



# Immunic Therapeutics

Developing Selective Oral Drugs in Immunology

NASDAQ: IMUX

Piper Jaffray 31st Annual Healthcare Conference

December 5, 2019



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## Our Vision

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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**
- **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

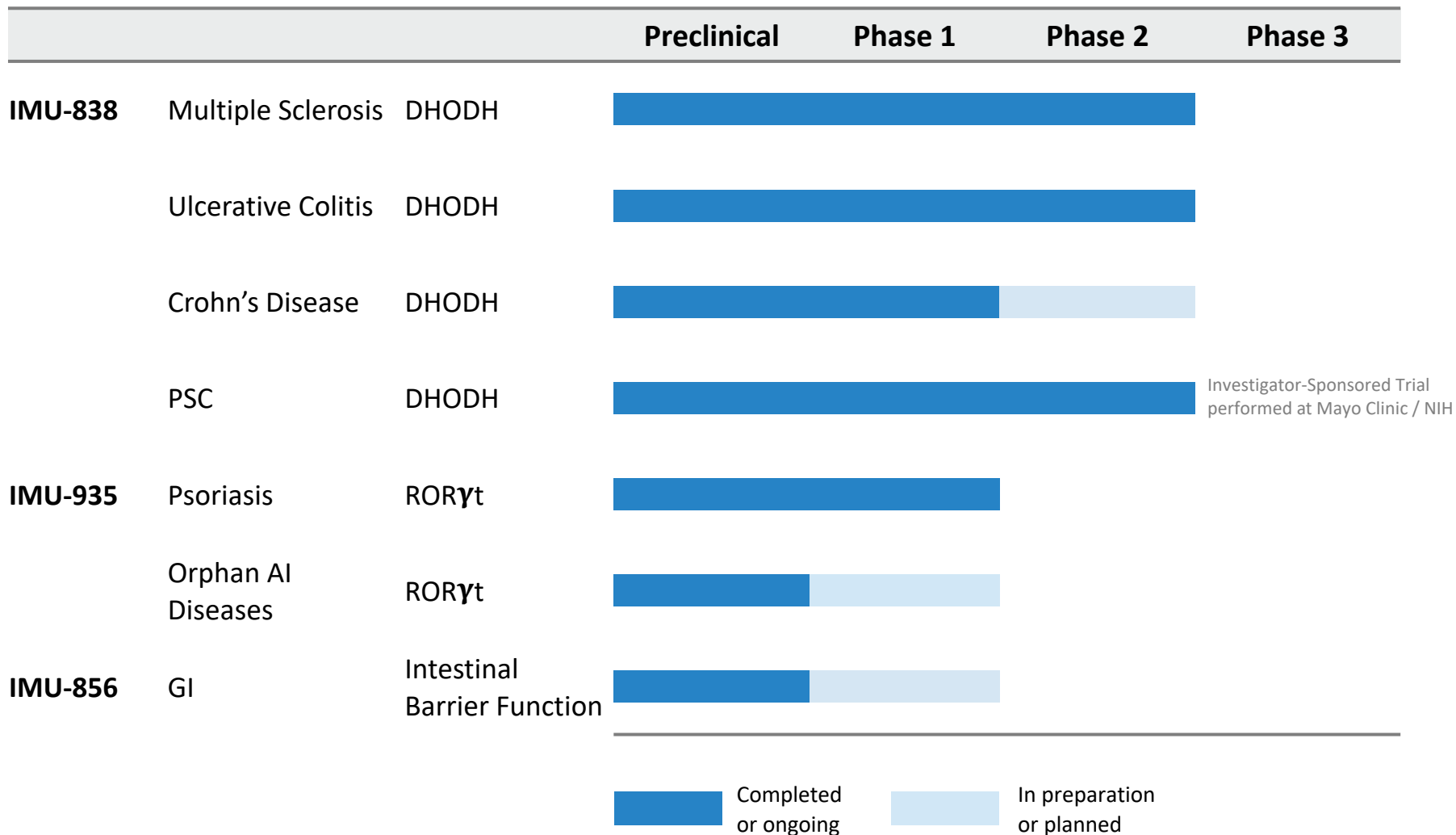
Experienced global management team

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

Strong balance sheet

- Well financed with cash runway to near-term value-driving events
- Cash position: USD 30.5 million (as of September 30, 2019)
- **Cash expected to last into Q4 2020**

