



Immunic
THERAPEUTICS

Immunic Therapeutics

Developing Selective Oral Drugs in Immunology

NASDAQ: IMUX | October 2021

Cautionary Note Regarding Forward-Looking Statements

→ This presentation contains “forward-looking statements” that involve substantial risks and uncertainties for purposes of the safe harbor within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These include statements regarding management’s intentions, plans, beliefs, expectations or forecasts for the future, and, therefore, you are cautioned not to place undue reliance on them. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. Immunic undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise, except to the extent required by law. We use words such as “anticipates,” “believes,” “plans,” “expects,” “projects,” “future,” “intends,” “may,” “will,” “should,” “could,” “estimates,” “predicts,” “potential,” “continue,” “guidance,” and similar expressions to identify these forward-looking statements that are intended to be covered by the safe-harbor provisions of the Private Securities Litigation Reform Act of 1995.

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→ Forward-looking statements included in this presentation are based on information available to Immunic as of the date of this presentation. Immunic does not undertake any obligation to update such forward-looking statements except as required by applicable law.

Our Mission



We are developing a pipeline of next-generation selective oral therapies focused on offering patients with chronic inflammatory and autoimmune diseases new and clinically meaningful treatment options.



Leadership Team



Company is Led by an Experienced Management Team



Daniel Vitt,
PhD
CEO &
President



Duane
Nash, MD,
JD, MBA
Executive
Chairman



Andreas
Muehler,
MD, MBA
CMO



Hella
Kohlhof,
PhD
CSO



Patrick
Walsh
CBO



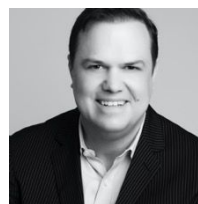
Inderpal
Singh
General
Counsel



Glenn
Whaley
Principal
Financial and
Accounting
Officer



Renowned International Board of Directors



Duane
Nash, MD,
JD, MBA
Executive
Chairman



Daniel Vitt,
PhD
CEO &
President of
Immunix



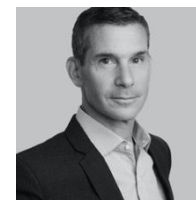
Tamar
Howson,
CFA
Independent
Director



Barclay
"Buck" A.
Phillips
Independent
Director



Joerg
Neermann,
PhD
Independent
Director



Vincent
Ossipow,
PhD, CFA
Omega
Funds



Jan Van den
Bossche,
CFA
Fund+

Development Pipeline

Program	Target	Preclinical	Phase 1	Phase 2	Phase 3	Key 2021/22 Milestones
IMU-838	DHODH	Relapsing-Remitting Multiple Sclerosis (RRMS)				<ul style="list-style-type: none">Phase 3 RRMS: first-patient-in expected in Q4/2021Phase 2 UC: last-patient-in expected in Q4/2021; top-line data expected in Q2/2022
		Progressive Multiple Sclerosis (PMS)				
		Ulcerative Colitis (UC)				
		Crohn's Disease (CD)				
		Primary Sclerosing Cholangitis (PSC)				
IMU-935	RORyt	Psoriasis				<ul style="list-style-type: none">Phase 1 healthy volunteers: unblinded SAD/MAD safety data expected in Q4/2021Phase 1b psoriasis: initial data expected in Q2/2022Phase 1 CRPC: expected to start in Q4/2021
		Castration-Resistant Prostate Cancer (CRPC)				
		Guillain-Barré Syndrome (GBS)				
IMU-856	Intestinal Barrier Function	Gastrointestinal Diseases				<ul style="list-style-type: none">Phase 1 healthy volunteers: unblinded SAD/MAD safety data expected in Q1/2022

■ Completed or ongoing ■ In preparation or planned

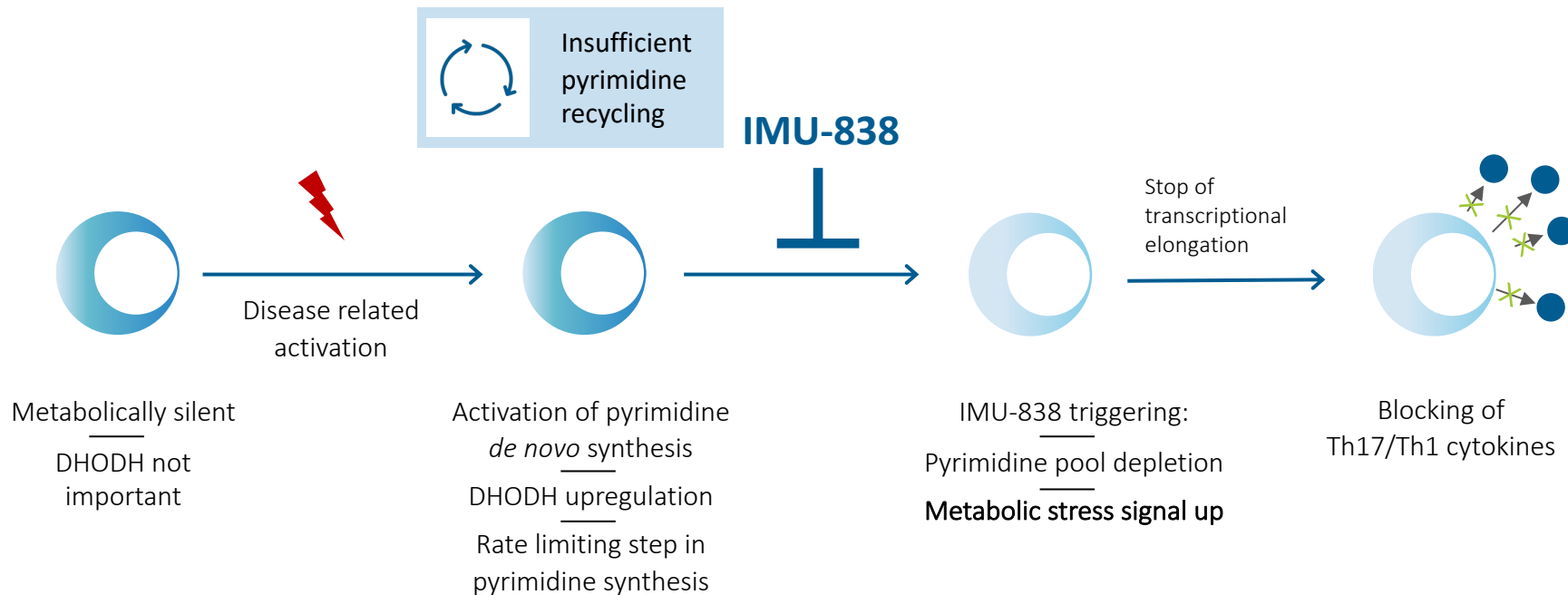
Blocking DHODH Leads to a Selective Effect on Overactivated Lymphocytes Without Broader Immunosuppression

Lymphocyte

Activated Lymphocyte

“Stressed” Lymphocyte

Pharmacological Effects



Selective targeting of hyperactivated immune cells without affecting normal immune function

No negative effect observed on:

- White blood cell count
- Rates of infection or malignancy
- Vaccination efficacy^[1]

Illustration adapted from Tan et al., 2016, Mol Cell 62; [1] Bar-Or A, Freedman MS, Kremenchutzky M, et al. Neurology. 2013;81(6):552-558
DHODH: dihydroorotate dehydrogenase



Phase 2 Clinical Trial in RRMS Successfully Completed

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

Successful MS Therapy Requires Efficacy, Safety and Tolerability



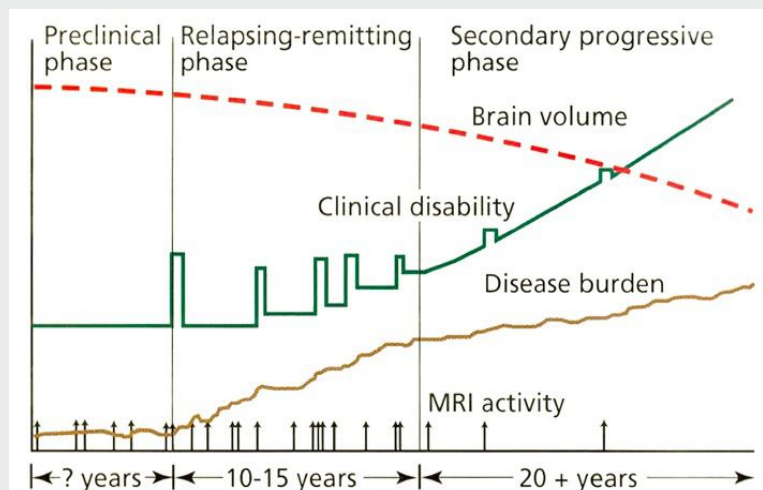
Lifelong Disease

- **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



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
- 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**

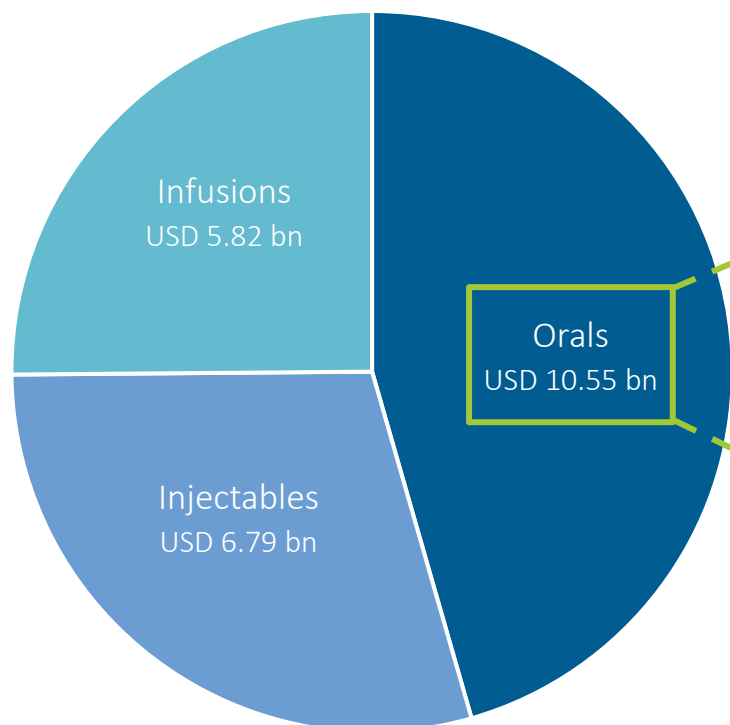
PML: progressive multifocal leukoencephalopathy

