



**Immunic**  
THERAPEUTICS

# Immunic Therapeutics

IMU-838 Phase 2 Top-Line Data EMPHASIS Trial in RRMS

NASDAQ: IMUX | August 3, 2020



# 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 PSLRA.

→ 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 for patients with relapsing-remitting multiple sclerosis or other conditions, if any, that may be supported by the Company’s phase 2 EMPHASIC 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 Capital 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 filings with the Securities and Exchange Commission (“SEC”).

→ 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.

# Development Pipeline

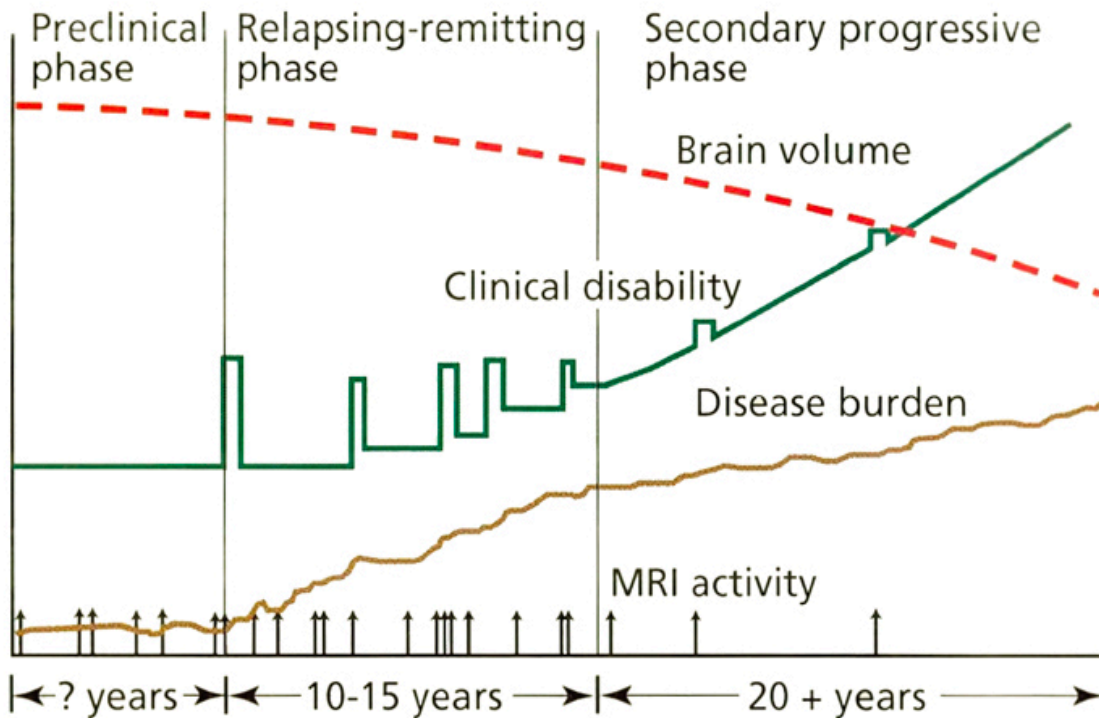
Program	Indication	Target	Preclinical	Phase 1	Phase 2	Phase 3
<b>IMU-838</b>	Multiple Sclerosis	DHODH	Completed or ongoing	Completed or ongoing	Completed or ongoing	In preparation or planned
	Ulcerative Colitis	DHODH	Completed or ongoing	Completed or ongoing	Completed or ongoing	
	Crohn's Disease	DHODH	Completed or ongoing	Completed or ongoing		
	PSC	DHODH	Completed or ongoing	Completed or ongoing	Completed or ongoing	Investigator-Sponsored Trial performed at Mayo Clinic / NIH
	COVID-19*	DHODH	Completed or ongoing	Completed or ongoing	Completed or ongoing	In preparation or planned
<b>IMU-935</b>	Psoriasis	ROR $\gamma$ t	Completed or ongoing	Completed or ongoing		
	Orphan AI Diseases	ROR $\gamma$ t	Completed or ongoing	In preparation or planned		
<b>IMU-856</b>	GI	Intestinal Barrier Function	Completed or ongoing	In preparation or planned		

■ 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

# Treatment Compliance and Persistence are Important Considerations for Life-Long Diseases such as Multiple Sclerosis (MS)

## MS Disease Course<sup>[1]</sup>



## Nonadherence or Nonpersistence of MS Treatments Can Lead to Greater Risk for Negative Clinical Outcomes<sup>[2]</sup>

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

	USA <sup>[3]</sup>	Canada <sup>[4]</sup>
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.

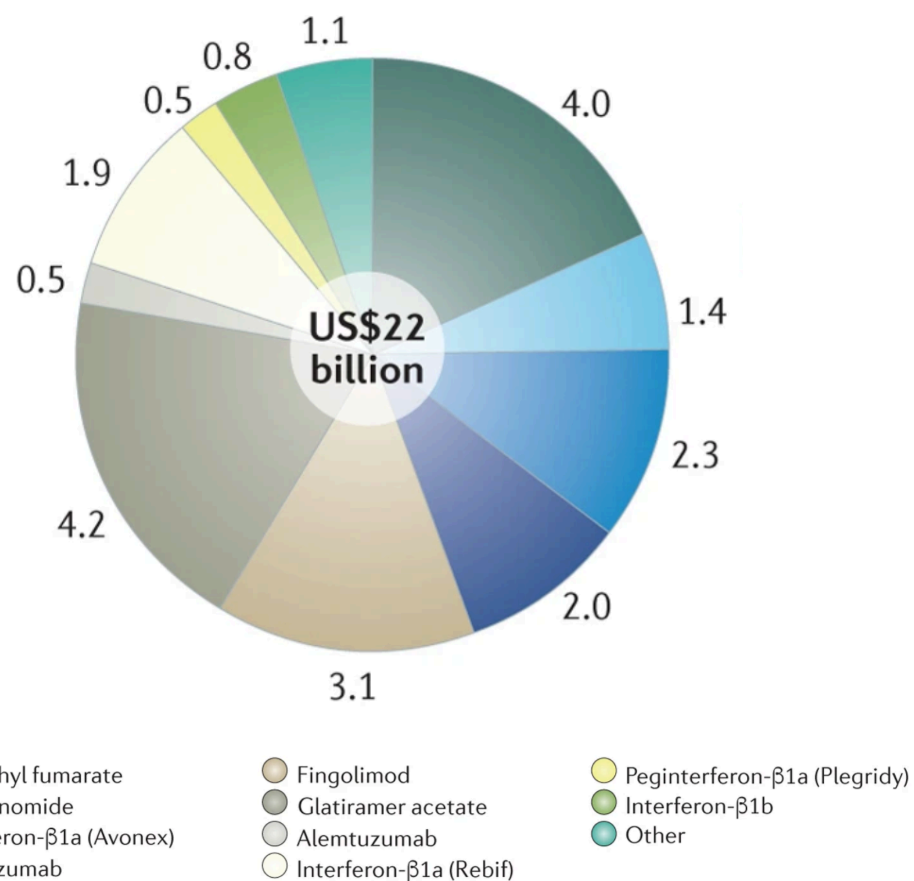
[1] Adapted from Fox RJ, Cohen JA: Multiple sclerosis: the importance of early recognition and treatment. Cleve Clin J of Med, 2001; 68:157-70

