Immunic THERAPEUTICS

Immunic Therapeutics

Developing Selective Oral Drugs in Immunology

NASDAQ: IMUX

BIO-Europe, November 12th 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: 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

			Preclinical	Phase 1	Phase 2	Phase 3
IMU-838	Multiple Sclerosis	DHODH				
	Ulcerative Colitis	DHODH				
	Crohn's Disease	DHODH				
	PSC	DHODH				
IMU-935	Psoriasis	RORγt				
	Orphan AI Diseases	RORγt				
IMU-856	GI	Intestinal Barrier Function				

Investigator-Sponsored Trial performed at Mayo Clinic / NIH

Completed or ongoing

In preparation or planned

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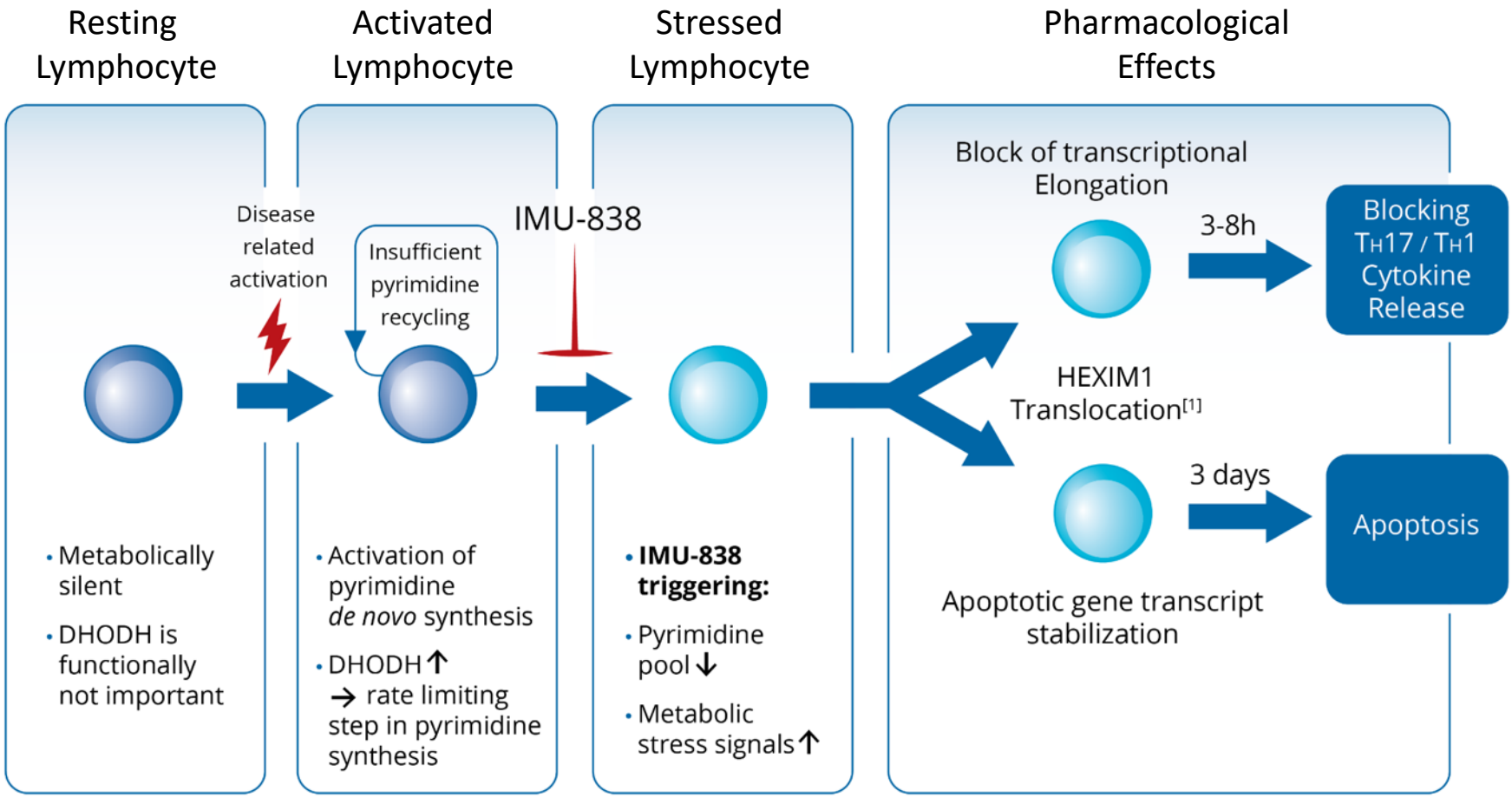
IMU-838 in Multiple Sclerosis

