Immunic Therapeutics

Developing Selective Oral Drugs in Immunology

NASDAQ: IMUX | Jefferies Virtual Healthcare Conference | June 4, 2020

Cautionary Note Regarding Forward-Looking Statements

Certain statements contained in this presentation regarding matters that are not historical facts are forward-looking statements within the meaning of Section 21E of the Securities and Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995, known as the PSLRA. 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 PSLRA.

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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 Vision

We are developing new therapies with best-in-class potential for the treatment of chronic inflammatory and autoimmune diseases.

Key Investment Highlights

Three potential best-in-class oral therapies

- IMU-838: Potent DHODH inhibitor currently tested in **three phase 2 studies**
- IMU-935: **Oral IL-17 inhibitor** with substantial potential
- IMU-856: Novel target – potentially disease modifying for GI disorders

High value markets

- Autoimmune & immunology with **high unmet medical needs**
- **Huge potential for the treatment of COVID-19**
- **Large markets** for IBD, MS and psoriasis with multibillion USD sales potential

Strong IP position

- IMU-838: Granted patents **until 2031**, patent application coverage **until 2038**
- IMU-935: **New compound IP** filed in 2017
- IMU-856: Compound patent filed in 2018

Experienced global management team

- Experienced management team with strong track record and over 90 years of leadership experience in the pharmaceutical industry
- Headquartered in New York with R&D operations in Munich, Germany

Strong balance sheet

- Expected cash runway through near-term value inflection points
- Cash position of USD 18.6 million (as of March 31, 2020)
- **Raised approximately USD 17.3 million in April 2020**

Immunic THERAPEUTICS

Leadership Team

Company is led by an experienced management team

Daniel Vitt, PhD
CEO & President of Immunic

Duane Nash, MD, JD, MBA
Executive Chairman

Andreas Muehler, MD, MBA
CMO

Hella Kohlhof, PhD
CSO

Manfred Groeppel, PhD
COO

Glenn Whaley, CPA
Vice President Finance, 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
LSP

Vincent Ossipow, PhD, CFA
Omega Funds

Jan Van den Bossche
Fund+

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Development Pipeline

Program	Indication	Target	Preclinical	Phase 1	Phase 2	Phase 3
IMU-838	Multiple Sclerosis	DHODH				
	Ulcerative Colitis	DHODH				
	Crohn's Disease	DHODH				
	PSC	DHODH				Investigator-Sponsored Trial performed at Mayo Clinic / NIH
	COVID-19	DHODH				
IMU-935	Psoriasis	RORγt				
	Orphan AI Diseases	RORγt				
IMU-856	GI	Intestinal Barrier Function				

■ Completed or ongoing ■ In preparation or planned

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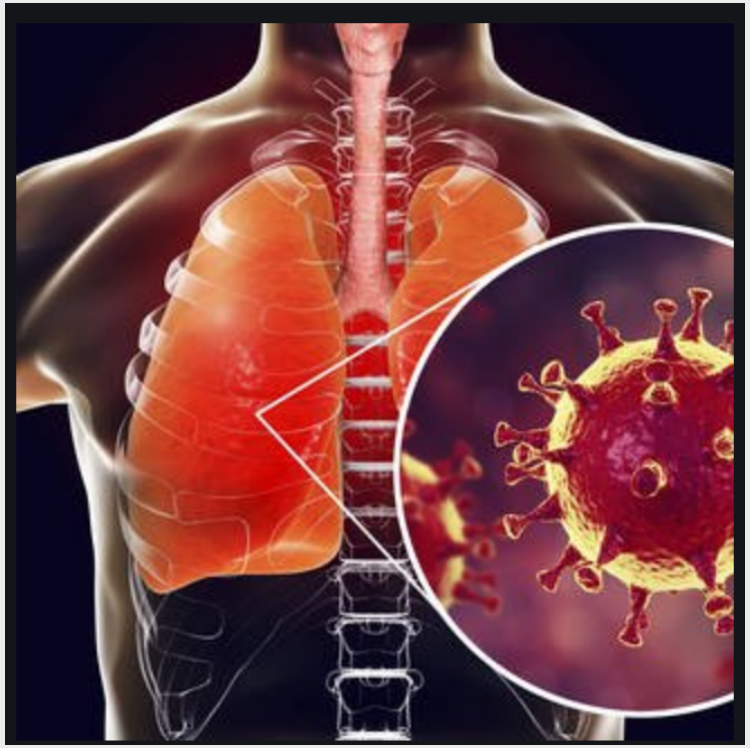
IMU-838 Fighting COVID-19

Leveraging DHODH's Broad-Spectrum Antiviral Activity

IMU-838: Triple Attack on COVID-19

IMU-838 is an advanced clinical drug candidate with attractive pharmacokinetic, safety and tolerability profile with more than **650 individuals exposed to date**



IMU-838 attacks COVID-19 disease by three complementary mechanisms:

1. Inhibition of **virus replication** by depletion of nucleotide pool
2. Insufficient first immune response due to SARS-CoV-2 encoded interferon antagonists
   Induction of **innate immune response** by DHODH inhibition independent of interferon signaling
3. Excessive activation of adaptive immune response – “cytokine storm”
   Inhibition of “overreacting”, **cytokine high** producing immune cells

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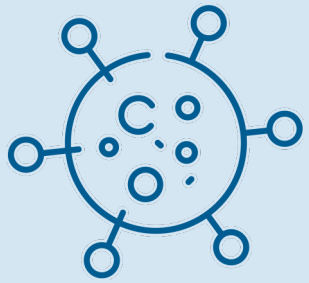
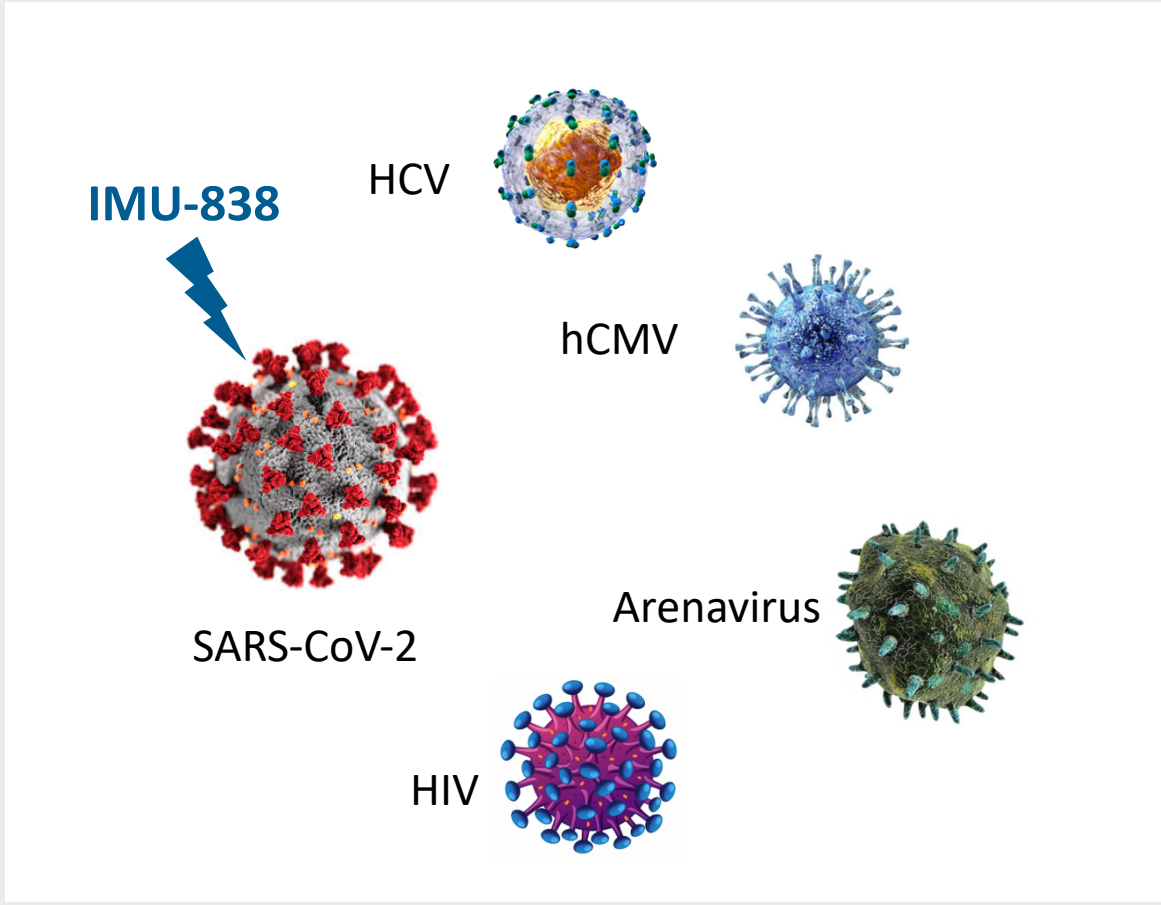
IMU-838: Activity Against SARS-CoV-2 and Other Viruses



