Immunic Therapeutics

Developing Selective Oral Drugs in Immunology

NASDAQ: IMUX | July 1, 2021 | IMU-838 in Multiple Sclerosis

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 aimed at offering patients with chronic inflammatory and autoimmune diseases new and clinically meaningful treatment options.

Immunic THERAPEUTICS

Development Pipeline

Program	Indication	Target	Preclinical	Phase 1	Phase 2	Phase 3
IMU-838	Relapsing-Remitting Multiple Sclerosis	DHODH	■	■	■	■
	Progressive Multiple Sclerosis	DHODH	■	■	■	
	Ulcerative Colitis	DHODH	■	■	■	
	Crohn's Disease	DHODH	■	■		
	Primary Sclerosing Cholangitis	DHODH	■	■	■	
IMU-935	Psoriasis	RORγt	■	■		
	Guillain-Barré Syndrome	RORγt	■	■		
IMU-856	Gastrointestinal Diseases	Intestinal Barrier Function	■	■		

■ Completed or ongoing ■ In preparation or planned

Immunic THERAPEUTICS

IMU-838 is Targeted to be the Easy-to-Use Approach for Patients With Multiple Sclerosis (MS)

IMU-838 is **intended** to be:

- the **once-daily medication** for MS patients with a well-balanced combination of a **favorable safety and convenience** profile with **robust clinical activity**

Benefits for Patient

- Noticeable efficacy and potential to prevent and/or delay disability worsening
- Outstanding safety profile of an oral drug without adverse events disturbing quality-of-live
- No/low PML risk
- Long treatment duration through less risk for discontinuation, high patient compliance

Advantages for Neurologist

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

PML: progressive multifocal leukoencephalopathy

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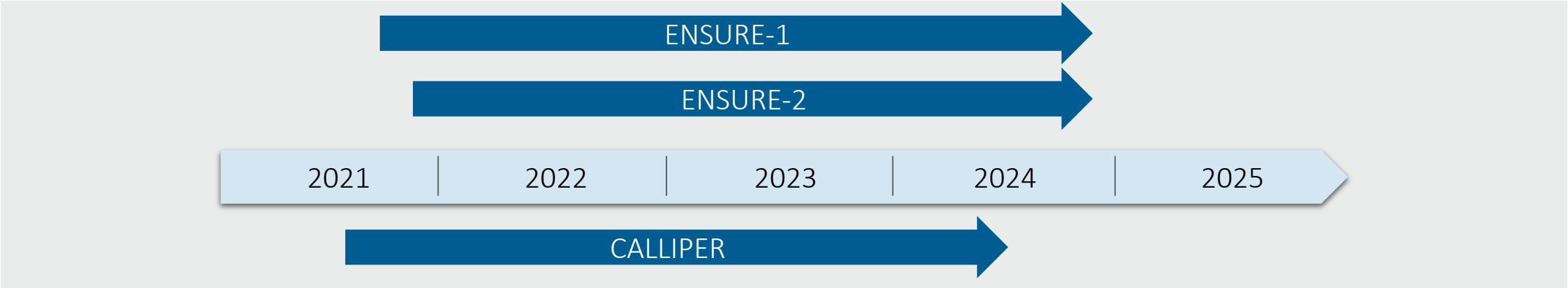
IMU-838: Phase 3 and Approval Strategy in Multiple Sclerosis

Phase 3 ENSURE Program in RRMS

- Two identical pivotal trials in RRMS patients
- Placebo-controlled
- Goal: Regulatory approval of IMU-838
- Dosage: 30 mg IMU-838 QD

Phase 2 CALLIPER Trial in PMS

- Phase 2 trial in PMS patients
- Goal: Corroborate IMU-838's potential for neuroprotective activity (slowing brain atrophy, delaying disability worsening)
- Dosage: 45 mg IMU-838 QD



QD: quaque die = once-daily

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IMU-838 in Multiple Sclerosis (MS)

Phase 3 ENSURE Program in Relapsing-Remitting Multiple Sclerosis (RRMS)

Phase 3 ENSURE Program of IMU-838 in RRMS

- U.S. Food and Drug Administration cleared Immunic's investigational new drug (IND) application
- Dosing of the first patient expected in H2/2021

ENSURE: Overview Pivotal Phase 3 Program in RRMS

Coordinating Investigator

Robert J. Fox, M.D.
Cleveland Clinic

Included Patient Population: Relapsing Forms of MS

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

EDSS: Expanded Disability Status Scale
Lublin FD, et al. Neurology. 2014;83(3):278-286