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

[1] http://hugin.info/152918/R/2233891/878937.PDF Accessed April 3, 2019

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
  - 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

* clinicaltrials.gov: NCT03846219

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

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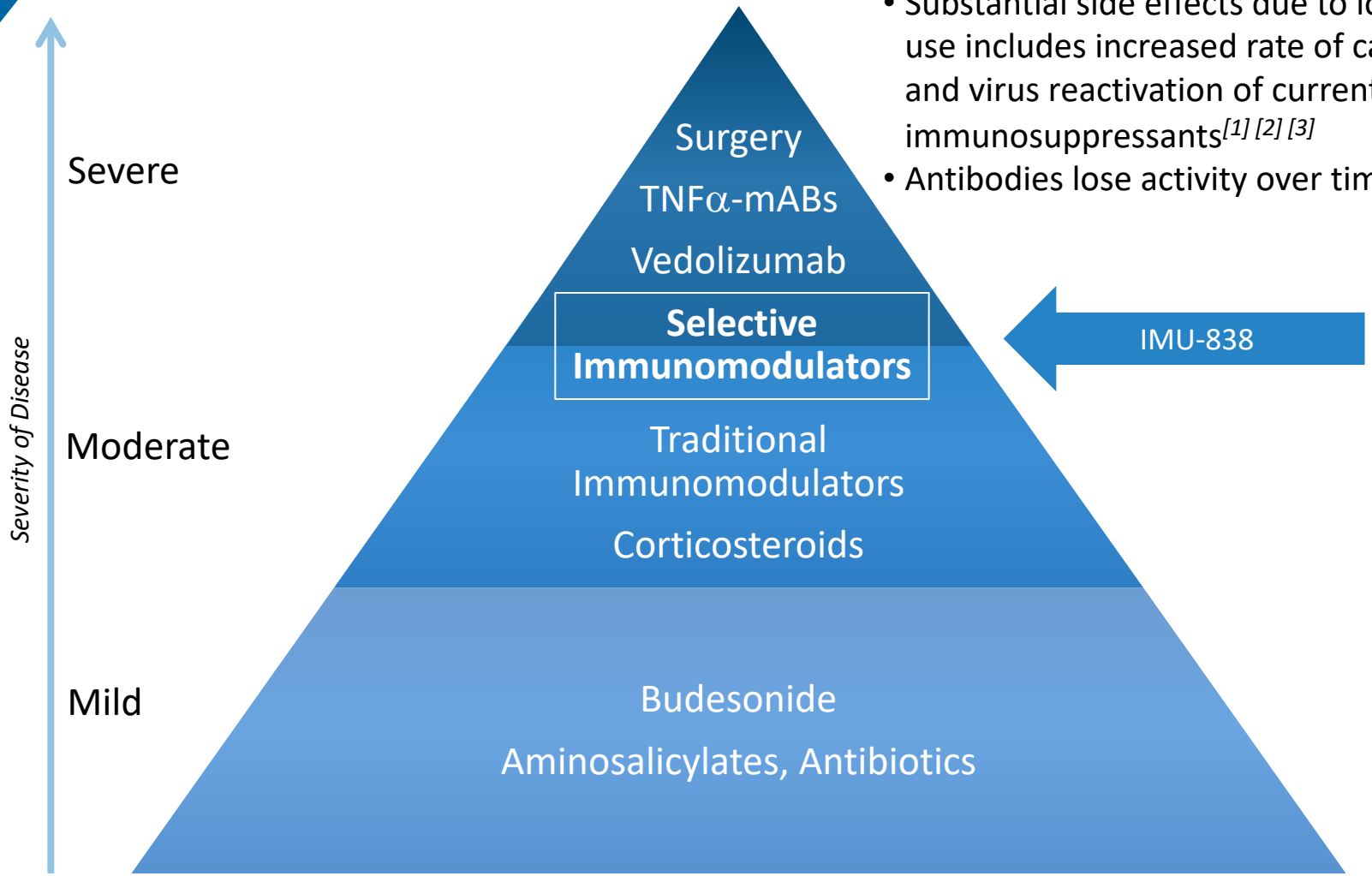
IMU-838 in Inflammatory Bowel Disease (IBD)

