Immunic THERAPEUTICS

Immunic Therapeutics

NASDAQ: IMUX

IBD Innovate Conference:
Product Development for Crohn's and Colitis
December 4, 2019

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Company and Product Overview

Our Vision

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

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				

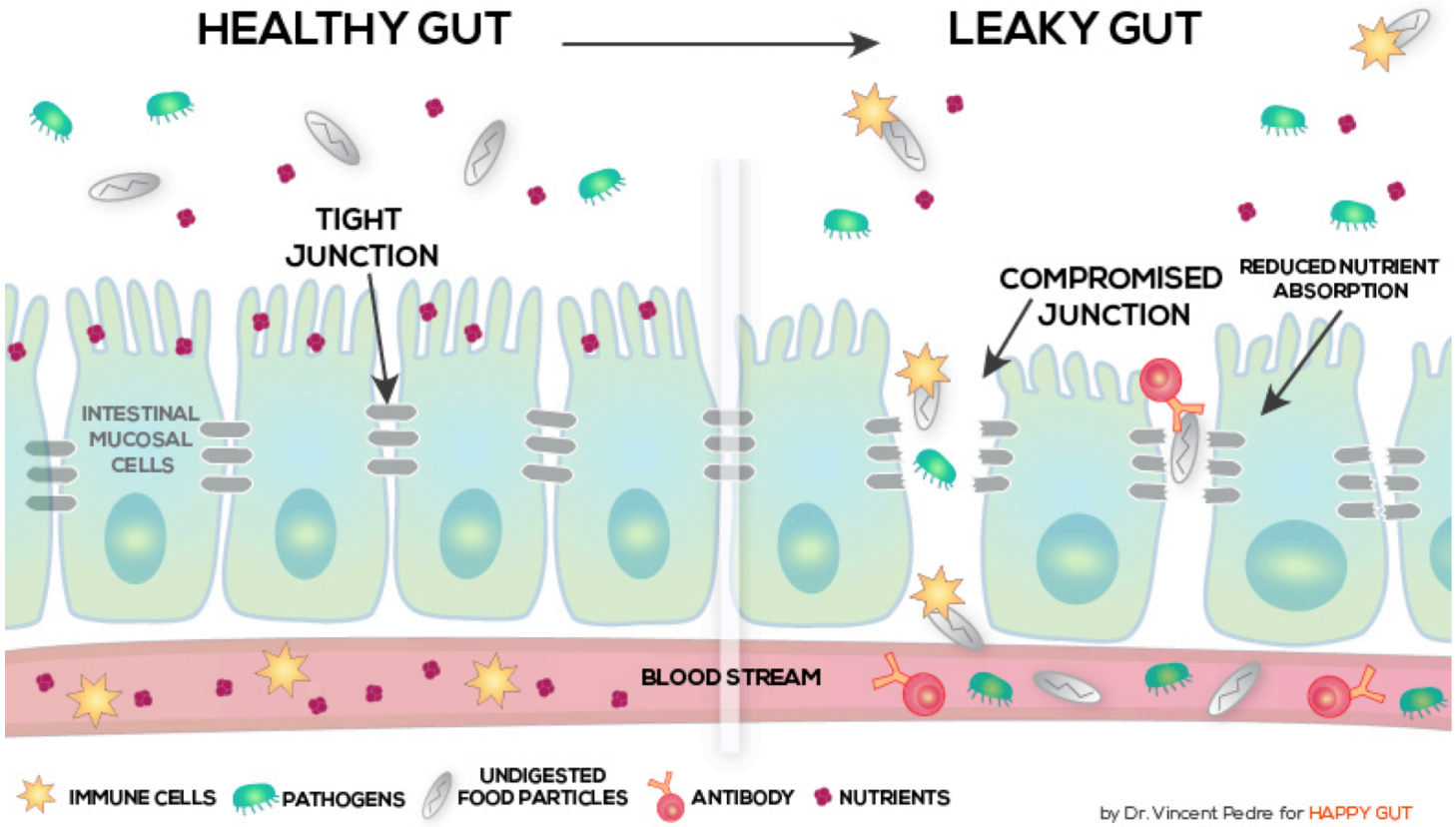
Investigator-Sponsored Trial performed at Mayo Clinic / NIH

