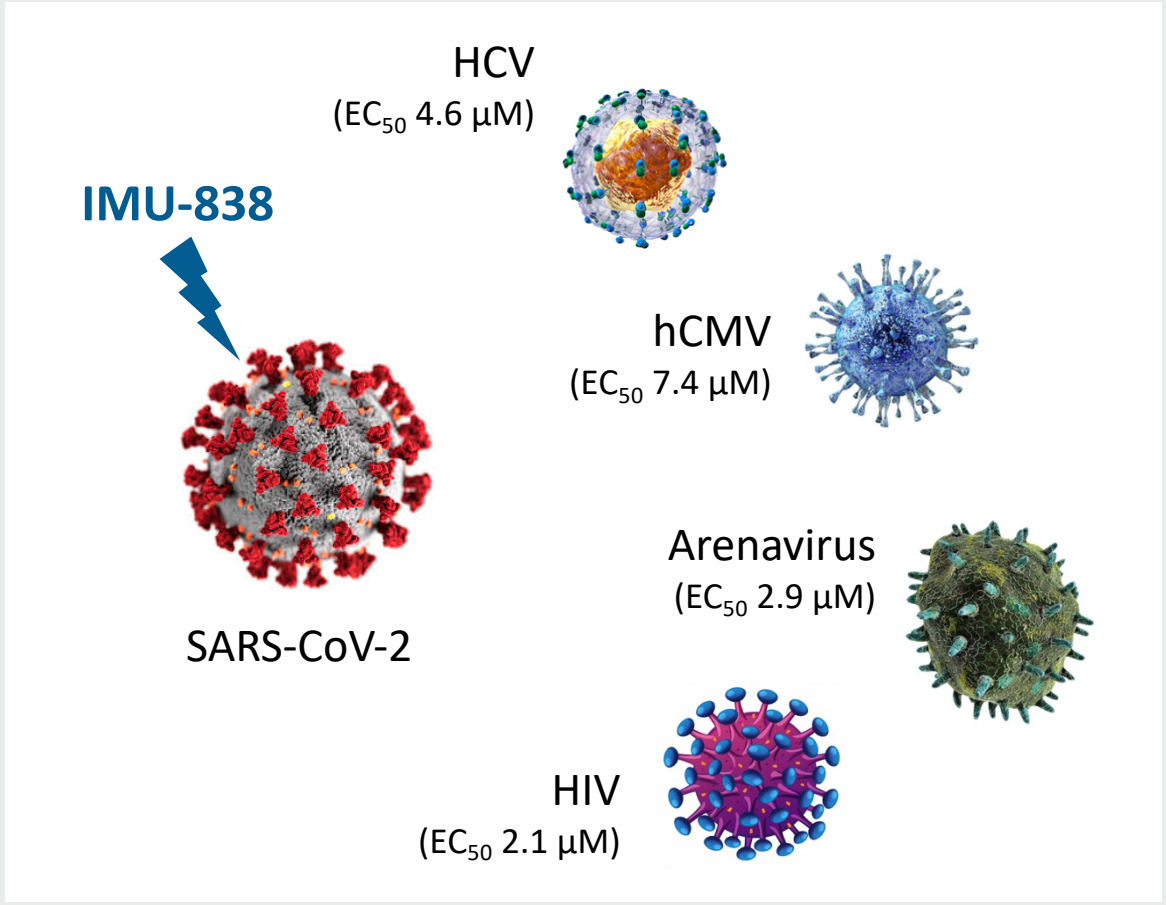
IMU-838 Fighting COVID-19

Leveraging DHODH's Broad-Spectrum Antiviral Activity

IMU-838 Antiviral Activity Against SARS-CoV-2 and Other Viruses



- IMU-838 is active against SARS-CoV-2
- IMU-838 has shown broad-spectrum antiviral activity against different pathogenic viruses with EC_{50} values in single digit µM range