[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, Nakhai-pour HR, Haddad P, Schecter R 2019 PLoS ONE 14(1): e0210417. <https://doi.org/10.1371/journal.pone.0210417>

# The Global MS Drug Market was 22 Billion USD in 2016



- Global market of MS drugs was USD 22 billion in 2016<sup>[1]</sup>
- Currently approved drugs include oral and injectable drugs
  - Early injectables
    - Interferons (e.g. Rebif®, Avonex®)
    - Glatiramer acetate
  - Oral drugs
    - Teriflunomide
    - Dimethyl fumarate
    - S1P modulators: Fingolimod, Siponimod, Ozanimod
  - High activity DMTs, infusions
    - Natalizumab
    - Ocrelizumab

[1] Westad, A., Venugopal, A. & Snyder, E. The multiple sclerosis market. Nature Reviews Drug Discovery 16, 675–676 (2017).

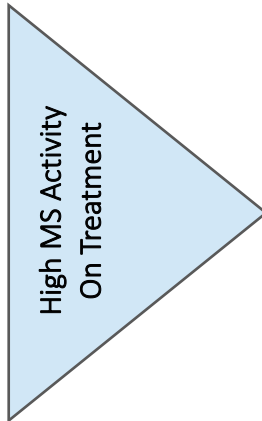
# Current Treatment of Relapsing-Remitting Multiple Sclerosis (RRMS)

## Escalation Treatment Approach in RRMS

### Base Medications

Treatment-naïve Patients  
Low-to-moderate disease activity

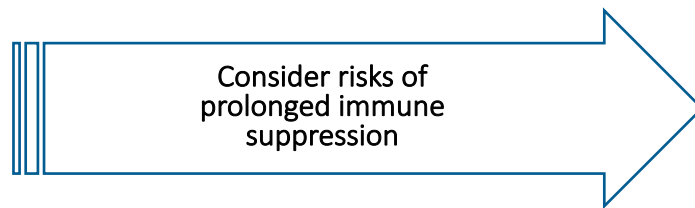
- Interferons
- Glatiramer acetate
- Dimethyl fumarate
- Teriflunomide



### Escalation Treatments

2nd/3rd Line Treatments  
High disease activity

- Fingolimod
- Siponimod
- Natalizumab
- Alemtuzumab
- Ocrelizumab
- Cladribine



- Currently, there is no specific guidance on which therapies/medications are used in which sequence.
- Typically, treatments are escalated over time considering:
  - Persistent high MS disease activity under treatment with base medications (relapse(s), disability worsening, MRI lesions),
  - Risks of long-term immunosuppression,
  - Patient preferences or risks perceptions, and
  - Safety/tolerability aspects.

Currently unaddressed medical need:  
**Oral base medications for MS patients with balance of  
good safety/tolerability/convenience profile  
and robust clinical activity**

Left: Adapted from F.1. F. Grand'Maison, Neural Regeneration Research, 2018, 13, 1871-1874

# IMU-838: Target Profile in Relapsing-Remitting Multiple Sclerosis



IMU-838 is Intended to be a Selective Once Daily Medication for RRMS Patients With a Well-Balanced Combination of Favorable Safety and Convenience Profile with Robust Clinical Activity



## For Patient

- Convenient safety profile of an oral drug without adverse events disturbing social activities
- No/low PML risk
- Long treatment duration through less risk for discontinuation, high patient compliance



## For Neurologist

- Robust clinical activity
- Easy on- and off-dosing
- Few monitoring requirements for treating neurologists
- No black box warning for hepatotoxicity



Phase 2 Top-Line Data EMPhASIS Trial

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# IMU-838 in Relapsing-Remitting Multiple Sclerosis (RRMS)



# EMPhASIS: Phase 2 Study Overview in RRMS



Coordinating Investigator

Robert Fox (Cleveland Clinic)



## Blinded Treatment Period

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



## Population: RRMS With Relevant Disease Activity

- Male or female (  $18 \geq \text{age} \leq 55$  )
- RRMS diagnosis (Revised McDonald criteria 2017)
- Evidence of disease activity based on relapse and MRI criteria
- Baseline EDSS:  $0 \geq \text{EDSS} \leq 4.0$
- Performed in Central and Eastern Europe

