



Immunic Therapeutics

Developing Selective Oral Drugs in Immunology

NASDAQ: IMUX



Cantor Global Healthcare Conference – October 4, 2019



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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: High demand target 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 36.1 million (as of August 8, 2019)
- **Cash expected to last into Q4 2020**

Immunic Leadership Team

Company is led by an experienced management team



Daniel Vitt, PhD
CEO & President



Andreas Muehler, MD, MBA
CMO



Hella Kohlhof, PhD
CSO



Manfred Groeppel, PhD
COO



Sanjay S. Patel, CFA
CFO

Renowned international board of directors



Duane Nash, MD, JD, MBA
Former Director of
Vital Therapies



Joerg Neermann, PhD
LSP



Vincent Ossipow, PhD, CFA
Omega Funds

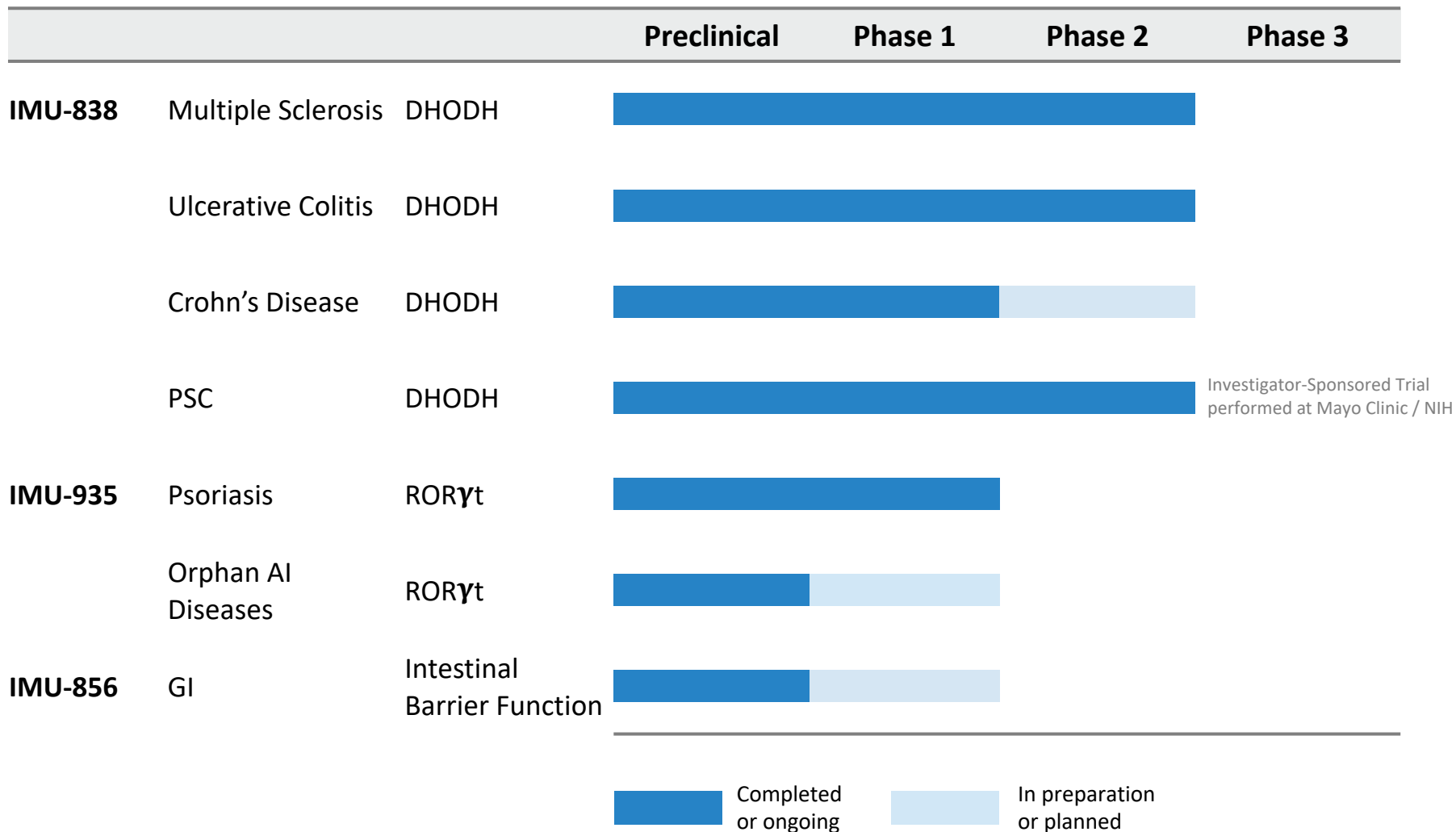


Jan Van den Bossche
Fund+



Daniel Vitt, PhD
CEO & President of Immunic

Development Pipeline

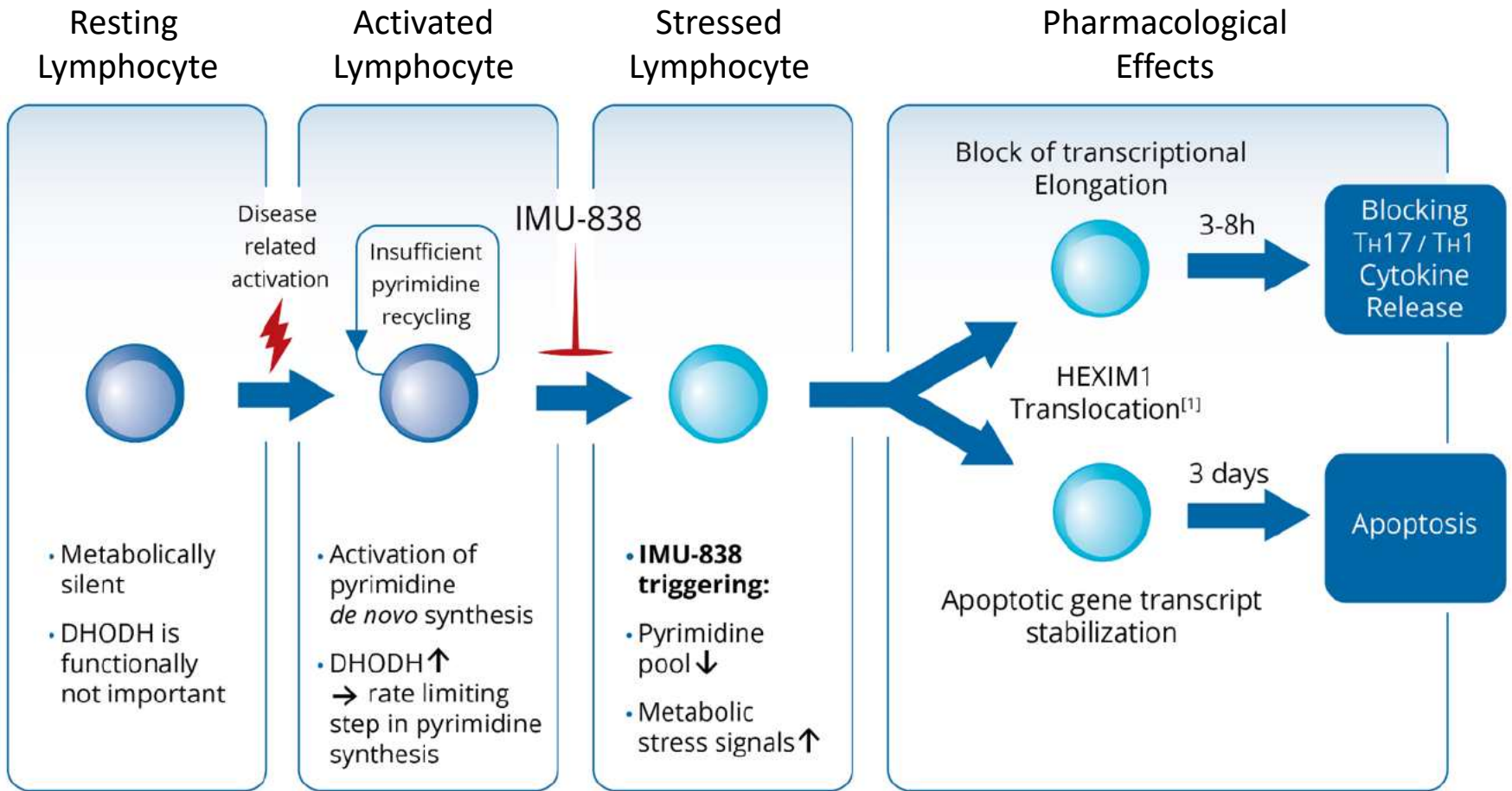


IMU-838 in Multiple Sclerosis

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^[1]**

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^{[1] [2] [3] [4]}
 - Pharmacokinetic parameters^{[5] [6]}
 - Safety profile^{[7] [8] [9] [10]}
 - Drug-drug interaction potential^[6]