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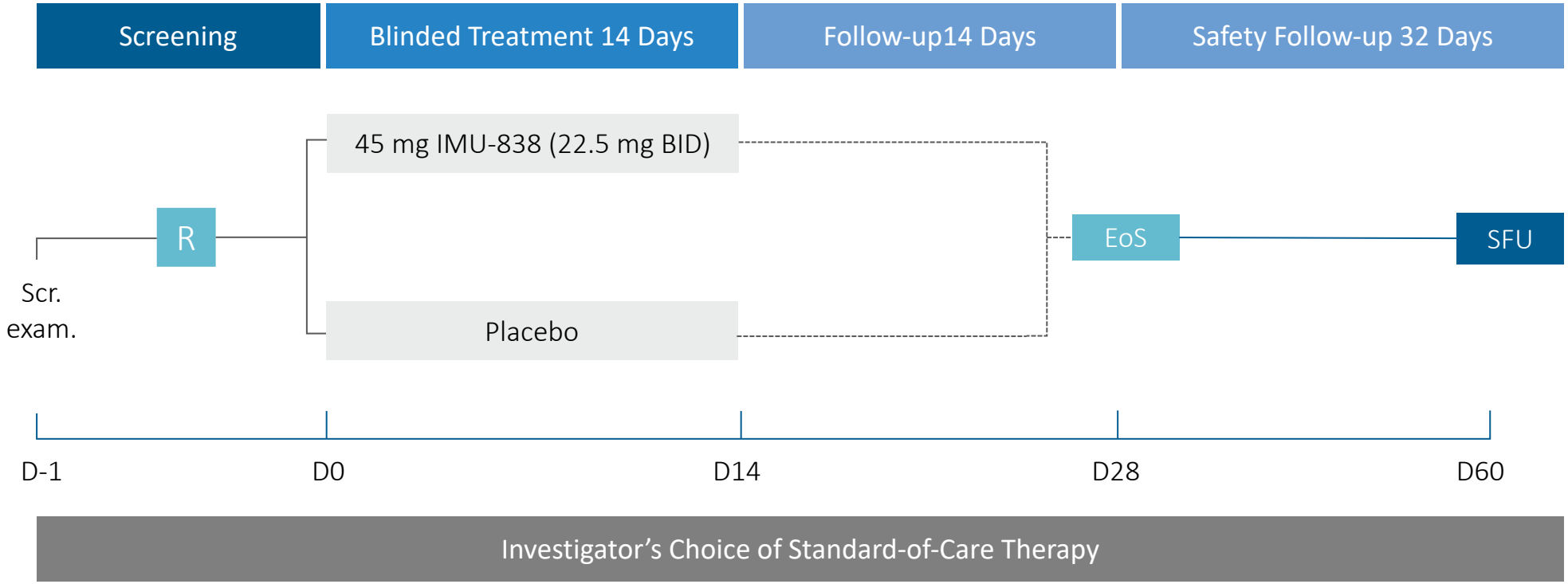
CALVID-1: Study Flow Chart
NCT04379271



BID: bis in die = two times daily; D: day; EoS: end of study; Scr.: screening; exam.: examination; SFU: safety follow-up
Stratification for randomization done for age category (≥65 years, < 65 years) and antiviral treatment as part of standard-of-care at time of randomization

- n=204 patients
- 20 clinical sites in the United States and Europe

- USD 29 million EIB venture loan accessible for further phase 2/3 development

Proportion of Patients with Clinical Recovery

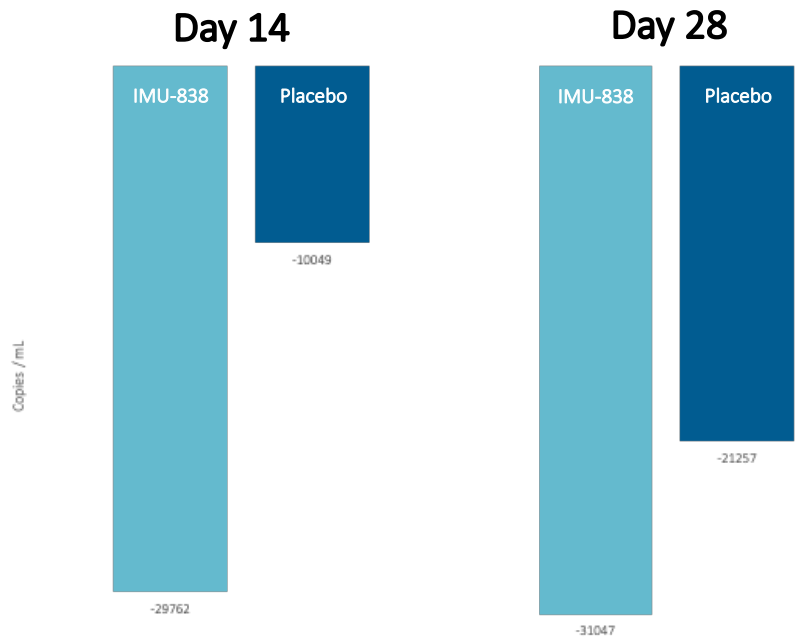
IMU-838 Increases the Number of Patients Achieving Clinical Recovery

Proportion of Patients With Clinical Recovery (Based on Symptoms Body Temperature, Respiratory Frequency and Blood Oxygenation)	IMU-838		Placebo	
	N	%	N	%
Day 7	15	18.5	10	12.8
Day 28	57	71.3	58	66.7

Full analysis set (FAS, n=99 for IMU-838, n=103 for Placebo)
Clinical recovery is defined as as axillary temperature <= 36.6 °C, or oral temperature <= 37.2 °C, or rectal or tympanic temperature <= 37.8 °C, and respiratory frequency <= 24 times/min without oxygen inhalation and oxygen saturation >= 98%. Clinical recovery is only assumed if it is confirmed in the evening and at the next visit (if applicable).

