Immunic Therapeutics

Developing Selective Oral Therapies in Immunology

NASDAQ: IMUX | February 2022

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, 2021, 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+

Multiple Clinical Data Readouts for All Three Development Programs Expected Throughout 2022

Program	Target	Preclinical	Phase 1	Phase 2	Phase 3	Key Milestones
Vidofludimus Calcium (IMU-838)	DHODH	Relapsing Multiple Sclerosis (RMS) – ENSURE Trials				▪ RMS interim analysis planned after approx. half of the events occurred ▪ PMS interim analysis planned after half of the patients completed 24 weeks of treatment ▪ June 2022: top-line UC data expected
		Progressive Multiple Sclerosis (PMS) – CALLIPER Trial				
		Ulcerative Colitis (UC) – CALDOSE-1 Trial				
		Crohn's Disease (CD)				
		Primary Sclerosing Cholangitis (PSC)				
IMU-935	IL-17 / RORγt	Psoriasis				▪ H2/2022: initial psoriasis data expected
		Castration-Resistant Prostate Cancer (CRPC)				▪ Q3/2022: initial CRPC safety data expected
IMU-856	Intestinal Barrier Function	Gastrointestinal Diseases				▪ Q3/2022: SAD/MAD safety data expected

■ Completed or ongoing ■ In preparation or planned

Immunic THERAPEUTICS

Vidofludimus Calcium (IMU-838)

Vidofludimus Calcium is Uniquely Positioned in Multiple Large Indications

There is an opportunity across multiple large indications to address the needs of patients who are seeking best-in-class treatment

Large Existing Markets[1]

- USD 20 billion+ in MS sales in major markets
- USD 15-20 billion in major markets in IBD, with ~USD 9 billion from biologics alone[2,3]

Multi-Billion Revenue Opportunity

Gap in Treatment Options

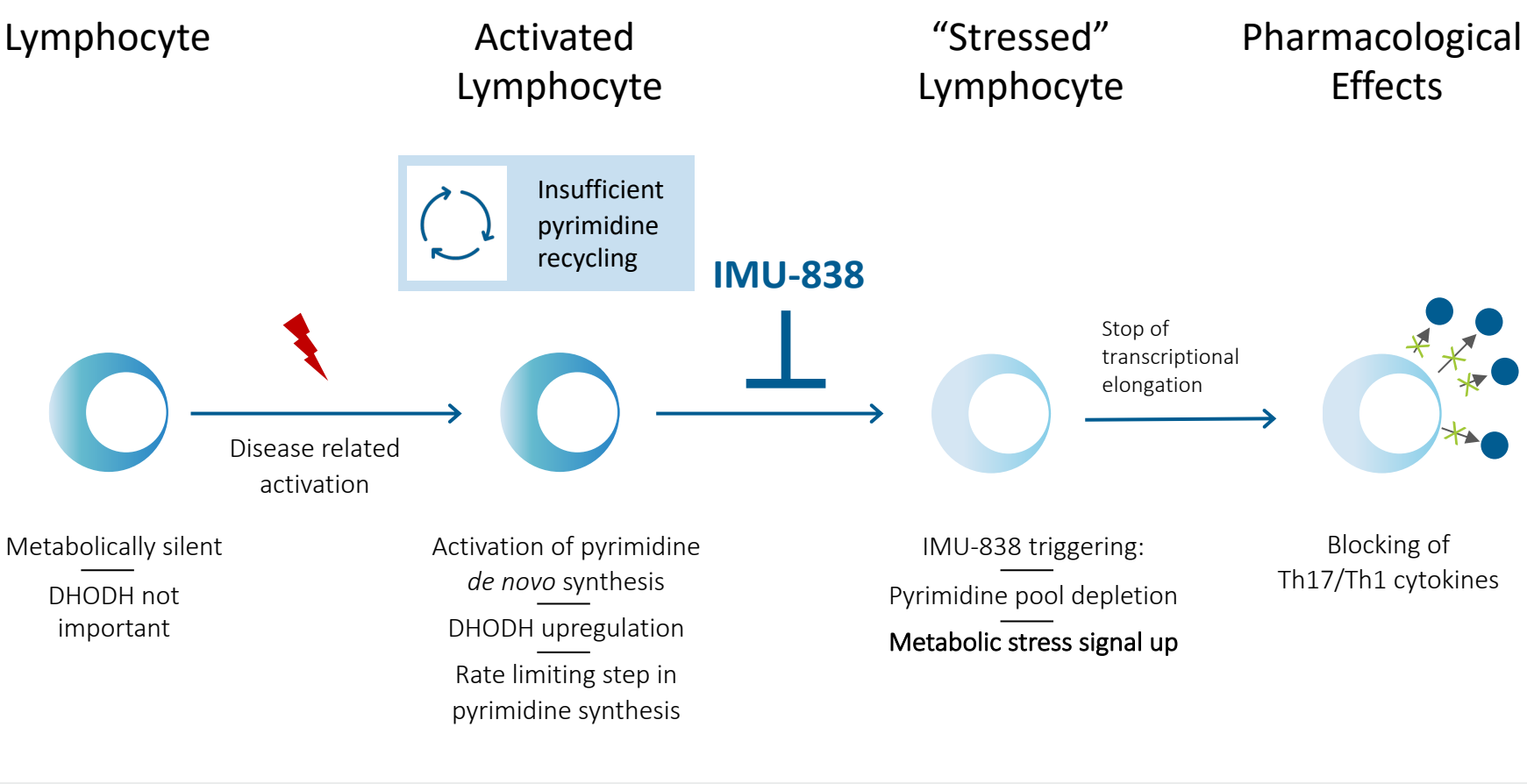
- MS (40%) and UC (25-40%) have significant group of untreated patients[1]
- Multiple issues with existing therapies

Potential to Leverage Current Treatment Algorithms

- Treatment intensity is escalated as disease severity increases
- Patient and physician emphasis on safety and tolerability in early treatment

[1] Decision Resources Group [2] Jefferies 2021 IBD Deep Dive [3] https://www.fiercepharma.com/marketing/ibd-market-set-for-major-growth-abbvie-stands-to-benefit-analyst

Vidofludimus Calcium Selectively Targets Only Hyperactive Immune Cells



Preserves normal immune cell function and numbers

→ No nonspecific immunosuppression

→ Maintains vaccination efficacy[1]

→ No negative effect observed on white blood cell count or rates of infection or malignancies

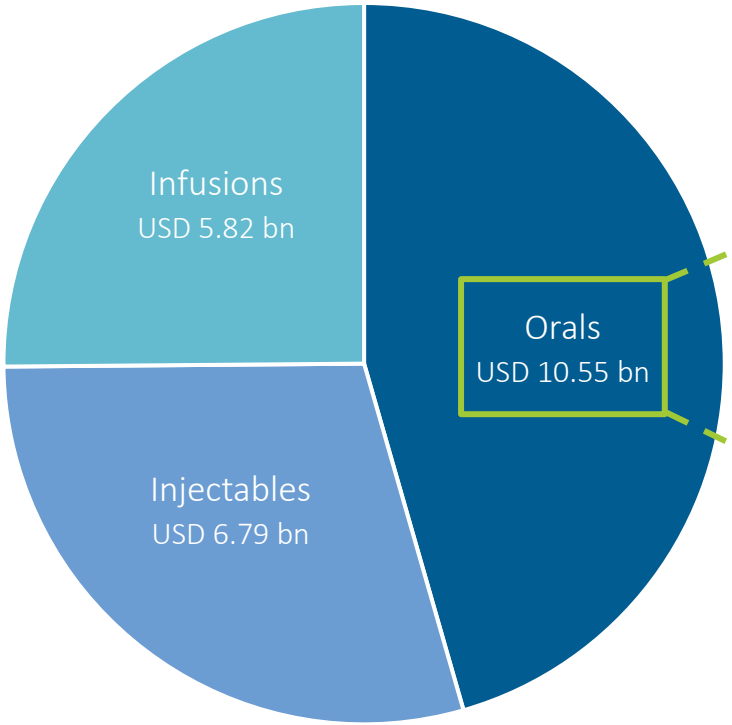
Illustration adapted from Tan et al., 2016, Mol Cell 62; [1] Bar-Or A, Freedman MS, Kremenchutzky M, et al. Neurology. 2013;81(6):552-558
DHODH: dihydroorotate dehydrogenase

Vidofludimus Calcium in Multiple Sclerosis (MS)

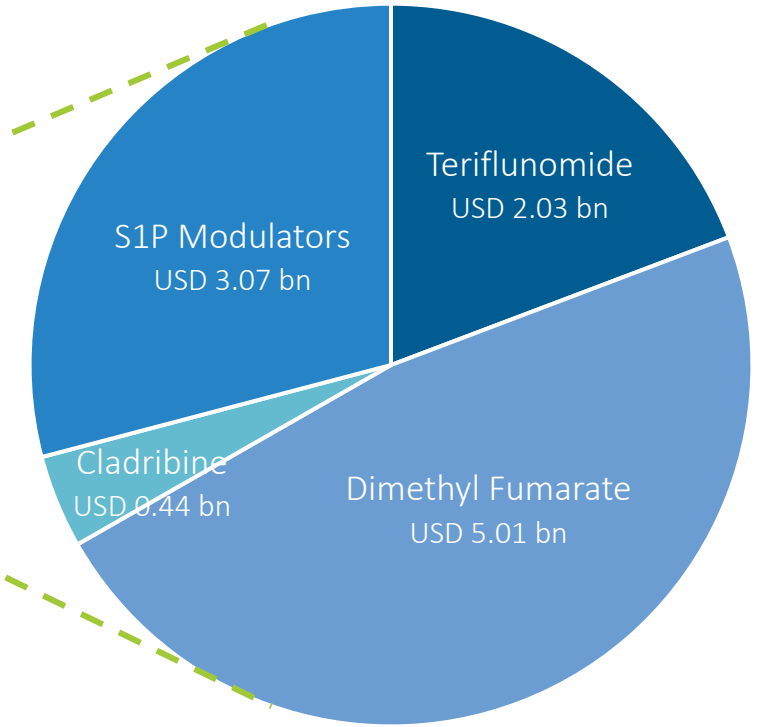
”Designed to be the Easy-to-Use, Uniquely Safe, Well-Tolerated and Efficacious MS Treatment”

