FIRST IN HUMAN TRIAL OF IMU-856, AN ORALLY AVAILABLE EPIGENETIC MODULATOR OF BARRIER REGENERATION FOR THE TREATMENT OF CELIAC DISEASE

Franziska Buriánek, Doris Pröbstl, Evelyn Peelen, Juliano Fonseca, Amelie Schreieck, Martina Wirth, Inge Kehler, Daniel Vitt, Hella Kohlhof, Andreas Muehler

Immunic AG, Gräfelfing, Germany

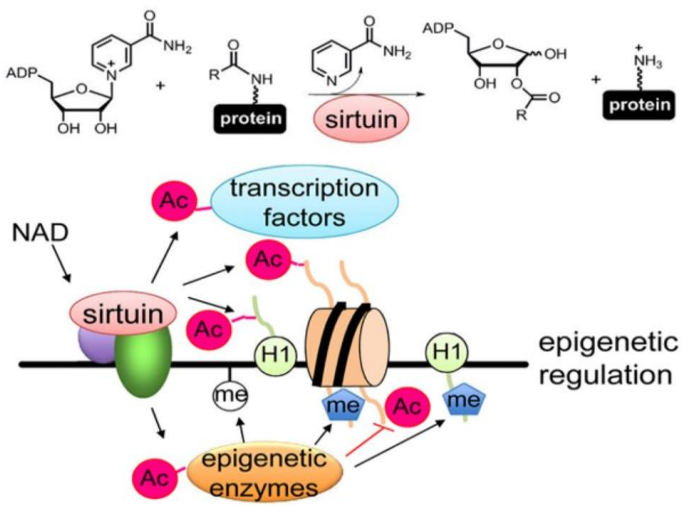
Abstract # 4025905

DDW2024
Digestive Disease Week®
MAY 18–21, 2024 | WASHINGTON, D.C.
EXHIBIT DATES: MAY 19–21, 2024
@DDWMeeting | #DDW2024

SIRT6 MODULATES CELLULAR PROCESSES BY GENE EXPRESSION THROUGH ITS DEACETYLASE ACTIVITY AND MODULATION OF PROTEIN INTERACTION NETWORKS

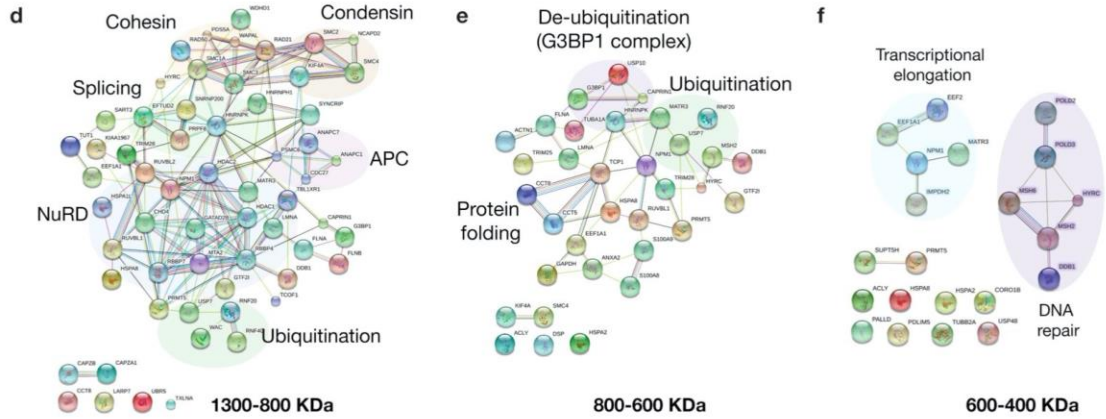
Function #1 – Deacetylase Activity

Modification of the chromatin structure and accessibility of DNA/promotor regions



Function #2 – Protein Interaction independent of enzymatic activity

Impact on processes like chromatin remodeling, mitotic chromosome segregation, protein homeostasis, and transcriptional elongation