IMU-838 Showed Activity Against COVID-19 on Several Readouts

Decrease of SARS-CoV-2 Viral Load[1]



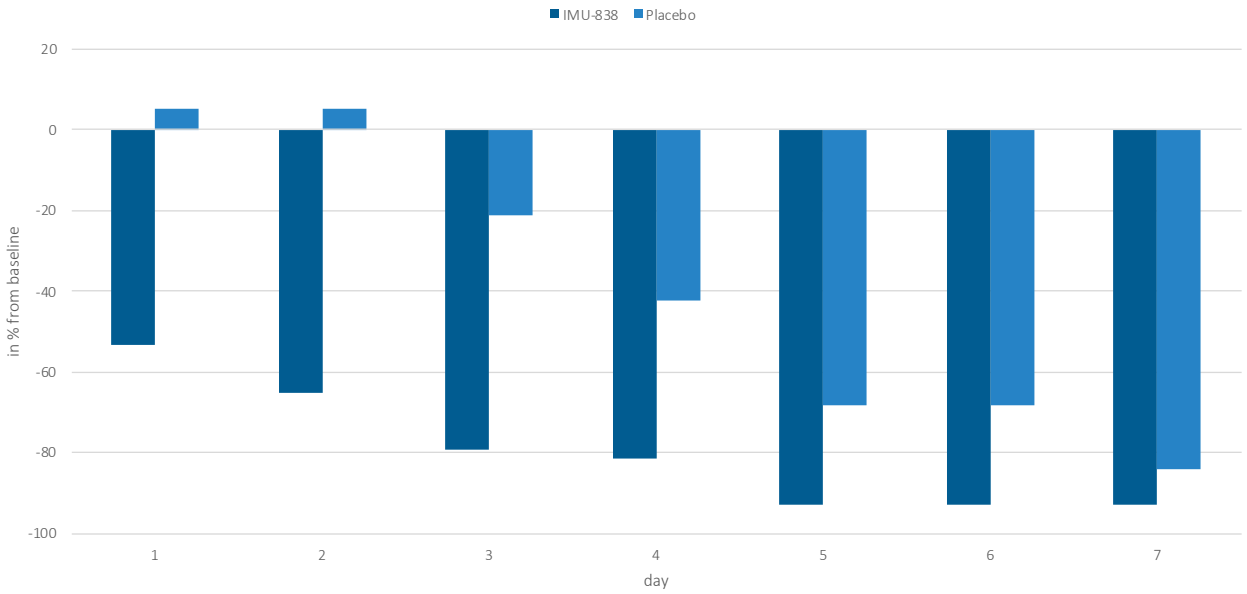
Time to Clinical Improvement[2]

- Regarding 75% probability of clinical improvement, **IMU-838 patients showed a 2.9 days advantage** versus placebo
- For high-risk patients[3], this advantage increased to 3.8 days
- For elderly patients **(≥ 65 years), this advantage increased to 4.8 days**