Completed or ongoing

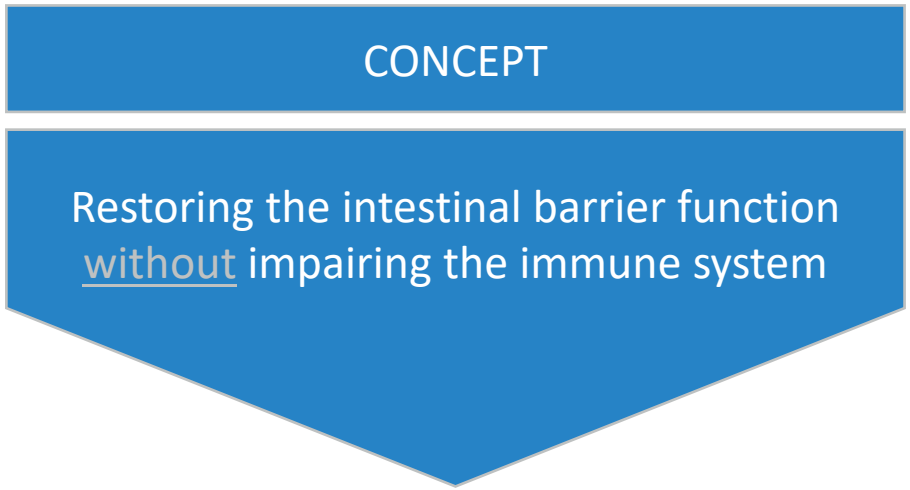
In preparation or planned

IMU-856
Concept

Barrier Function Hypothesis: Bacterial Penetration Through Weakened Cellular Adhesion Causes Immune Overstimulation