New Oral Treatment with Promising Safety Profile

IBD: Therapeutic Pyramid

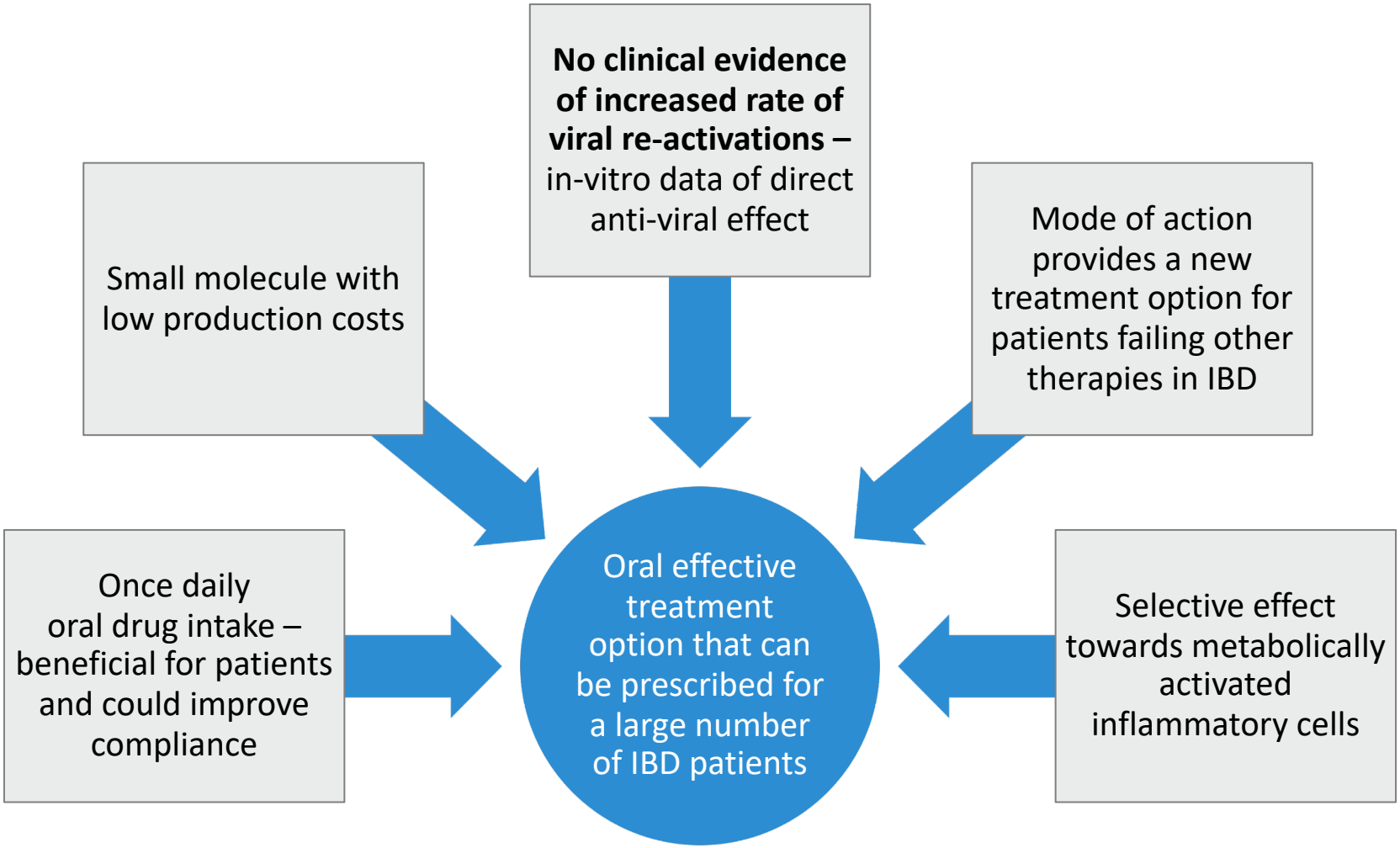


Current solutions have limitations

- Substantial side effects due to long-term use includes increased rate of cancer risk and virus reactivation of currently used immunosuppressants[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.