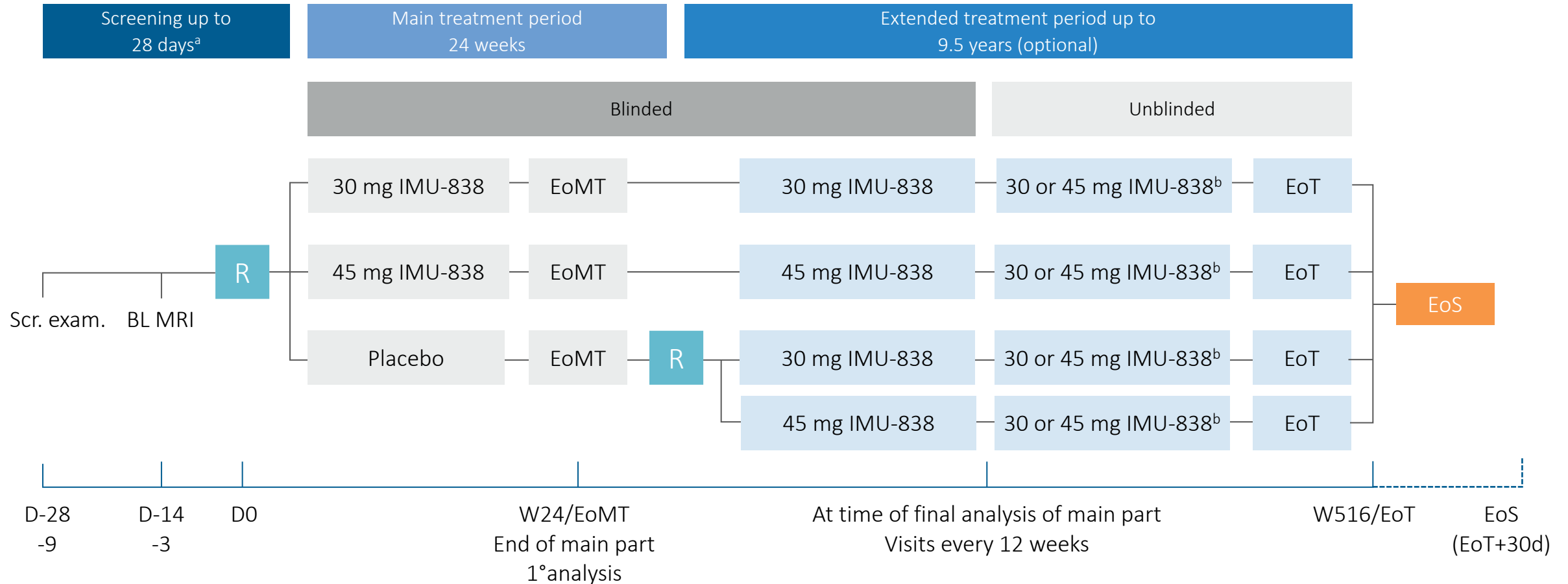


## Extended Treatment Period

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

[www.clinicaltrials.gov](http://www.clinicaltrials.gov): NCT03846219

# EMPhASIS: Phase 2 Trial Design in RRMS

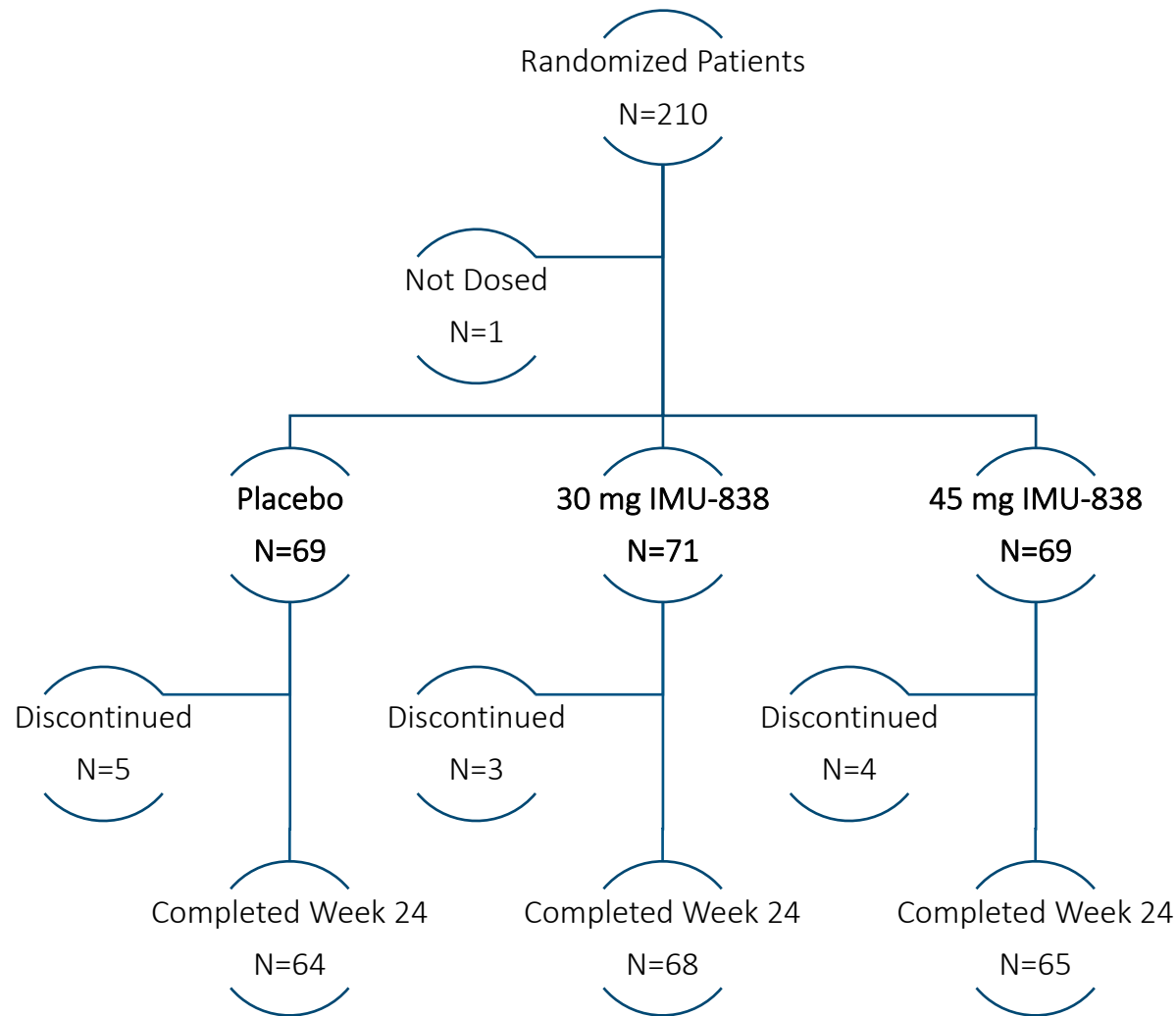


a) Can be interrupted/extended, if the baseline MRI must be repeated due to poor quality (to be done as soon as possible). If results of the central MRI assessment are not available in time for randomization, the screening period can be extended by up to 7 days, if needed.