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

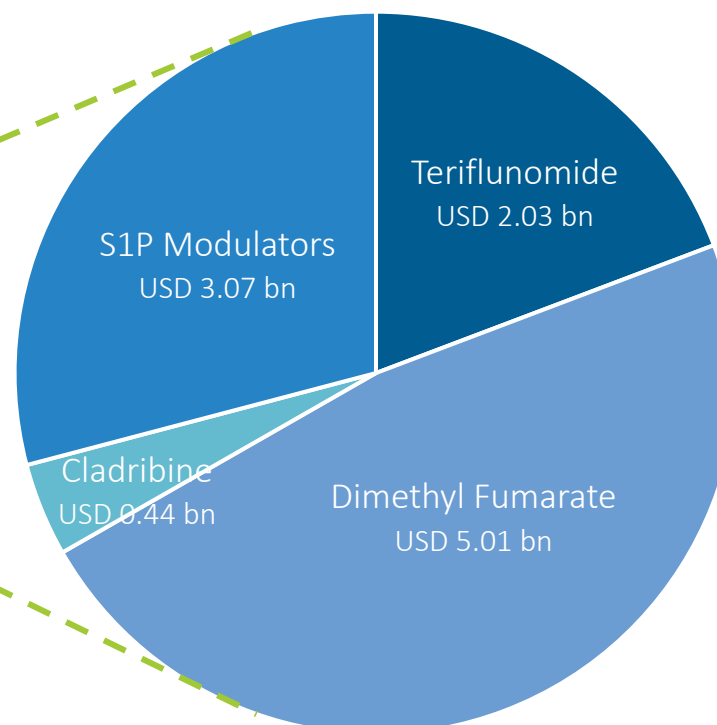
The Global MS Drug Market is Crowded But Enormous

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*



















































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-life
- A solution particularly for early diagnosed patients who need an easy-to-use base medication

* 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

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

IMU-838 is Targeted to be the Easy-to-Use Approach for MS Patients



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**



Intended 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-life
- No/low PML risk
- Long treatment duration through less risk for discontinuation, high patient compliance

PML: progressive multifocal leukoencephalopathy



Intended Advantages for Neurologist

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

Phase 2 Data of IMU-838 in RRMS: Primary and Key Secondary Endpoints Met, Showing Strong Activity on MRI Lesions

Double-Blind, Placebo-Controlled, Randomized, Parallel-Group Phase 2 Trial

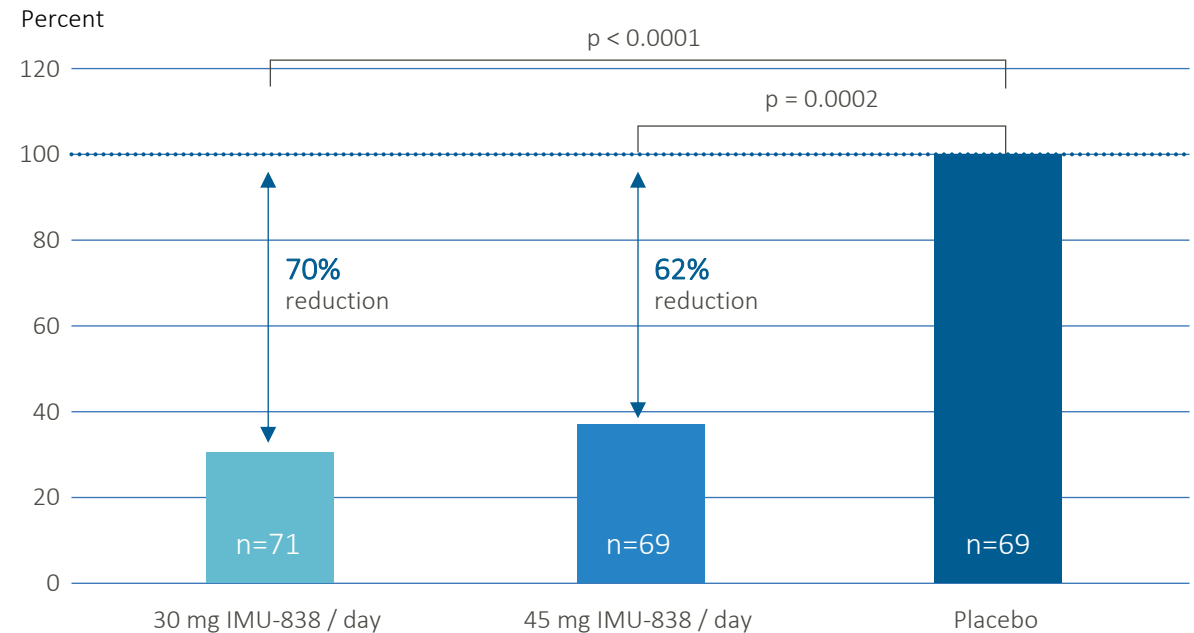
- Blinded main treatment period of 24 weeks
- Extended treatment period of up to 9.5 years to observe long-term safety
- 210 patients randomized in 36 centers across four European countries

Key Study Endpoints

Cumulative number of new combined unique active (CUA) magnetic resonance imaging (MRI) lesions up to week 24

- Primary endpoint: Difference between 45 mg/day IMU-838 and placebo
- Key secondary endpoint: Difference between 30 mg/day IMU-838 and placebo

Suppression of CUA MRI Lesions IMU-838 Versus Placebo Over 24 Weeks



10 mg dose of IMU-838 in sub-cohort 2 of additional 59 patients demonstrated a placebo-adjusted reduction of 32% in CUA MRI lesions at week 12

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.

Phase 2 Data of IMU-838 in RRMS: Demonstrated Robust Activity



The **Robust MRI Lesion Suppression of IMU-838** Observed in the Phase 2 Trial Compares Favorably to Other First-Line and Oral Base Medications Commercially Available in RRMS.*

	IMU-838	Glatiramer Acetate ^[1]	Teriflunomide ^[2]	Dimethyl Fumarate ^[3]	Fingolimod ^[4]	Ozanimod ^[5]
Administration	Oral	Injectable	Oral	Oral	Oral	Oral
Daily Dose	30 mg QD	20 mg QD	14 mg QD	240 mg TID	1.25 mg QD	1 mg QD
MRI Endpoint	Cumulative CUA lesions	Cumulative Gd lesions	Mean CUA lesions/scan	Cumulative Gd lesions	Cumulative Gd lesions	Cumulative Gd lesions
Treatment Duration	24 weeks	9 months	36 weeks	24 weeks	6 months	24 weeks
Suppression of MRI Activity	70%	29%	61%	69%	43%	86%

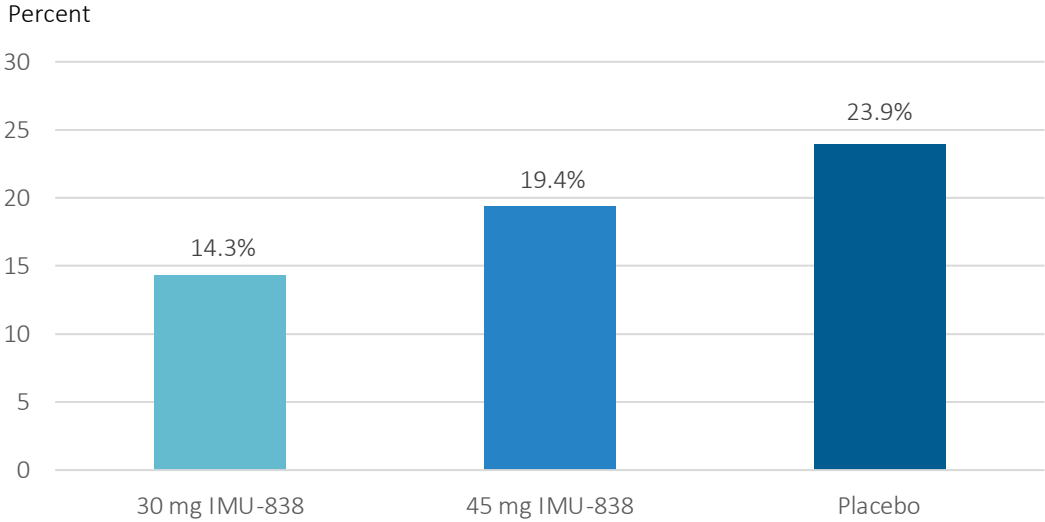
*The table summarizes the data on treatment/study discontinuation rates of the commercial dose in phase 2 trials of RRMS drugs. If the commercial dose was not included in the phase 2 trials, the dose closest to the commercial dose was shown. This high-level comparison is provided for illustrative purposes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

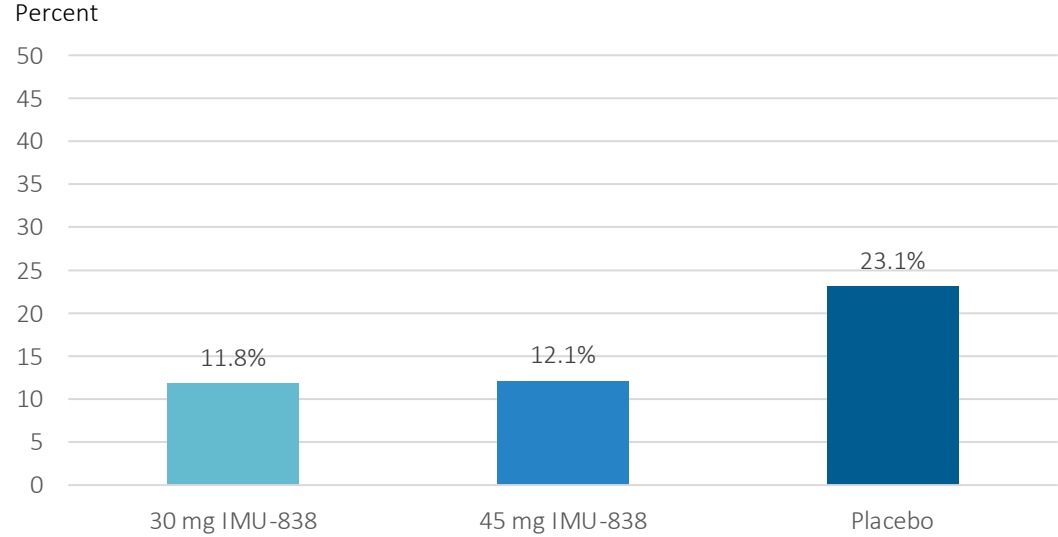
[1] Comi et al. Ann Neurol. 2001;49(3):290-297 [2] O'Connor et al. Neurology. 2006;66(6):894-900 [3] Kappos et al. Lancet. 2008;372(9648):1463-1472 [4] Kappos et al. N Engl J Med. 2006;355(11):1124-1140 [5] Cohen JA, Arnold DL, Comi G, et al. Lancet Neurol. 2016;15(4):373-381

Phase 2 Data of IMU-838 in RRMS: Positive Signals on Relapse and Unconfirmed Disability