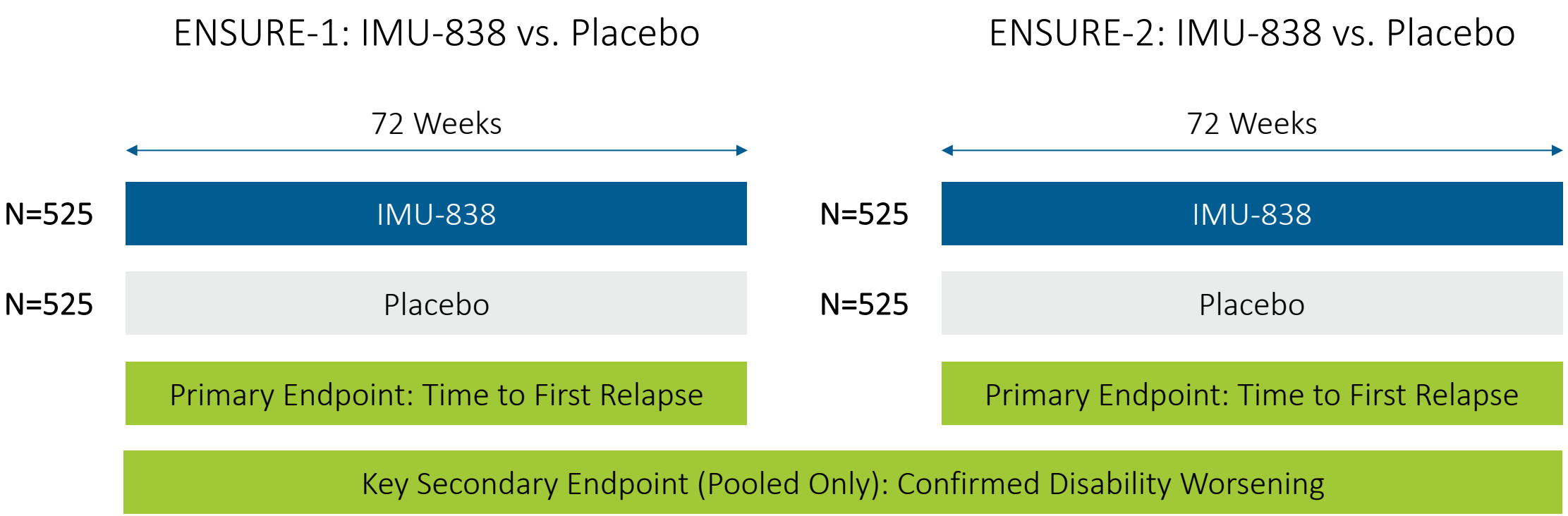
Two Multicenter, Randomized, Double-Blind Phase 3 Trials

- Approximately 1,050 patients in each trial
- More than 100 sites in the United States, Latin America, Central and Eastern Europe, and India in each trial
- Randomization to either 30 mg IMU-838 or placebo once-daily

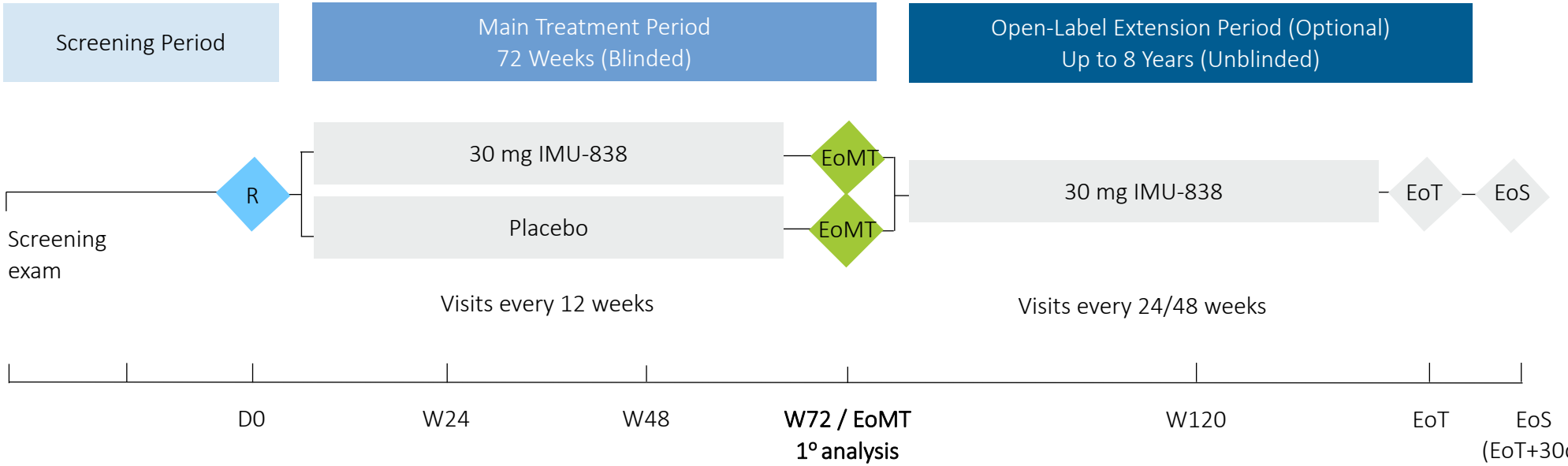
Treatment Schedule

- Trials will be run concurrently
- 72-week double-blind treatment periods
- Optional, approximately 8-year, open-label extension periods
- Interim analysis to assess event rates is planned to occur after a certain number of relapses have occurred in the double-blind treatment periods