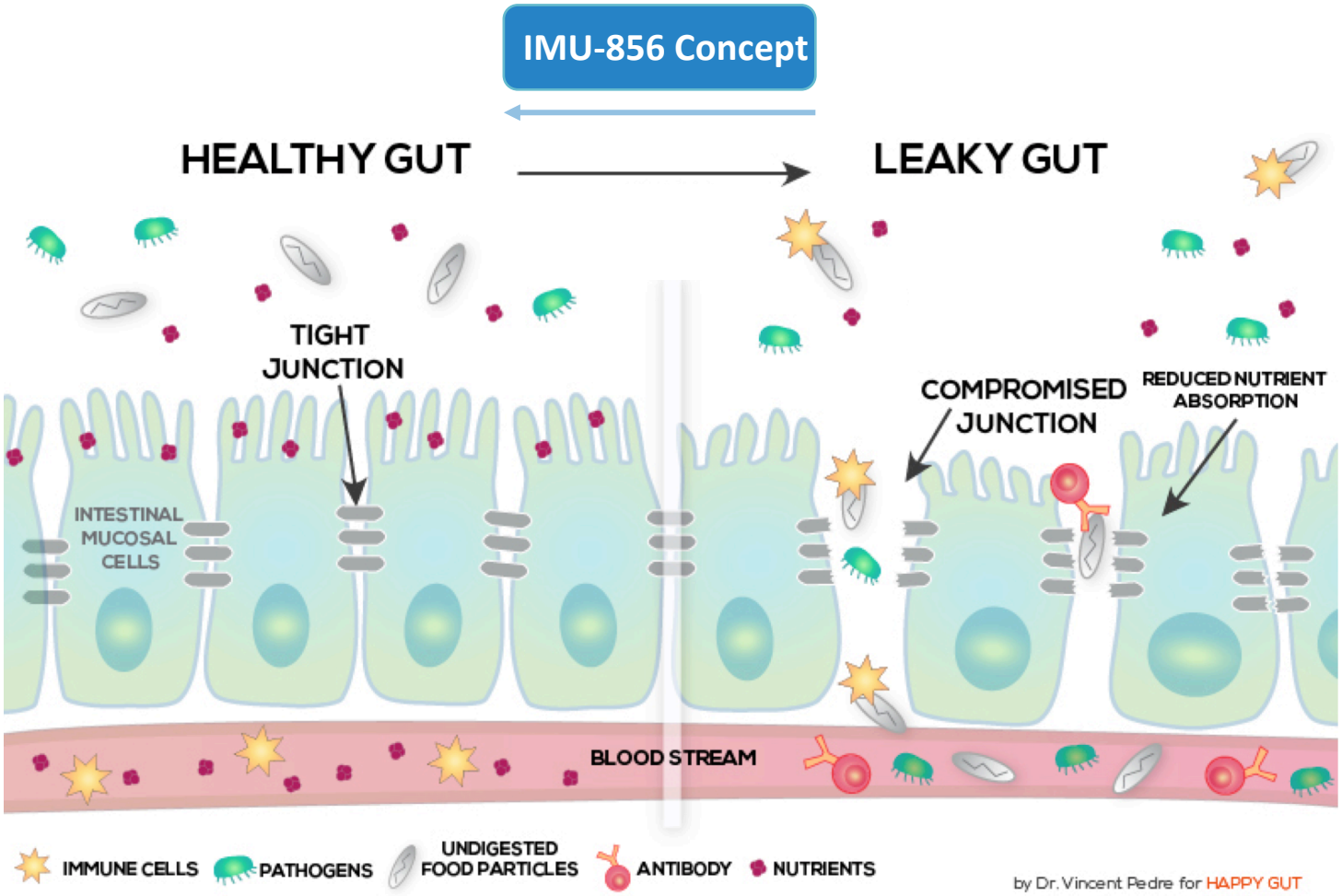


IMU-856: Breakthrough Concept



"IMU-856 has the potential to revolutionize the way of treating multiple diseases related to intestinal barrier function"

IMU-856: Breakthrough Concept



IMU-856 Background

IMU-856: Background

Daiichi-Sankyo

IMU-856 was discovered and developed by **Daiichi Sankyo Venture Science Labs** up to non-GLP safety stage

Novel target

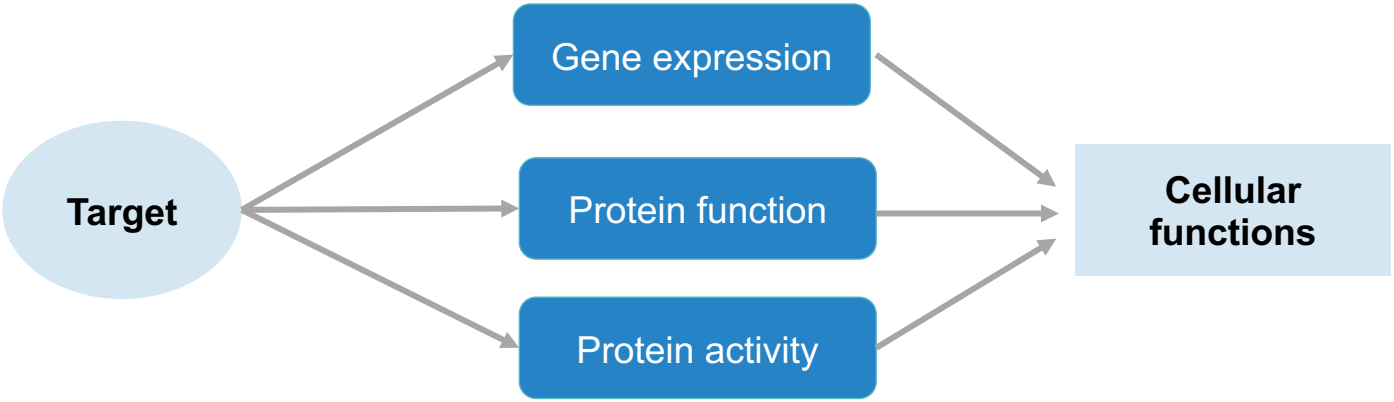
The target was identified in a knock-out animal model

Immunic has an **exclusive option** for the global exclusive license to IMU-856

IMU-856
Target

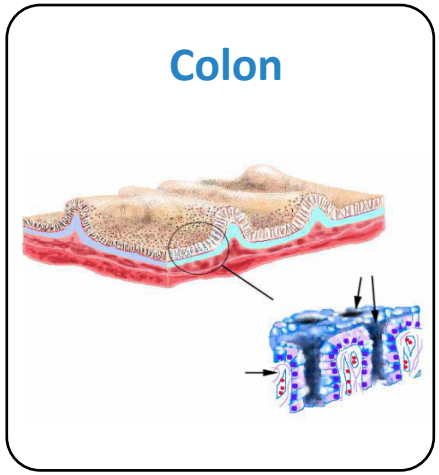
IMU-856's Target: An Epigenetic Regulator…

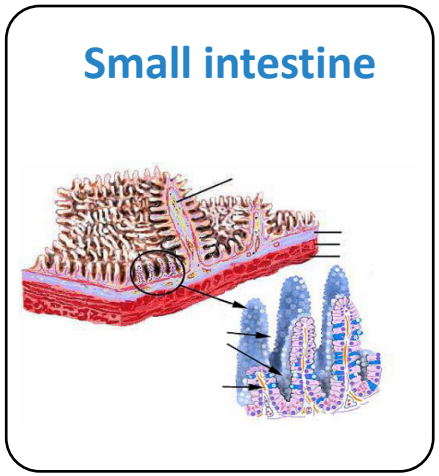
- … influencing the tightly regulated network of genes and proteins associated with epithelial cell interaction/adhesion through its enzyme activities.

