Immunic Therapeutics

Developing Selective Oral Drugs in Immunology

NASDAQ: IMUX | November 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.

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 and the Company’s other product candidates to safely and effectively target and treat the diseases mentioned herein; the impact of future preclinical and clinical data on IMU-838 and the Company’s other product candidates; the availability or efficacy of Immunic’s potential treatment options that may be supported by trial data discussed herein; expectations regarding potential market size; the timing of the availability of data from Immunic’s clinical trials; the timing of any planned investigational new drug application or new drug application; Immunic’s plans to research, develop and commercialize its current and future product candidates; Immunic’s ability to successfully collaborate with existing collaborators or enter into new collaboration agreements, and to fulfill its obligations under any such collaboration agreements; the clinical utility, potential benefits and market acceptance of Immunic’s product candidates; Immunic’s commercialization, marketing and manufacturing capabilities and strategy; Immunic’s ability to identify additional products or product candidates with significant commercial potential; developments and projections relating to Immunic’s competitors and industry; the impact of government laws and regulations; Immunic’s ability to protect its intellectual property position; Immunic’s listing on The Nasdaq Global Select Market; expectations regarding the capitalization, resources and ownership structure of the company; the executive and board structure of the company; Immunic’s estimates regarding future revenue, expenses, capital requirements and need for additional financing; the nature, strategy and focus of the company; and the other risks set forth in the company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2020, filed with the Securities and Exchange Commission.

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

Our 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.

Immunic THERAPEUTICS

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 Immunic

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+

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Development Pipeline

Program	Target	Preclinical	Phase 1	Phase 2	Phase 3	Key 2021/22 Milestones
vidofludimus calcium (IMU-838)	DHODH	Relapsing Multiple Sclerosis (RMS)				▪ Phase 2 UC: top-line data expected in Q2/2022
		Progressive Multiple Sclerosis (PMS)				
		Ulcerative Colitis (UC)				
		Crohn's Disease (CD)				
		Primary Sclerosing Cholangitis (PSC)				
IMU-935	RORγt	Psoriasis				▪ Phase 1 healthy volunteers: unblinded SAD/MAD safety data expected in Q4/2021 ▪ Phase 1b psoriasis: initial data expected in Q2/2022 ▪ Phase 1 CRPC: trial expected to start in Q4/2021
		Castration-Resistant Prostate Cancer (CRPC)				
		Guillain-Barré Syndrome (GBS)				
IMU-856	Intestinal Barrier Function	Gastrointestinal Diseases				▪ Phase 1 healthy volunteers: unblinded SAD/MAD safety data expected in Q3/2022

▪ Completed or ongoing ▪ In preparation or planned

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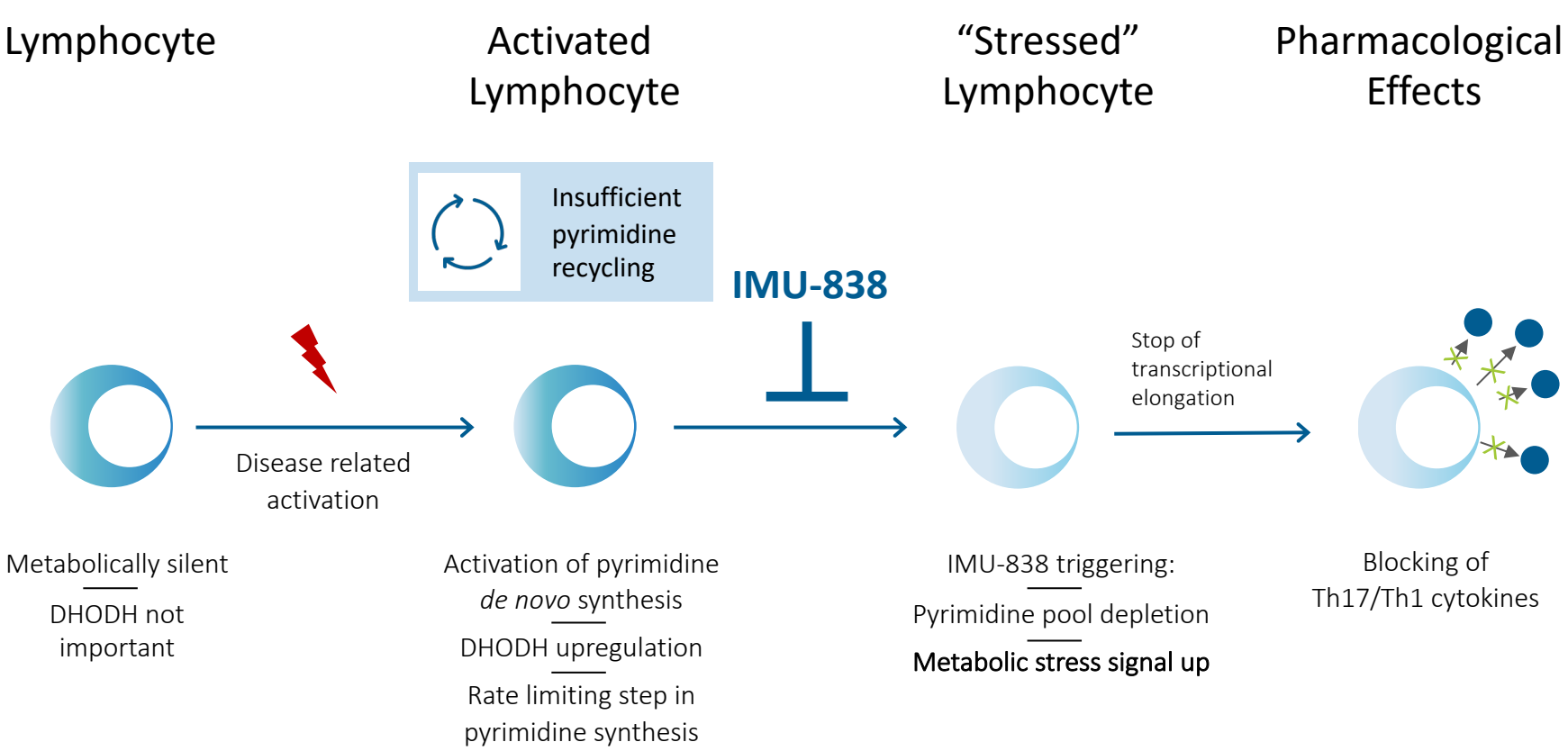
Blocking DHODH Leads to a Selective Effect on Overactivated Lymphocytes Without Broader Immunosuppression



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 Relapsing-Remitting Multiple Sclerosis (RRMS) Successfully Completed

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

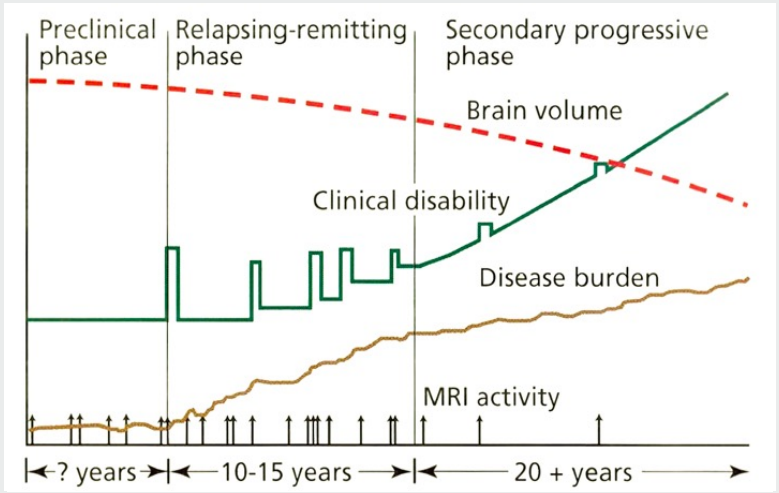
Successful MS Therapy Requires Efficacy, Safety and Tolerability

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

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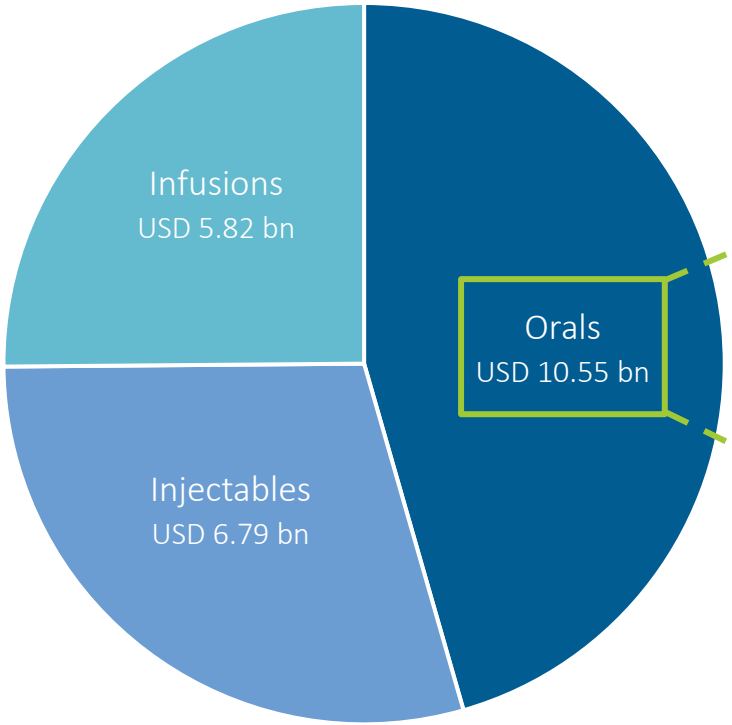
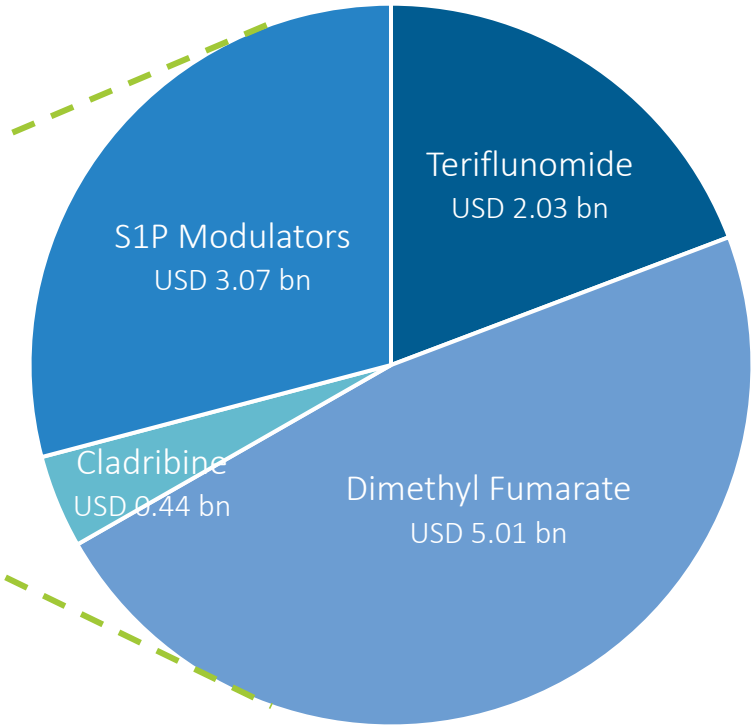
The Global MS Drug Market is Crowded But Enormous