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

# Patient Disposition and Treatment Discontinuations



Well Balanced Patient Population Across Treatment Groups:

		Placebo	30 mg IMU-838	45 mg IMU-838
Sex	Male	33%	44%	28%
	Female	67%	56%	72%
Age	≤ 40 yrs.	65%	62%	65%
	> 40 yrs.	35%	38%	35%
EDSS Baseline	≤ 2.5	48%	55%	59%
	> 2.5	52%	45%	41%
Prior MS Therapy	No	74%	72%	70%
	Yes	26%	28%	30%
Duration of Disease	≤ 4 yrs.	54%	52%	54%
	> 4 yrs.	46%	48%	46%
Relapses Last 24 Months	< 2	51%	45%	51%
	≥ 2	49%	55%	49%

# Primary and Key Secondary Efficacy Endpoints



## Key Study Endpoints

To evaluate the efficacy of IMU-838 as compared to placebo based on 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

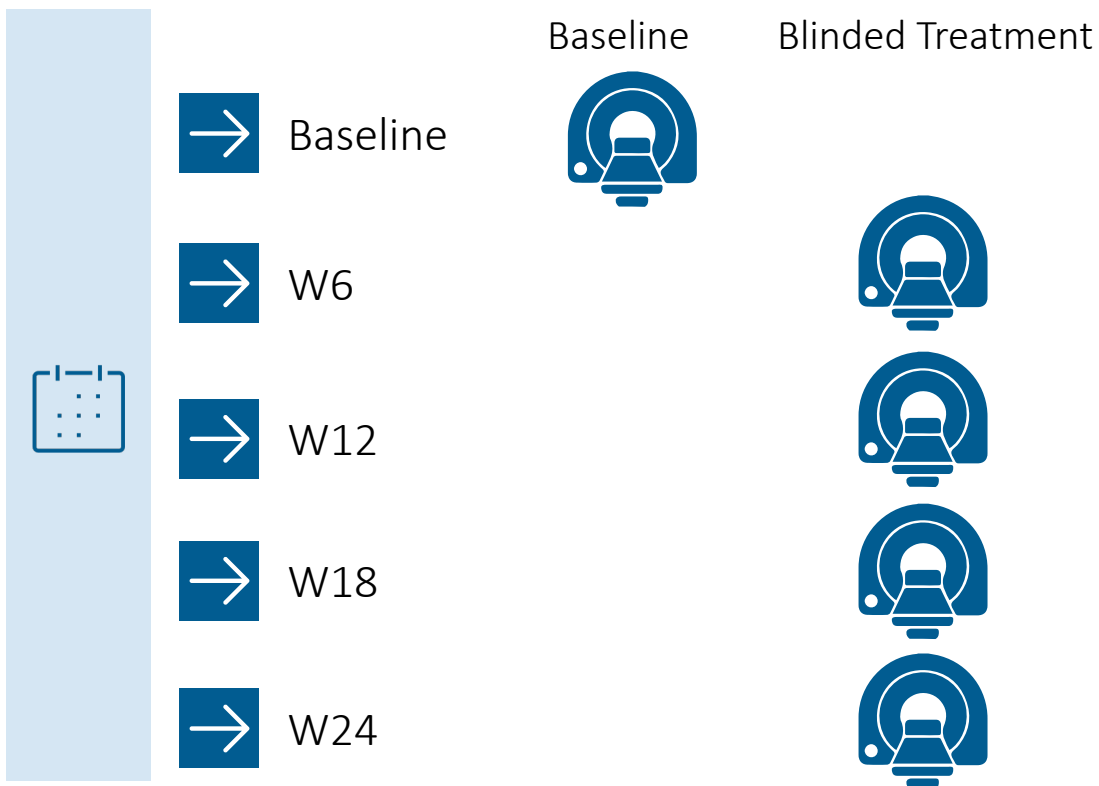


## Combined Unique Active (CUA) Lesions

Sum of the number of all new Gd-enhanced (Gd+) lesions on T1-weighted magnetic resonance imaging (MRI) and the number of all new or substantially enlarged lesions on T2-weighted MRI (non-enhancing on T1-weighted MRI), avoiding double counting.



All MRI Scans Were Assessed Centrally by an Independent MRI Reading Center Only







Phase 2 Top-Line Data EMPHASIS Trial

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# Efficacy



# EMPhASIS Trial NCT03846219

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Primary and Key Secondary  
Endpoints Met With High  
Statistical Significance

# Study Met Primary and Key Secondary Endpoints

## High Statistical Significance and Robust Results Regarding Suppression of CUA MRI Lesions

		Analysis Set	IMU-838	Placebo	Suppression of CUA MRI Lesions IMU-838 vs. Placebo	p-value (1-sided)
Primary Endpoint	45 mg IMU-838 vs. Placebo	Full Analysis Set*	N=69	N=69	<b>62%</b>	<b>0.0002</b>
Key Secondary Endpoint	30 mg IMU-838 vs. Placebo	Full Analysis Set*	N=71		<b>70%</b>	<b>&lt;0.0001</b>

CUA MRI Lesions: combined unique active magnetic resonance imaging lesions. Sum of the number of all new Gadolinium-enhanced lesions on T1-weighted magnetic resonance imaging (MRI) and the number of all new or substantially enlarged lesions on T2-weighted MRI (non-enhancing on T1-weighted MRI), avoiding double counting.

\*The Full Analysis set is the primary statistical analysis set as recommended as intent-to-treat (ITT) analysis by regulatory guidance. As per the pre-defined statistical analysis plan, it contains the data of all randomized patients who received at least one dose of IMP, analysis of all data as randomized and includes imputation of missing values.

