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IMU-856, an Orally Available Epigenetic Modulator of Barrier Regeneration, Showed Positive Effects on Gut Hormone Levels in Celiac Disease Patients in a Phase 1 Clinical Study

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October 6, 2025, Berlin
AS-UEG-2025-01463, ***OP053***

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Disclosure of Conflicts of Interest

I herewith declare the following paid or unpaid consultancies, business interests, or sources of honoraria payments for the past three years, and anything else which could potentially be viewed as a conflict of interest:

I am an employee of Immunic AG and own shares and stock options of the parent company of Immunic AG.

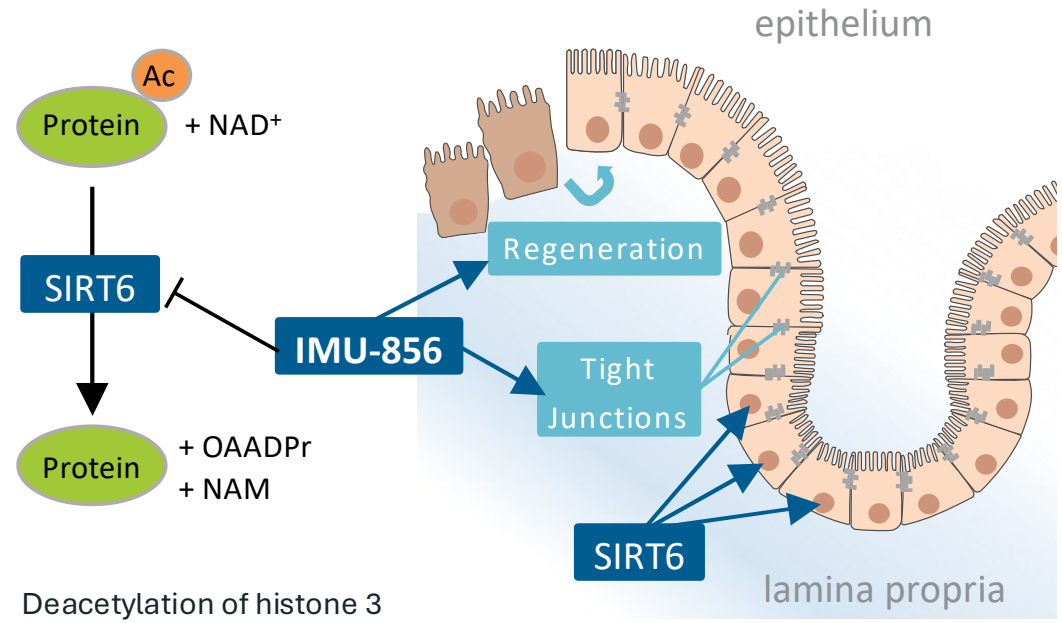
Disclaimer - Forward-Looking Statements

This presentation contains forward-looking statements regarding future events, development plans, clinical trial timelines, and potential product candidates. These statements are based on current expectations and are subject to risks and uncertainties. Actual results may differ materially.

This information is intended for scientific exchange with healthcare professionals and is not for promotional use.

Mode of Action of IMU-856

- IMU-856 is a highly selective and potent modulator of the enzymatic activity and stability of SIRT6 (sirtuin 6)
- IMU-856 promotes intestinal regeneration and improves barrier function in human cell and animal models
- No known effect on immune cells