Despite Limitations of Current Therapies, the Global MS Market Exceeds USD 23 Billion* Annually

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:

- An anti-inflammatory, with additional neuroprotective properties
- A safe and well-tolerated oral drug
- An easy-to-use therapy, allowing patients to maintain their normal quality-of-live

* 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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Treatment Escalation Remains the Typical Approach for Patients With Relapsing-Remitting Multiple Sclerosis (RRMS)

Treatments escalated due to:

1. Long time-course of disease
2. Lack of efficacy
   - Relapse(s)
   - Disability worsening
   - MRI lesions
3. Safety / tolerability issues
   - Side effect profile
   - Risk perception
   - Long-term immunosuppression
   - Delivery challenges

Base Therapy (Initiation)

- Tolerability often prioritized in the early disease stages (due to low disease burden)

Escalation (Switch)[1,2]

- Switch most often driven by either
  - Need for increased efficacy, or
  - Safety / tolerability / patient request

→ Existing treatment options do not adequately address near or long-term needs of patients

[1] DRG - Treatment Algorithms CDA Multiple Sclerosis US May 2021 [2] Spherix Real World Dynamix_DMT Switching in MS_US_2021

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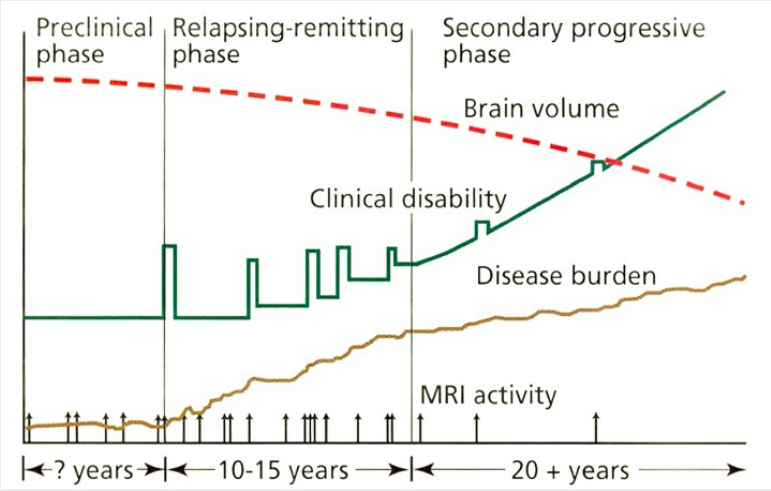
For Patients With Lifelong Illness, Disability is a Critical Concern

MS is a Lifelong Disease

- **Lifelong disease** requiring decades of therapy
- ~2.8 million people affected worldwide (~1M in US)[1]
- Often diagnosed in **younger adults** (3:1 women:men)



Therapeutic Goal: Preventing Disability Worsening

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

Need to Do so Without

- **Problematic side effects**
- **Cumulative health risks**: cancer, infections, cardiovascular and liver disease
- 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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Existing First-Line and Oral MS Therapies 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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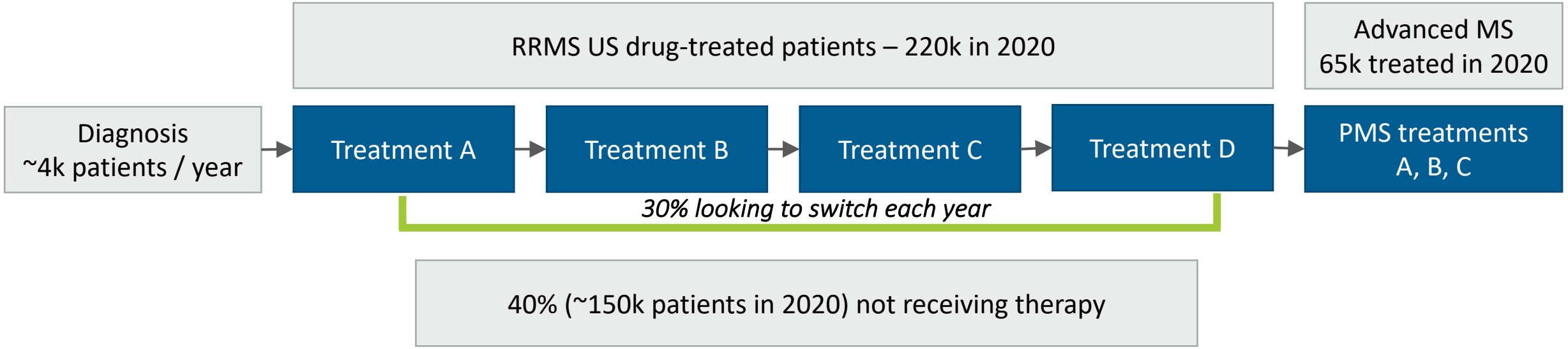
Vidofludimus Calcium Could Address the Limiting Factors of Other Therapies Across Multiple Segments of the MS Patient Journey

Illustrative Patient Flow



Market entry with differentiated profile plus current treatment switching patterns offers a USD 1 billion opportunity/year

Sources: DRG - Treatment Algorithms CDA Multiple Sclerosis US May 2021, KOL and community physician feedback
k: thousand

Vidofludimus Calcium is Targeted to Address Unmet Needs From Both the Patient and Provider Perspective

Intended Value for Patient: **Precision Solution**

- Noticeable efficacy
  - Improvements in relapses and lesions
  - Prevent and/or delay disability worsening
  - Confirmed reduction in neurofilament light chain
- Category leading safety and tolerability profile
  - Low adverse events → Not disturbing quality-of-life
  - No/low infection risk (inclusive of PML)
- Oral and easy to manage

Intended Value for Neurologist: **Seamless Fit for Patient**

- Specific to disease causing cells
- Applicable throughout patient journey
- Strong clinical activity
- Long-term utility with low discontinuation rates
- Easy on- and off-dosing
- Reduced monitoring requirements

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

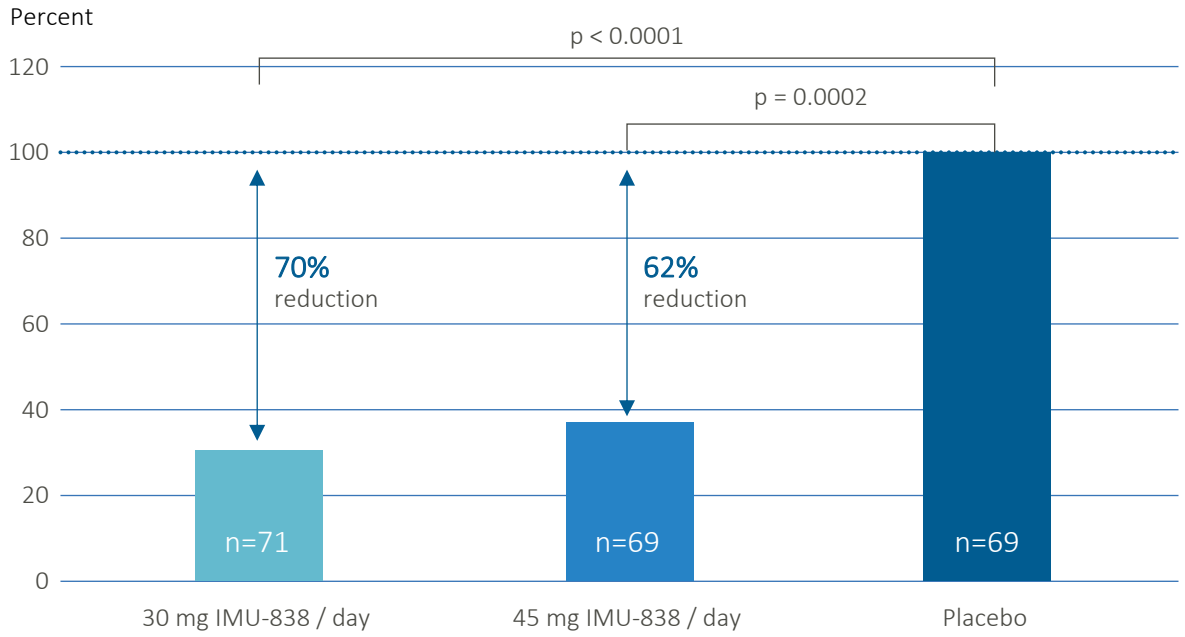
- Blinded main treatment period of 24 weeks
- Extended treatment period of up to 9.5 years to observe long-term safety
- 210 patients randomized in 36 centers across four European countries

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 Highly Significant MRI Lesion Suppression of Vidofludimus Calcium