[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

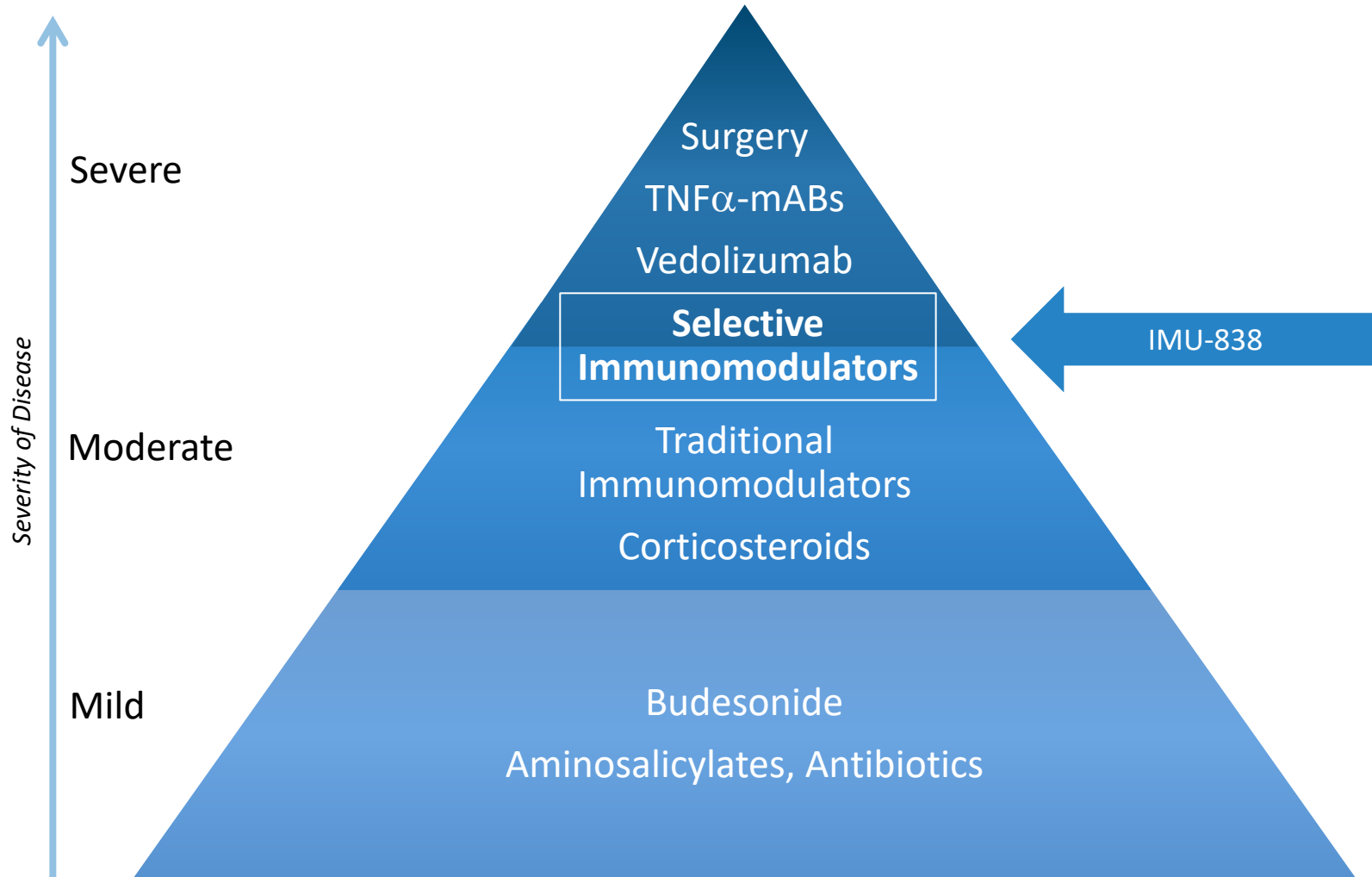
- **Phase 2 trial** in patients with relapsing-remitting multiple sclerosis (RRMS)*
- **Study Design**
 - Planning to enroll 195 patients in four countries
 - Primary endpoint: cumulative number of combined unique active (CUA) MRI lesions, up to week 24
 - Central reading of MRI
- **Timelines**
 - Study started in February 2019
 - Currently estimated to deliver **top-line data in Q3 2020**
 - Positive data would allow for quick start of **phase 3 study** in RRMS

IMU-838 in Inflammatory Bowel Disease (IBD)