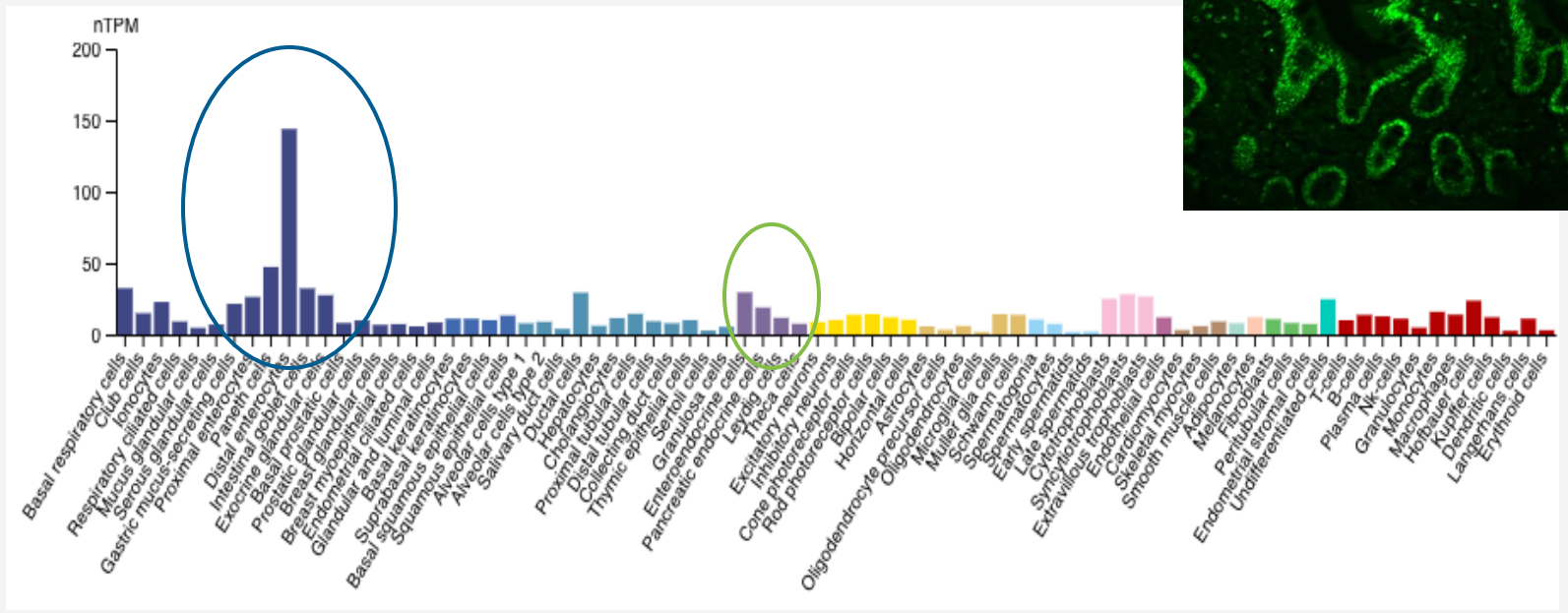


Deacetylation of histone 3 (H3K9ac, H3K56ac) and non-histone proteins (e.g. transcription factors, other epigenetic proteins)

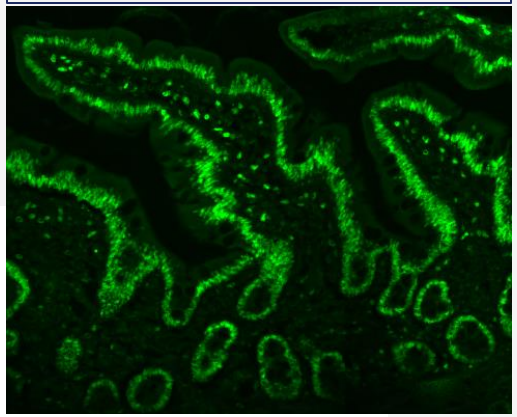
E-Poster (*PP0290*): Dr. Marta Alexdottir, Nordic Bioscience
BIOMARKERS OF EXTRACELLULAR MATRIX REMODELING REFLECT PHARMACODYNAMIC EFFECTS OF IMU-856, AN ORAL EPIGENETIC MODULATOR OF BARRIER REGENERATION

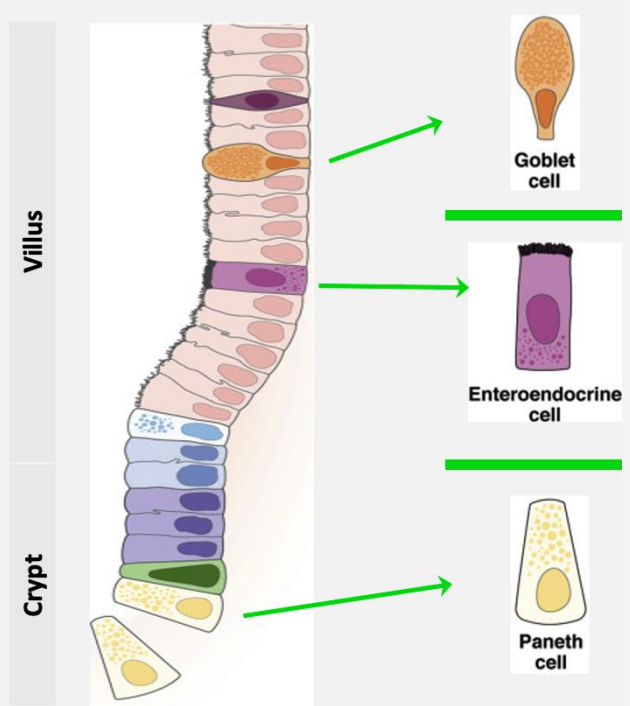
SIRT6 is Highly Expressed in Intestinal Epithelial Cells Including All Secretory Cell Types

