



**Immunic**  
THERAPEUTICS

# Immunic Therapeutics

Developing Selective Oral Therapies in Immunology

NASDAQ: IMUX | May 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.

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

# Our Mission



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



# Leadership Team



## Company is Led by an Experienced Management Team



Daniel Vitt,  
PhD  
CEO &  
President



Duane  
Nash, MD,  
JD, MBA  
Executive  
Chairman



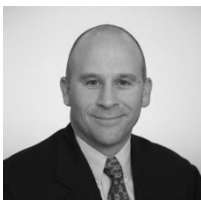
Andreas  
Muehler,  
MD, MBA  
CMO



Hella  
Kohlhof,  
PhD  
CSO



Patrick  
Walsh  
CBO



Glenn  
Whaley  
CFO



Inderpal  
Singh  
General  
Counsel



## Renowned International Board of Directors



Duane  
Nash, MD,  
JD, MBA  
Executive  
Chairman



Daniel Vitt,  
PhD  
CEO &  
President of  
Immunicon



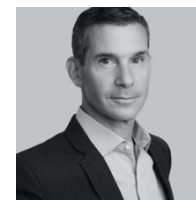
Tamar  
Howson,  
CFA  
Independent  
Director



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				<ul style="list-style-type: none"><li>▪ RMS interim analysis planned after approx. half of the events occurred</li><li>▪ PMS interim analysis planned after half of the patients completed 24 weeks of treatment</li><li>▪ June 2022: top-line UC data expected</li></ul>
		Progressive Multiple Sclerosis (PMS) – CALLIPER Trial				
		Ulcerative Colitis (UC) – CALDOSE-1 Trial				
		Crohn’s Disease (CD)				
Primary Sclerosing Cholangitis (PSC)						
IMU-935	IL-17 / RORyt	Psoriasis				<ul style="list-style-type: none"><li>▪ H2/2022: initial psoriasis data expected</li><li>▪ Q3/2022: initial CRPC safety data expected</li></ul>
		Castration-Resistant Prostate Cancer (CRPC)				
IMU-856	Intestinal Barrier Function	Celiac Disease				<ul style="list-style-type: none"><li>▪ Q3/2022: SAD/MAD safety data expected</li></ul>

■ Completed or ongoing   ■ In preparation or planned



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# 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<sup>[1]</sup>

- 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<sup>[2,3]</sup>



## Gap in Treatment Options

- MS (40%) and UC (25-40%) have significant group of untreated patients<sup>[1]</sup>
- 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>

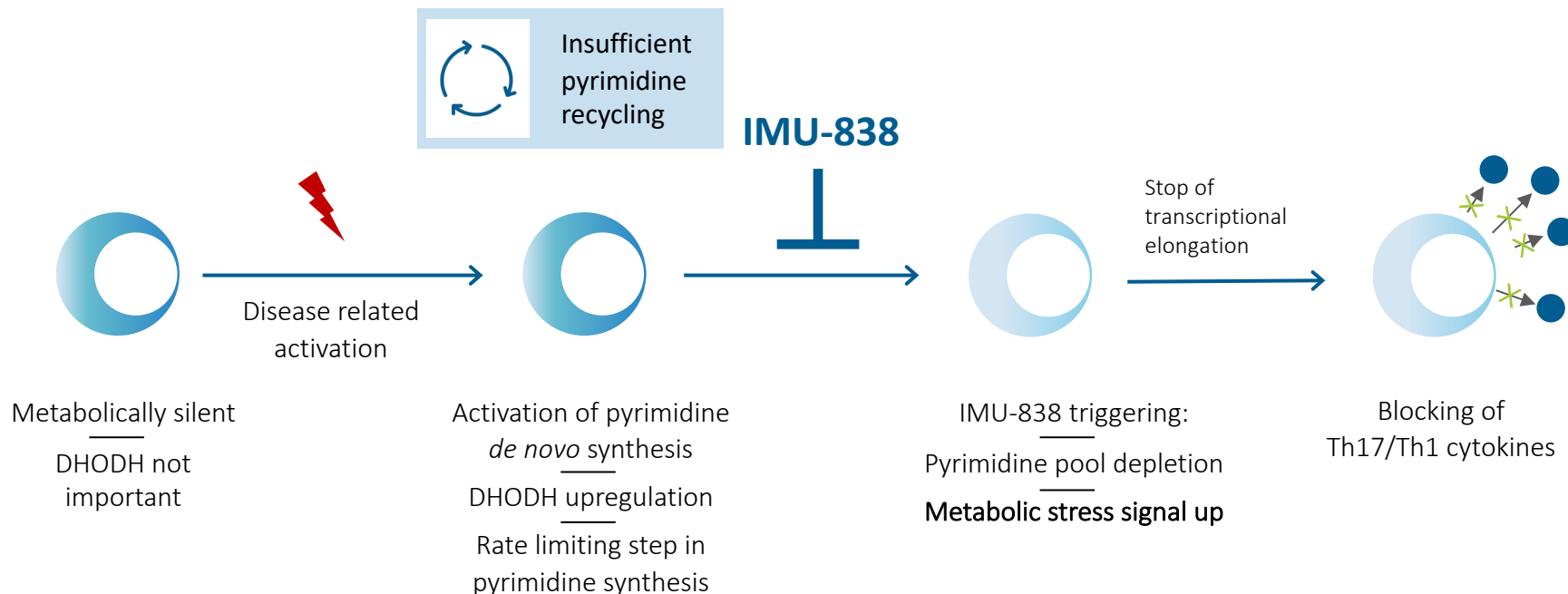
# Vidofludimus Calcium Selectively Targets Only Hyperactive Immune Cells

Lymphocyte

Activated  
Lymphocyte

“Stressed”  
Lymphocyte

Pharmacological  
Effects



Preserves normal  
immune cell function  
and numbers

→ No nonspecific  
immunosuppression

→ Maintains  
vaccination  
efficacy<sup>[1]</sup>

→ 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; Th: T helper



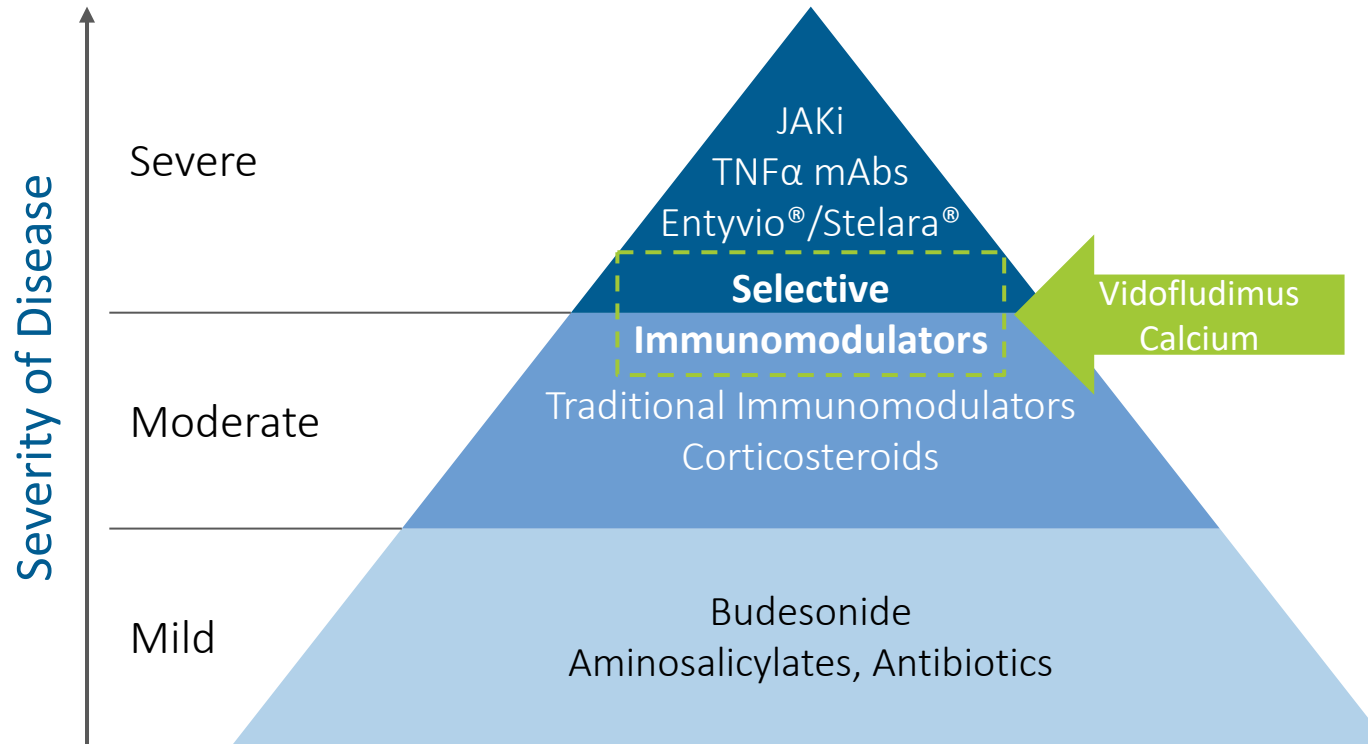


Vidofludimus Calcium in Inflammatory Bowel Disease (IBD)

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“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 Moderate-to-Severe IBD Patients