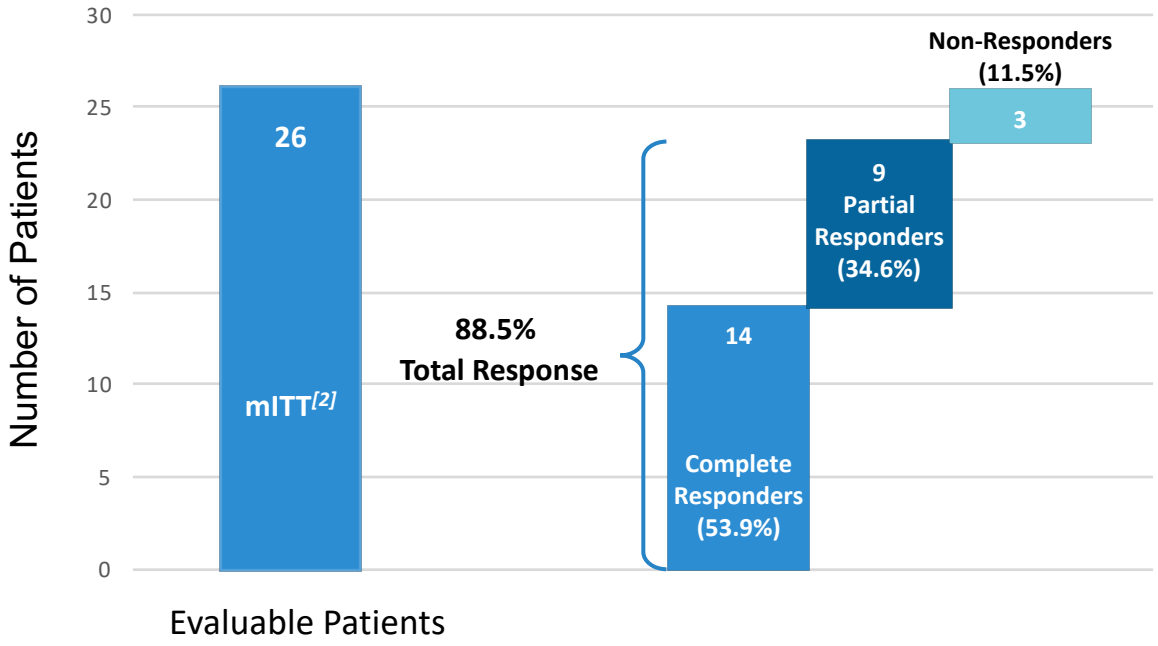
IMU-838: Key Strengths That Address Limitation of Existing Therapies in IBD



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

[1] Herrlinger et.al., 2011, Gastroenterology *140*:588.
[2] mITT: modified intent to treat