ENSURE: Overview Pivotal Phase 3 Program in RRMS



ENSURE: General Phase 3 Study Design in RRMS



- **Primary endpoint:** delaying the occurrences of relapses based on time to first relapse*
- **Key secondary endpoints:** volume of new T2-lesions, time to confirmed disability progression, time to sustained clinically relevant changes in cognition, percentage of whole brain volume change, grey matter volume, and white matter volume

D: day; EoMT: end of main treatment period; EoS: end of study; EoT: end of treatment; R: randomization; W: week
* First relapse that occurred at least two weeks after the start of treatment administration and before the end of the double-blind treatment period (censored at 72 weeks)

ENSURE: Powering Assumptions and Interim Analysis

Event-Based Sample Size Calculation

- Primary endpoint for both trials is time to first relapse up to 72 weeks
- Each trial is 90% powered at a 0.025 significance level (log rank)
- Assuming hazard ratio between treatment arms of 0.67

Interim Analysis

- After approximately half of the events in the double-blind treatment period
- Not intended as a futility analysis
- Merely intended to inform potential sample size adjustment and help ensure that final study readout is not planned to occur before sufficient events have been achieved

ENSURE is Intended to Provide a Straightforward Path to Regulatory Approval

- IMU-838 development goals in MS: achieve market approval and confirm product differentiation based on safety, tolerability, efficacy and neuroprotective properties of IMU-838.
- Immunic believes that the phase 3 program provides a simple and straightforward path towards potential regulatory approval of IMU-838 in RRMS.
- Supportive phase 2 CALLIPER trial in PMS is designed to corroborate IMU-838's neuroprotective potential and to support differentiated profile.

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02

IMU-838 in Multiple Sclerosis (MS)

Phase 2 CALLIPER Trial in Progressive Multiple Sclerosis (PMS)

Progressive Multiple Sclerosis (PMS) is Characterized by Gradual Accrual of Disability Independent of Relapses Over Time

- PMS includes both primary progressive MS (PPMS) and secondary progressive MS (SPMS).
- PPMS is characterized by steadily worsening neurologic function from the onset of symptoms without initial relapse or remissions.
- SPMS is identified following an initial relapsing remitting course, after which the disease becomes more steadily progressive, with or without other disease activity present.

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Robert J. Fox, M.D.
Cleveland Clinic

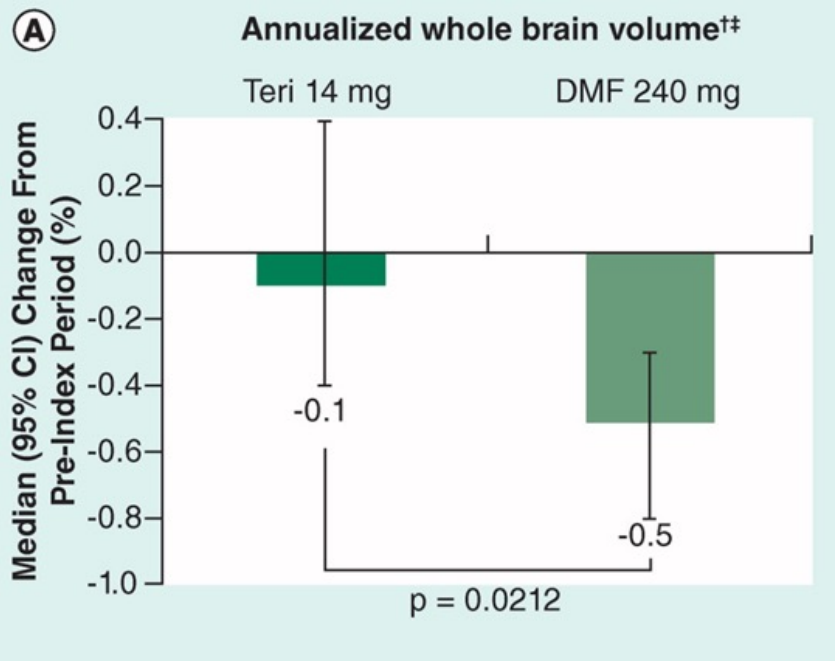
"Disability progression is a principal concern for clinicians and patients of both PMS and RRMS. The ongoing disability worsening, even in periods without relapse, not only diminishes quality-of-life but can also ultimately lead to profound impairments in patient mobility. There is a clear unmet need for new therapeutic options which can help delay or arrest this process."

Dr. Fox receives compensation as a chair of the steering committees for the ENSURE and CALLIPER programs.