Total 2020 Sales in G7 Countries*: USD 23.24 Billion

Oral MS Drugs Have Substantial Market Share*



vidofludimus calcium 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-live
- 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

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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

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Targeted to be the Easy-to-Use Approach for MS Patients

vidofludimus calcium 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-live
- No/low PML risk
- Long treatment duration through less risk for discontinuation, high patient compliance

Intended 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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Phase 2 Data in RRMS: Primary and Key Secondary Endpoints Met, Showing Strong Activity on MRI Lesions

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

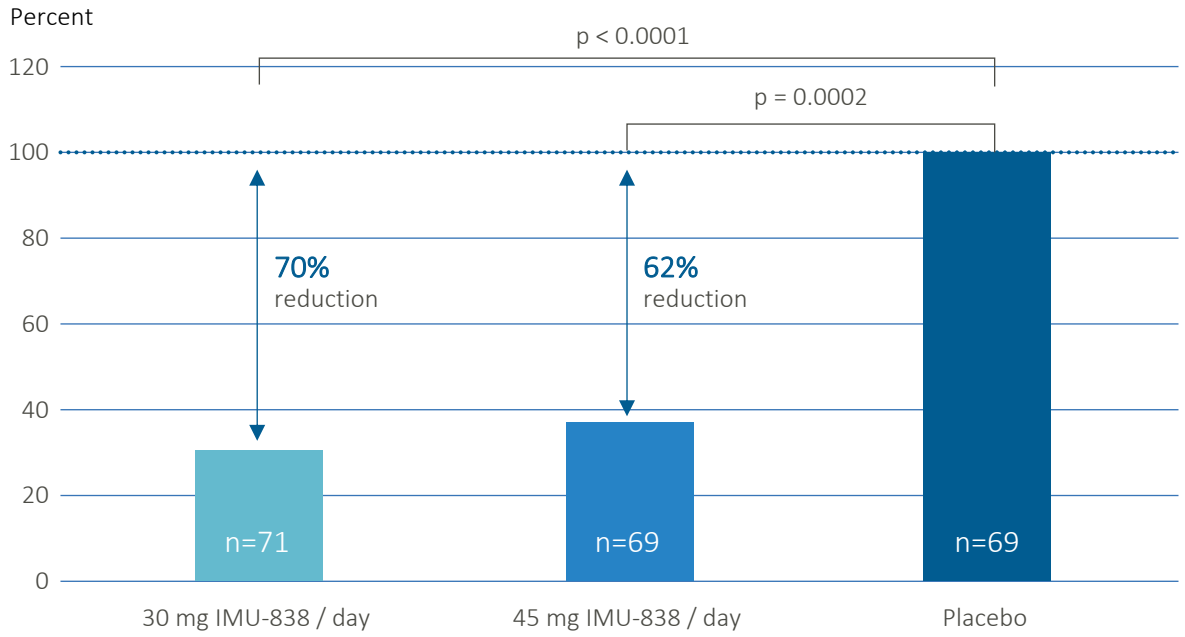
- Blinded main treatment period of 24 weeks
- Extended treatment period of up to 9.5 years to observe long-term safety
- 210 patients randomized in 36 centers across four European countries

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 vidofludimus calcium and placebo
- Key secondary endpoint: Difference between 30 mg/day vidofludimus calcium and placebo

Suppression of CUA MRI Lesions: vidofludimus calcium Versus Placebo Over 24 Weeks



10 mg dose of vidofludimus calcium 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.

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Phase 2 Data in RRMS: Demonstrated Robust Activity

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

	vidofludimus calcium	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

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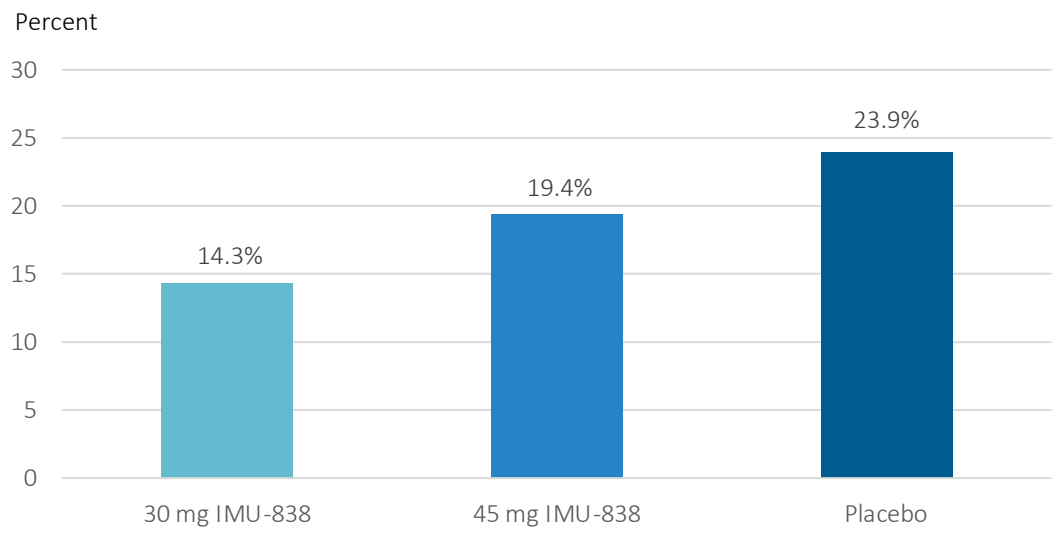
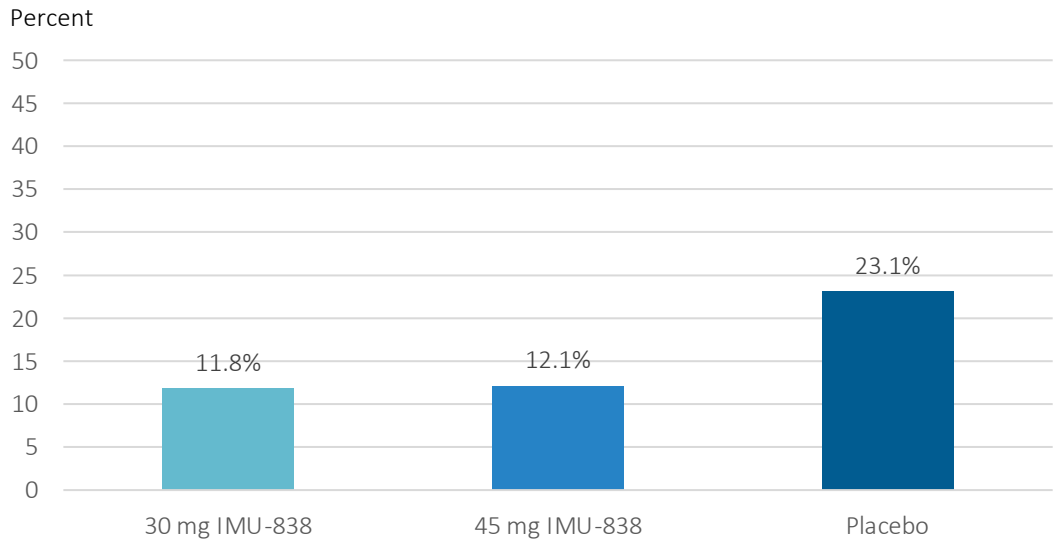
Phase 2 Data in RRMS: Positive Signals on Relapse and Unconfirmed Disability

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.