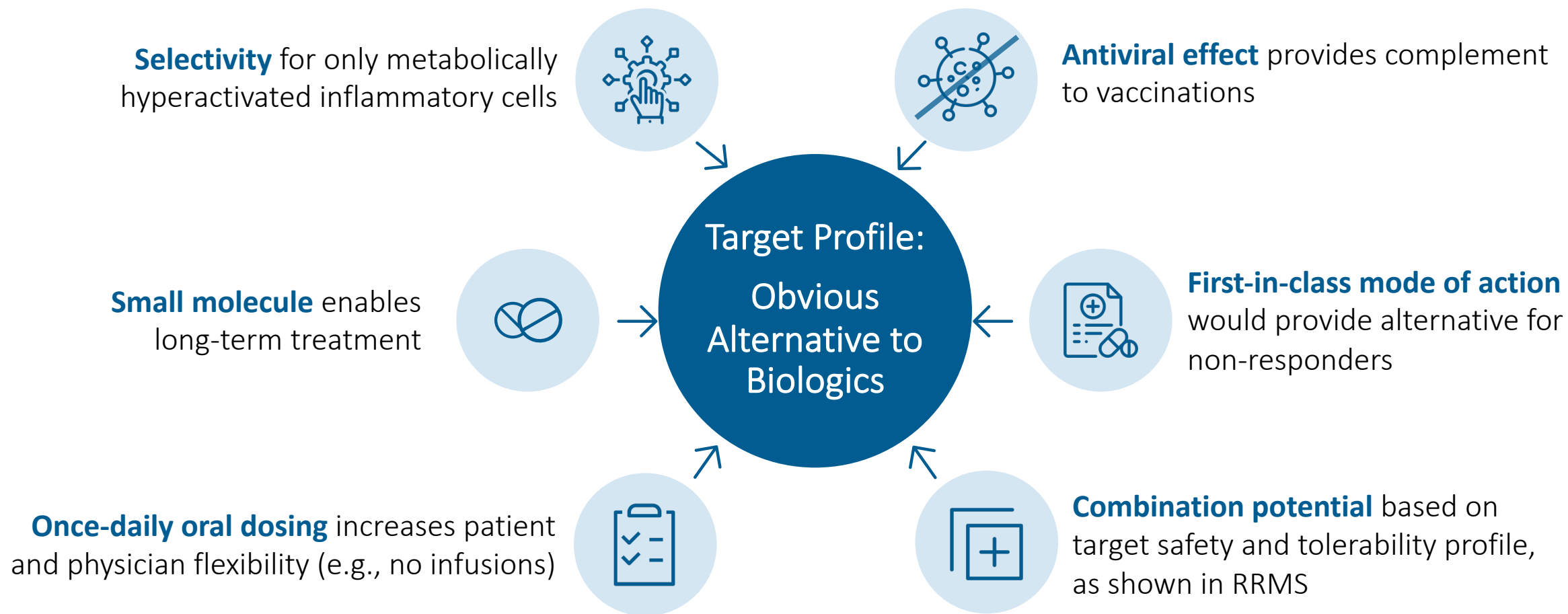


## Goal: New Standard of Care

- 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

JAKi: Janus kinase inhibitors; TNF: tumor necrosis factor; mAb: monoclonal antibody; RRMS: relapsing-remitting multiple sclerosis

# Vidofludimus Calcium is Targeted to Address Limitations of Existing IBD Therapies



# Strong Indications for Vidofludimus Calcium's Activity in IBD



## Crohn's Investigations Confirm DHODH Activity

Investigator-initiated studies of leflunomide in adults with CD:

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



## 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, and 91.7% in ulcerative colitis

[1] Holtmann, MH., et al. Dig Dis Sci (2008) 53: 1025 [2] Prajapati, DN al. Journal of Clinical Gastroenterology: 2003(37): 125  
CD: Crohn's disease; RRMS: relapsing-remitting multiple sclerosis



## EMPhASIS Trial: Phase 2 Data 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



## CALDOSE-1 Trial: Interim Analysis

- Performed by an unblinded data review committee
- Analysis based on all available clinical, endoscopic, biomarker, pharmacodynamic, and safety data
- Established a potentially broad effective dose range
- No intolerable dose identified; no safety signal observed



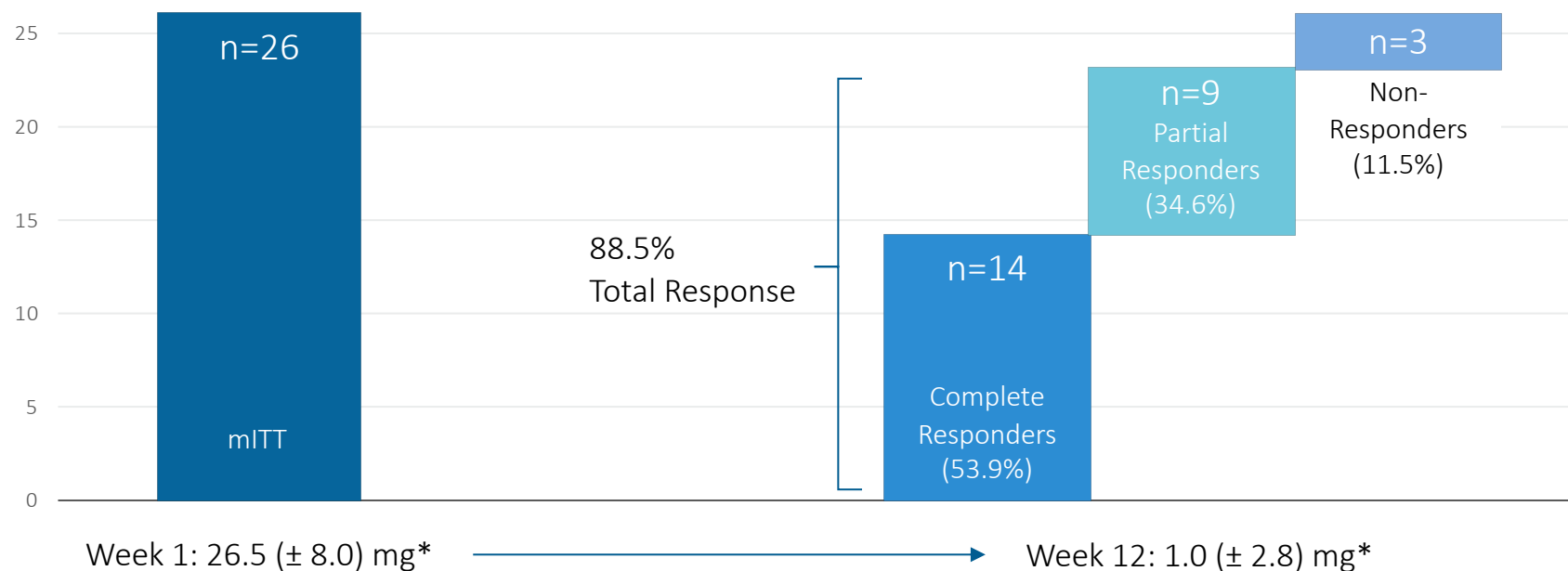
# ENTRANCE Study: Primary Efficacy Results



## ENTRANCE Study:

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

Number of Patients



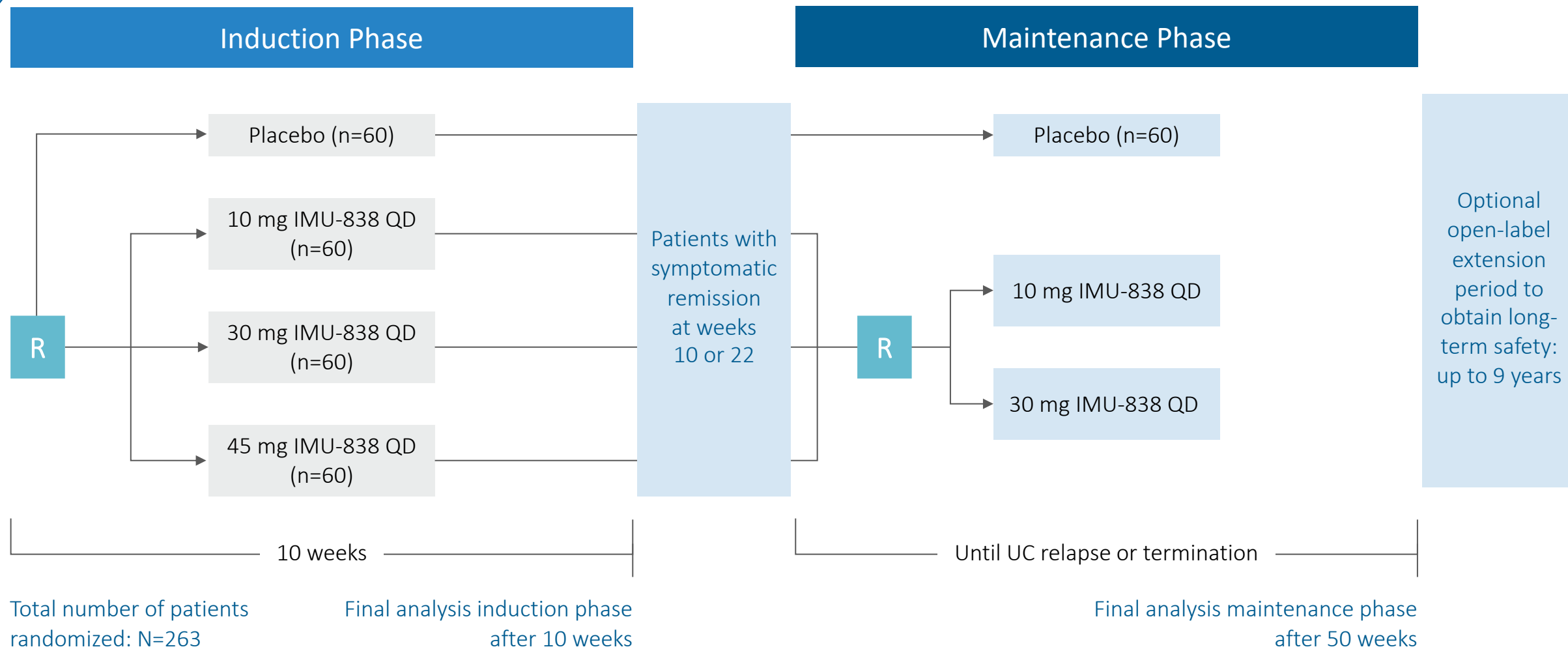
Vidofludimus had response rates of: 85.7% in Crohn's disease  
91.7% in ulcerative colitis