Proportion of Patients With Relapse up to Week 24



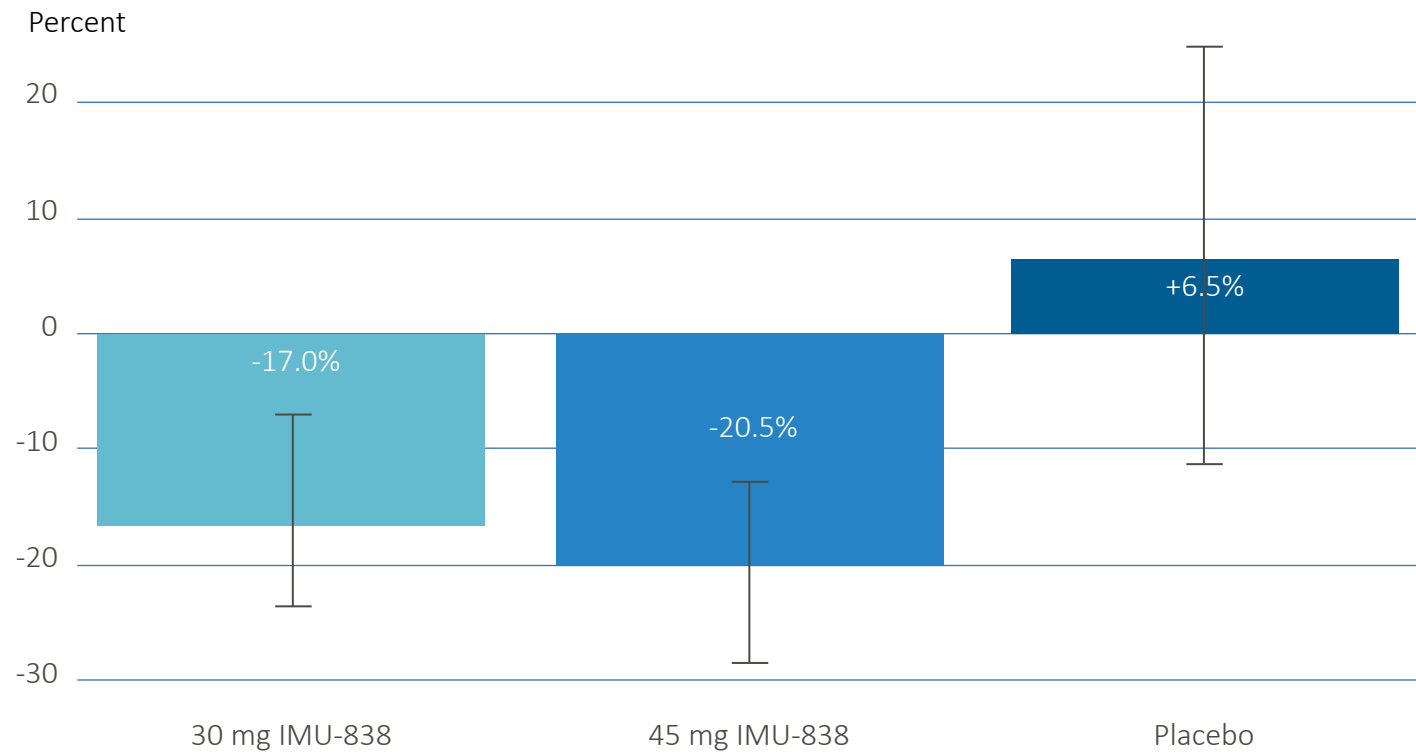
Proportion of Patients With Unconfirmed Disability Progression up to Week 24



Left: For patients with relapse up to week 24 the time to first relapse is calculated as date of first relapse - date of first IMP. Patients without relapse up to week 24 were censored at the last visit date during the main treatment period, e.g., censoring time is calculated as last visit date - date of first IMP + 1. Censored observations are marked with circles. Right: EDSS (Expanded Disability Status Scale) 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.

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

Phase 2 Data of IMU-838 in RRMS: 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 Benefit to Patients.*

	IMU-838	Glatiramer Acetate ^[1]	Teriflunomide ^[2]	Dimethyl Fumarate ^[3]	Fingolimod ^[4]	Ozanimod ^[5]
Administration	Oral	Injectable	Oral	Oral	Oral	Oral
Daily Dose	30 mg QD	20 mg QD	14 mg QD	240 mg TID	1.25 mg QD	1 mg QD
Treatment Period	24 weeks	9 months	36 weeks	24 weeks	6 months	24 weeks
Active Treatment	2.8%	5.9%	19.3%	15.6%	5.4%	2.2%
Placebo	7.2%	5.8%	6.6%	9.2%	6.5%	3.3%

*The table summarizes the data on treatment/study discontinuation rates of the commercial dose in phase 2 trials of RRMS drugs. If the commercial dose was not included in the phase 2 trials, the dose closest to the commercial dose was shown. This high-level comparison is provided for illustrative purposes only, is based on publicly available data and does not purport to be a comprehensive comparison or depiction of the other trials. Larger data sets than presented in this presentation are publicly available for certain of the compounds included on this slide. Please note that these results are taken from placebo-controlled trials, and these medications have not been tested in head-to-head assessments.

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] Cohen JA, Arnold DL, Comi G, et al. Lancet Neurol. 2016;15(4):373-381

IMU-838: Attractive Pharmacokinetic, Safety and Tolerability Profile Observed in Multiple Clinical Trials

- Safety profile similar to placebo: no general safety signals observed in clinical trials so far
- No increased rates of diarrhea, neutropenia, or alopecia
- No increased rates of infections and infestations or hematology values

- Drug exposure tested in more than 800 human subjects and patients to date
- Low rates of adverse events and treatment-emergent adverse events
- No signal for hepatotoxicity or elevations of liver enzymes and no Hy's law cases have been observed in the IMU-838 program, including the phase 2 EMPHASIS trial



Phase 2 EMPHASIS Trial: No Signal for an Increase of Infections and Infestations

TEAE of SOC: Infections and Infestations	30 mg IMU-838	45 mg IMU-838	Placebo
Patients with TEAE	18.3%	23.2%	23.2%

TEAE: treatment-emergent adverse events; SOC: system organ class



Phase 2 EMPHASIS Trial: Absence of Hepatotoxicity Signals

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)

IMU-838's Safety Profile to Date 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

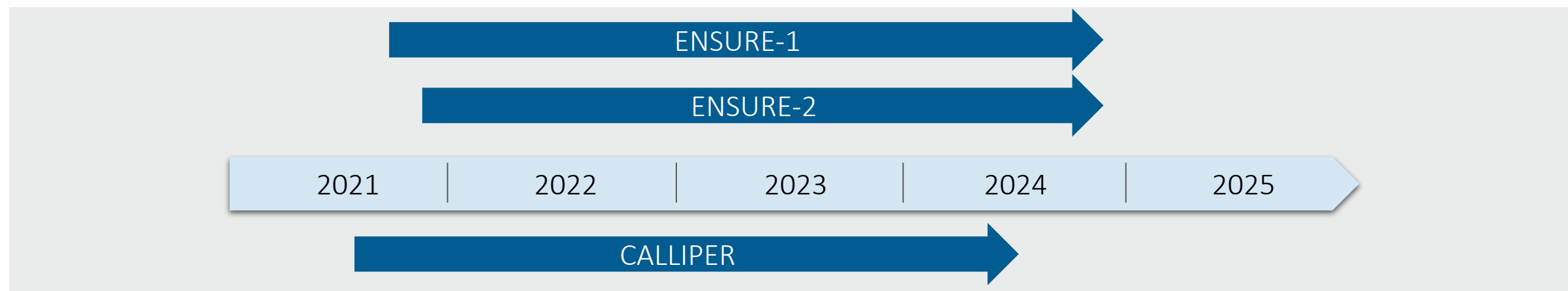
IMU-838: Phase 3 and Approval Strategy in Multiple Sclerosis

Phase 3 ENSURE Program in RRMS

- Two identical pivotal trials in RRMS patients
- 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: Demonstrate IMU-838's potential for neuroprotective activity
- Dosage: 45 mg IMU-838 QD



QD: quaque die = once-daily

ENSURE: Overview Pivotal Phase 3 Program in RRMS



Coordinating Investigator

Robert J. Fox, M.D.
Cleveland Clinic



Included Patient Population: Relapsing Forms of MS

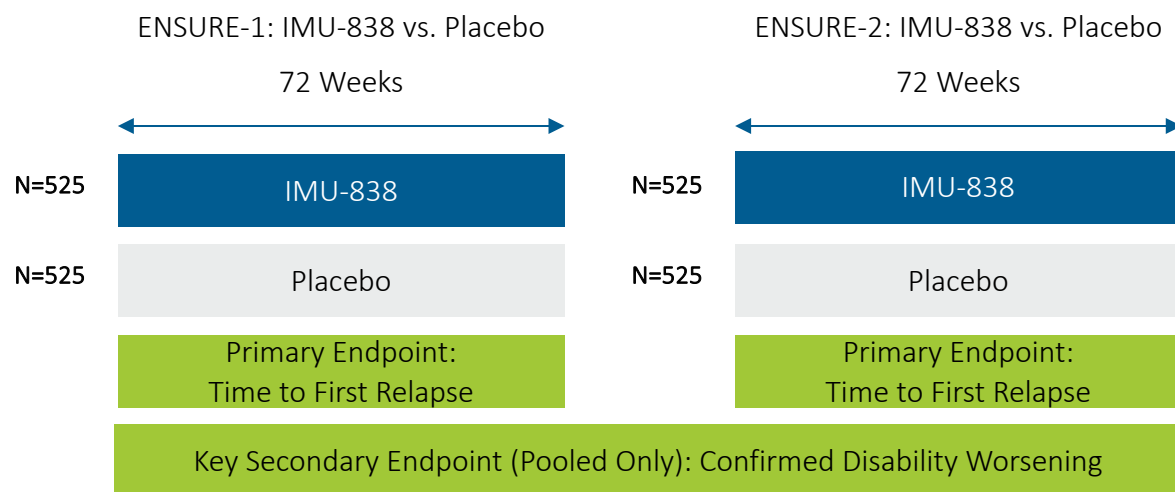
- Adult patients aged 18 to 55 years
- Established diagnosis of MS (Revised McDonald criteria 2017)
- Confirmed relapsing MS (1996 Lublin criteria)
- Active disease as defined by Lublin 2014
- EDSS score at screening between 0 to 5.5

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



Two Multicenter, Randomized, Double-Blind Phase 3 Trials

- 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
- Dosing of the first patient expected in [Q4/2021](#)



CALLIPER: Phase 2 Trial Intended to Run Concurrently With and to Complement the Phase 3 Program in RRMS



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

PPMS: primary progressive multiple sclerosis; SPMS: secondary progressive multiple sclerosis; EDSS: Expanded Disability Status Scale
* NCT05054140



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

- Approximately 450 patients in more than 70 sites in North America, Western, Central and Eastern Europe
- Randomization to either 45 mg IMU-838 or placebo once-daily
- Primary endpoint: annualized rate of percent brain volume change up to 120 weeks