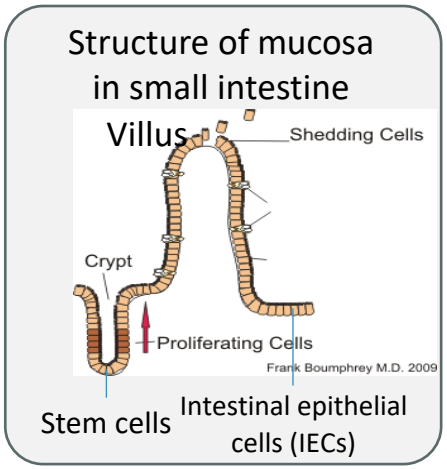


Target Expression and K.O. Model

- Target is predominantly expressed in intestinal epithelial cells (IECs) in intestinal crypts
  - In colon and in small intestine



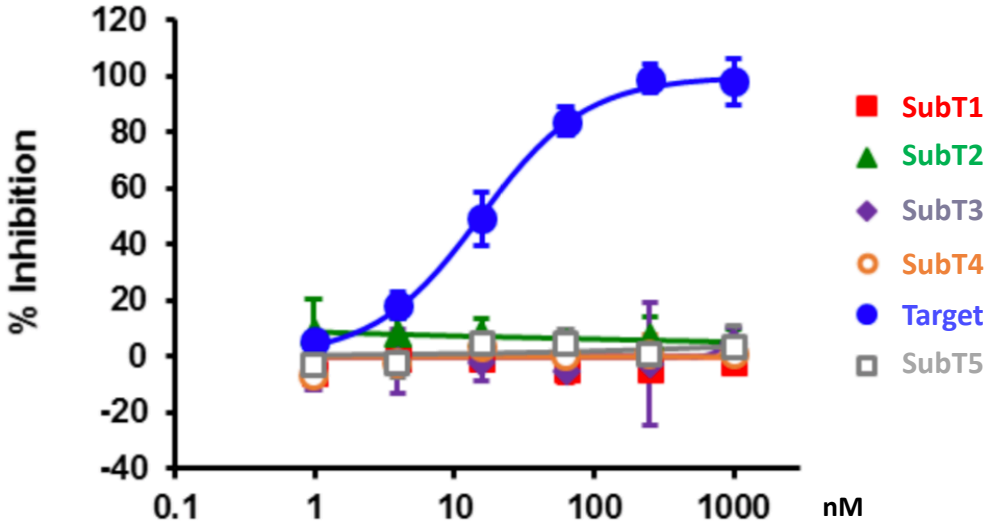




- K.O. of target in IECs led to delayed and milder onset of colitis when induced by DSS treatment

IMU-856 Pharmacology

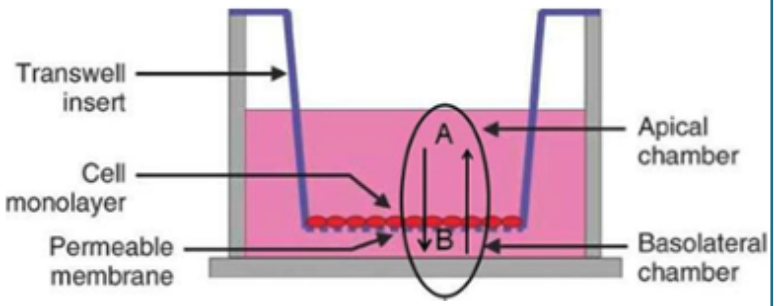
IMU-856: Selectivity



IMU-856 inhibits the Target's enzyme activity
A unique binding mode allows high selectivity over other subtypes