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

# CALDOSE-1: Phase 2 Trial Design in UC

NCT03341962



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

# 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



### Patient Population:

- Male and female patients, aged 18 to 80 years
- Previous treatment failure with immuno-modulators, steroids or biologicals
- Active symptoms defined as a Mayo stool frequency score of  $\geq 2$  and a modified Mayo endoscopy subscore of  $\geq 2$  at the screening flexible sigmoidoscopy (independent central reader)



### Primary Endpoint:

Proportion of patients with symptomatic remission and endoscopic healing at **week 10**



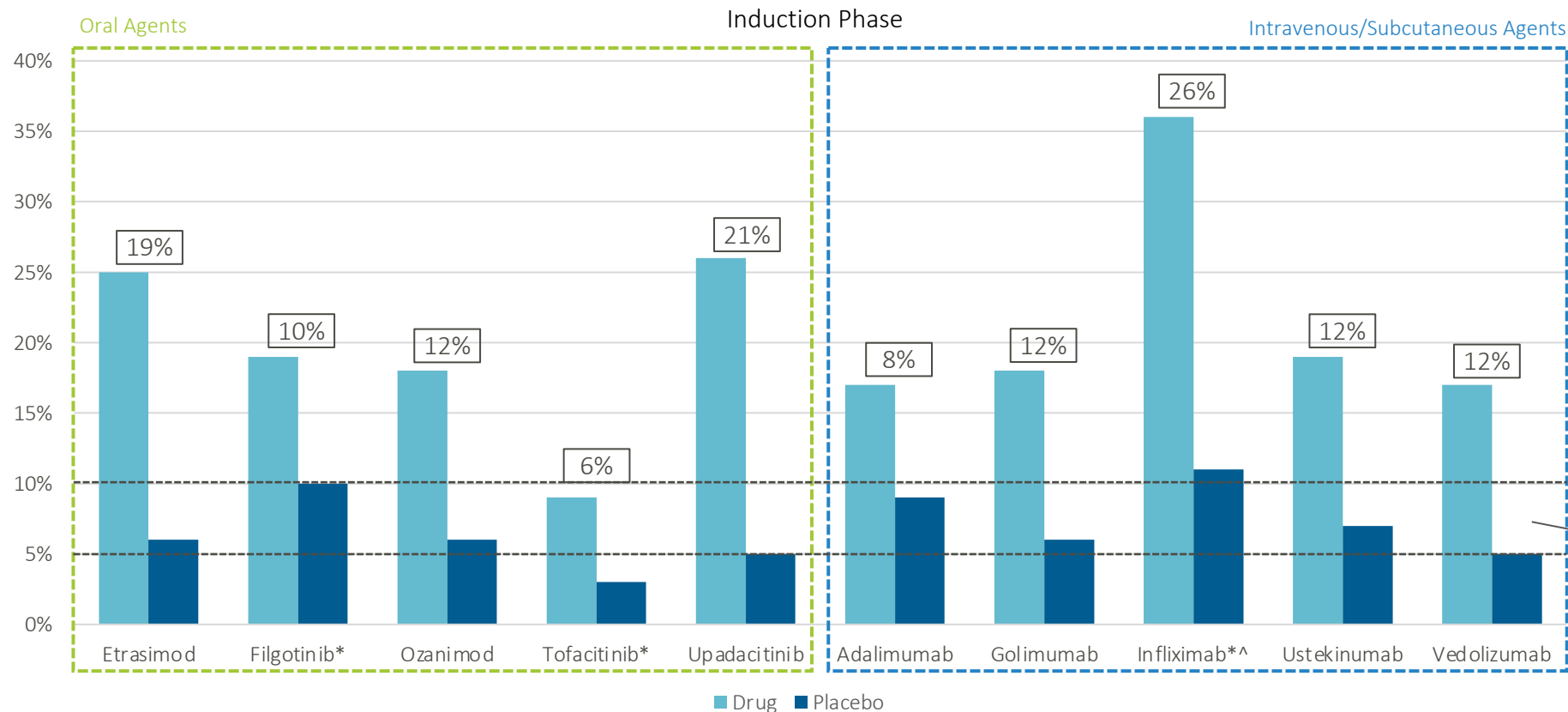
### Timelines:

Currently estimated to deliver top-line data in **June of 2022**

IND: investigational new drug

# UC Drugs Treatment Effect in Clinical Remission Rate

## FDA 2016 Guideline



\*Average of clinical study results ^Naïve to tumor necrosis factor (TNF) blocker  
Source: Jefferies Group LLC (2021): IBD Deep Dive - The Current and Emerging Landscape





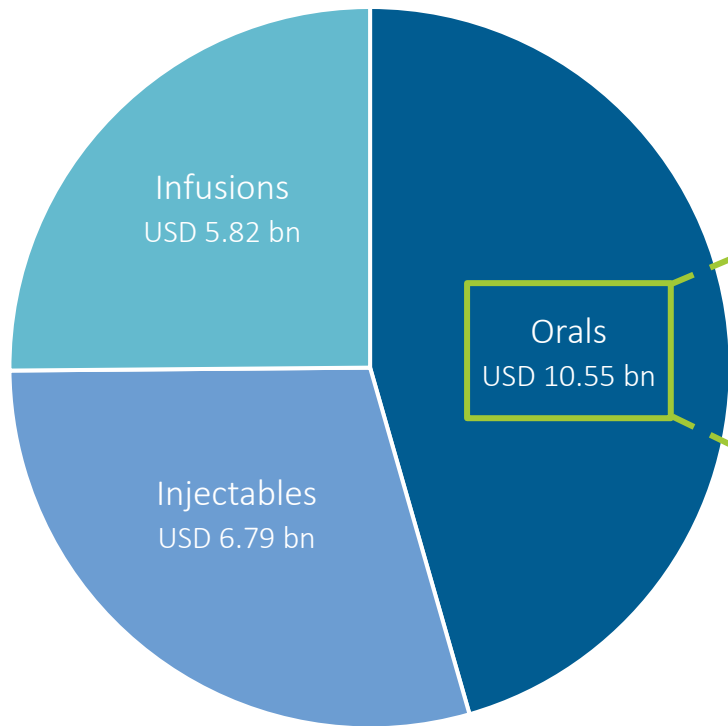
Vidofludimus Calcium in Multiple Sclerosis (MS)

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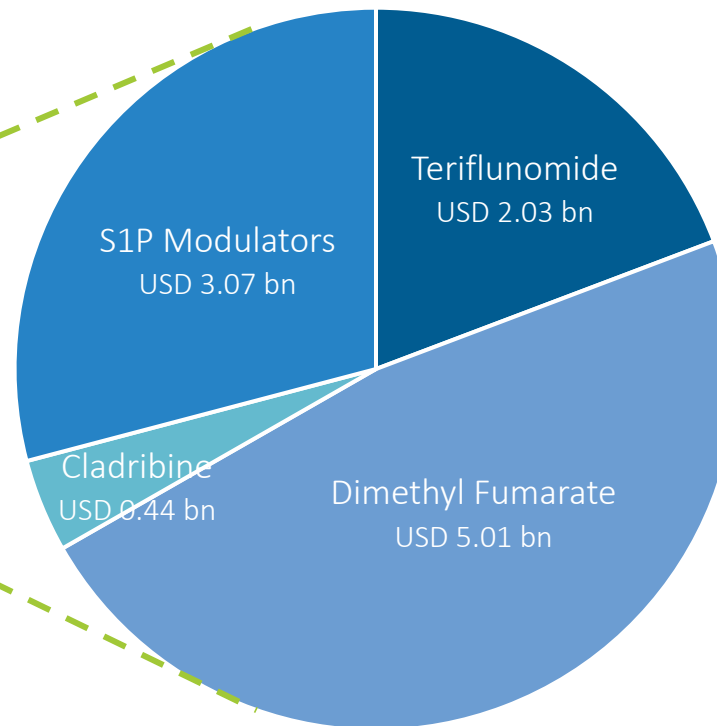
“Designed to be the Easy-to-Use,  
Uniquely Safe, Well-Tolerated and  
Efficacious MS Treatment”