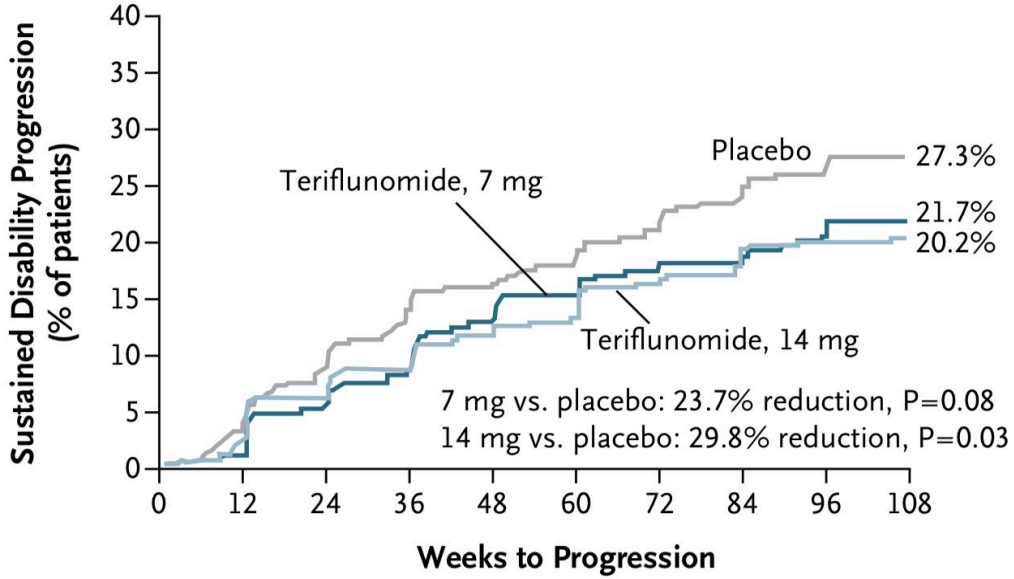
DHODH Provides Proven Mechanism for Neuroprotection

DHODH Inhibitors Have Successfully Shown Neuroprotective Effects

Teriflunomide has **demonstrated a clear and statistically significant advantage regarding brain atrophy** in RRMS patients as compared to dimethyl fumarate[1]



Teriflunomide has **demonstrated a clear effect slowing disability progression** in RRMS patients as compared to placebo[2]



CI: confidence interval; Teri: teriflunomide; DMF: dimethyl fumarate

[1] Zivadinov, et al. J Comp Eff Res. 2019;8(5):305-316

[2] O'Connor PW et al. N Engl J Med. 2011; 365:1293–303; Confavreux C et al. Lancet Neurol. 2014; 13:247–56.. (TEMSO study)

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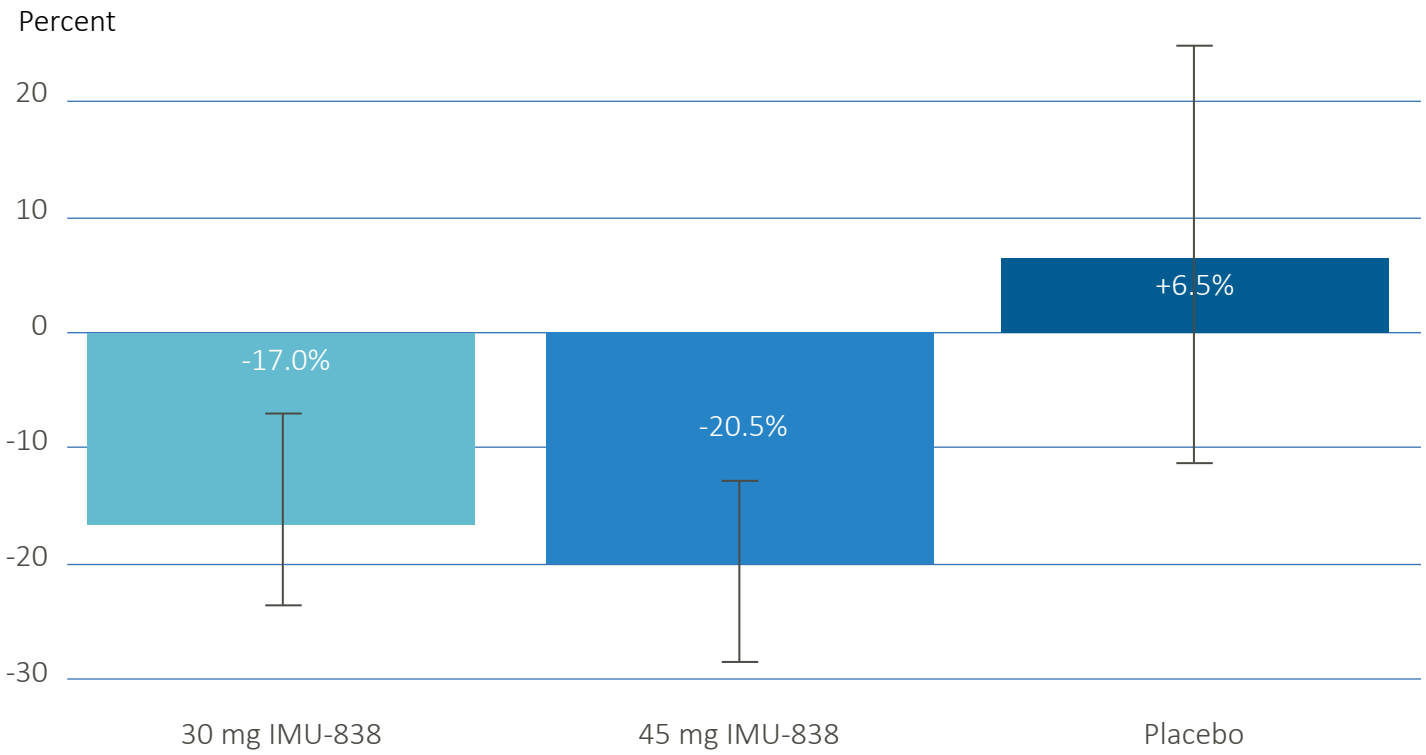
Phase 2 Data of IMU-838 in RRMS Showed Evidence of Potential Neuroprotective Activity