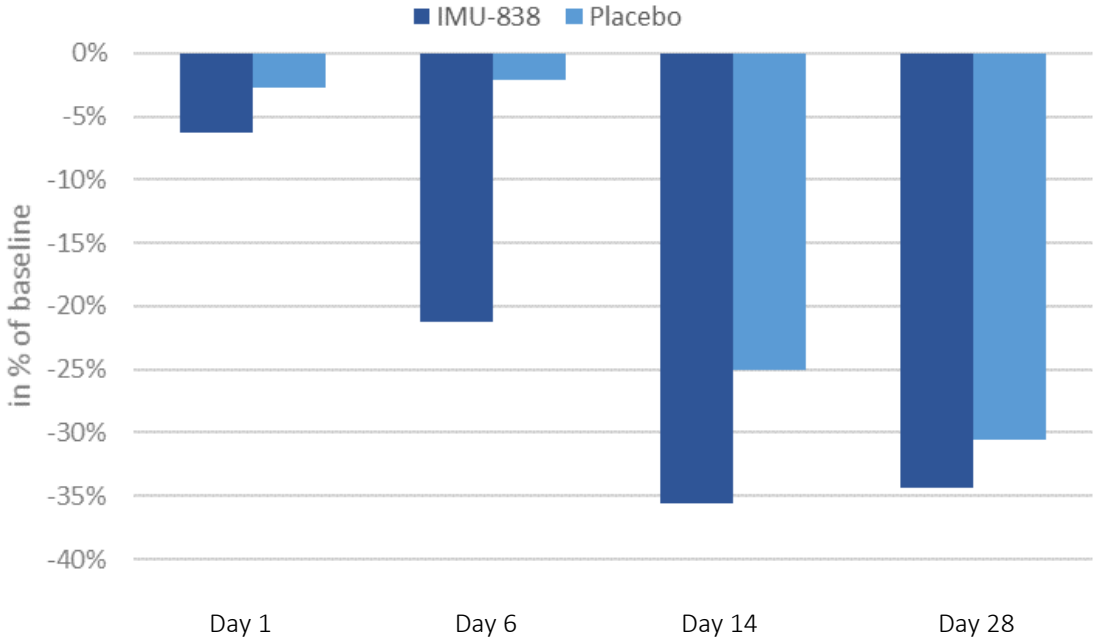
[1] Modified full analysis set (N = 90 for IMU-838, N = 91 Placebo). The viral load is set 0 cp/mL if the test result is 'No SARS-CoV2 detected' and set to 1018 cp/mL if the test result is '< 1018 cp/mL SARS-CoV2 detected'. Only patients with viral load measured from nasopharyngeal swab and results provided by the central laboratory are included. Analysis is based on the median of viral titers (as assessed by the central virology laboratory) on each individual day.
[2] Modified full analysis set (mFAS), all patients (n=61 for IMU-838, n=69 for Placebo), high-risk patients (n=41 for IMU-838, n=41 for Placebo), elderly patients (n=17 for IMU-838 , n=17 for Placebo), N.C.= not calculated because of too few patients in this category
[3] High-risk factors are age ≥65 years, cardiovascular disease (including hypertension), pre-existing pulmonary disease, diabetes, malignancy, medical conditions leading to immunodeficiency, current or recent (within three months) immunosuppressive treatment.
Clinical improvement is defined as an improvement of at least two points on the derived WHO nine-category ordinal scale, or live discharge from hospital without oxygen supplementation, whichever comes first. The WHO nine-category ordinal scale is derived using SARS-CoV-2 test results provided by the central laboratory (only nasopharyngeal swabs). The evaluations of high-risk and elderly populations are a post hoc analysis and were not pre-specified in the statistical analysis plan.

IMU-838 Shown Activity against COVID-19 on Several Readouts

Clear Signal on C-Reactive Protein (CRP)[1]



D-Dimer Substantially Reduced[2]



[1] Systemic inflammation, as measured by CRP, is strongly associated with thrombotic events, kidney injury, critical illness, and mortality in COVID-19 patients. (Smilowitz et al. C-reactive protein and clinical outcomes in patients with COVID-19. Eur Heart J. 2021 Jan 15:ehaa1103). Safety analysis set (n= 99 for IMU-838, n= 103 for Placebo). Analysis is based on the median of CRP on each individual day

[2] D-dimer is commonly elevated in patients with COVID-19. D-dimer levels correlate with disease severity and are a reliable prognostic marker for in-hospital mortality in patients admitted for COVID-19. (Yao et al. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. j intensive care 8, 49 (2020)). D-dimer levels are also correlated with thromboembolic events in COVID-19 patients (Vidali et al. D-dimer as an indicator of prognosis in SARS-CoV-2 infection: a systematic review, ERJ Open Research Apr 2020, 6 (2) 00260-2020). Safety analysis set (n= 99 for IMU-838, n= 103 for Placebo); Analysis is based on the median of D-dimer on each individual day

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Summary of the Overall Rate of Adverse Events

No General Safety Signals, as Compared to Placebo

	45 mg IMU-838			Placebo			Total		
	Number of AEs (N#)	No. of patients with AE (N)	Patients with AE (%)	Number of AEs (N#)	No. of patients with AE (N)	Patients with AE (%)	Number of AEs (N#)	No. of patients with AE (N)	Patients with AE (%)
Any TEAE	290	73	73.7	242	67	65.0	532	140	69.3
Any SAE	2	2	2.0	5	4	3.9	7	6	3.0
Any TEAE Related to Study Medication and/or Study Procedure	25	18	18.2	12	10	9.7	37	28	13.9
Any TEAE Leading to Withdrawal of Study Drug	3	2	2.0	3	2	1.9	6	4	2.0
Any TEAE of Increased Severity Related to COVID-19	**9**	**7**	**7.1**	**17**	**13**	**12.6**	**26**	**20**	**9.9**