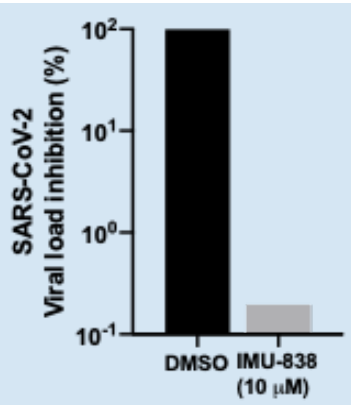
- IMU-838 is active against SARS-CoV-2
- IMU-838 has shown **broad-spectrum antiviral activity** against different pathogenic viruses with EC_{50} values in single digit µM range



IMU-838: SARS-CoV-2 Preclinical Testing

Collaboration partners in Germany and the United States

A549-ACE2



IMU-838 demonstrated inhibition of SARS-CoV-2 replication

A549-ACE2 cells (human lung epithelial cells, overexpressing ACE2 receptor)

- Virus RNA reduction – RT-qPCR
- $EC_{99.9}$ ~10 µM

Vero76 (monkey kidney)

- Cytopathic effect – EC_{50} 5.7 µM
- Virus yield reduction – EC_{90} 7 µM

VeroE4 cells (monkey kidney)

- Virus RNA reduction – RT-qPCR
- EC_{90} < 10 µM

Further testing ongoing in

Huh7 (liver) and CaCo2 (colon) cells

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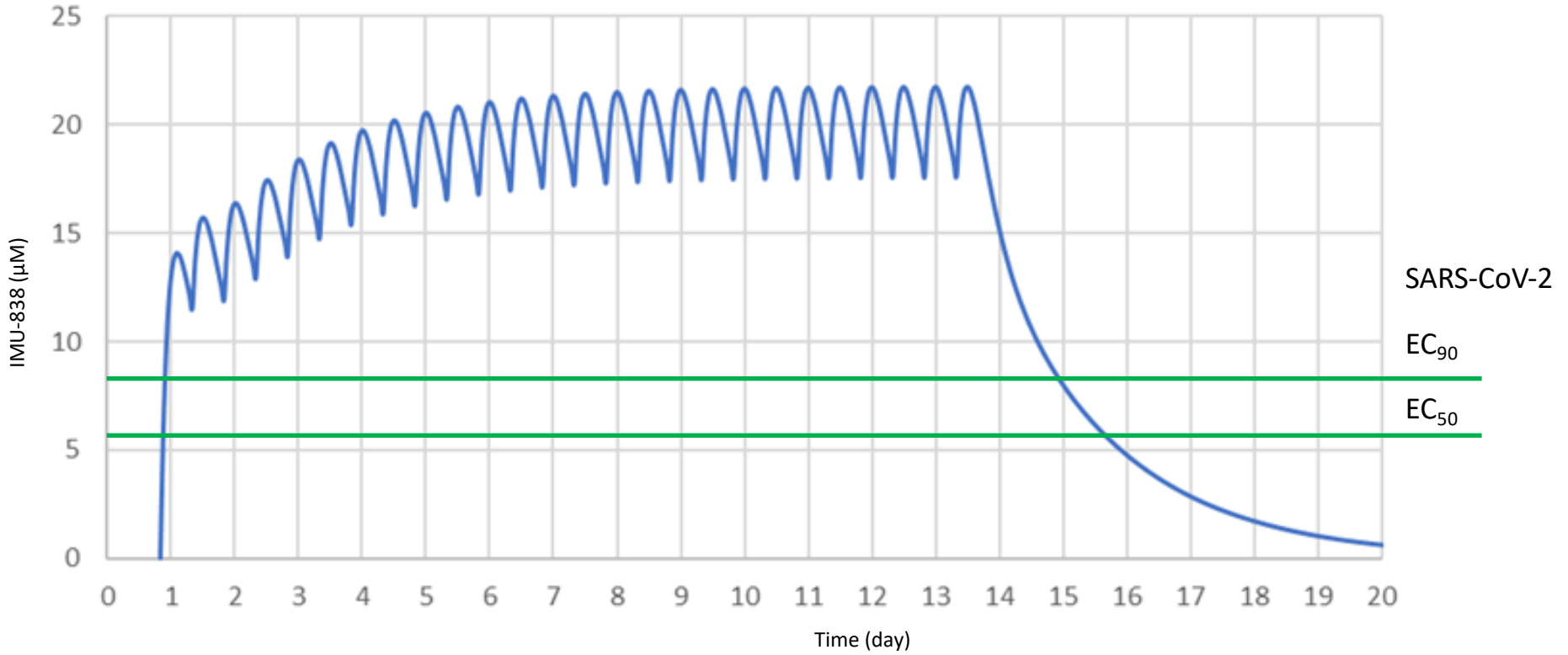
Anticipated Pharmacokinetic Profile 22.5 mg BID 14-day Treatment in Phase 2 IMU-838 in COVID-19 Patients

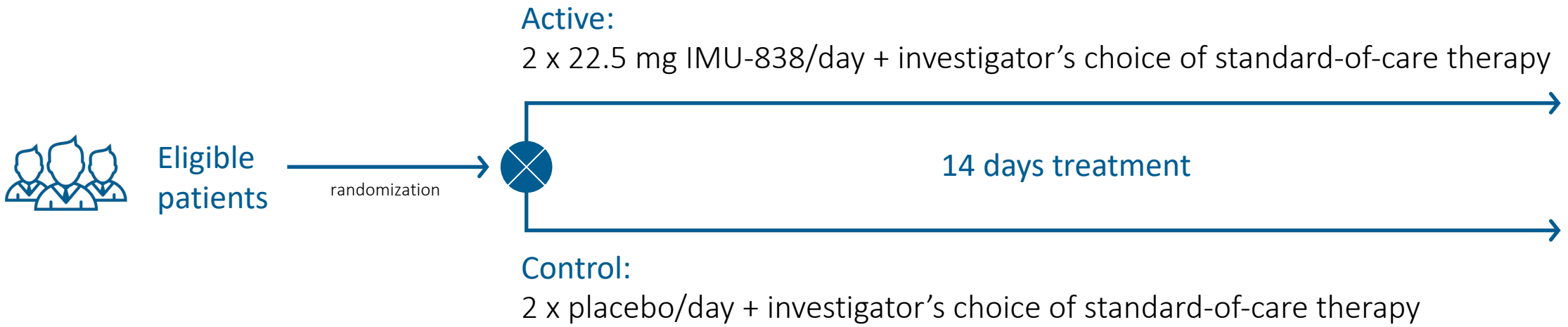


Proposed dosing regimen ensures that therapeutic levels of IMU-838 are reached starting from first dose

Based on Population Pharmacokinetic Model for IMU-838 as described in the following publication: Muehler et al. Eur J Drug Metab Pharmacokinet. 2020 May 2. doi: 10.1007/s13318-020-00623-7

CALVID-1: Phase 2 Clinical Trial Design in COVID-19

Prospective, multicenter, randomized, placebo-controlled, double-blind phase 2 clinical trial



n = 230 patients

About 10-35 clinical sites
in the United States and Europe

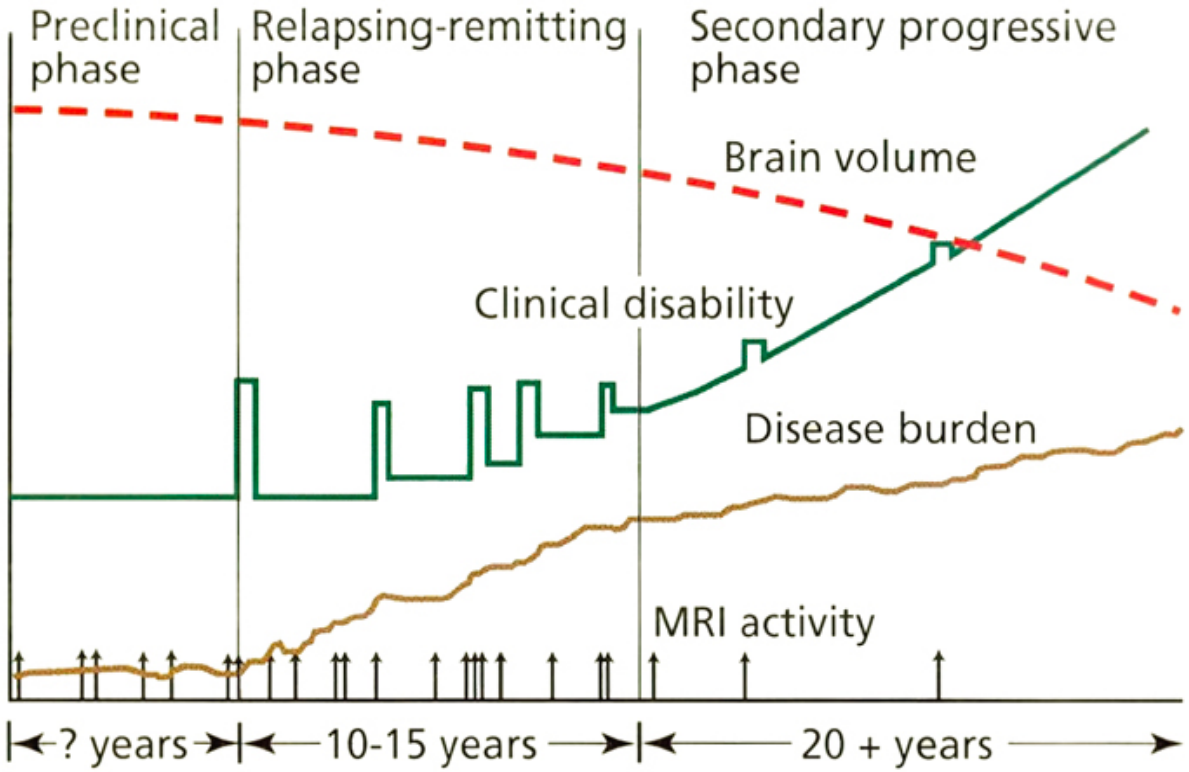
Coordinating Investigator:
Neera Ahuja, MD (Stanford University)