# Perspective of IMU-838 Data Versus Other Phase 2 Trials in RRMS



## IMU-838 Data on Suppression of MRI Activity Compares Favorably to Other First-Line and Oral Medications in RRMS\*

	IMU-838	IMU-838	Glatiramer acetate <sup>[1]</sup>	Teriflunomide <sup>[2]</sup>	Dimethyl fumarate <sup>[3]</sup>	Fingolimod <sup>[4]</sup>	Siponimod <sup>[5]</sup>
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	<b>62%</b>	<b>70%</b>	<b>29%</b>	<b>61%</b>	<b>69%</b>	<b>43%</b>	<b>70%</b>

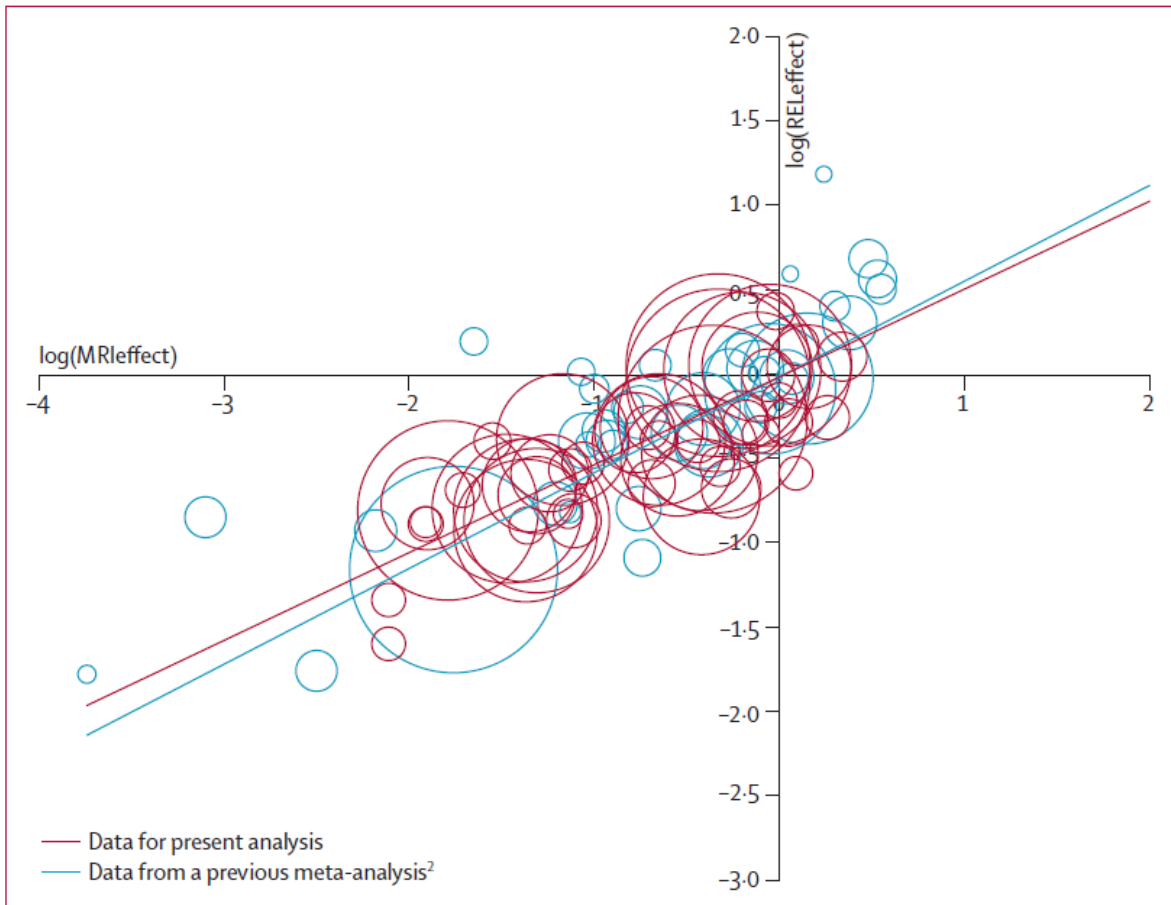
\*The table summarizes the data on treatment/study discontinuation rates of the commercial dose in phase 2 trials of RRMS drugs. If the commercial dose was not included in the phase 2 trials, the dose closest to the commercial dose was shown. This high-level comparison is provided for illustrative purposes 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 are 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.



# Meta-Analysis: Prediction of Relapse Reduction From MRI Activity



- Meta-analysis of 54 published trials for the treatment of relapsing-remitting multiple sclerosis<sup>[1]</sup>
- Allows a robust estimation of the association between the effect on MRI lesions and the effect of treatment on relapses with high correlation factor
$$\log(\text{REL-effect}) = 0.00 + 0.53 \log(\text{MRI-effect})$$
$$R^2=0.76$$
- Predicts that relapse-related activity (likely) follows the MRI activity

Both treatment effects are expressed as rate ratios on a log scale. Every circle represents a comparison of the experimental group versus the control group, with the size of the circles representing the weight of the comparison, proportional to trial size and duration. The straight lines represent the weighted regression, which show the effect on relapses predicted by the observed effects on MRI.  $\log(\text{RELeffect})$ =logarithm of the relapse rate ratio.  $\log(\text{MRIeffect})$ =logarithm of the MRI lesion rate ratio.

[1] Sormani MP, Bruzzi P. MRI lesions as a surrogate for relapses in multiple sclerosis: a meta-analysis of randomised trials. *Lancet Neurol.* 2013;12(7):669-676.

# Secondary Endpoints: New Gadolinium-Enhancing MRI Lesions

## Number of Patients Without Any Gadolinium MRI Lesions Over Entire 24-Week Treatment Period\*

Treatment Group	Number of Patients Without Any Gadolinium MRI Lesions Over Entire 24-Week Treatment Period	
	(N)	(%)
30 mg IMU-838	42/71	59.2%
45 mg IMU-838	34/69	49.3%
Placebo	26/69	37.7%

## Cumulative number of new enhancing Gadolinium-enhancing MRI lesions at Week 24\*

Treatment group	N	Mean cumulative number of Gd-Lesions	Suppression of Gd-Lesions IMU-838 vs. Placebo
		(N)	(%)
30 mg IMU-838	71	4.5	65%
45 mg IMU-838	69	4.0	69%
Placebo	69	13.0	N/A

\*MRI examinations were done at weeks 6, 12, 18 and 24 of the blinded treatment period.