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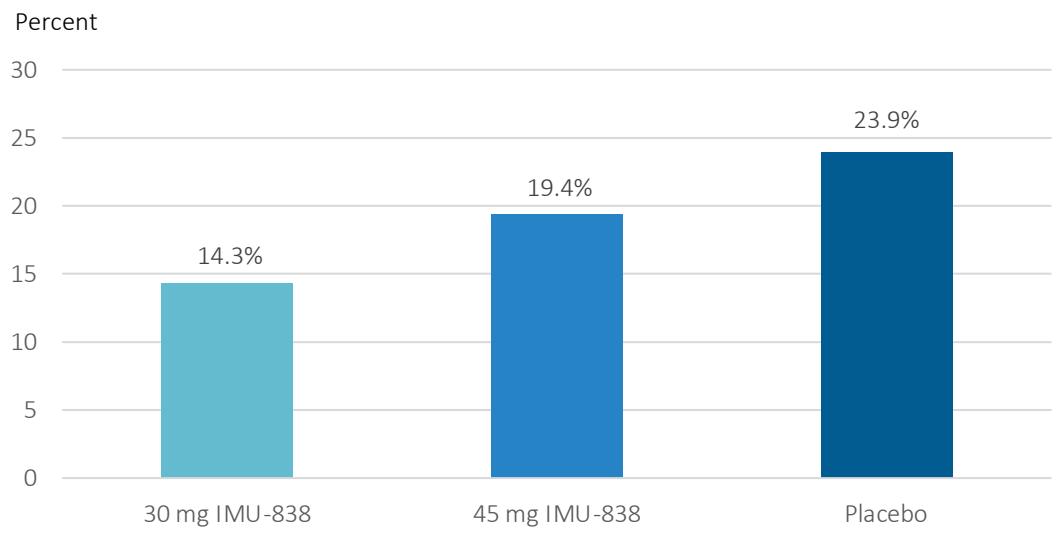
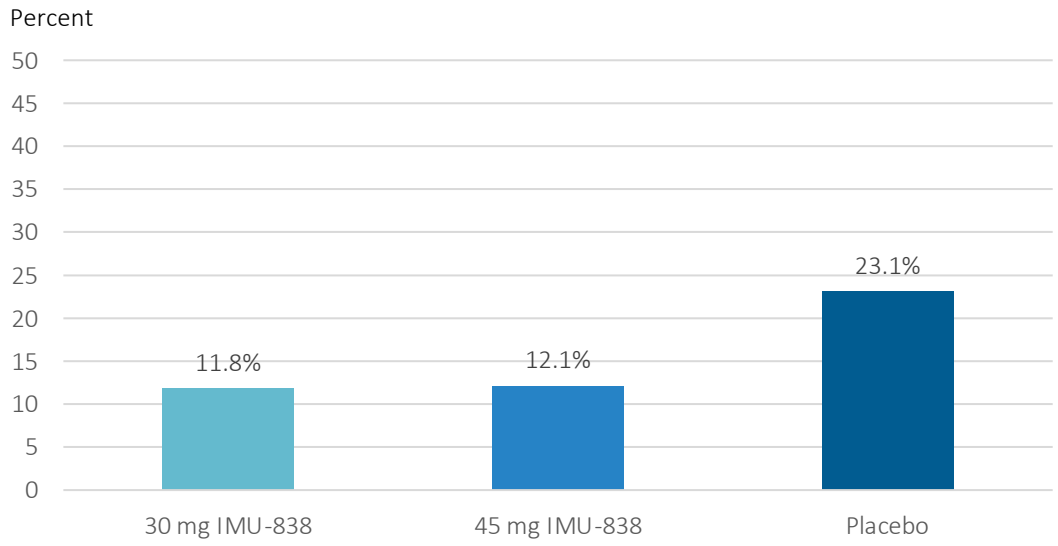
Phase 2 Data in RRMS: Positive Signals on Relapse and Unconfirmed Disability

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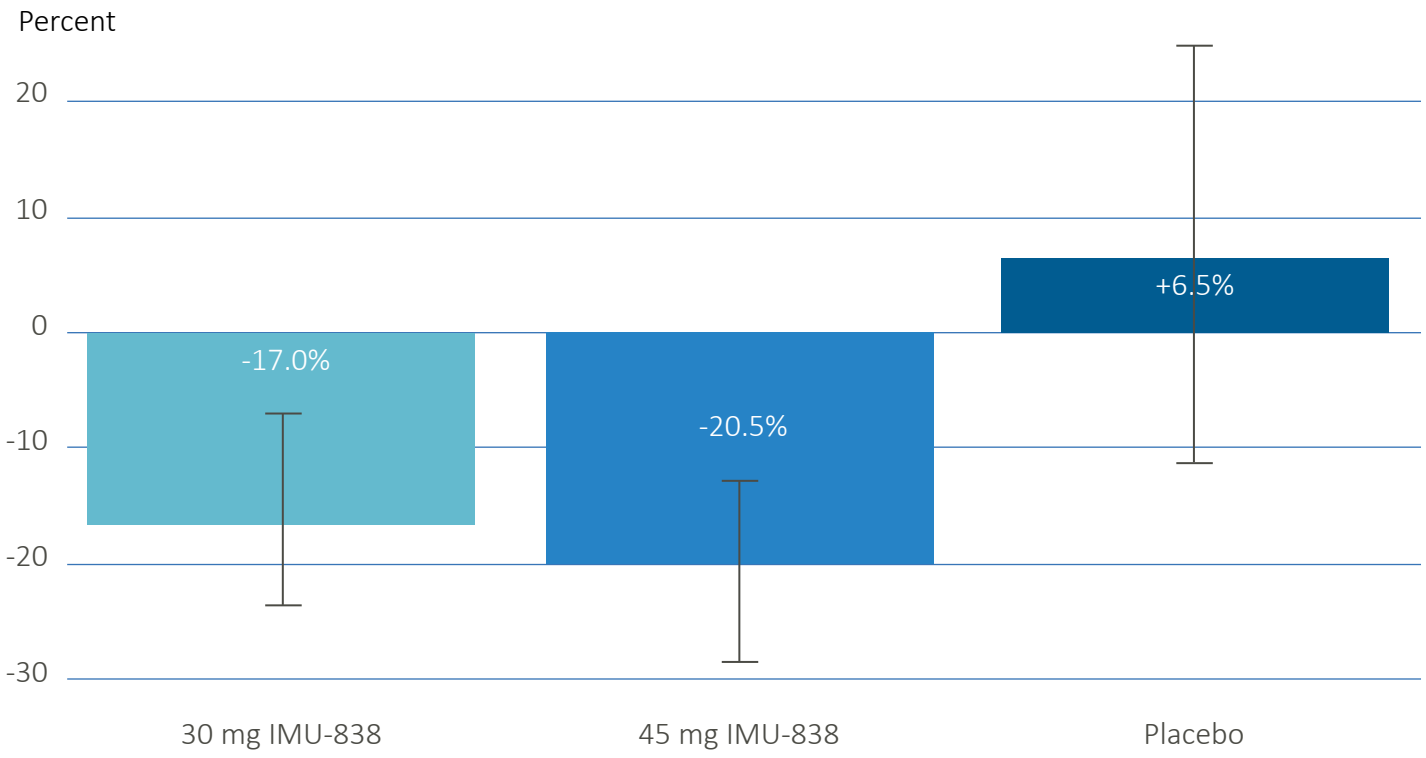
Phase 2 Data in RRMS: Showed Evidence of Potential Neuroprotective Activity

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



NfL has been shown consistently to correlate with disease activity in neurological disorders.

NfL has become one of the most important serum biomarkers for axonal damage.

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

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Phase 2 Data in RRMS: Indicated Patients Feel Well-Treated With Vidofludimus Calcium

Reflected in **Low Discontinuation Rates** for Vidofludimus Calcium-Treated RRMS Patients, Considerably Lower Than Placebo*

	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 1,100 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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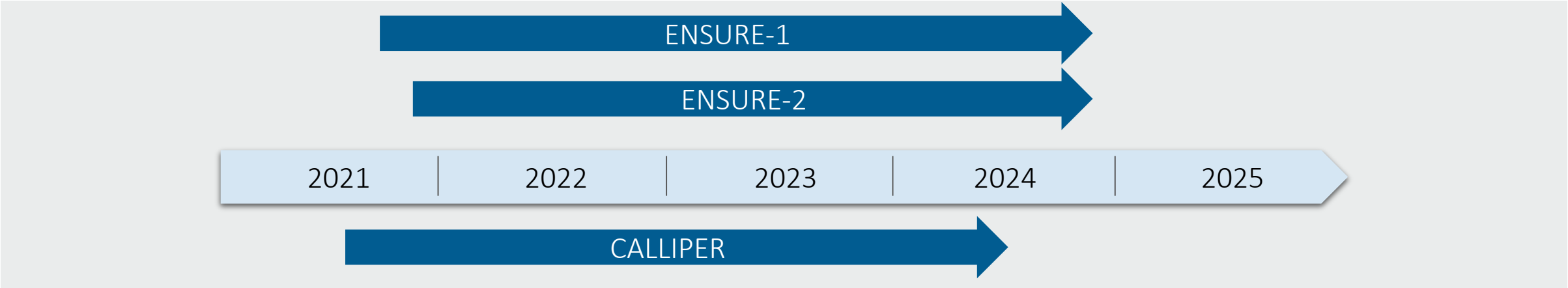
Phase 3 and Approval Strategy in MS

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
- ClinicalTrials.gov: NCT05134441 & NCT05201638

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
- ClinicalTrials.gov: NCT05054140