IMU-838: Clinical Phase 2 in UC Ongoing

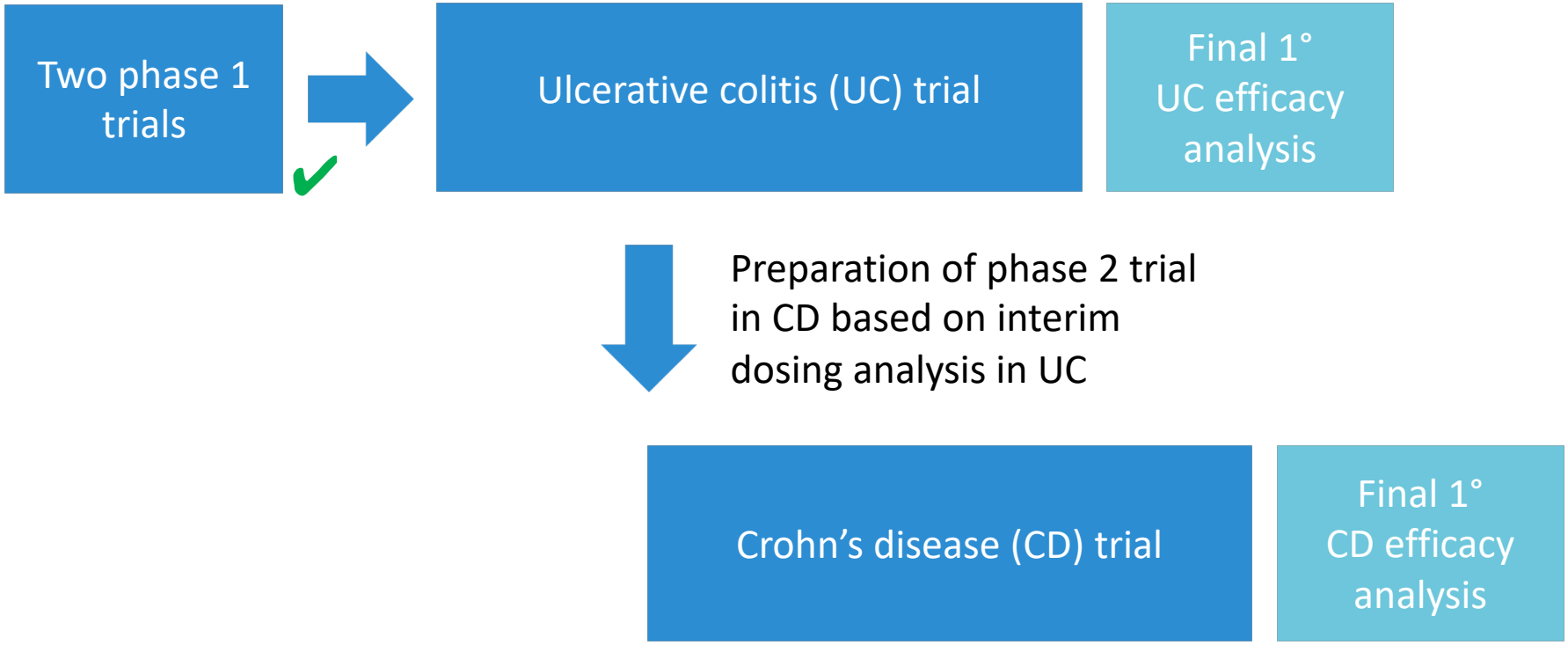
- Active IND in the US; study started in April 2018
- Study design*
  - Central endoscopy assessment for active disease for study eligibility in order to reduce placebo rate
  - Endpoint measuring proportion of patients with symptomatic remission and endoscopic healing at week 10
  - Number of patients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