Highest mRNA Expressions in Paneth Cells, Enterocytes, Goblet Cells and Enteroendocrine Cells such as L-Cells



Duodenal biopsy of celiac disease patient





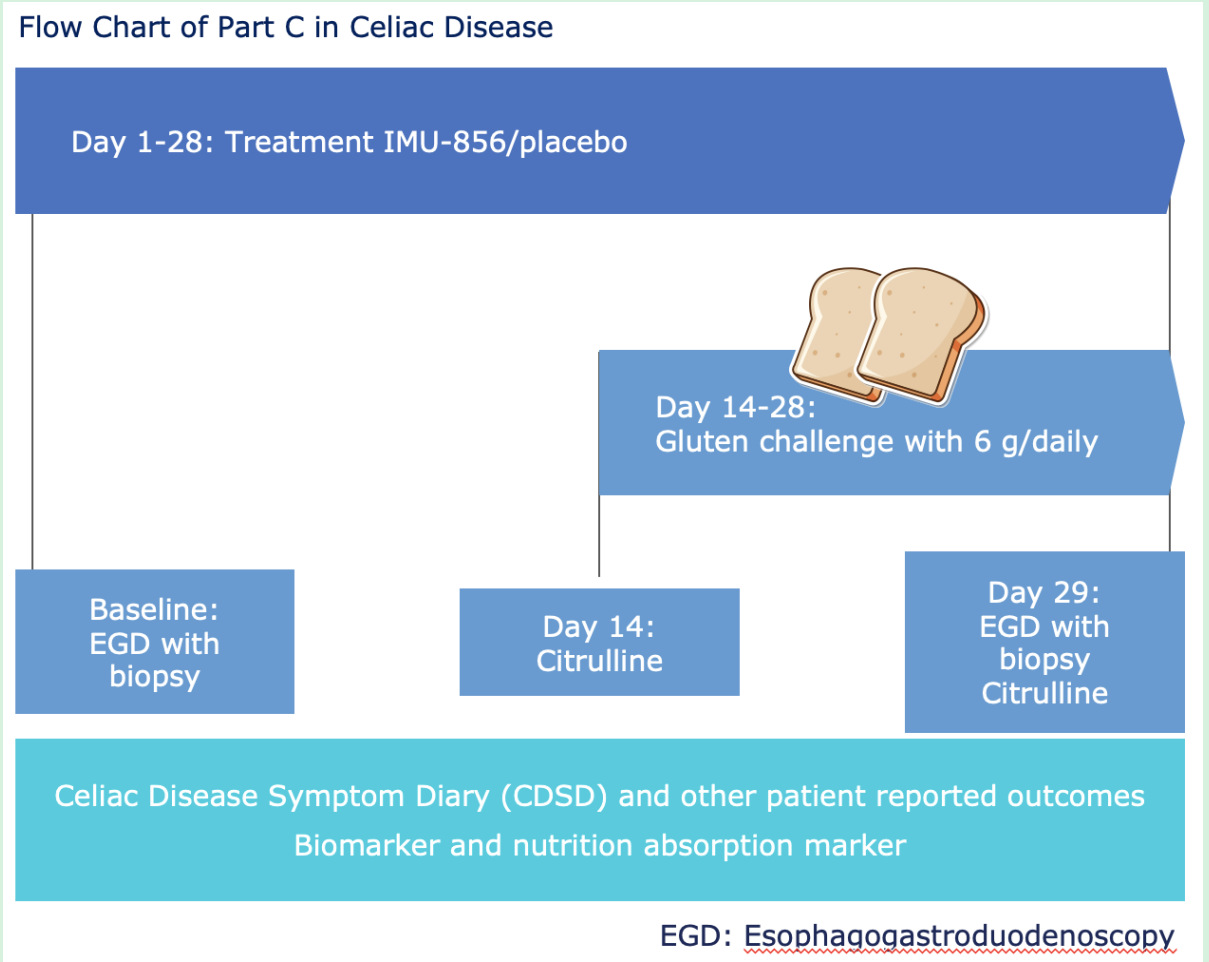
Left: https://www.proteinatlas.org/ / Right: Peterson, L., Artis, D. Nat Rev Immunol 14, 141–153 (2014); SIRT: sirtuin; mRNA: messenger ribonucleic acid; nTPM: normalized transcript per million