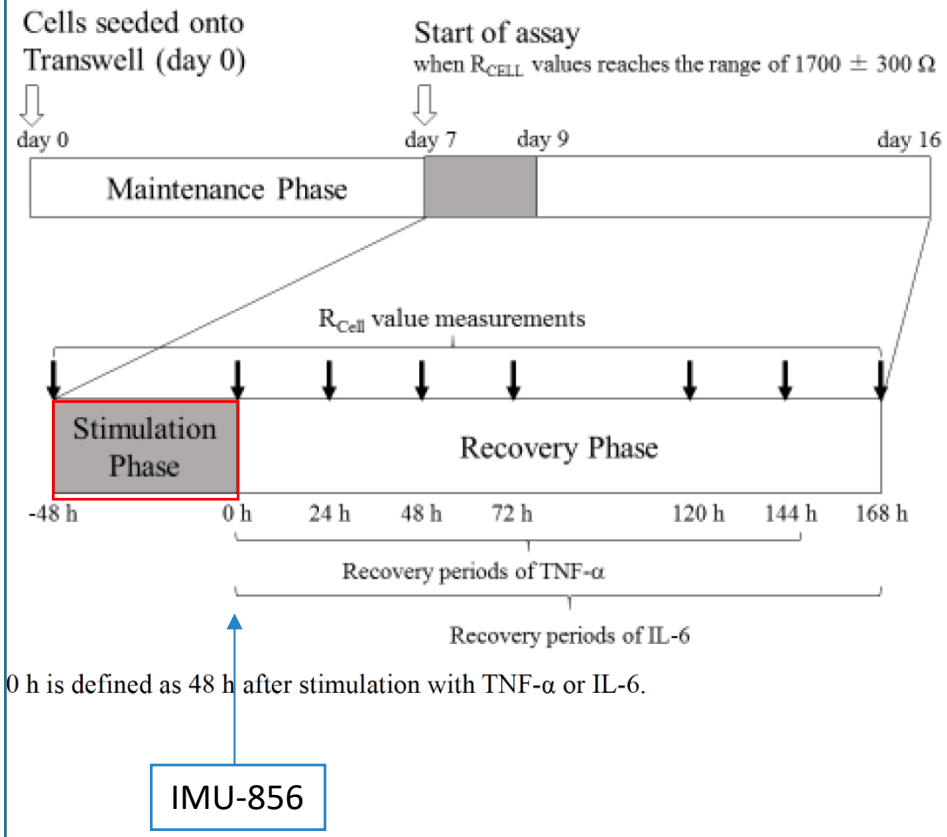
IMU-856: Impact on Intestinal Permeability

Intestinal permeability was measured as TEER* after barrier-disrupting stimulation in Caco-2 cells**



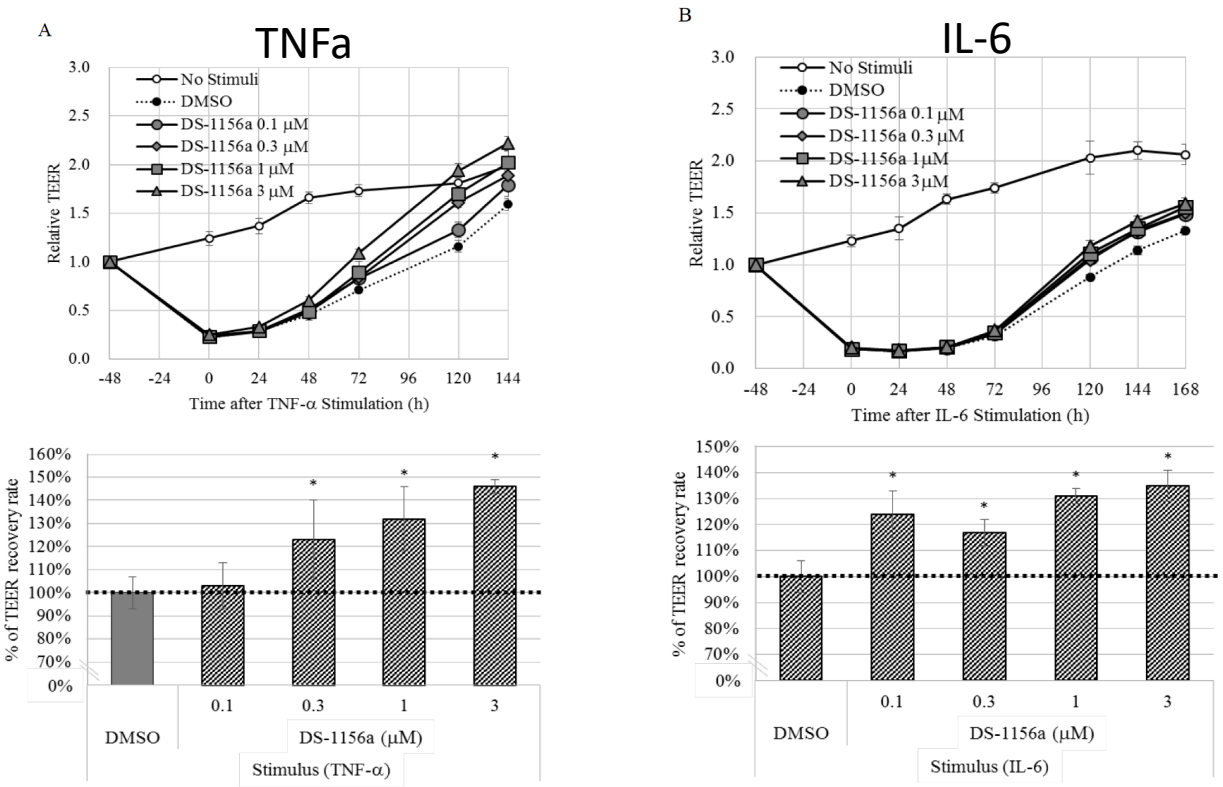
*TEER: transepithelial electrical resistance