QD: quaque die = once-daily

ENSURE: Ongoing Pivotal Phase 3 Program in RMS
NCT05134441

Coordinating Investigator

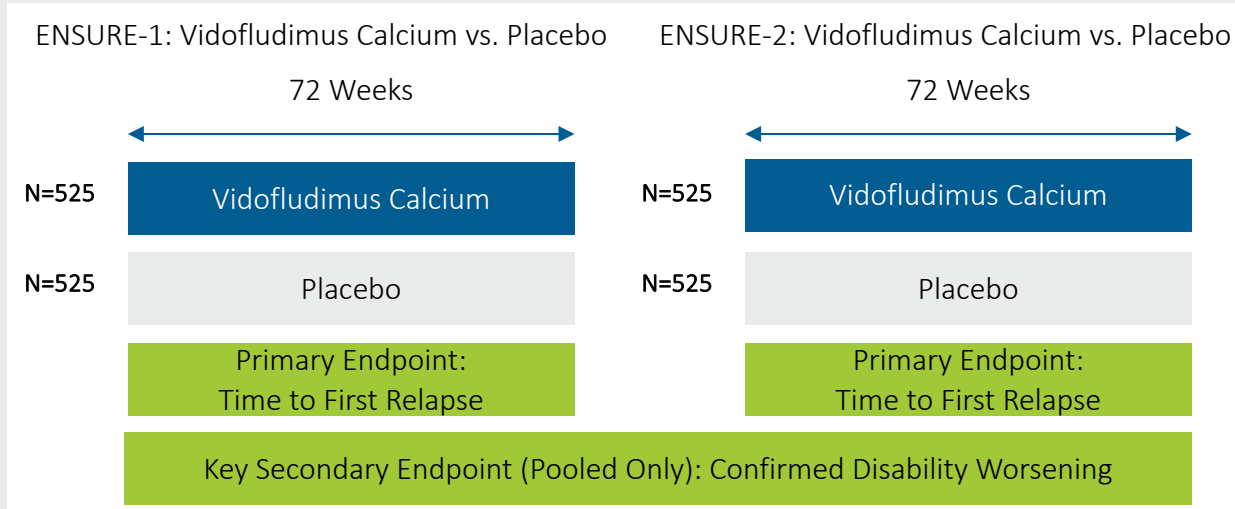
Robert J. Fox, M.D.
Cleveland Clinic

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

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

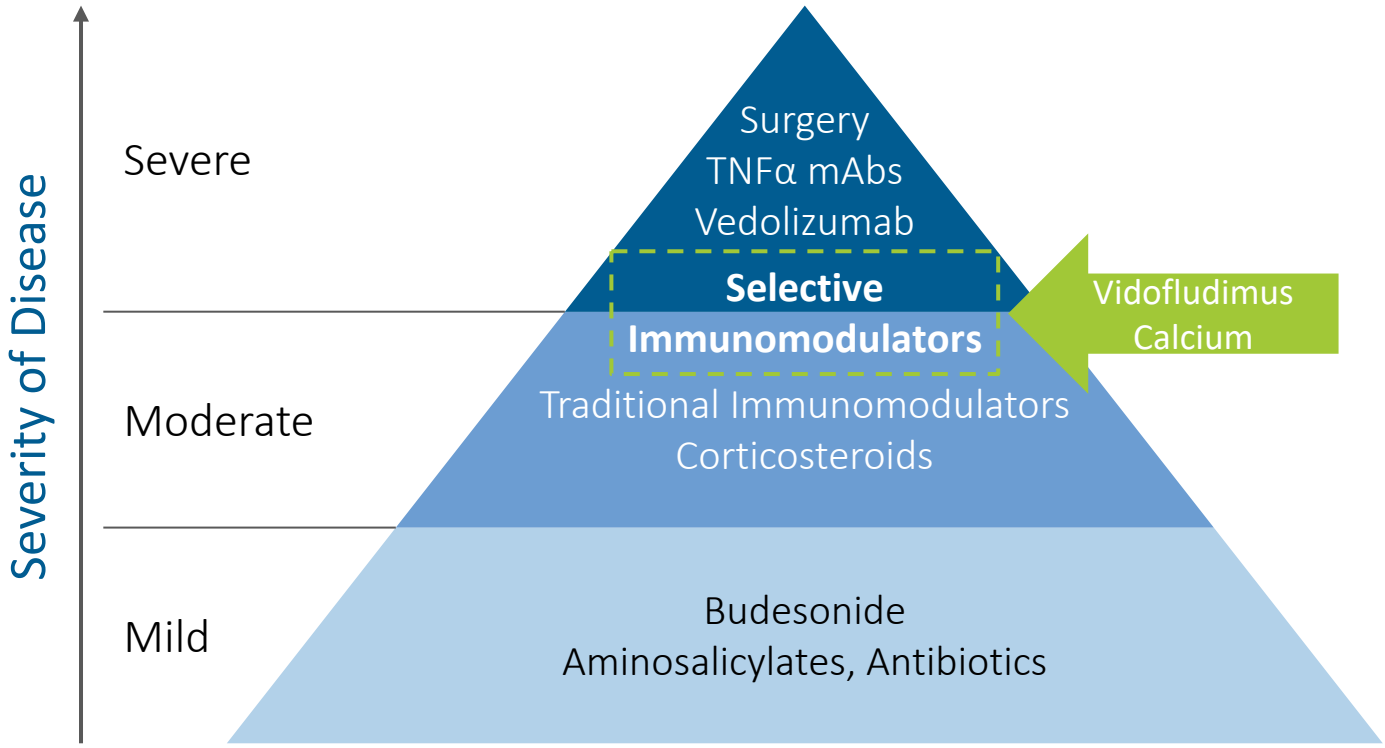
- Immunic believes that the phase 3 **ENSURE program provides a straightforward path towards potential regulatory approval** of vidofludimus calcium in RMS.
- CALLIPER is designed to corroborate vidofludimus calcium's neuroprotective potential to support differentiated profile.*
- CALLIPER is targeted for underserved PMS patients, with assessments of long-term patient outcomes.

* 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.

Vidofludimus Calcium in Inflammatory Bowel Disease (IBD)

“Targeted to be a First-in-Class Therapy to Elevate the Standard of Care for Treating IBD”

Vidofludimus Calcium is Targeted to Become the New Standard of Care for IBD Patients



Goal: New Standard of Care

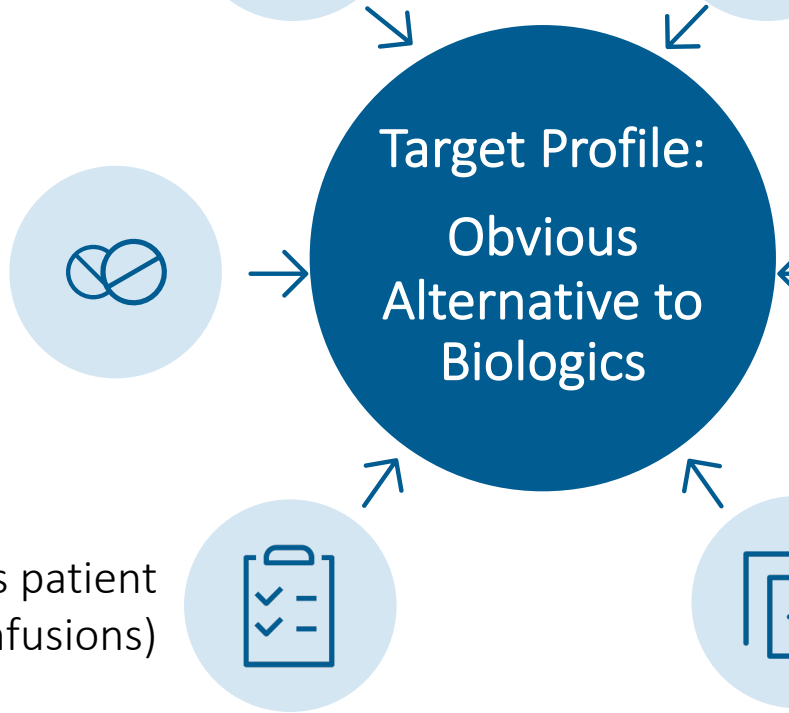
- Highly selective
- First-in-class oral, providing increased flexibility and clear switch opportunity for physician and patient
- Leading safety and tolerability (consistent with data shown in RRMS phase 2 trial)
- Potential for combination treatment

TNF: tumor necrosis factor; mAb: monoclonal antibody

Vidofludimus Calcium is Targeted to Address Limitations of Existing IBD Therapies

Selectivity for only metabolically hyperactivated inflammatory cells

Antiviral effect provides complement to vaccinations



Small molecule enables long-term treatment

First-in-class mode of action would provide alternative for non-responders

Once-daily oral dosing increases patient and physician flexibility (e.g., no infusions)

Combination potential based on target safety and tolerability profile, as shown in RRMS

Strong Indications for Vidofludimus Calcium's Activity in IBD

ENTRANCE Study: IBD Activity of Vidofludimus

Phase 2a study of vidofludimus in corticosteroid-dependent patients after two unsuccessful withdrawal attempts:

- Endpoint: remission at week 12 with successful full or partial steroid tapering
- Vidofludimus showed response rates of:
  - 85.7% in Crohn's disease
  - 91.7% in ulcerative colitis

Crohn's Investigations Confirm DHODH Activity

Investigator-initiated studies of leflunomide (another DHODH inhibitor) in adult patients with CD:

- CD activity index decreased from 219 to 87 and steroid intake from 25 to 3 mg/day[1]
- Significant reduction in Harvey-Bradshaw score[2]
- However, adverse side effects, in particular diarrhea, were frequent in this patient population

Phase 2 Data of IMU-838 in RRMS

Safety data confirmed biological selectivity of target with placebo-like tolerability profile

Strong performance on efficacy-related endpoints

- Primary and key secondary endpoints met with high statistical significance
- Strong inhibition of MRI lesion activity

[1] Holtmann, MH., et al. Dig Dis Sci (2008) 53: 1025
[2] Prajapati, DN al. Journal of Clinical Gastroenterology: 2003(37): 125

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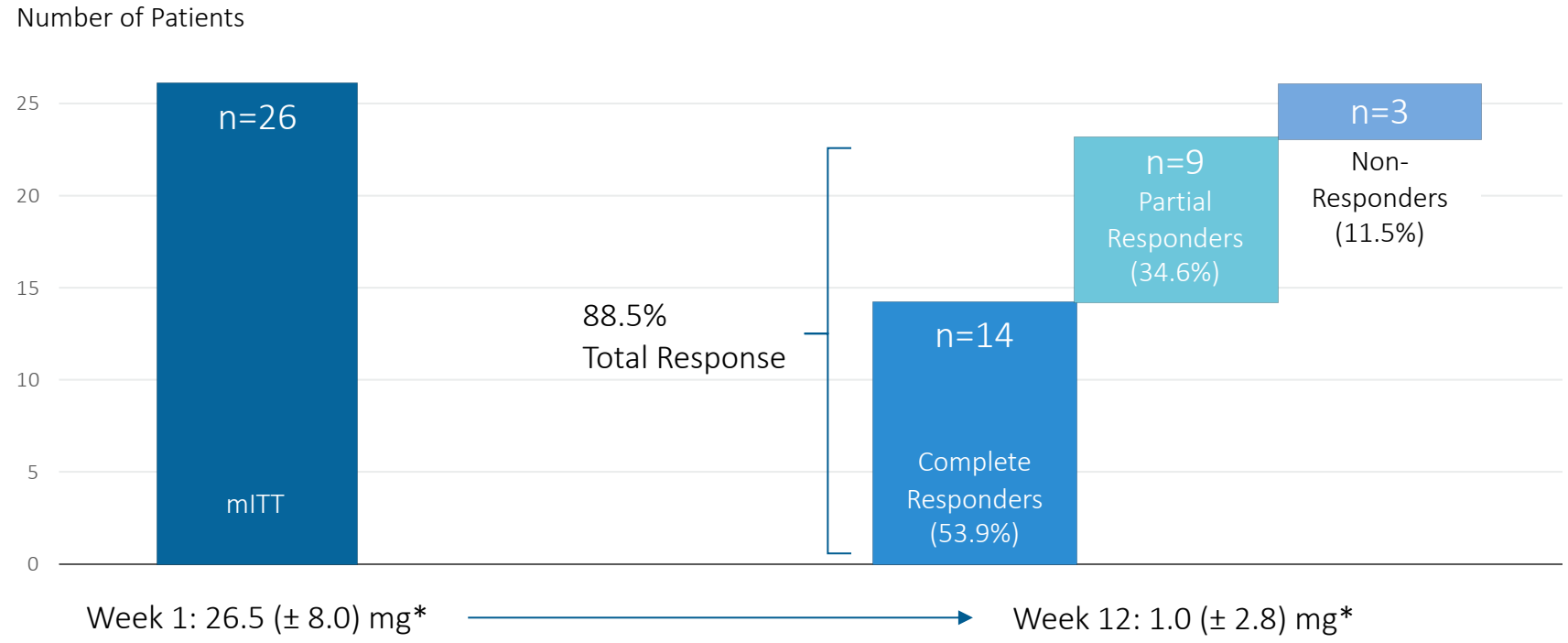
ENTRANCE Study: Primary Efficacy Results