Phase 1b Clinical Trial of IMU-856 in Celiac Disease Designed as a Gluten Challenge Trial

- Population of well-controlled celiac disease patients with gluten challenge of 6 g/day for 15 days
- Dosing: 80 and 160 mg PO once daily of IMU-856
- N=43 (IMU-856 80 mg: N=14, IMU-856 160 mg: N=15)

- **Proof of concept study:**
  - histological changes
  - blood biomarkers
  - nutrient uptake
  - disease-related symptoms

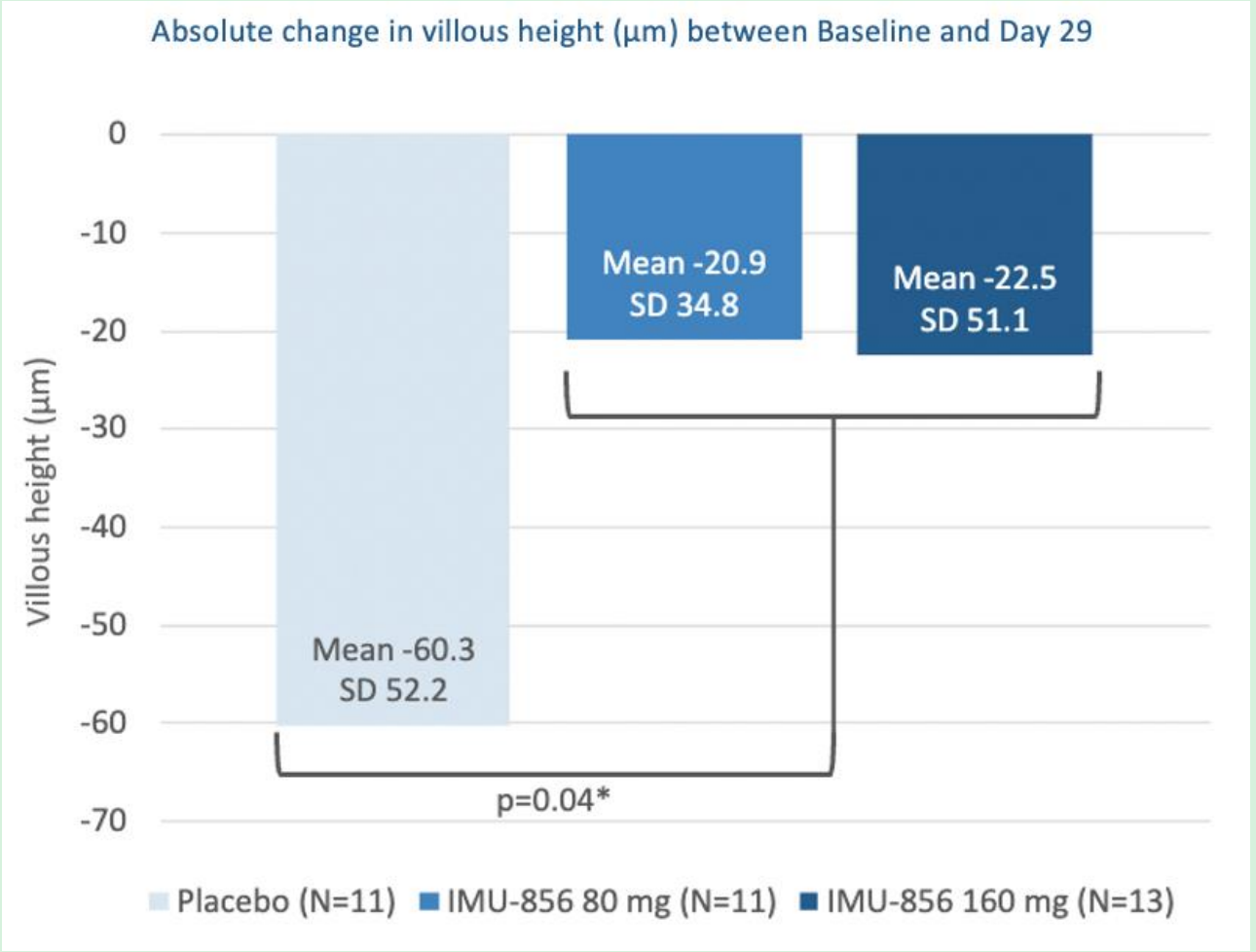
- IMU-856 observed to be **safe and well-tolerated**