www.clinicaltrials.gov: NCT04379271

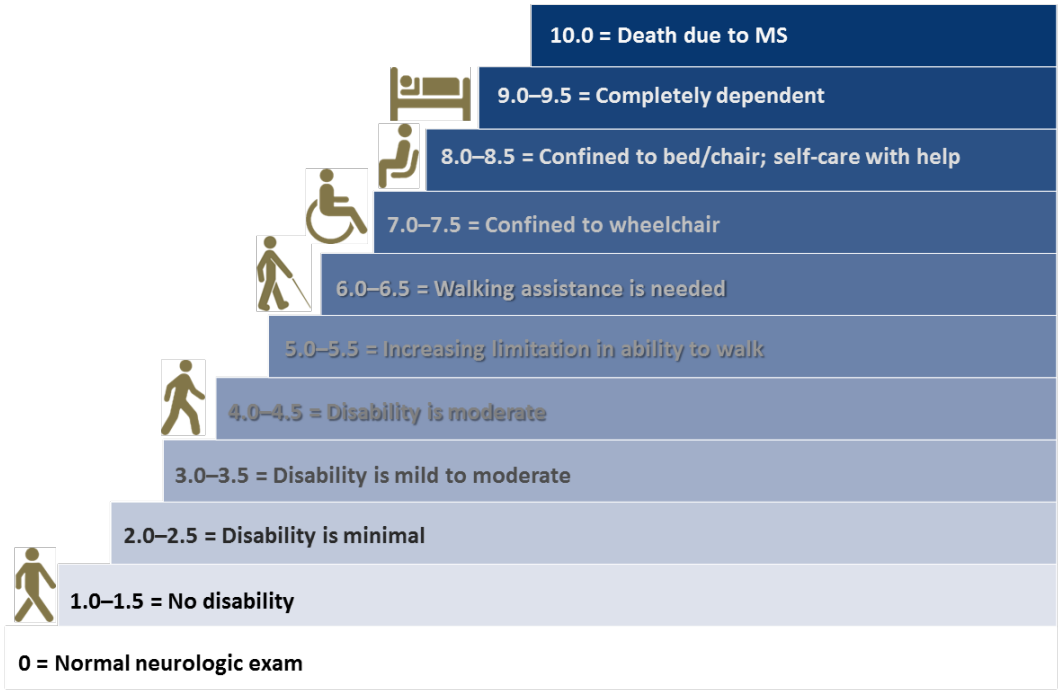
IMU-838 in Relapsing-Remitting Multiple Sclerosis (RRMS)

Mode of Action of IMU-838 Enables Broad Therapeutic Use

Natural History of Relapsing Multiple Sclerosis



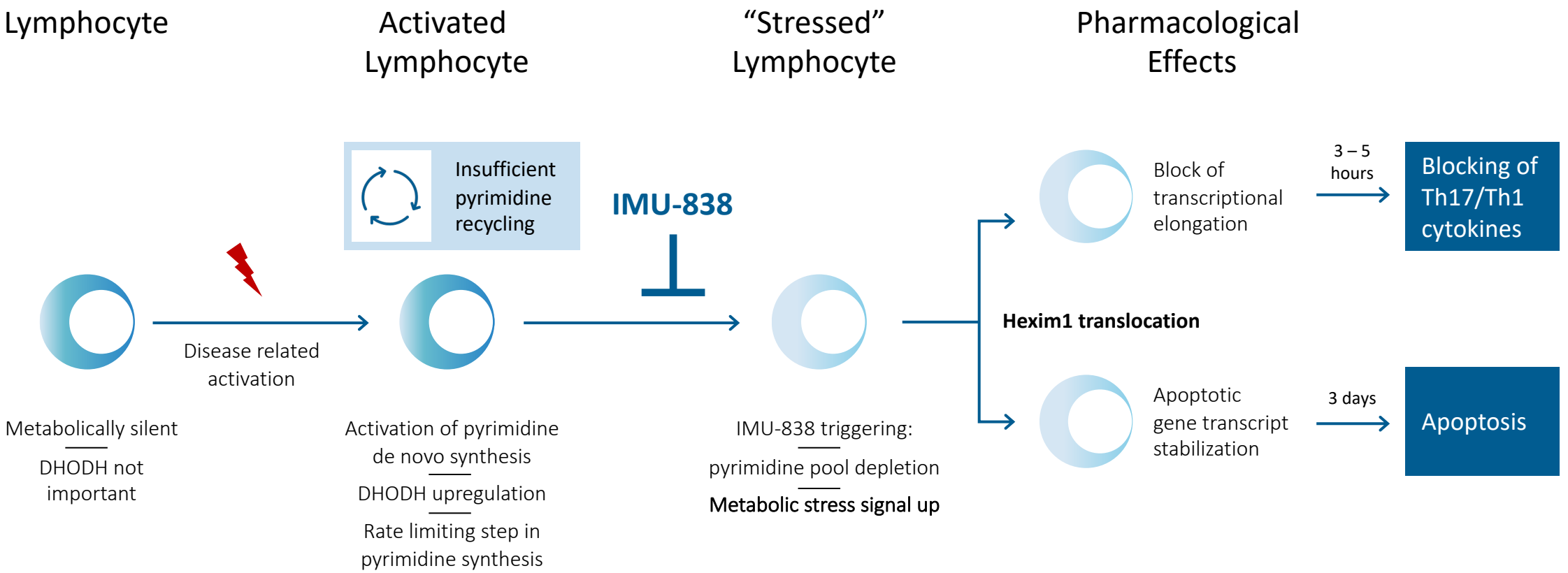
MS Disease Course*



Expanded Disability Status Scale – EDSS*

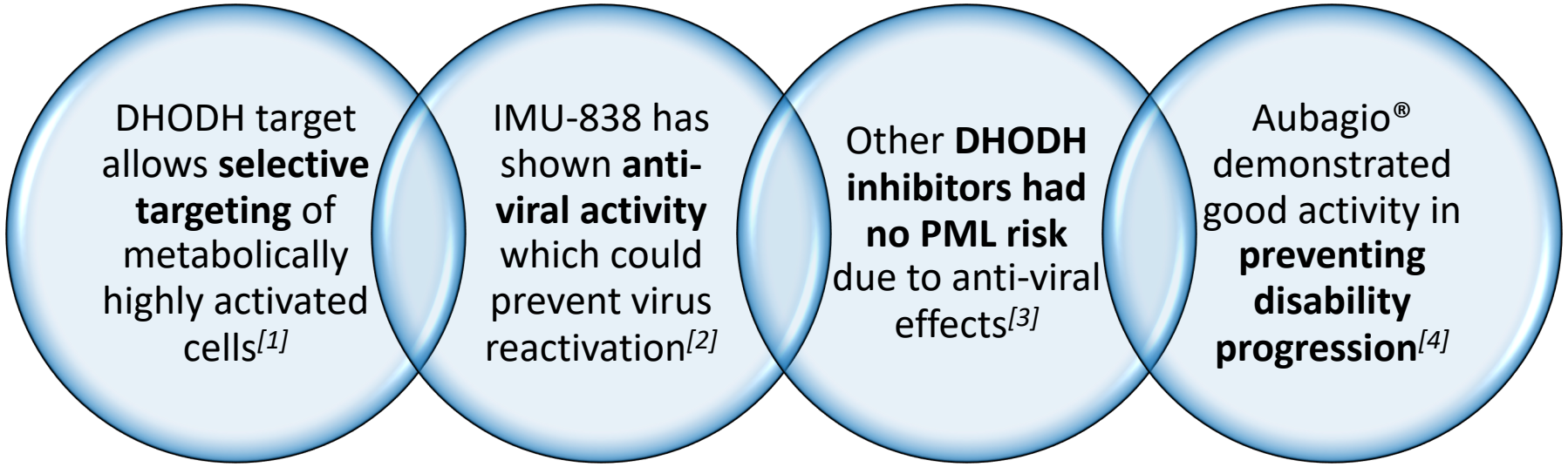
Adapted from: Fox RJ, Cohen JA: Multiple sclerosis: the importance of early recognition and treatment. Cleve Clin J of Med, 2001; 68:157–70