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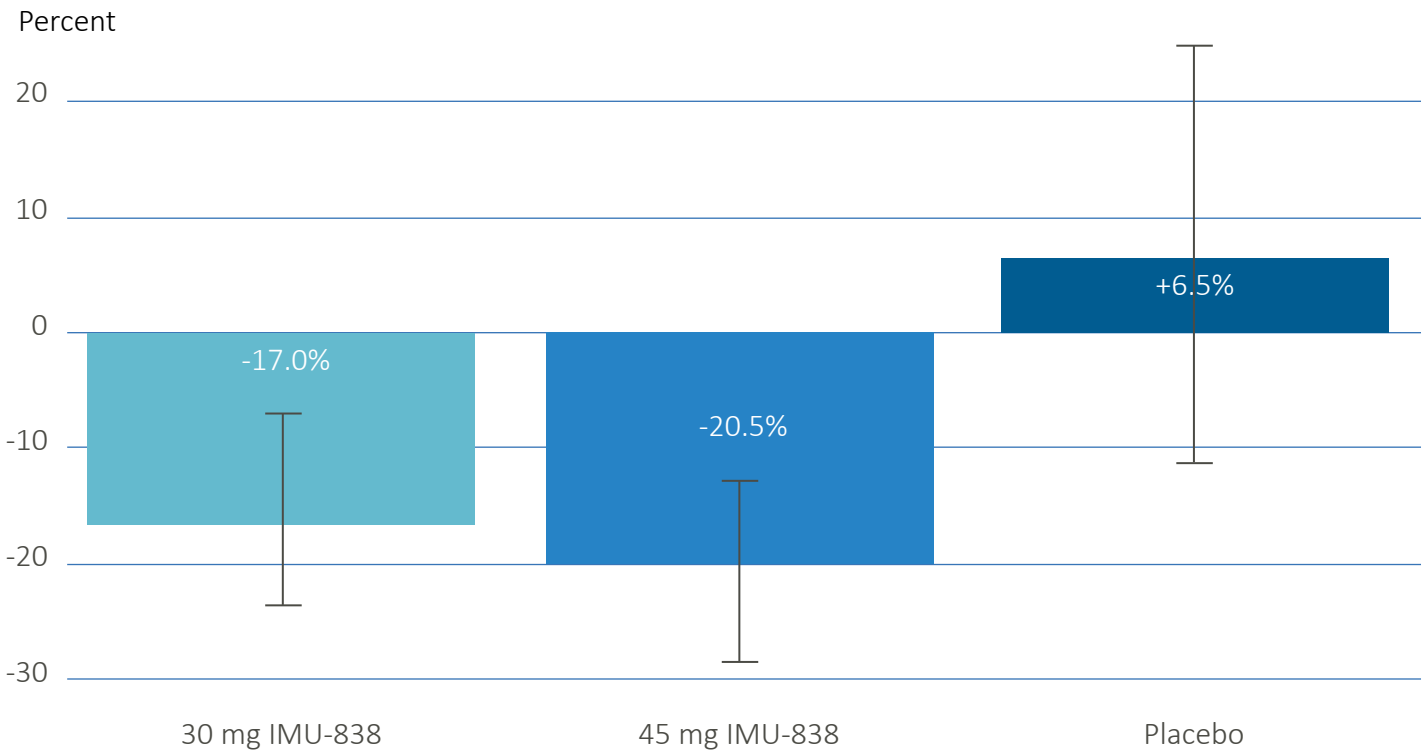
Phase 2 Data in RRMS: Showed Evidence of Potential Neuroprotective Activity

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 Data in RRMS: Low Discontinuation Rates

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

	vidofludimus calcium	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

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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 signals for hepatotoxicity or elevations of liver enzymes and no Hy's law cases observed in the vidofludimus calcium 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)

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vidofludimus calcium's Safety Profile to Date is Unique

	vidofludimus calcium[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

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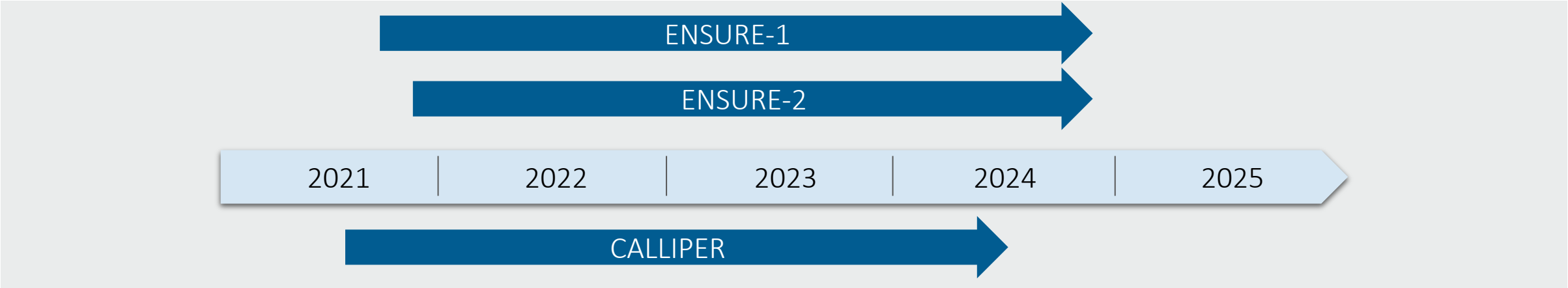
Phase 3 and Approval Strategy in MS

Phase 3 ENSURE Program in RMS

- Two identical pivotal trials in RMS patients
- Goal: Regulatory approval of vidofludimus calcium
- Dosage: 30 mg vidofludimus calcium QD

Phase 2 CALLIPER Trial in PMS

- Phase 2 trial in PMS patients
- Goal: Demonstrate vidofludimus calcium's potential for neuroprotective activity
- Dosage: 45 mg vidofludimus calcium QD



QD: quaque die = once-daily

ENSURE: Ongoing Pivotal Phase 3 Program in RMS

Coordinating Investigator

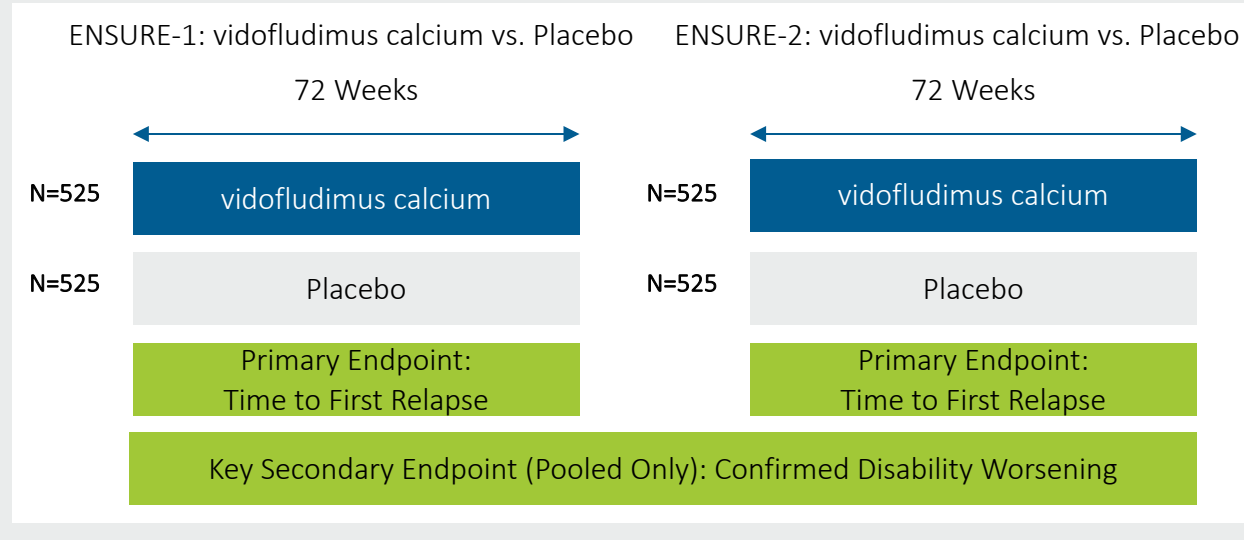
Robert J. Fox, M.D.
Cleveland Clinic

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

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 30 mg vidofludimus calcium or placebo QD



EDSS: Expanded Disability Status Scale; QD: quaque die = once-daily
Lublin FD, et al. Neurology. 2014;83(3):278-286

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

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 in more than 70 sites in North America, Western, Central and Eastern Europe
- Randomization to 45 mg vidofludimus calcium or placebo QD
- Primary endpoint: annualized rate of percent brain volume change up to 120 weeks

Treatment Schedule

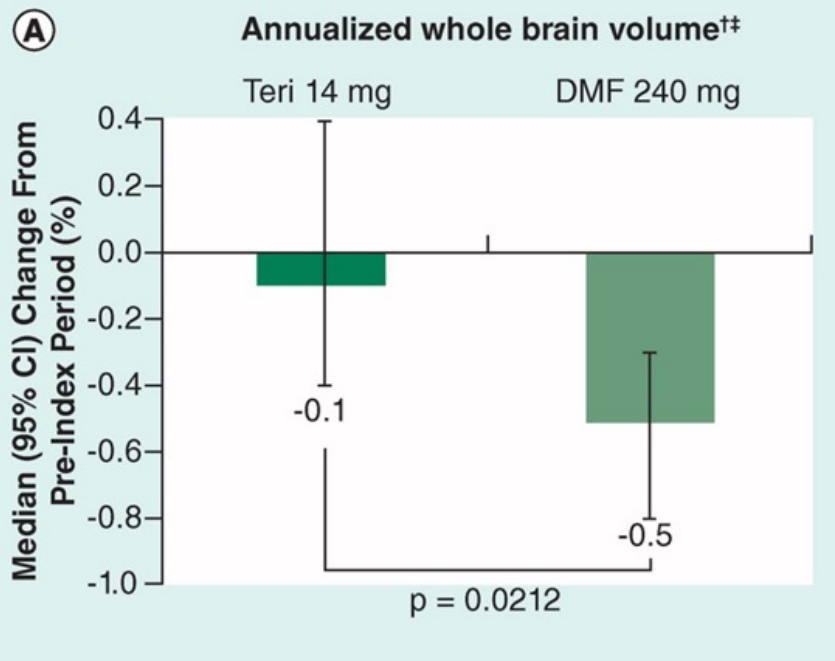
- Blinded 120-week main treatment period
- Optional, approximately 8-year, open-label extension period
- Interim analysis of serum neurofilament light chain planned after approximately half of the enrolled patients have completed 24-weeks of treatment