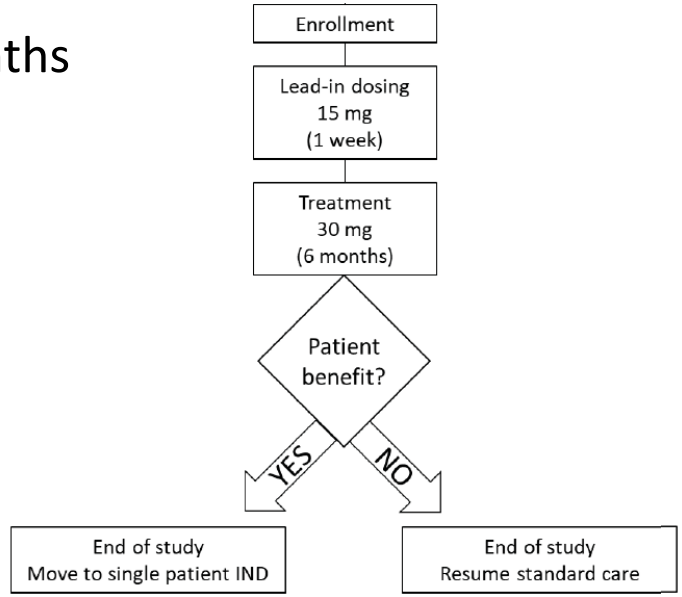
* clinicaltrials.gov: NCT03341962

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

* clinicaltrials.gov: NCT03722576

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IMU-935

Unique RORγt Inverse Agonist

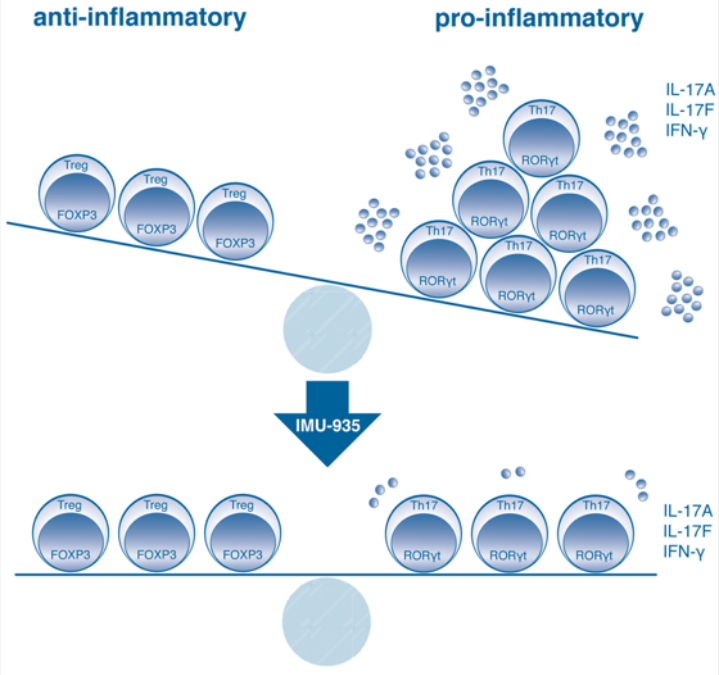
Autoimmune Diseases and IMU-935

Challenge:

- 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]

Solution:

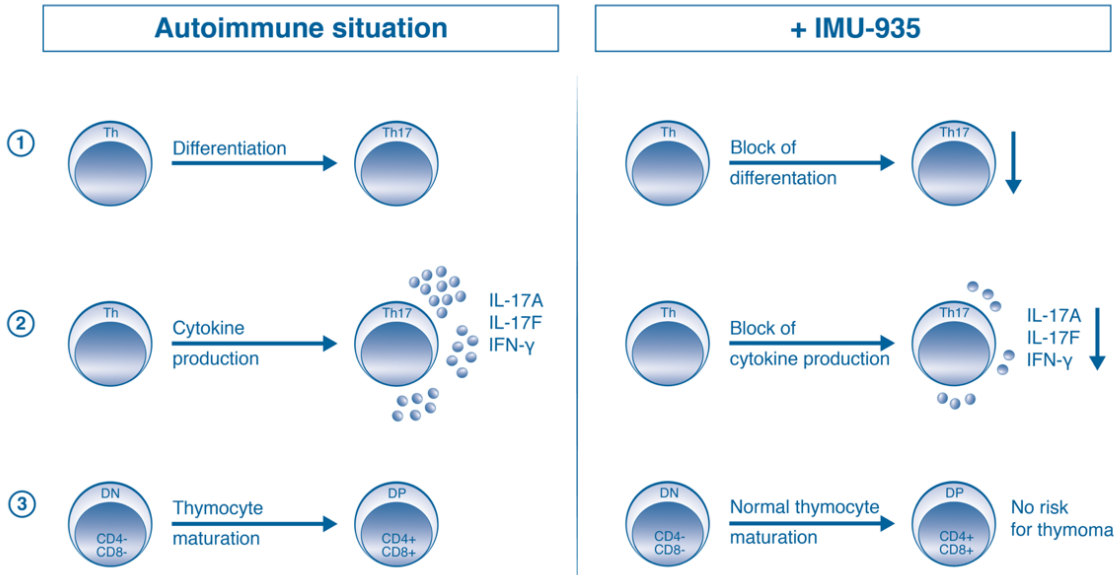
- IMU-935 is a potent small molecule targeting RORγt