Safety analysis set (n=99 for IMU-838, n=103 for Placebo)
AE: adverse event; TEAE: treatment-emergent adverse event; SAE: serious adverse event
Adverse events as coded by MedDRA version 23.0

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IMU-838 in Primary Sclerosing Cholangitis (PSC)

Investigator-Sponsored Trial Performed at Mayo Clinic

IMU-838 in PSC: Phase 2 Proof-of-Concept Study
NCT03722576

Principal Investigator

Elizabeth Carey, MD (Mayo Clinic)

Study Timelines

- Study started in August 2019
- Enrollment took place between July 2019 and September 2020, but almost all enrollment occurred in 2019 and early 2020
- The ongoing pandemic situation triggered the principal investigator's decision to terminate the study in late 2020

Investigator-Sponsored Trial Conducted at Two Mayo Clinic Sites

- Single-arm, open-label, exploratory study which planned to enroll 30 patients, aged 18 to 75 years
- Supported by National Institutes of Health (NIH) grant
- Study was performed at tertiary referral centers for PSC patients:
  - Mayo Clinic, Phoenix, Arizona (Elizabeth Carey, MD)
  - Mayo Clinic, Rochester, Minnesota (John E. Eaton, MD)
- Immunic provided the study medication
- Dosing: 30 mg of IMU-838 once daily for a period of 24 weeks
- Primary objective: change in serum alkaline phosphatase (ALP) at week 24, as compared to baseline
- Together with the investigators, Immunic determined to readout data of the 18 patients who were enrolled prior to the COVID-19 pandemic*

* During the COVID-19 pandemic, recruitment for this study was hampered, as patients with PSC are at a high risk of COVID-19 infections and were advised to avoid travel and unnecessary social contacts such as those required to participate in a clinical trial.

Primary Objective: Change in Serum Alkaline Phosphatase

The Primary Objective Was to Determine Whether IMU-838 Reduces Serum ALP in Adult Patients Diagnosed With PSC[1]

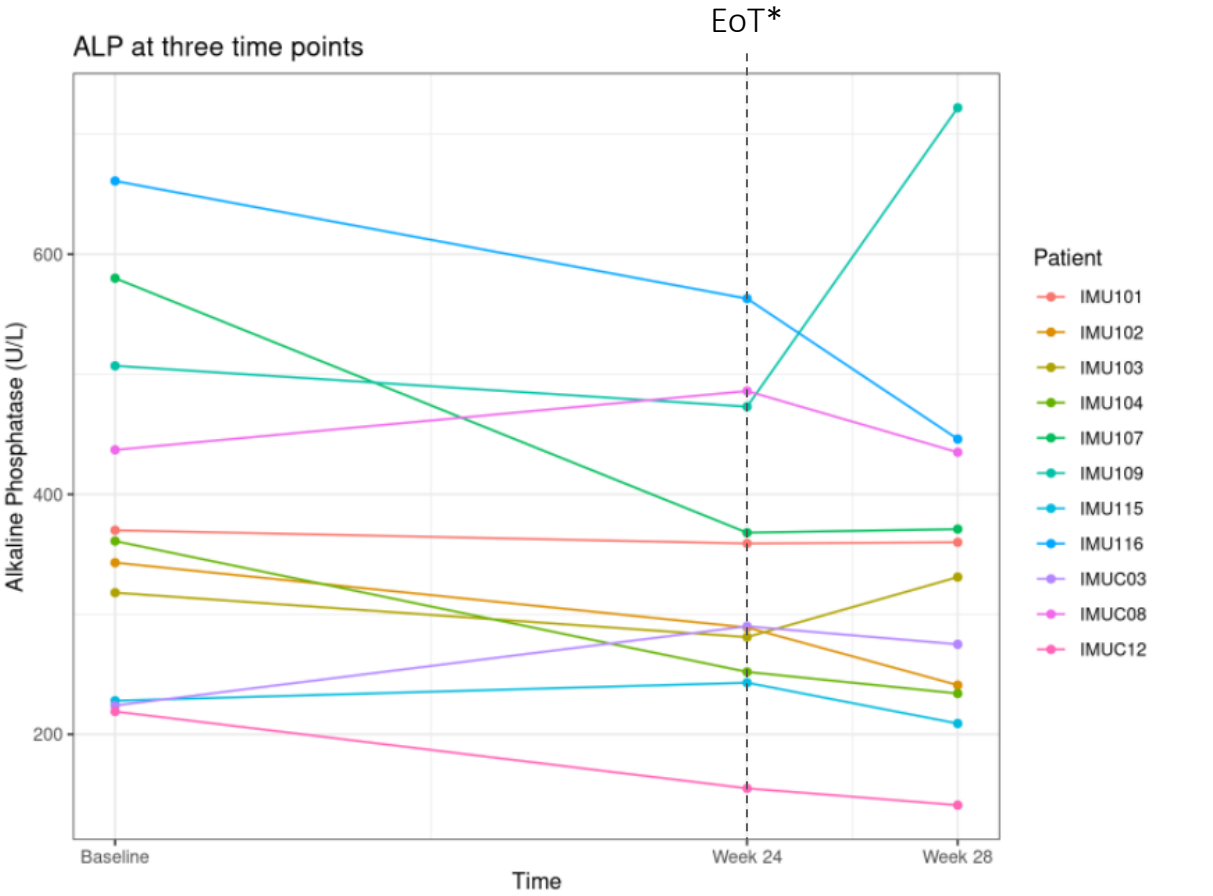
	Positive Outcome N (%)	95% CI
ALP Reduction ≥25% and AST Increase ≤33% Between Baseline and Week 24 (ITT, N=18)	3/18 (16.7%)	3.6%, 41.4%
ALP Reduction ≥25% and AST Increase ≤33% Between Baseline and Week 24 (PP, N=11)	**3/11 (27.3%)**	**6.0%, 61.0%**