PPMS: primary progressive multiple sclerosis; SPMS: secondary progressive multiple sclerosis; EDSS: Expanded Disability Status Scale; QD: quaque die = once-daily
* NCT05054140

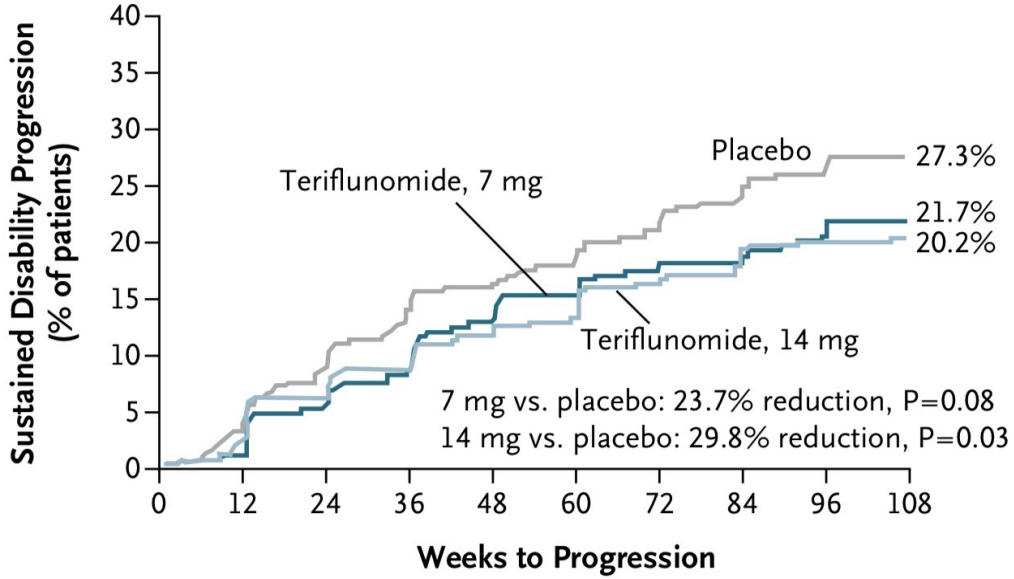
DHODH Provides Proven Mechanism for Neuroprotection

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)

Immunic THERAPEUTICS

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

- vidofludimus calcium development goals in MS: achieve market approval and confirm product differentiation based on safety, tolerability, efficacy and neuroprotective properties of vidofludimus calcium.
- Immunic believes that the phase 3 ENSURE program provides a simple and straightforward path towards potential regulatory approval of vidofludimus calcium in RMS.
- CALLIPER is designed to corroborate vidofludimus calcium'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 RMS. The CALLIPER trial, by itself, is not intended to support regulatory approval of vidofludimus calcium in PMS.

Well-Differentiated From Current Treatments

"Immunic believes that the ENSURE and CALLIPER programs along with vidofludimus calcium's strong safety and tolerability profile may allow for a meaningful clinical differentiation of vidofludimus calcium from other oral MS medications and an attractive commercial positioning."

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:
  - vidofludimus calcium, ponesimod, masitinib, ublituximab, ibudilast, evobrutinib, tolebrutinib, fenebrutinib, glatiramer acetate depot
- Among those, **vidofludimus calcium was considered the most interesting** with 77% of neurologists considering vidofludimus calcium for the next switch to DMT (possibly and very likely)
- Of the drugs analyzed, vidofludimus calcium 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

Potential for Full Prescription Coverage at Attractive Pricing Range

Immunic Hired Third-Party Pricing Experts to Perform Landscape Analysis for vidofludimus calcium 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**.

- vidofludimus calcium 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:

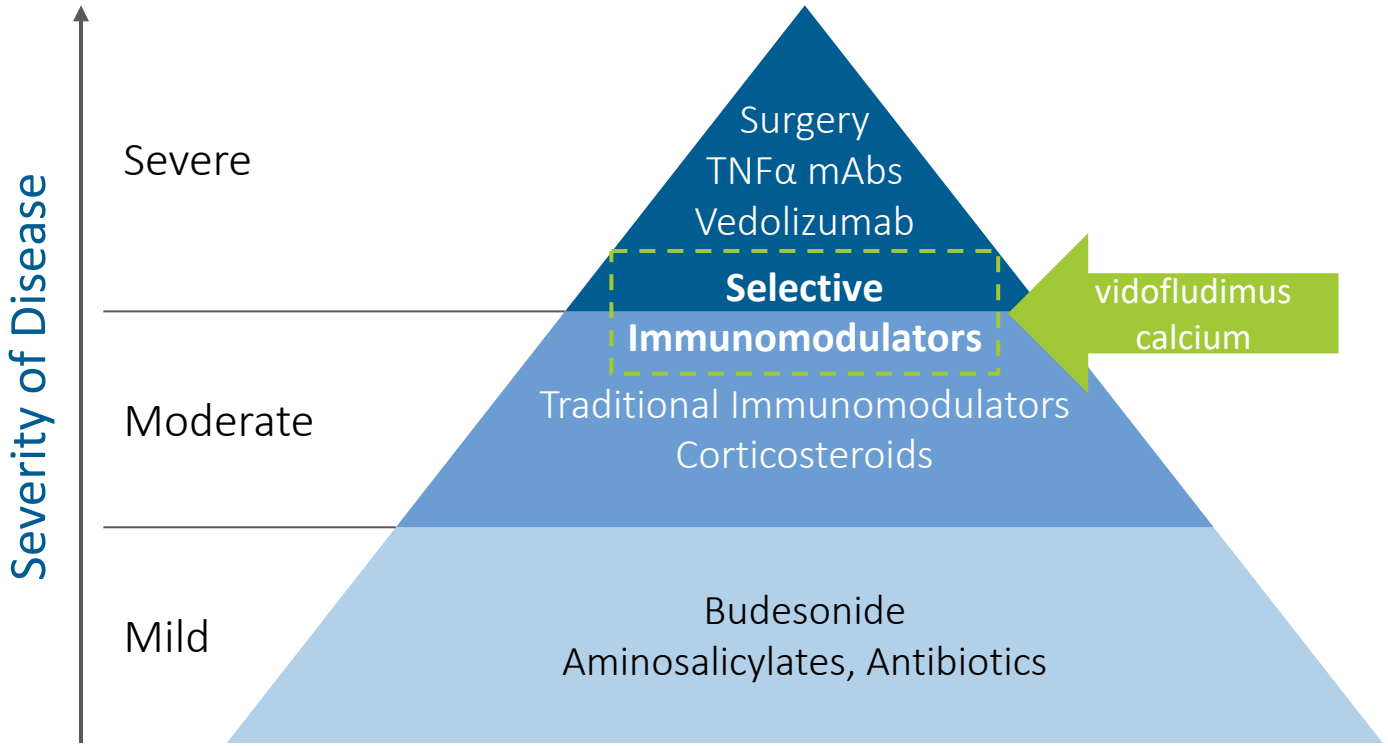
- Coverage is **not sensitive** to vidofludimus calcium pricing despite the presence of generics.
- **Full prescription coverage by payers is achievable for vidofludimus calcium** at an attractive pricing range of USD 50-60 thousand annually, **independent of future generic pricing.**

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

vidofludimus calcium in Inflammatory Bowel Disease (IBD)