Mode of Action: DHODH Targeting Leads to Metabolic Stress in Metabolically Activated Cells



Adapted from Tan et al., 2016, Mol Cell 62

Key Advantages of Targeting DHODH



[1] Klotz et al., Sci. Transl. Med. 11, eaao5563, 2019
[2] Marschall et al., Antiviral Res., 2013;10:640-648
[3] Chahin S and Berger JR. J. Neurovirol. 2015;21:623-631
[4] Confavreux C et al. Lancet Neurol. 2014;13:247–56

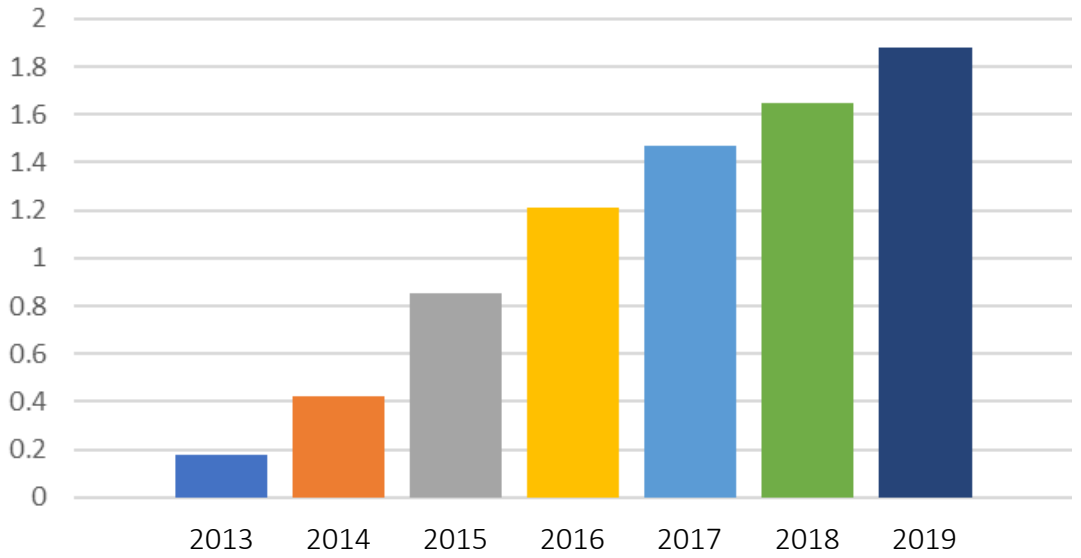
MS Opportunity

Aubagio® (teriflunomide) is currently the **only approved** DHODH inhibitor for MS

- Aubagio® is indicated for the treatment of relapsing forms of MS, to include clinically isolated syndrome, RRMS, and active secondary progressive disease, in adults.
- Clinical data suggests that DHODH inhibition leads to sustained activity even after multiple prior DMT[2]
- Teriflunomide's slowed atrophy compares favorably to ocrelizumab[3]

Global Sales Aubagio® in MS[1]

Worldwide Sales (in € B)



[1] Sanofi Annual Reports, https://www.sanofi.com/-/media/Project/One-Sanofi-Web/Websites/Global/Sanofi-COM/Home/en/investors/docs/press-releases/Q42018results.pdf?la=en&hash=9E677FE77C61BB895BCC44A229407ED8
[2] O'Connor et al, NEJM 2011 - Radue et al, Neurol 2017
[3] Radue et al, Neurol 2017

Challenges of Aubagio®

- Aubagio® hits off targets, e.g. protein kinases **EGFR and Aurora A**[1,2], leading to off-target toxicities[3]
  - Diarrhea (in 13 to 14 % of patients)[4]
  - Hair loss (in 10 to 13 % of patients)[4]
  - Neutropenia (in 4 to 6 % of patients)[4]
- Aubagio® has a half-life of about 18 to 19 days in humans[3-6]; wash-out takes more than **six months**
  - Emergency treatment discontinuations limited due to **long wash-out period,** require accelerated wash-out procedures[4]
- Frequent screening required (black box warning for **hepatotoxicity**)[4]

[1] Büttner R, et al. Blood 130 (suppl 1): 4426 abstract, 2017
[2] Cada DJ, et al. Hosp Pharm, 2013;48:231-240
[3] O'Connor et al, NEJM 365: supplementary appendix, 2011
[4] Summary of Product Characteristics Aubagio®
[5] FDA CDER Medical Review Teriflunomide, 2012
[6] O'Connor et al, NEJM, 2011;365:1293-1303

IMU-838: A New, ”Easy-to-Use” Treatment Option for RRMS

- IMU-838 **does not inhibit kinases,** such as EGFR and Aurora A, at relevant concentrations
  - **No decrease of bone marrow cellularity observed** in animal experiments at high doses[1]
  - **No increased rate of diarrhea, neutropenia or alopecia** observed so far[2]
- Convenient **half-life of ~30 hours**, reaching steady state in 5 to 7 days[3]
- IMU-838 likely not to require accelerated wash-out procedures for treatment discontinuations
  - Most patients with **undetectable blood levels at 10 days** after last dose[3]

[1] Kulkarni et al., Am. J. of Pathology, 2010;176: 2840 – 2847
[2] Muehler et al., Drugs in R&D. 2019 Dec;19(4):351-366
[3] Muehler et al., ECTRIMS 2019, Abstract A-1026-0031-00242

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EMPhASIS: Phase 2 Study Overview in RRMS

Coordinating Investigator

Robert Fox, MD (Cleveland Clinic)

Population: RRMS With Relevant Disease Activity

- Male or female (18 ≥ age ≤ 55)
- RRMS diagnosis (Revised McDonald criteria 2017)
- Evidence of disease activity based on relapse and MRI criteria
- **Baseline EDSS: 0 ≤ EDSS ≥4.0**

Main Treatment Period

- MRI endpoint **new combined unique active lesions**
- Parallel group design with placebo control
- Overall blinded **treatment period 24 weeks**
- **MRI every six weeks**