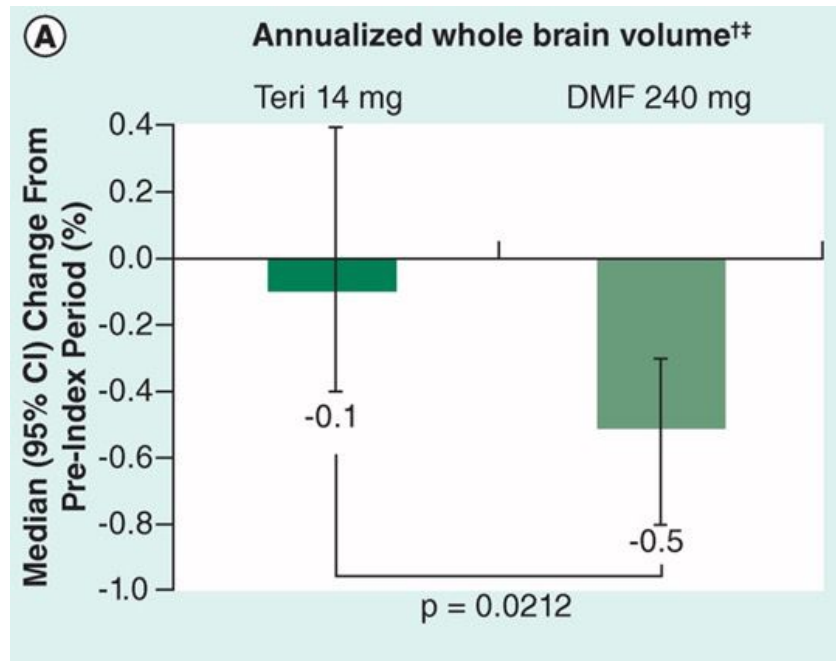
Treatment Schedule

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

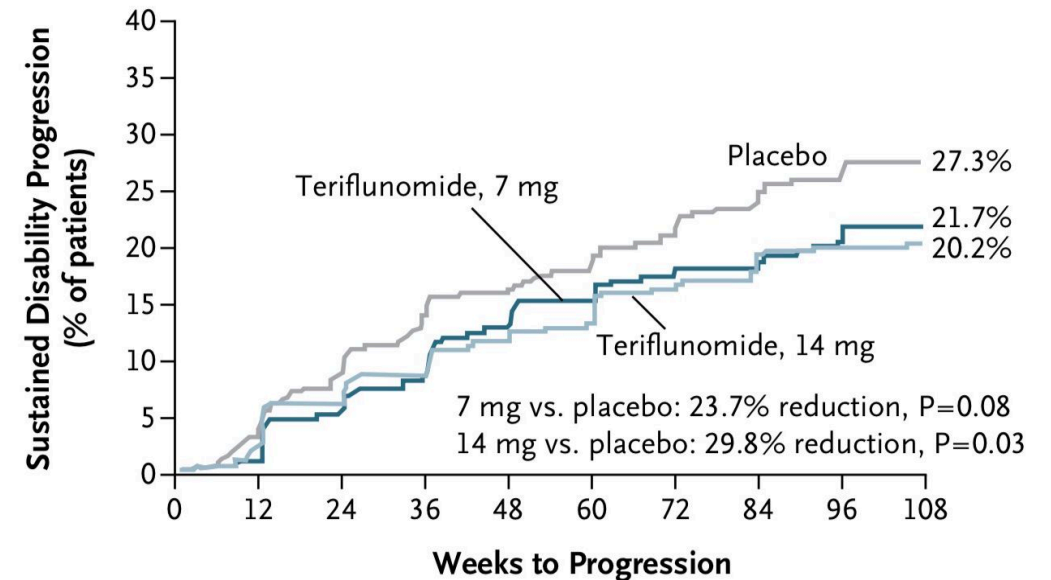
DHODH Provides Proven Mechanism for Neuroprotection

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)

MS Program is Intended to Provide a Straightforward Path to Regulatory Approval in RRMS



- 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 ENSURE program provides a simple and straightforward path towards potential regulatory approval of IMU-838 in RRMS.
- CALLIPER is designed to corroborate IMU-838's neuroprotective potential, as exemplified by slowing of brain atrophy, and delay in disability worsening, to support differentiated profile.*

* 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.



Well-Differentiated From Current Treatments

“Immunic believes that the ENSURE and CALLIPER programs along with 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.”

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



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



- 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).

IMU-838: Potential for Full Prescription Coverage 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**.

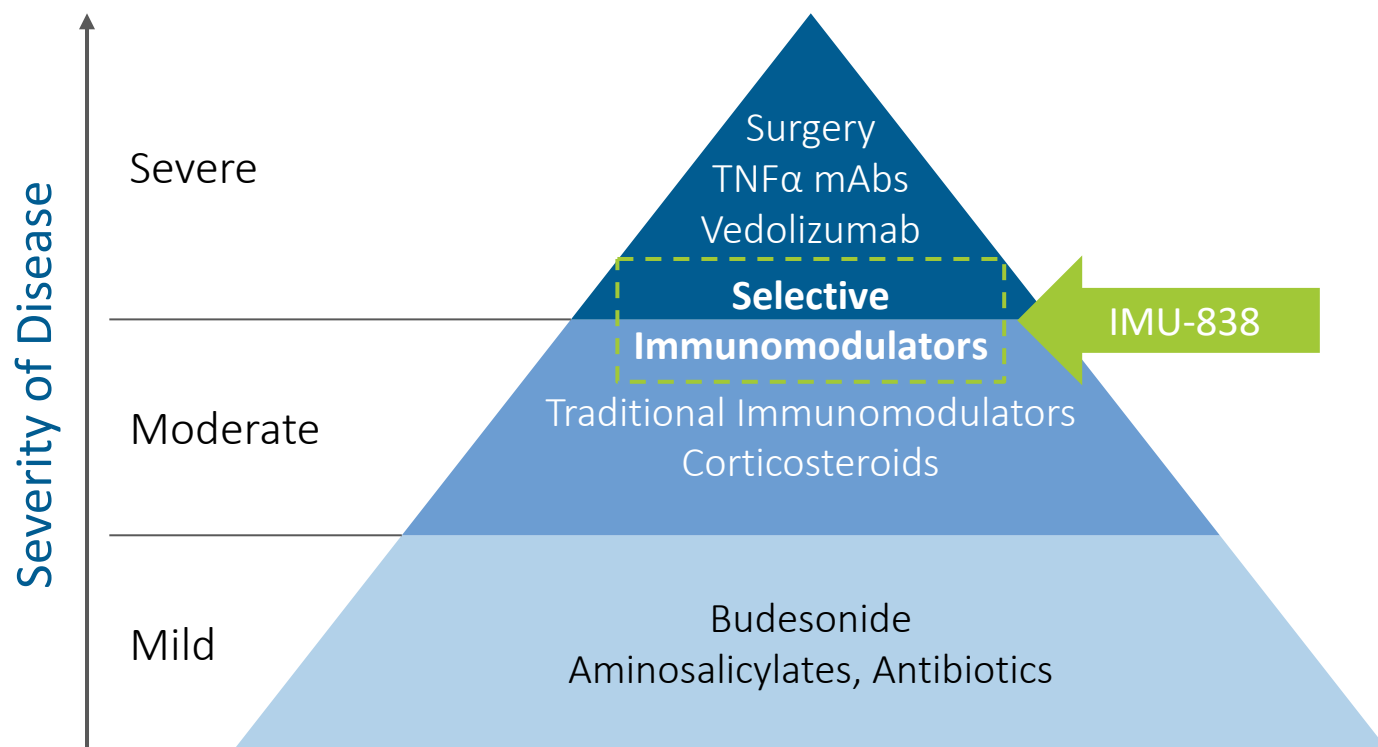
[1] Payer's analysis performed by Medical Marketing Economics (MME), LLC



IMU-838 in Inflammatory Bowel Disease (IBD)

IMU-838 is Targeted to be a
First-in-Class Treatment Option With an
Excellent Safety Profile

IBD: Therapeutic Pyramid

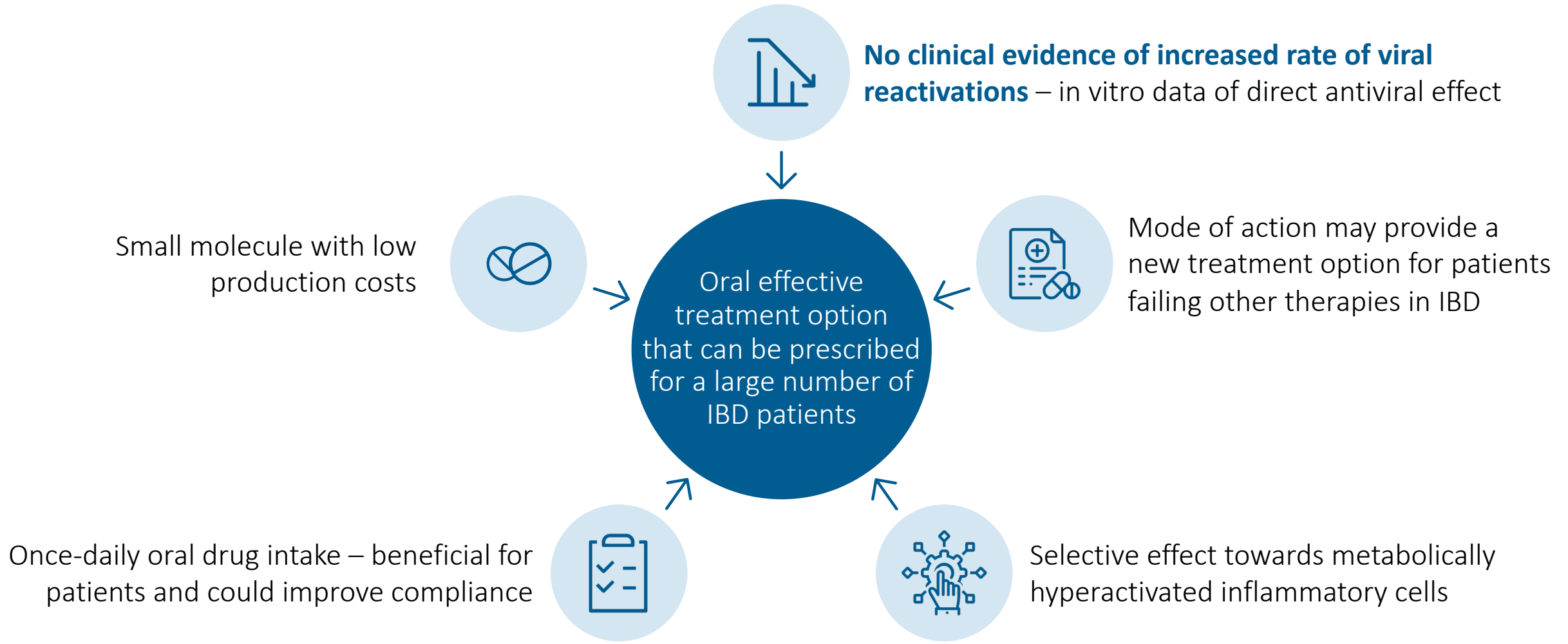


Current Solutions Have Limitations

- 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]
- In the absence of potential 'game changing' new therapies, combination approaches may become more relevant. Due to its unique properties, IMU-838 might be a perfect combination candidate.