The ALP Value Statistically Significantly (p=0.041) Decreased in the PP Population[2]

	Estimate of Change Every 30 Days (95% CI)	p-value
ALP Change Between Baseline and Week 24 (ITT, N=18)	-2.11 (-9.62, 5.40)	0.578
ALP Change Between Baseline and Week 24 (PP, N=11)	**-5.76 (-11.29, -0.23)**	**0.041**

[1] The definition of the primary objective was patients who achieve a reduction of ALP at week 24 which is greater or equal to 25%, as compared to baseline, while the AST increase at week 24 is no more than 33%, as compared to baseline.
[2] Model adjusted for age at baseline and gender
ALP: alkaline phosphatase; AST: aspartate aminotransferase; PP: per-protocol; ITT: intend-to-treat, CI: confidence interval

Individual ALP Changes Over Treatment Period



- Consistent individual pattern of a stable decrease in ALP values between baseline and Week 24 (24-week treatment period)
- While the decrease in ALP values was moderate, no patient of the PP population showed an increase of more than 20% of ALP at Week 24, as compared to baseline
- After treatment cessation at Week 24, a total of 2 patients showed a strong rebound effect at Week 28

ALP: alkaline phosphatase, Treatment period between baseline and Week 24. Follow-up period (without treatment) between Week 24 and Week 28, Per Protocol (PP) Population (n=11)
*EoT: End of Treatment

IMU-838 in PSC: Outlook

As an Orally Available DHODH Inhibitor With a Prominent Influence on Th17 Induced Inflammatory Processes, IMU-838 is a Promising Approach for the Treatment of PSC

- The encouraging results regarding biochemical parameters and safety suggest that IMU-838 merits further clinical testing in PSC
- Immunic is in discussions with investigators and leading clinical experts to further evaluate the data set and to explore potential next steps
- Immunic believes that dose optimization would be needed for potential future trials, which would also require assessment of pharmacokinetics in hepatic impaired patients

Immunic THERAPEUTICS

IMU-935

Unique RORγt Inverse Agonist

Autoimmune Diseases and IMU-935

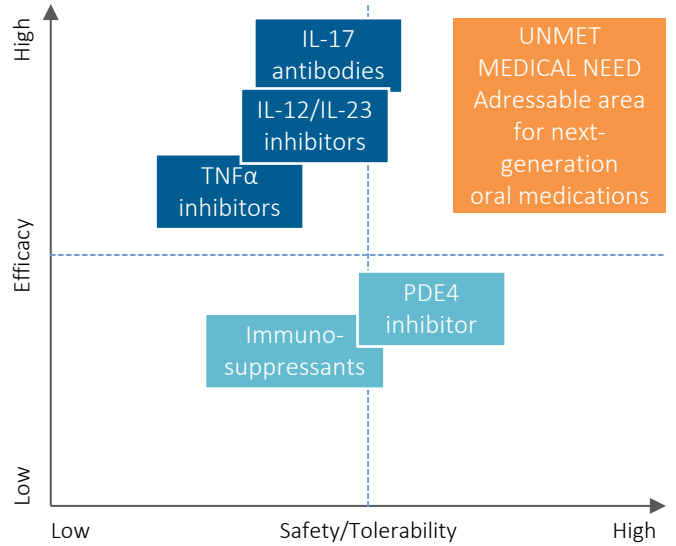
IL-17 in Autoimmune Diseases

- Autoimmune diseases are frequent diseases affecting millions of patients worldwide[1]
- Th17/IL-17/RORγt axis is important in auto immunity related diseases[2]
- Antibodies targeting this axis successfully demonstrated this concept but bear the disadvantage of being a non-oral drug[2]