# Development Pipeline

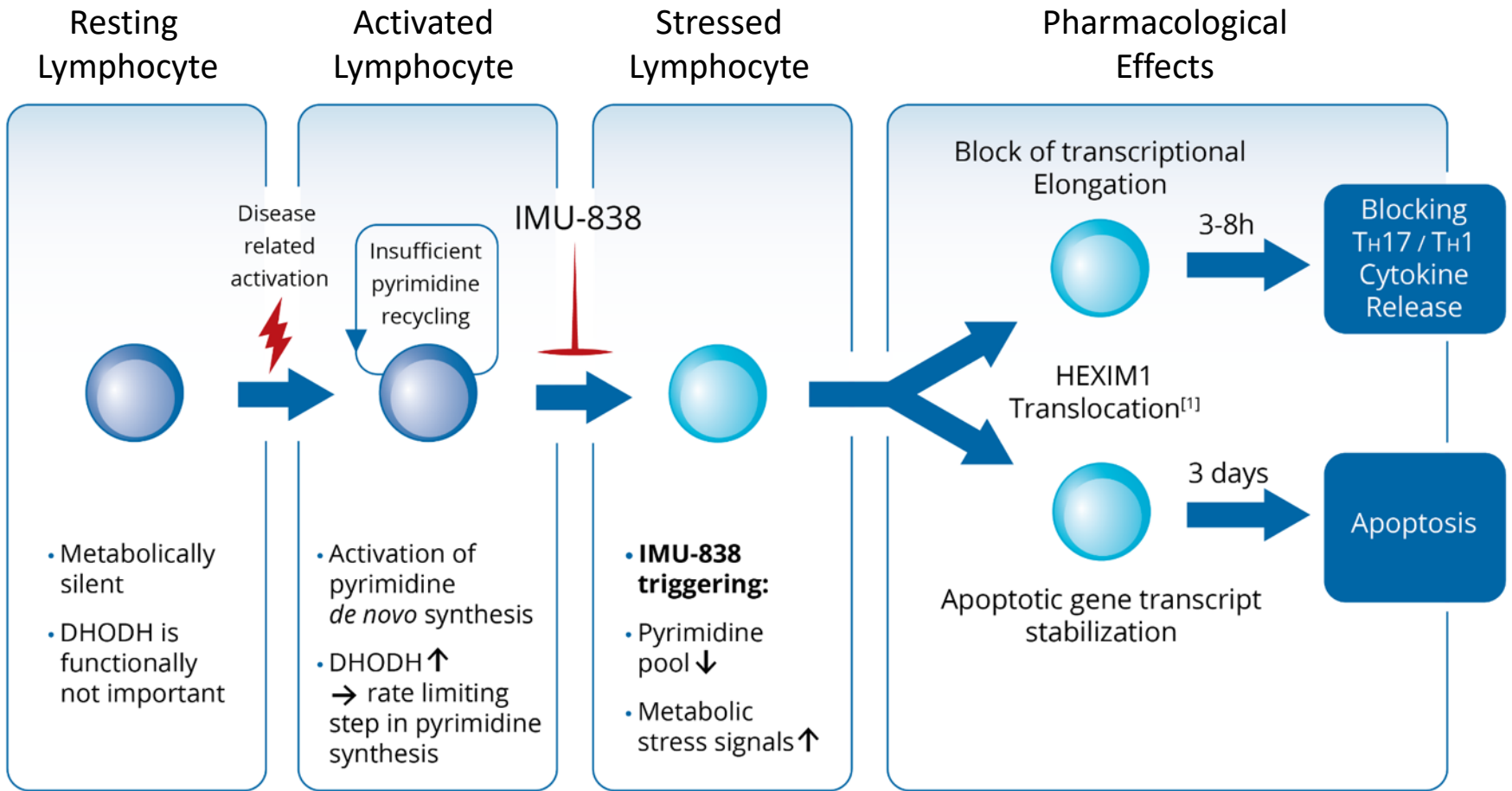


# IMU-838 in Multiple Sclerosis

Mode of Action of IMU-838 Enables Broad  
Therapeutic Use



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



[1] Tan et al., 2016, Molecular Cell 62, 34-46

# MS Opportunity

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

Despite its substantial side effects, Aubagio® reached sales of **around USD 1.8 billion in 2018**<sup>[1]</sup>

**IMU-838** has the potential to be a **best-in-class DHODH inhibitor** and **MS drug** due to improved safety and pharmacokinetics profile



# IMU-838: Potential Advantages in MS

- Potential advantages of IMU-838 therapy compared with Aubagio® (teriflunomide):
  - Selectivity and sensitivity<sup>[1] [2] [3] [4]</sup>
  - Pharmacokinetic parameters<sup>[5] [6]</sup>
  - Safety profile<sup>[7] [8] [9] [10]</sup>
  - Drug-drug interaction potential<sup>[6]</sup>

[1] FDA CDER Pharmacological Review Teriflunomide 2012

[2] Merrill JE, et al. J Neurol 256: 89-103, 2009

[3] Büttner R, et al. Blood 130 (suppl 1): 4426 abstract, 2017

[4] Cada DJ, et al. Hosp Pharm 48: 231-240, 2013 )

[5] FDA CDER Clinical Pharmacology and Biopharmaceutics Review Teriflunomide 2012

[6] Summary of Product Characteristics Aubagio®

[7] SmPC Aubagio®

[8] FDA CDER Medical Review Teriflunomide, 2012

[9] O'Connor et al, NEJM 365: 1293-1303, 2011

[10] O'Connor et al, NEJM 365: supplementary appendix, 2011



# IMU-838: Phase 2 Clinical Trial in RRMS

- Phase 2 trial in patients with relapsing-remitting multiple sclerosis (RRMS)\*
- Study Design
  - Primary endpoint: cumulative number of combined unique active (CUA) MRI lesions, up to week 24
  - Central reading of MRI
  - Study enrolled 210 patients in 36 centers across four European countries
- Timelines
  - Study started in February 2019; enrollment of 210 patients was completed in October 2019 – after 8.5 months only
  - Currently estimated to deliver top-line data in Q3 2020
  - Positive data would allow for quick start of phase 3 study in RRMS

