Immunic THERAPEUTICS

Changing Paradigms

IMU-856: Celiac Disease Clinical Phase 1b Results

NASDAQ: IMUX | May 4, 2023

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This presentation contains “forward-looking statements” that involve substantial risks and uncertainties for purposes of the safe harbor within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. 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 Private Securities Litigation Reform Act of 1995.

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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 does not undertake any obligation to update such forward-looking statements except as required by applicable law.

Today’s Highlights

Positive Phase 1b Results of IMU-856 in Celiac Disease

- Regeneration and protection of the gut wall proven for the first time in patients, establishing a new concept for healthy gut in gastrointestinal disorders
- Consistent clinical benefit seen across four dimensions of clinical outcome for celiac disease patients
- Shown to be safe and well-tolerated in this trial
- Preparing clinical phase 2b testing in ongoing active celiac disease

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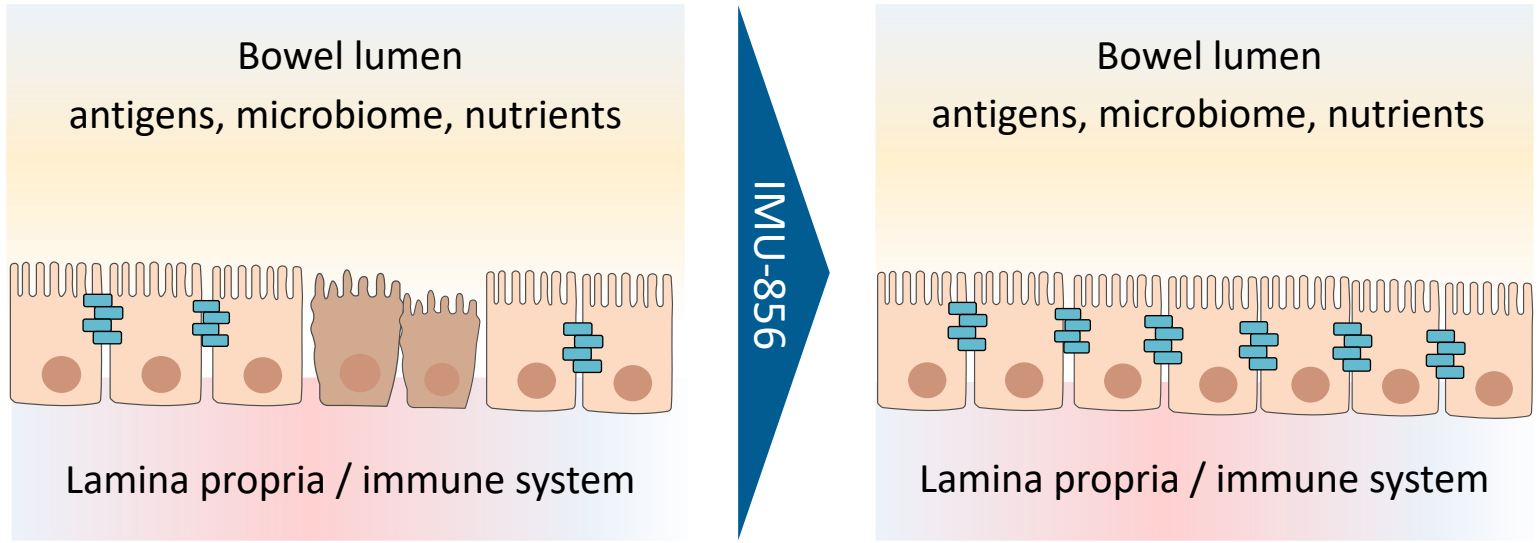
IMU-856 could become a game changer in the way we treat gastrointestinal diseases.

Once-Daily, Oral IMU-856 Aims to **Regenerate the Gut Wall** and Barrier Function by a New Epigenetic Mechanism



IMU-856:

- Epigenetic modulator aimed to regenerate gut wall and restore barrier
- Provides protection and enhances transport of nutrients

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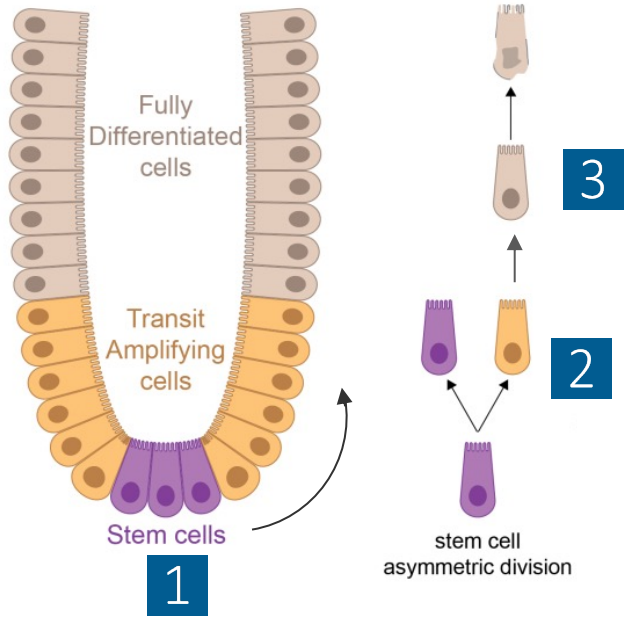
IMU-856 Enhances the Natural Regenerative Process in the Gut

Gut wall renewal is a normal physiological process

1. Regeneration begins in the crypts, where intestinal stem cells are located
2. Stem cells undergo asymmetric division thereby producing fully differentiated epithelial gut cells and renewing intestinal stem cells
3. These new epithelial cells are renewing the lining of crypts and villi to maintain healthy gut and proper intestinal barrier

→ IMU-856 is an epigenetic regulator which enhances this natural tissue renewal phenotype

Asymmetric cell division renews stem cells and regenerates the gut wall

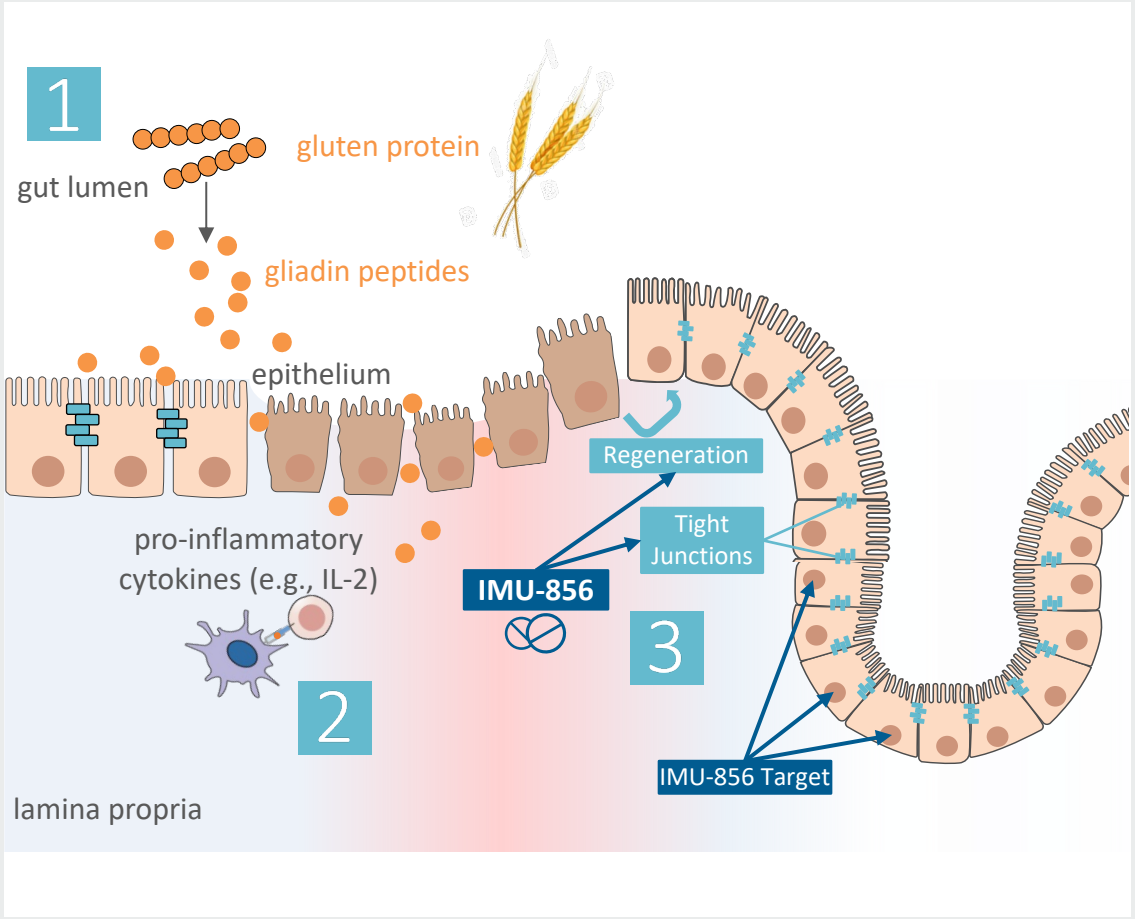


Adapted from Mamis et al., 2023, cbioRxiv

*IMU-856 is a completely new approach for the treatment of gastrointestinal diseases by **restoring a healthy gut** by renewal of the gut wall.*

First Proof-of-Concept for Gastrointestinal Disorders in Celiac Disease

Celiac Disease is a Serious Life-Long Disease



Celiac disease is a **multifactorial, complex autoimmune disease** caused by an immune reaction against a degradation product of gluten and is strongly associated with **specific HLA class II gene variants** (HLA-DQ2 and -DQ8)[1]

1
- Gluten is degraded into **gliadin peptides** which are taken up by the bowel epithelium (trans- or paracellular)

2
- In patients with a specific HLA protein (DQ2 and DQ8) composition, deaminated gliadin (by TG2) is recognized by CD4+ T cells and can trigger an immune response which leads upon continued gliadin uptake to
  - **Increased intestinal permeability**
  - **Epithelial and mucosal damage** with negative changes of the gut architecture, including villous atrophy leading to malabsorption of nutrients