Goal

- Develop an orally available and potent IL-17 inhibitor for the safe and efficacious treatment of autoimmune diseases
- Small molecule inhibitor of RORγt functions in autoimmune disease state without affecting physiological functions of RORγt

Unmet Need in Psoriasis Care



Strong Medical Need for Oral IL-17 Pathway Inhibitors such as IMU-935

[1] Rose, Noel R. American journal of epidemiology 2016; 183.5: 403-406
[2] Fasching, Patrizia, et al. Molecules 2017 22.1: 134

IMU-935: Cytokine Inhibition in Low Nanomolar Range

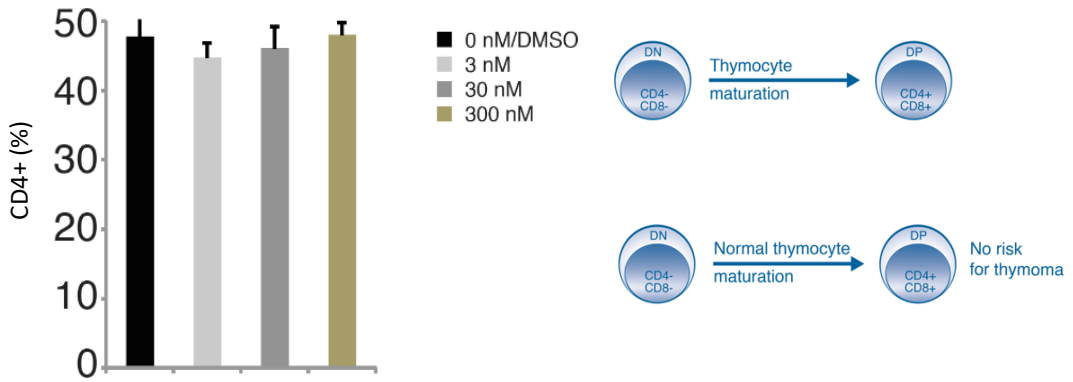
Effect of the Development Compound IM105935 (IMU-935) in Stimulated Human PBMC

Inhibition of RORγ (20 nM) and DHODH (240 nM) leads to synergistical inhibition of cytokines with IC_{50} of 3-5 nM in stimulated human lymphocytes

	IC_{50} (µM)
IL-17A	0.005
IL-17F	0.004
IFNγ	0.003
IL-1a and b	no inhibition
IL-4,5,6,8	no inhibition
RORγ (MST)	0.024
RORγ (cellular, reporter assay)	0.020
DHODH	0.240
Th17 differentiation (murine)	150 nM

Read-out: effect on cytokine production after 48 hours in PBMC

IMU-935 Maintains Normal Thymocyte Maturation and Retains Basal Activity of RORγt



IMU-935 allows normal thymocyte maturation from murine DN towards matured CD4+ thymocytes (CD4+ and CD4+/CD8+)

PBMC: peripheral blood mononuclear cells

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IMU-935: Phase 1 Study Performed in Australia

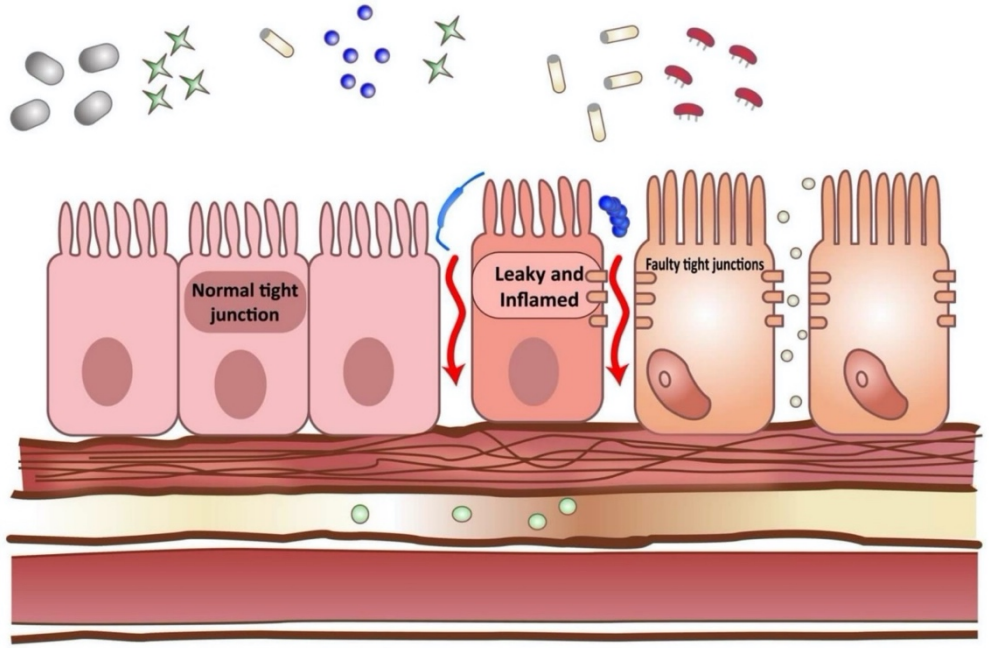
- Double-blind, placebo-controlled clinical phase 1 study performed by Immunic subsidiary in Australia started in September 2019
- Phase 1 study performed in three parts
  - Part A: Single ascending dose (SAD) study in healthy volunteers
  - Part B: 14-day multiple ascending dose (MAD) study in healthy volunteers
  - Part C: 4-week safety study in psoriasis patients
- Timelines
  - Safety data from the SAD and MAD parts expected to be available in H2/2021
  - Initiation of Part C in psoriasis expected around mid-2021
- Immunic has identified Guillain-Barré syndrome as a suitable orphan autoimmune indication for phase 2 development, in addition to the previously planned development in psoriasis.