[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

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



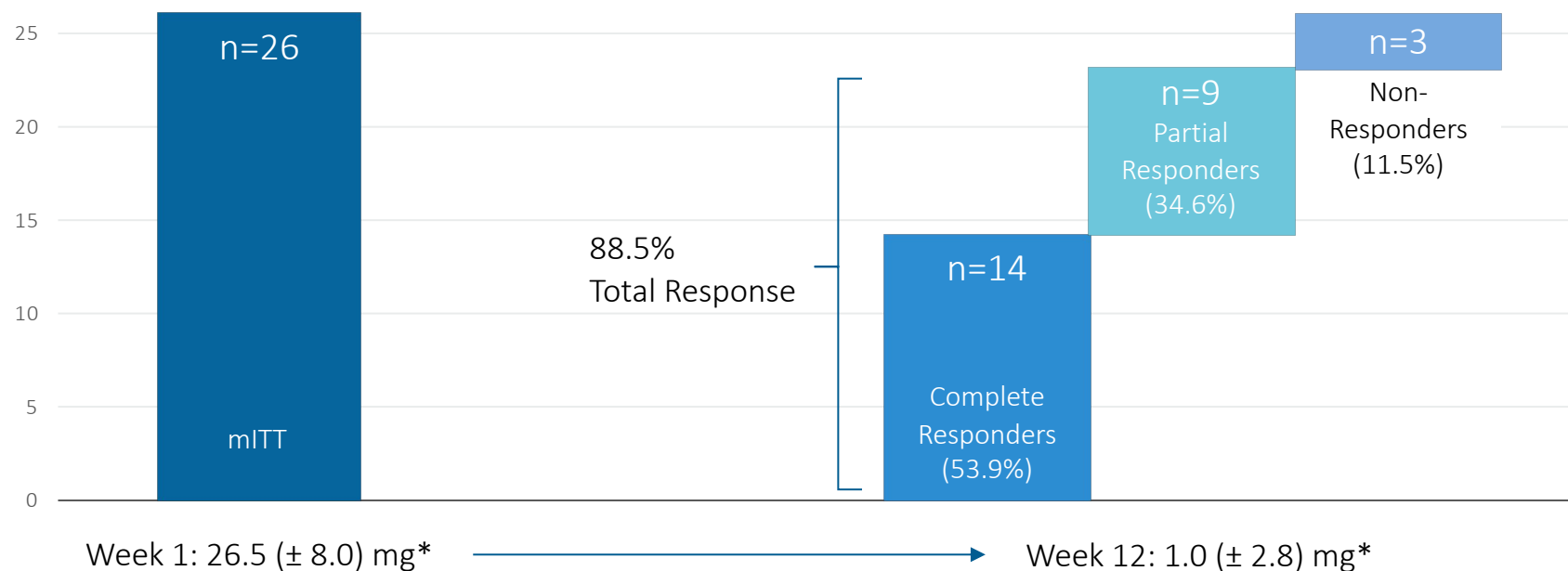
ENTRANCE Study: Primary Efficacy Results



ENTRANCE Study:

- Study performed with active moiety vidofludimus
- All patients failed two attempts to taper down steroids
- Open-label, dosing of 35 mg vidofludimus QD
- Primary efficacy endpoint: steroid-free/steroid-reduced remission (week 12)

Number of Patients



IMU-838 had response rates of:

85.7% in Crohn's disease

91.7% in ulcerative colitis

Herrlinger et.al., 2011, Gastroenterology 140:588

*Mean dose of steroid equivalent in mg per day; mITT: modified intent to treat; QD: quaque die = once-daily

ENTRANCE: Steroid-Sparing

Development of prednisolone intake over 12 weeks (mITT):

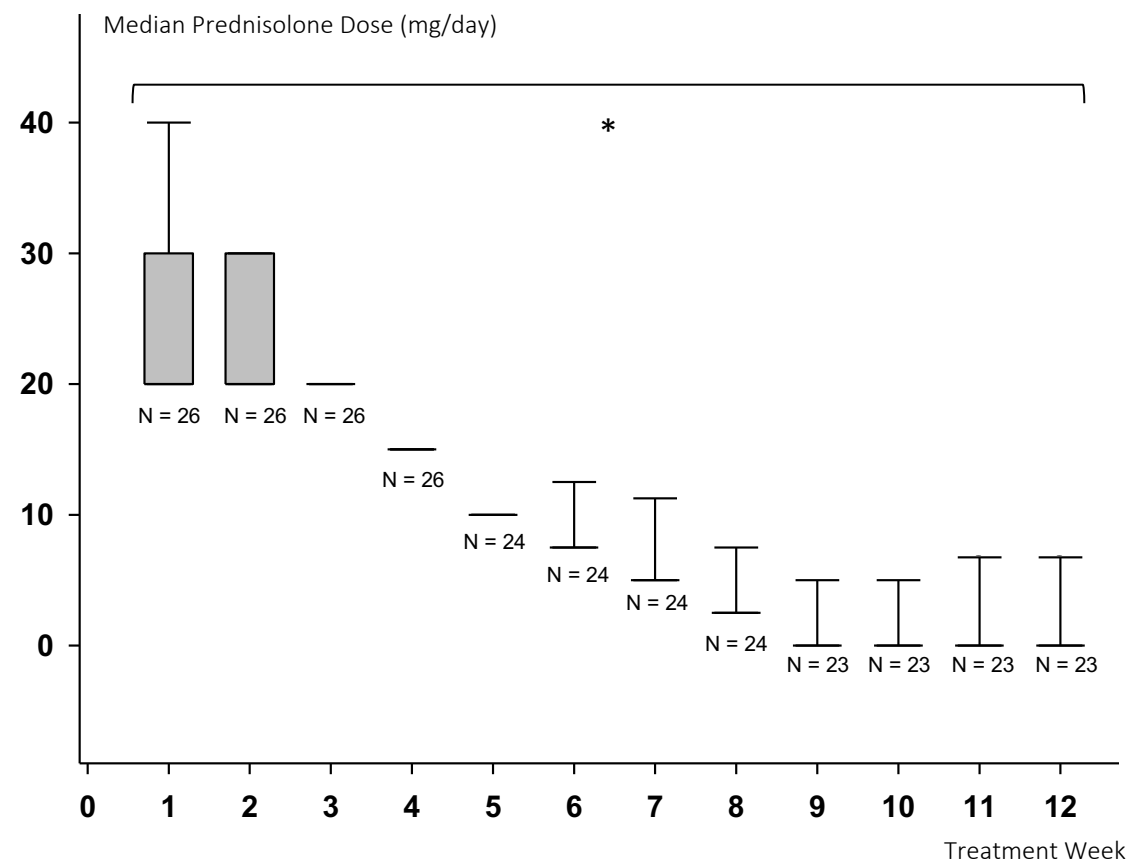
mg/day	W1	W2	W3	W4	W5	W6
A	20 (20 – 40)	20 (20 – 30)	20 (20 – 20)	15 (15 – 15)	10 (10 – 20)	7.5 (7.5 – 20)
B	26.5 (± 8.0)	24.6 (± 5.1)	20 (± 0.0)	15 (± 0.0)	10.6 (± 2.2)	8.5 (± 2.9)

mg/day	W7	W8	W9	W10	W11	W12
A	5 (5 – 15)	2.5 (2.5 – 15)	0 (0 – 15)	0 (0 – 10)	0 (0 – 10)	0 (0 – 10)
B	5.9 (± 2.8)	3.4 (± 2.9)	1.3 (± 3.4)	0.9 (± 2.5)	1.1 (± 2.7)	1.0 (± 2.8)



Mean consumption of prednisolone significantly (* $p < 0.001$) decreased from 26.5 mg/day (± 8.0) to 1.0 mg/day (± 2.8)

A: Median (Range); B: Mean (SD); W: week; mITT: modified intent to treat
Herrlinger et al. Poster, ECCO 2011



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, pharmacodynamic, 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**



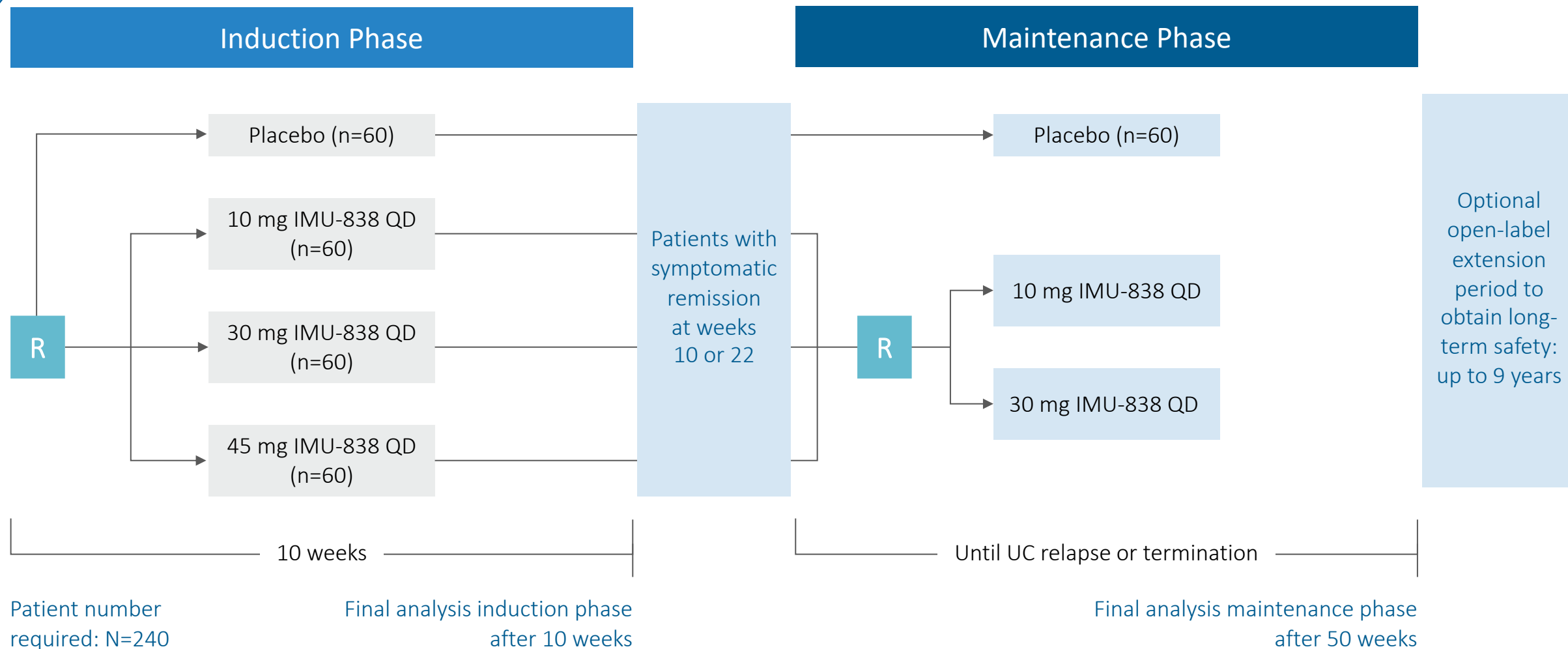
Timelines:

Recruitment expected to be completed in **Q4/2021**
Currently estimated to deliver top-line data in **Q2/2022**

IND: investigational new drug

CALDOSE-1: Phase 2 Trial Design in UC

NCT03341962



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



Potentially Applicable to a Wide Range of Diseases

IMU-838: Clinical Activity in Further Indications



IMU-838: Opportunities Beyond MS and IBD

Primary Sclerosing Cholangitis (PSC)

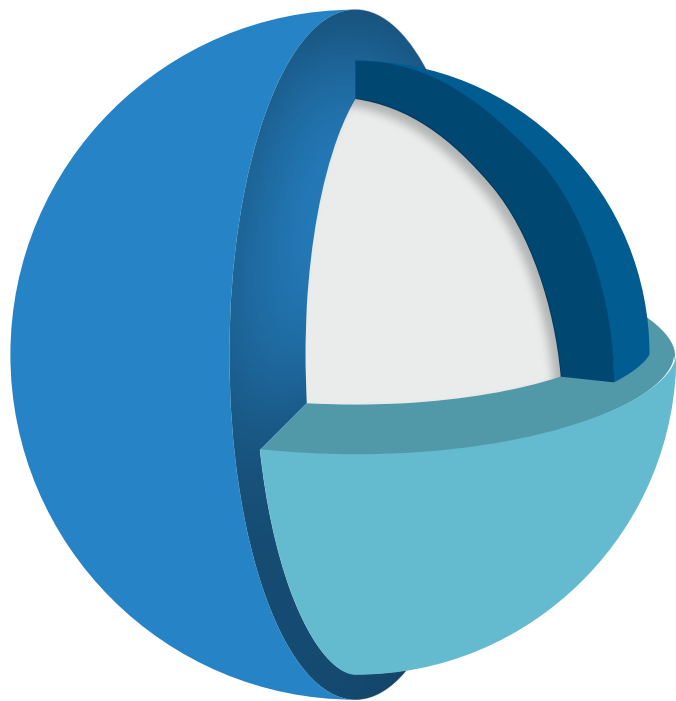
- IMU-838 showed a statistically significant reduction of serum ALP levels in PSC patients treated in a small, instigator-sponsored phase 2 trial which was conducted at Mayo Clinic
- Immunic is exploring PK and dose optimization in hepatic impaired patients in order to consider potential future clinical activities in PSC

COVID-19

- Backed by its broad-spectrum antiviral activity demonstrated *in vitro*, IMU-838 showed evidence of clinical activity and reduction of virus levels in COVID-19 patients in a phase 2 clinical trial
- Utilizing its DHODH inhibitor platform, Immunic is exploring combination therapy approaches with a focus on pandemic preparedness, thereby also considering activity against other viruses such as influenza

IMU-838: IP Position

IMU-838 is Protected by Several Layers of Patents:



- Patent on the specific salt form and pharmaceutical composition of IMU-838, granted in the United States, Europe and other key markets – expires in 2031
- New patent filed in 2017 on the dosing regimen protecting the applied dosing scheme of the ongoing and planned therapeutic studies – expires in 2038, if granted
- New patent filed in 2018 on the specific polymorph of IMU-838 used in current studies – expires in 2039, if granted
- New patent filed in 2020 on IMU-838's antiviral activity for use in COVID-19 – expires in 2041, if granted
- Another level of protection can be expected by data exclusivity in the United States and in Europe based on IMU-838's classification as a New Chemical Entity (NCE)



IMU-935: An Oral IL-17 Inhibitor

Uniquely Acting and Highly Selective
ROR γ t Inverse Agonist

Autoimmune Diseases and IMU-935



IL-17 in Autoimmune Diseases

- Autoimmune diseases affect millions of patients worldwide^[1]
- Th17/IL-17/ROR γ t axis plays an important role in auto immunity-related diseases^[2]
- Antibodies targeting this axis corroborate IL-17's role in autoimmune diseases, but are more complex, costly and less patient friendly than oral drugs^[2]



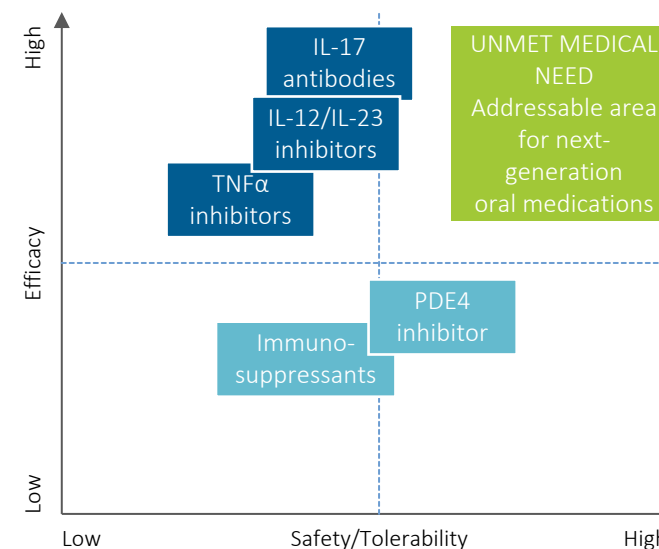
Goal

- Develop an orally available and potent IL-17 inhibitor for the safe and efficacious treatment of autoimmune diseases
- Small molecule inhibitor of the pathologic functions of ROR γ t in autoimmune diseases without affecting physiological functions of ROR γ t

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

Th: T helper; IL: interleukin; TNF: tumor necrosis factor; PDE4: phosphodiesterase type 4; ROR γ : retinoic acid receptor-related orphan nuclear receptor gamma

Unmet Need in Psoriasis Care



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

Current Landscape of Oral IL-17 Inhibitors^[1]

Product	Developer	Development Stage	Indications
IMU-935	Immunic	Phase 1b	Psoriasis, Castration-Resistant Prostate Cancer, Guillain-Barré Syndrome
AUR-101	Aurigene	Phase 2	Psoriasis
bevurogant	Boehringer Ingelheim	Phase 2	Plaque psoriasis, psoriatic arthritis
cedirogant	AbbVie	Phase 1b	Plaque psoriasis
SAR-441169	Sanofi Genzyme	Phase 1	Not disclosed
JTE-761	Japan Tobacco	Phase 1	Not disclosed

[1] Gege, C. (2021). Expert Opinion on Drug Discovery

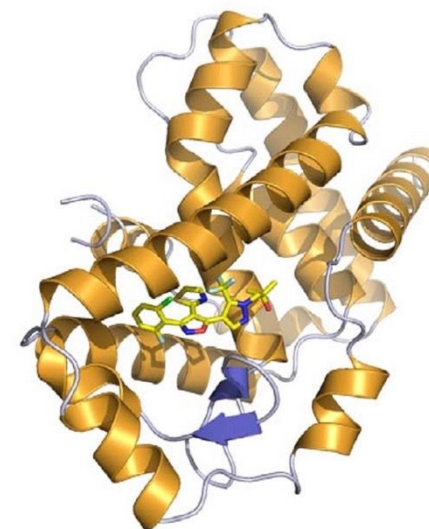
IMU-935 Has Been Observed to be Potent in Human Cells

Effect of IMU-935 in Stimulated Human PBMC at Nanomolar Concentrations

→ Inhibition of ROR γ (20 nM) and DHODH (240 nM) leads to synergistic inhibition of cytokines associated with autoimmune diseases with IC₅₀ of 3-5 nM in stimulated human lymphocytes

	IC ₅₀ (μ M)
IL-17A	0.005
IL-17F	0.004
IFN γ	0.003
IL-1a and b	no inhibition
IL-4,5,6,8	no inhibition
ROR γ (MST)	0.024
ROR γ (cellular, reporter assay)	0.020
DHODH	0.240
Th17 differentiation (murine) ^[1]	0.135

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

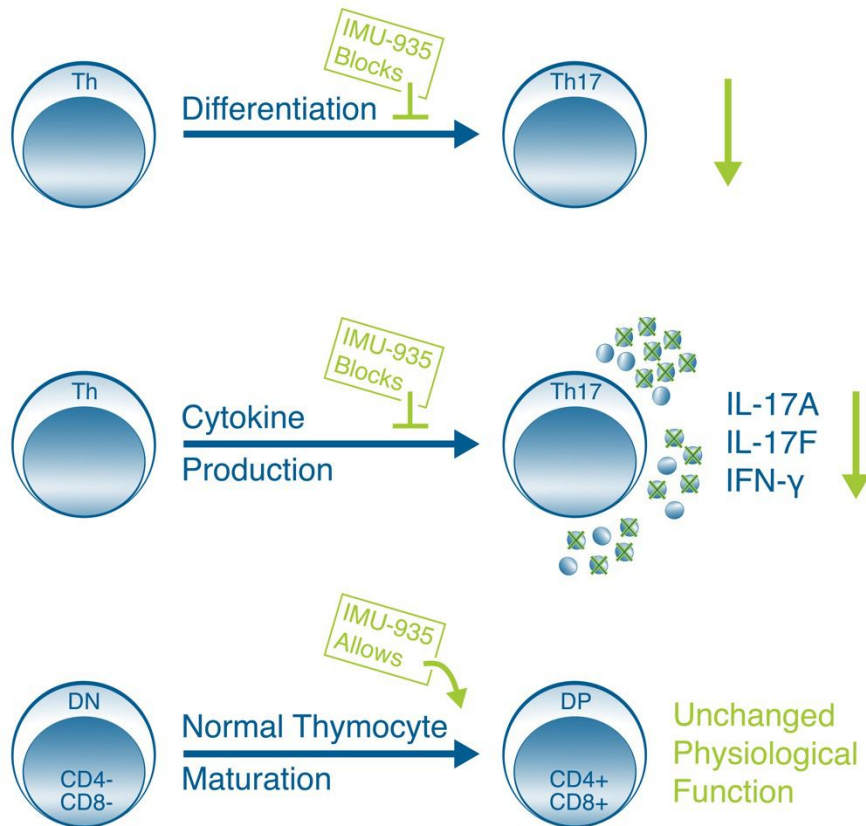


Co-crystal structure (Resolution 2.6 Å) of a closely related derivative compound binds to hydroxycholesterol binding site of ROR γ

PBMC: Peripheral Blood Mononuclear Cells; Th: T helper; IL: interleukin; IFN: interferon; MST: microscale thermophoresis