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

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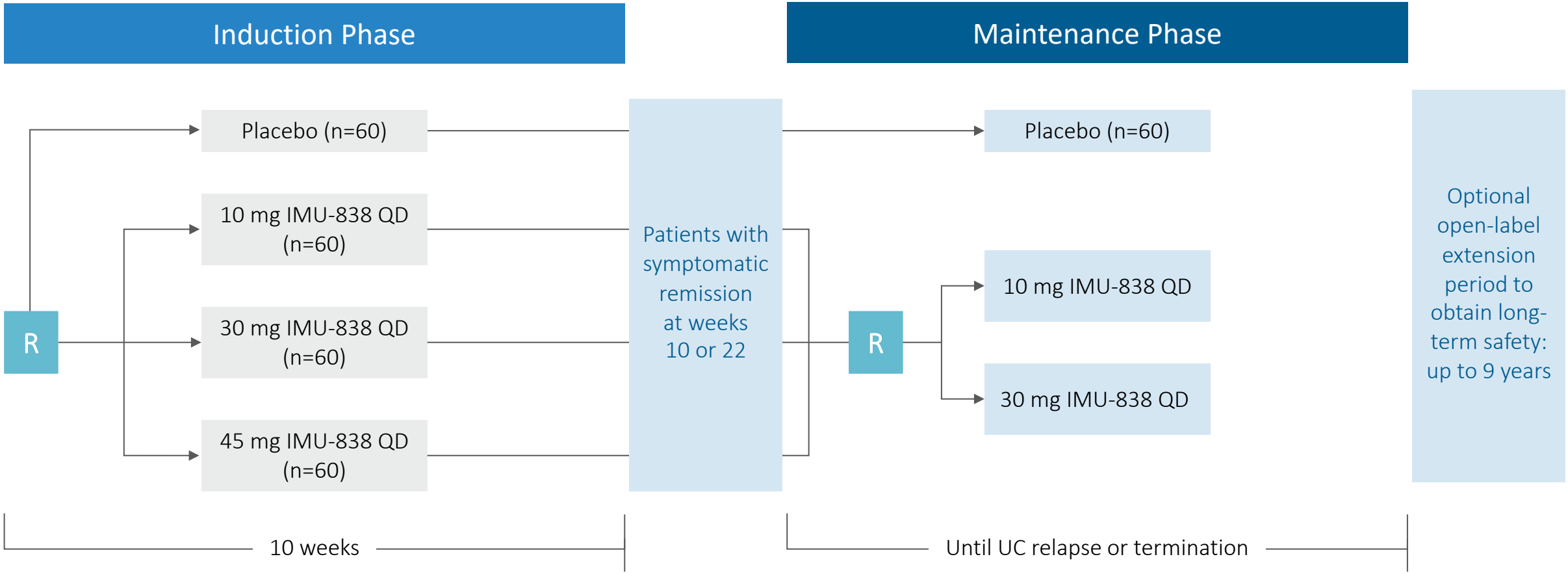
CALDOSE-1: Phase 2 Trial Design in UC

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

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 June of 2022

IND: investigational new drug

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

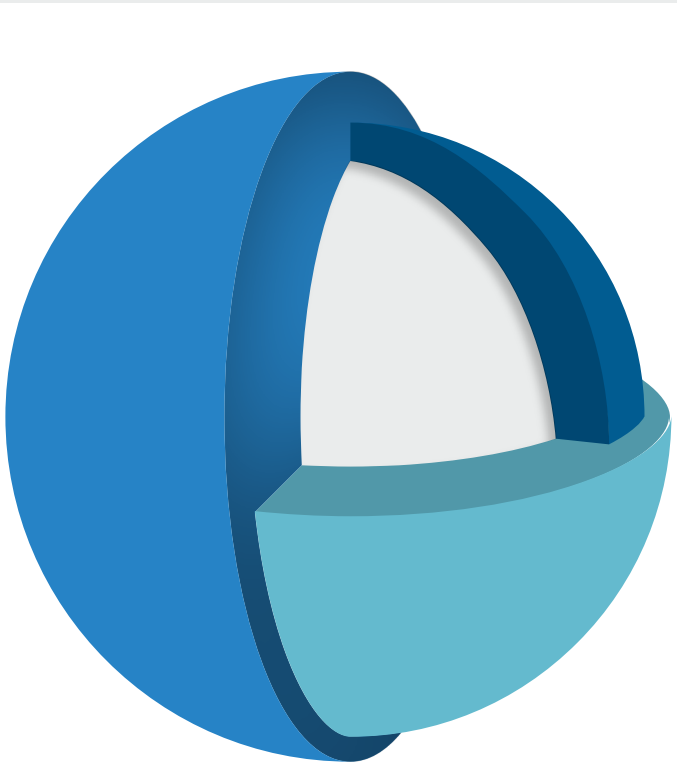
COVID-19

- 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: A Potentially Best-in-Class Oral IL-17 Inhibitor

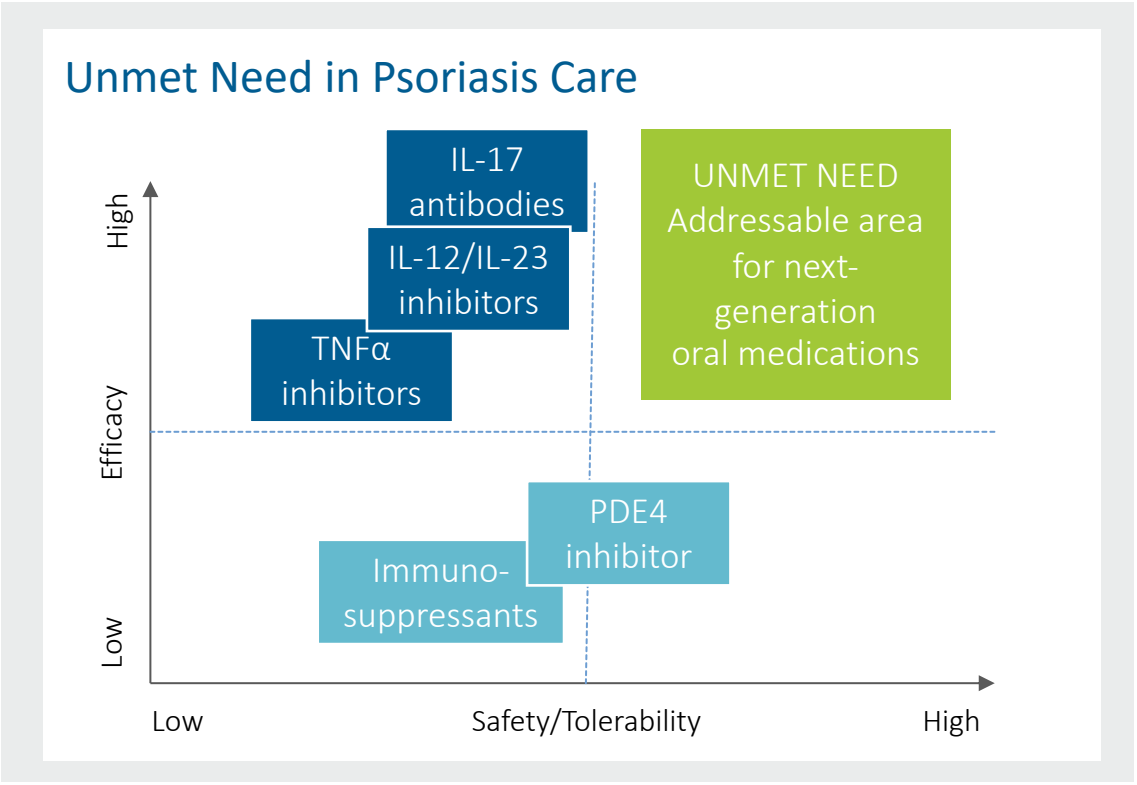
Uniquely Acting and Highly Selective RORγt Inverse Agonist

Clear Need for Potent and Specific Inhibition of IL-17 in Multiple Autoimmune Diseases

IL-17 is Significant in Many Autoimmune Diseases

- Imbalance between regulatory T cells (T_{regs}) and Th17 cells contributes to autoimmune diseases, with Th17 cells secreting pro-inflammatory cytokines such as IL-17[1]
- RORγt is a master regulator of Th17 development and expression of IL-17[2]
- Multiple diseases are driven by IL-17; many represent significant market opportunities beyond MS and IBD[3]:
  - Psoriasis (USD 18 billion)
  - Psoriatic arthritis (USD 7 billion)
  - Rheumatoid arthritis (USD 32 billion)

Goal: Develop a Potent, Specific, and Orally Available IL-17 Inhibitor

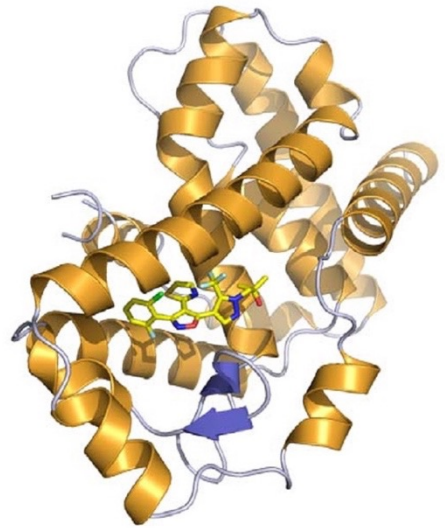


[1] Fasching, Patrizia, et al. Molecules 2017 22.1: 134 [2] Bassolas-Molina, Helena et.al., Front. Immunol., 22 October 2018 [3] DRG Clarivate 2020 G7 Markets
Th: T helper; IL: interleukin; TNF: tumor necrosis factor; PDE4: phosphodiesterase type 4; RORγ: retinoic acid receptor-related orphan nuclear receptor gamma

IMU-935 Inhibits Cytokines Associated With Autoimmune Diseases With an 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
Th17 differentiation (murine)[1]	0.135