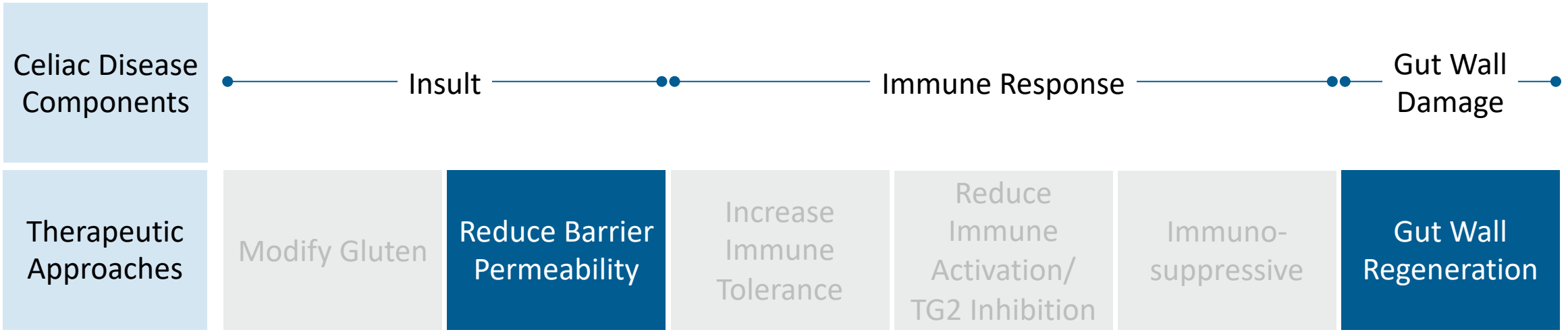
3
- Hypothesis for IMU-856's mode of action:
  - Restores villous architecture by triggering regenerative processes of the epithelial lining
  - Improves intestinal barrier function

Picture: self-drawn; [1] Caio et al. BMC Medicine (2019) 17:142
HLA: human leukocyte antigen; TG2: tissue transglutaminase 2; CD: cluster of differentiation; IL: interleukin

IMU-856 Addresses Two Key Pathological Aspects of Celiac Disease

IMU-856 Mode of Action

Orally available and systemically acting small molecule modulator that targets a protein which serves as a transcriptional regulator of intestinal barrier function and regeneration of bowel epithelium

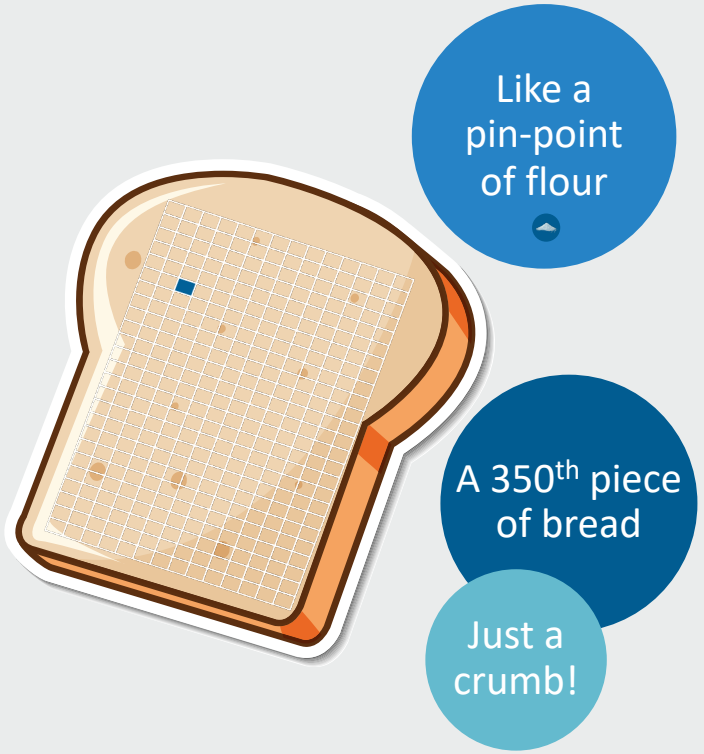


TG: transglutaminase

Celiac Disease Currently Has No Adequate Treatment Options

- Two million patients diagnosed with celiac disease in the US; more than one million more undiagnosed[1,2]
- Most studies report between **24% and 47%**[3-8] of patients with signs and symptoms of ongoing active celiac disease (OACD) **despite a gluten-free diet,** most likely due to continuous (inadvertent) gluten exposure
- **Only established therapeutic option is a life-long strict adherence to a gluten-free diet**[9], which involves complete avoidance of proteins from wheat, barley, and rye
- Gluten challenge is an accepted concept for clinical trials in celiac disease

10 mg of gluten is the total limit for all foods combined for the entire day.



How much is 10 mg of gluten?

[1] Singh et al., Clinical Gastroenterology and Hepatology 2018;16:823–836 [2] Choung et al., Mayo Clin Proc. 2016 Dec 5:S0025-6196(16)30634-6 [3] Lebwohl et al., Aliment Pharmacol Ther. 2014 March ; 39(5): 488–495 [4] Lanzini et al., Aliment Pharmacol Ther. 2009; 29(12):1299–308 [5] Ciacci et al., Digestion. 2002; 66(3):178–85 [6] Selby et al., Scand J Gastroenterol. 1999; 34(9):909–14 [7] Rubio-Tapia et al., Am J Gastroenterol. 2010; 105(6):1412–20 [8] Sharkey et al., Aliment Pharmacol Ther. 2013; 38(10):1278–91 [9]: https://nationalceliac.org/celiac-disease-questions/understanding-gluten-levels/ (text and picture)

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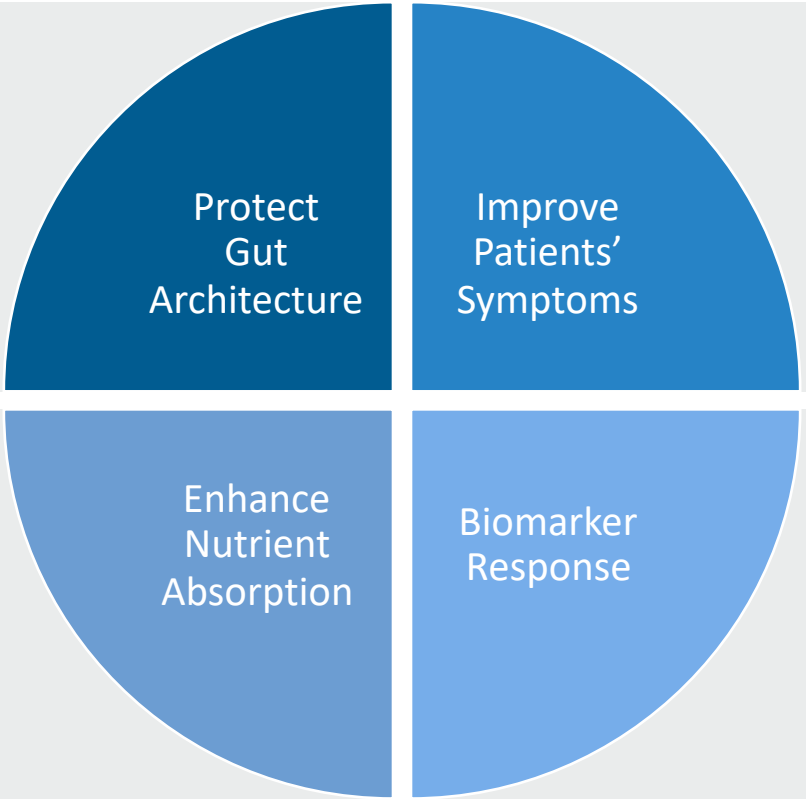
IMU-856 Shows Positive Effects in Main Four Dimensions of Clinical Outcome in Celiac Disease Patients

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



IMU-856 reduces/reverses gluten-induced symptoms reported by patients

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

IMU-856 dampens gluten-induced immune activation, as measured by IL-2, and shows positive impact on citrulline

All these effects achieved without any known suppression of the immune system

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Trial Design

Phase 1b Clinical Trial of IMU-856

Trial Design Phase 1 Clinical Trial of IMU-856

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

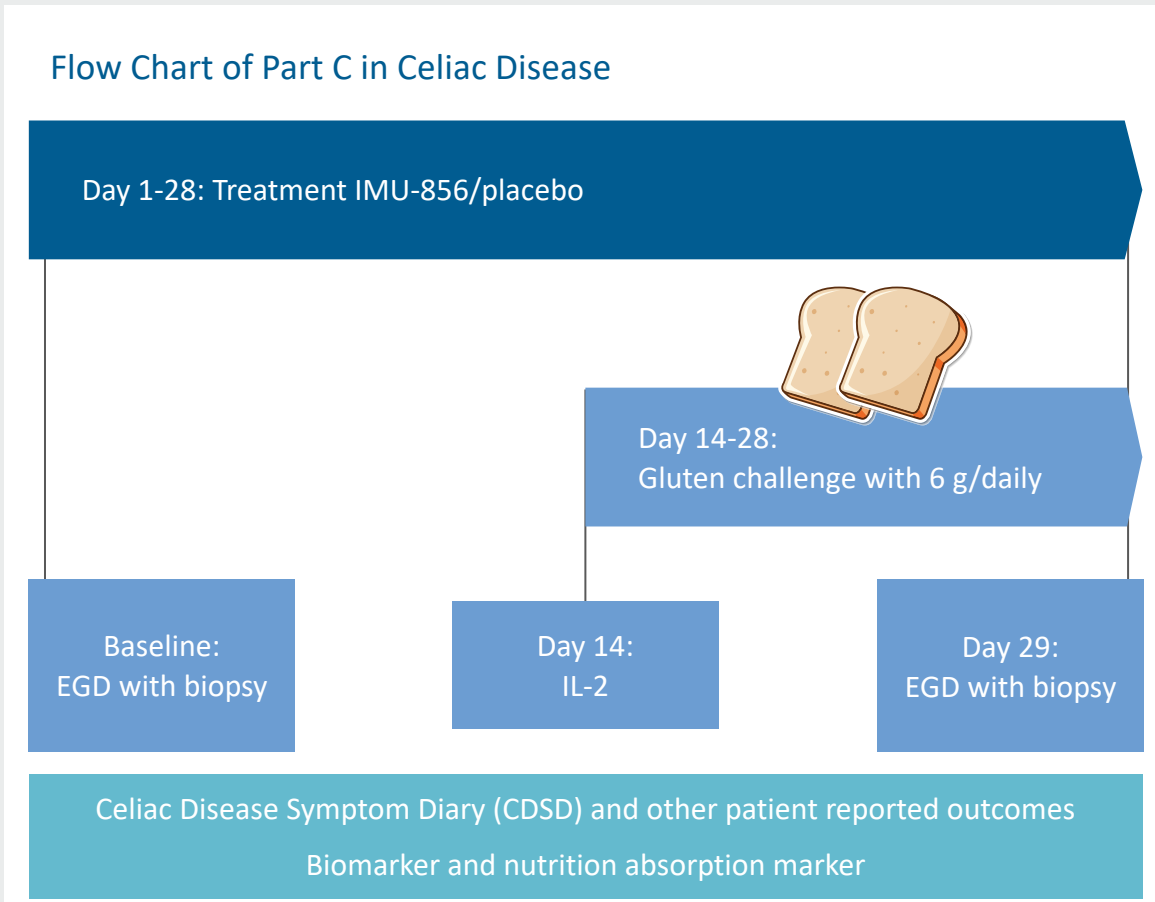
- Planned dosing completed: 80 and 160 mg QD of IMU-856
- 43 patients with celiac disease enrolled (IMU-856: N=29)
- Provided proof-of-concept of IMU-856's mode of action