# 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-life

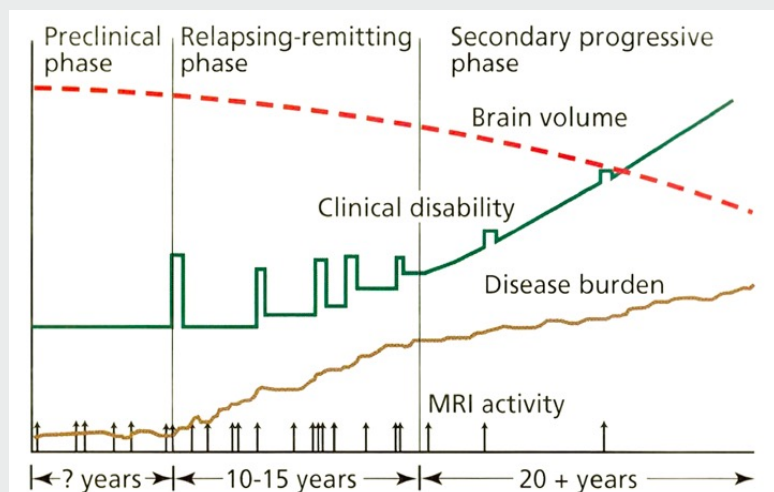
\* Sales numbers in G7 countries (US, UK, Canada, Japan, Germany, France, Italy) in USD billion; S1P: sphingosine-1-phosphate  
Source: Multiple Sclerosis Landscape and Forecast by Decision Resources Group Part of Clarivate

# 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)<sup>[1]</sup>
- 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; M: million

[1] MS International Federation (2020): Atlas of MS. <https://www.atlasofms.org/map/global/epidemiology/number-of-people-with-ms>; illustration adapted from Fox RJ, Cohen JA. Cleve Clin J of Med, 2001; 68:157-70

# 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)<sup>[1,2]</sup>

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



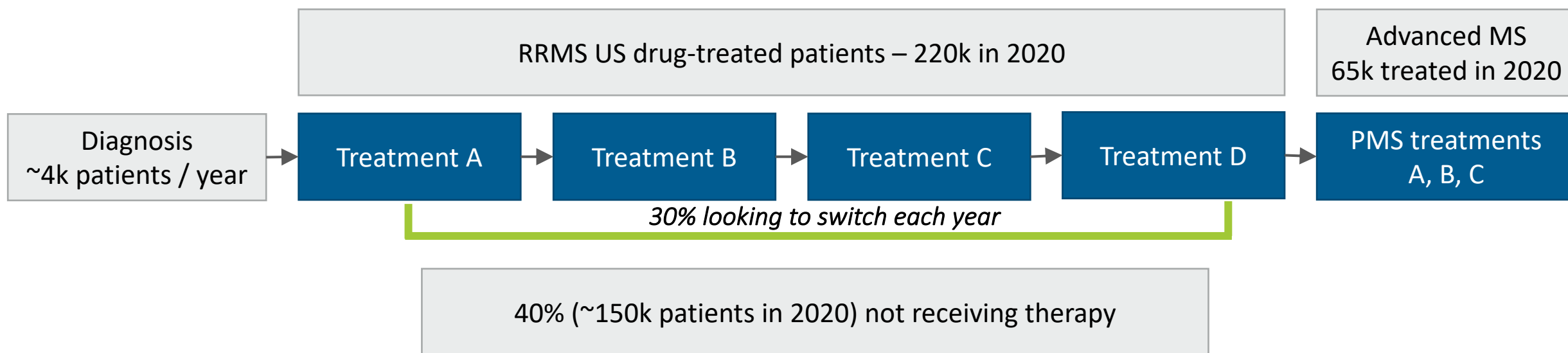
Existing treatment options do not adequately address near or long-term needs of patients

[1] DRG - Treatment Algorithms CDA Multiple Sclerosis US May 2021 [2] Spherix Real World Dynamix\_DMT Switching in MS\_US\_2021



# 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; RRMS: relapsing-remitting multiple sclerosis

# 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

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



## Intended Value for Patient

- Clear therapeutic benefits
  - Reduction of relapses and MRI lesions
  - Prevent and/or delay disability worsening
  - Confirmed reduction in neurofilament light chain
- Outstanding safety and tolerability profile
  - Low rate of adverse events → not disturbing social and work life
  - No/low infection risk (inclusive of PML)
- Oral, easy to manage medication



## Intended Value for Neurologist

- Selective targeting of disease-related immune cells while preserving important immune functions
- Applicable for different disease stages in the journey of an MS patient
- Reliable clinical activity
- Long-term utility with low discontinuation rates
- Easy on- and off-dosing
- Reduced monitoring requirements

PML: progressive multifocal leukoencephalopathy

# EMPhASIS Trial: Strong Reduction of MRI Lesion Activity

## Pooled Cohorts 1 & 2

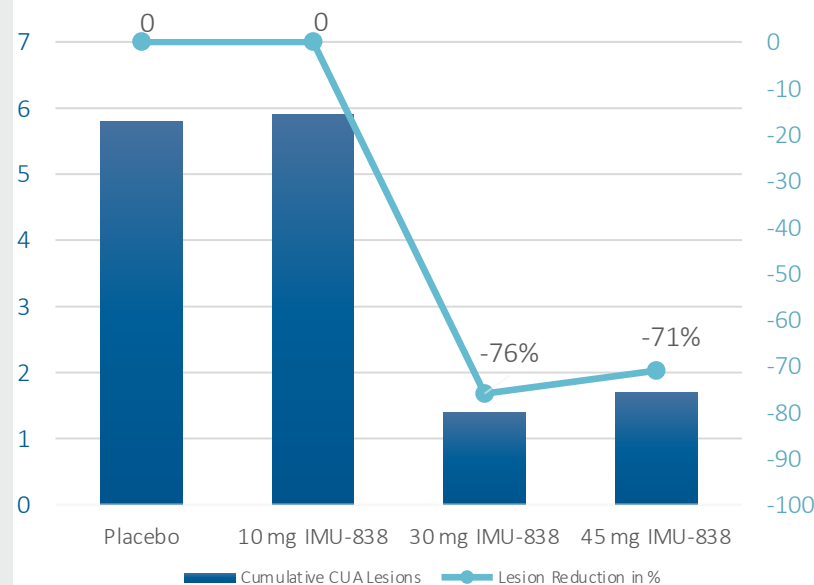
### Double-Blind, Placebo-Controlled, Randomized, Parallel-Group Phase 2 Trial in RRMS

- Blinded main treatment period of 24 weeks
- Randomized 268 patients in 36 centers across four European countries
- Cohort 1: 30 and 45 mg or placebo
- Cohort 2: 10 mg or placebo
- Extended treatment period of up to 9.5 years to observe long-term safety

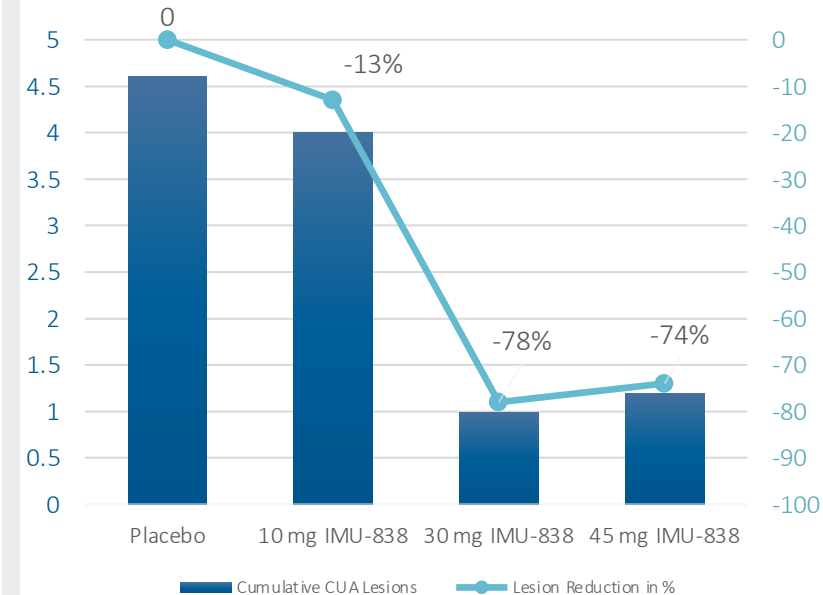
### Efficacy Endpoints

- Cumulative number of new CUA and Gd+ MRI lesions up to week 24
- Primary endpoint: Difference in CUA MRI lesions between 45 mg/day vidofludimus calcium and placebo
- Primary and key secondary endpoints met with high statistical significance (primary:  $p = 0.0002$  / key secondary:  $p < 0.0001$ )

Reduction in Cumulative CUA Lesions up to Week 24



Reduction in Gd+ Lesions up to Week 24



As Cohort 2 only allowed MRI machines of 1.5T, pooled data of Cohorts 1 & 2 only include patients that were evaluated at MRI field strength of 1.5 Tesla. Modified full analysis set C1/C2 (N10 = 47, N30 = 65, N45 = 66, NPBO C1 = 59, NPBO C2 = 12)

Data displayed are as adjusted mean values. Estimates are adjusted for baseline volume of T2 lesions and baseline number of Gd+ lesions (0,  $\geq 1$ ) using a generalized linear model with a negative binomial distribution and a logarithmic link function. Log transformation of time from first investigational medicinal product (IMP) dose to date of last MRI assessment with non-missing values is used as offset term.