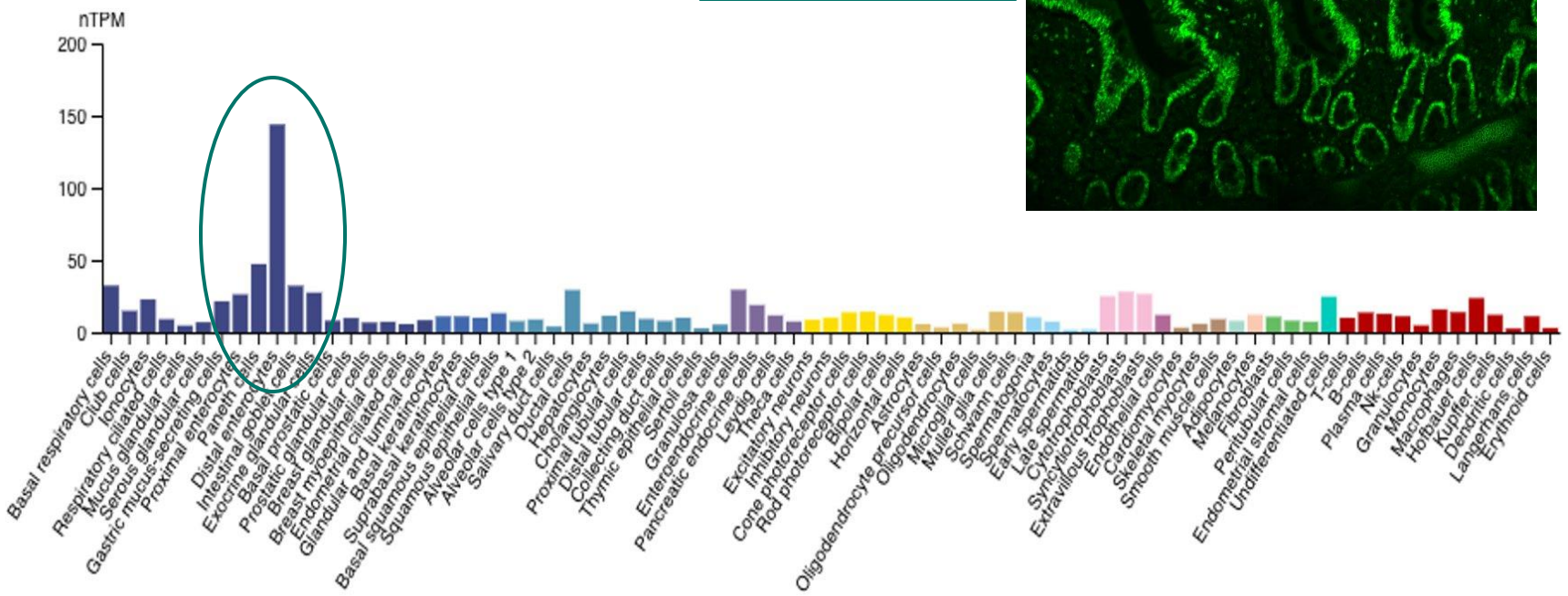


@DDWMeeting| #DDW2024

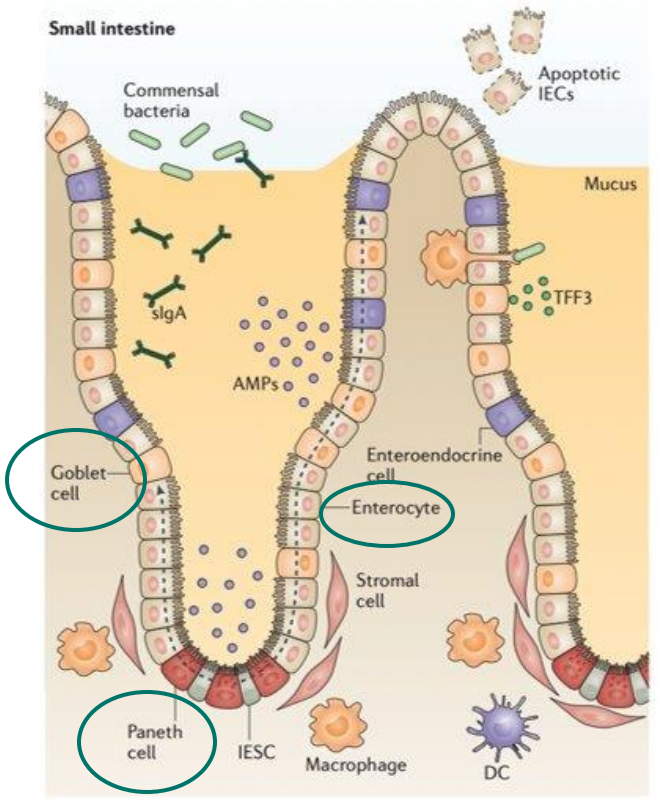
DDW2024
Digestive Disease Week®
MAY 18-21, 2024 | WASHINGTON, D.C.
EXHIBIT DATES: MAY 19-21, 2024

Left: Chem. Rev. 2015, 115, 6, 2350–2375; Right: Simeoni et al. 2013, Scientific ReportsSimeoni et al. Scientific Reports. 2013

SIRT6 IS MAINLY EXPRESSED IN GUT EPITHELIAL CELLS – HIGHEST MRNA EXPRESSION IN PANETH CELLS, ENTEROCYTES AND GOBLET CELLS