QD: quaque die = once-daily

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

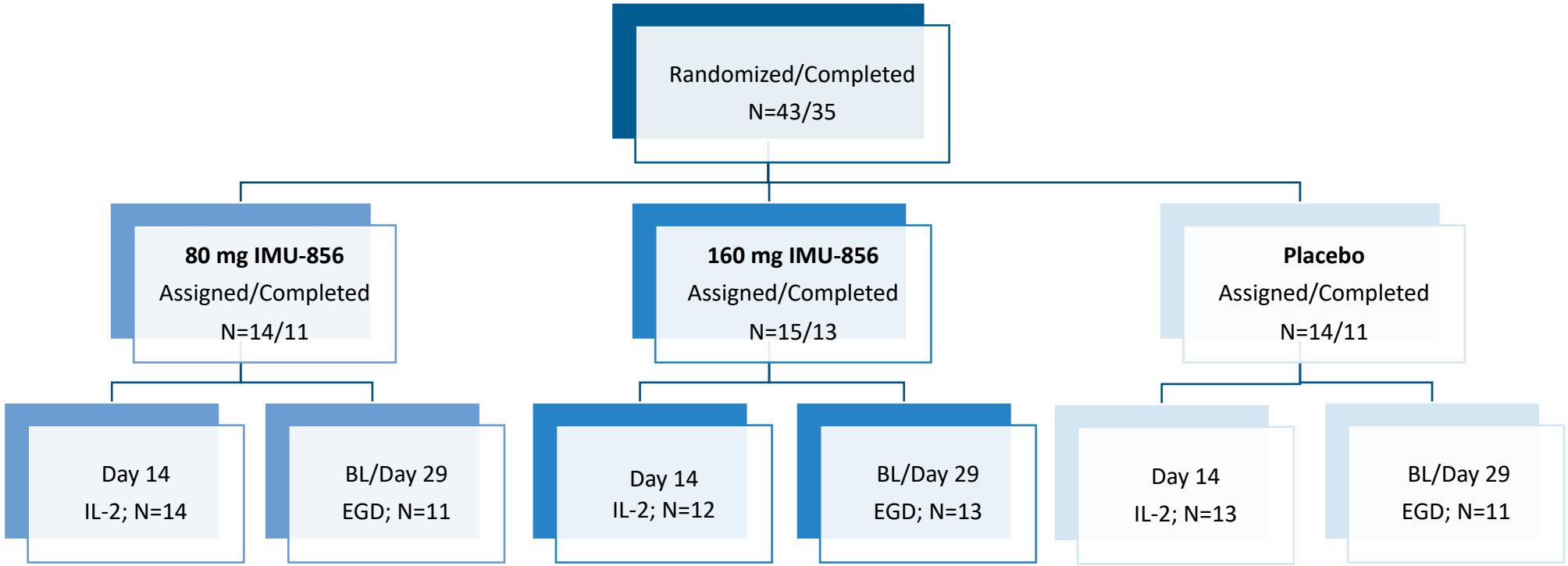
Proof-of-Concept Study

- Part C planned to include a well-controlled celiac disease patient population
- 100% seronegative patients (indicating absence of ongoing substantial gluten exposure)
- Performed at sites in Australia and New Zealand
- Designed to assess safety, tolerability and pharmacokinetics of IMU-856
- Measured histologic changes, blood biomarkers, nutrient uptake and disease-related symptoms



EGD: esophagogastroduodenoscopy; IL: interleukin

Patients Per Treatment Group



Reasons for Early Termination	IMU-856 80 mg	IMU-856 160 mg	Placebo
Gluten intolerance	N=3	-	N=2
Personal reasons	-	N=1	-
Unrelated viral illness	-	-	N=1
Unrelated biliary colic	-	N=1	-

IL: interleukin; BL: Baseline; EGD: esophagogastroduodenoscopy

Distribution of Q-MARSH Histology Score at Baseline

Approximately 60% of IMU-856 Treated Patients Already in FDA Required Phase 2/3 Population Category

Q-MARSH N (%)		IMU-856 80 mg (N=14)	IMU-856 160 mg (N=15)	All Active (N=29)	All Placebo (N=14)
M0		1 (7.1)	1 (6.7)	2 (6.9)	0
M1		1 (7.1)	2 (13.3)	3 (10.3)	3 (21.4)
M2		2 (14.3)	5 (33.3)	7 (24.1)	8 (57.1)
Ongoing Active Celiac Disease (OACD)	M3a	10 (71.4)	6 (40.0)	16 (55.2)	3 (21.4)
	M3b	0	1 (6.7)	1 (3.4)	0
	M3c	0	0	0	0
Vh:Cd (Mean)		1.71	1.86	1.79	2.01

- Inclusion criteria representing well-controlled celiac disease:
  - At least one year of gluten-free diet
  - Seronegative status
  - Absence of signs and symptoms of villous atrophy
- IMU-856 treatment arms showed a higher proportion of patients **with a more severe disease (Q-Marsh scores of M3a or worse)**:
  - More severe baseline inflammation measured as e.g., lower Vh:Cd ratio leads to stronger histologic and symptomatic worsening during gluten challenge[1]
- Patient population in this phase 1b trial for the IMU-856 treatments already close to those required in FDA guidelines for regulatory relevant phase 3 studies

The table displays the overall patient population of N=43 patients and data from histology at screening, including 8 patients that discontinued prematurely before Day 29 and for which histologic change are not available in this study.

[1] Stamnaes, medRxiv 2020.05.04.20090977; doi: https://doi.org/10.1101/2020.05.04.20090977; Vh:Cd: Villous height:Crypt depth; FDA: U.S. Food and Drug Administration

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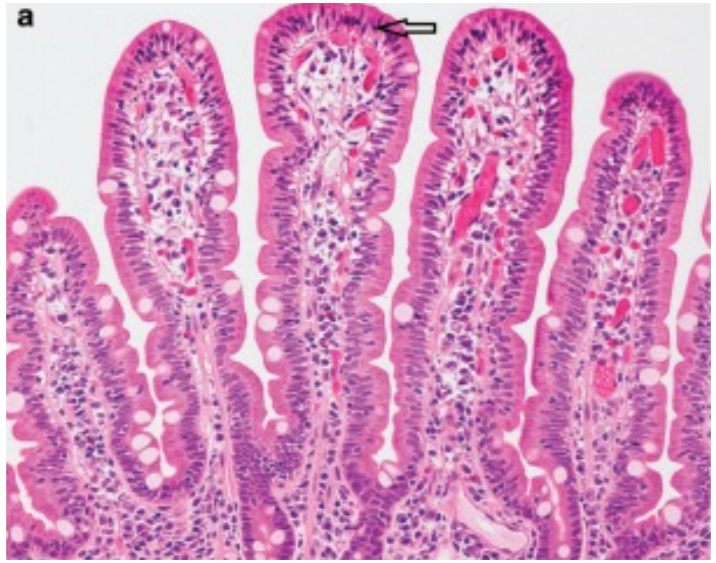
Protects Gut Architecture

Phase 1b Clinical Trial of IMU-856

Histological Hallmarks of Celiac Disease

A Well-Controlled Celiac Disease

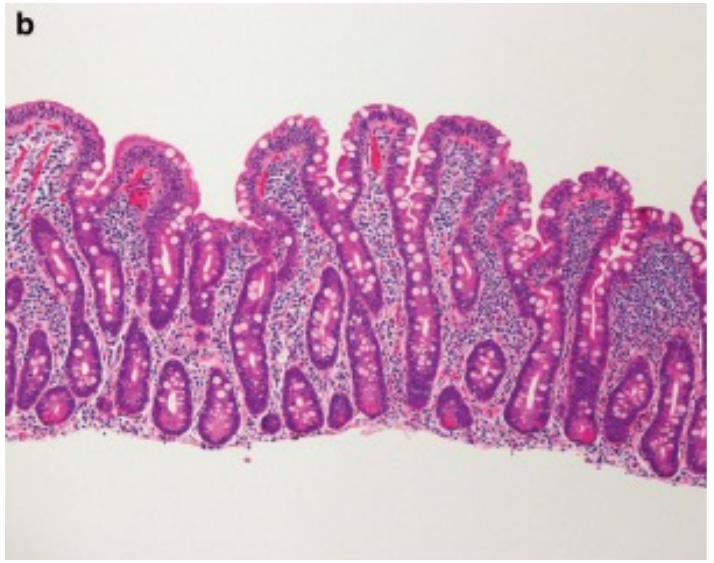
- Villi with normal appearance



Gluten Exposure

B Ongoing Active Celiac Disease (OACD)