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

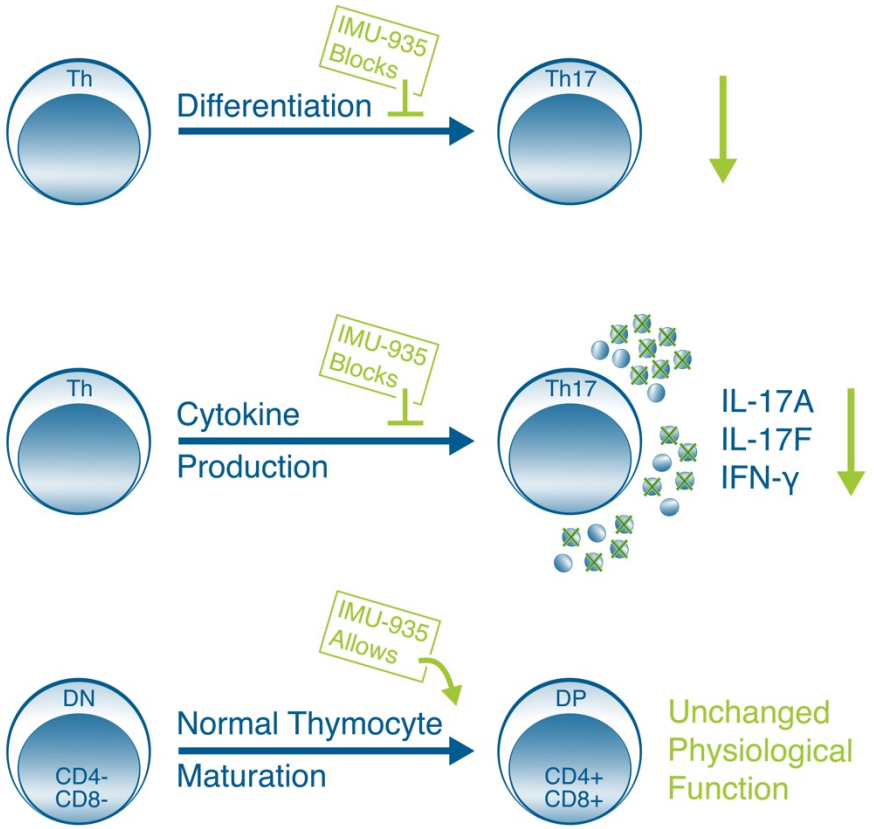


Co-crystal structure (Resolution 2.6 A) of a closely related derivative compound binds to hydroxycholesterol binding site of RORγ

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

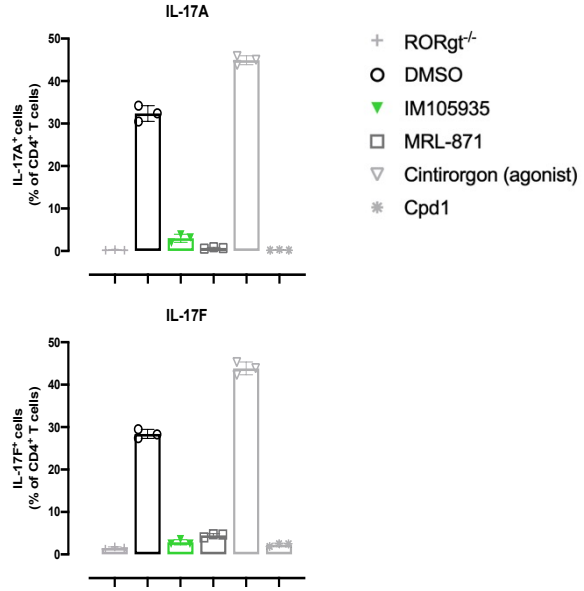


- The differentiation towards Th17 cells is inhibited by IMU-935
- The production of IL-17A and IL-17F is inhibited by IMU-935
- The physiological maturation of T cells within the thymus is not affected by IMU-935

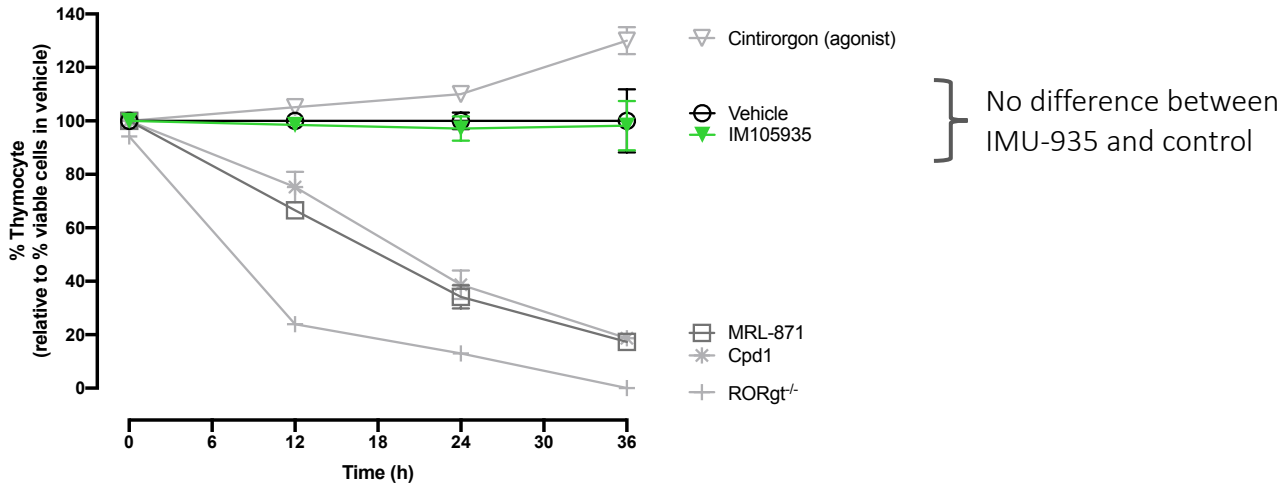
Th: T helper; IL: interleukin; IFN: interferon; DN: double-negative; DP: double-positive; CD: cluster of differentiation

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.



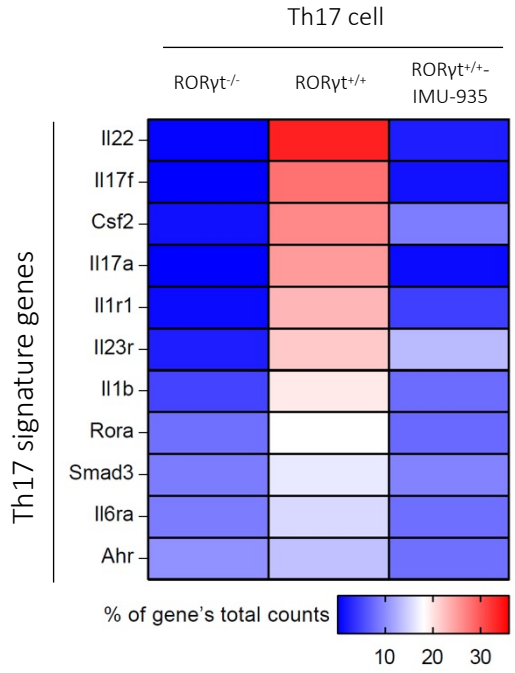
Impact on Th17 differentiation at 500 nM

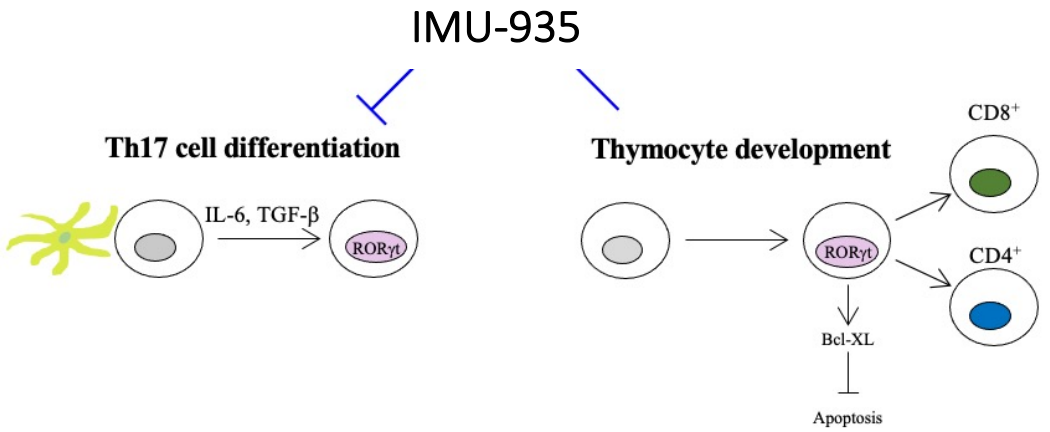


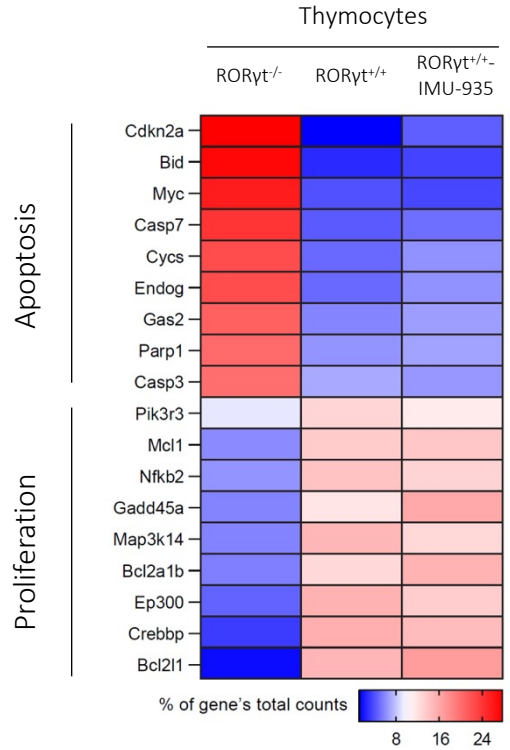
Impact on thymocyte viability at 1000 nM

