



Immunic Therapeutics

NASDAQ: IMUX



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

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- 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 undertakes any obligation to update such forward- looking statements to reflect events or circumstances after the date of this presentation.

Company and Product Overview

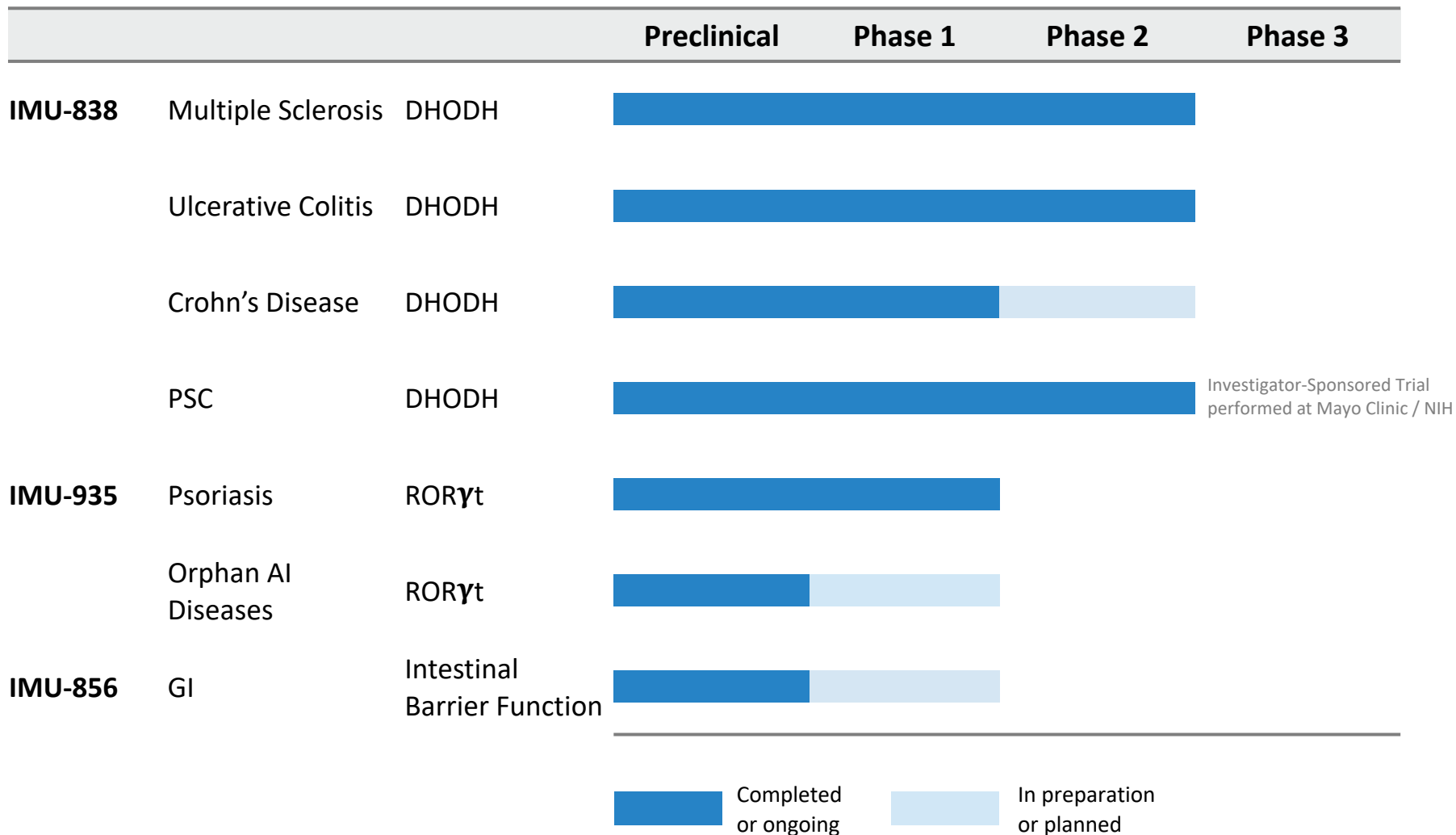




Our Vision

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

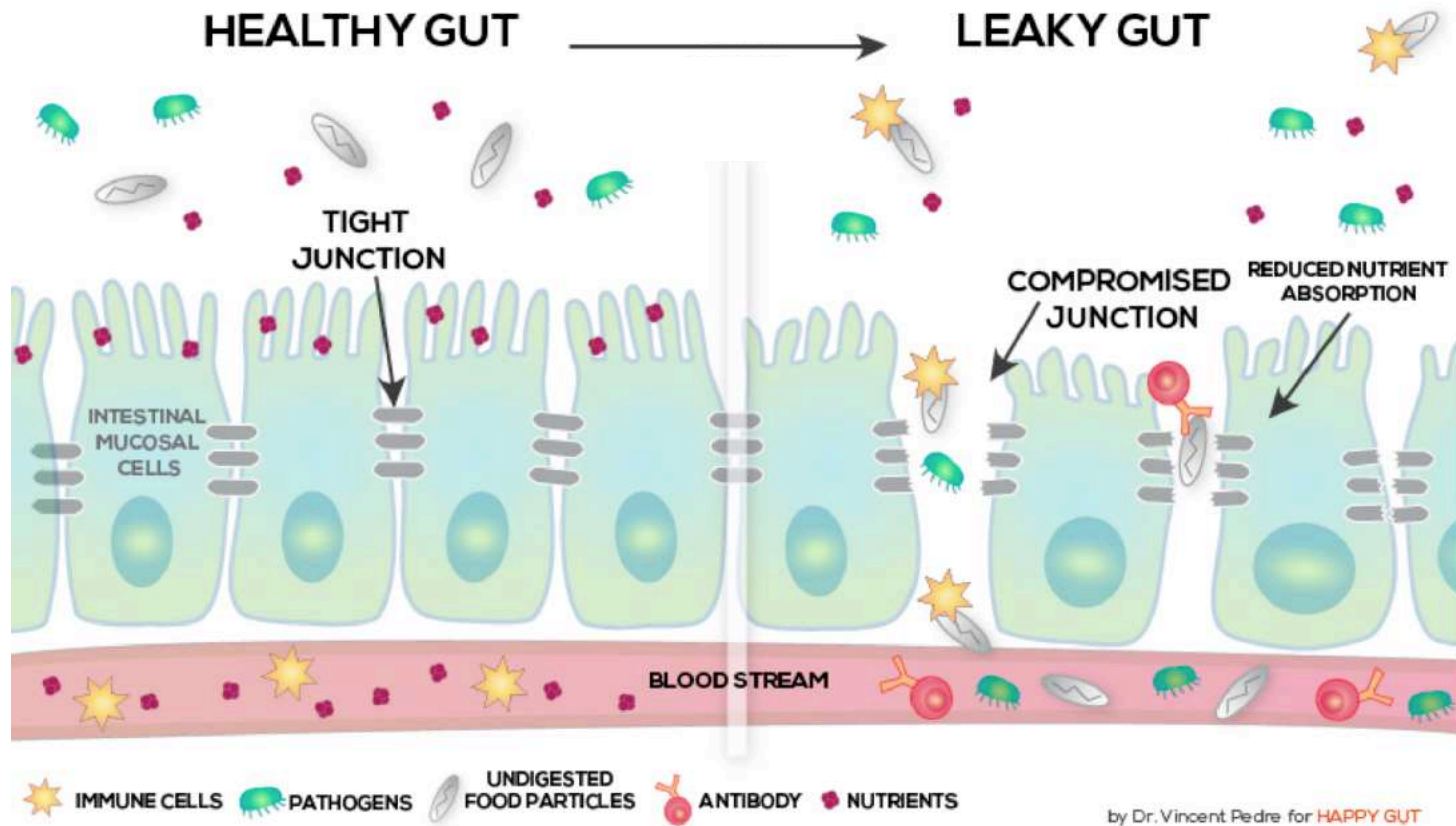
Development Pipeline



IMU-856 Concept



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





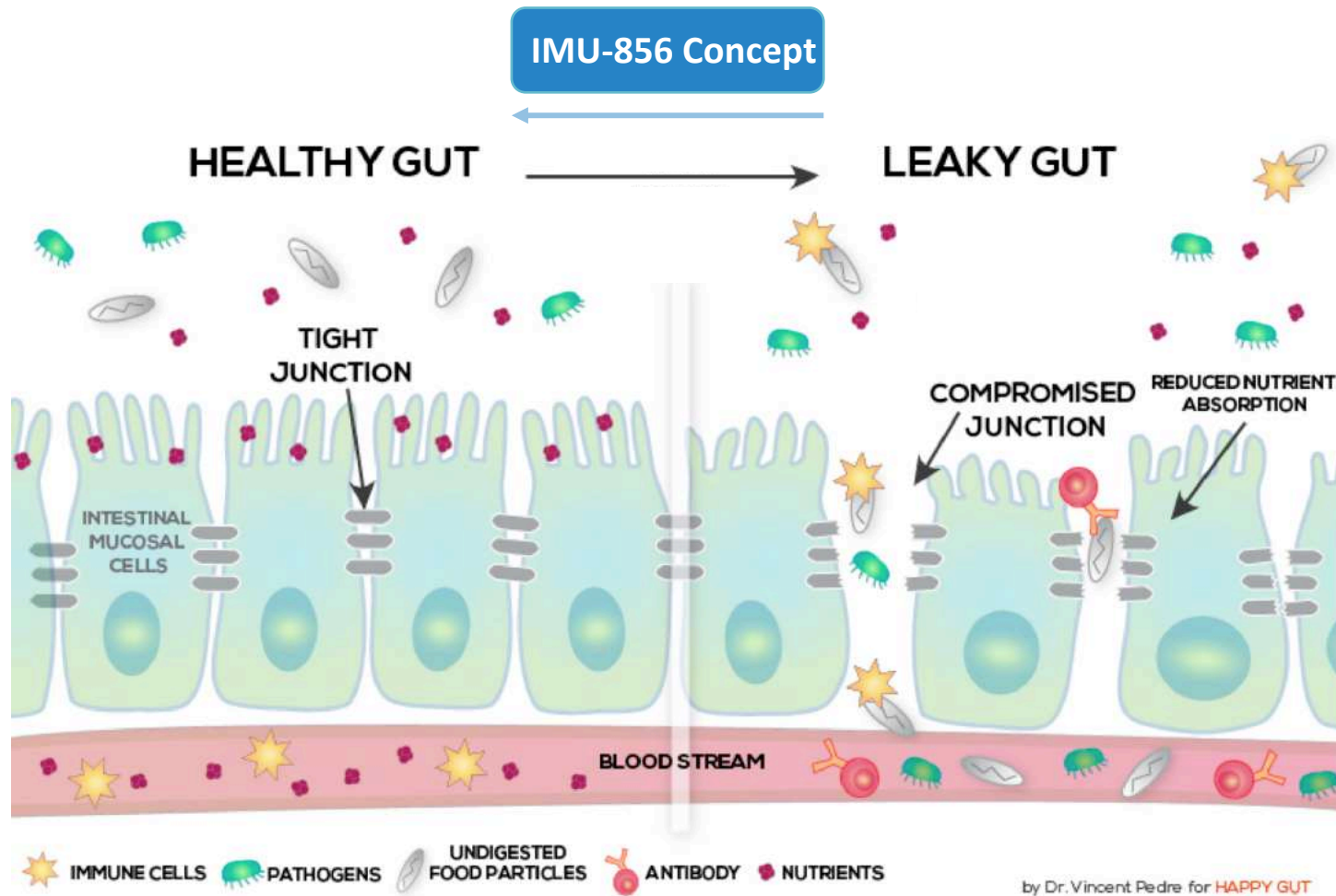
IMU-856: Breakthrough Concept

CONCEPT