- Villous height:Crypt depth ratio decreases



Kamboj et al., Clinical and Translational Gastroenterology (2017) 8, e114

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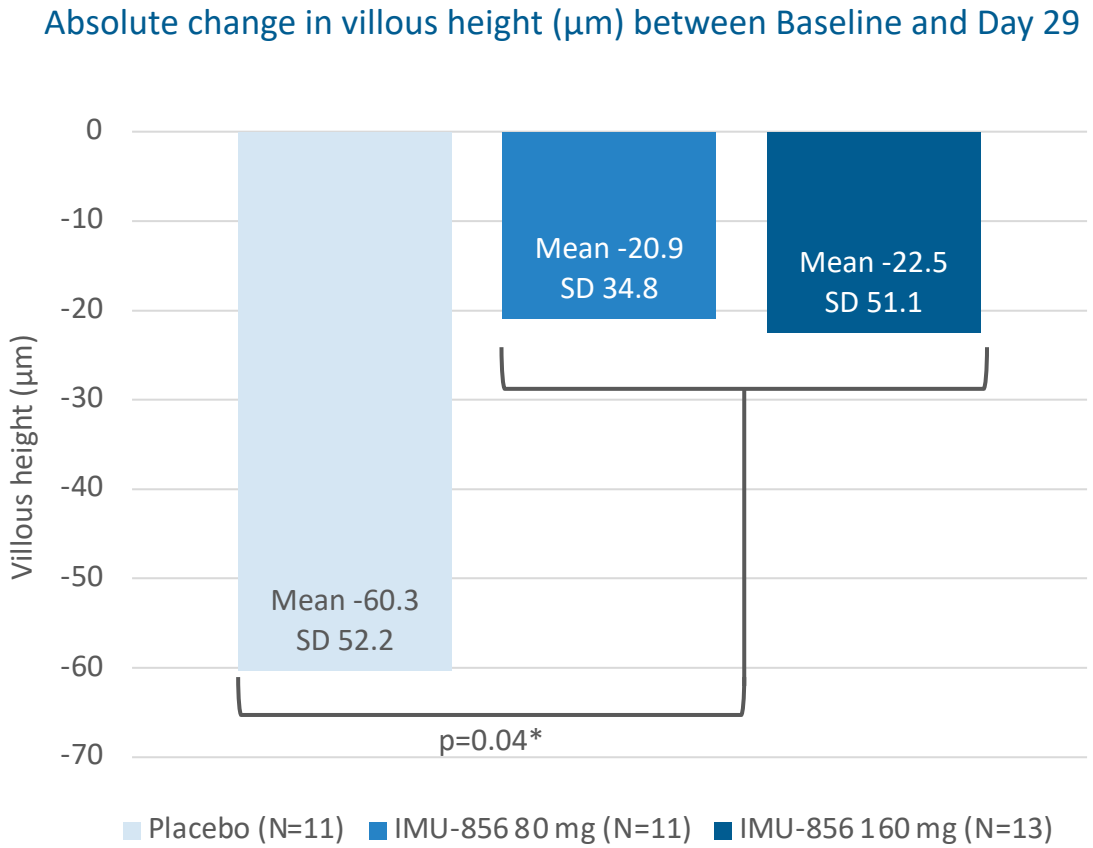
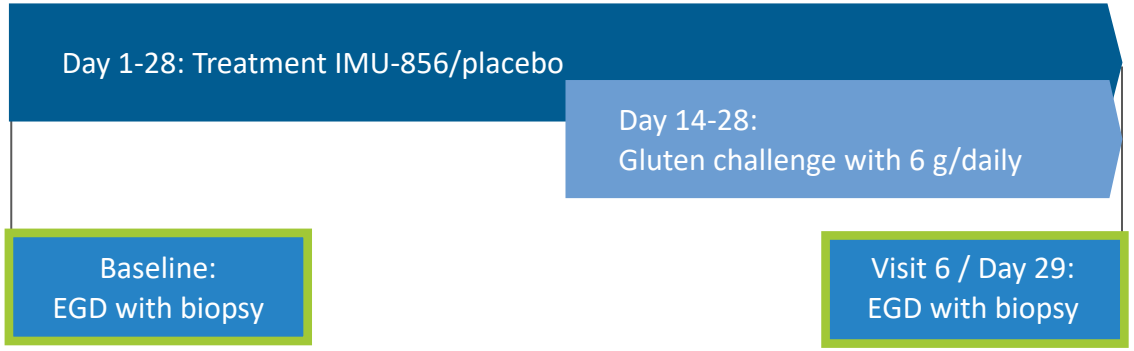
IMU-856 Protects Villous Height as Compared to Placebo



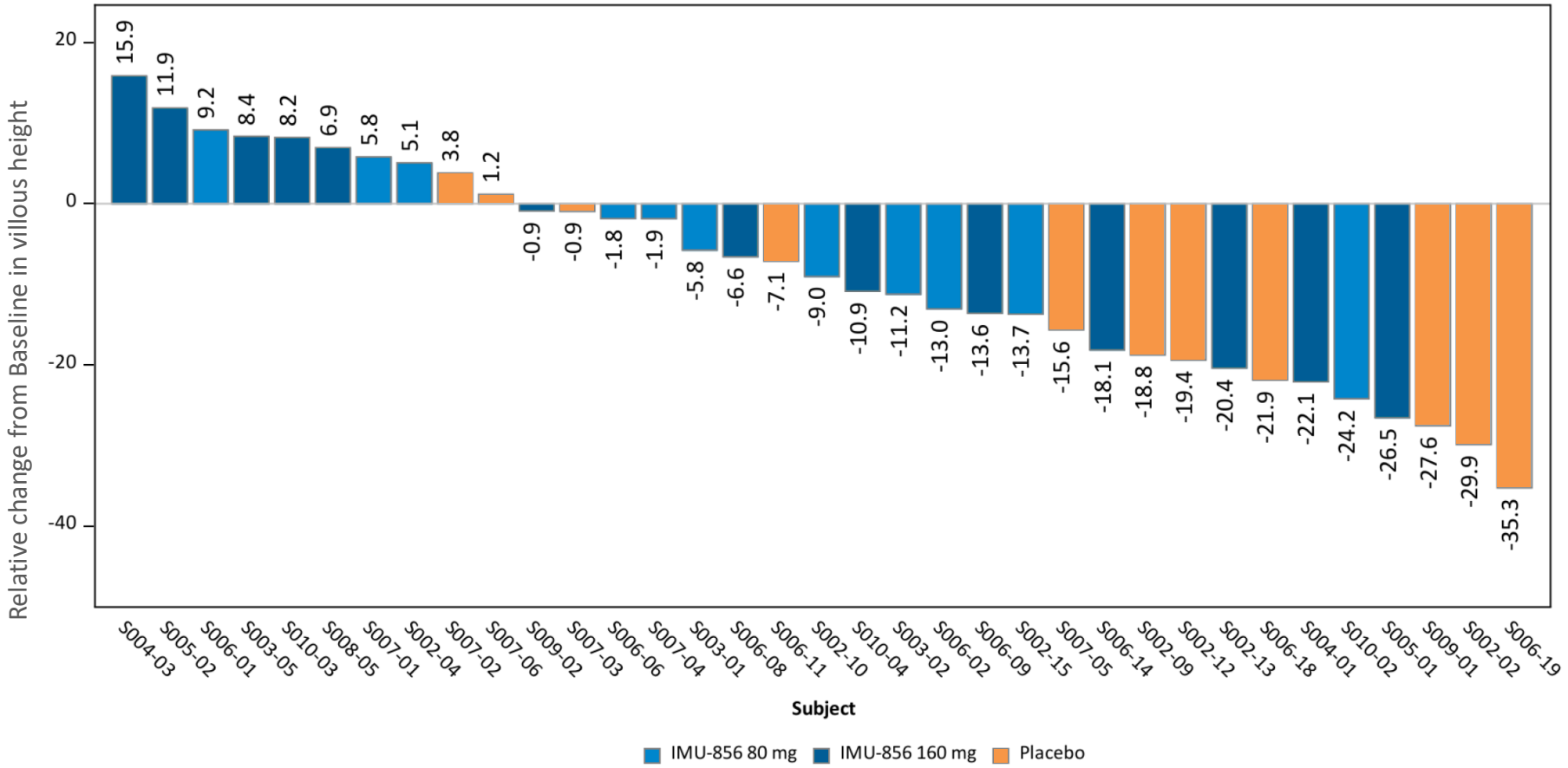


- Substantial protection for IMU-856 treatment groups as compared to placebo
- Reached statistical significance* for this objective readout which is known to be relevant to influence future medical complications of celiac disease
- Assessed by central pathology laboratory and blinded pathology reader

* 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. Central pathology laboratory: Jilab Inc. Tampere, Finland
EGD: esophagogastroduodenoscopy; SD: standard deviation

Individual Patient Data for Changes in Villous Height

Dose-Dependent Shift in Histological Protection From Placebo to 160 mg of IMU-856



Waterfall plot for relative changes in villous height (in % of baseline) for individual patients. Disease Analysis Set: N=35 included in histology analysis set. Of the 43 randomized patients, 8 patients could not be included in this analysis due to early termination before Day 29.

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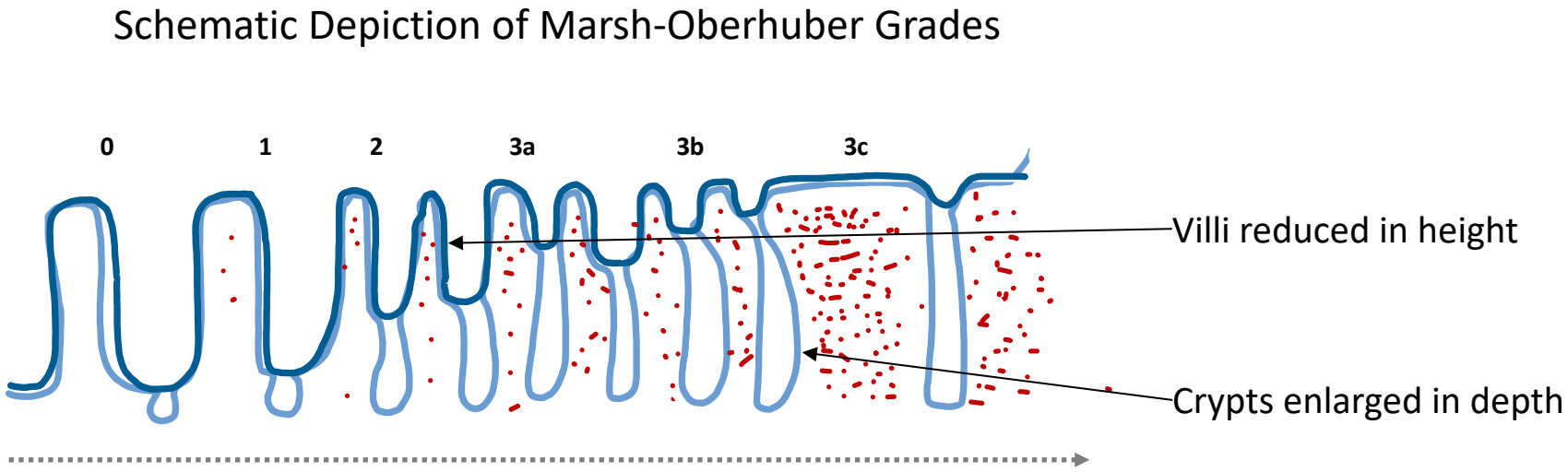
Staging of Celiac Disease: Q-Marsh Histological Scores



Healthy mucosa
- Little malabsorption
- No villous atrophy
- Little crypt hyperplasia
- Increased IELs