Sun, Zuoming. City of Hope, 2021, unpublished

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







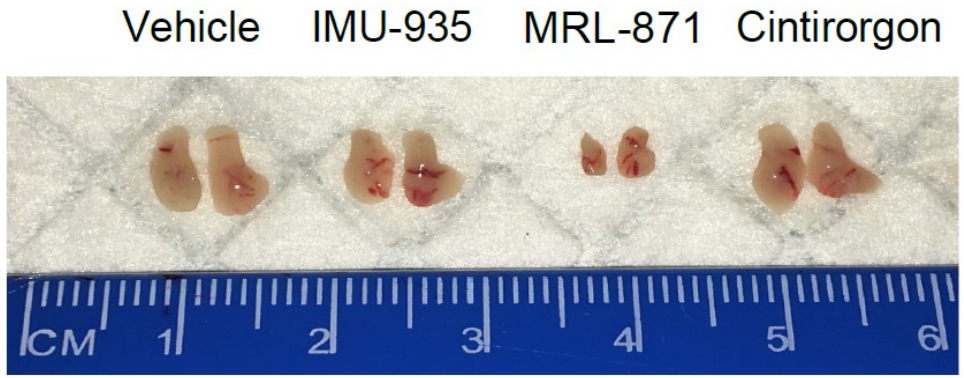
Similar gene expression pattern for Th17 signature genes in **RORγt knockout and wild type cells treated with IMU-935**

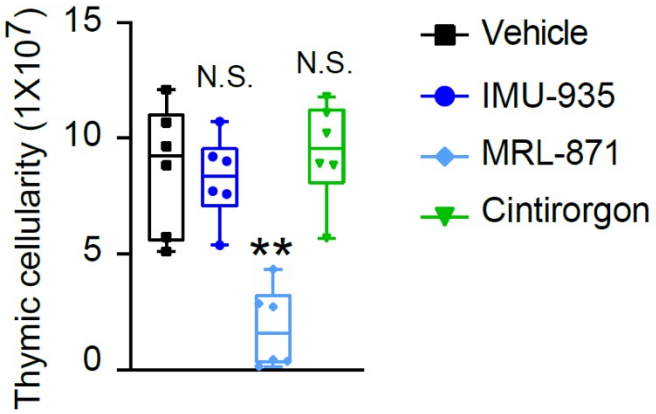
Different gene expression pattern for apoptosis and proliferation signature genes in **RORγ knockout** and **IMU-935 treatment**, but similar for RORγ+/+

Zuoming Sun, City of Hope, 2021

IMU-935 Allows Normal Thymocyte Maturation *In Vivo*
Acute Model, 3 Days of Treatment

- IMU-935 (100 mg/kg BID), MRL-871 (100 mg/kg BID) and Cintirorgon (30 mg/kg BID) were tested for 3 days in C57BL/6j mice



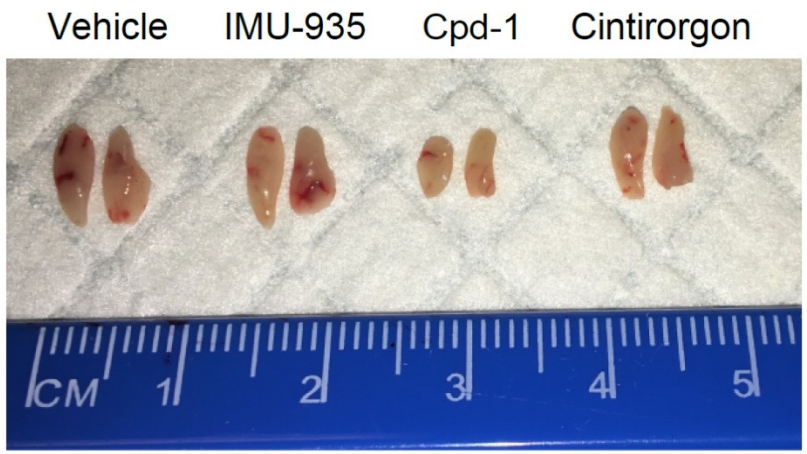


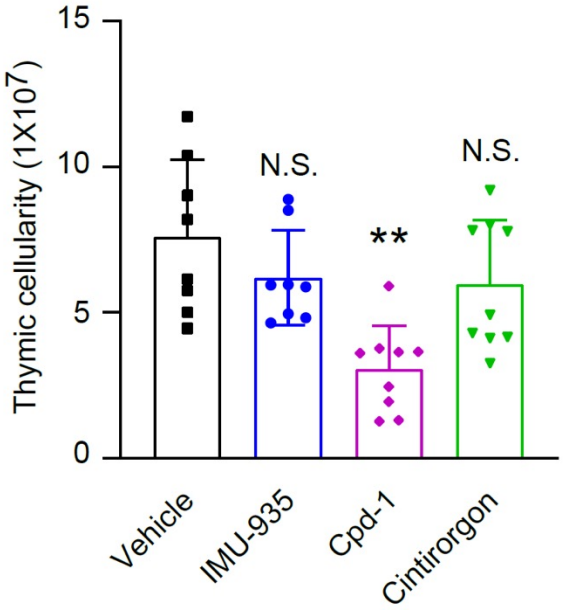
In contrast to MRL-871, **IMU-935 does not impact thymus size, thymocyte cell numbers or thymocyte maturation** in an acute mouse model.

Guo et al., 2016, Cell Reports (MRL-871), Guntermann et al., 2017, JCI Insight (Cpd1), Mahalingam et al., 2019, Clin Cancer Res. (Cintirorgon)
Sun, Zuoming. City of Hope, 2021, unpublished

IMU-935 Allows Normal Thymocyte Maturation *In Vivo*
Chronic Model, 28 Days of Treatment

- C57BL/6j mice (male, 9wks, n=8-9 per group) were administrated with IMU-935 (100 mg/kg), Cpd1 (40 mg/kg), or Cintirorgon (30 mg/kg) for 4 weeks (BID)





In contrast to Cpd1, **IMU-935 does not impact thymus size, thymocyte cell numbers or thymocyte maturation** in a chronic mouse model.

Guo et al., 2016, Cell Reports (MRL-871), Guntermann et al., 2017, JCI Insight (Cpd1), Mahalingam et al., 2019, Clin Cancer Res. (Cintirorgon)
Sun, Zuoming. City of Hope, 2021, unpublished

Phase 1 Clinical Trial: Trial Design and Current Status

PART A

Evaluation of single ascending doses (SAD)

—

Healthy human subjects randomized to receive single dose of IMU-935 or placebo

- Dose escalation completed: 100, 200, 300 and 400 mg of IMU-935
- Final PK analysis ongoing
- 79 subjects enrolled
- IMU-935 was well-tolerated and showed dose-linear PK

PART B

Evaluation of multiple ascending doses (MAD)

—

Healthy human subjects randomized to receive 14-day treatment of IMU-935 or placebo

- Dose escalation completed: 150 mg QD and 150 mg BID of IMU-935
- Final PK analysis ongoing
- 15 subjects enrolled
- IMU-935 was well-tolerated and steady-state was achieved after 3-6 days of dosing

PART C

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

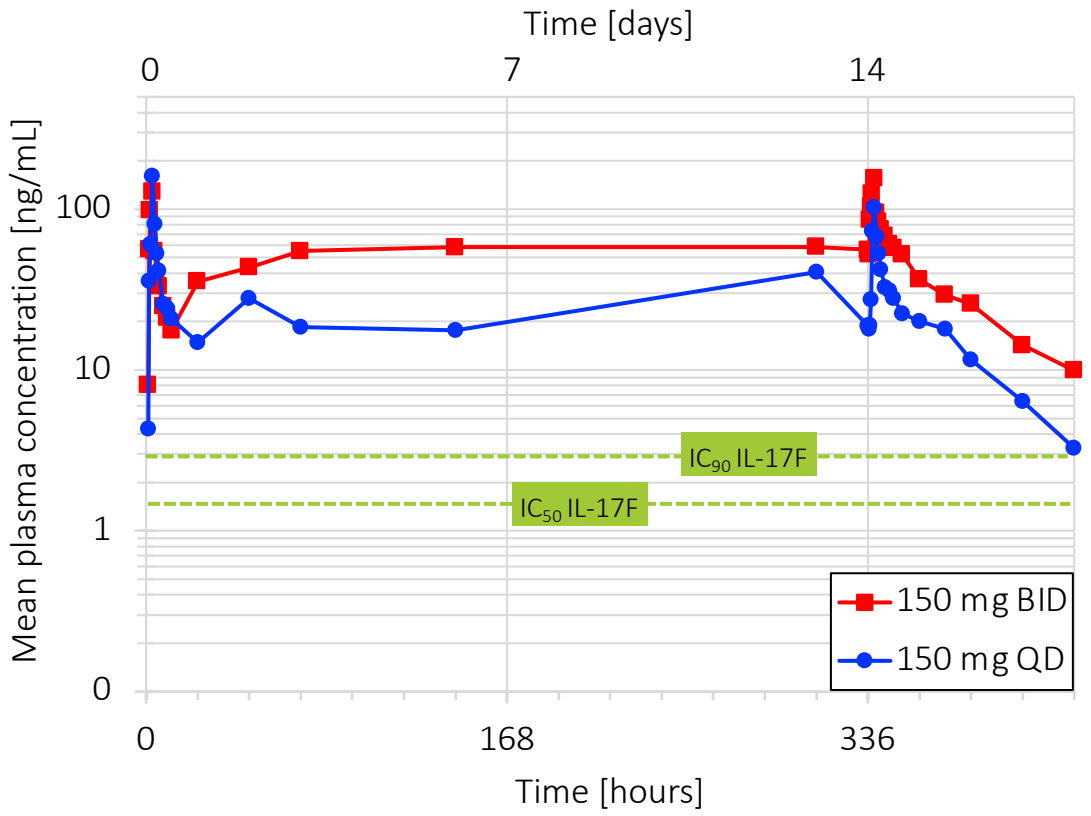
- 150 mg QD and 150 mg BID of IMU-935
- Approximately 52 patients planned to be enrolled
- Initial data expected to be available in H2/2022

PK: pharmacokinetic; QD: quaque die = once-daily; BID: bis in die = two times daily

Phase 1 Clinical Trial: Pharmacokinetic Results

Part B: Summary of QD and BID Dosing Regimen for IMU-935

IMU-935 concentration time profiles (log-linear scale)



Favorable PK Properties for IMU-935 at Steady-State Observed

Pharmacokinetic parameters in steady-state (mean)	150 mg QD	150 mg BID
$C_{max, ss}$ (ng/mL)	124	206
$C_{min, ss}$ (ng/mL)	15.7	48.5
$T_{max, ss}$ (hr)	2.8	2.4
$t_{1/2, ss}$ (hr)	29.0	38.0
AUC_{last} (hr*ng/mL)	1540	3040

Non-compartmental analysis

- Fast achievement of steady-state within first week and stable steady-state trough levels over 14-day treatment period.
- Accumulation factors of 1.29 (150 mg QD) and 2.21 (150 mg BID) allowing predictable trough levels.