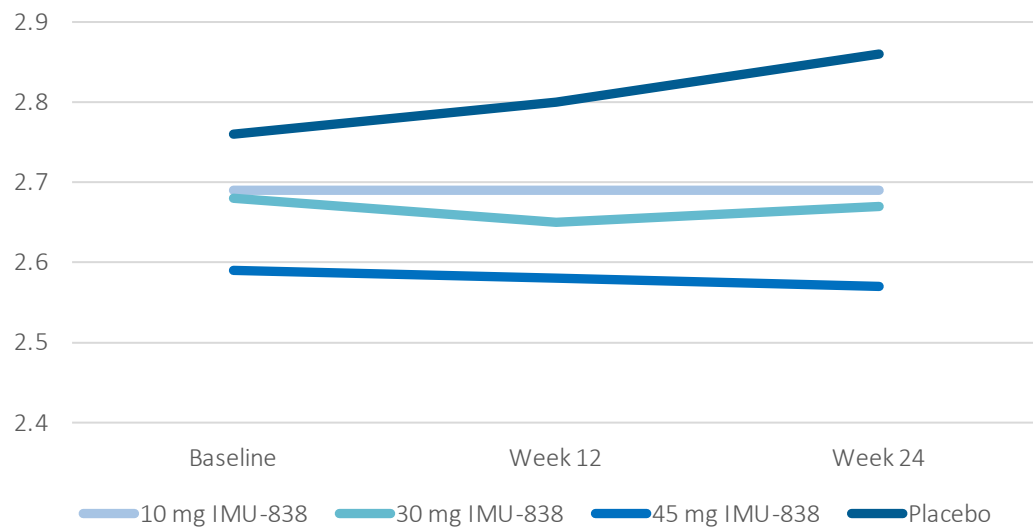
RRMS: relapsing-remitting multiple sclerosis; MRI: magnetic resonance imaging; CUA: cumulative unique active, Gd+: gadolinium-enhancing



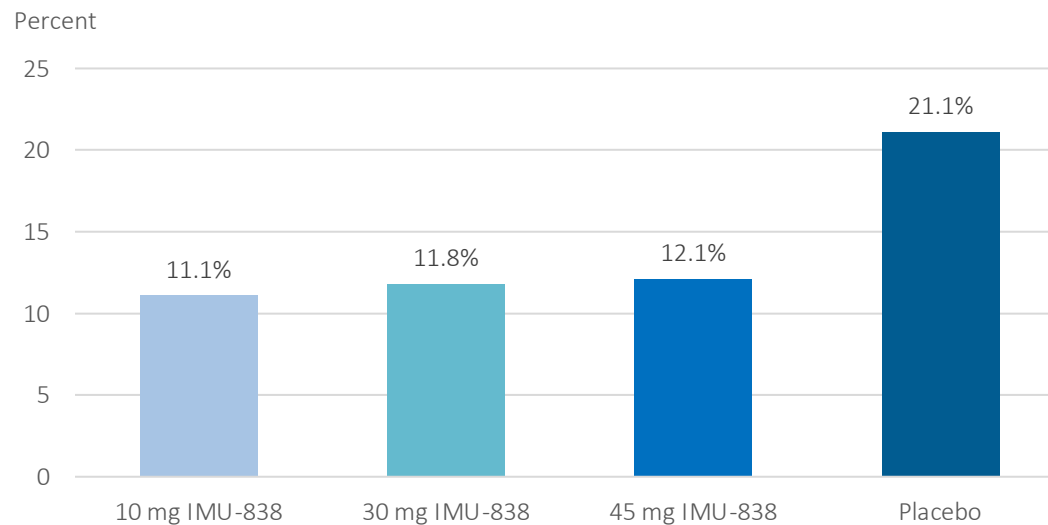
# EMPhASIS Trial: Encouraging Signals of Neuroprotective Effects

## Based on EDSS Assessments, Pooled Cohorts 1 & 2

Change of EDSS from Baseline to Week 24

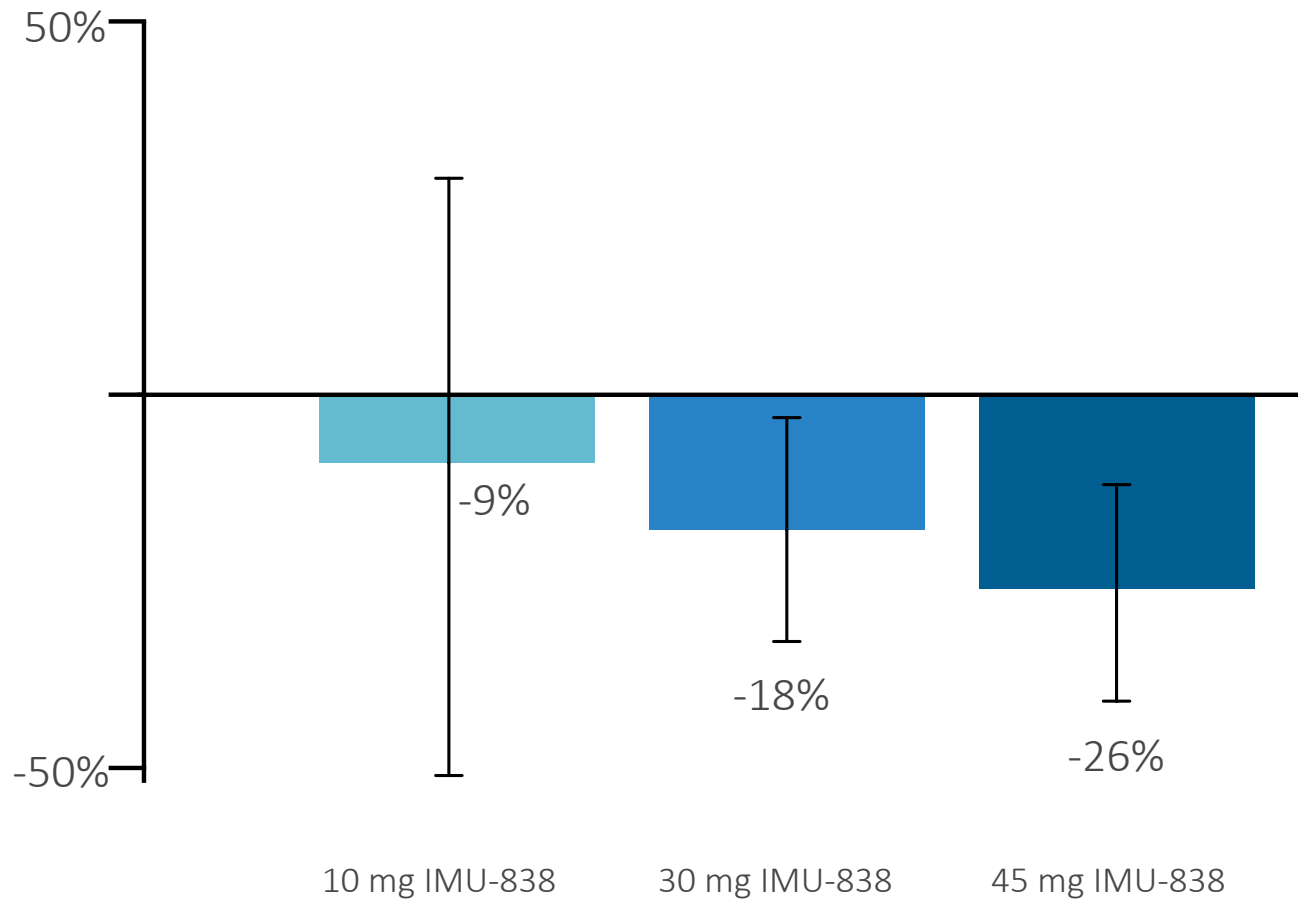


Proportion of Patients With Unconfirmed EDSS Progression up to Week 24



Displayed are mean values, combined data for Cohort 1 and 2 patients  
EDSS: Expanded Disability Status Scale

# EMPhASIS Trial: Relative Change of Serum NfL Concentrations Versus Placebo After 24 Weeks, Pooled Cohorts 1 & 2



The relative change of serum neurofilament light chain versus placebo is proportional to vidofludimus calcium dose.

- May reflect increasing trough levels and related improved effects of vidofludimus calcium
- Should favor higher doses when neuroprotective effects are more important

Displayed are median values of differences between percentage change of serum neurofilament light chain concentration (Hodges-Lehmann estimation), treatment vs. placebo, combined data for Cohort 1 and 2 patients  
NfL: neurofilament

# EMPhASIS Trial: 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 <sup>[1]</sup>	Teriflunomide <sup>[2]</sup>	Dimethyl Fumarate <sup>[3]</sup>	Fingolimod <sup>[4]</sup>	Ozanimod <sup>[5]</sup>
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; RRMS: relapsing-remitting multiple sclerosis

[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

# Vidofludimus Calcium Showed Interesting Hints for Clinical Anti-SARS-CoV-2 Activity



Treatment Tends to Decrease the Number of Opportunistic COVID-19 Infections

	IMU-838 (10 mg QD)	Placebo
Any Infection	17% (8/47)	33% (4/12)
COVID-19	<b>8.5%</b> (4/47)	<b>25%</b> (3/12)

Phase 2 EMPHASIS Trial in RRMS  
Number of reported COVID-19 infections in Cohort 2



Treatment Does Not Interfere With Antibody Development During SARS-CoV-2 Infection

	Day 6		Day 14		Day 28	
	IgA	IgG	IgA	IgG	IgA	IgG
Placebo	84%	88%	94%	94%	97%	99%
Vidofludimus Calcium	86%	93%	97%	97%	95%	100%

Phase 2 CALVID-1 Trial in COVID-19  
Proportion of patients with anti-SARS-CoV-2 IgA or IgG antibodies

COVID-19: coronavirus disease 2019; SARS-CoV-2: severe acute respiratory syndrome coronavirus; RRMS: relapsing-remitting multiple sclerosis; QD: quaque die = once-daily; IgA: immunoglobulin A; IgG: immunoglobulin G

# 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



## 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



## 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)

# Vidofludimus Calcium's Safety Profile to Date is Unique

	Vidofludimus Calcium <sup>[1]</sup>	Teriflunomide <sup>[2]</sup>	Dimethyl Fumarate <sup>[3]</sup>	Cladribine <sup>[4]</sup>	Fingolimod <sup>[5]</sup>	Siponimod <sup>[6]</sup>	Ponesimod <sup>[7]</sup>	Ozanimod <sup>[8]</sup>
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



# 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

## 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.

QD: quaque die = once-daily

\* 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.