Well-Controlled CelD
- Minimal malabsorption
- Partial villous atrophy
- Some crypt hyperplasia
- Increased IELs

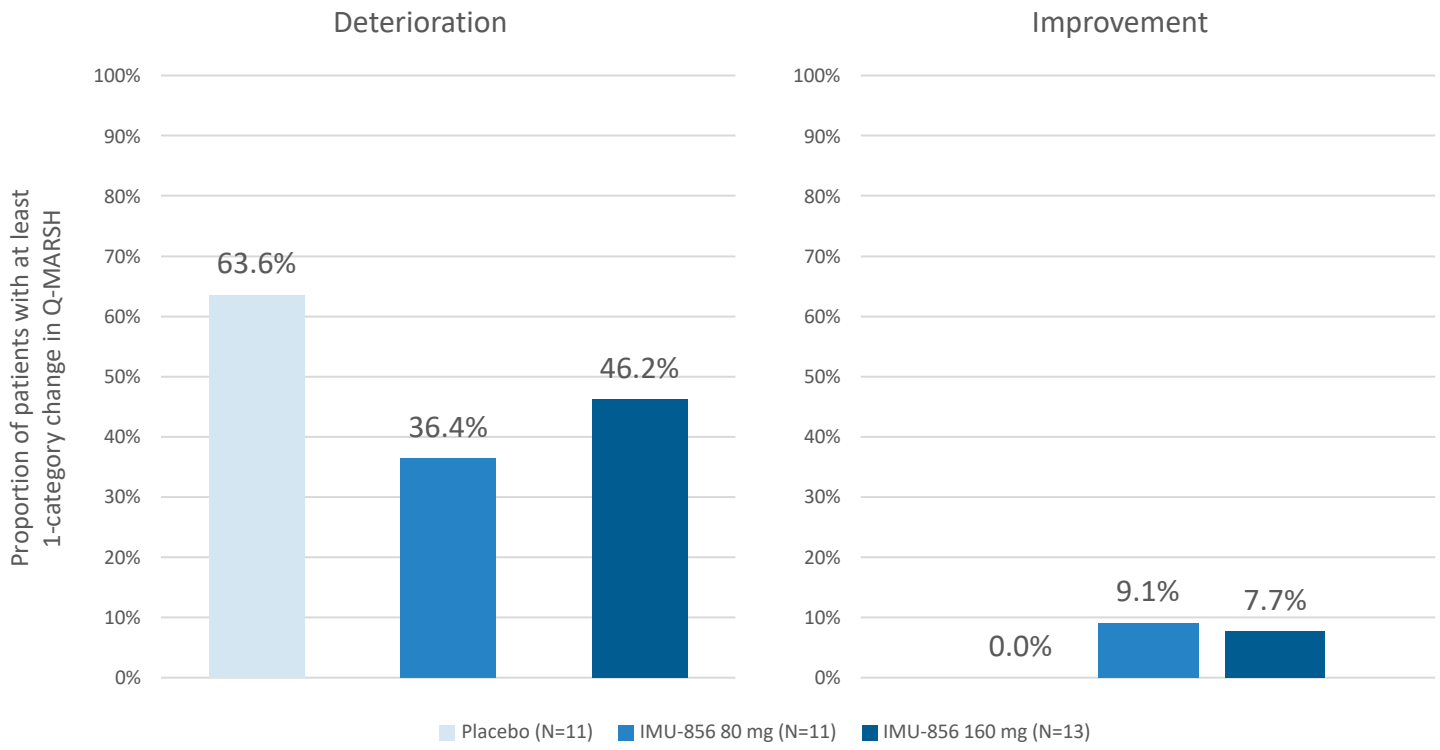
Ongoing Active CelD
- Extensive malabsorption
- Complete villous atrophy
- Marked crypt hyperplasia
- Increased IELs

Adapted from Adelman et al, Am J Gastroenterol 2018; 113:339–347
IEL: intraepithelial lymphocytes; CelD: celiac disease

IMU-856 Shows Signal Preventing Histological Damage (Q-Marsh)

Change in Q-MARSH between Baseline and Day 29

Deterioration/improvement defined as at least a decrease/increase of 1 category in Q-MARSH score on Day 29 as compared to Baseline



Worsening

Marsh Oberhuber Class	Villous height:Crypt depth Ratio
M0	≥2,8 (≥2.3)
M1	≥2,8 (≥2.3)
M2	2.0-2.79 (1.8-2.29)
M3a	1.2-1.99 (1.1-1.79)
M3b	0.50-1.19 (0.5-1.09)
M3c	0.0-0.49

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 grams daily. Central pathology laboratory: Jilab Inc. Tampere, Finland; EGD: esophagogastroduodenoscopy

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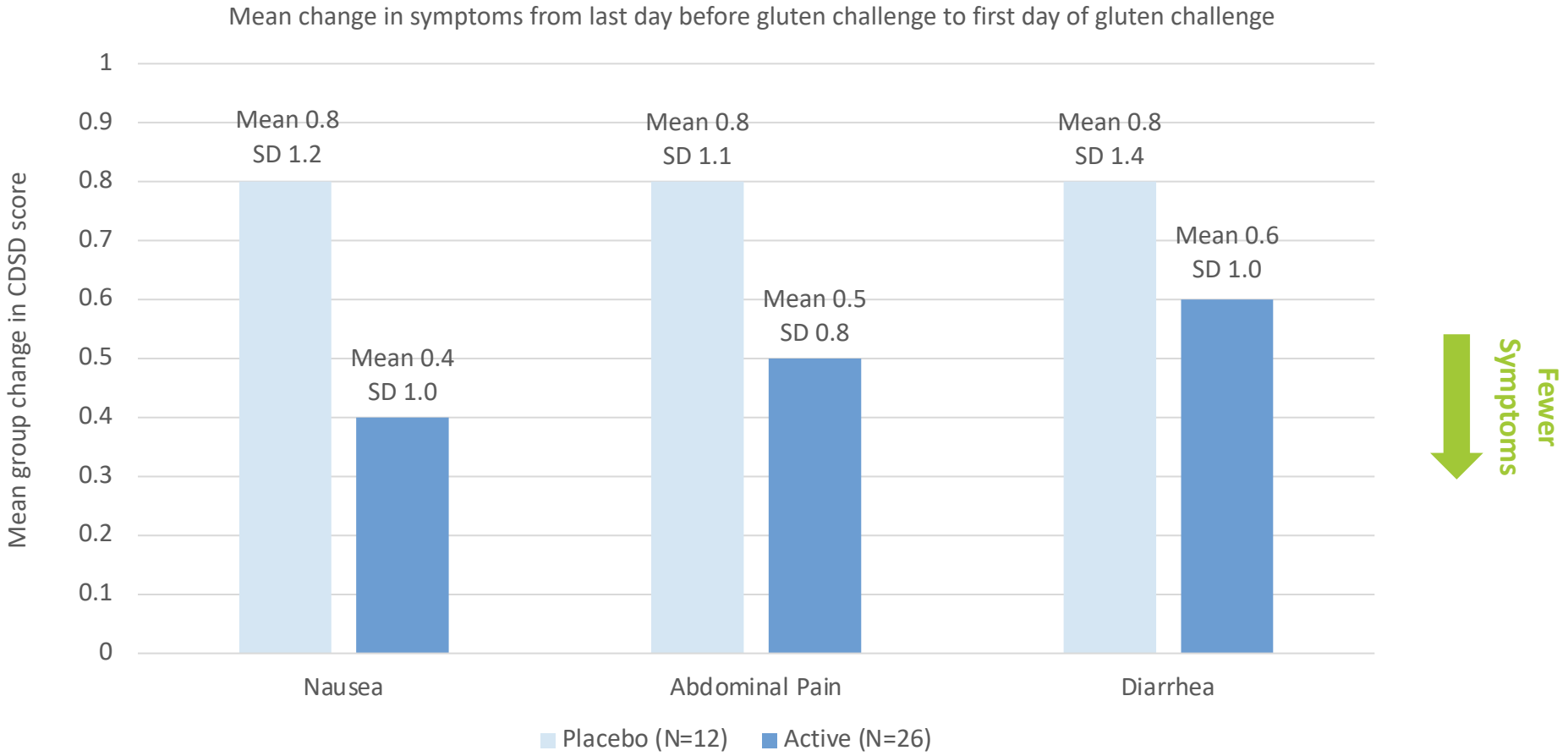
Improves Patients' Symptoms