# Potential Positioning of IMU-838 in RRMS

Protection against virus reactivations and potentially PML

Unique property of DHODH inhibitors on slowing disability progression

Suggestion of **sustained activity** even after multiple prior DMT

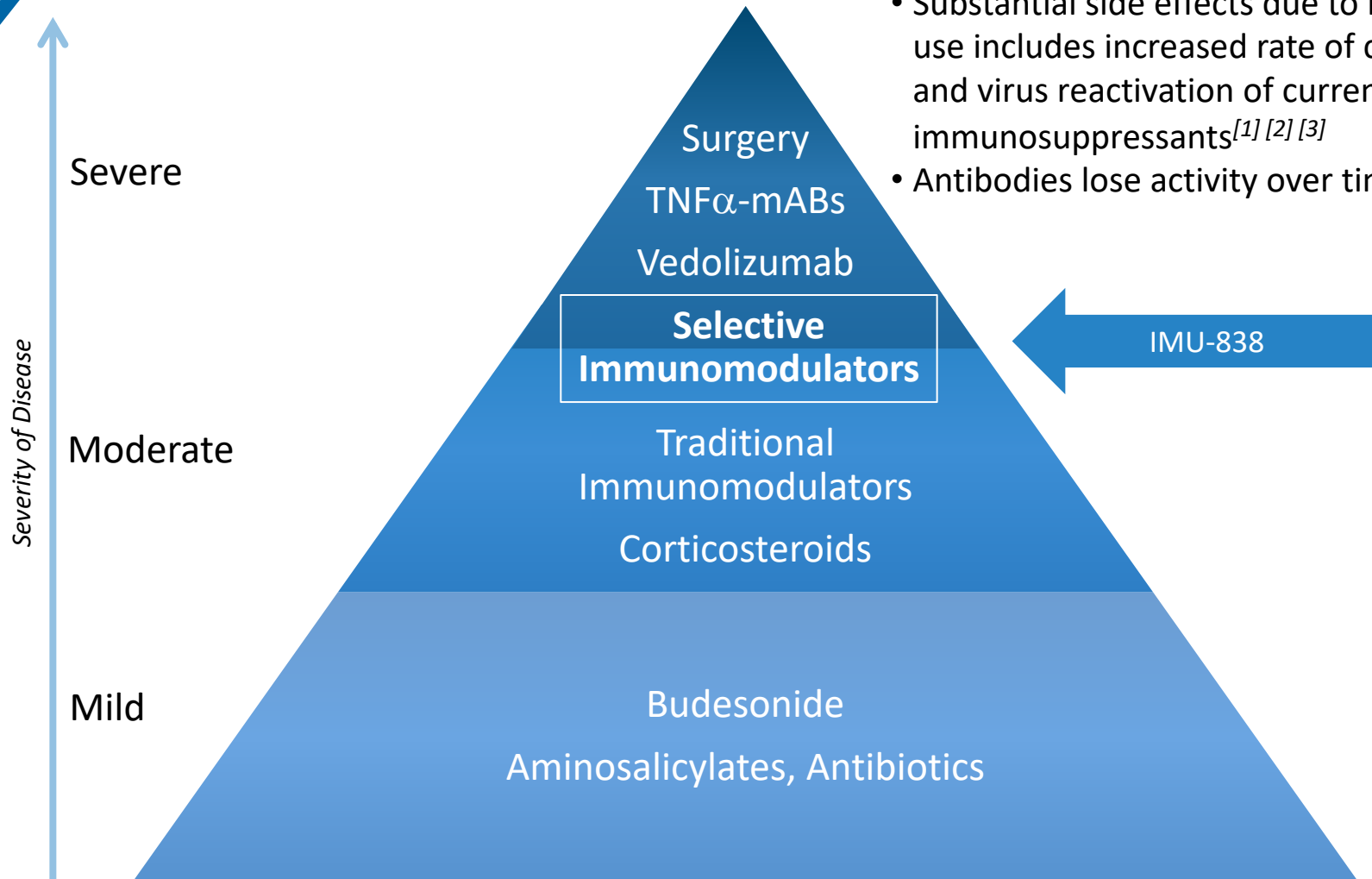
Unique safety profile may allow (for the first time) **combination/maintenance therapies** with highly effective DMTs

# IMU-838 in Inflammatory Bowel Disease (IBD)

New Oral Treatment 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<sup>[1] [2] [3]</sup>
- Antibodies lose activity over time<sup>[4]</sup>

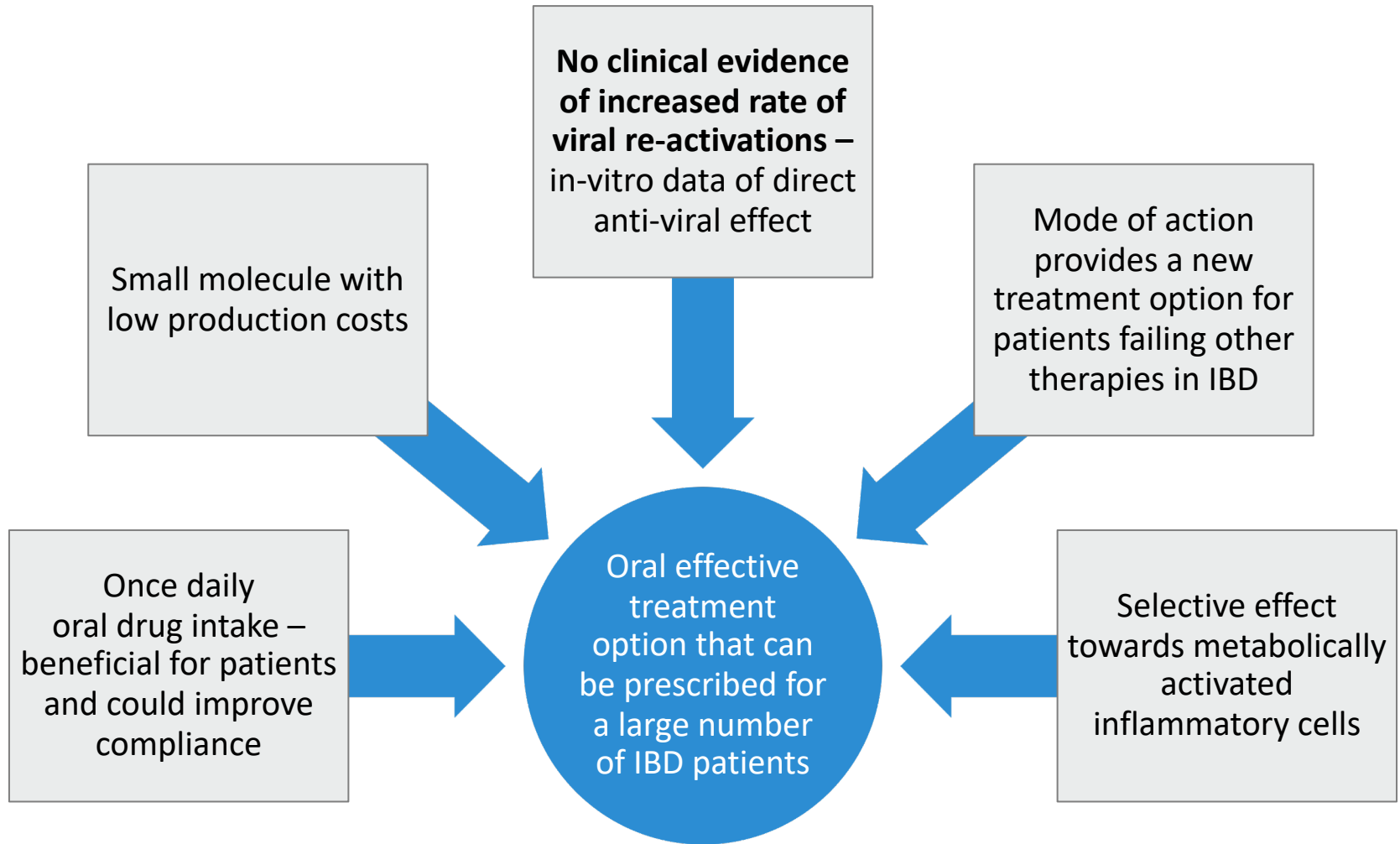
[1] Present, Daniel H., et al. *Annals of internal medicine* 1989; 111.8: 641-649.