Robust Decrease in Serum Neurofilament Light Chain (NfL)[1]



NfL has been shown consistently to correlate with disease activity in neurological disorders and has become one of the most important serum biomarkers for axonal damage over the past few years.

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

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Phase 2 CALLIPER Trial of IMU-838 in PMS

- U.S. Food and Drug Administration cleared Immunic's investigational new drug (IND) application
- Dosing of the first patient expected in Q3/2021

CALLIPER: Phase 2 Trial Overview in PMS

Coordinating Investigator

Robert J. Fox, M.D.
Cleveland Clinic

Included Patient Population: Progressive Forms of MS

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

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

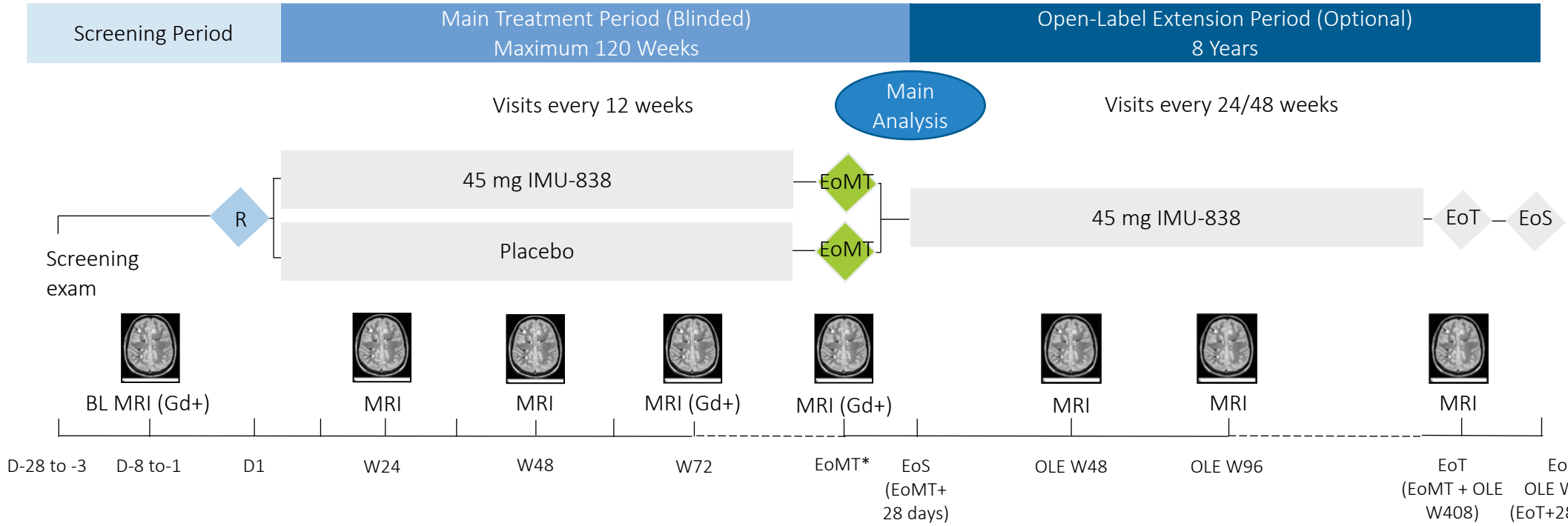
- Approximately 450 patients
- More than 70 sites in North America, Western, Central and Eastern Europe
- Randomization to either 45 mg IMU-838 or placebo once-daily