Daveson, A James M et al., The Lancet Gastroenterology & Hepatology, Volume 10, Issue 1, 44 - 54

IMU-856 Protected Against Gluten-Induced Decrease in Villous Height as Compared to Placebo

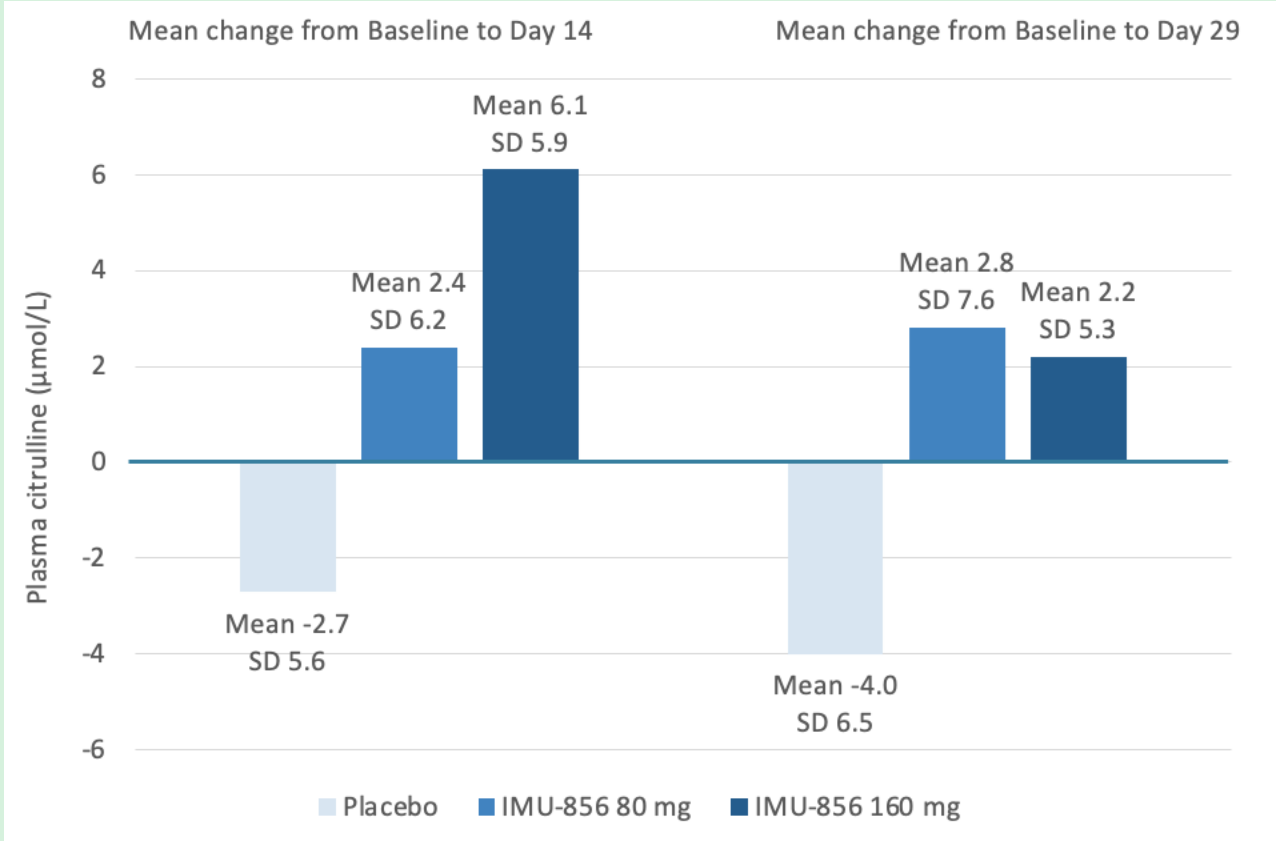
- Substantial protection for IMU-856 treatment groups as compared to placebo
- Reached statistical significance*
- Assessed by central pathology laboratory and blinded pathology reader