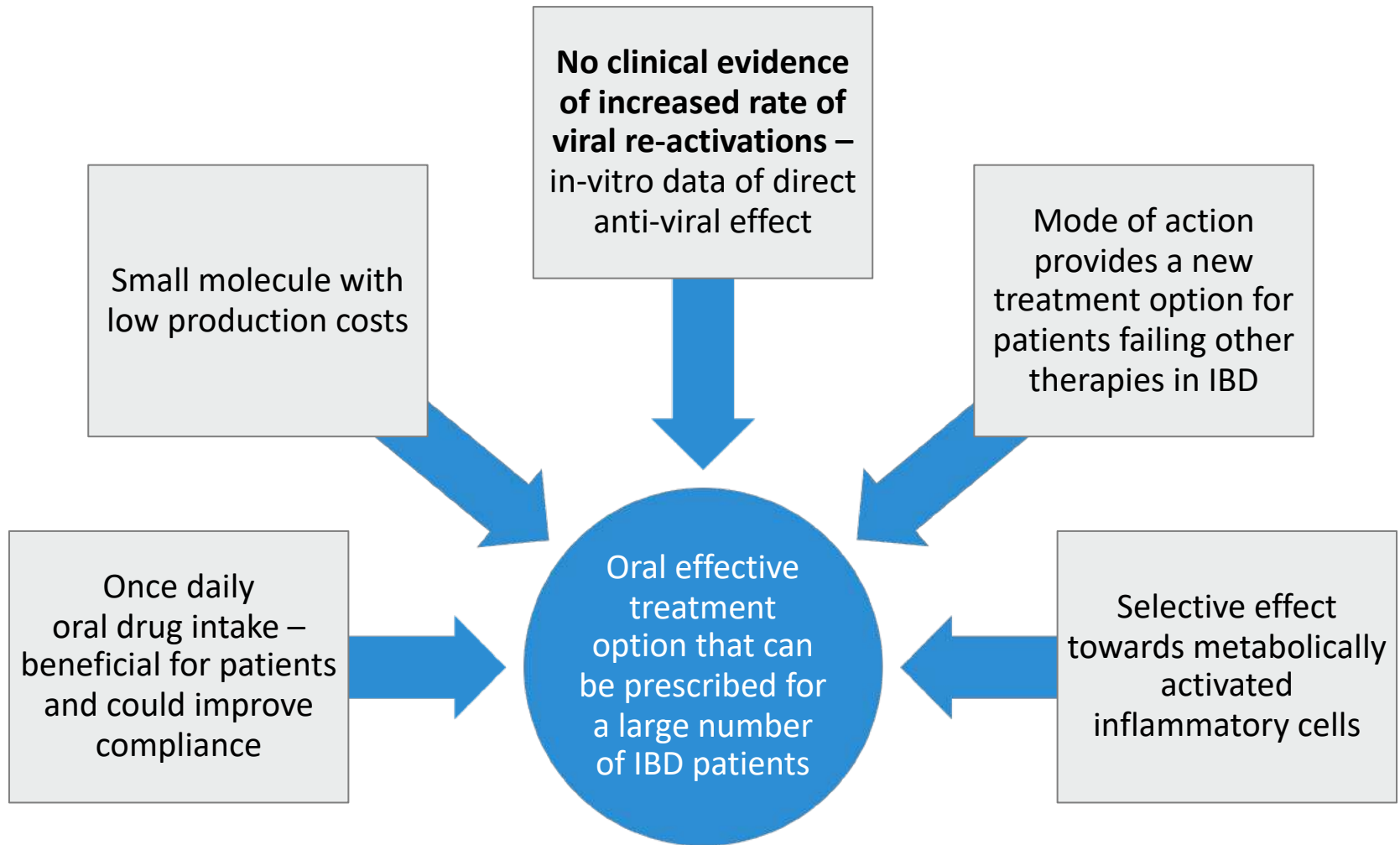
New Oral Treatment with Promising Safety Profile