Treatment Schedule

- Blinded 120-week main treatment period
- Optional, approximately 8-year, open-label extension period
- Interim analysis planned after approximately half of the enrolled patients have completed 24-weeks of treatment: unblinded analysis of serum neurofilament light chain

PPMS: primary progressive multiple sclerosis; SPMS: secondary progressive multiple sclerosis; EDSS: Expanded Disability Status Scale

CALLIPER: Phase 2 Trial Design in PMS



- **Primary endpoint:** annualized rate of percent brain volume change (PBVC) during the main treatment period 45 mg IMU-838 vs. placebo
- **Key secondary endpoints:** annualized rate of change in whole brain atrophy and time to 24-week confirmed disability progression

*EoMT: at W120 or when last enrolled patient reaches W72
BL: baseline; D: day; EoMT: end of main treatment period; EoS: end of study; EoT: end of treatment; Gd+: with Gadolinium contrast; M: month; MRI: magnetic resonance imaging; OLE: open-label extension; R: randomization; W: week

CALLIPER is Designed to Support IMU-838's Overall Positioning and the Phase 3 Program in RRMS

- CALLIPER is intended to run concurrently with and to complement the phase 3 program in RRMS.
- CALLIPER is designed to corroborate IMU-838's neuroprotective potential, as exemplified by slowing of brain atrophy, and delay in disability worsening.*
- Immunic believes that, if the CALLIPER trial is successful in showing a beneficial effect of IMU-838, this data, along with the ENSURE program and IMU-838's strong safety and tolerability profile may allow for a meaningful clinical differentiation of IMU-838 from other oral MS medications and an attractive commercial positioning.

* Although a supportive trial, Immunic does not believe that data from the CALLIPER trial are a pre-condition for filing a New Drug Application in RRMS. The CALLIPER trial, by itself, is not intended to support regulatory approval of IMU-838 in PMS.

03

IMU-838 is Designed to be an Easy-to-Use, Uniquely Safe, Well-Tolerated and Efficacious MS Treatment

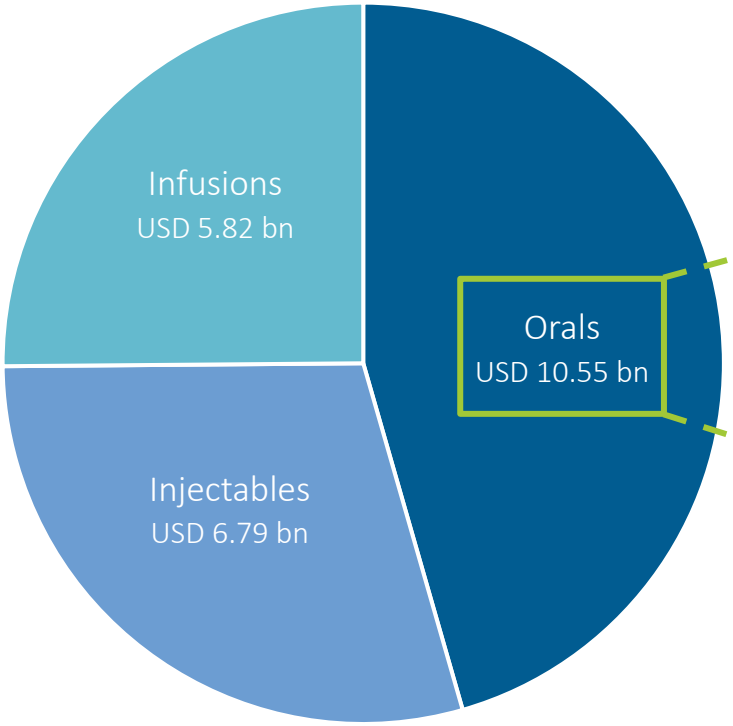
MS drug market exceeds USD 23 billion, but still needs:

- A robust anti-inflammatory, with additional **neuroprotective properties**
- A **safe and well-tolerated oral** drug, allowing patients to maintain their normal quality-of-live
- A solution particularly for **early diagnosed patients** who need an **easy-to-use base medication**