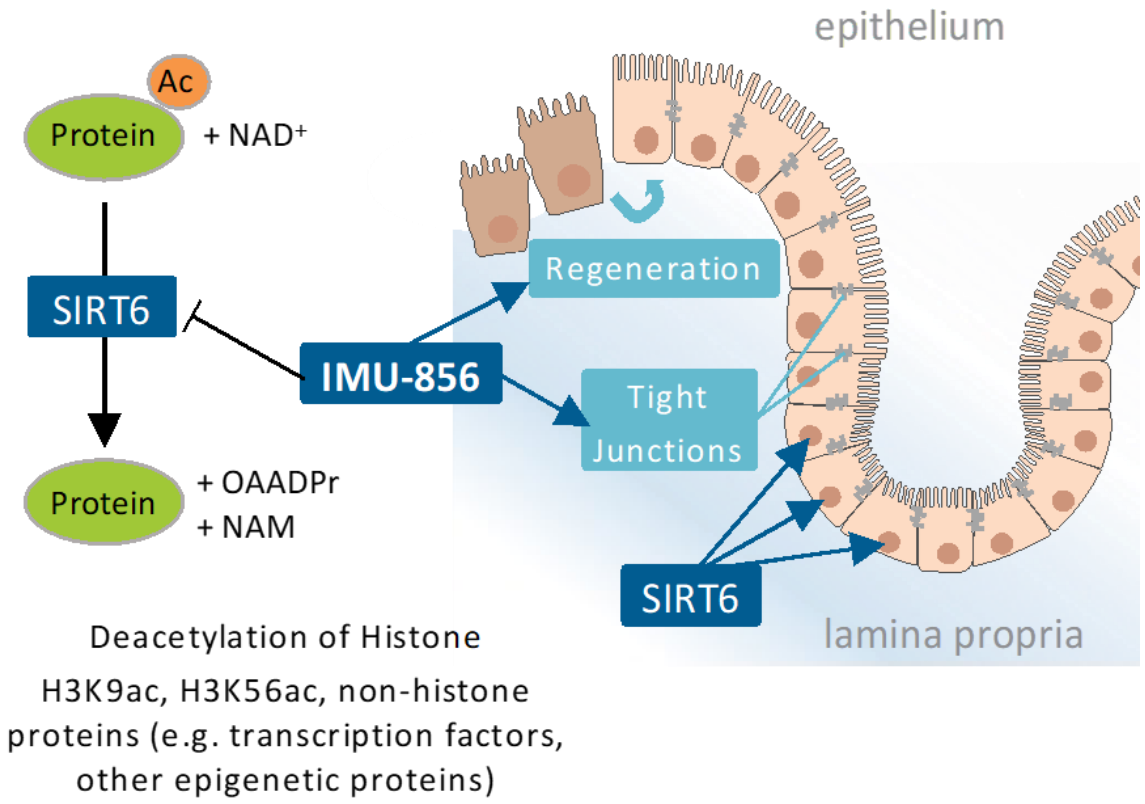


Duodenal biopsy celiac disease patient



Left graph: https://www.proteinatlas.org/; Right image: Peterson, L., Artis, D. Nat Rev Immunol 14, 141–153. 2014.
Duodenal Biopsy: Jilab Inc. / Immunic AG

IMU-856 MODE OF ACTION: RESTORATION OF INTESTINAL BARRIER FUNCTION AND INDUCTION OF PHYSIOLOGIC REGENERATION



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

- ❑ 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

IMU-856 PHASE 1/1B CLINICAL TRIAL DESIGN

A THREE-PART, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 1/1B STUDY OF IMU-856 IN HEALTHY VOLUNTEERS AND CELIAC DISEASE PATIENTS

PART A

Evaluation of single ascending doses (SAD)

Healthy human subjects randomized to receive single dose of IMU-856 or placebo

- Planned dose escalation completed: 10, 20, 40, 80, 120 and 160 mg of IMU-856
- 45 subjects enrolled (IMU-856: N=33)
- IMU-856 was well-tolerated and showed dose-linear pharmacokinetics

PART B

Evaluation of multiple ascending doses (MAD)

Healthy human subjects randomized to receive 14-day treatment of IMU-856 or placebo

- Planned dose escalation completed: 40, 80 and 160 mg QD of IMU-856
- 26 subjects enrolled (IMU-856: N=19)
- IMU-856 was well-tolerated and steady-state trough levels were achieved within first week of dosing

PART C

Evaluation of patients with celiac disease receiving 28-day treatment of IMU-856 or placebo