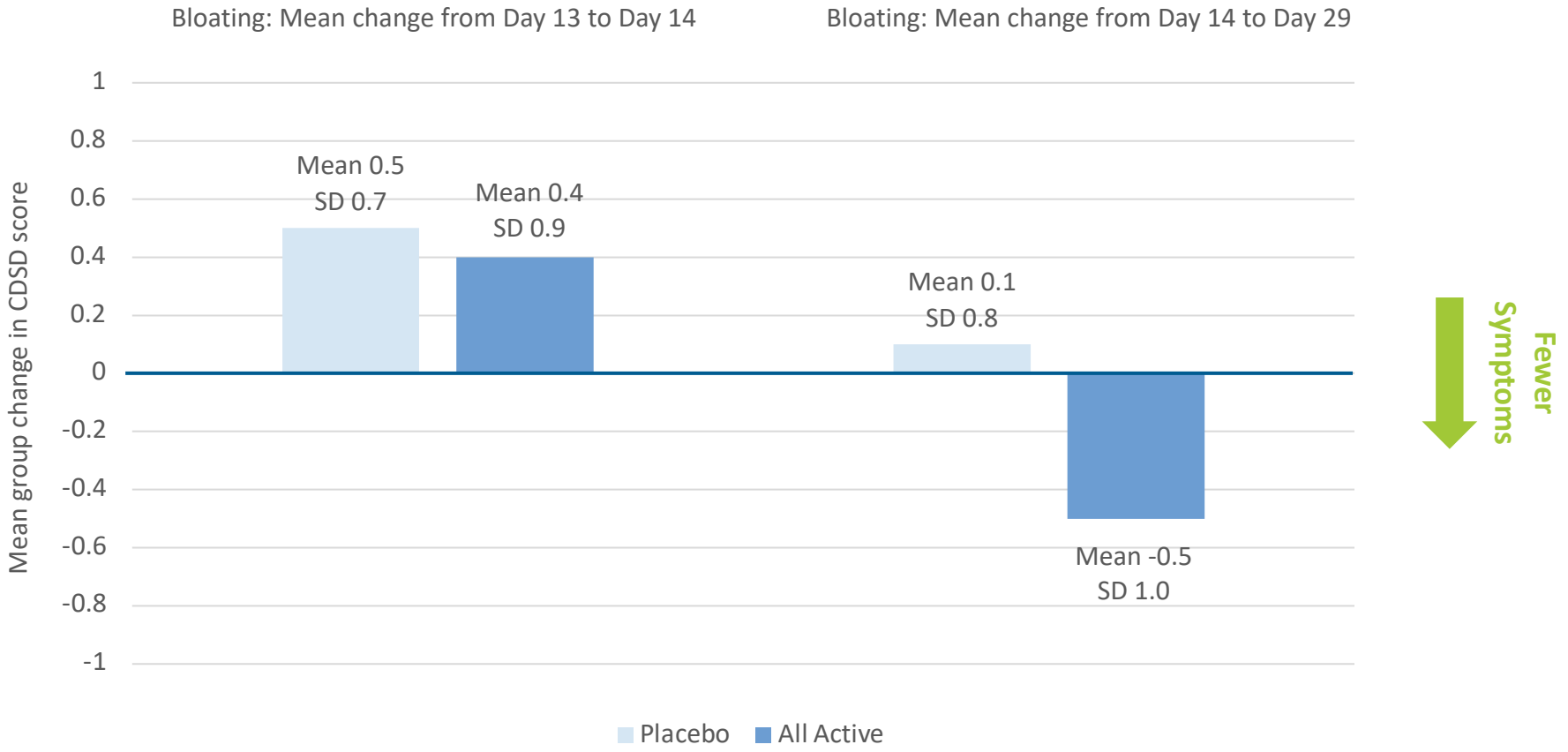
Phase 1b Clinical Trial of IMU-856

IMU-856 Treated Patients Have Fewer Symptoms After First Day of Gluten Challenge Than Placebo Patients (on Day 14)



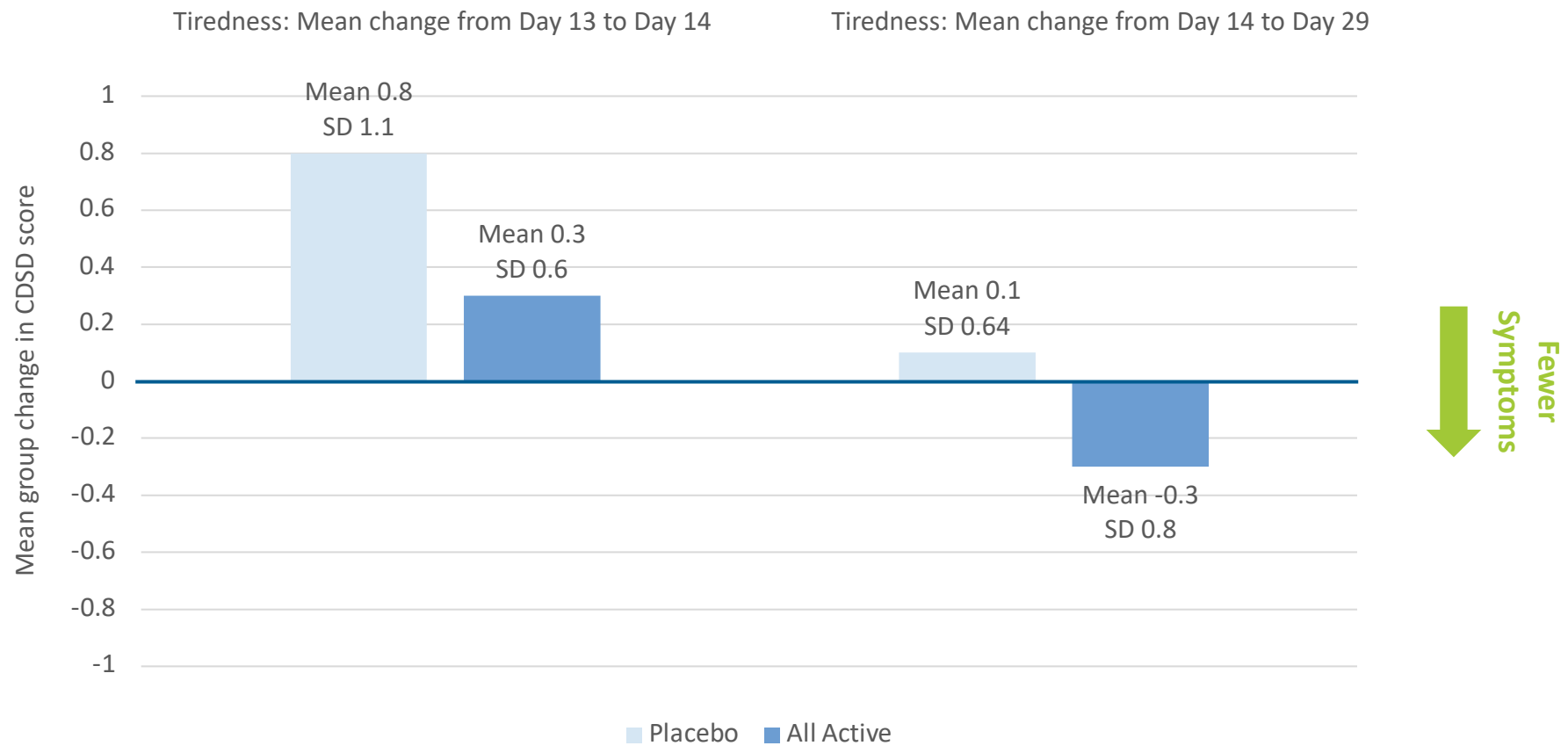
Assessed via Celiac Disease Symptom Diary (CDSD)
Fewer symptoms includes either less patients with symptoms or less severity of symptoms; SD: standard deviation

IMU-856 Treated Patients Recover From Bloating Symptoms on Continued Treatment During Gluten Challenge



Assessed via Celiac Disease Symptom Diary (CDSD). Day 13: Last day before Gluten Challenge. Day 14: First Day of Gluten Challenge. Day 29: First Day after Completion of Gluten Challenge
Fewer symptoms includes either less patients with symptoms or less severity of symptoms; SD: standard deviation

IMU-856 Treated Patients Recover From Tiredness Symptoms on Continued Treatment During Gluten Challenge



Assessed via Celiac Disease Symptom Diary (CDSD). Day 13: Last day before Gluten Challenge. Day 14: First Day of Gluten Challenge. Day 29: First Day after Completion of Gluten Challenge
Fewer symptoms includes either less patients with symptoms or less severity of symptoms; SD: standard deviation

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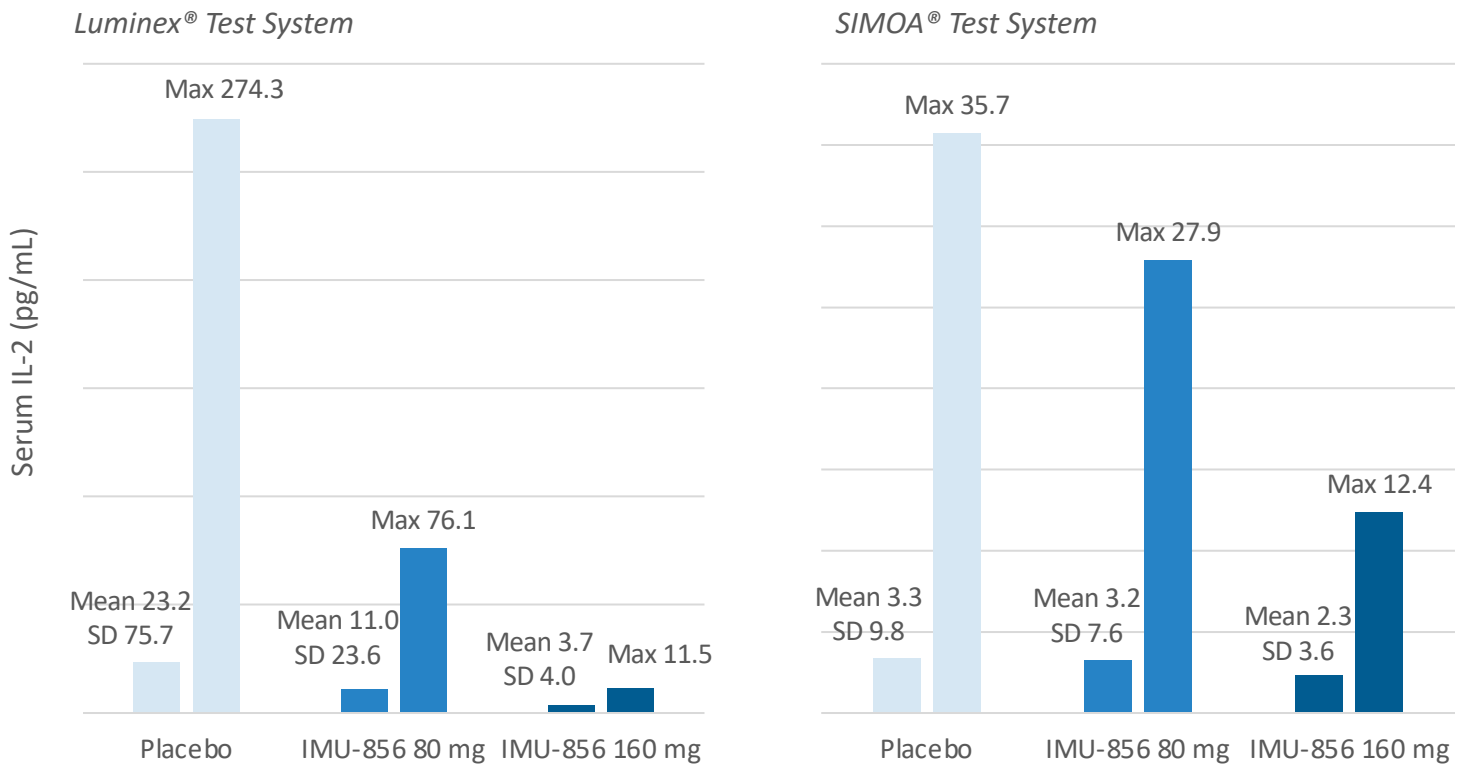
Biomarker Response

Phase 1b Clinical Trial of IMU-856

IMU-856 Dampens Acute IL-2 Immune Response on First Day of Gluten Challenge

Mean absolute change and maximum change in serum IL-2 (in pg/mL) from pre-gluten to 4 hours post-gluten on first day of gluten challenge



IMU-856 dampens gluten-induced acute immune response, as measured by IL-2 release, in a dose-dependent fashion. A wide inter-individual range of IL-2 response leads to large SD, especially in the placebo group. The inter-individual variance regarding IL-2 response decreases with increasing dose levels.