# ENSURE Program: Ongoing Pivotal Phase 3 Trials in RMS

## NCT05134441 & NCT05201638



Coordinating Investigator

Robert J. Fox, M.D.  
Cleveland Clinic



Included Patient Population:  
Relapsing Forms of MS

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

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

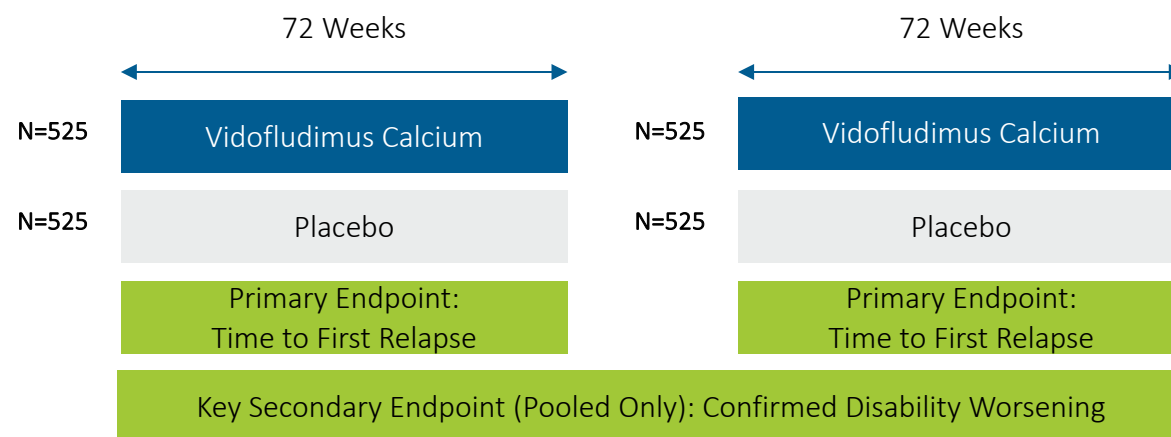


Two Multicenter, Randomized,  
Double-Blind Phase 3 Trials

- Approximately 1,050 patients in each trial
- More than 100 sites in the United States, Latin America, Central and Eastern Europe, and India in each trial
- Randomization to 30 mg vidofludimus calcium or placebo QD

ENSURE-1: Vidofludimus Calcium vs. Placebo

ENSURE-2: Vidofludimus Calcium vs. Placebo



# CALLIPER Trial: 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

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

\* NCT05054140



## 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



Potentially Applicable to a Wide Range of Diseases

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## 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)





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

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Uniquely Acting and Highly Selective  
ROR $\gamma$ t Inverse Agonist

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



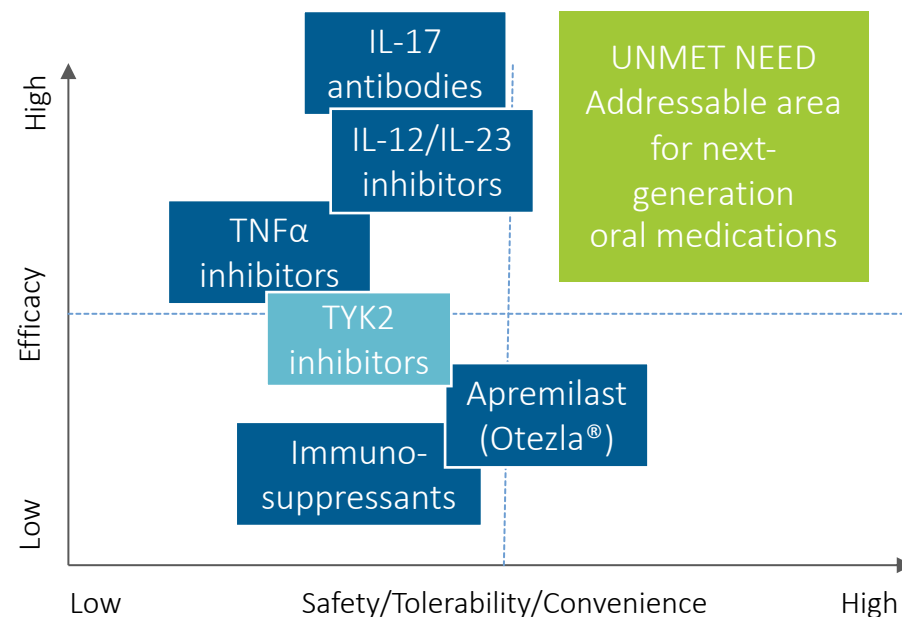
## IL-17 is Significant in Many Autoimmune Diseases

- 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<sup>[1]</sup>
- ROR $\gamma$ t is a master regulator of Th17 development and expression of IL-17<sup>[2]</sup>
- Multiple diseases are driven by IL-17; many represent significant market opportunities<sup>[3]</sup>:
  - 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

### Unmet Need in Psoriasis Care

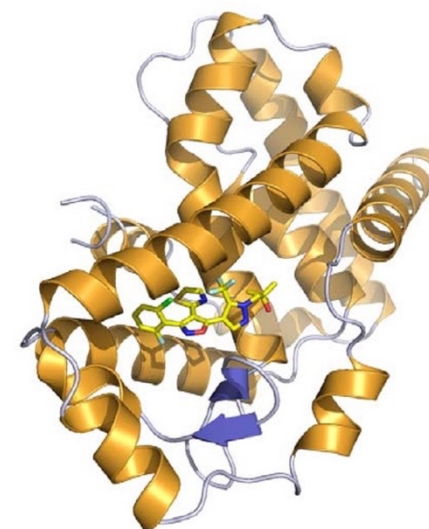


[1] Fasching, Patrizia, et al. Molecules 2017 22.1: 134 [2] Bassolas-Molina, Helena et al., Front. Immunol., 22 October 2018 [3] DRG Clarivate 2020 G7 Markets  
Th: T helper; IL: interleukin; TNF: tumor necrosis factor; TYK2: Tyrosine kinase 2; ROR $\gamma$ : retinoic acid receptor-related orphan nuclear receptor gamma

# IMU-935 Inhibits Cytokines Associated With Autoimmune Diseases With an IC<sub>50</sub> of 3-5 nM in Stimulated Human Lymphocytes

	IC <sub>50</sub> (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) <sup>[1]</sup>	0.135

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

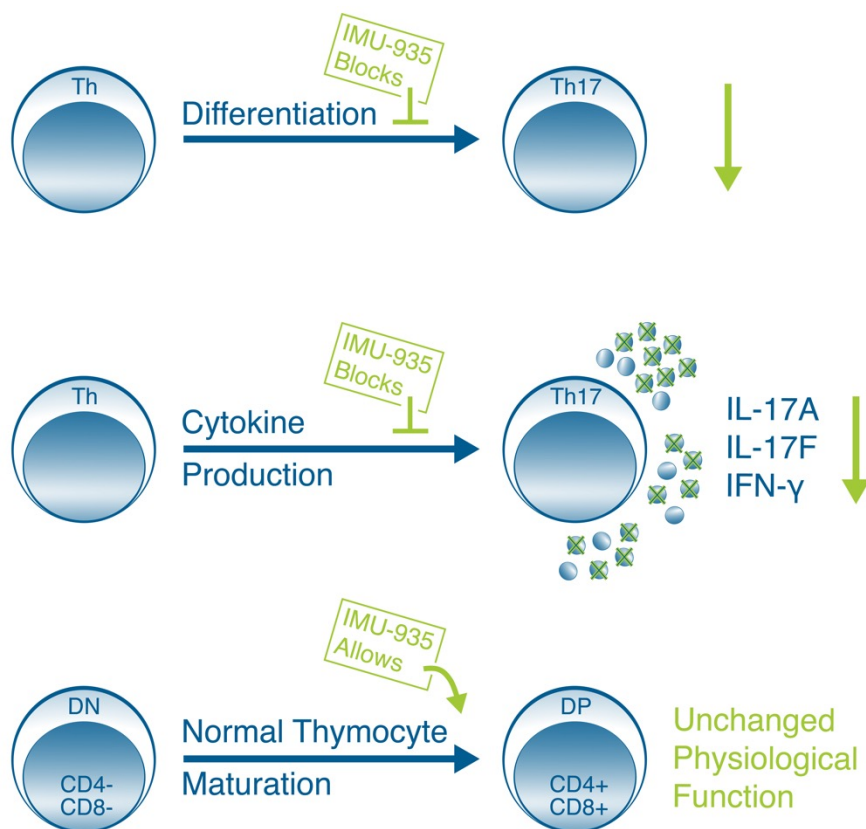


Co-crystal structure (Resolution 2.6 Å) of a closely related derivative compound binds to hydroxycholesterol binding site of RORγ