**Caco-2 cells: Human intestinal epithelial cell lines



IMU-856 was able to maintain epithelial barrier integrity

IMU-856: Impact on Barrier Function



IMU-856 was able to restore barrier function in cytokine challenged Caco-2 cells

IMU-856: Pharmacology

		IMU-856
In vitro cell-free	Protein based test, IC_{50}	15 nM
In vitro cell	biomarker in HT-29 cells, EC_{50}	4.3 nM
Selectivity	Other proteins of same family	No inhibition (1 μM)
	87 kinds of enzymes, receptors and channels	No effects (10 μM)
Species differences	Human / Mouse / Rat / Monkey (cell-free test, IC_{50})	15/41/28/31 nM
In vivo IBD models	Mouse DSS models (PAD*)	<1 mg/kg/day

IMU-856 shows pharmacological activity at low concentrations in vitro, cellular and in vivo

*PAD = pharmacological active dose

IMU-856: In-Vivo Activity

Colitis Induction	Setting	Duration	Treatment setting	Doses	Efficacy demonstrated?
1.5% DSS	Induction	8 days	Prevention	0.1, 0.3, 1mg/kg	Yes Read out: colon length
1.5% DSS	Induction	6 days	Prevention	0.3mg/kg +/- Tacrolimus	Yes Read out: colon length
3% DSS	Chronic, recovery	3 cycles (6+4 days)	Prevention	0.1, 0.3, 1mg/kg	Yes Read out: colon length
1.5% DSS	Chronic, recovery	1 cycle (7+4 days)	Prevention	0.1, 0.3, 1mg/kg	Yes Read out: colon length
2.8% DSS	Therapeutic	8 days, 1-5 DSS, 4-8 treatment	Therapeutic	1mg/kg	Yes Read out: Diarrhea score, histological score

IMU-856 is active in several DSS Colitis Models

IMU-856: Activity

Diarrhoea Score

Raw data in *Appendix 1. Raw Data*.

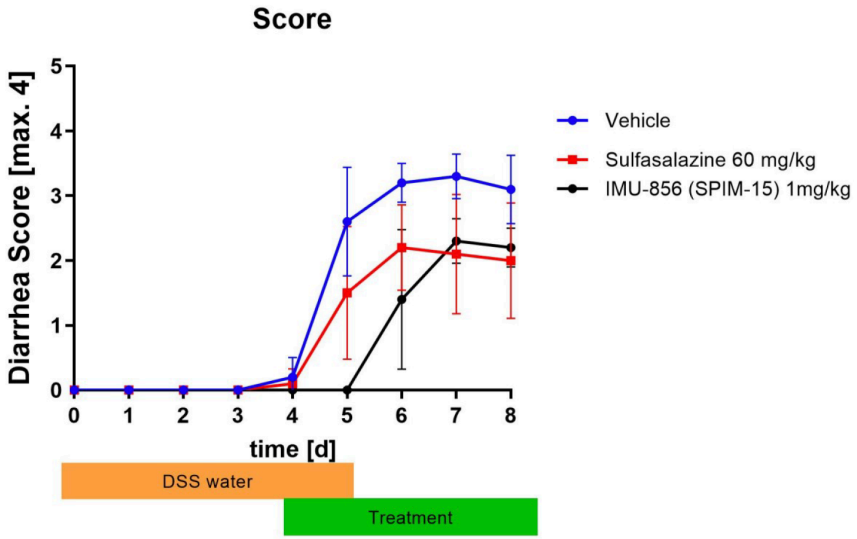
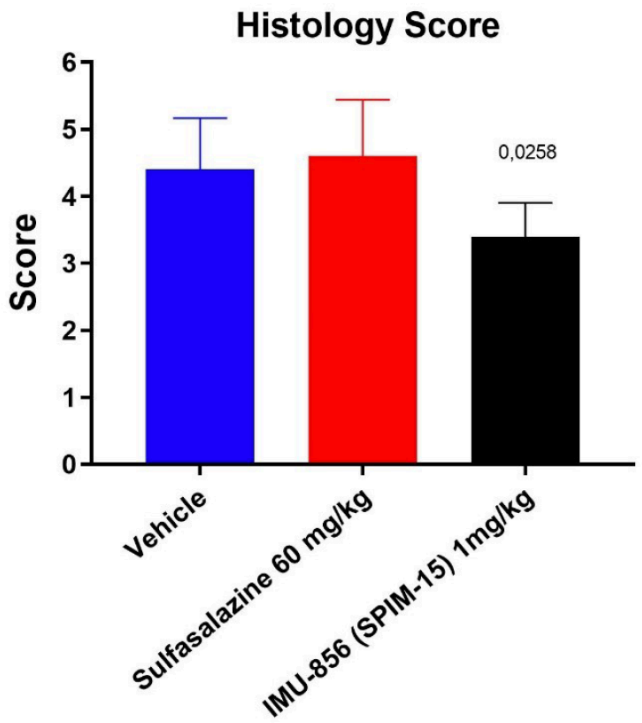