[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.

# IMU-838: Key Strengths That Address Limitation of Existing Therapies in IBD

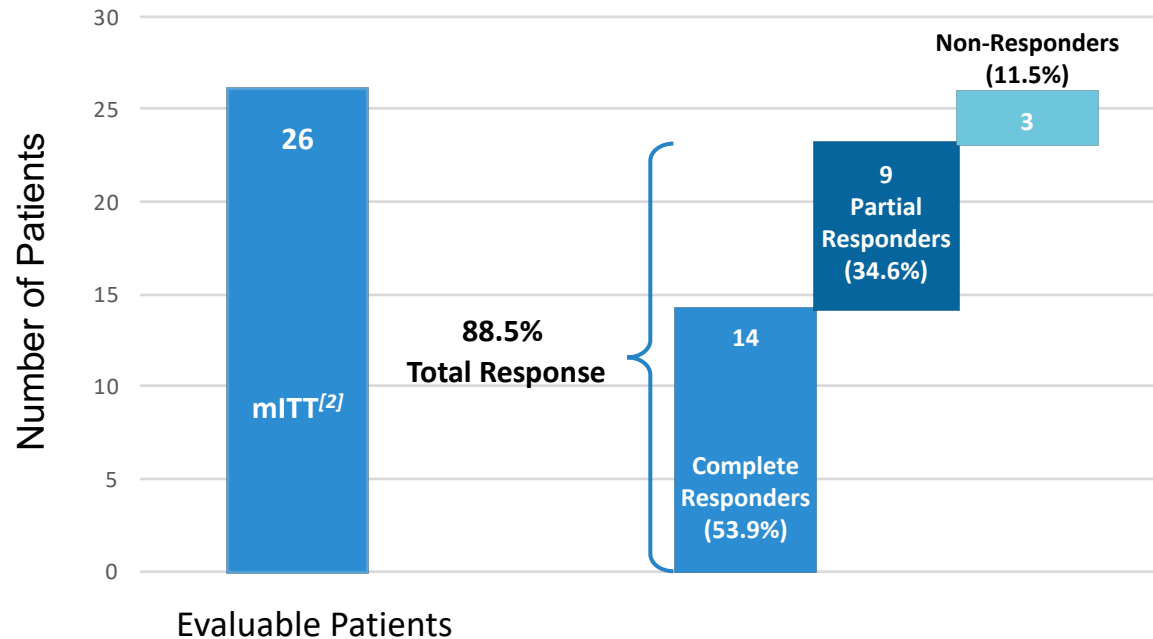




# IBD Phase 2a ENTRANCE: Primary Efficacy Results

## ENTRANCE study:<sup>[1]</sup>

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

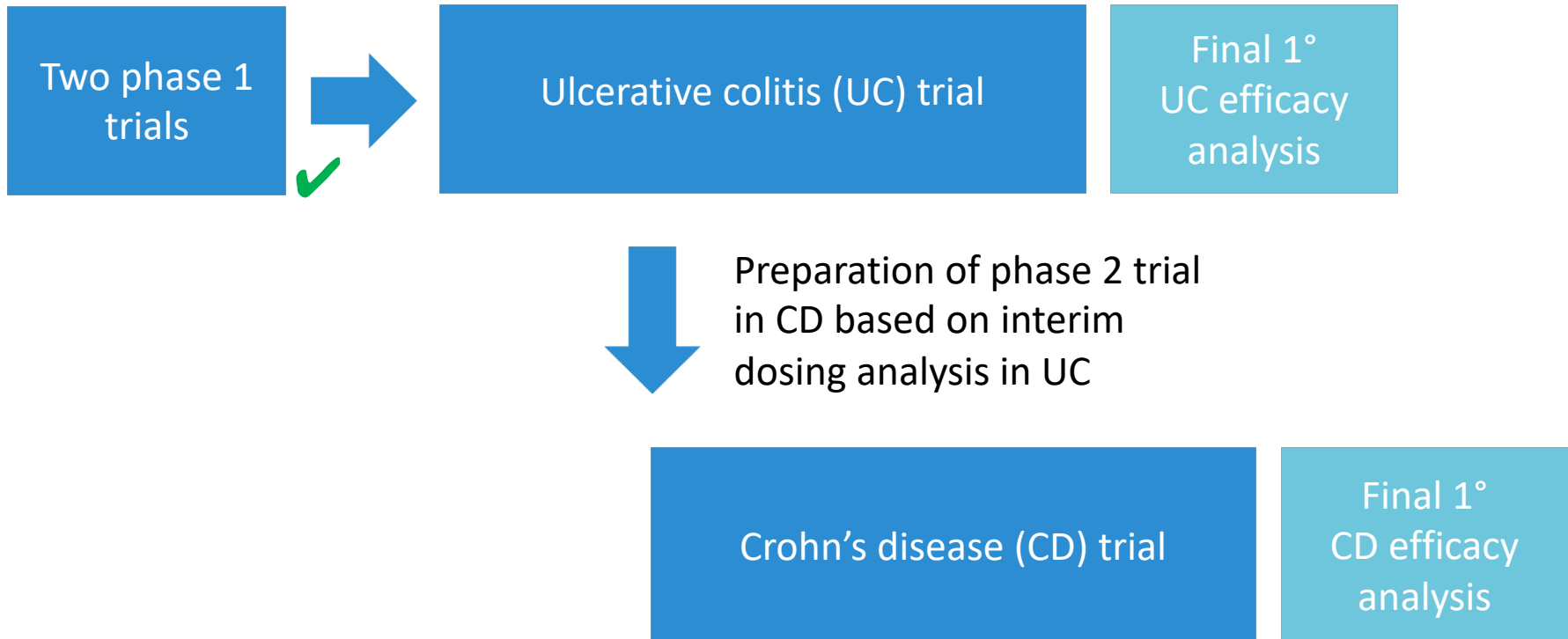


IMU-838 had response rates of:  
85.7% in Crohn's disease  
91.7% in ulcerative colitis

# IMU-838: Clinical Phase 2 in UC Ongoing

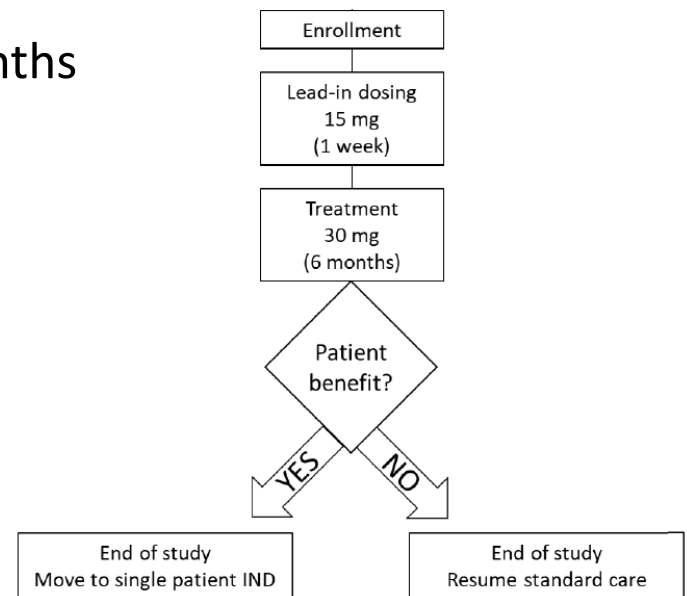
- Active IND in the US; study started in April 2018
- Study design\*
  - Central endoscopy assessment for active disease for study eligibility in order to reduce placebo rate
  - Endpoint measuring proportion of patients with symptomatic remission and endoscopic healing at week 10
  - Number of patients estimated to be 240
- Currently more than 70 active sites in 10 countries
  - USA, Western, Central and Eastern Europe
- Interim dosing analysis performed end of August 2019
  - Performed by an unblinded, independent data review committee
  - Immunic hypothesized 30 mg to be the lowest effective dose and therefore anticipated that the 10 mg dose might be discontinued
    - 10 mg surprisingly also showed hints of activity
    - All three doses are being continued

# IBD: Overall Study Program



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

- Ongoing investigator-sponsored trial (IST): 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 by Prof. Keith Lindor, MD, and Elisabeth Carey, MD, supported by NIH funding
  - Dosing: 30 mg IMU-838 qd for six months
  - Primary endpoint: change in serum alkaline phosphatase (ALP) at six months compared to baseline
- Study started in August 2019
- Positive data should enable immediate start of a pivotal trial in this orphan indication by Immunic