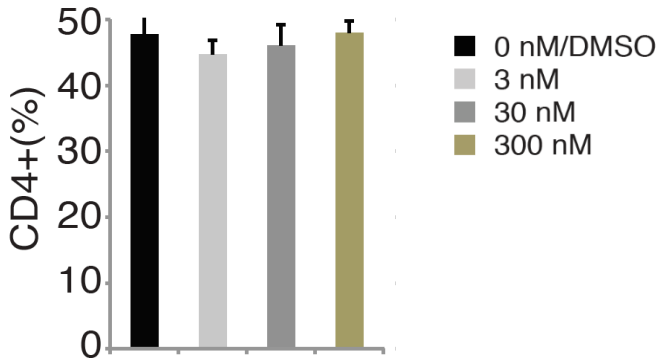


[1] Rose, Noel R. American journal of epidemiology 2016; 183.5: 403-406.
[2] Fasching, Patrizia, et al. *Molecules* 2017 22.1: 134.

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.
- Result: **IMU-935 allows normal thymocyte maturation** from double negative towards matured CD4+ thymocytes (CD4+ and CD4+/CD8+).



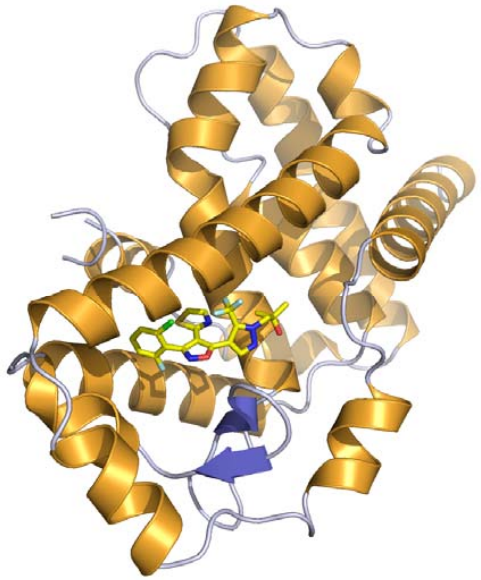


IMU-935: Cytokine Inhibition in Low Nanomolar Range

- Effect of the development compound IM105935 (IMU-935) in stimulated human PBMCs
  - Inhibition of 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, rep.)	0.020
DHODH	0.240
Th17 differentiation	0.150

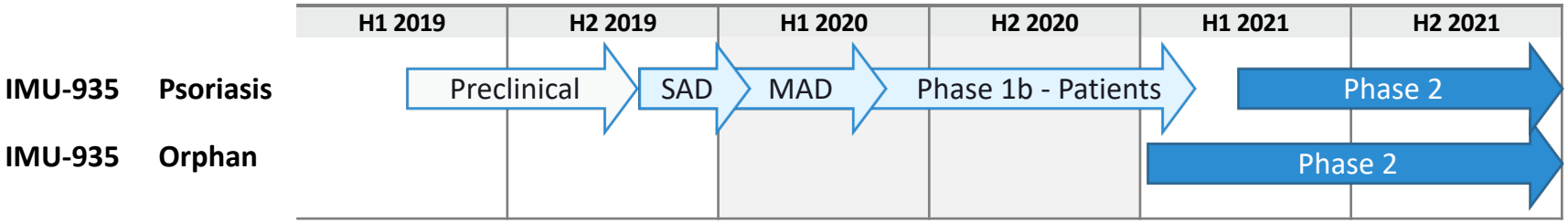
Read-out: effect on cytokine production after 48 hours in PBMCs