* Wilcoxon Two-Sample Test comparison between pooled IMU-856 groups and placebo, performed as post-hoc exploratory statistical analysis. Disease Analysis Set: N=35/43 included in histology analysis set. 8 patients not included in this analysis due to early termination. Gluten Challenge for 15 days with 6 g daily. EGD: esophagogastroduodenoscopy; SD: standard deviation. Central pathology laboratory: Jilab Inc., Tampere, Finland

IMU-856 Showed Signal for Improved Enterocyte Mass and Function

- Citrulline is a biomarker for enterocyte functional mass[1]
- Plasma citrulline levels are known to correlate with villous atrophy
- IMU-856 increased citrulline levels dose proportionally before gluten challenge, whereas levels were reduced in placebo treated celiac disease patients

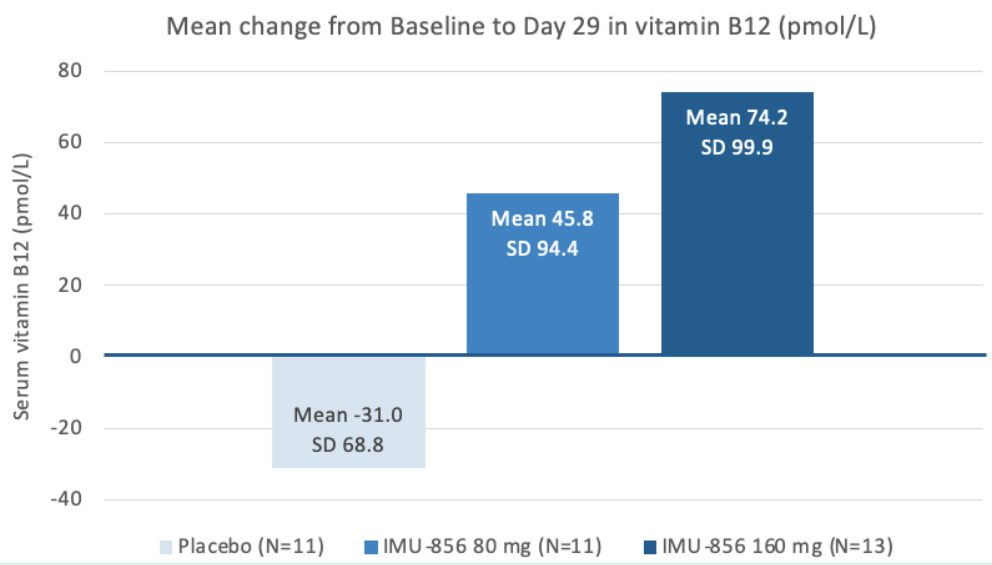


[1] Singh et al., J. Clin. Med. 2019, 8, 885; doi:10.3390/jcm8060885;

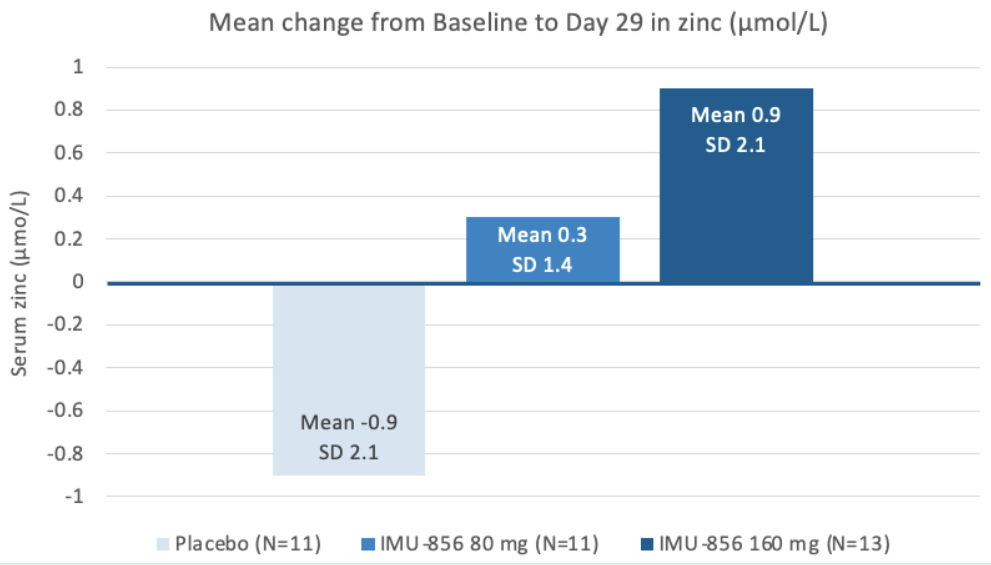
Number of Patients:
Placebo: N=13 for Mean Change Baseline to Day 14, N=11 for Mean Change Baseline to Day 29;
IMU-856 80 mg: N=14 for Mean Change Baseline to Day 14, N=11 for Mean Change Baseline to Day 29;
IMU-856 160 mg: N=13 for Mean Change Baseline to Day 14, N=13 for Mean Change Baseline to Day 29;
SD: standard deviation