Restoring the intestinal barrier function
without impairing the immune system

“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



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

Novel target

The target was identified in a knock-out animal model



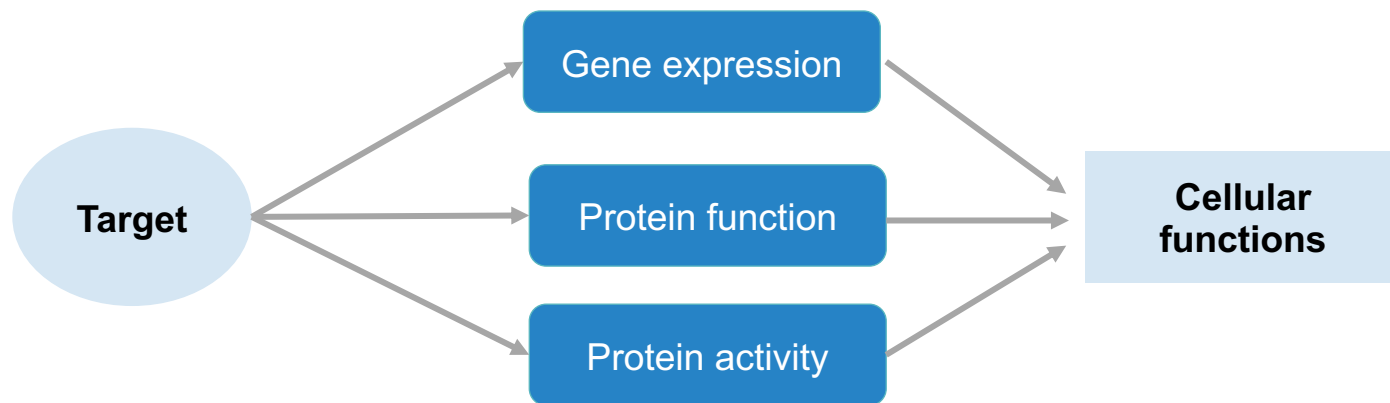
Immunic has an **exclusive option** for the global exclusive license to IMU-856