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

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



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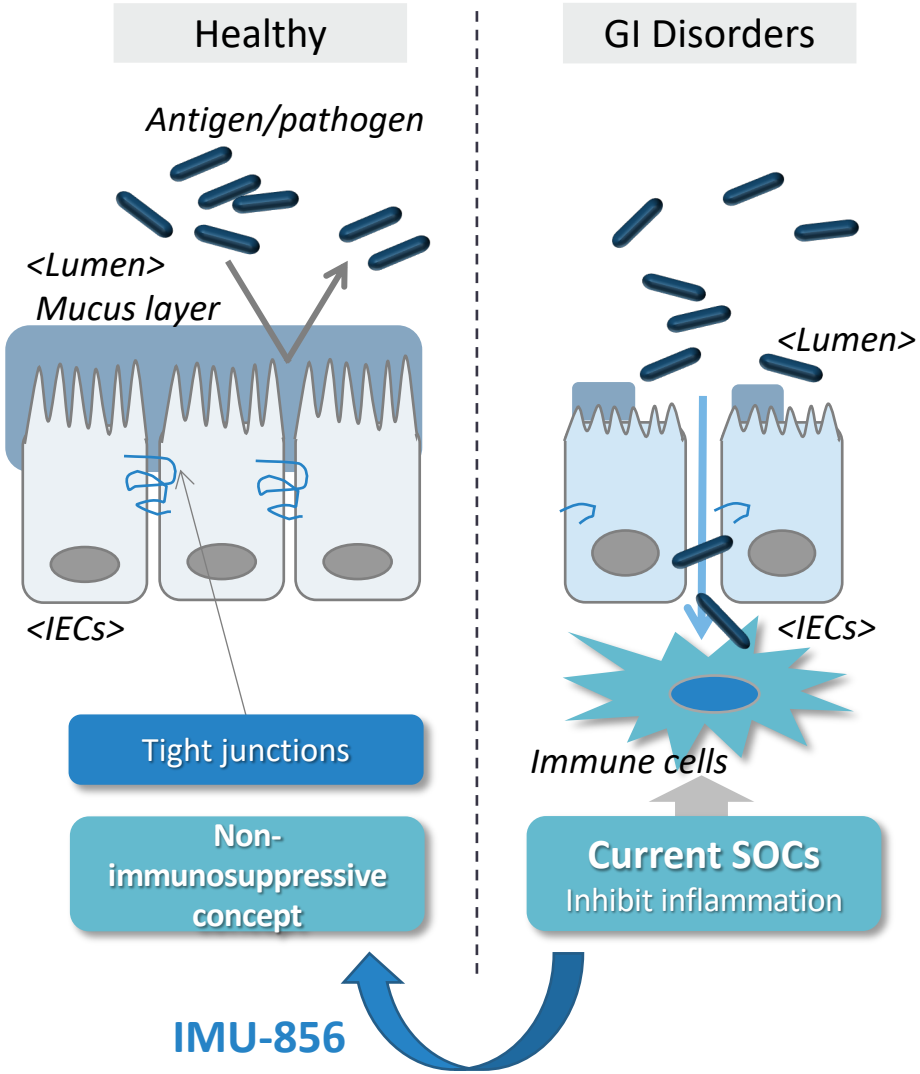
IMU-856

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**

Source: Adopted from Daiichi Sankyo Venture Science Labs, November 2018

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 New York City
- 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 – 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


Australia
Melbourne
small
IBD
best-in-class
drug
selective
inhibitors
preclinical
RORγt
NASDAQ
colitis
multiple
ulcerative
psoriasis
Crohn's
IMU-856
programs
chronic
Halle/Saale
MayoClinic
Germany
agonist
inflammatory
USA
development
diseases
IMUX
bowel
biotech
Immunic
Munich
novel
candidates
autoimmune
Martinsried
DaiichiSankyo
oral
healthcare
immunology
molecule
sclerosis
clinical
proof-of-concept
immune
inverse
DHODH
IMU-935
PSC
therapies
intestinal
IMU-838
barrier
function
specialist

Immunic THERAPEUTICS

Thank You!

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