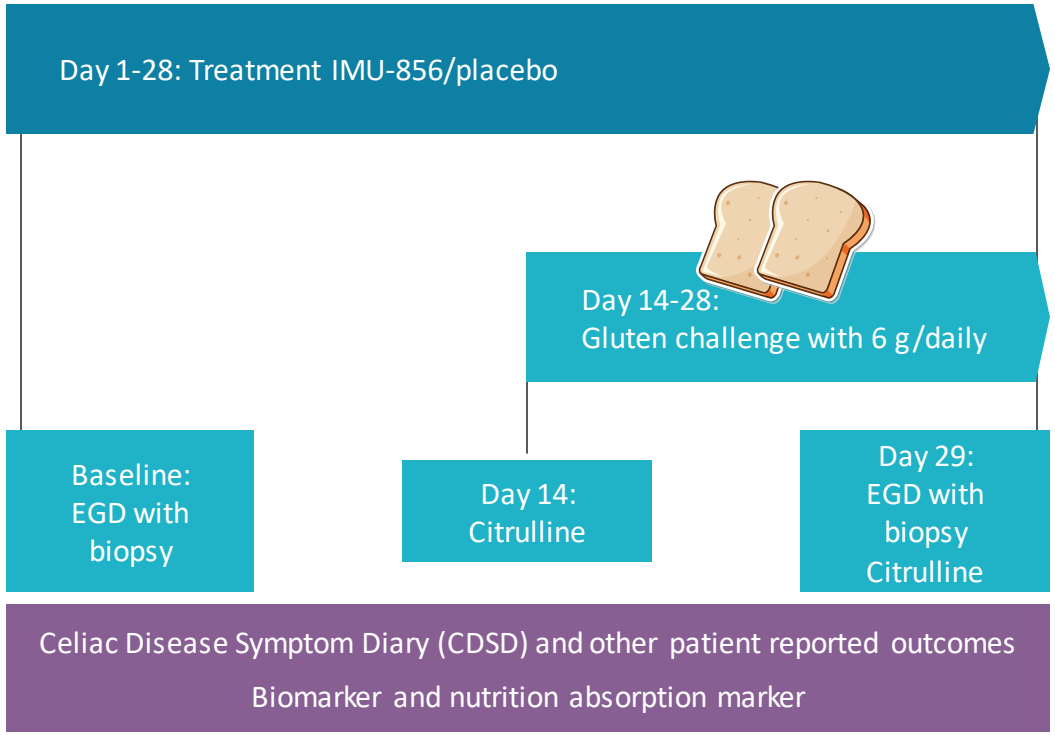
- Planned dosing completed: 80 and 160 mg QD of IMU-856
- 43 patients with celiac disease enrolled (IMU-856: N=29)
- Provided proof-of-concept of IMU-856's mode of action

PHASE 1B CLINICAL TRIAL OF IMU-856 IN CELIAC DISEASE DESIGNED AS A GLUTEN CHALLENGE TRIAL

Proof-of-Concept Study

- ❑ Conducted in a population of well-controlled celiac disease patients with planned gluten challenge of 6g/day for 15 days
- ❑ Dosing: 80 and 160 mg PO once daily of IMU-856
- ❑ N=43 (IMU-856 80mg: N=14, IMU-856 160mg: N=15)
- ❑ Performed at sites in Australia and New Zealand
- ❑ Proof of concept study:
  - histological changes
  - blood biomarkers
  - nutrient uptake
  - disease-related symptoms

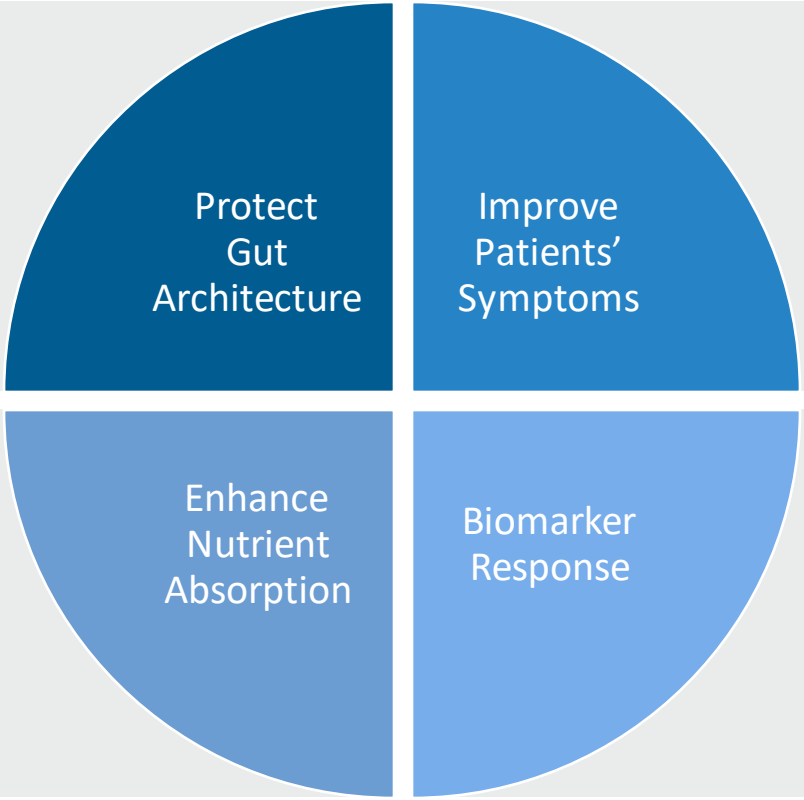
Flow Chart of Part C in Celiac Disease



DDW2024
Digestive Disease Week®
MAY 18-21, 2024 | WASHINGTON, D.C.
EXHIBIT DATES: MAY 19-21, 2024