IMU-856 Treatment Resulted in Dose Linear Enhanced Uptake of Actively Transported Essential Nutrients Vitamin B12 and Zinc

Vitamin B12



Zinc



IMU-856 Substantially Increased GLP-1 in Celiac Disease Patients

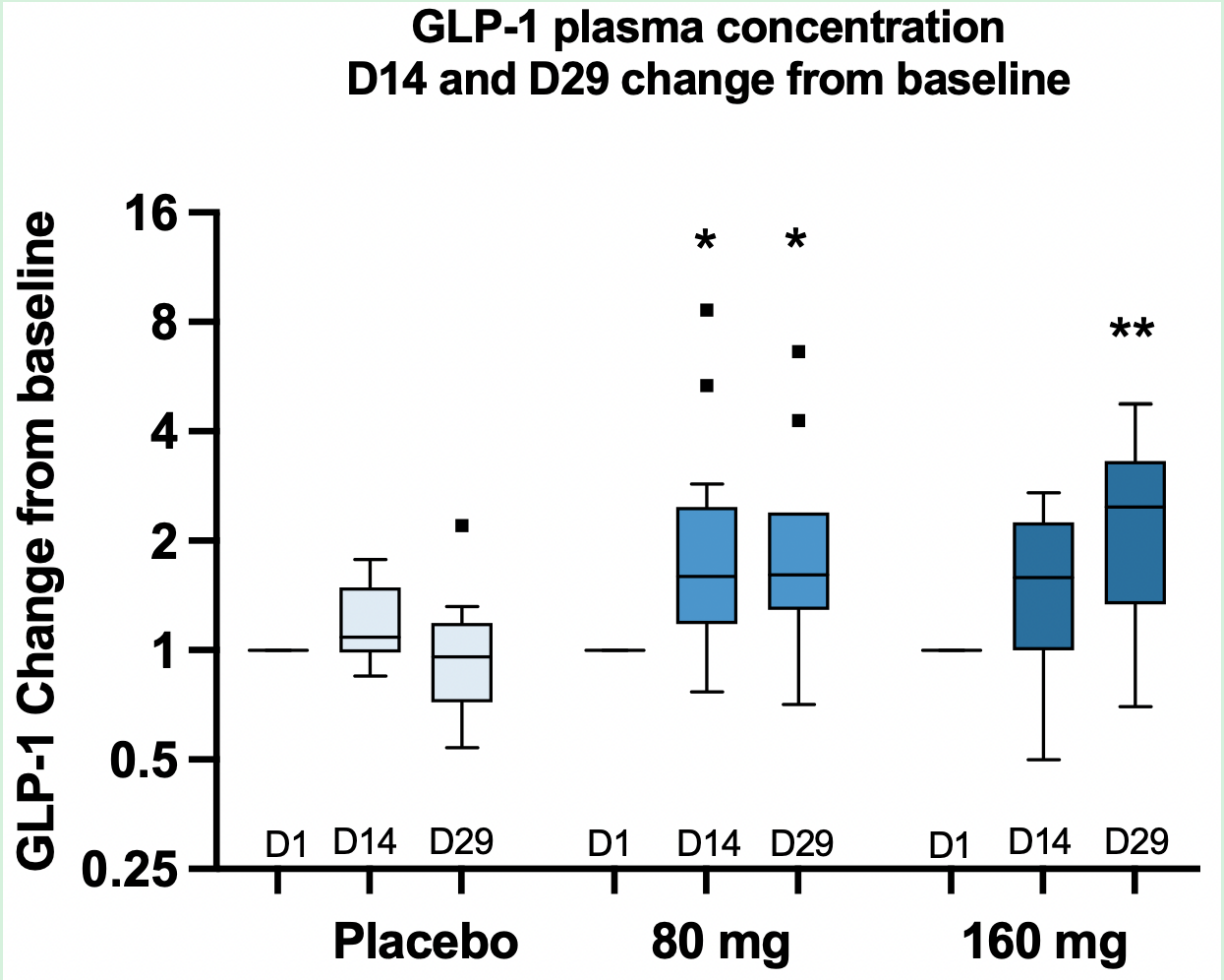
GLP-1

- Peptide hormone secreted in response to **nutrient ingestion** and neuroendocrine stimulation
- GLP-1 increase leads to slow gut motility, lower food intake, increase satiety and induce insulin secretion

- Patients measured for plasma GLP-1 concentrations:
  - N=11 (placebo)
  - N=13 (80 mg)
  - N=13 (160 mg)

- 3 timepoints per treatment arm:
  - Left: Day 1 (baseline)
  - Middle: Day 14 (before start of gluten challenge)
  - Right: Day 29 (after last treatment on Day 28)