Extended Treatment Period

- Up to 9.5 years
- Extension study for obtaining long-term safety

www.clinicaltrials.gov: NCT03846219

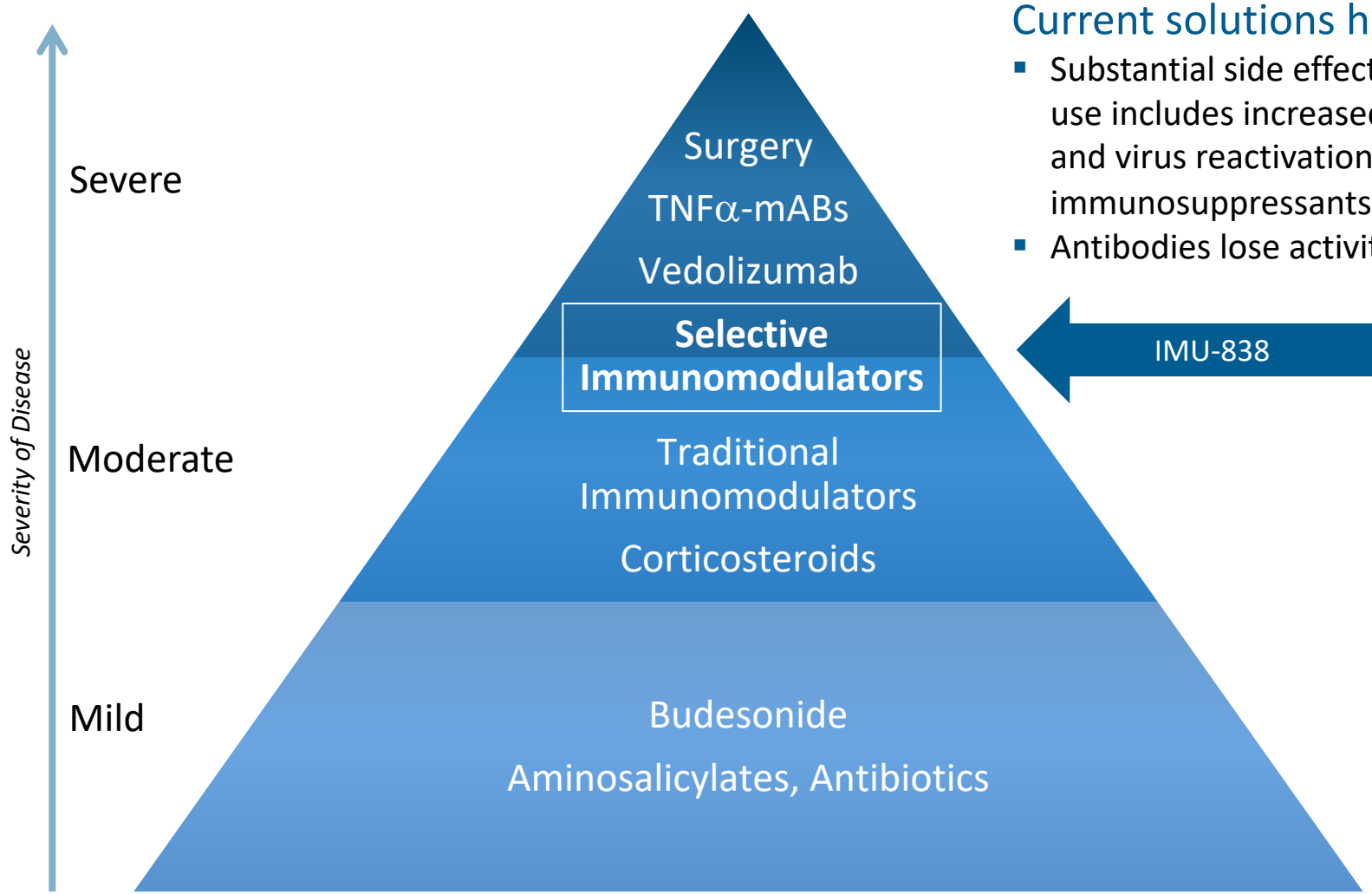
IMU-838: Potential Positioning in RRMS

1	2	3	4	5
Unique properties known from DHODH inhibitors regarding disability progression	Suggestion of sustained activity even after multiple prior DMT	Known protection against John Cunningham virus reactivations and resulting PML	Pharmacokinetic profile (short blood half-life) allowing for convenient treatment interruptions and no need for accelerated washout procedures	Unique safety profile of IMU-838 may open the opportunity of de-escalation following anti-B-cell biologics

IMU-838 in Inflammatory Bowel Disease (IBD)

New Oral Treatment Option with Promising Safety Profile

IBD: Therapeutic Pyramid



Current solutions have limitations

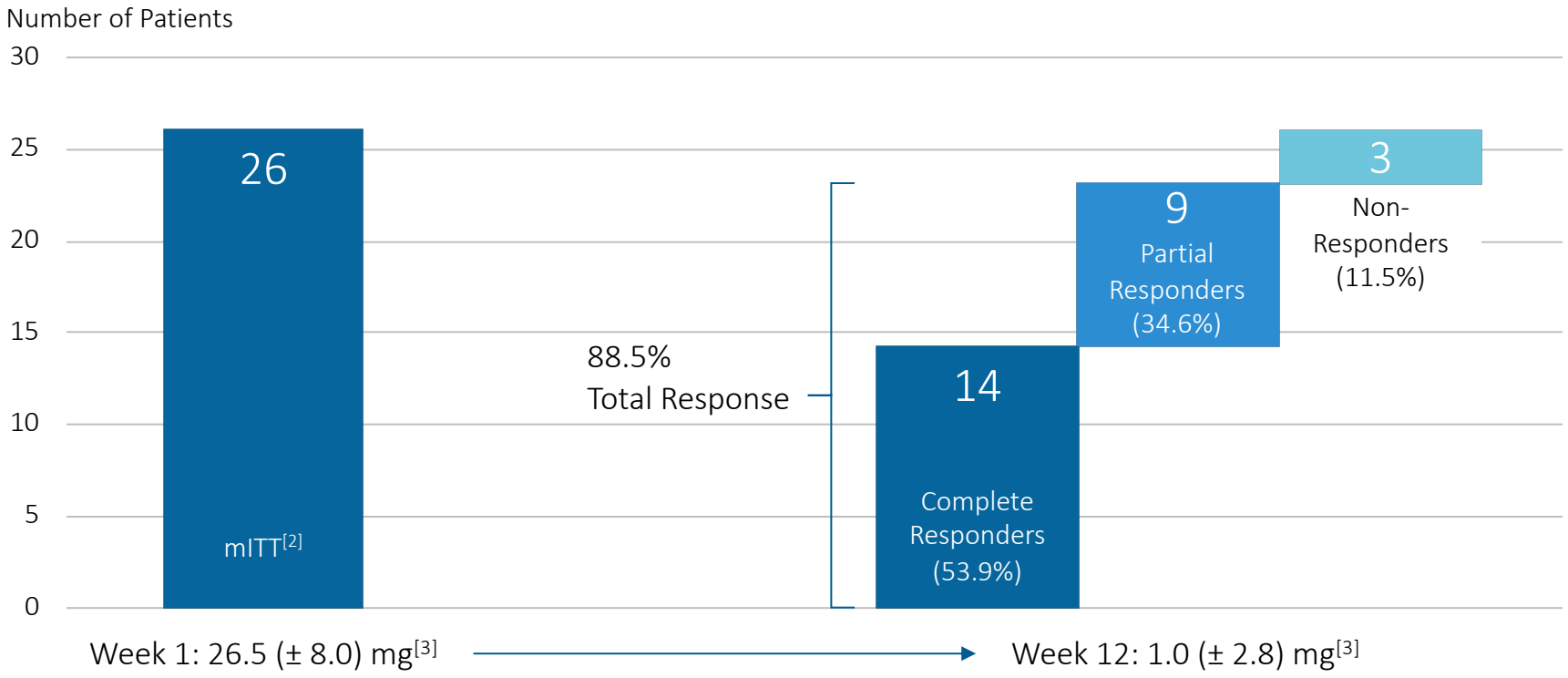
- Substantial side effects due to long-term use includes increased rate of cancer risk and virus reactivation of currently used immunosuppressants[1] [2] [3]
- Antibodies lose activity over time[4]

[1] Present, Daniel H., et al. Annals of internal medicine 1989; 111.8: 641-649
[2] Dayharsh, Gerald A., et al. Gastroenterology 2002; 122.1: 72-77
[3] Winthrop, Kevin L., et al. Arthritis & rheumatology 2014; 66.10: 2675-2684
[4] Roda, Giulia, et al. Clinical and translational gastroenterology 2017; 7.1: e135

ENTRANCE Study: Primary Efficacy Results

ENTRANCE Study:[1]

- 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)



IMU-838 had response rates of:

85.7 % in Crohn's disease

91.7 % in ulcerative colitis

[1] Herrlinger et.al., 2011, Gastroenterology 140:588
[2] mITT: modified intent to treat
[3] Mean dose of steroid equivalent in mg per day

CALDOSE-1: Clinical Phase 2 in UC Ongoing

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

Active IND in the United States

Overall number of patients: 240

Currently more than 65 active sites in 9 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 ≥2 and a modified Mayo endoscopy subscore of ≥2 at the screening flexible sigmoidoscopy (independent central reader)

Induction period: 10 weeks

Maintenance period: up to week 50

Open-label extension period:

- Up to 9 years
- Extension study for obtaining long-term safety

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

Currently estimated to deliver top-line data end of 2021

www.clinicaltrials.gov: NCT03341962

CALDOSE-1: Interim Analysis Established Potentially Broad Effective Dose Range

Performed by an unblinded data review committee (DRC) in August 2019

Analysis based on all available clinical, endoscopic, biomarker, PD, and safety data

1 Potentially broad effective dose range in UC patients

Doses of 10 to 45 mg may be effective in UC

2 Interim analysis confirmed the good safety profile

- No intolerable dose identified
- No safety signal observed

The interim analysis supported that IMU-838 is a safe oral medication in patients with UC with a broad therapeutic index.