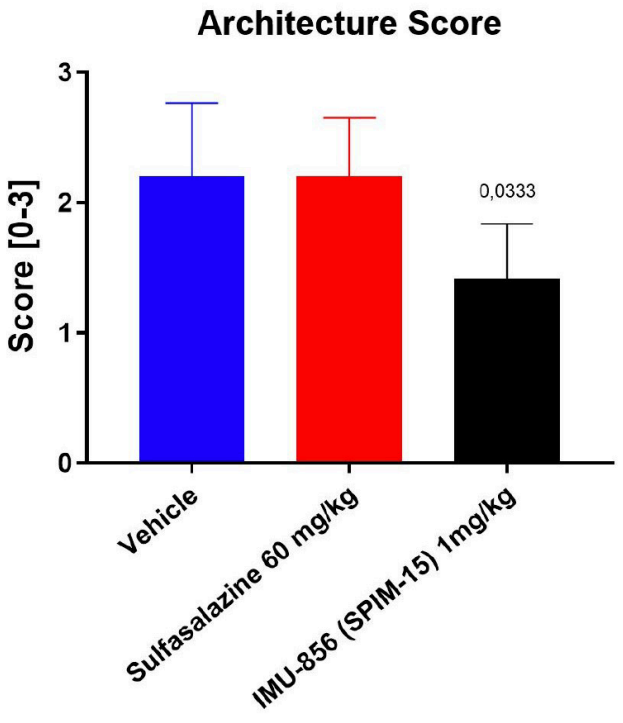
Figure 3: Diarrhoea Score along the study. Diarrhoea scoring scheme: 0 = normal consistency; 1 = soft; 2 = pasty, unshaped, not sticking to anus; 3 = diarrhoea, sticking to anus, diarrhoea with macroscopic bleeding. Values are displayed as mean ± 95% CI.