Study Flow Chart

# IMU-935

Unique ROR $\gamma$ t Inverse Agonist



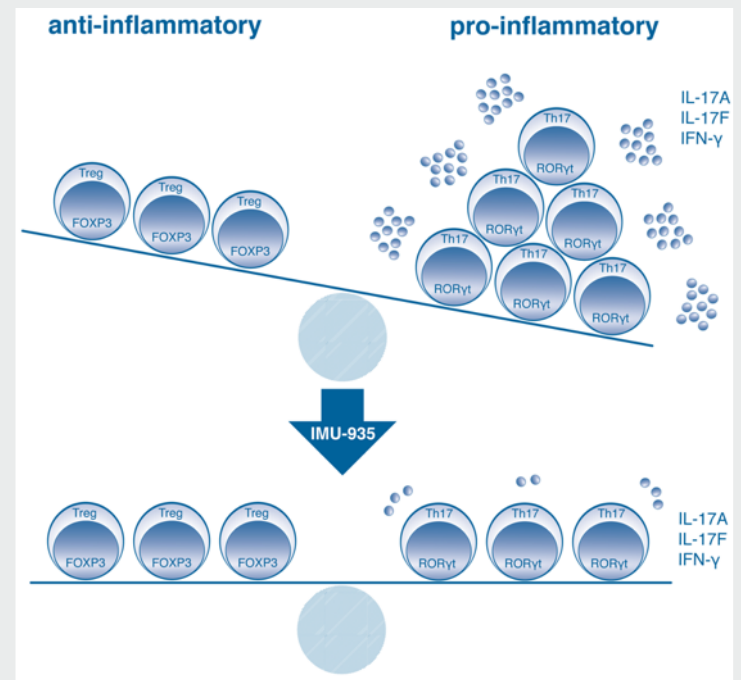
# Autoimmune Diseases and IMU-935

## Challenge:

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

## Solution:

- IMU-935 is a potent small molecule targeting ROR $\gamma$ t



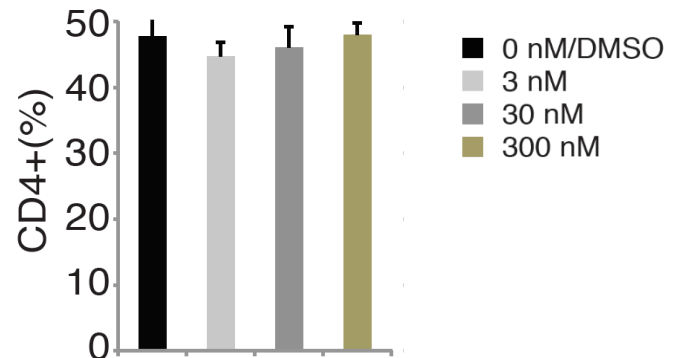
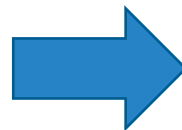
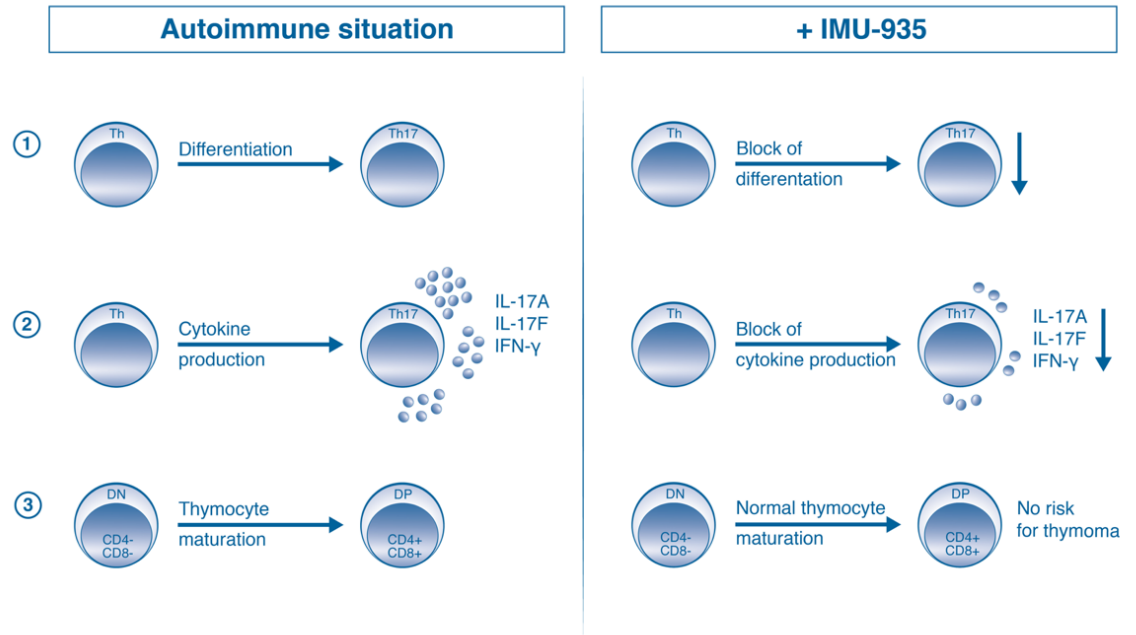
[1] Rose, Noel R. American journal of epidemiology 2016; 183.5: 403-406.

[2] Fasching, Patrizia, et al. *Molecules* 2017 22.1: 134.



# IMU-935: Main Functions of ROR $\gamma$ t

- The differentiation towards Th17 cells is inhibited by IMU-935.
- The production of IL-17A and IL-17F is inhibited by IMU-935.
- Result: **IMU-935 allows normal thymocyte maturation** from double negative towards matured CD4+ thymocytes (CD4+ and CD4+/CD8+).