IMU-856 Target



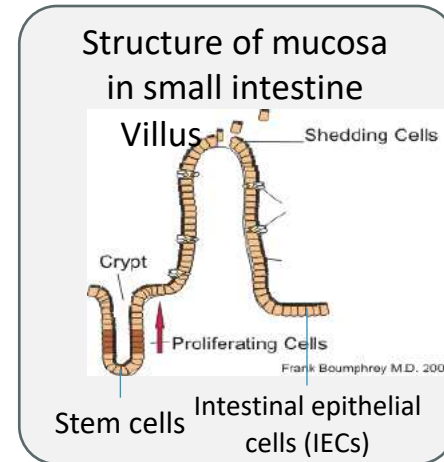
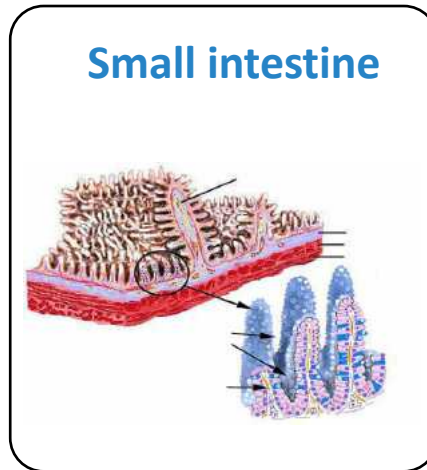
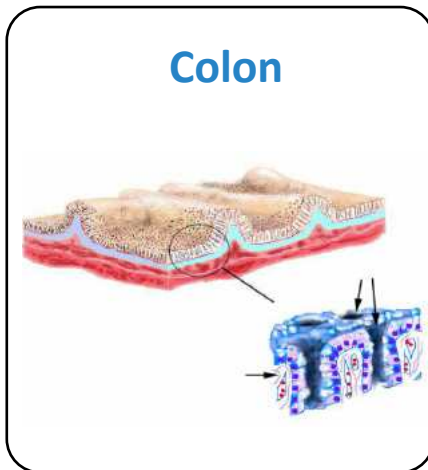
IMU-856's Target: An Epigenetic Regulator...

- ... 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



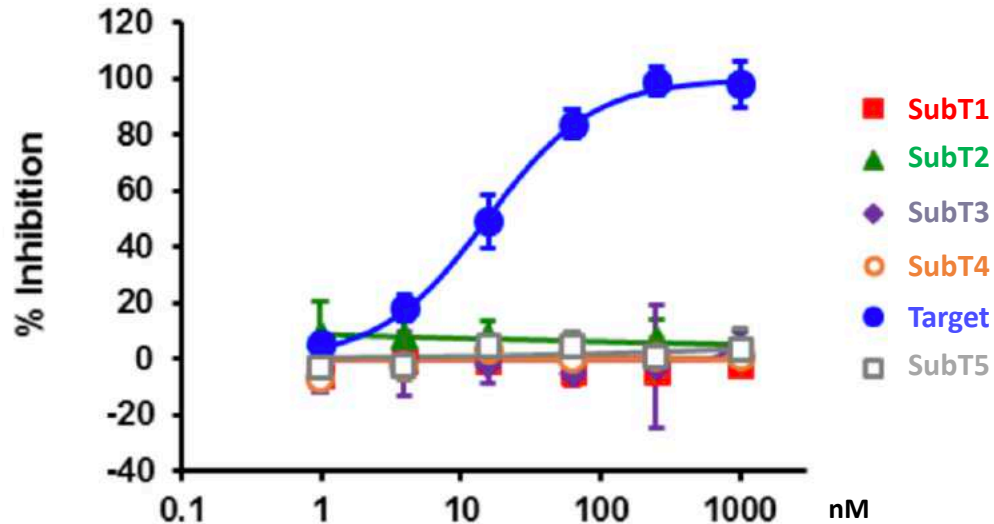
- K.O. of target in IECs led to delayed and milder onset of colitis when induced by DSS treatment