IBD: Therapeutic Pyramid



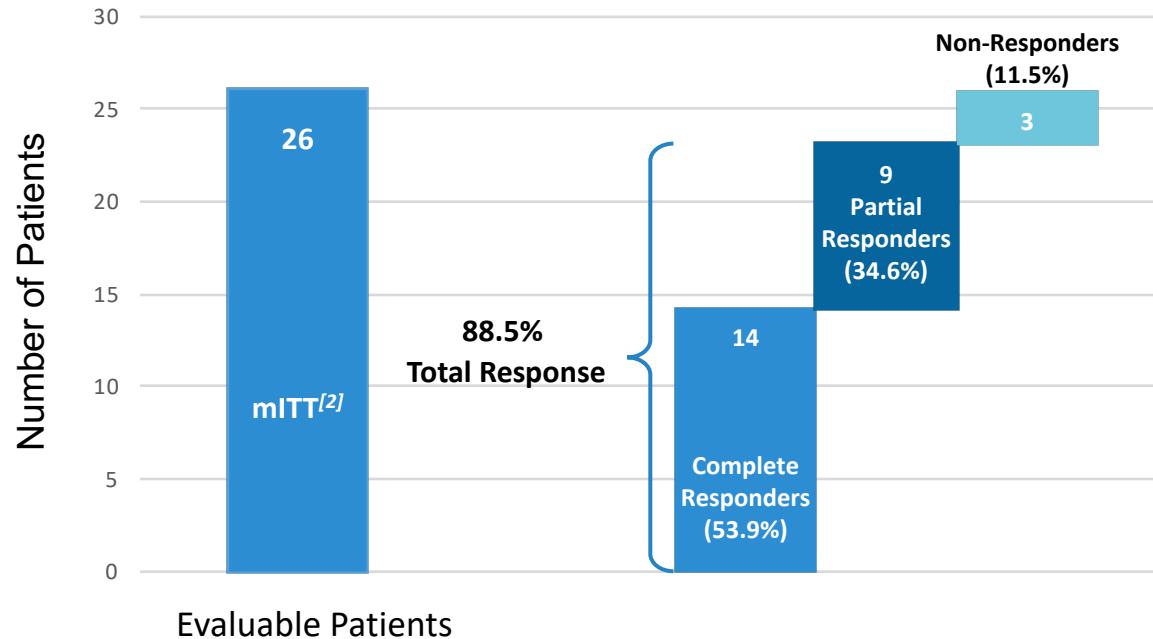
IMU-838: Key Strengths That Address Limitation of Existing Therapies in IBD



IBD Phase 2a ENTRANCE: Primary Efficacy Results

ENTRANCE study:^[1]

- 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)

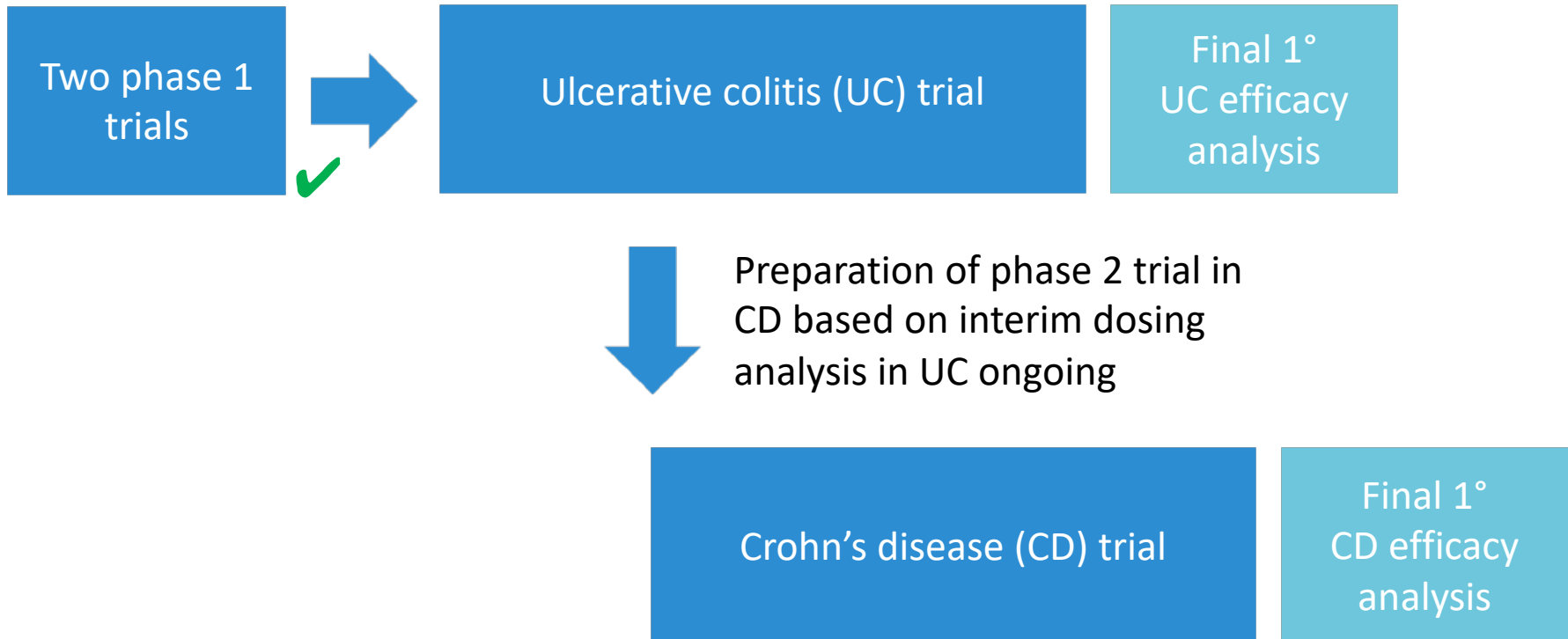


IMU-838 had response rates of:
85.7% in Crohn's disease
91.7% in ulcerative colitis