# Secondary Endpoints: Relapse-Related Endpoints

## Effect on Annualized Relapse Rate (ARR)

Treatment Group	N	Adjusted Mean ARR	Relapse Suppression Versus Placebo
30 mg IMU-838	71	0.39	28%
45 mg IMU-838	69	0.48	10%
Placebo	69	0.53	N/A

## Relapse-Free Patients Over Entire 24-Week Treatment Period

Treatment Group	Number of Patients Free of Relapse During Entire 24-Week Treatment Period	
	(N)	(%)
30 mg IMU-838	60/70	85.7%
45 mg IMU-838	54/67	80.6%
Placebo	51/67	76.1%

Given the study's relatively small sample size and short duration of blinded treatment (24 weeks), statistical testing of relapse rates was not included in the trial's statistical analysis plan. Nonetheless, a positive signal was detected.



# Conclusions Regarding Efficacy

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- **Primary and key secondary endpoints met** with high statistical significance
- All other secondary endpoints, including those based on other MRI parameters and on clinical endpoints such as relapse event, also provided a noticeable signal and numerical benefit for the IMU-838 treatment groups, as compared to placebo
- Data on inhibition of MRI lesions encouraging
- IMU-838 data on suppression of MRI activity compares favorably to other first-line and oral medications in RRMS





Phase 2 Top-Line Data EMPHASIS Trial

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# Safety

# Overall Rate of Patients With Treatment Emergent Adverse Events

Treatment Group	Number of TEAE	Number of Patients with TEAE
30 mg IMU-838	70	32/71 (45.1%)
45 mg IMU-838	59	28/69 (40.6%)
Placebo	62	30/69 (43.5%)

There were 3 patients with serious treatment-emergent adverse events (SAE) in this trial:

- Placebo: Squamous cell carcinoma of the cervix
- 30 mg: open fracture, ureterolithiasis/tubulointerstitial nephritis
- 45 mg: no treatment-emergent SAE reported

There were no on-study deaths in this trial.

TEAE: treatment-emergent adverse event

# Reasons for Treatment Discontinuations due to Adverse Events

Treatment Discontinuation Before Week 24 (all dosed patients until end of blinded treatment)		
Placebo	7.2 %	5/69
All IMU-838	5.0 %	7/140
30 mg IMU-838	4.2 %	3/71
45 mg IMU-838	5.8 %	4/69

Reasons for Treatment Discontinuation Before Week 24	Placebo (N=69)	30 mg IMU-838 (N=71)	45 mg IMU-838 (N=69)
Number of patients discontinued treatment related to adverse events (investigator decision due to AE, or fulfilling study stopping rules for hepatic events)	N=3	N=0	N=2
Number of events leading to discontinuations	4	N/A	3

## Adverse events leading to treatment discontinuations

### Placebo

- N=2 liver enzyme elevations
- N=1 cervix carcinoma
- N=1 hematuria

### 30 mg IMU-838

- No events

### 45 mg IMU-838

- N=2 liver enzyme elevations
- N=1 rash

# Perspective of IMU-838 Treatment Discontinuation Rates Versus Other Phase 2 Trials in RRMS



## IMU-838 Discontinuation Rate Compares Favorably to Other First-Line and Oral Medications in RRMS\*

	IMU-838	IMU-838	Glatiramer acetate <sup>[1]</sup>	Teriflunomide <sup>[2]</sup>	Dimethyl fumarate <sup>[3]</sup>	Fingolimod <sup>[4]</sup>	Siponimod <sup>[5]</sup>
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	<b>5.8%</b>	<b>4.2%</b>	<b>5.9%</b>	<b>19.3%</b>	<b>15.6%</b>	<b>5.4%</b>	<b>14.3%</b>
Placebo	<b>7.2%</b>	<b>7.2%</b>	<b>5.8%</b>	<b>6.6%</b>	<b>9.2%</b>	<b>6.5%</b>	<b>8.9%</b>

\*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 are 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.

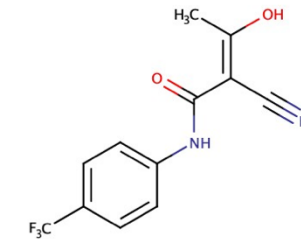
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[1] Comi et al. *Ann Neurol.* 2001;49(3):290-297. [2] O'Connor et al. *Neurology.* 2006;66(6):894-900. [3] Kappos et al. *Lancet.* 2008;372(9648):1463-1472. [4] Kappos et al. *N Engl J Med.* 2006;355(11):1124-1140. [5] Selmaj et al. *Lancet Neurol.* 2013;12(8):756-767.

# IMU-838: Second Generation, Highly Selective DHODH Inhibitor With Distinct Chemical Structure

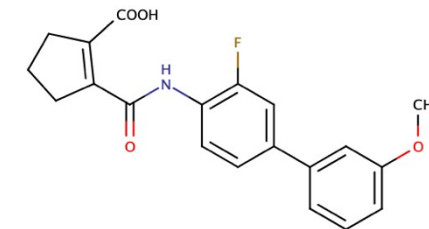
- **Aubagio® hits off targets**, e.g. protein kinases EGFR and Aurora A<sup>[1,2]</sup>, leading to off-target toxicities<sup>[3]</sup>
- Aubagio® has a half-life of about 18 to 19 days in humans<sup>[3-6]</sup>; wash-out takes more than six months → emergency treatment discontinuations require 11-day accelerated washout procedure<sup>[5]</sup>
- Frequent screening required (black box warning for hepatotoxicity)<sup>[4]</sup>

teriflunomide (Aubagio®)



- **IMU-838 (vidofludimus calcium) and leflunomide/teriflunomide are structurally unrelated**
- Immunic has carefully monitored all liver events throughout the entire IMU-838 development program
- **To date, no signal has been observed for hepatotoxicity anywhere in the entire IMU-838 development program**

vidofludimus\* (IMU-838)