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

[1] Zuoming Sun, City of Hope, 2019

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



→ The differentiation towards Th17 cells is inhibited by IMU-935

→ The production of IL-17A and IL-17F is inhibited by IMU-935

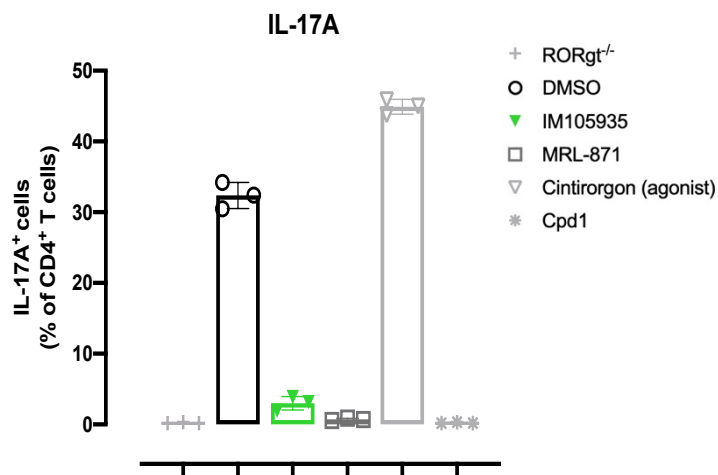
→ The physiological maturation of T cells within the thymus is not affected by IMU-935

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

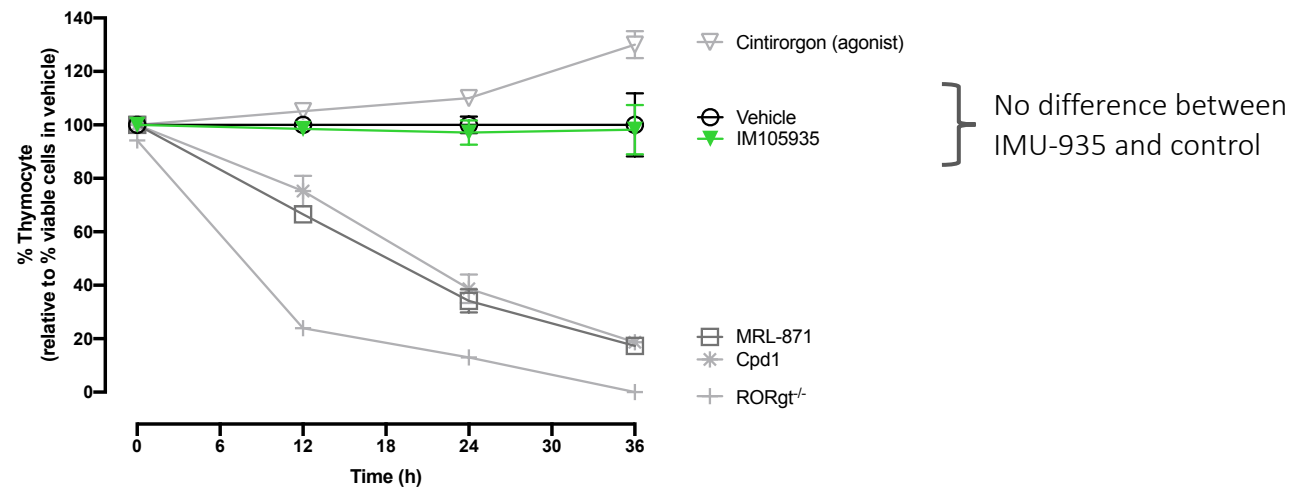
# IMU-935 Does Not Induce Thymocyte Apoptosis



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

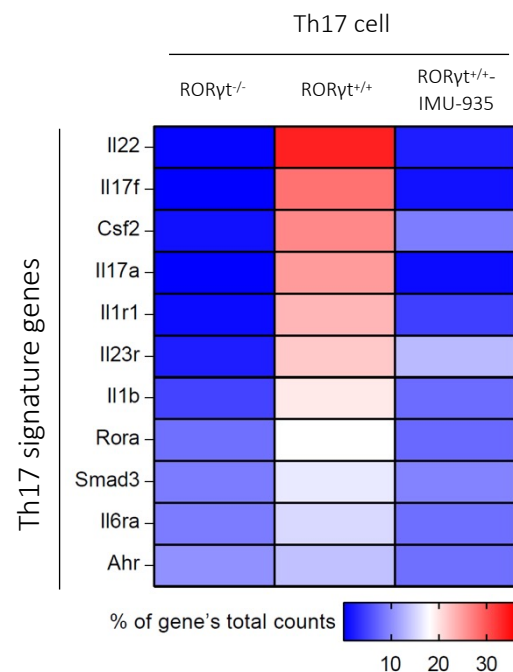


Impact on Th17 differentiation at 500 nM

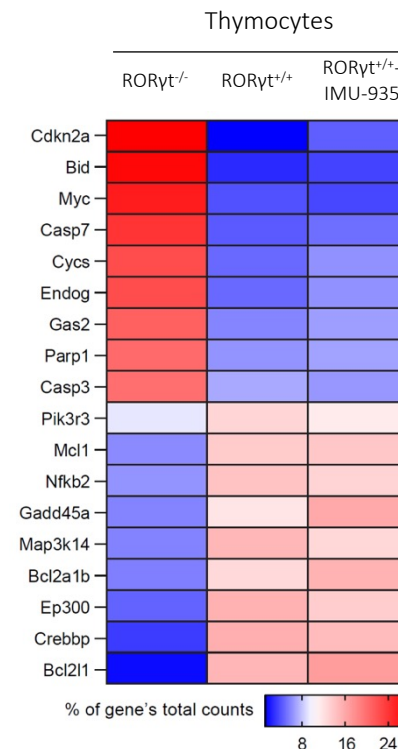
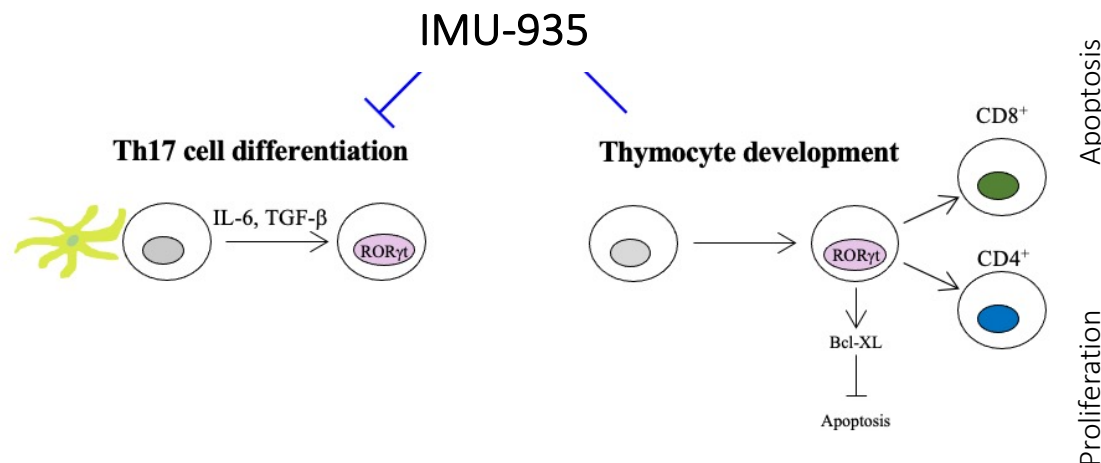


Impact on thymocyte viability at 1000 nM

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



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



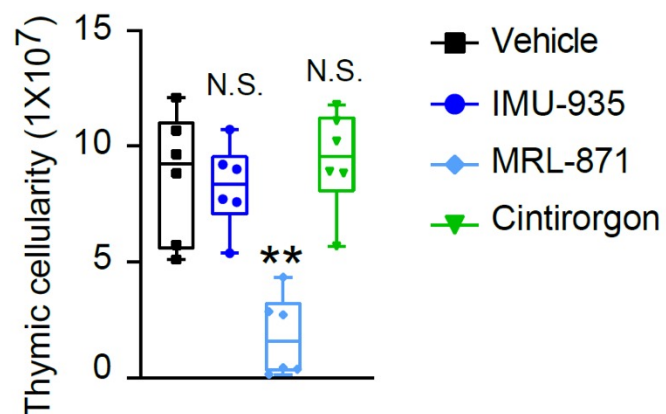
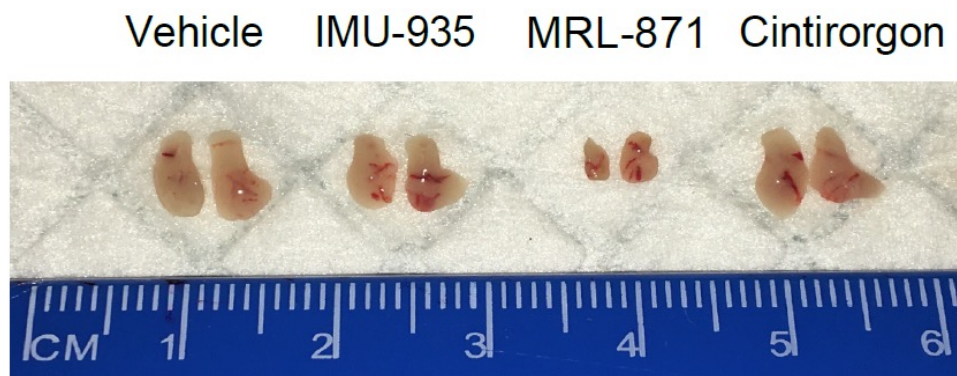
Different gene expression pattern for apoptosis and proliferation signature genes in RORγt knockout and IMU-935 treatment, but similar for RORγt<sup>+/+</sup>