IMU-856 is active in a therapeutic DSS Colitis Model

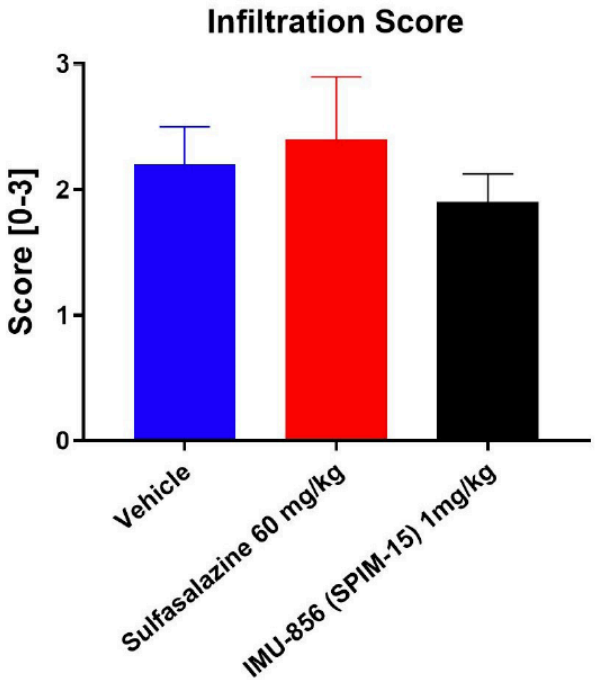
IMU-856 Improves Colonic Histology

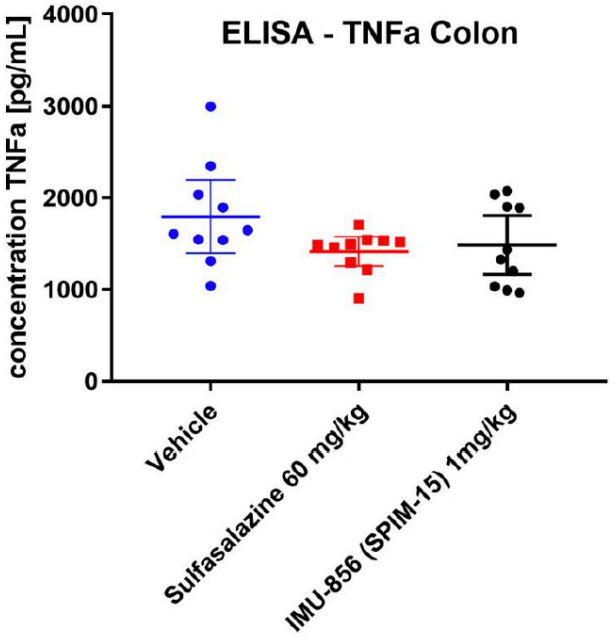
Colon histopathology





IMU-856: No/Less Impact on Immune Cells





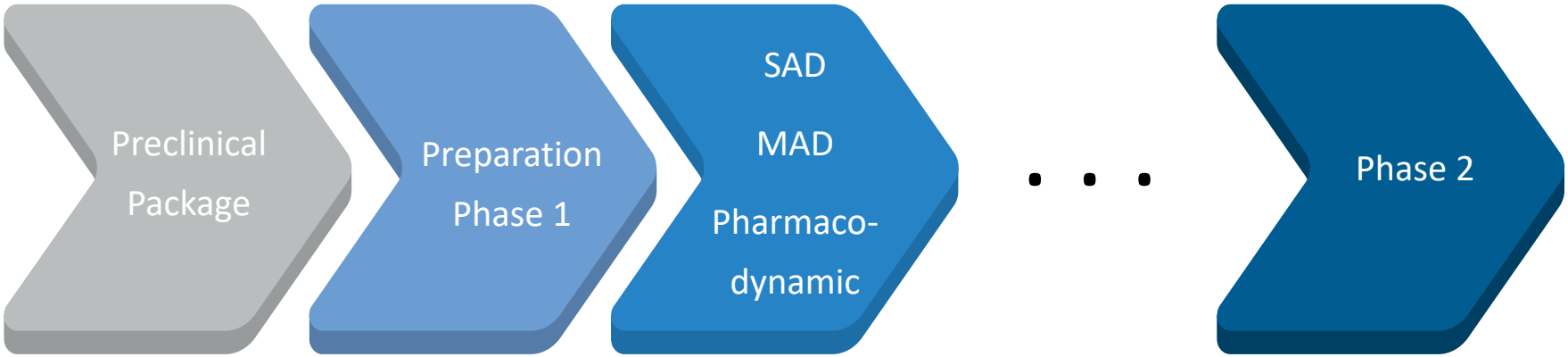
IMU-856
Safety

IMU-856: Preclinical Safety Assessment

- Safety package to initiate phase 1 clinical trial has been performed
  - hERG, AMES, micronucleus (non-GLP)
  - 28 day subchronic toxicity studies in rats and monkeys
  - Respiratory, CNS, Cardiac safety
- Safety margin between efficacy in mice and NOAEL in rats is factor 50

IMU-856
Further Development

IMU-856: Development Overview



IMU-856: Preliminary Development Plan*

Possible indications: CD and UC; IBS-D and ICI colitis

Phase 0: Validation of the Lactulose/mannitol test (ongoing)	Phase 1 SAD: FPI H1 2020 Phase 1 MAD (14 days): FPI H1 2020 Phase 1b (14 days) POC: pharmacodynamic study • Safety and PK in patients • Proof of concept based on established PD tests for intestinal permeability	Phase 2: Intended lead indication IBS-D

IMU-856: Highlights

IMU-856…		
… targets a yet undisclosed and novel target which modulates the intestinal barrier function.	… is an orally available, very selective and potent small molecule with beneficial safety and physicochemical properties.	… could be a disruptive treatment for several gut barrier associated diseases without compromising the immune system.


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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