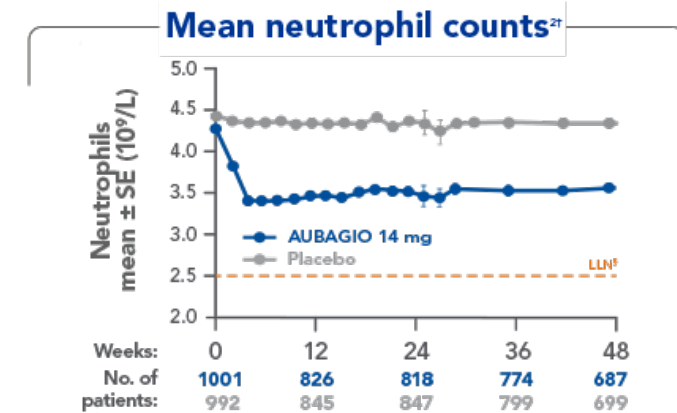
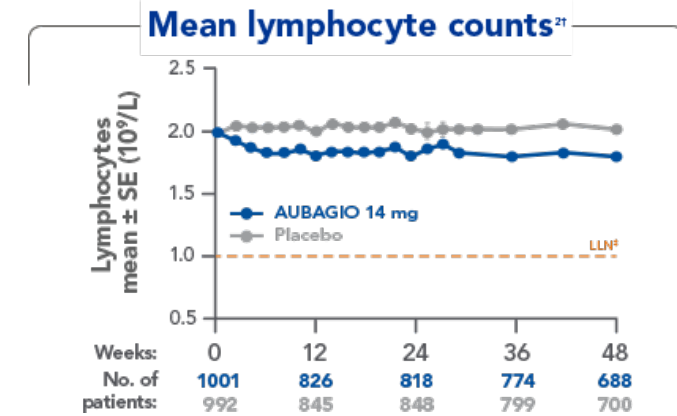
[1] Büttner R, et al. Blood 130 (suppl 1): 4426 abstract, 2017 [2] Cada DJ, et al. Hosp Pharm, 2013;48:231-240 [3] O'Connor et al, NEJM 365: supplementary appendix, 2011

[4] Summary of Product Characteristics Aubagio® [5] FDA CDER Medical Review Teriflunomide, 2012 [6] O'Connor et al, NEJM, 2011;365:1293-1303 [5] More information available at: [https://www.aubagiohcp.com/content/pdf/drug\\_elimination\\_guide.pdf](https://www.aubagiohcp.com/content/pdf/drug_elimination_guide.pdf)

\* Vidofludimus is the active moiety of IMU-838.

# Teriflunomide Has a Safety and Tolerability Profile Not Expected From Selective DHODH Inhibition

Adverse Event	Aubagio® 14 mg (n=1002)	Aubagio® 7 mg (n=1045)	Placebo (n=997)
Headache	16%	18%	15%
ALT increased	15%	13%	9%
Diarrhea	14%	13%	8%
Alopecia	13%	10%	5%
Nausea	11%	8%	7%



[1] Aubagio® (teriflunomide) Prescribing Information US FDA. Medical Review for teriflunomide. August 25, 2012

[2] O'Connor et al, NEJM 365: supplementary appendix, 2011

# Previous COMPONENT\* Trial of Vidofludimus

Incidence of Liver Events <sup>[1]</sup>		
Liver Event TEAE By Preferred Term	Vidofludimus 35 mg n = 122	Placebo n = 119
Biliary Colic	0 (0.0%)	1 (0.8%)
Hepatic Pain	0 (0.0%)	1 (0.8%)
Hepatic Steatosis	0 (0.0%)	1 (0.8%)
Hepatocellular Injury	1 (0.8%)	0 (0.0%)
g-Glutamyl Transferease Increased	1 (0.8%)	1 (0.8%)
Alanine Aminotransferase Increased	0 (0.0%)	1 (0.8%)
Hepatic Enzyme Increased	0 (0.0%)	1 (0.8%)
<b>Patients with Liver Events (%)</b>	<b>2 (1.6%)</b>	<b>6 (5.0%)</b>

Vidofludimus is the active moiety of IMU-838. TEAE: treatment emergent adverse events

\*The COMPONENT trial was a randomized, double blind, placebo-controlled, parallel group, multicenter phase 2 clinical trial to assess the safety and efficacy of vidofludimus in combination with methotrexate (MTX) in patients with rheumatoid arthritis (RA) who were not responding sufficiently to MTX monotherapy.

[1] Muehler A, Kohlhof H, Groeppel M, Vitt D. The Selective Oral Immunomodulator Vidofludimus in Patients with Active Rheumatoid Arthritis: Safety Results from the COMPONENT Study. *Drugs R D.* 2019;19(4):351-366.



# EMPhASIS Trial: Detailed Assessment of Liver Events (1): Overall Rate of Liver and Renal Events

There Was No Increase in Liver or Renal Events for the Pooled IMU-838 Treatment Arms Versus Placebo During Blinded Treatment Period

Treatment Group	Rate of Patients With Treatment-Emergent Adverse Events (TEAE)	
	With any TEA fulfilling predefined criteria as liver event	With any TEA fulfilling predefined criteria as renal event
IMU-838	4.3% (6/140)	2.1% (3/140)
Placebo	4.3% (3/69)	1.4% (1/69)

TEAE: treatment-emergent adverse events

Renal events are TEAE with predetermined adverse event preferred terms related to renal function from MedRA Systems Organ Classes 'Renal and urinary disorder' or 'Investigations'.

Liver events are TEAE with predetermined adverse event preferred terms related to liver function from MedRA Systems Organ Classes 'Investigations' or 'Hepatobiliary disorders'.

# EMPhASIS Trial: Detailed Assessment of Liver Events (2)

## Liver Enzyme Elevations

Very few cases of increases of alanine aminotransferase increases (ALT) or aspartate aminotransferase (AST) above the different thresholds of upper limit of normal (ULN)