- Up to 2.5-fold increase in GLP-1 levels compared to baseline



y-axis log2 scale, statistics: two-sided Mann-Whitney U - treatment vs placebo at Day 14 and Day 29

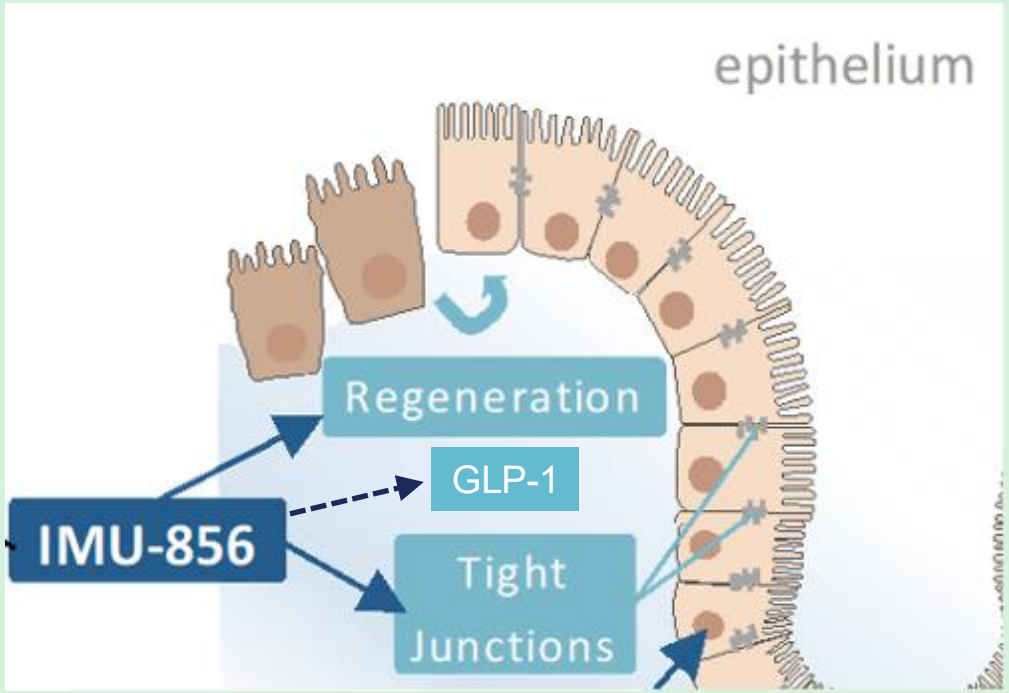
IMU-856 – From Proof of Concept in Celiac Disease to IBD and Beyond

IMU-856 → Enterocytes 

- Regenerates gut barrier (cell renewal / differentiation)
- Drives gut barrier tightness (via tight junction proteins)

IMU-856 ⇢ Enteroendocrine cells 

- Increases GLP-1 hormone secretion
  →influence on gastric emptying
  →anti-inflammatory properties
  →intestinotrophic effects → intestinal health and repair



Immunic THERAPEUTICS

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Thank you very much for your attention.