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

IBD: Therapeutic Pyramid

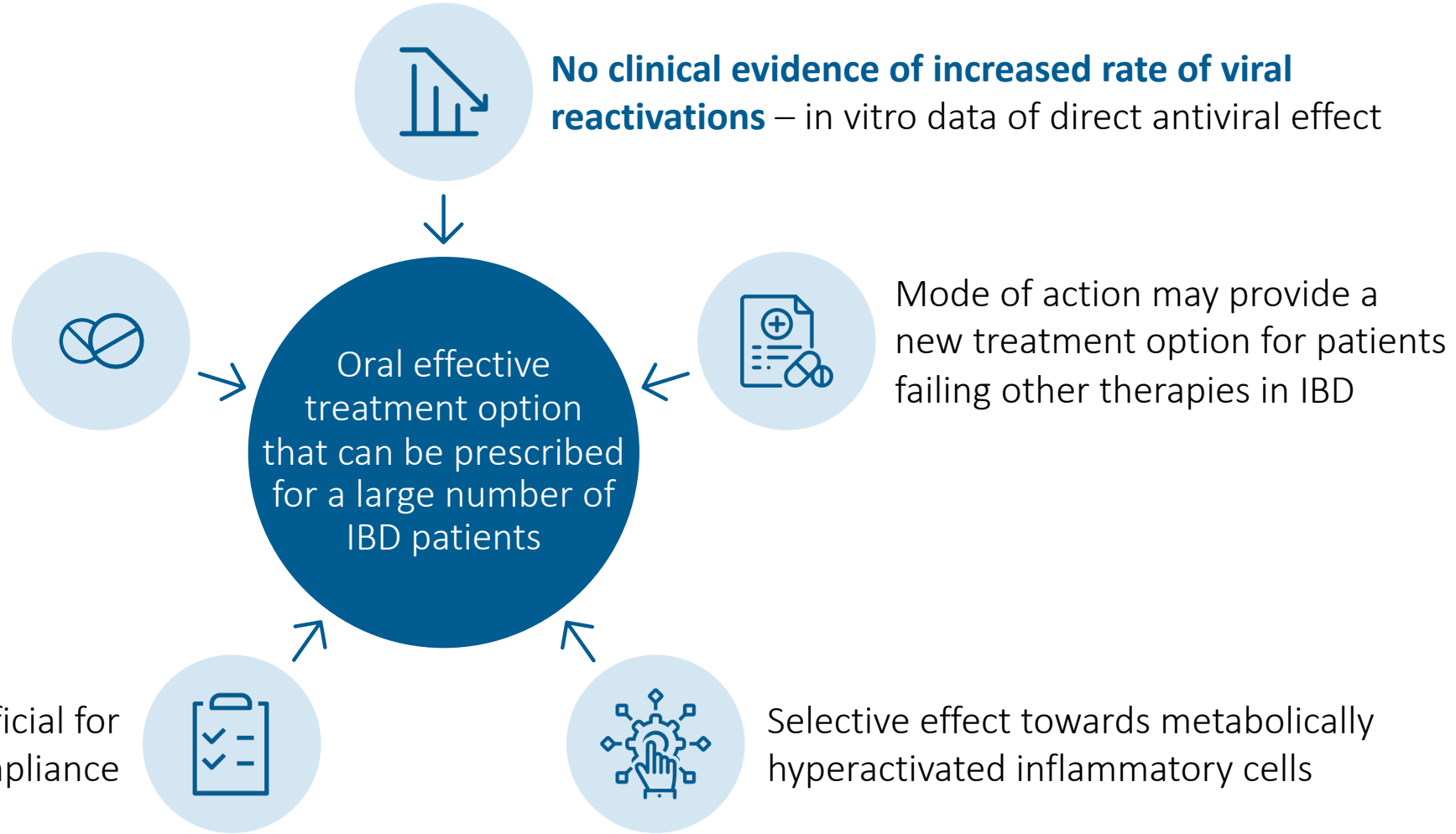


Current Solutions Have Limitations

- 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, vidofludimus calcium 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

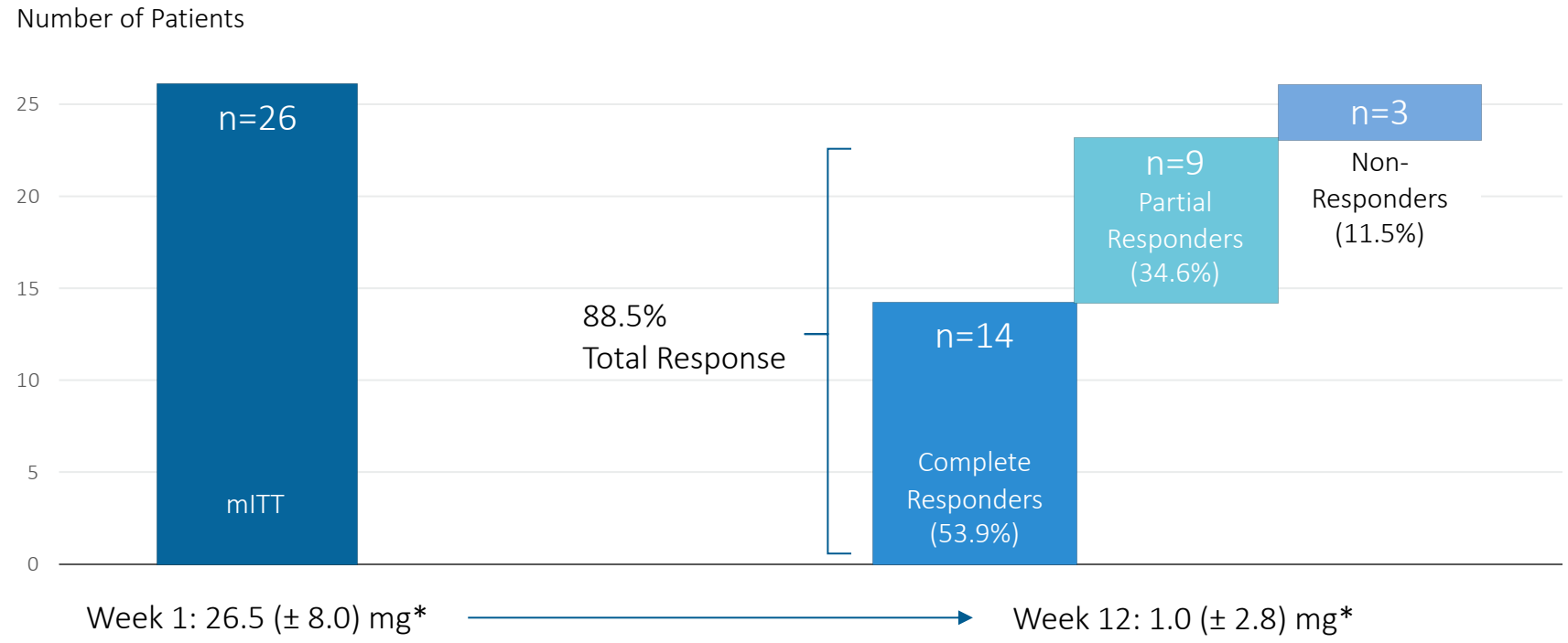
vidofludimus calcium: Key Strengths Designed to Address Limitation of Existing Therapies in IBD



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)



vidofludimus 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

Immunic THERAPEUTICS

ENTRANCE Study: Steroid-Sparing

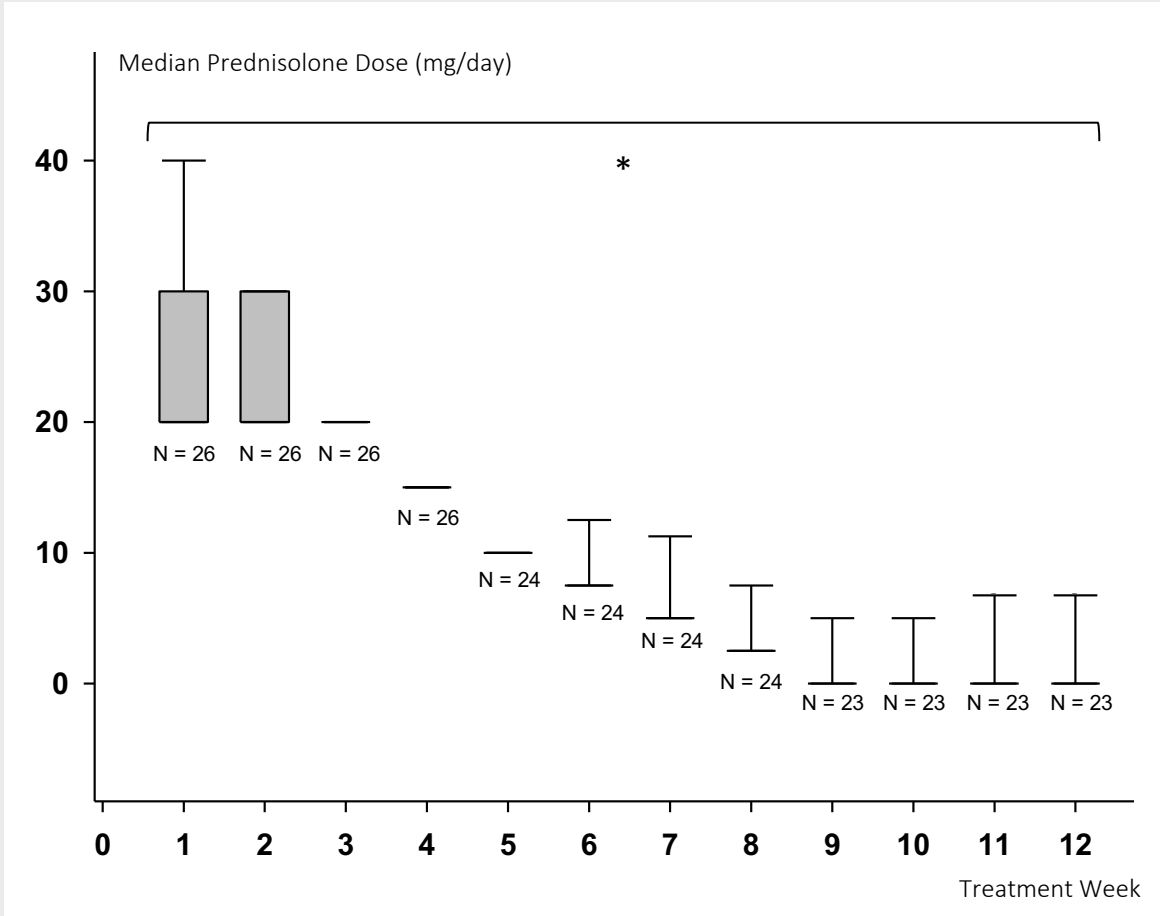
Development of prednisolone intake over 12 weeks (mITT):

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



Immunic THERAPEUTICS

CALDOSE-1: Clinical Phase 2 Trial in UC
NCT03341962

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

Active IND in the United States

Total Number of Patients Randomized: 263

More Than 100 Sites in 19 Countries: USA, Western, Central and Eastern Europe

Interim Analysis Established Potentially Broad Effective Dose Range:

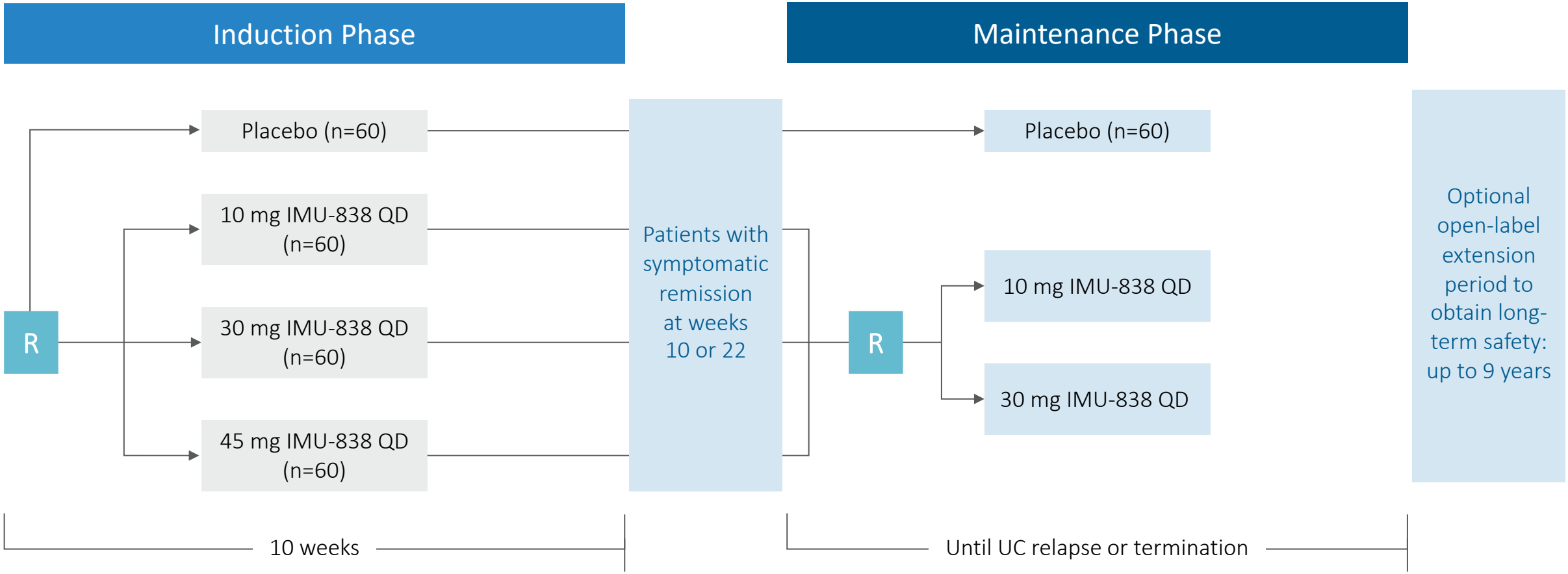
- Performed by an unblinded data review committee in August 2019
- Analysis based on all available clinical, endoscopic, biomarker, pharmacodynamic, and safety data
- No intolerable dose identified
- No safety signal observed

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

Timelines:
Currently estimated to deliver top-line data in Q2/2022

IND: investigational new drug

CALDOSE-1: Phase 2 Trial Design in UC
NCT03341962



Total number of patients randomized: N=263

Final analysis induction phase after 10 weeks

Final analysis maintenance phase after 50 weeks

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

Potentially Applicable to a Wide Range of Diseases

Clinical Activity of vidofludimus calcium in Further Indications

vidofludimus calcium: Opportunities Beyond MS and IBD

Primary Sclerosing Cholangitis (PSC)

- vidofludimus calcium 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

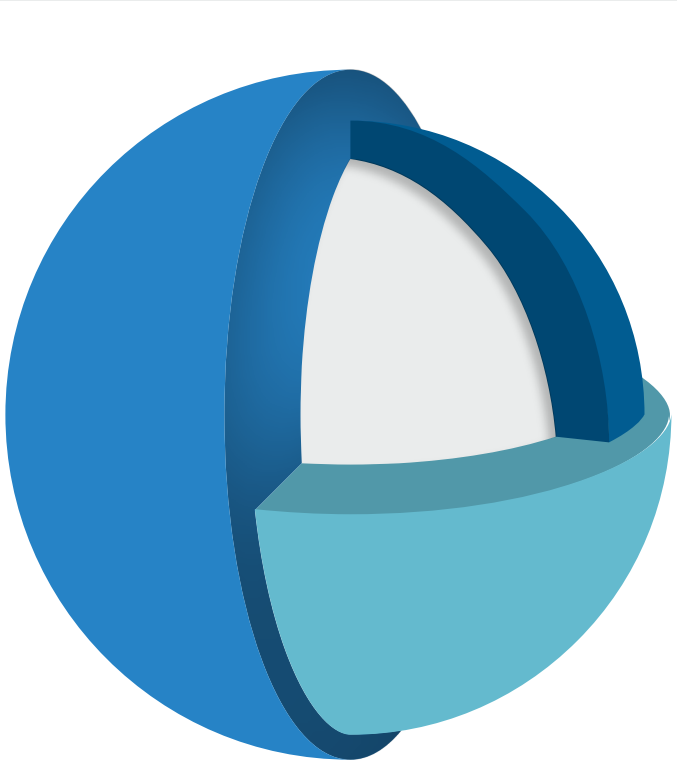
COVID-19

- Backed by its broad-spectrum antiviral activity demonstrated *in vitro*, vidofludimus calcium 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

ALP: alkaline phosphatase; PK: pharmacokinetics

vidofludimus calcium: IP Position

vidofludimus calcium is Protected by Several Layers of Patents:



- Patent on the specific salt form and pharmaceutical composition of vidofludimus calcium, 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 vidofludimus calcium used in current studies – expires in 2039, if granted
- New patent filed in 2020 on vidofludimus calcium‘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 vidofludimus calcium’s classification as a New Chemical Entity (NCE)

Immunic THERAPEUTICS

IMU-935: An Oral IL-17 Inhibitor

Uniquely Acting and Highly Selective RORγt Inverse Agonist

Autoimmune Diseases and IMU-935

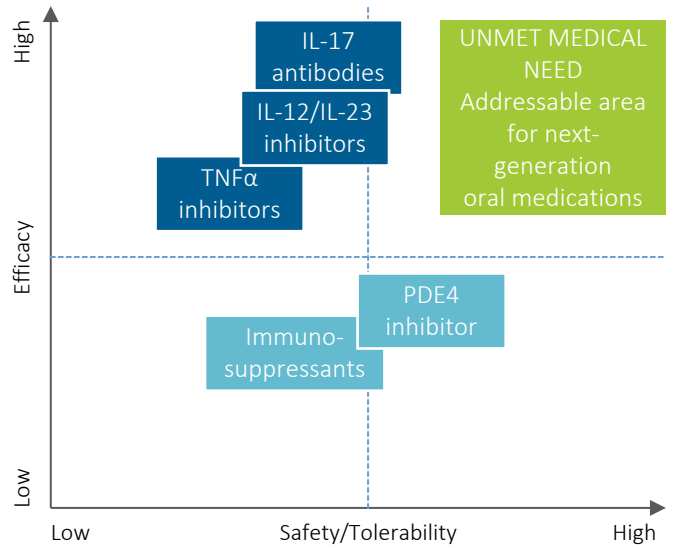
IL-17 in Autoimmune Diseases

- Autoimmune diseases affect millions of patients worldwide[1]
- Th17/IL-17/RORγt 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 RORγt in autoimmune diseases without affecting physiological functions of RORγt

Unmet Need in Psoriasis Care



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

[1] Rose, Noel R. American journal of epidemiology 2016; 183.5: 403-406 [2] Fasching, Patrizia, et al. Molecules 2017 22.1: 134
Th: T helper; IL: interleukin; TNF: tumor necrosis factor; PDE4: phosphodiesterase type 4; RORγ: retinoic acid receptor-related orphan nuclear receptor gamma

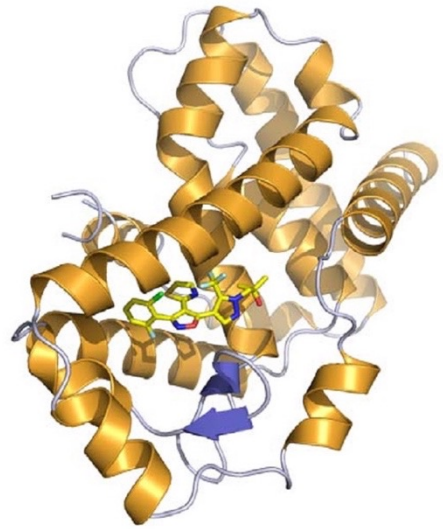
IMU-935 Has Been Observed to be Potent in Human Cells

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

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

	IC_{50} (µM)
IL-17A	0.005
IL-17F	0.004
IFNγ	0.003
IL-1a and b	no inhibition
IL-4,5,6,8	no inhibition
RORγ (MST)	0.024
RORγ (cellular, reporter assay)	0.020
DHODH	0.240
Th17 differentiation (murine)[1]	0.135

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

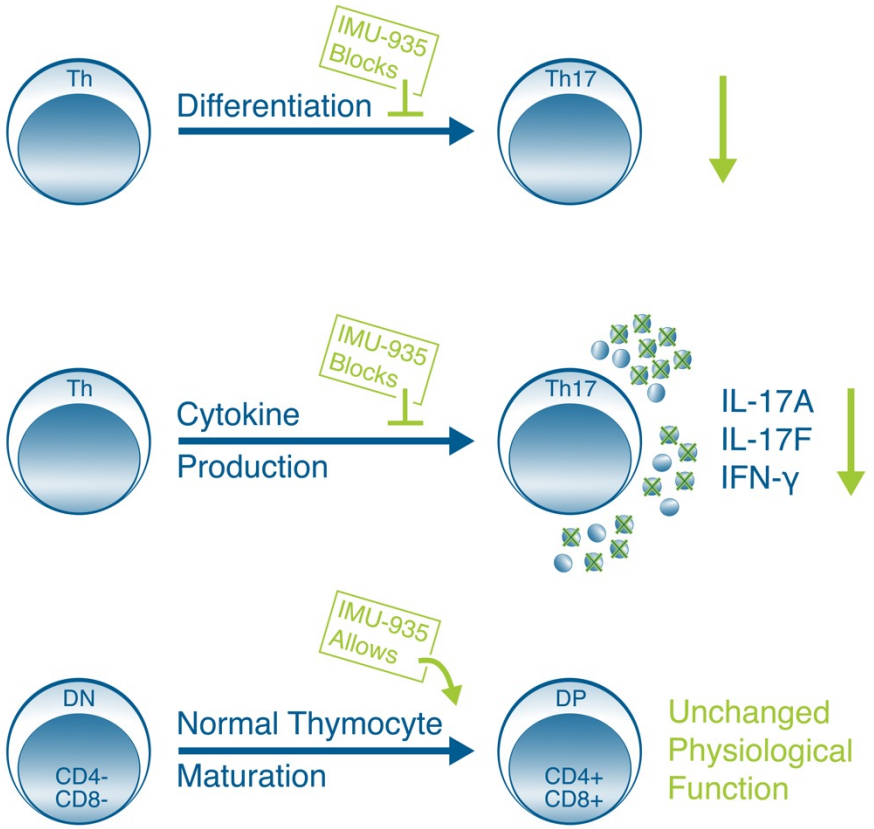


Co-crystal structure (Resolution 2.6 A) of a closely related derivative compound binds to hydroxycholesterol binding site of RORγ