Interim data, PK analysis ongoing

QD: quaque die = once-daily; BID: bis in die = two times daily; PK: pharmacokinetic; ss: steady-state; C_{max}: maximum plasma drug concentration; T_{max}: time to reach maximum plasma concentration; hr: hours; $t_{1/2}$: half-life; AUC_{last}: area under the concentration-time curve from dosing to last measurement

Accumulation factors were calculated as the relationship of $AUC_{0\text{-}tau}$ of Day 14/Day 1 (after first dosing).

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Phase 1 Clinical Trial: Summary of Safety and Tolerability Findings
Part B

Daily Dosing of IMU-935 in Healthy Human Subjects Over 14 Days Was Found to Have a Favorable Safety and Tolerability Profile

- No serious adverse events
- No dose-dependency in adverse events
- No maximum tolerated dose reached
- No trends for post-dose changes in any laboratory parameter
- No adverse events regarding any laboratory parameter
- No medically relevant changes in vital signs or 12-lead electrocardiograms as compared to placebo

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Phase 1 Clinical Trial: Ongoing Part C in Psoriasis Patients

Study Design

- Double-blind, placebo-controlled dose escalation study to evaluate safety, tolerability, pharmacodynamics and exploratory efficacy of IMU-935 in patients with moderate-to-severe psoriasis
- Psoriasis patients will receive 28 days of daily treatment
- Up to 52 psoriasis patients will be enrolled in 2 cohorts:
  - First cohort will receive a low dose of IMU-935 (150 mg QD) or placebo at a ratio of 3:1
  - Second cohort will receive a high dose of IMU-935 (150 mg BID) or placebo at a ratio of 3:1
- Initial results from part C are expected to be available in H2/2022

QD: quaque die = once-daily; BID: bis in die = two times daily

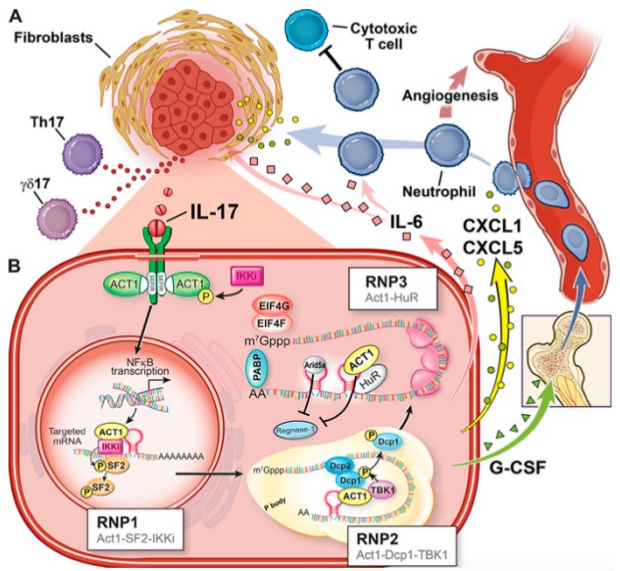
IMU-935 As Treatment Option in Castration-Resistant Prostate Cancer Targeting Key Resistance Mechanism

Inhibition of RORγ

- The androgen-receptor mutant variant AR-V7 lacks the ligand-binding domain – which is the target of enzalutamide and abiraterone – and 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



RORγ in Myeloid-Derived Suppressor Cells

- Myeloid-specific expression of RORγ marks advanced cancer inflammation.
- Expansion of circulating RORγ+ myeloid cells is associated with an increased number of MDSCs. Inhibition of RORγ in myeloid cells reprograms cancer myelopoiesis in favor of effector APCs with antitumoral effects.[1]
- IL-17 mediates the induction, recruitment and expansion of MDSCs.

AR-V7: androgen receptor variant 7/mutated form; MDSC: myeloid-derived suppressor cells; APC: antigen presenting cells; Th: T helper; IL: interleukin

[1] Strauss et al., Cellular & Molecular Immunology (2021); Illustration: Zhao, J., Chen, X., Herjan, T., Li, X.; J Exp Med 6 January 2020; 217 (1): e20190297

Immunic THERAPEUTICS

Phase 1 Clinical Trial of IMU-935 in CRPC
NCT05124795

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
- Main treatment will be single agent IMU-935 for 3 cycles of 28 days each
- Dose escalation follows a Bayesian optimal interval (BOIN) design
- An expansion cohort can be added at a therapeutically active dose level
- Patients who benefit can receive extended treatment
- At each dose level:
  - A safety analysis after 28 days will be performed to consider start of next dose
  - An interim activity analysis after 3 months of treatment will be performed
  - A main cohort analysis will be performed when the last patient in treatment reaches the 6 months follow-up visit

Principal Investigator

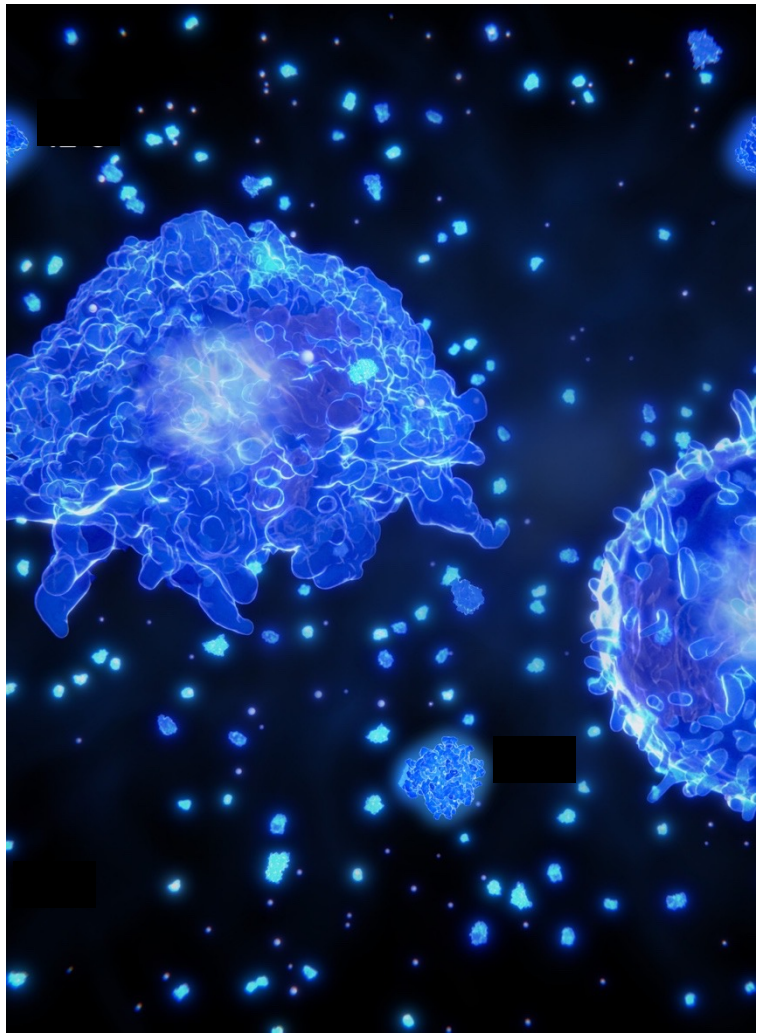
Johann Sebastian de Bono, M.D., Ph.D.

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-935: A Potentially Best-in-Class Oral IL-17 Inhibitor



- IMU-935 showed a very **favorable safety, tolerability and PK profile** in this phase 1 clinical trial with no serious adverse events seen in the SAD and MAD parts.
- In particular, IMU-935 was **safe and well-tolerated** in 14-day repeated oral dosing in healthy human subjects at doses expected to exceed required therapeutic dosing.
- IMU-935's outstanding **selectivity profile on Th17 over thymocyte development** was confirmed in an impressive fashion in a mouse model.
- IMU-935 is currently being tested in psoriasis patients with initial data expected in H2/2022 – setting the stage for a potential **best-in-class oral** psoriasis therapy.
- IMU-935 may offer **extensive potential** beyond psoriasis in other autoimmune diseases.

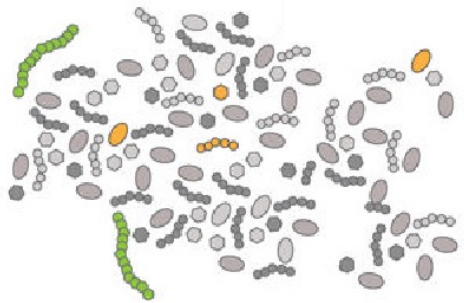
IMU-856

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

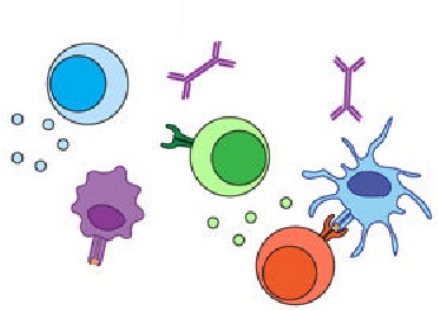


Influencing the Microbiome

- 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)

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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 human subjects (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

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Summary

Multiple Clinical Data Readouts for All Three Development Programs Expected Throughout 2022

Advanced clinical pipeline:
three differentiated products in various phases of clinical development

Oral IL-17 inhibitor IMU-935:
proof-of-concept data in psoriasis expected in H2/2022; further development in CRPC

RMS phase 3 program of vidofludimus calcium ongoing, to be supported by neuroprotective data from PMS phase 2 trial

IMU-856 for intestinal barrier function:
unblinded phase 1 safety data expected in Q3/2022

UC phase 2 data of vidofludimus calcium expected in June of 2022

Cash runway through Q1/2023

Shares outstanding: 27,906,942 (as of February 18, 2022)

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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