- Such cases are comparable between IMU-838 treatments arms and placebo

### Liver Enzyme Elevations

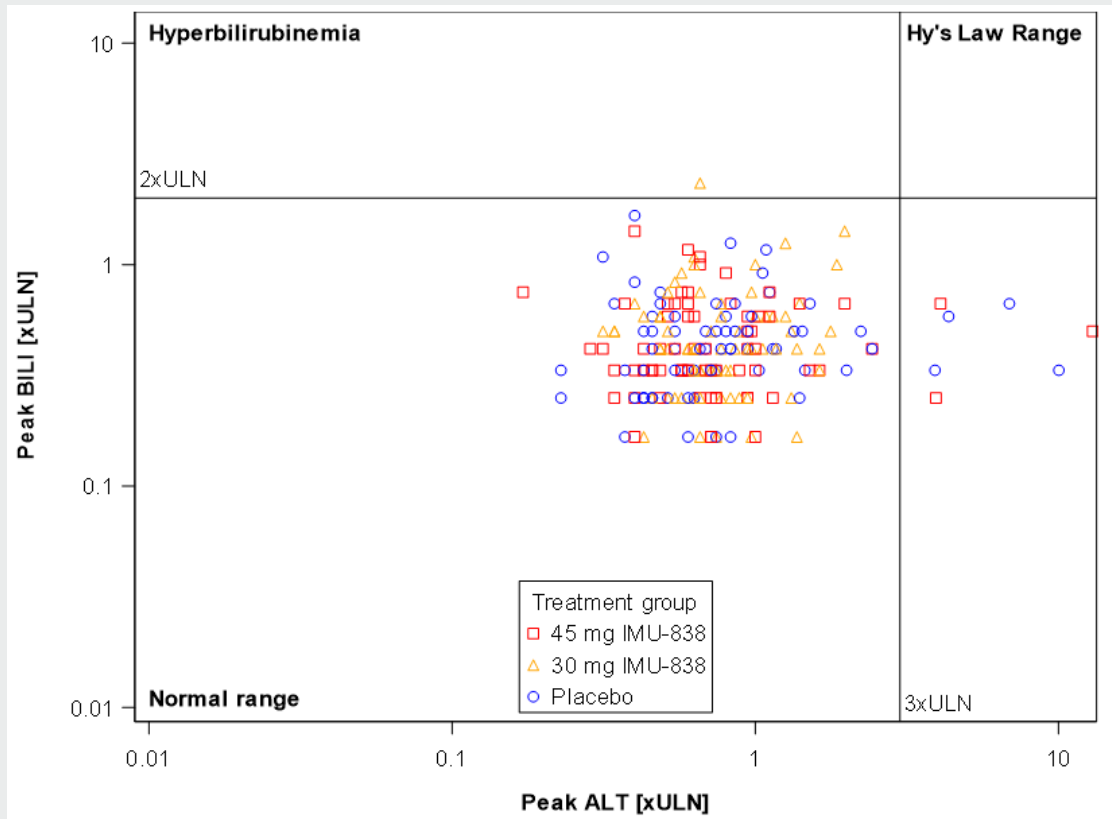
	30 mg IMU-838	45 mg IMU-838	Placebo
Number of Patients Evaluated	71	69	69
ALT or AST >5xULN	0 (0%)	1 (1.4%)	2 (2.9%)
ALT or AST >10xULN	0 (0%)	1 (1.4%)	1 (1.4%)
ALT or AST >15xULN	0 (0%)	0 (0%)	0 (0%)

ULN: upper limit normal

# EMPhASIS Trial: Detailed Assessment of Liver Events (3)

## Hy's Law Assessment

### Hy's Law Assessment



Very few cases of increases of alanine aminotransferase (ALT) above 3xULN, or bilirubin (BILI) >2x ULN:

- Such cases are comparable between IMU-838 treatment arms and placebo
- There are no Hy's Law cases with concurrent increases of ALT and BILI (there are no such cases in the entire development program of IMU-838)

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



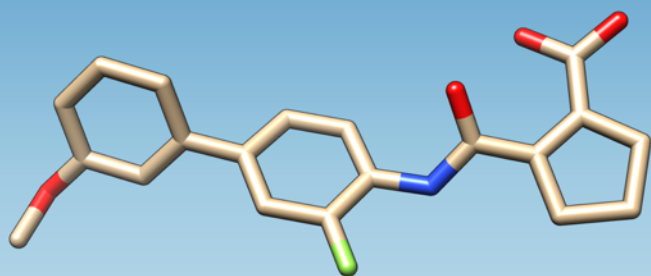
## Conclusions Regarding Safety

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- Consistent with prior data sets in other patient populations, administration of IMU-838 in this trial was observed to be well-tolerated, thereby also providing further evidence of a favorable safety profile of IMU-838 in the RRMS patient population.
  - In general, safety profile is similar to placebo group
- Very low rate of treatment discontinuations
  - IMU-838 discontinuation rate compares favorably to many other medications in RRMS
- Favorable safety profile of IMU-838 observed
  - No increase in liver and renal events, as compared to placebo
  - No signal for any hepatotoxicity or elevations of liver enzymes

# Status Quo and Outlook

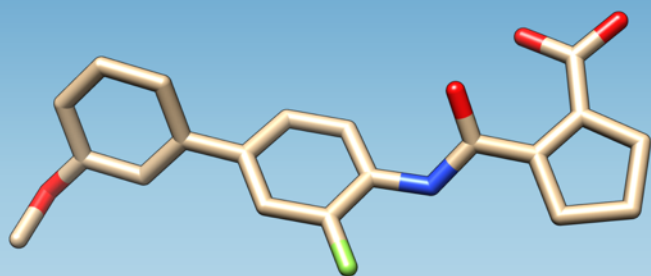
## Available Top-Line Data Announced Today



- 1** Analysis of the full EMPHASIS data is ongoing and is intended to be presented at the joint **ACTRIMS-ECTRIMS scientific meeting on September 11 to 13, 2020**
- 2** **More detailed safety data** (in particular, diarrhea, alopecia, neutropenia) are not yet available, however such events, based on the blinded safety monitoring during the trial, were very rare and no other conclusions are expected as known from already established safety profile
- 3** Immunic now **continuing preparations for clinical phase 3 program**
- 4** Immunic intends to give more guidance on next step for the phase 3 program once the full data is available and discussions with experts as well as regulatory authorities have been completed

# Summary

## Positive Clinical Activity Data Achieved and Unique Safety Properties of IMU-838 Further Support Potential as Best-in-Class Drug Candidate



- 1 IMU-838 showed compelling clinical activity in this phase 2 trial
- 2 Unique safety properties compared with current RRMS treatment options
- 3 We believe it would allow for a safe and easy-to-use treatment option of early RRMS in patients with mild-to-moderate disease activity
- 4 Preparations of phase 3 program ongoing

# Thank You!

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