[1] Zuoming Sun, City of Hope, 2019

IMU-935 Selectively Inhibits Th17 Differentiation and IL-17 Secretion

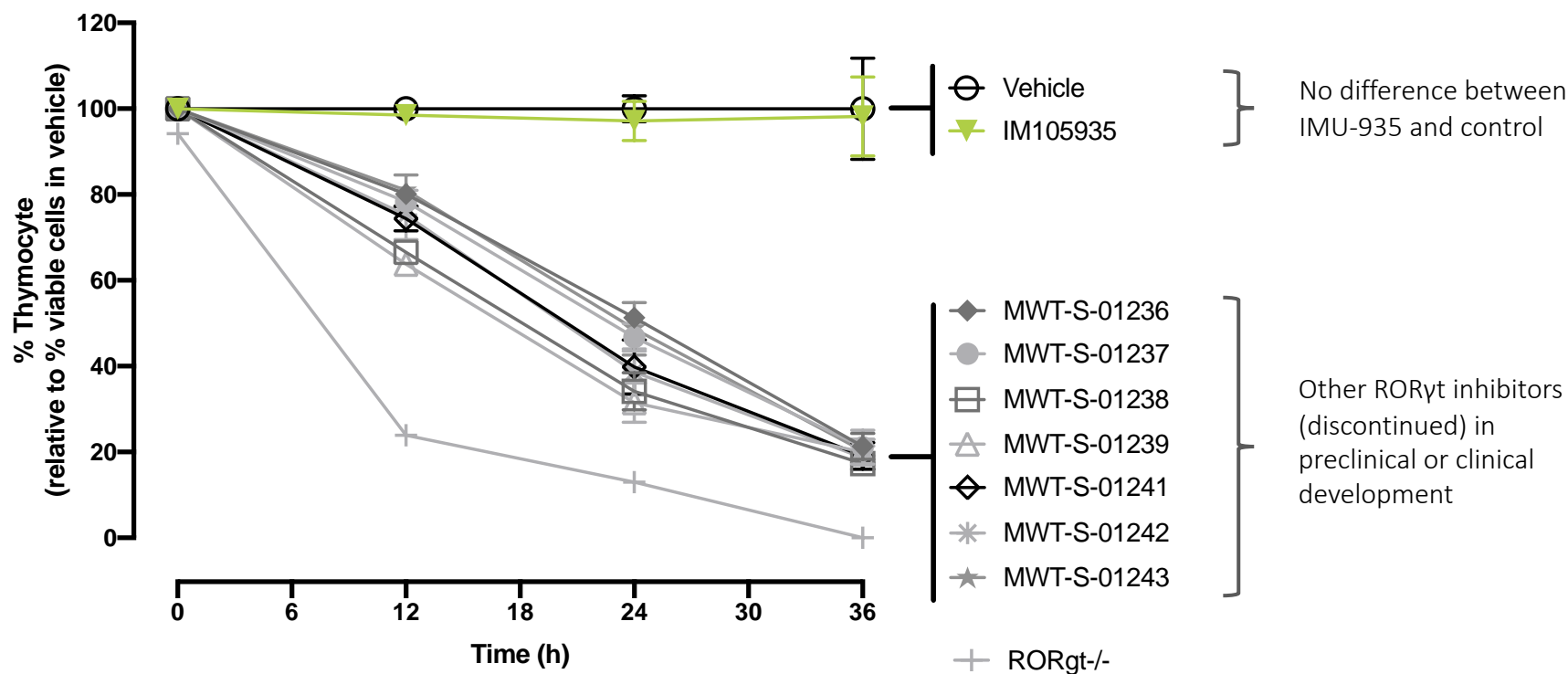


- The differentiation towards Th17 cells is inhibited by IMU-935
- The production of IL-17A and IL-17F is inhibited by IMU-935
- The physiological maturation of T cells within the thymus is not affected by IMU-935

IMU-935 Does Not Induce Thymocyte Apoptosis

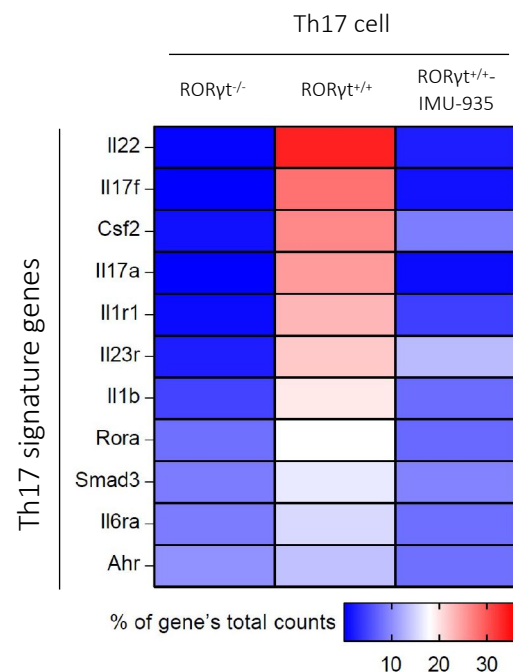


In Contrast to IMU-935, Comparator Compounds Have a Negative Impact on Thymocyte Viability and Therefore Bear the Risk of Lymphoma.

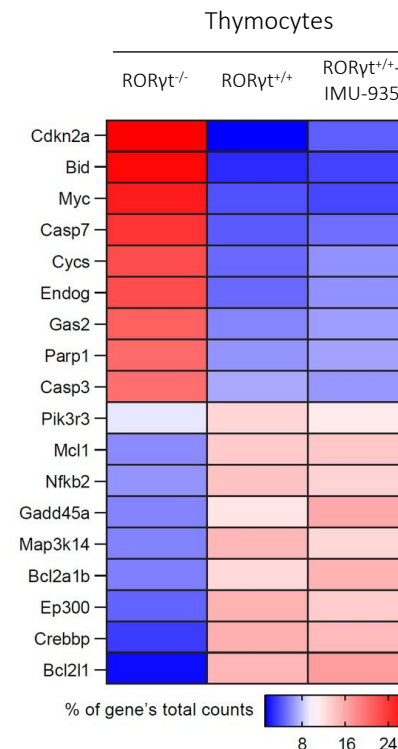
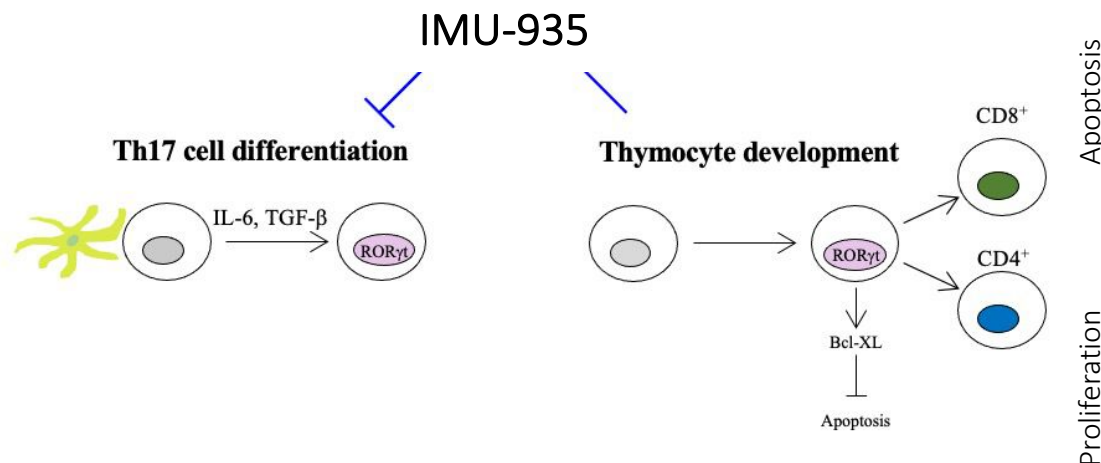


Sun, Zuoming. City of Hope, 2021, unpublished

IMU-935 Blocks Th17 Differentiation But Allows Normal Thymocyte Maturation: Gene Expression Profiles



Similar gene expression pattern for Th17 signature genes in RORγt knockout and wild type cells treated with IMU-935



Different gene expression pattern for apoptosis and proliferation signature genes in RORγt knockout and IMU-935 treatment, but similar for RORγt^{+/+}

Phase 1 Clinical Trial of IMU-935: Design and Status

PART A

Evaluation of
single ascending doses (SAD)

—
Healthy volunteers
randomized to receive single
dose of IMU-935 or placebo

- Dose escalation completed: 100, 200, 300 and 400 mg of IMU-935
- 79 subjects enrolled (still blinded)
- IMU-935 was well-tolerated and showed dose-linear PK
- Food effect cohort ongoing

PK: pharmacokinetics

PART B

Evaluation of
multiple ascending doses (MAD)

—
Healthy volunteers randomized
to receive 14-day treatment of
either IMU-935 or placebo

- Currently ongoing
- First multiple dose cohort completed (data evaluation ongoing, still blinded)

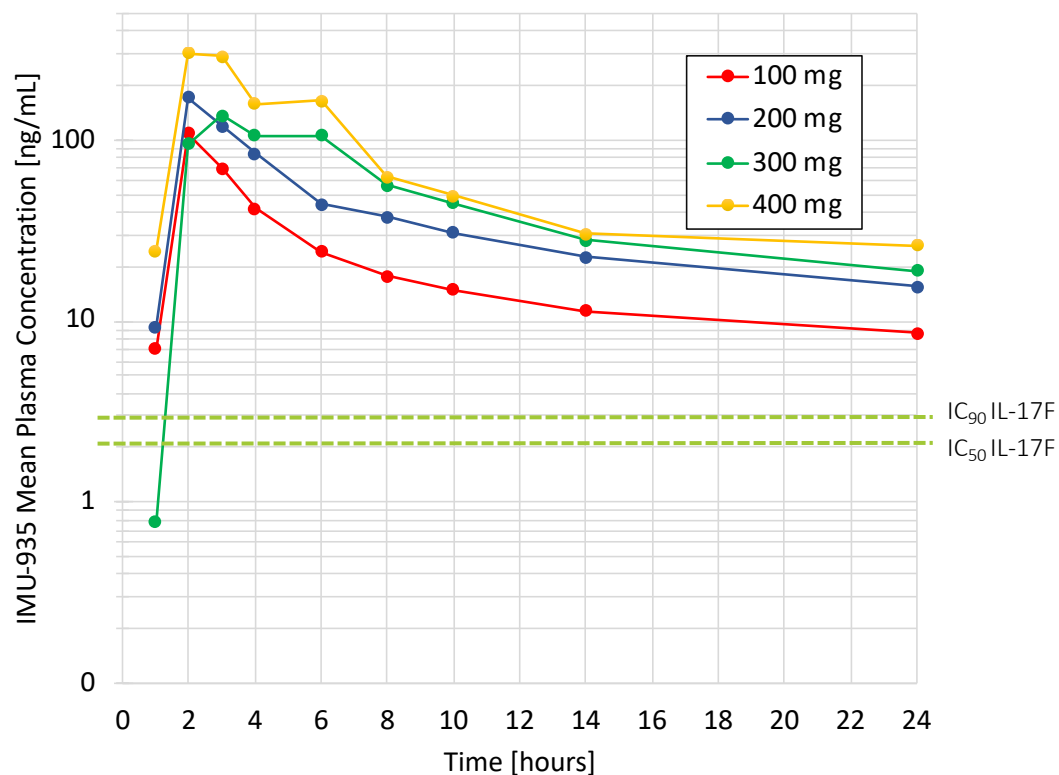
PART C

Evaluation of
moderate-to-severe psoriasis
patients receiving 28-day
treatment of either
IMU-935 or placebo