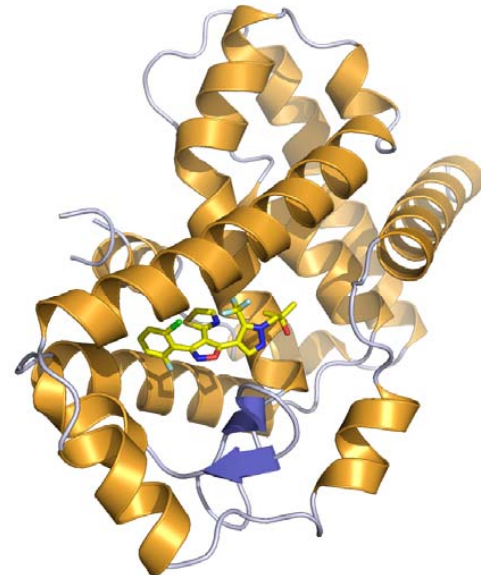


# IMU-935: Cytokine Inhibition in Low Nanomolar Range

- Effect of the development compound IM105935 (IMU-935) in stimulated human PBMCs
  - Inhibition of ROR $\gamma$  (20 nM) and DHODH (240 nM) leads to synergistical inhibition of cytokines with IC<sub>50</sub> of 3-5 nM in stimulated human lymphocytes

	IC <sub>50</sub> ( $\mu$ M)
IL-17A	0.005
IL-17F	0.004
IFN $\gamma$	0.003
IL-1a and b	no inhibition
IL-4,5,6,8	no inhibition
ROR $\gamma$ (MST)	0.024
ROR $\gamma$ (cellular, rep.)	0.020
DHODH	0.240
Th17 differentiation	0.150

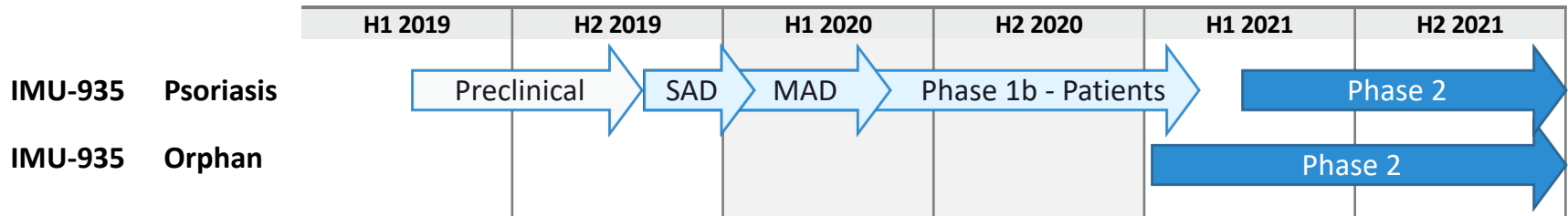
Read-out: effect on cytokine production after 48 hours in PBMCs



Resolution 2.6 Å of a closely related derivative compound binds to hydroxycholesterol binding site of ROR $\gamma$

# IMU-935: Project Status

- Clinical phase 1 program started in September 2019
  - Ongoing double-blind, placebo-controlled, single and multiple ascending dose trials of IMU-935 in healthy volunteers
  - Extension of these studies to assess safety and mechanism-related biomarkers in patients with mild to moderate psoriasis is planned to start next year – would potentially offer early read-out of activity based on four-week treatment
- Identification of suitable orphan indications with high unmet medical need for accelerated development is ongoing

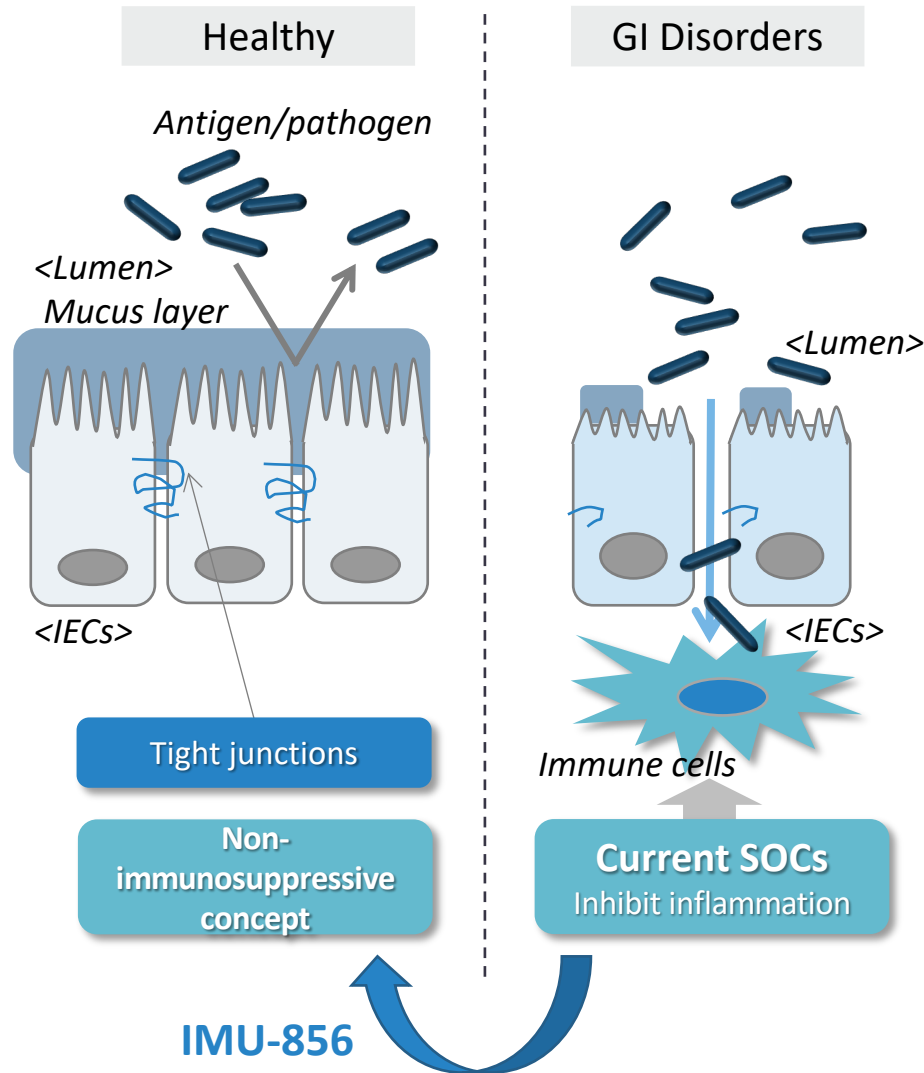


# IMU-856

Restoring Intestinal Barrier Function



# IMU-856: Targeting Gut Barrier Function With New Mode of Action



- IMU-856 is a potent inhibitor of a **novel target** which was validated in a knock-out animal model
- Targeting restoration of the intestinal barrier function without impairing the immune system
- Small **orally available** molecule suitable for once daily dosing
- Obtained through option and licensing agreement with **Daiichi Sankyo Venture Science Labs**