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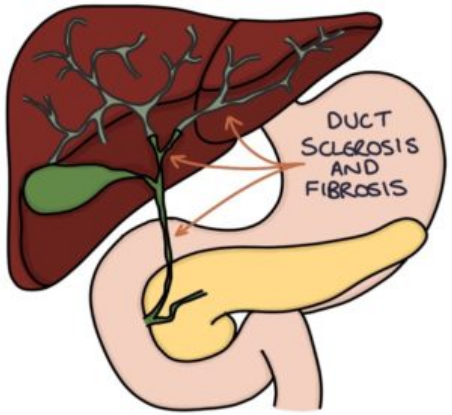
IMU-838 in Primary Sclerosing Cholangitis (PSC)

Investigator-Sponsored Trial Performed at the Mayo Clinic

Orphan Disease Primary Sclerosing Cholangitis

Rare progressive liver disease without approved pharmaceutical treatments



- Ongoing trial targeted to allow Immunic to gauge clinical activity of IMU-838 in patients with PSC
- If successful, this indication may allow an accelerated path to regulatory approval

IMU-838: Phase 2 Proof-of-Concept Study in PSC

Principal Investigator

Elizabeth Carey, MD (Mayo Clinic)

Investigator-Sponsored Trial in Patients with PSC

- Single-arm, open-label, exploratory study planning to enroll 30 patients, aged 18 to 75 years
- Conducted at two Mayo Clinic sites in Arizona and Minnesota
- Supported by NIH grant
- Immunic provides the study medication to clinical sites
- Dosing: 30 mg IMU-838 qd for up to six months
- Primary endpoint: change in serum alkaline phosphatase (ALP) at six months compared to baseline

Study Started in August 2019

Currently about half of the patients enrolled

Expected Results: Early 2021

www.clinicaltrials.gov: NCT03722576

IMU-935

Unique RORγt Inverse Agonist

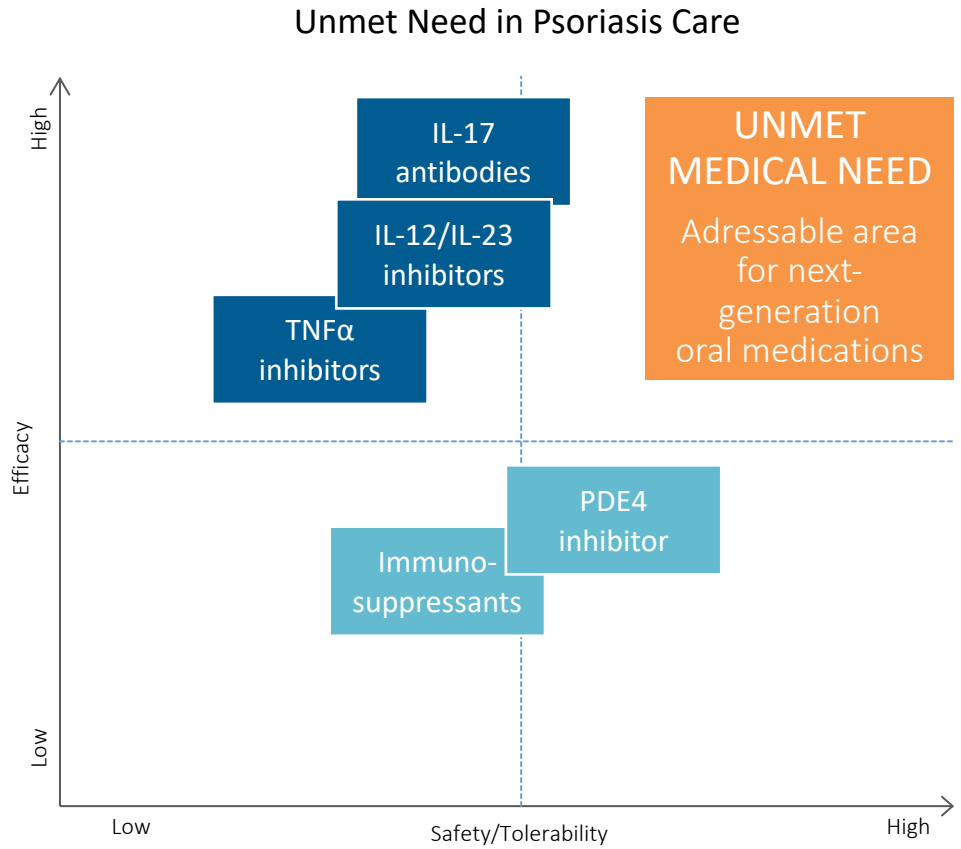
Autoimmune Diseases and IMU-935

IL-17 in Autoimmune Diseases

- Autoimmune diseases are frequent diseases affecting millions of patients worldwide[1]
- Th17/IL-17/RORγt axis is important in auto immunity related diseases[2]
- Antibodies targeting this axis successfully demonstrated this concept but bear the disadvantage of being a non-oral drug[2]

Goal

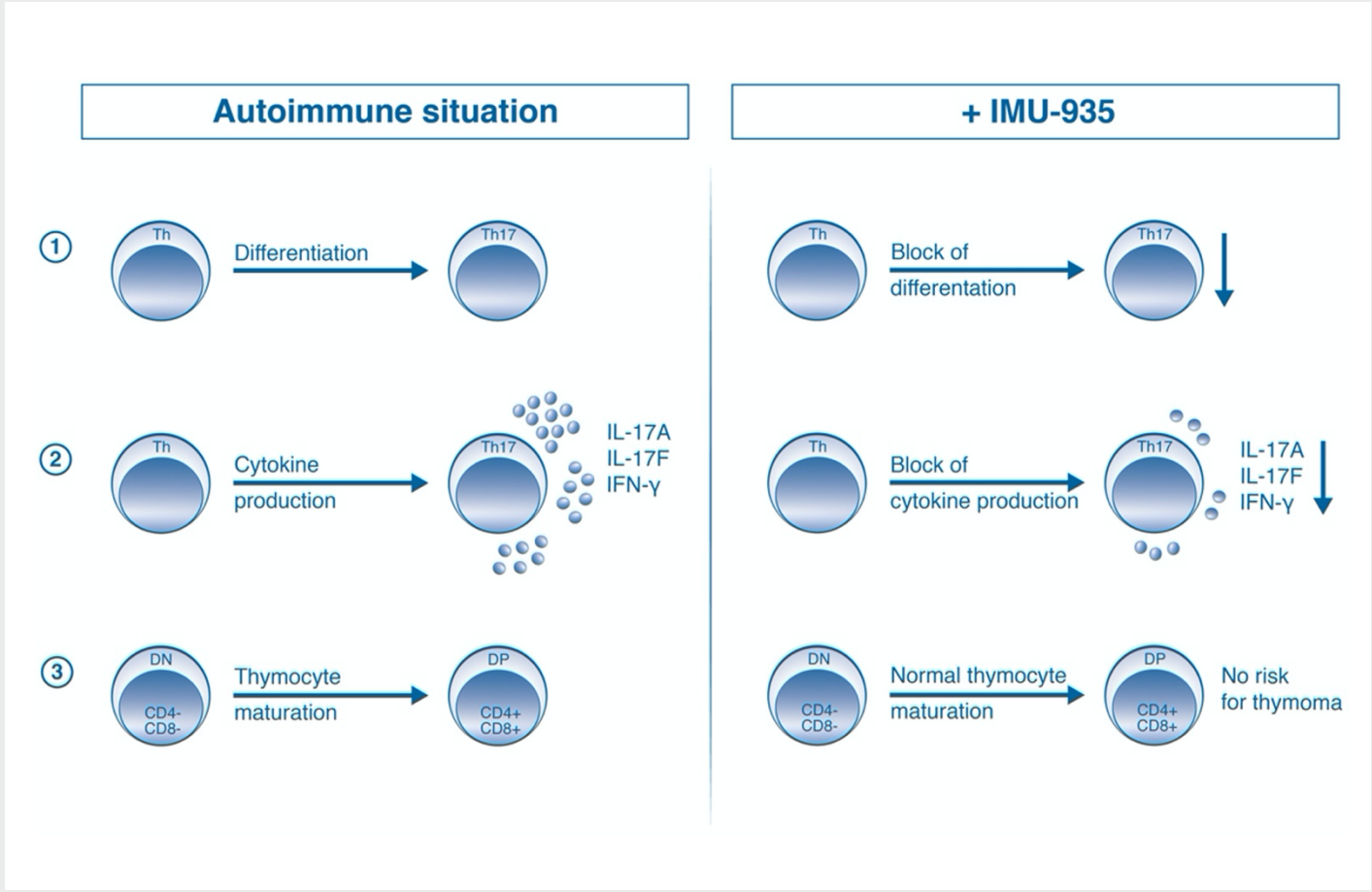
- Develop an orally available and potent IL-17 inhibitor for the safe and efficacious treatment of autoimmune diseases
- Small molecule inhibitor of RORγt functions in autoimmune disease state without affecting physiological functions of RORγt



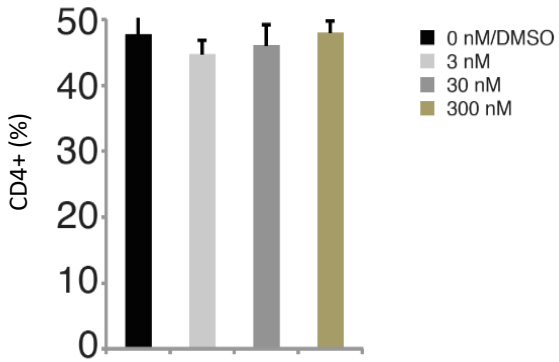
Strong medical need for oral IL-17 pathway inhibitors such as IMU-935