IMU-838: Clinical Phase 2 in UC Ongoing

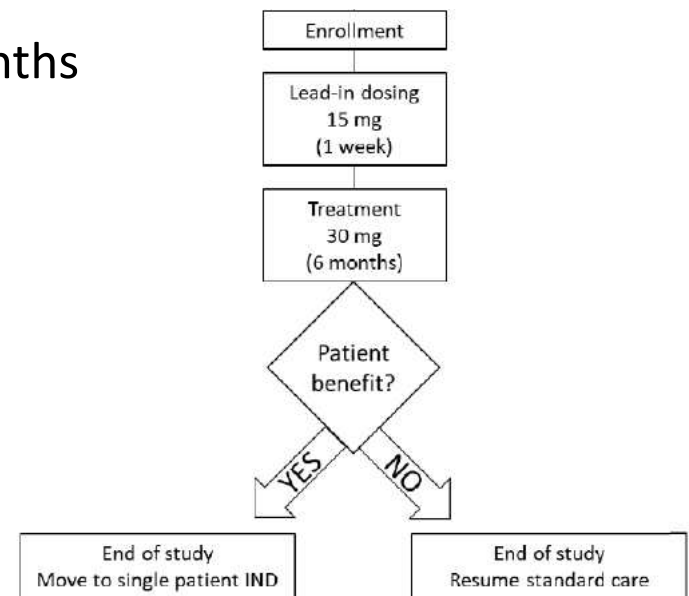
- Active IND in the US; study started in April 2018
- Study design*
 - Central endoscopy assessment for active disease for study eligibility in order to reduce placebo rate
 - Endpoint measuring proportion of patients with symptomatic remission and endoscopic healing at week 10
 - Number of patients 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 γ t Inverse Agonist



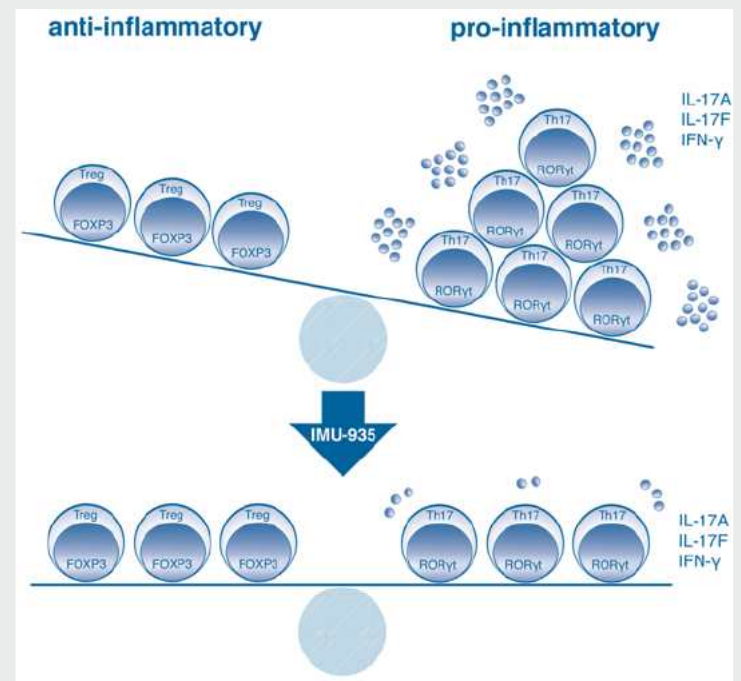
Autoimmune Diseases and IMU-935

Challenge:

- Autoimmune diseases are frequent diseases affecting millions of patients worldwide^[1]
- Th17/IL-17/ROR γ t 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]