# 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.

# 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

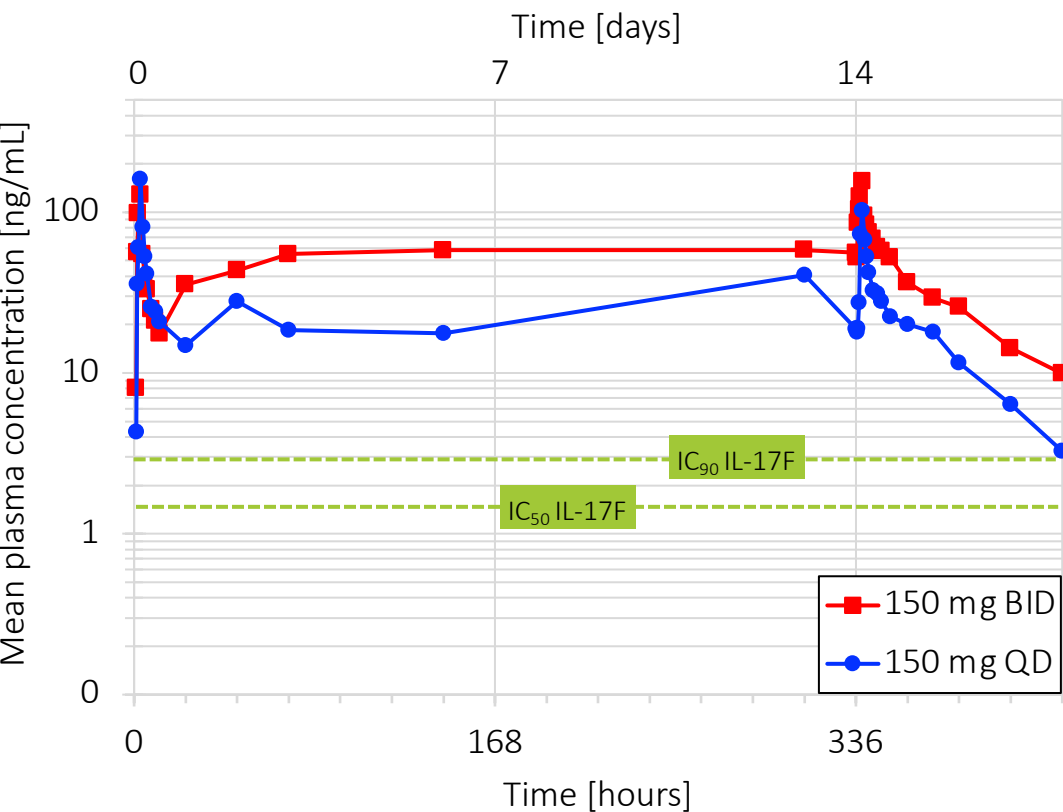
- 150 mg QD and 150 mg BID of IMU-935
- Approximately 40 patients planned to be enrolled
- Initial results expected to be available in H2/2022

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 <sub>max, ss</sub> (ng/mL)	124	206
C <sub>min, ss</sub> (ng/mL)	15.7	48.5
T <sub>max, ss</sub> (hr)	2.8	2.4
t <sub>1/2, ss</sub> (hr)	29.0	38.0
AUC <sub>last</sub> (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<sub>max</sub>: maximum plasma drug concentration; T<sub>max</sub>: time to reach maximum plasma concentration; hr: hours; t<sub>1/2</sub>: half-life; AUC<sub>last</sub>: area under the concentration-time curve from dosing to last measurement  
Accumulation factors were calculated as the relationship of AUC<sub>0-τ</sub> of Day 14/Day 1 (after first dosing).

# 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

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- 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

# Phase 1 Clinical Trial: Ongoing Part C in Psoriasis Patients



## Trial Design

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- 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
- Psoriasis patients will be enrolled in 2 cohorts:
  - First cohort of up to 16 patients will receive a low dose of IMU-935 (150 mg QD) or placebo at a ratio of 3:1
  - Second cohort of up to 24 patients 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



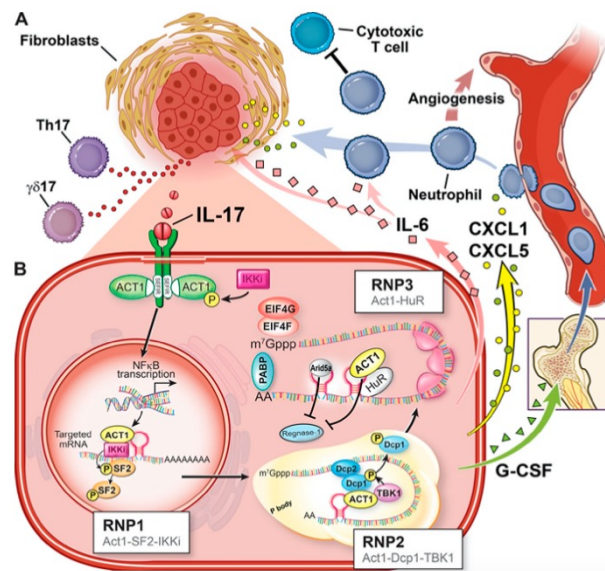
## Inhibition of RORγ

- 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.<sup>[1]</sup>
- 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

# Phase 1 Clinical Trial of IMU-935 in CRPC

## NCT05124795



### Trial 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



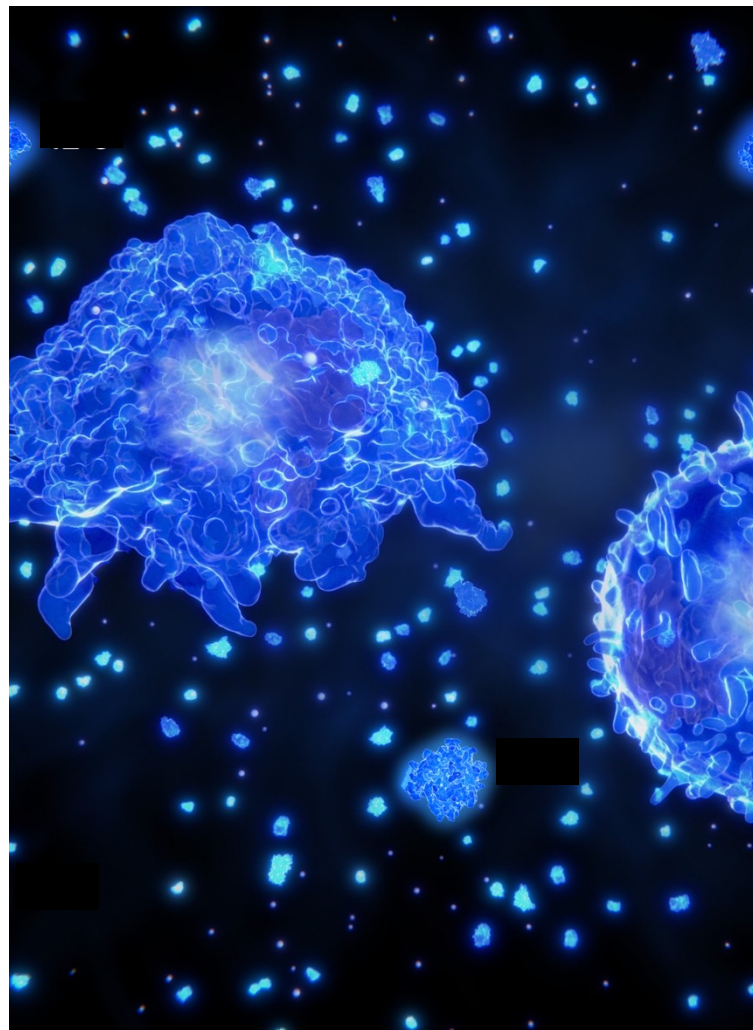
Principal Investigator

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

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## Restoring Intestinal Barrier Function

# IMU-856: Hypothesis of Therapeutic Approach



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

Microbiota

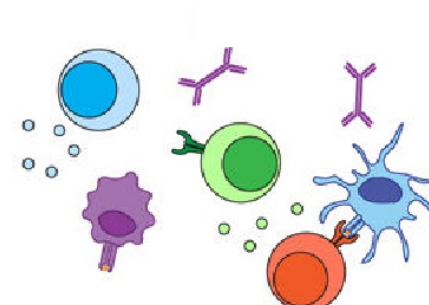


## Influencing the Microbiome

- Changes in nutrition are driving the increase in disease rates
- Diversity of microbiome is good, but data on pathogenicity of particular species is often inconsistent
- Effects of probiotics on disease have been shown (supportive)

Gut Wall

Immune System



## Focus on Immunosuppression

- Stimulation of the immune system by the microbiome cannot be prevented
- Suppression of the secondary inflammatory process
- Usually has unintended consequences in terms of adverse events (infections, malignancies, inability to vaccinate)

# IMU-856: Phase 1 Clinical Trial Performed in Australia

Double-Blind, Randomized, Placebo-Controlled Phase 1 Trial



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



Phase 1 clinical trial performed in three parts:

- Safety and pharmacokinetics in healthy human subjects (Part A: single ascending doses, Part B: multiple ascending doses)
- Part C includes a celiac disease patient population, designed to assess safety and tolerability of IMU-856 as well as pharmacokinetics and disease markers



Safety data from the SAD and MAD parts expected to be available in Q3/2022



Immunic Therapeutics

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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 into Q3/2023  
Shares outstanding: 30,540,383 (as of May 2, 2022)

# Thank You!



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