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

IMU-935: Main Functions of RORγt



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



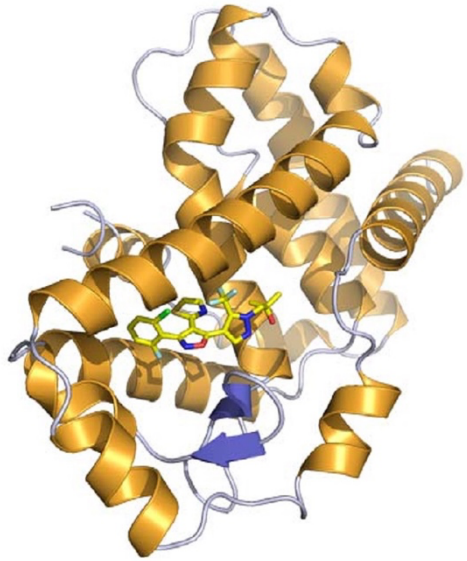
IMU-935: Cytokine Inhibition in Low Nanomolar Range

Effect of the development compound IM105935 (IMU-935) in stimulated human PBMCs

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

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

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



Resolution 2.6 A of a closely related derivative compound binds to hydroxycholesterol binding site of RORγ

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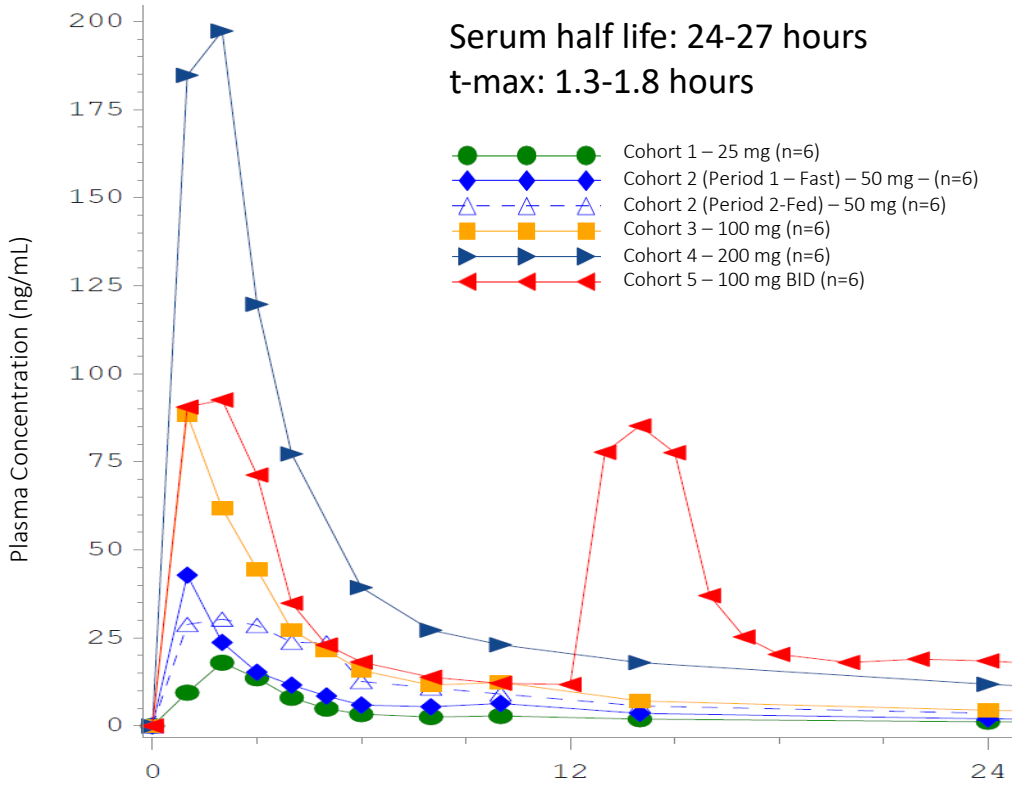
IMU-935: Phase 1 Study Performed in Australia

- Double-blind, placebo-controlled clinical phase 1 study performed by Immunic subsidiary in Australia
- Availability of experienced early phase CROs and phase 1 units
  - CMAX phase 1 Unit (Adelaide/SA)
  - Avance Clinical CRO (Adelaide/SA)
- Started in September 2019
- Phase 1 study performed in three parts
  - Part A: Single ascending dose (SAD) study in healthy volunteers
  - Bart B: 14-day multiple ascending dose (MAD) study in healthy volunteers
  - Part C: 4-week safety study in psoriasis patients

IMU-935: Pharmacokinetic Results of Single Ascending Dose Cohorts 1-5 Predictable Dose-Linear Pharmacokinetics



Average pharmacokinetic variables

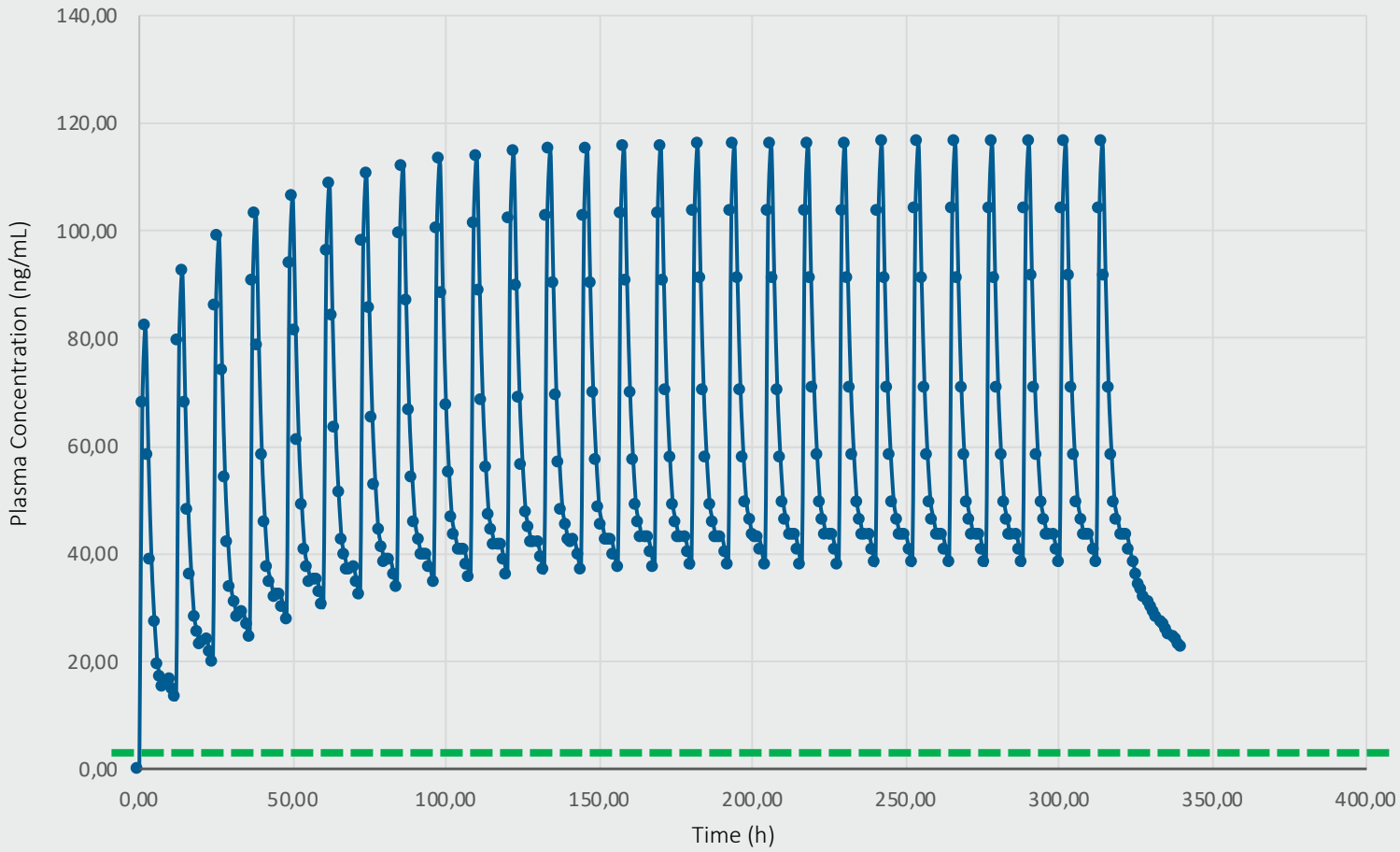
Dose	C-max ng/mL	T-max (hours)	AUC-24h (h* ng/mL)
25 mg	22.8	1.83	91.9
50 mg (fast)	49.6	1.50	176
50 mg (fed)	46.5	2.67	260
100 mg	95.7	1.33	399
200 mg	199	1.83	1000

Preliminary data

IMU-935: Pharmacokinetic Modeling of Multiple Dose

Prediction of multiple dose pharmacokinetics (75 mg IMU-935 BID)