IMU-856

Pharmacology



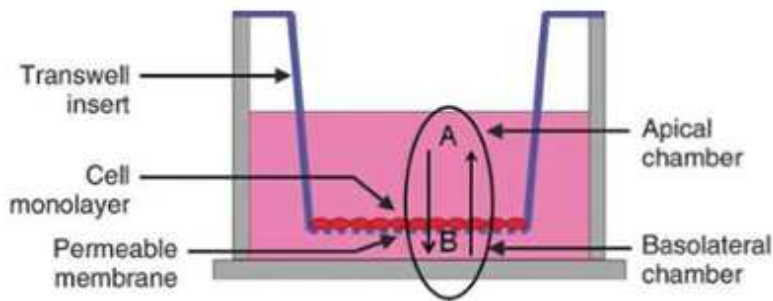
IMU-856: Selectivity



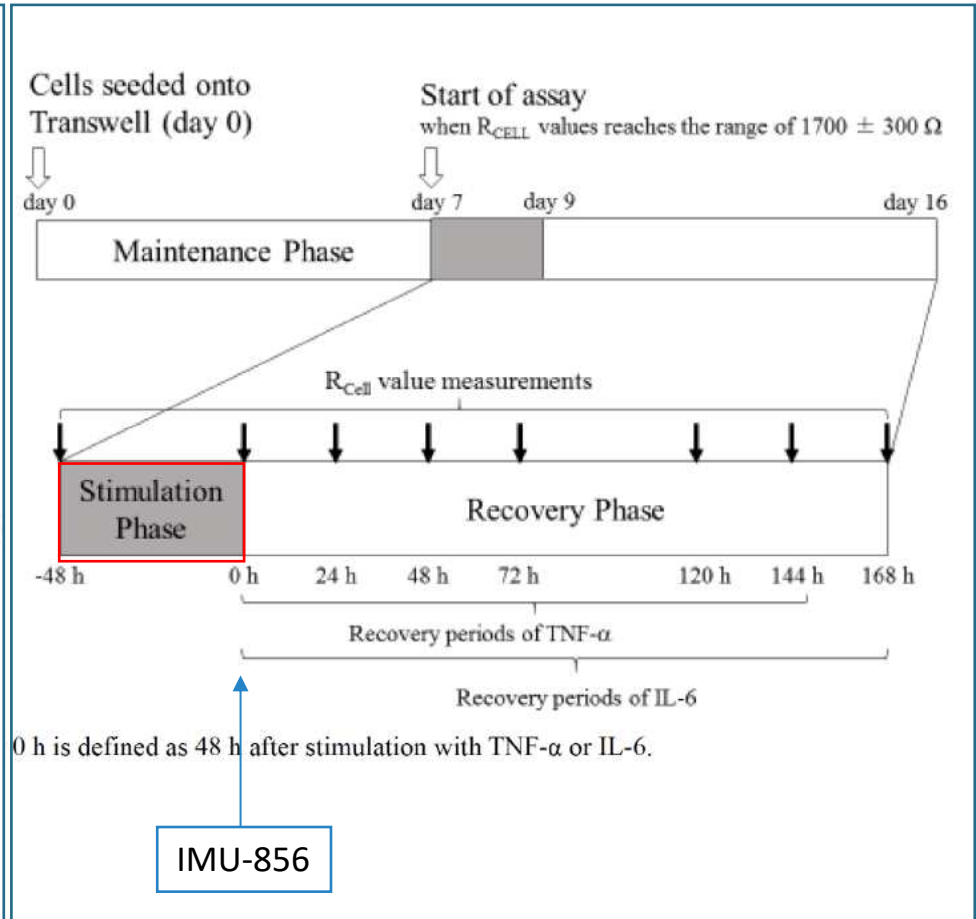
IMU-856 inhibits the Target's enzyme activity
A unique binding mode allows high selectivity over other subtypes