IMU-856 SHOWED POSITIVE EFFECTS IN FOUR MAIN DIMENSIONS OF CLINICAL OUTCOME IN CELIAC DISEASE

IMU-856 effectively protected against gluten-induced intestinal damage, as measured by villous height



IMU-856 reduced/reversed gluten-induced symptoms reported by patients

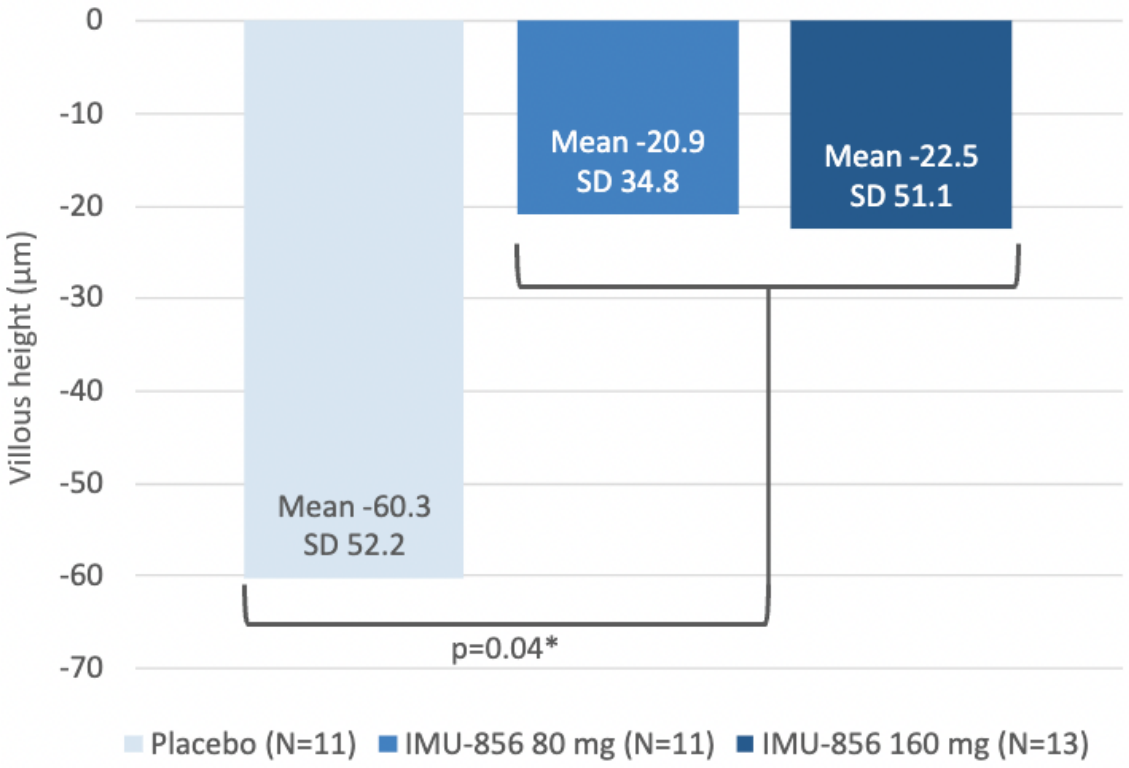
IMU-856 restored villi absorptive function resulting in improved uptake of nutrients such as vitamin B12 and zinc

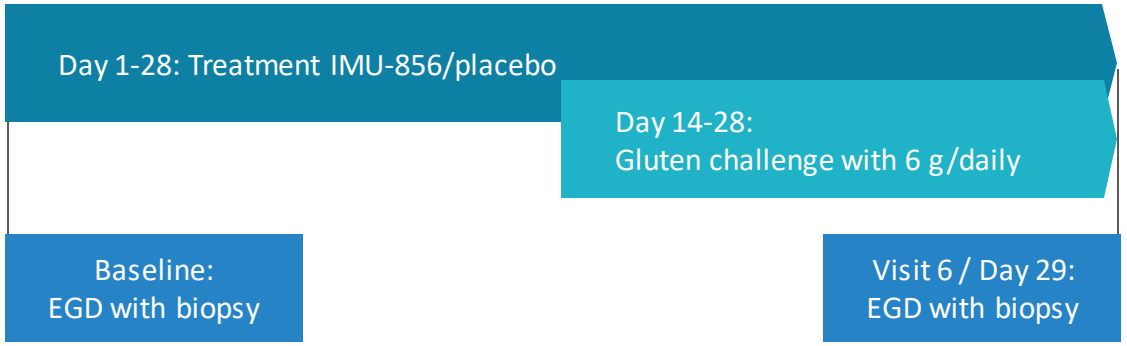
IMU-856 improved blood biomarker such as citrulline levels