## IMU-856: Development Plan

- Possible GI indications
  - IBD, IBS-D, ICI
- Clinical development plan
  - Phase 1 single and multiple ascending dose studies are expected to start in H1 2020
- IMU-856 has substantial potential for the treatment of further diseases outside GI
- Product is covered by a global PCT patent application



# Summary



# Financial Summary

- Nasdaq: **IMUX**
- Headquarters in New York
- Shares outstanding: 10.1 million (as of November 1, 2019)
- Cash position of USD 30.5 million (as of September 30, 2019)
- **Cash runway** expected to be sufficient beyond important value inflection points **into Q4 2020**
- Immunic's reverse takeover with Vital Therapies was supported by a committed investor base **investing approximately USD 30 million in April 2019**

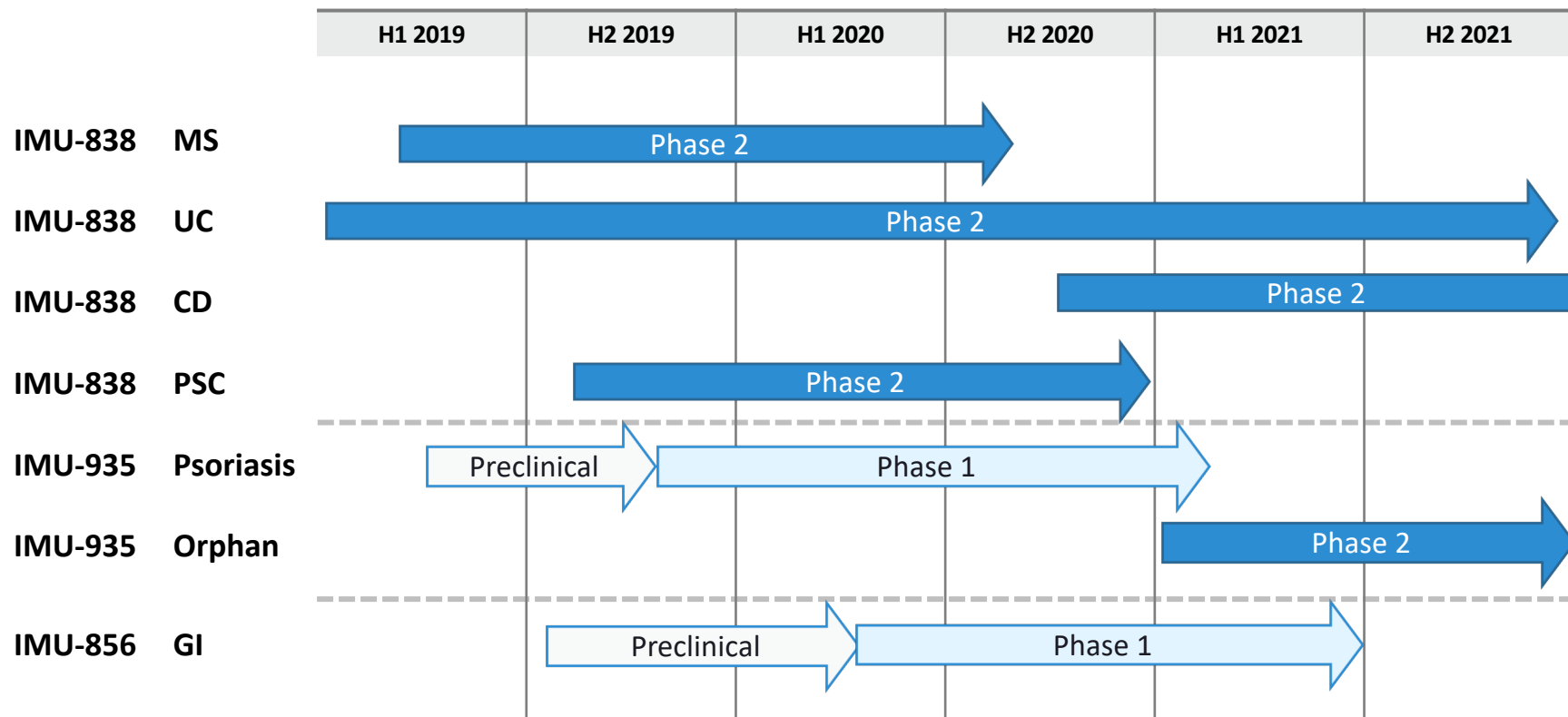




# Key Investment Highlights – Three Oral Drugs in Development

- IMU-838 currently tested in **three phase 2 trials**
- RRMS **phase 2 data** of IMU-838 expected in Q3 2020
- Very promising **data from interim dosing analysis** of UC phase 2
- Three oral programs in active development – each with unique positioning
  - Phase 1 of **IMU-935** started in Sep 2019 – 1<sup>st</sup> data expected Q1 2020
  - **IMU-856** could be a **disruptive technology** for treating GI diseases like IBS-D and IBD – restoring intestinal barrier function

# Significant News Flow Potential From Three Development Programs









# Thank You!

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