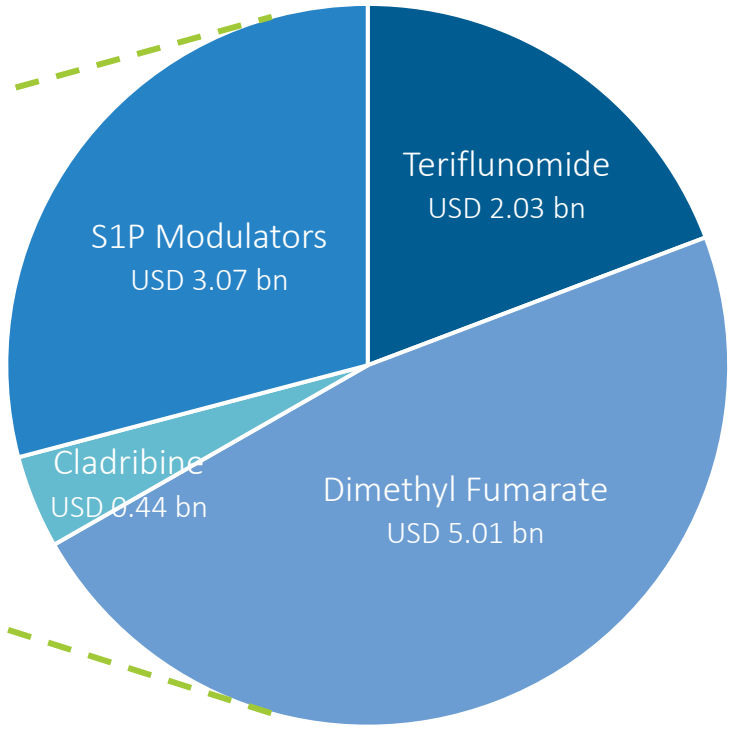
The Global MS Drug Market is Crowded But Enormous

Total 2020 Sales in G7 Countries*: USD 23.24 Billion

Oral MS Drugs Have Substantial Market Share*



IMU-838 Aims at Significant Share of USD 10+ Billion Oral MS Drug Market*



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

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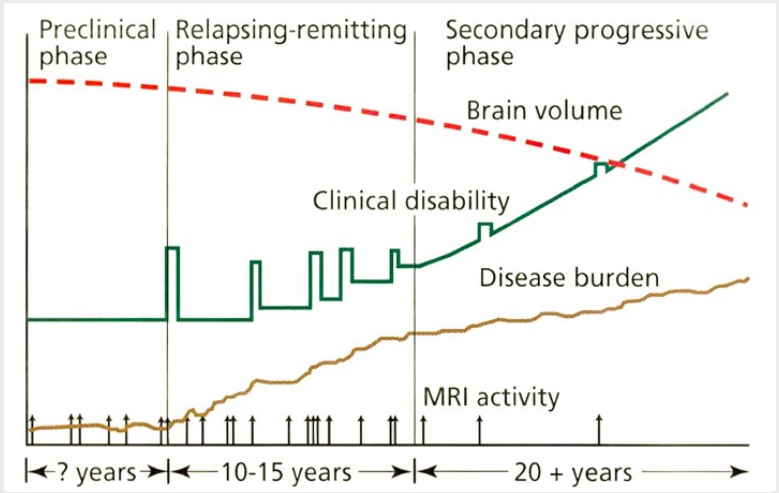
Successful MS Therapy Requires Efficacy, Safety and Tolerability

Lifelong Disease

- **Lifelong disease** requiring decades of therapy
- ~2.8 million people affected worldwide (~1 million in the US)[1]
- Typically diagnosed in **younger adults** with a 3:1 preference for women
- Patients can expect to be on therapy for 40+ years

Therapeutic Goal: Preventing Disability Worsening

- Historical focus has been on prevention of relapses
- Unmet need is prevention of **disability worsening**



Need to Do so Without

- **Problematic side effects** which worsen quality-of-life and/or decrease compliance (leading to worse outcomes)
- Health risks, which can add up **cumulatively** over life-time of therapy, such as:
  - Cancer risk
  - Infection risk, incl. PML risk
  - Cardiovascular risk
  - Liver risk
- Need for **significant monitoring** (inconvenience, expense, false positives, etc.)

PML: progressive multifocal leukoencephalopathy

[1] MS International Federation (2020): Atlas of MS. https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms

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Existing First-Line and Oral MS Drugs Leave Much to be Desired

	Glatiramer Acetate	Interferons	Teriflunomide	Dimethyl Fumarate	Cladribine	S1P Modulators
Oral?	🔴	🔴	🟢	🟢	🟢	🟢
Relapse Reduction	🟡	🟡	🟡	🟢	🟢	🟢
Prevention of Disability Worsening	🟡	🔴	🟢	🟡	🟢	🟢
Tolerability	🟢	🔴	🟡	🟡	🟡	🟡
Safety	🟢	🟢	🟡	🟡	🔴	🟡
Absence of Infection Risk	🟢	🟢	🟢	🔴	🔴	🔴
Vaccination Possible?	🟢	🟢	🟢	🔴	🔴	🔴
Low Monitoring Requirements	🟢	🟡	🔴	🔴	🔴	🔴

🟢 Favorable Profile / Yes 🟡 Clinical Concern / Risk 🔴 Substantial Risk / No

This classification is based on Immunic assumptions according to clinical trial results as well as FDA labels of the drugs displayed.
S1P: sphingosine-1-phosphate