PBMC: Peripheral Blood Mononuclear Cells; Th: T helper; IL: interleukin; IFN: interferon; MST: microscale thermophoresis
[1] Zuoming Sun, City of Hope, 2019

Immunic THERAPEUTICS

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

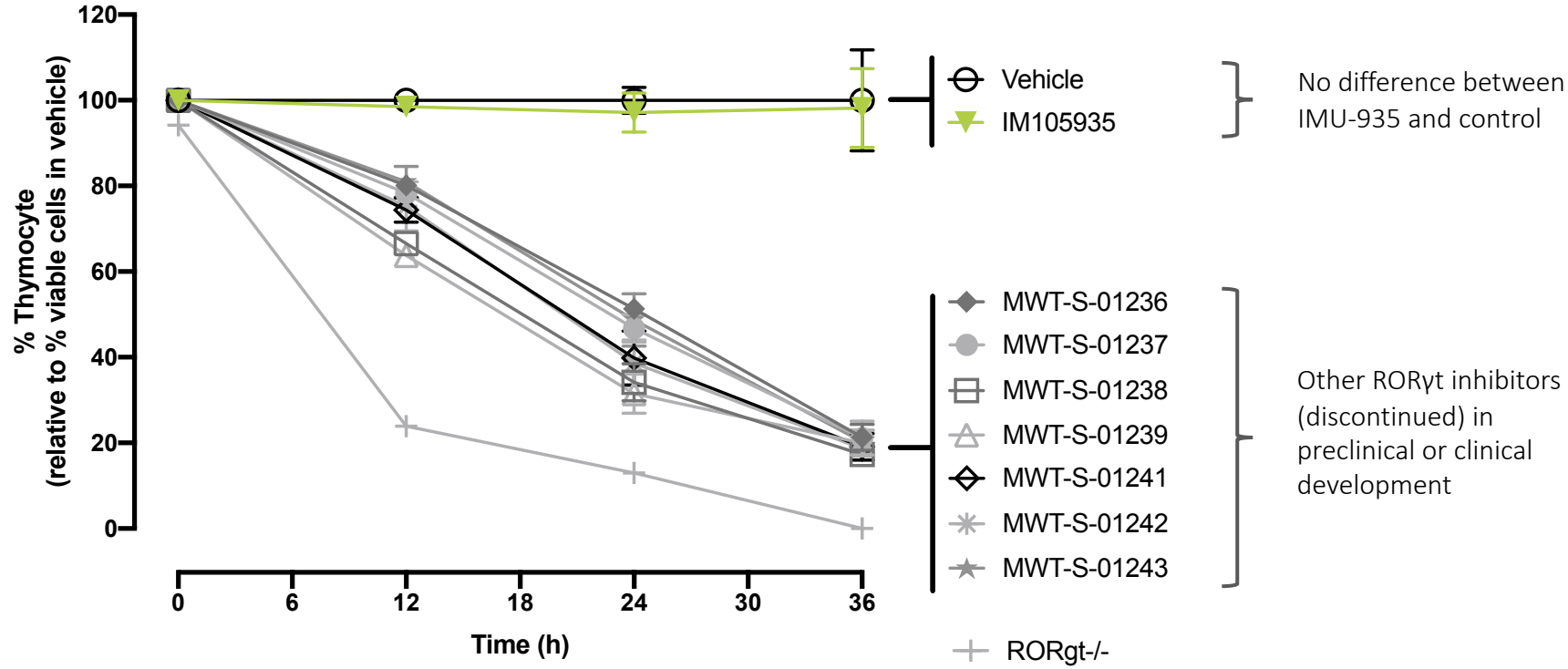


- The differentiation towards Th17 cells is inhibited by IMU-935
- The production of IL-17A and IL-17F is inhibited by IMU-935
- The physiological maturation of T cells within the thymus is not affected by IMU-935

Th: T helper; IL: interleukin; IFN: interferon; DN: double-negative; DP: double-positive; CD: cluster of differentiation

IMU-935 Does Not Induce Thymocyte Apoptosis

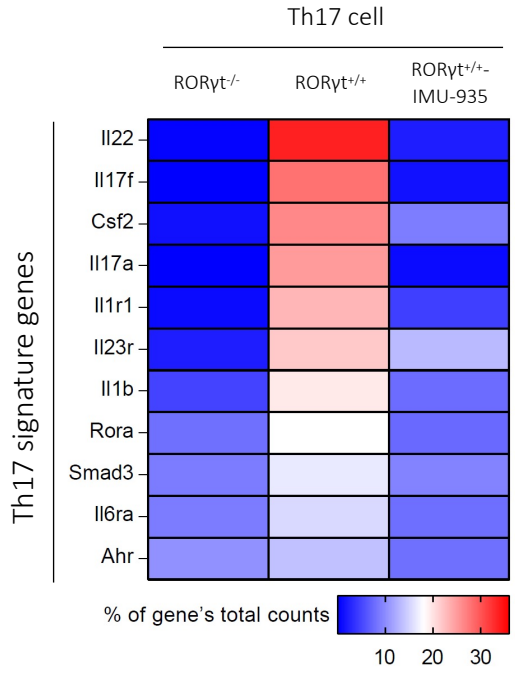
In Contrast to IMU-935, Comparator Compounds Have a Negative Impact on Thymocyte Viability and Therefore Bear the Risk of Lymphoma.

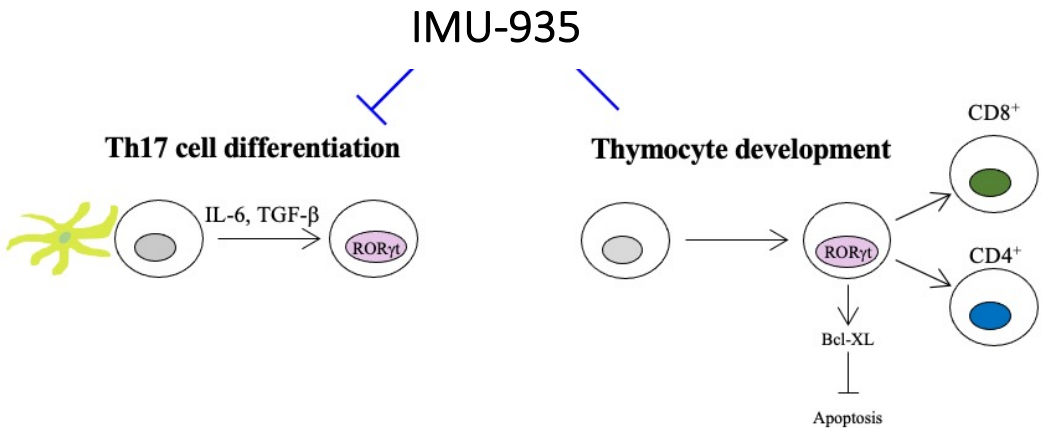


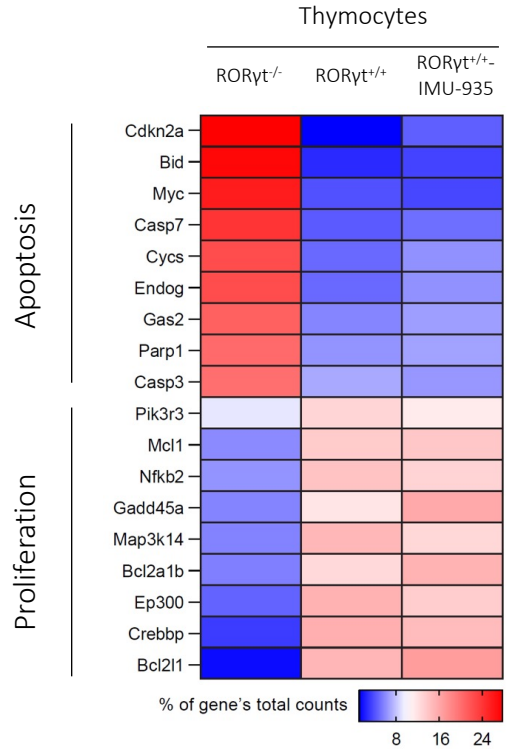
Sun, Zuoming. City of Hope, 2021, unpublished

Immunic THERAPEUTICS

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 **RORγ knockout** and **IMU-935 treatment**, but similar for RORγ+/+

Zuoming Sun, City of Hope, 2021

Immunic THERAPEUTICS

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

PART B

Evaluation of multiple ascending doses (MAD)

—

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

- Experimental phase completed
- 15 subjects enrolled (still blinded)
- IMU-935 was well-tolerated and showed trough levels in the anticipated therapeutically active range