IMU-856: Impact on Intestinal Permeability

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

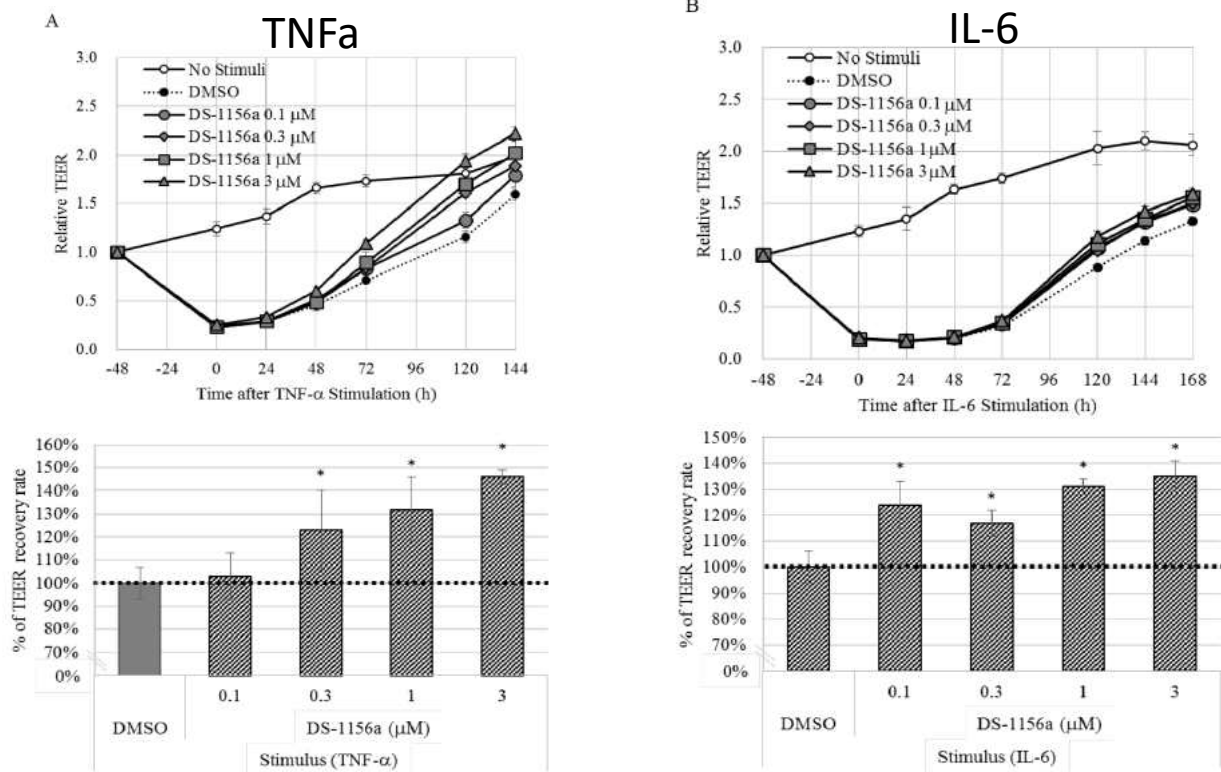


*TEER: transepithelial electrical resistance
**Caco-2 cells: Human intestinal epithelial cell lines



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
<i>In vitro</i> cell-free	Protein based test, IC ₅₀	15 nM
<i>In vitro</i> 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
<i>In vivo</i> IBD models	Mouse DSS models (PAD*)	<1 mg/kg/day

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

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*.