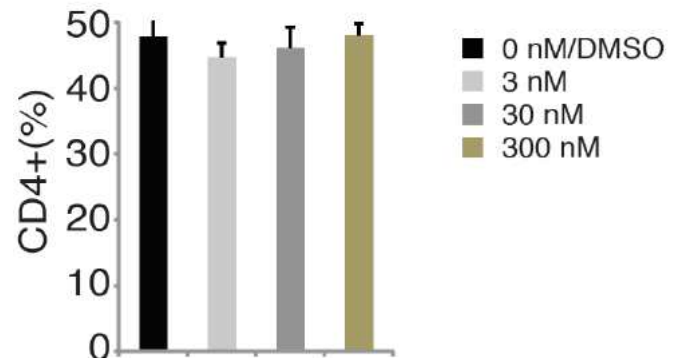
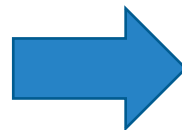
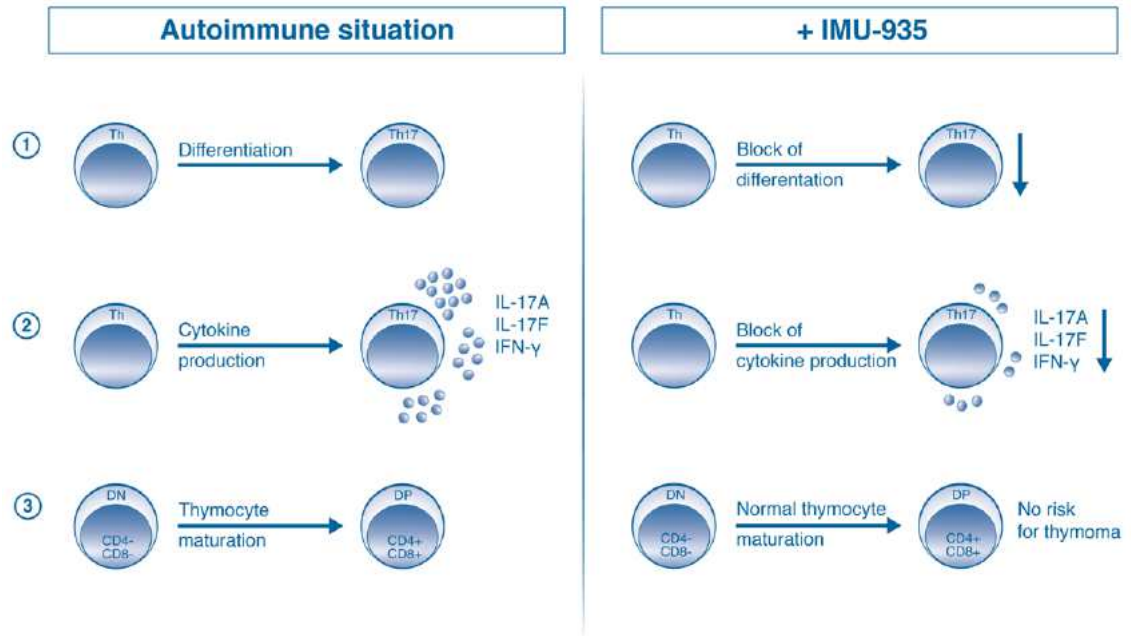
Solution:

- IMU-935 is a potent small molecule targeting ROR γ t



IMU-935: Main Functions of ROR γ 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+).

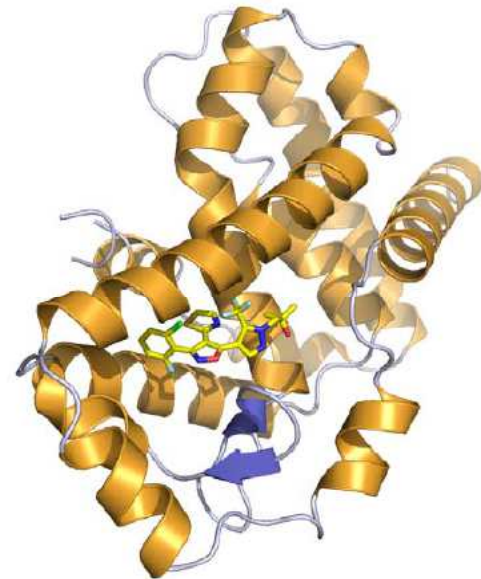


IMU-935: Cytokine Inhibition in Low Nanomolar Range

- Effect of the development compound IM105935 (IMU-935) in stimulated human PBMCs
 - Inhibition of ROR γ (20 nM) and DHODH (240 nM) leads to synergistical inhibition of cytokines with IC₅₀ of 3-5 nM in stimulated human lymphocytes

	IC ₅₀ (μ M)
IL-17A	0.005
IL-17F	0.004
IFN γ	0.003
IL-1a and b	no inhibition
IL-4,5,6,8	no inhibition
ROR γ (MST)	0.024
ROR γ (cellular, rep.)	0.020
DHODH	0.240
Th17 differentiation	0.150