N=39/43 included in IL-2 analysis set. 3 patients not included in this analysis due to early termination and 1 incomplete IL-2 sampling due to site error

Methods used for IL-2 analysis: Milliplex® Human High Sensitivity T Cell Magnetic Bead Panel, 3 plex (Luminex®) and Simoa® CorPlex™ Human IL-2 Kit (Quanterix); IL: interleukin; SD: standard deviation

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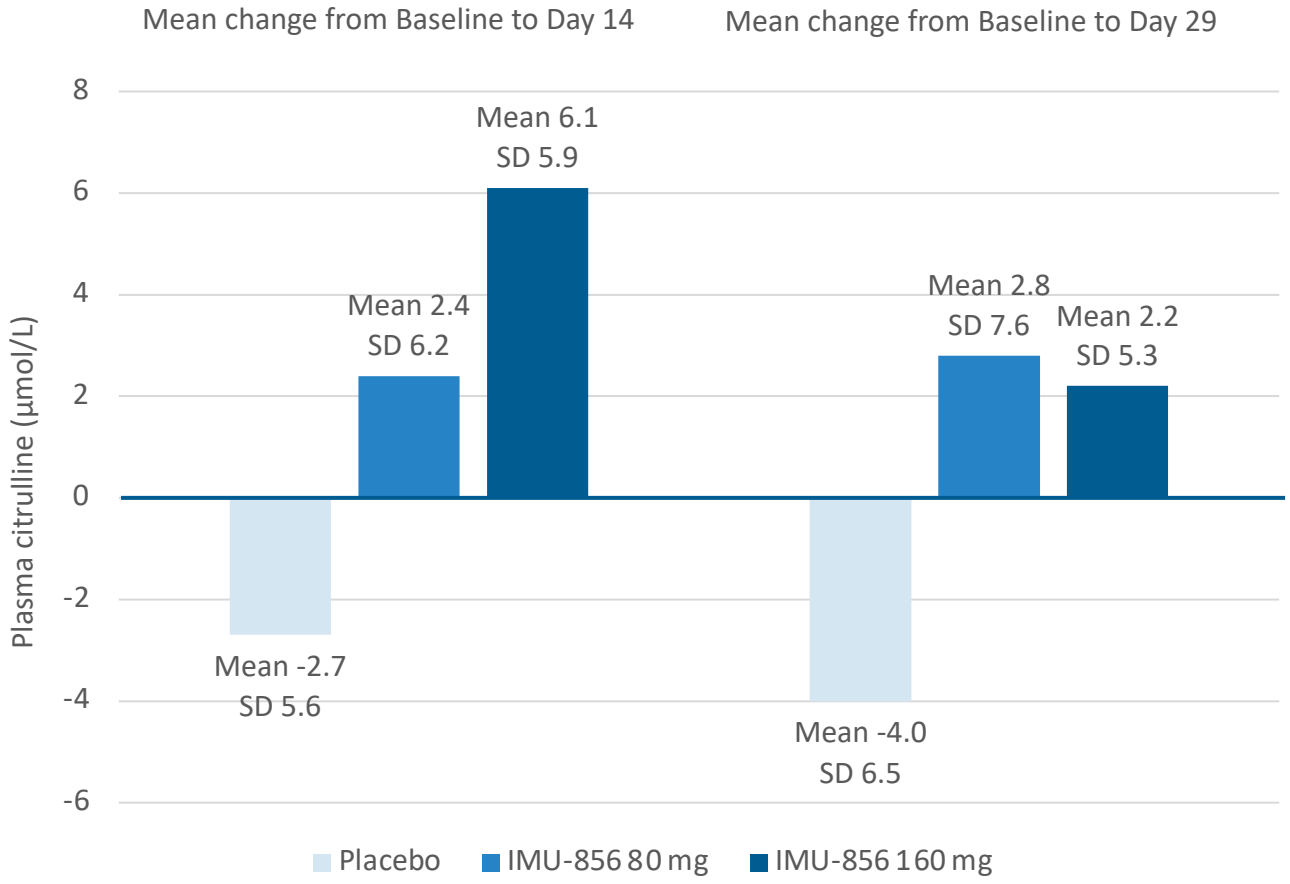
IMU-856 Shows Signal for Improving Citrulline

Biomarker Reflecting the Health Status and Function of Enterocytes



Citrulline is a non-essential amino acid that is mainly produced by the enterocyte and, hence, the level of citrulline in plasma can represent the synthetic function of the enterocytes[1]

Plasma citrulline levels are known to be related to villous atrophy

- Citrulline levels increase with gluten-free diet and with improvement of enteropathy[2]
- 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 [2] Fragkos et al., United Eur. Gastroenterol. J. 2018, 6, 181–191 &/ 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

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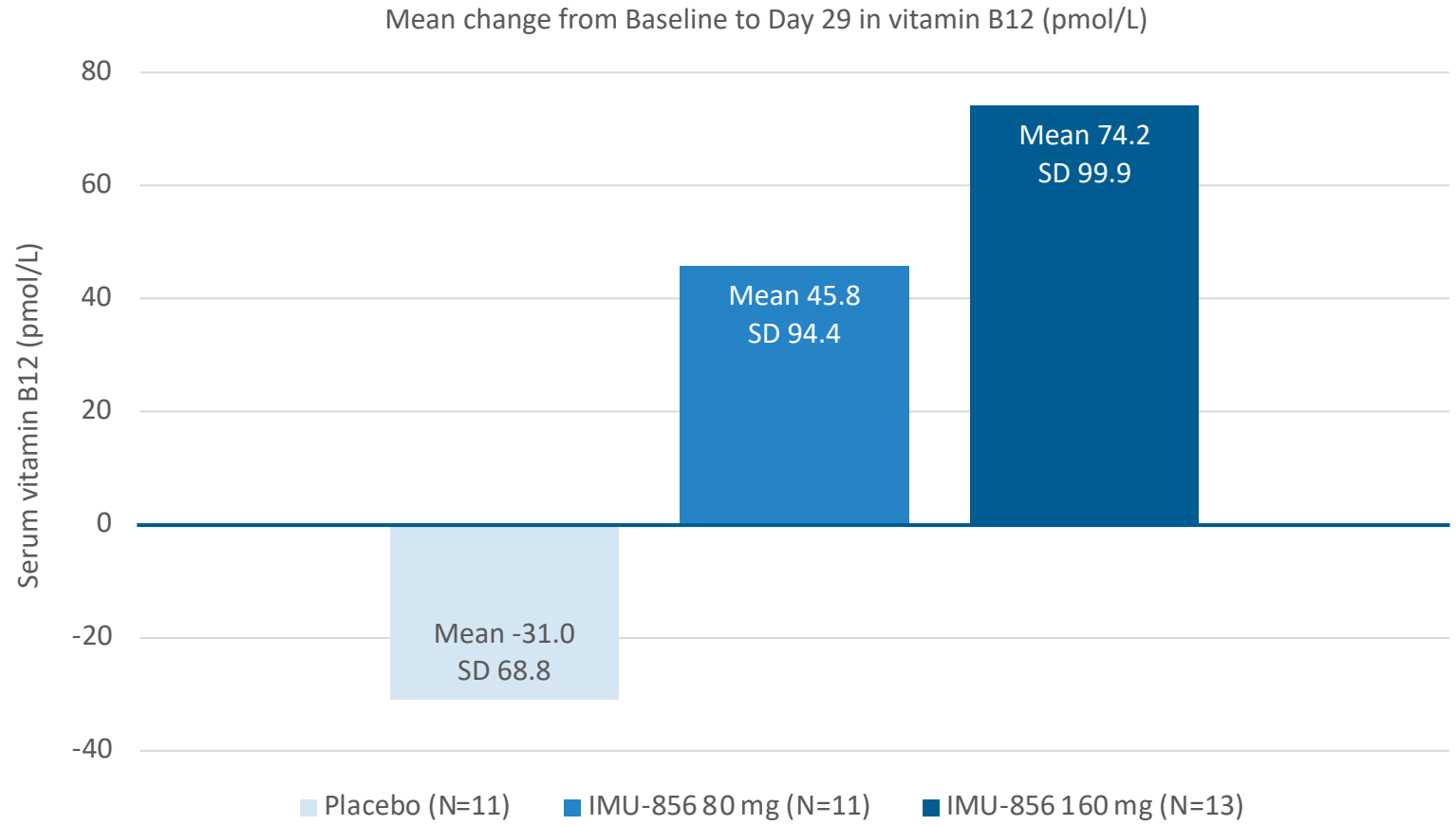
Enhances Nutrient Absorption