- All these effects are achieved without any known or observed suppression of immune cells
- IMU-856 was observed to be safe and well-tolerated in this trial

IMU-856 PROTECTED AGAINST GLUTEN-INDUCED DECREASE IN VILLOUS HEIGHT AS COMPARED TO PLACEBO

Absolute change in villous height (µm) between Baseline and Day 29





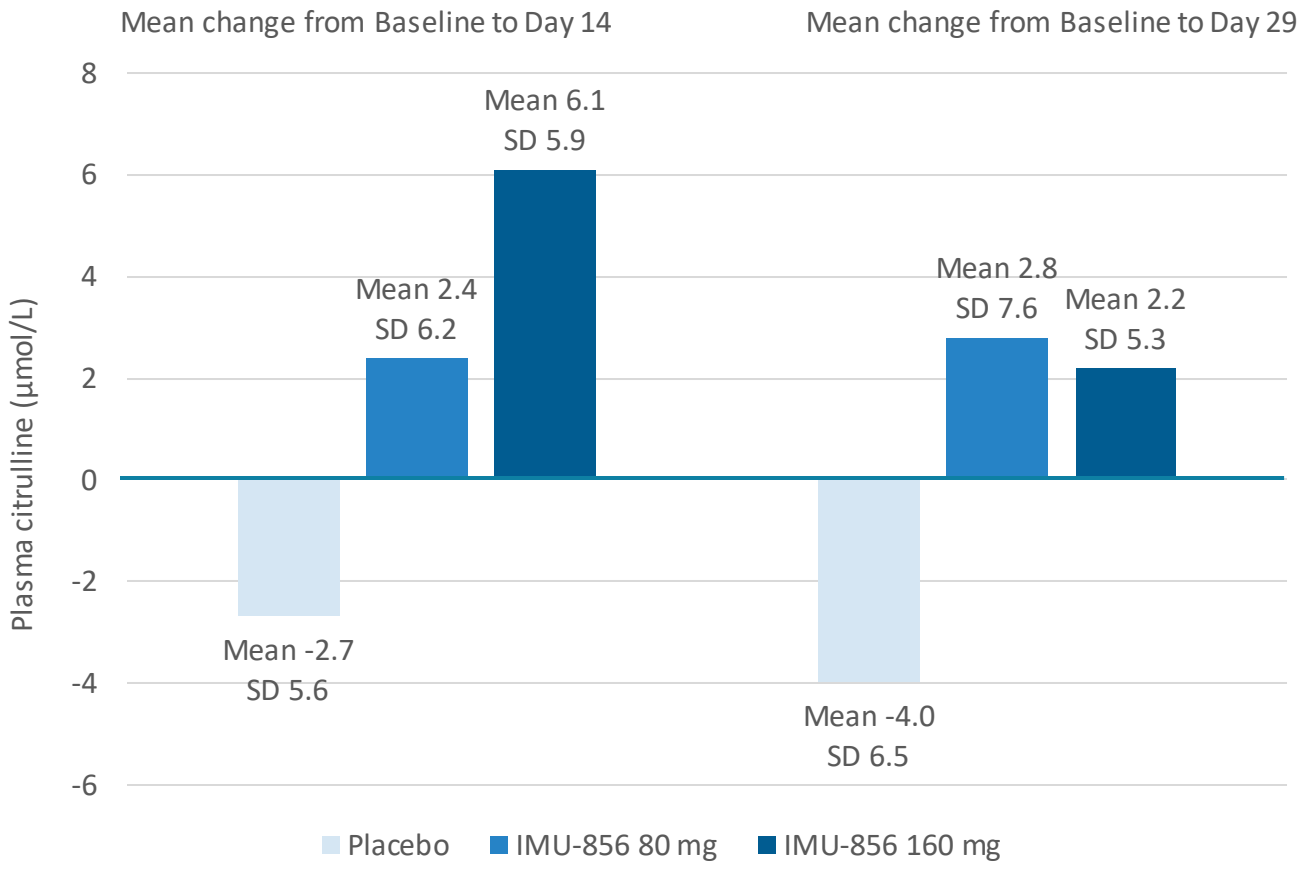
- ❑ Substantial protection for IMU-856 treatment groups as compared to placebo
- ❑ Reached statistical significance*
- ❑ Assessed by central pathology laboratory and blinded pathology reader

@DDWMeeting| #DDW2024

DDW2024
Digestive Disease Week®
MAY 18-21, 2024 | WASHINGTON, D.C.
EXHIBIT DATES: MAY 19-21, 2024