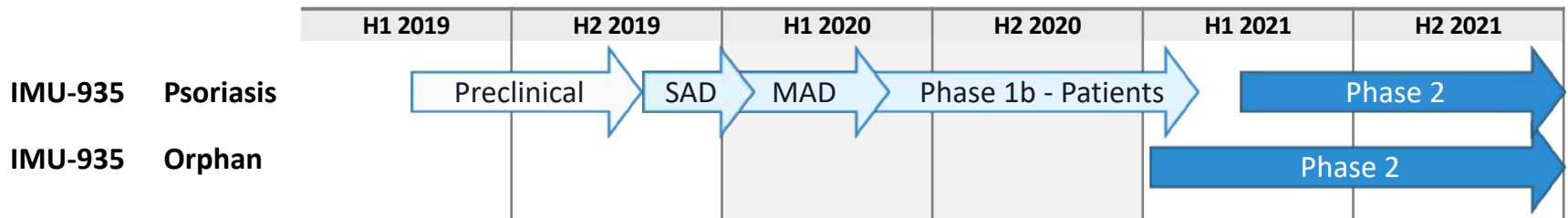
Read-out: effect on cytokine production after 48 hours in PBMCs



Resolution 2.6 Å of a closely related derivative compound binds to hydroxycholesterol binding site of ROR γ

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
- Expansion to orphan indications with high unmet medical need for accelerated development is ongoing

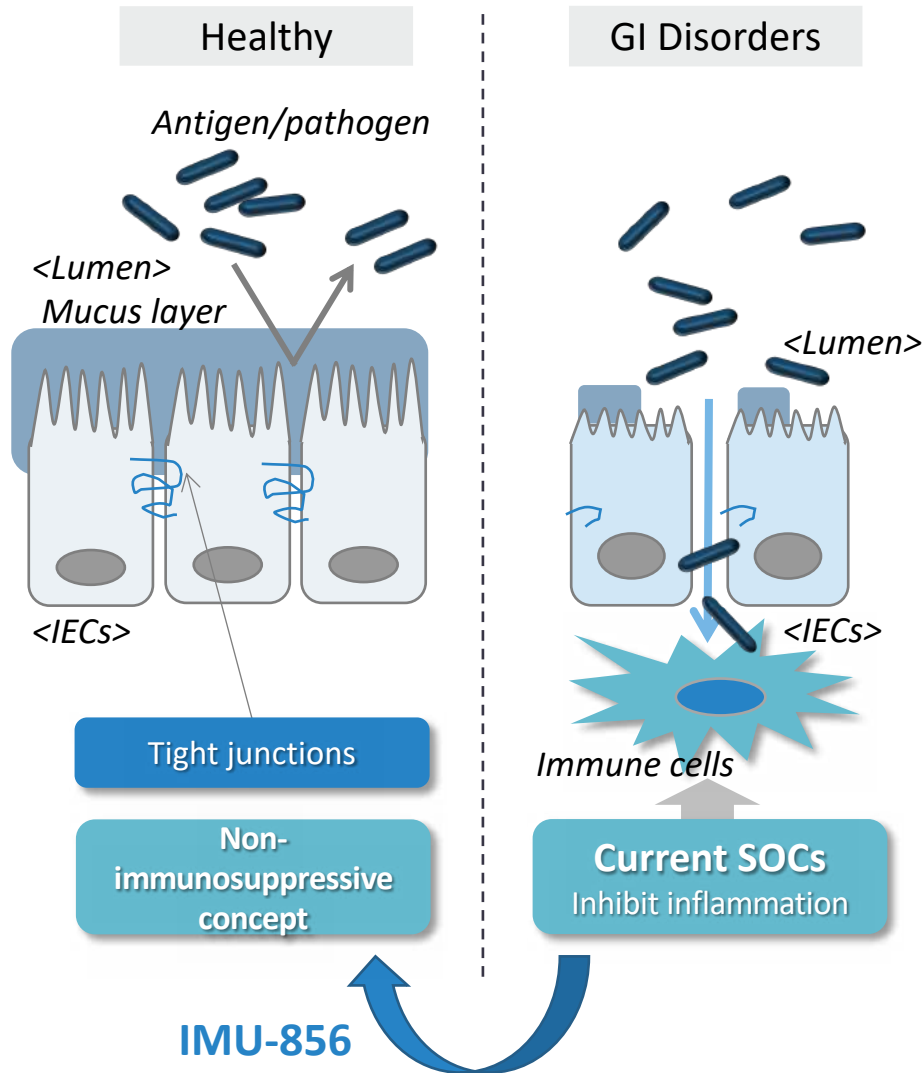


IMU-856

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 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, e.g. CNS
- Product is covered by a global PCT patent application

Summary



Financial Summary

- Nasdaq: **IMUX**
- Headquarters in San Diego – plan to relocate to East Coast in 2019
- Shares outstanding: 10.0 million (as of August 8, 2019)
- Cash position of USD 36.1 million (as of August 8, 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 – 1st data expected Q1 2020
 - **IMU-856** could be a **disruptive technology** for treating GI diseases like IBS-D and IBD – restoring intestinal barrier function



Thank You!

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