- Initial human data expected to be available in Q2/2022

Phase 1 Clinical Trial: Interim SAD Pharmacokinetic Results

New Formulation With Dose-Linear AUC



Plasma half-life new formulation: 17-26 h
 T_{max} : 2.2-3.8 h

Average Pharmacokinetic Variables

Dose	C_{max} ng/mL	T_{max} (hours)	AUC_{inf} (h* ng/mL)
100 mg (3N)	119	2.20	755
200 mg (4N)	195	2.83	1440
300 mg (5N)	182	3.83	1710
400 mg (6N)	479	2.83	2940

Preliminary data

AUC: area under the curve; h: hours; C_{max} : maximum (peak) plasma drug concentration; T_{max} : time to reach maximum (peak) plasma concentration; AUC_{inf} : area under the concentration-time curve to infinity

IMU-935 As Treatment Option in Castration-Resistant Prostate Cancer – Synergistic Effects by Targeting ROR γ and ROR γ t



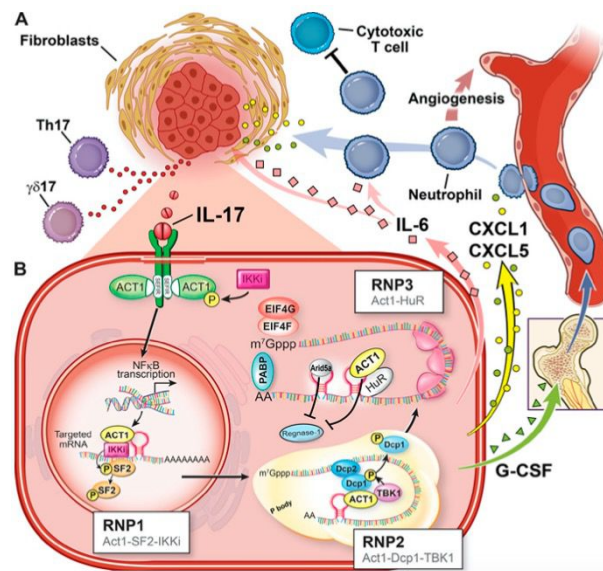
Inhibition of ROR γ

- The androgen-receptor mutant variant AR-V7 lacks the ligand-binding domain, which is the target of enzalutamide and abiraterone, but remains constitutively active as a transcription factor.
- IMU-935 represses the mutated androgen receptor AR-V7 expression – and subsequent target genes.



Inhibition of IL-17 by ROR γ t Regulation

- IL-17 contributes to the formation, growth and metastasis of cancers.
 - Induces mitogenic signaling



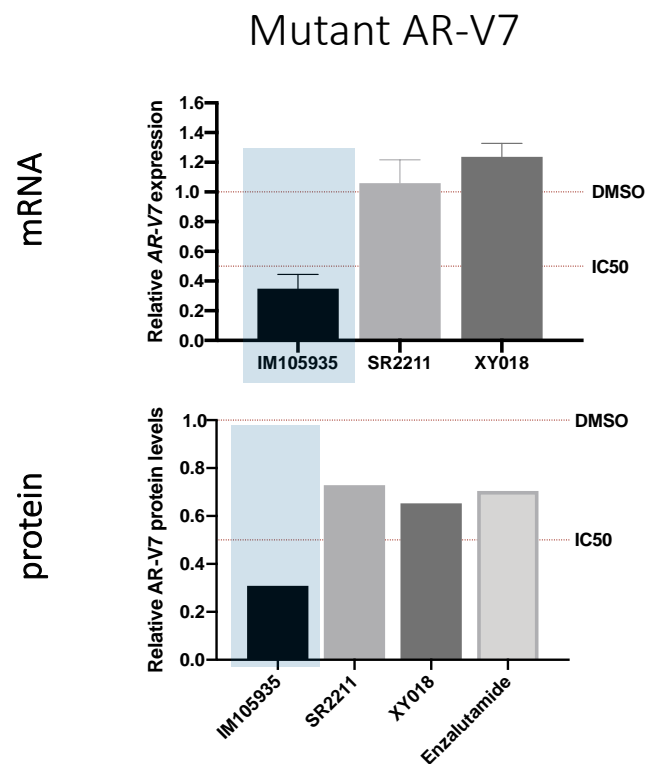
Differentiation of MDSCs

- IL-17 mediates the induction, recruitment and expansion of MDSCs.
- Next to IL-17 suppression via ROR γ t inhibition, IMU-935 also targets DHODH. Targeting this enzyme is an additional route to stop these tumor supportive cells.
- Supportive data regarding cell differentiation has been observed in AML cell lines using closely related molecules.

AR-V7: androgen receptor variant 7/mutated form; MDSC: myeloid-derived suppressor cells; AML: acute myeloid leukemia; Th: T helper; IL: interleukin
Illustration: Zhao, J., Chen, X., Herjan, T., Li, X.; J Exp Med 6 January 2020; 217 (1): e20190297

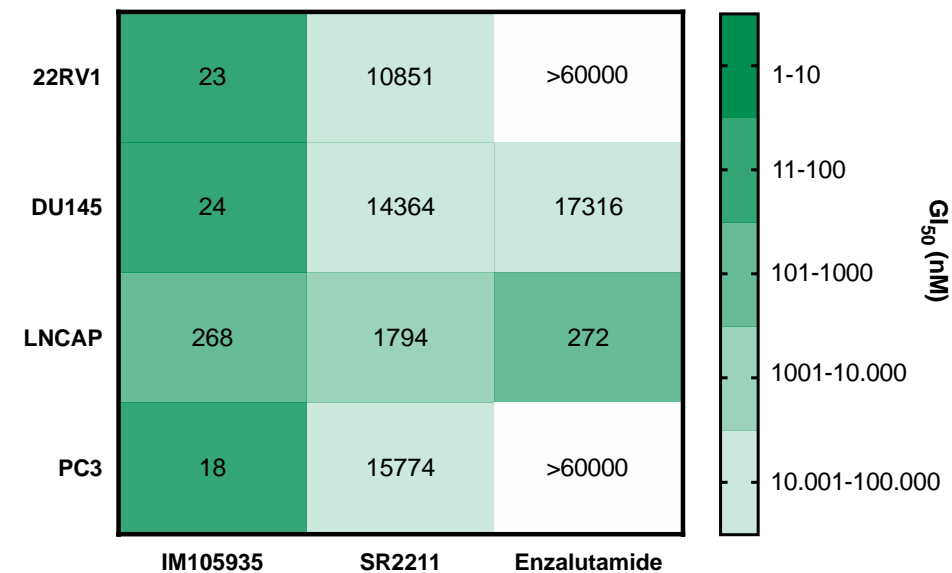
IMU-935 Demonstrated ROR γ -Dependent Effects in CRPC Cells

IMU-935 Has Been Shown to Repress Expression of Mutated AR



IMU-935 Potently Inhibited Proliferation of Different Prostate Cell Lines

72h, 2d culture, read out protein staining/number of cells



AR-FL: androgen receptor full length/wildtype; AR-V7: androgen receptor variant 7/mutated form; mRNA experiment: 1 μ M, 48h; protein expression: 6 μ M, 48h; SR2211 and XY018 are ROR γ inverse agonists

Phase 1 Clinical Trial of IMU-935 in CRPC

Expected to Start in Q4/2021



Study Design

- Open-label dose escalation trial to evaluate safety, tolerability, anti-tumor activity, and pharmacokinetics of IMU-935 in patients with progressive, metastatic castration-resistant prostate cancer
- Dose escalation follows a Bayesian optimal interval (BOIN) design
- An expansion cohort can be added at a therapeutically active dose level
- Main treatment will be single agent IMU-935 for 3 cycles of 28 days each
- Patients who benefit can receive extended treatment
- At each dose level:
 - A safety analysis will be performed to consider start of next dose cohort
 - An interim activity analysis will be performed upon completion of 3 months treatment
 - A main cohort analysis will be performed when the last patient in treatment reaches the 6 months follow-up visit



Principal Investigator

Johann Sebastian de Bono, M.D., Ph.D.

Regius Professor of Cancer Research and
Professor in Experimental Cancer Medicine
The Institute of Cancer Research and The Royal
Marsden NHS Foundation Trust
London, United Kingdom



IMU-856

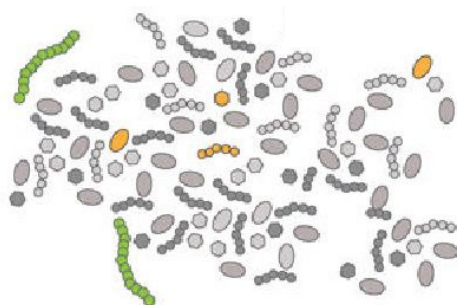
Restoring Intestinal Barrier Function

IMU-856: Hypothesis of Therapeutic Approach



Strengthening the Bowel Barrier Function Leads to Compartmentalization of Microbiome and Intestinal Immune System and Prevents Immune Stimulation That Drives Disease Processes

Microbiota

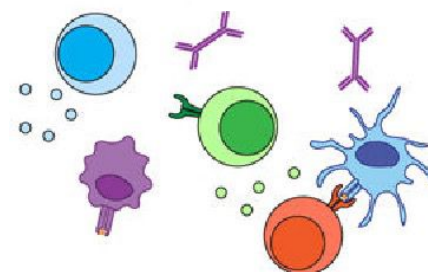


Influencing the Microbiome

- 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 events (infections, malignancies, inability to vaccinate)

IMU-856: Phase 1 Study Performed in Australia

Double-Blind, Randomized, Placebo-Controlled Phase 1 Study Performed in Three Parts



Exclusive global rights to commercialization of IMU-856 in all countries obtained through option and licensing agreement with Daiichi Sankyo



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



Timelines

- Safety data from the SAD and MAD parts expected to be available in Q1/2022
- Initiation of Part C in patients expected in H1/2022



Immunic Therapeutics

Summary

Summary and Highlights



Advanced and well-balanced pipeline:
Three differentiated products in various phases of clinical development



Oral IL-17 inhibitor IMU-935:
Proof-of-concept data in psoriasis expected in Q2/2022; further development in CRPC and GBS



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



Shares outstanding: 26,249,439 (as of July 30, 2021)
Cash and cash equivalents of approx. USD 87.2 million (as of June 30, 2021); additional approx. USD 45.0 million raised in July 2021



Phase 3 program of IMU-838 in RRMS:
Expected to start in Q4/2021, to be supported by neuroprotective data from phase 2 trial in PMS



Raised net cash of approx. USD 186 million in 2020 and 2021, substantially extending cash runway beyond important inflection points

Thank You!



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