PART C

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

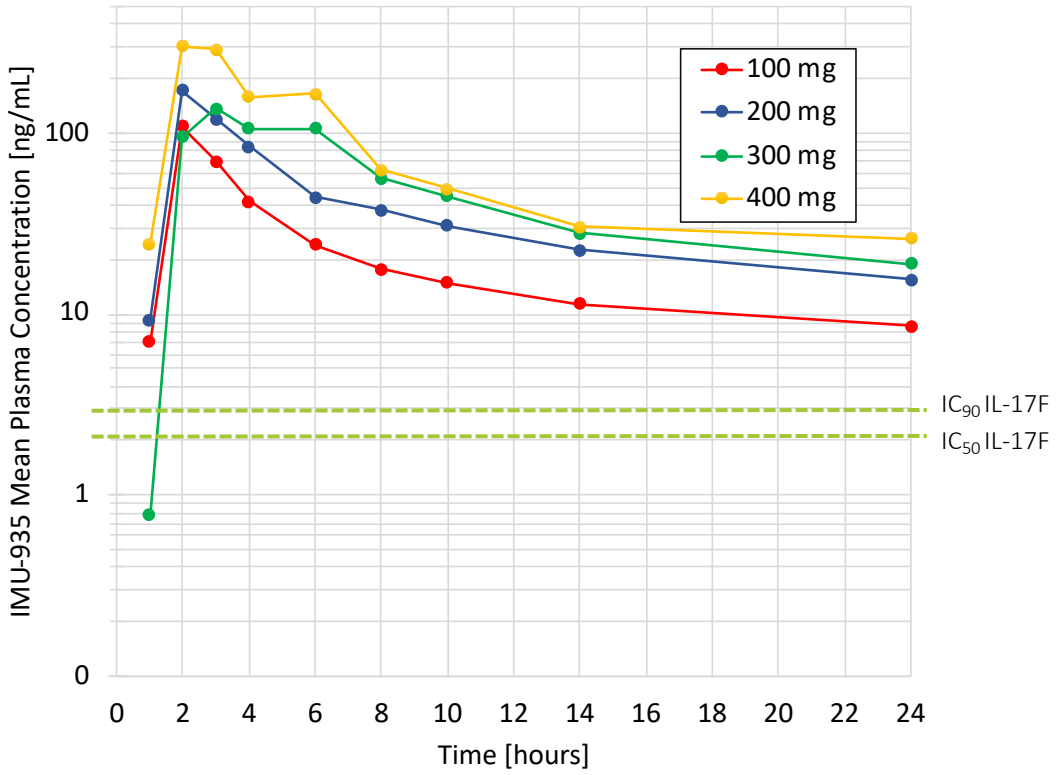
- Approximately 52 patients planned to be enrolled
- Initial human data expected to be available in Q2/2022

PK: pharmacokinetics

Immunic THERAPEUTICS

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

Immunic THERAPEUTICS

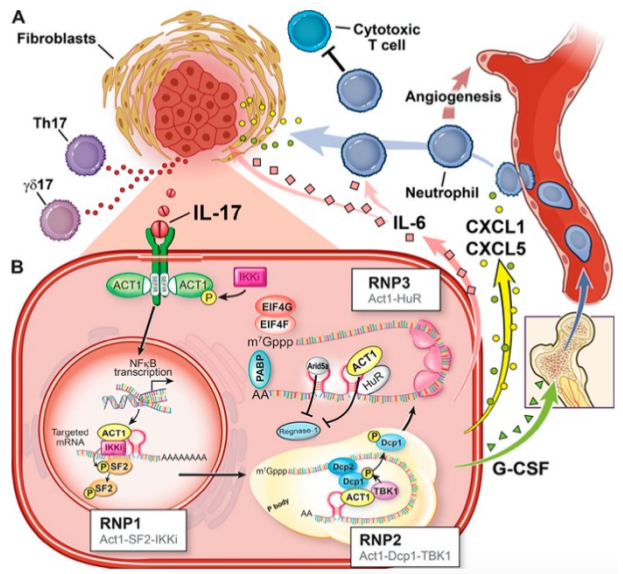
IMU-935 As Treatment Option in Castration-Resistant Prostate Cancer – Synergistic Effects by Targeting RORγ and RORγt

Inhibition of RORγ

- 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 RORγt Regulation

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



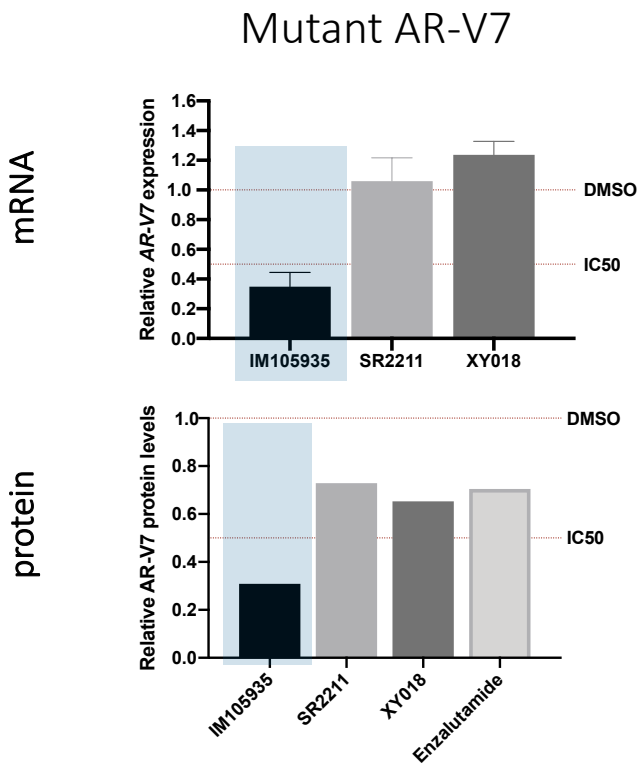
Differentiation of MDSCs

- IL-17 mediates the induction, recruitment and expansion of MDSCs.
- Next to IL-17 suppression via RORγt 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

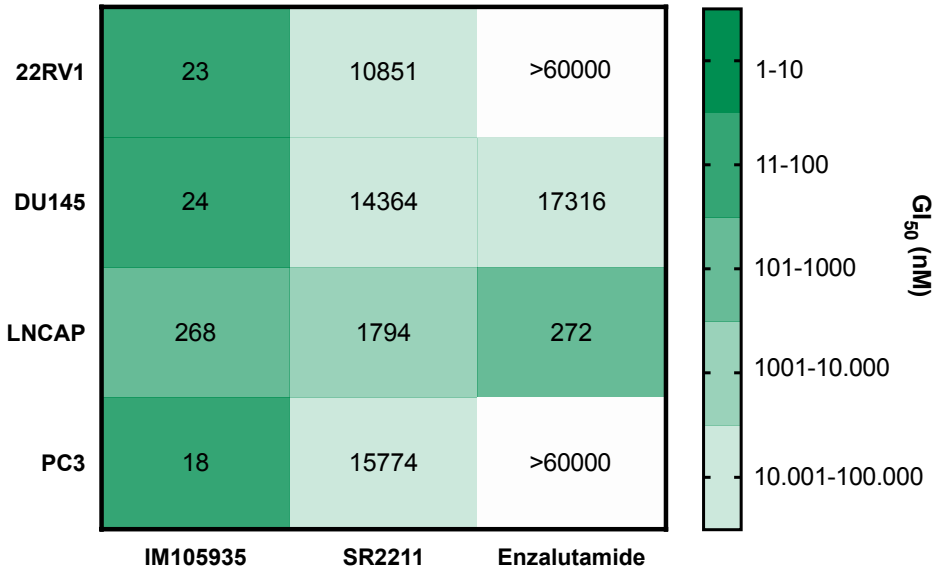
IMU-935 Demonstrated RORγ-Dependent Effects in CRPC Cells

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: 1µM, 48h; protein expression: 6µM, 48h; SR2211 and XY018 are RORγ 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

Immunic THERAPEUTICS

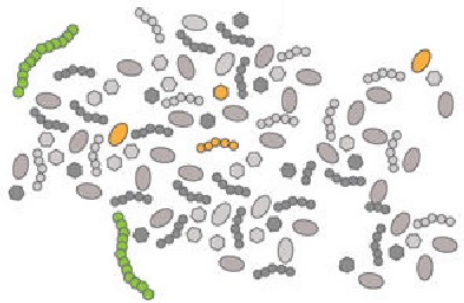
IMU-856

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

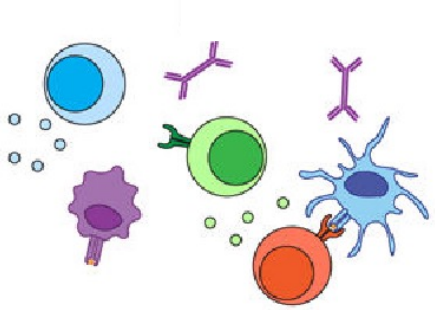


Influencing the Microbiome

- 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)

Immunic THERAPEUTICS

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 Q3/2022
  - 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:
vidofludimus calcium met all statistical endpoints and underlined favorable safety and tolerability profile

Shares outstanding: 26,249,439 (as of October 29, 2021)

Cash and cash equivalents of approx. USD 110.4 million (as of September 30, 2021)

Phase 3 program of vidofludimus calcium in RMS Ongoing, 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

Immunic THERAPEUTICS

Thank You!

Jessica Breu

Head of IR & Communications

Phone: +49-89-2080477-09

Email: ir@imux.com

Web: www.imux.com

Immunic, Inc.
1200 Avenue of the Americas
New York City, NY 10036
USA

Immunic AG
Gräfelfing (Munich)
Germany

Immunic Research GmbH
Weinberg Campus
Halle (Saale)
Germany

Immunic Australia Pty. Ltd.
Melbourne
Australia