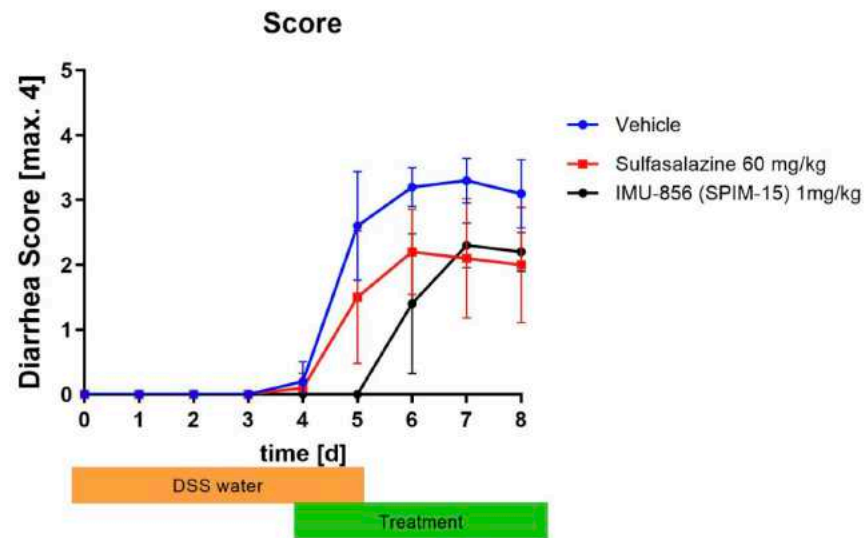
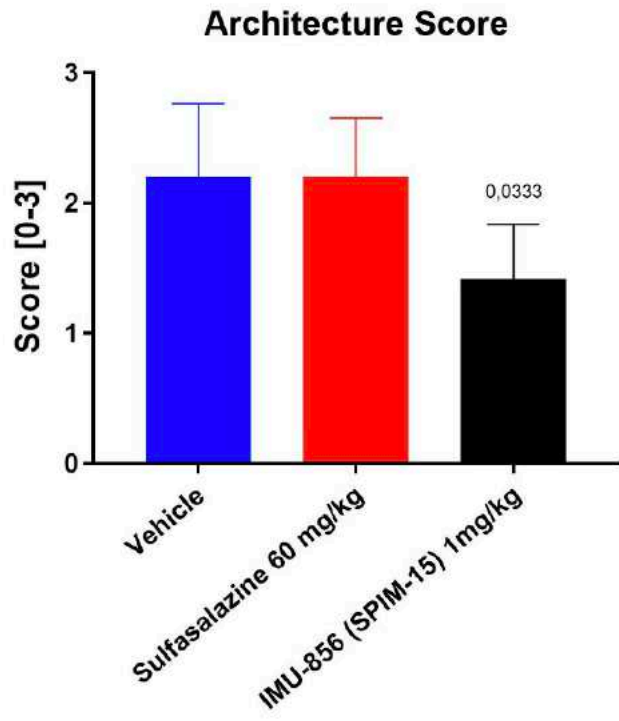
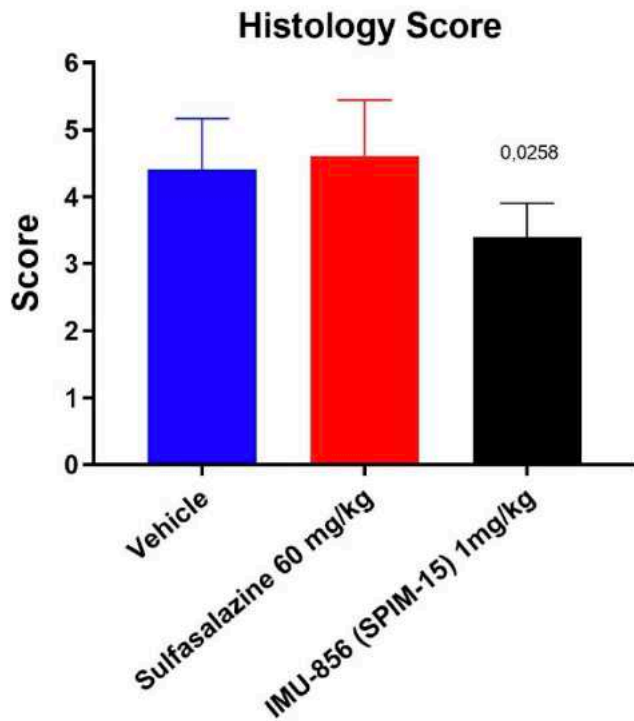


Figure 3: Diarrhoea Score along the study. Diarrhoea scoring scheme: 0 = normal consistency; 1 = soft; 2 = pasty, unshaped, not sticking to anus; 3 = diarrhoea, sticking to anus, diarrhoea with macroscopic bleeding. Values are displayed as mean \pm 95% CI.