Estimated accumulation factor for multiple dosing 1.22



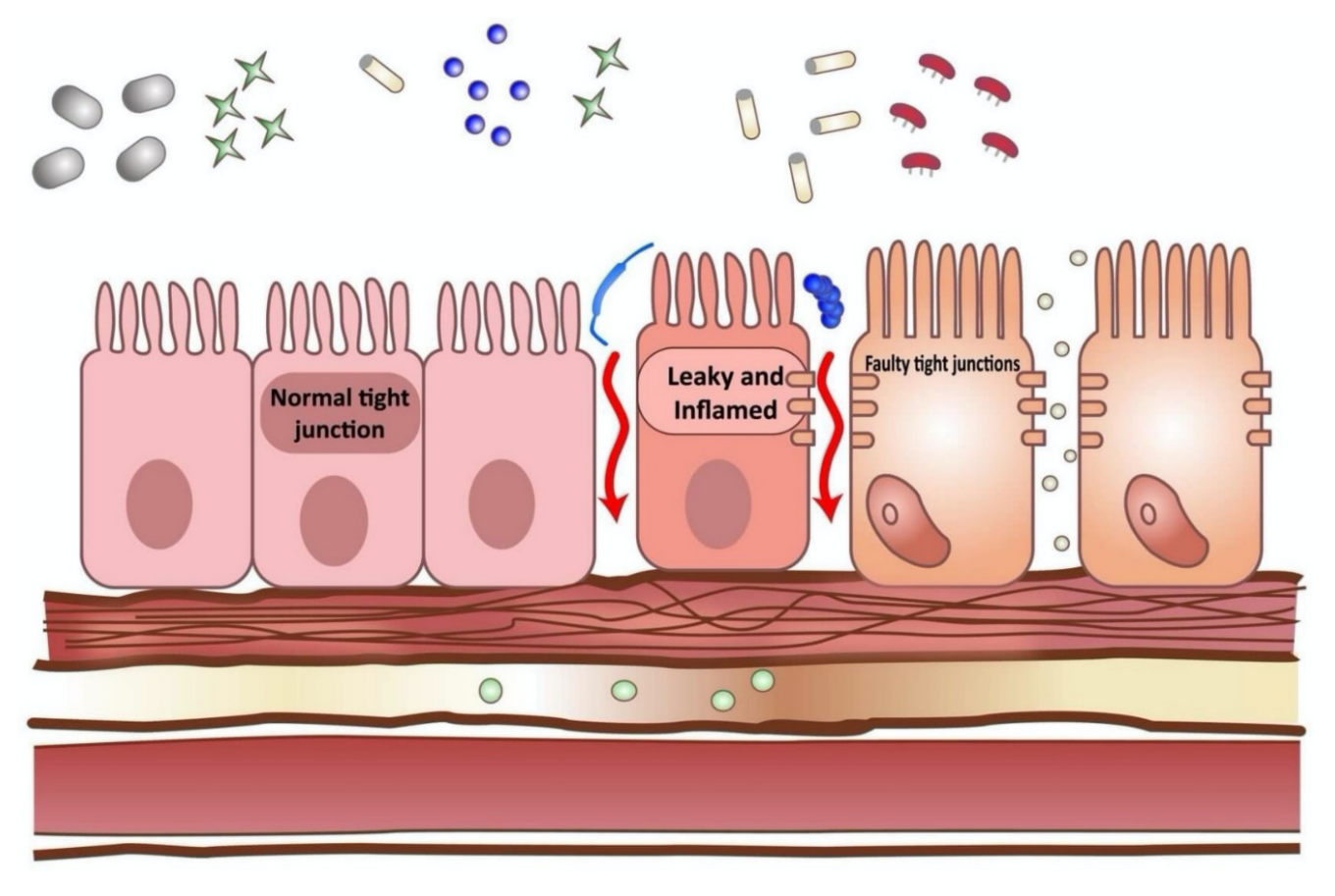
IC_{50} IL-17, IFNγ and Th17 diff.

IMU-856

Restoring Intestinal Barrier Function

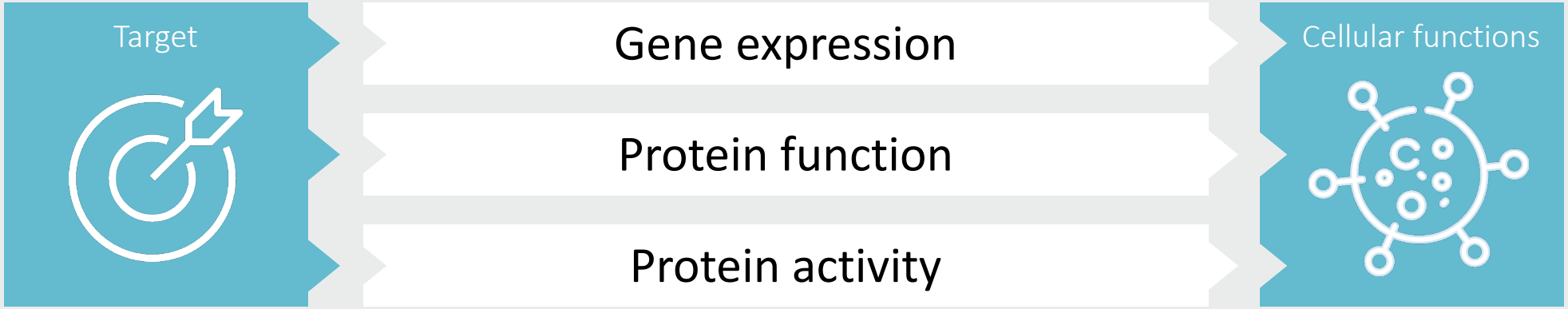
Concept of IMU-856: Restoring the Intestinal Barrier Function Without Impairing the Immune System

Increased bowel permeability connects the microbiome and the immune system



IMU-856's Target: An Epigenetic Regulator…

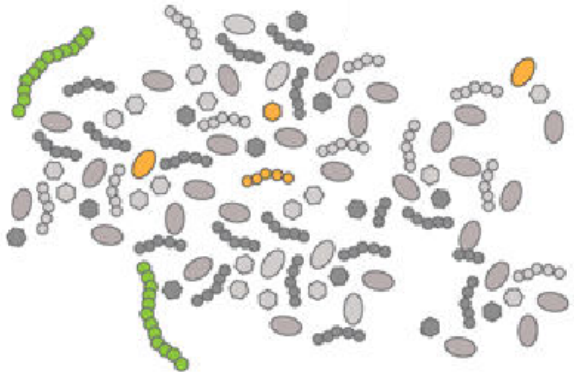
… influencing the tightly regulated network of genes and proteins associated with epithelial cell interaction/adhesion through its enzyme activities.



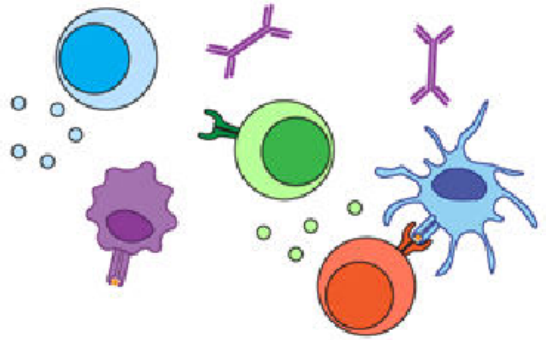
IMU-856: Hypothesis of Therapeutic Approach

Compartmentalize microbiome and immune system
By strengthening the bowel barrier function

Microbiota



Immune system



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)

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 event (infections, malignancies, inability to vaccinate)

IMU-856: Medical Positioning

"IMU-856 is a non-immunosuppressive treatment for gastrointestinal diseases."

"IMU-856 targets the disease-causing trigger"

Maintaining immunocompetency in patients may

- Avoid infections
- Allow vaccinations during therapy
- Maintain cancer surveillance

Potentially providing LONG-TERM SAFETY

Improvement of the bowel barrier function may

- Remove bacterial triggers for relapse
- Maintain remission
- Reduce symptoms

Potentially differentiating as MAINTENANCE DRUG

Immunic THERAPEUTICS

IMU-856: Development Concept

Option and licensing agreement with Daiichi Sankyo, option exercised in January 2020

- Immunic obtained exclusive rights to commercialization of IMU-856 in all countries, including the United States, Europe and Japan

Finalize preclinical work – H1/2020

Phase 1 starting with FPI – 2020

Includes patient population for confirmation of pharmacodynamic activity

- Safety and pharmacokinetics in healthy volunteers (Part A – SAD, Part B – MAD)
- In Part C, patients with IBS-D and IBD are planned to be included
- 2-sugar test performed for bowel permeability to monitor IMU-856 therapy effects during trials

Immunic Therapeutics

Summary

Summary and Highlights

Advanced and well-balanced pipeline:
Three products in development

Shares outstanding: 12.8 million
(as of May 1, 2020)

Phase 2 data read-outs ahead:
Several clinical phase 2 trials with IMU-838 expected to read-out in the next couple of months

Cash position of **USD 18.6 million**
(as of March 31, 2020)

USD 40 million ATM in place

Phase 2 in COVID-19 to start soon
IMU-838 is a potential COVID-19 solution
Broad-spectrum antiviral activity

Raised approximately USD 17.3 million
in April 2020 via a registered direct offering and ATM issuances, substantially extending cash runway beyond important value inflection points

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Thank You!

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