* 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 CITRULLINE LEVELS, A BIOMARKER FOR ENTEROCYTE FUNCTIONAL MASS

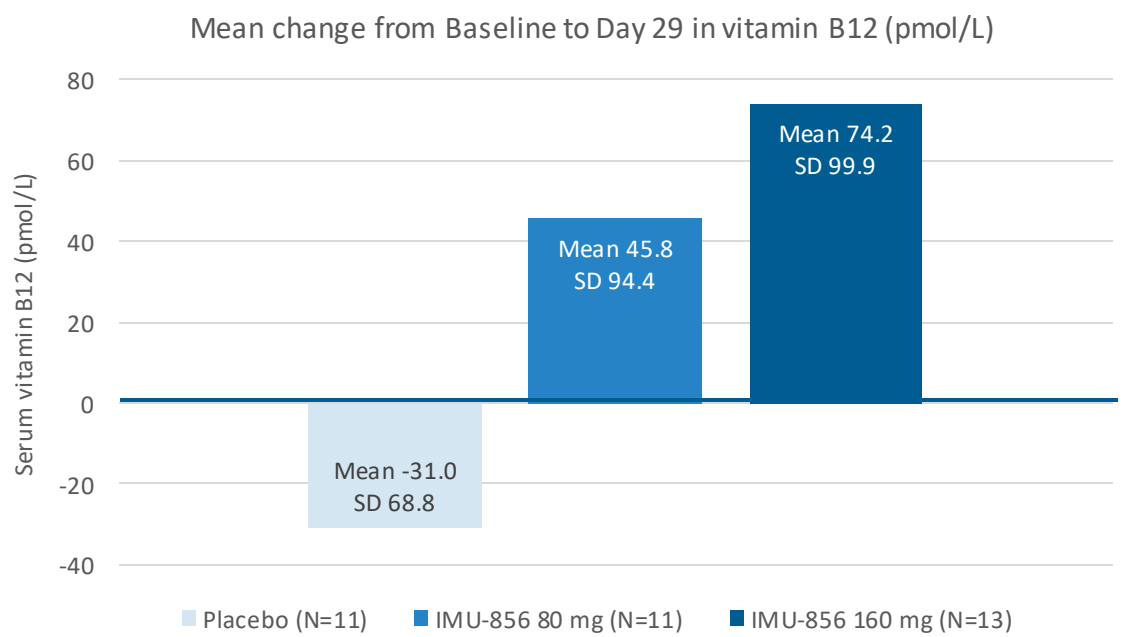


- Citrulline is a biomarker for enterocyte functional mass[1]
- Plasma citrulline levels are known to be related to villous atrophy
- IMU-856 increased citrulline levels dose proportionally, whereas being reduced in placebo treated celiac disease patients

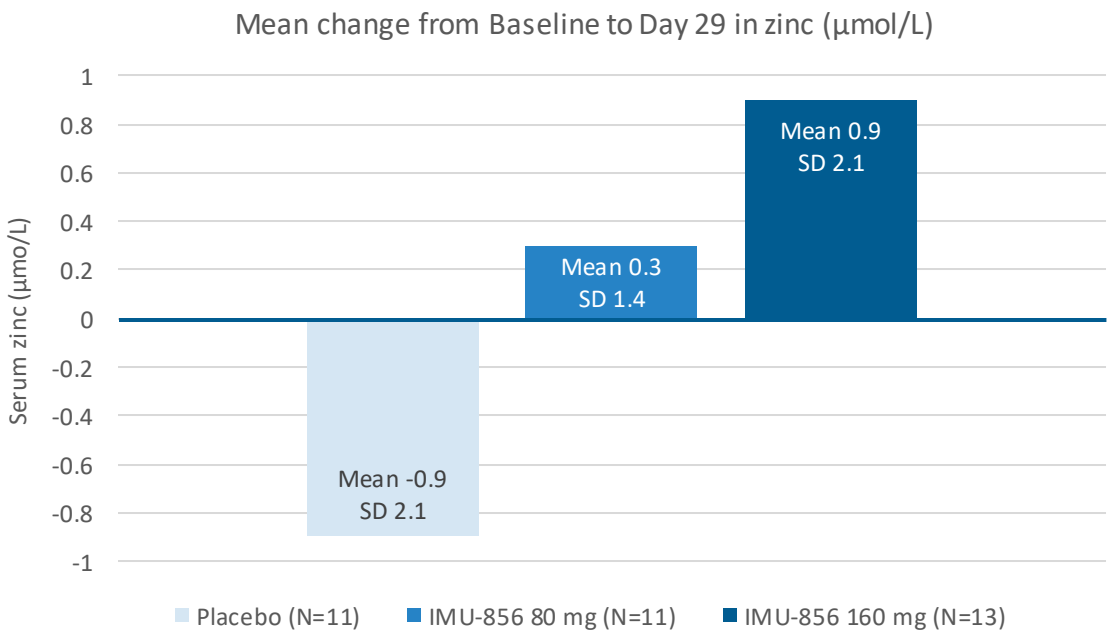
[1] Singh et al., J. Clin. Med. 2019, 8, 885; doi:10.3390/jcm8060885; Number of Patients: Placebo: N=13 for Mean Change Baseline to Day 14, N=11 for Mean Change Baseline to Day 29; IMU-856 80 mg: N=14 for Mean Change Baseline to Day 14, N=11 for Mean Change Baseline to Day 29; IMU-856 160 mg: N=13 for 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