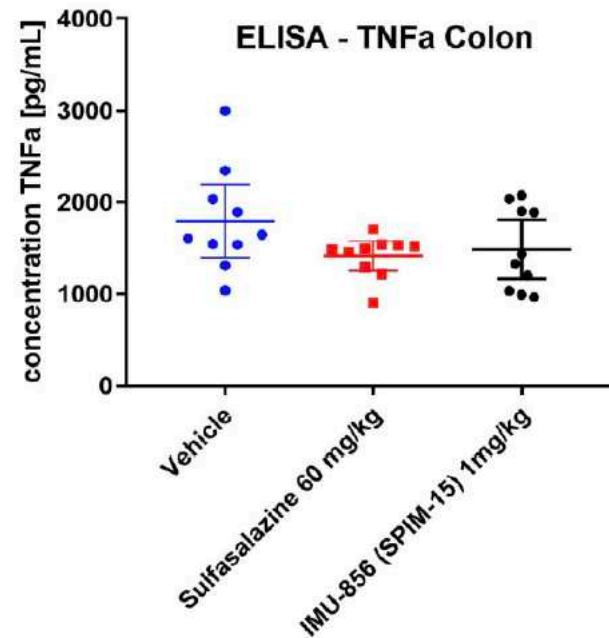
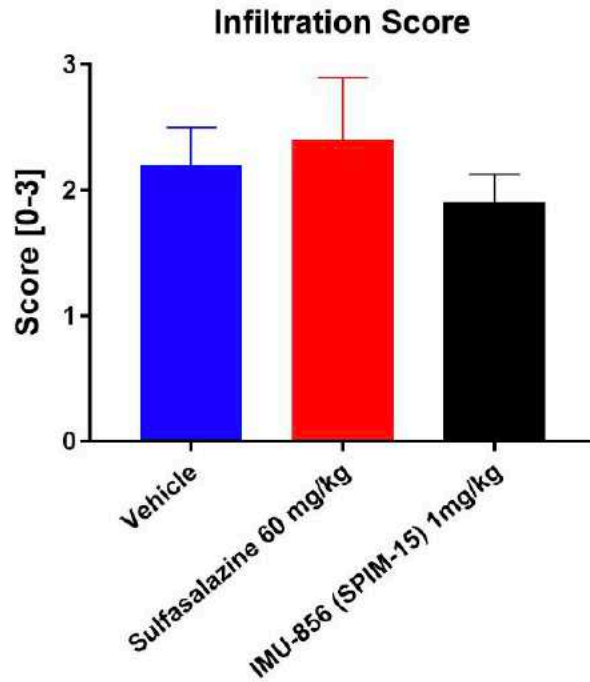
IMU-856 is active in a therapeutic DSS Colitis Model

IMU-856 Improves Colonic Histology

Colon histopathology



IMU-856: No/Less Impact on Immune Cells



IMU-856 Safety





IMU-856: Preclinical Safety Assessment

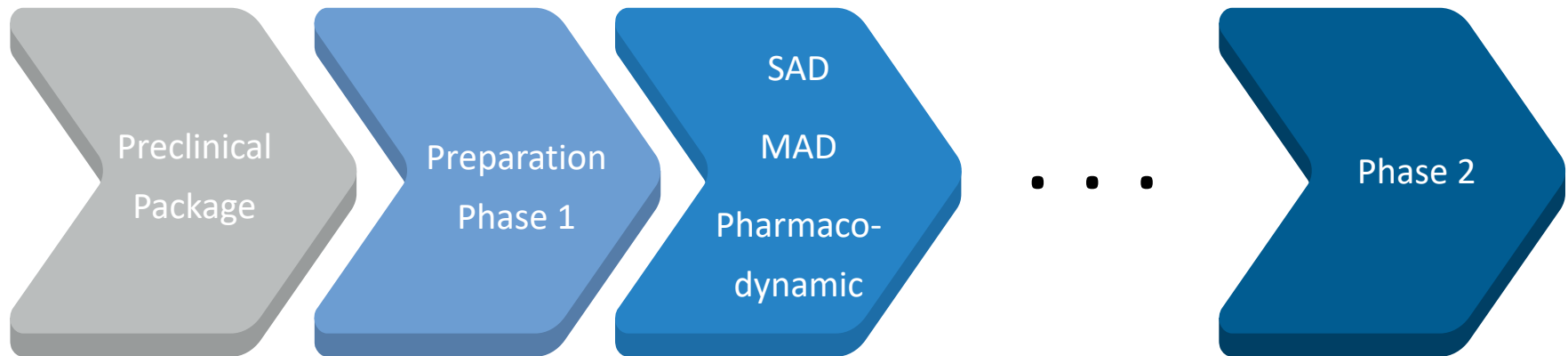
- Safety package to initiate phase 1 clinical trial has been performed
 - hERG, AMES, micronucleus (non-GLP)
 - 28 day subchronic toxicity studies in rats and monkeys
 - Respiratory, CNS, Cardiac safety
- Safety margin between efficacy in mice and NOAEL in rats is factor 50

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.





Thank You!

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