Immunic THERAPEUTICS

Strong Phase 2 Data of IMU-838 in RRMS Supports Desired Product Target Profile

Strong Phase 2 Data Underlines Robust Efficacy With Neuroprotective Potential

- **Suppression of MRI lesions ($p < 0.001$): met primary and key secondary endpoints**
- Positive signals on:
  - Annual relapse rate (ARR)
  - Time to relapse
  - Unconfirmed disability
  - Expanded disability status scale (EDSS)
- Robust decrease in serum neurofilament light chain provides **evidence of potential neuroprotective activity**

Phase 2 Data Also Confirms Best-in-Class Safety and Tolerability

- Administration of IMU-838 was observed to be **safe and well-tolerated**
- Very **low rate of treatment discontinuations**, even lower than in the placebo group, indicated an encouraging combination of tolerability and efficacy
- **No** signals for **hepatotoxicity or infections**, no liver and kidney events and no hematuria observed – **suggests less need for intensive monitoring**

No other drug, approved or in development, shares these unique attributes.

MRI: magnetic resonance imaging

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IMU-838's Safety Profile is Unique

	IMU-838[1]	Teriflunomide[2]	Dimethyl Fumarate[3]	Cladribine[4]	Fingolimod[5]	Siponimod[6]	Ponesimod[7]	Ozanimod[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 ☐ N/A

This classification is based on Immunic assumptions according to clinical trial results regarding likelihood and severity of risk as well as FDA labels of the drugs displayed: [1] https://www.immunic-therapeutics.com/2020/09/11/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] Gold et al., 2012 NEJM, Fox et al., 2012 NEJM [4] Giovannoni et al., 2010 NEJM [5] Kappos et al., 2010 NEJM, Cohen et al., 2010 NEJM [6] Kappos et al 2018 Lancet [7] Kappos et al., 2021 JAMA [8] Comi et al., 2020 Lancet, Cohen et al., 2020 Lancet

Immunic THERAPEUTICS

IMU-838: Already Viewed as Most Attractive DMT in Development

An Independent, Third-Party Study* Analyzed How MS Patients Are Switching Therapies

SPHERIX GLOBAL INSIGHTS

- Independent expert group, Spherix, asked real world treating physicians:
  - If current DMT is not successful for the patient, and based on what you know about the following DMTs in development, how likely would you be to switch the patient to one of these agents (assuming they are available)?
- Study **analyzed nine MS drugs**, then in development:
  - IMU-838, ponesimod, masitinib, ublituximab, ibudilast, evobrutinib, tolebrutinib, fenebrutinib, glatiramer acetate depot
- Among those, **IMU-838 was considered the most interesting** with 77% of neurologists considering IMU-838 for the next switch to DMT (possibly and very likely)
- Of the drugs analyzed, IMU-838 was the **only drug then in phase 2** development
- Immunic had not yet started significant medical affairs outreach

DMT: disease-modifying therapy

* "DMT Switching in Multiple Sclerosis 2021" report published end of March 2021. The 2021 audit included in the service captured chart data from 1,117 patients switched to a new DMT within the past three months (provided by 223 neurologists).

Immunic THERAPEUTICS

IMU-838: Full Prescription Coverage Achievable at Attractive Pricing Range

Immunic Hired Third-Party Pricing Experts to Perform Landscape Analysis for IMU-838 Pricing

Historically, **differentiated** innovator drugs have **not experienced price impacts** even when generics are approved for a related or similar molecule.

- For example, the genericization of Copaxone 20 mg did not impact the pricing of the 40 mg version of Copaxone.

Payer study[1] found coverage **insensitivity regarding generic pricing levels**.

- IMU-838 is considered **differentiated** from currently approved oral RRMS drugs, including Aubagio®:
  - Better safety
  - Better tolerability
  - Less monitoring likely to be required
  - Potential neuroprotective effects

Conclusions:

- Coverage is **not sensitive** to IMU-838 pricing despite the presence of generics.
- **Full prescription coverage by payers is achievable for IMU-838** at an attractive pricing range of USD 50-60 thousand annually, **independent of future generic pricing.**

[1] Payer's analysis performed by Medical Marketing Economics (MME), LLC

04

Immunic Therapeutics

Summary

IMU-838 is Targeted to be the Easy-to-Use Approach for Patients With Multiple Sclerosis (MS)

IMU-838 is **intended** to be:

- the **once-daily medication** for MS patients with a well-balanced combination of a **favorable safety and convenience** profile with **robust clinical activity**

- FDA clearance allows initiation of IMU-838 phase 3 ENSURE studies in RRMS and phase 2 CALLIPER study in PMS
- Phase 3 ENSURE program in RRMS comprises twin studies evaluating efficacy, safety, and tolerability of IMU-838 versus placebo, intended to provide straightforward path to regulatory approval
- Supportive phase 2 CALLIPER trial in PMS, designed to corroborate IMU-838's neuroprotective potential and to support differentiated profile
- Both ENSURE and CALLIPER expected to begin in H2/2021

Thank You!

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