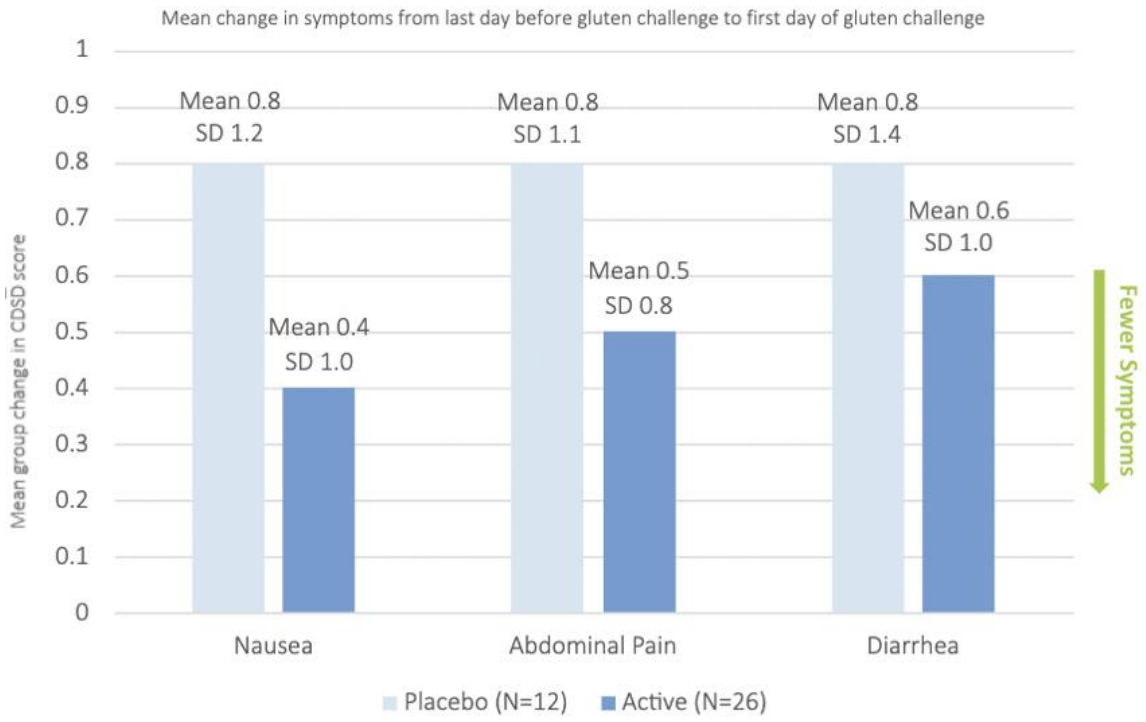
Zinc



DDW2024
Digestive Disease Week®
MAY 18-21, 2024 | WASHINGTON, D.C.
EXHIBIT DATES: MAY 19-21, 2024

IMU-856 REDUCED SYMPTOMS AFTER GLUTEN CHALLENGE AND WAS SAFE AND WELL TOLERATED

IMU-856 Treated Patients Had Fewer Symptoms On First Day Of Gluten Challenge Than Placebo Patients



Once-daily oral dosing of IMU-856 for 28 days proved to be safe and well-tolerated

- ❑ No dose-dependency in adverse events
- ❑ No IMP-related severe or serious adverse events or IMP-related study withdrawals
- ❑ No clinically relevant findings in any laboratory parameter, ECG, physical examination or vital signs
- ❑ Linear Pharmacokinetics that allow once-daily oral dosing
- ❑ IMU-856 may offer extensive potential beyond celiac disease in other gastrointestinal disease with epithelial damage or with compromised intestinal barrier function

@DDWMeeting| #DDW2024

Assessed via Celiac Disease Symptom Diary (CDSD); SD: standard deviation

DDW2024
Digestive Disease Week®
MAY 18-21, 2024 | WASHINGTON, D.C.
EXHIBIT DATES: MAY 19-21, 2024

THANK YOU VERY MUCH FOR YOUR ATTENTION

@DDWMeeting| #DDW2024

Immunic THERAPEUTICS

Contact Info
Dr. Franziska Buriánek
franziska.burianek@imux.com
Sr. Medical Director - Immunic AG
Gräfelfing, Germany

DDW2024
Digestive Disease Week®
MAY 18-21, 2024 | WASHINGTON, D.C.
EXHIBIT DATES: MAY 19-21, 2024

DISCLOSURE INFORMATION

Dr. Franziska Buriánek

I disclose the following financial relationship(s) with a commercial interest

- I am an employee of the trial sponsor