IMU-856

Restoring Intestinal Barrier Function

Concept of IMU-856: Restoring the Intestinal Barrier Function Without Impairing the Immune System

Increased Bowel Permeability Connects the Microbiome and the Immune System



Picture taken from https://vibrantblueoils.com/essential-oils-to-heal-and-seal-the-gut/

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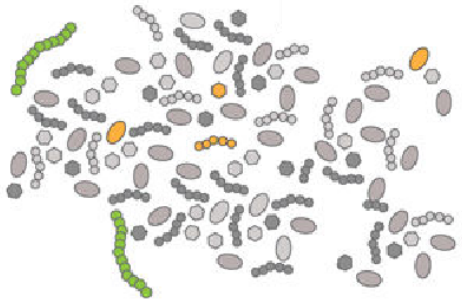
IMU-856: Hypothesis of Therapeutic Approach

Compartmentalize Microbiome and Immune System by Strengthening the Bowel Barrier Function

Microbiota

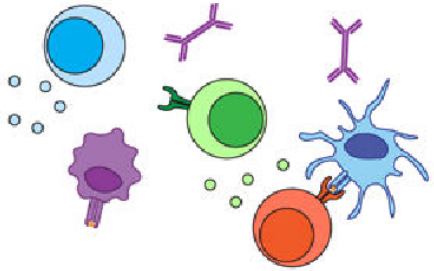


Influencing the Microbiome

- Changes in nutrition are driving the increase in disease rates
- Diversity of microbiome is good, but data on pathogenicity of particular species is often inconsistent
- Effects of probiotics on disease have been shown (supportive)

Gut wall

Immune System



Focus on Immunosuppression

- Stimulation of the immune system by the microbiome cannot be prevented
- Suppression of the secondary inflammatory process
- Usually has unintended consequences in terms of adverse event (infections, malignancies, inability to vaccinate)

Immunic THERAPEUTICS

IMU-856: Development Concept

- Exclusive global rights to commercialization of IMU-856 in all countries obtained through option and licensing agreement with Daiichi Sankyo
- Double-blind, randomized, placebo-controlled clinical phase 1 study performed by Immunic subsidiary in Australia started in August 2020
- Phase 1 study includes patient population for confirmation of pharmacodynamic activity:
  - Safety and pharmacokinetics in healthy volunteers (Part A: SAD, Part B: MAD)
  - In Part C, patients with several diseases involving bowel barrier dysfunction will be included
  - 2-sugar test performed for bowel permeability to monitor therapy effects
- Timelines
  - Safety data from the SAD and MAD parts expected to be available in H2/2021
  - Initiation of Part C in patients expected in H2/2021

Immunic Therapeutics

Summary

Summary and Highlights

Advanced and well-balanced pipeline:
Three products in clinical development

Additional clinical activity of IMU-838
demonstrated in COVID-19 and PSC; favorable safety and tolerability profile confirmed

Excellent phase 2 data in RRMS:
IMU-838 met all statistical endpoints and underlined favorable safety and tolerability profile

Shares outstanding: 21,168,240 (as of February 19, 2021)

Cash and cash equivalents of approx. USD 127.5 million (as of December 31, 2020)

Phase 3 program in RRMS expected to start in H2/2021 after end-of-phase 2 meetings with regulatory authorities

Raised approx. USD 144.4 million in 2020, substantially extending cash runway beyond important value inflection points

Thank You!

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