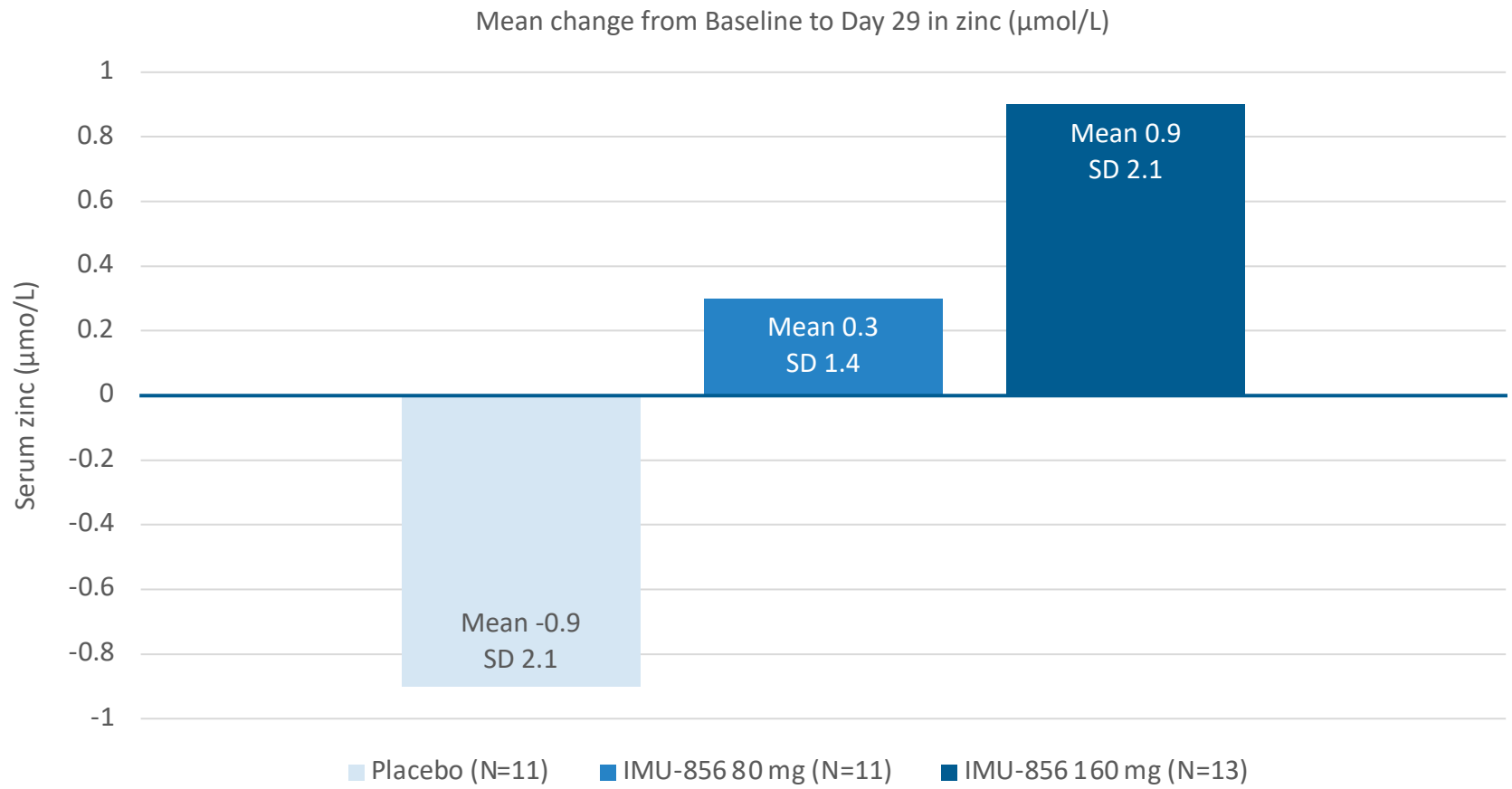
Phase 1b Clinical Trial of IMU-856

IMU-856 Shows Enhanced Uptake of Vitamin B12



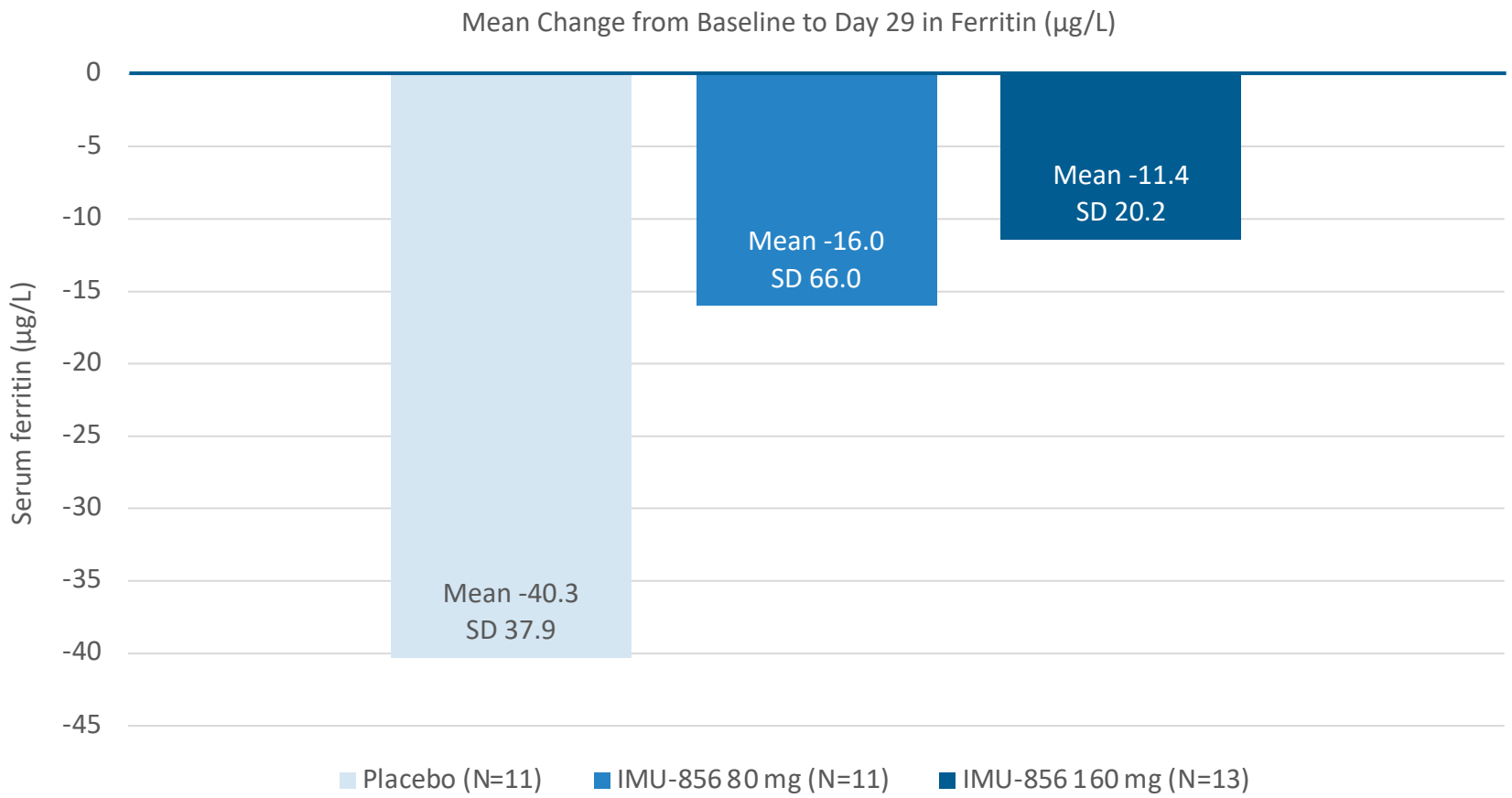
SD: standard deviation

IMU-856 Shows Enhanced Uptake of Zinc



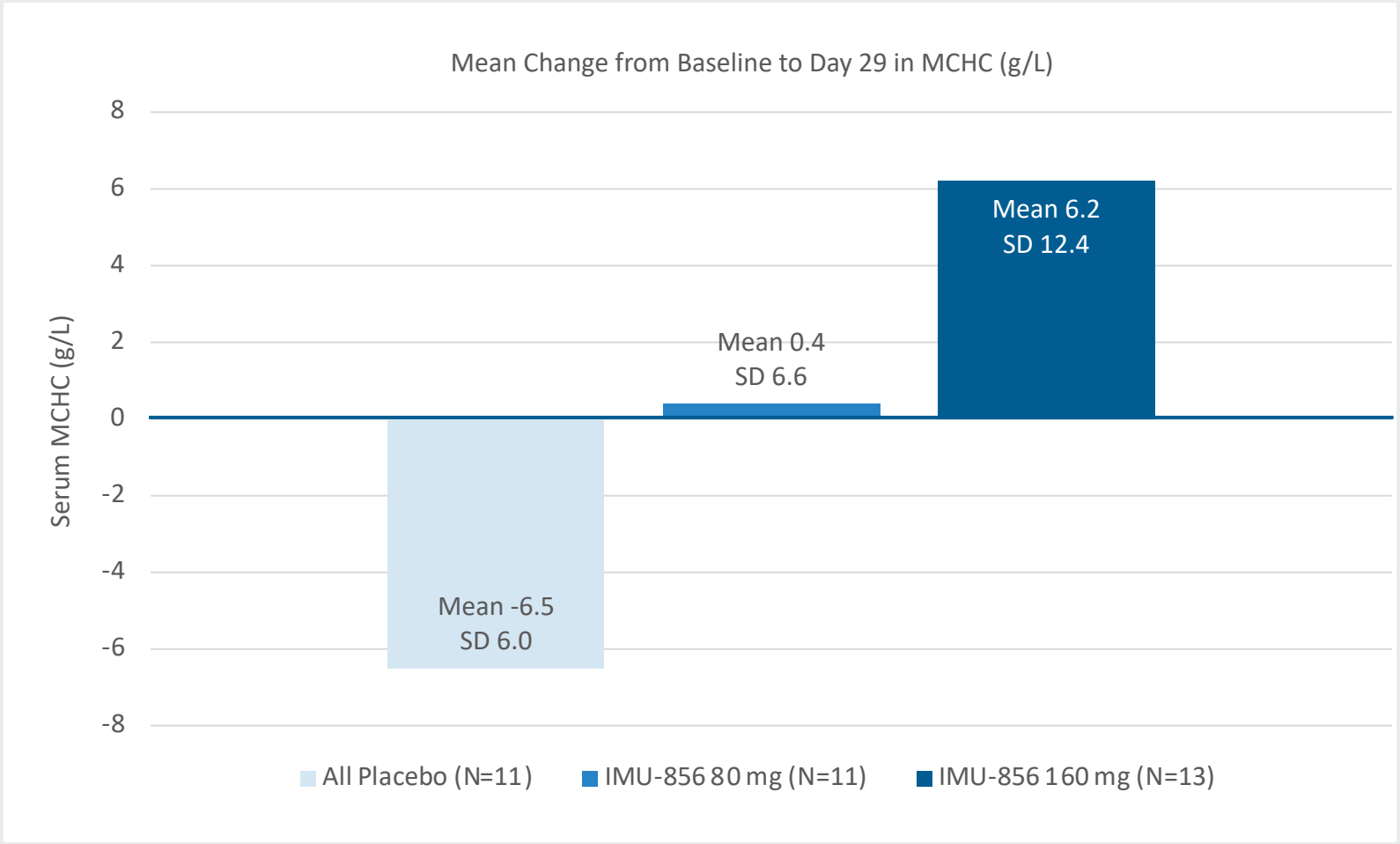
SD: standard deviation

IMU-856 Shows Amelioration of Gluten-Induced Iron Malabsorption – Ferritin Levels



SD: standard deviation

IMU-856 Shows Improvement in Red Blood Cell Function as a Consequence of Improved Iron Absorption



MCHC is a measure of the concentration of hemoglobin in red blood cells.

Since hemoglobin is the molecule to which oxygen attaches, MCHC is a measure of the average oxygen-carrying capacity of the red blood cells circulating in the body[1].

[1] https://www.verywellhealth.com/mean-cell-hemoglobin-concentration-4584155; MCHC: Mean Corpuscular Hemoglobin Concentration; SD: standard deviation

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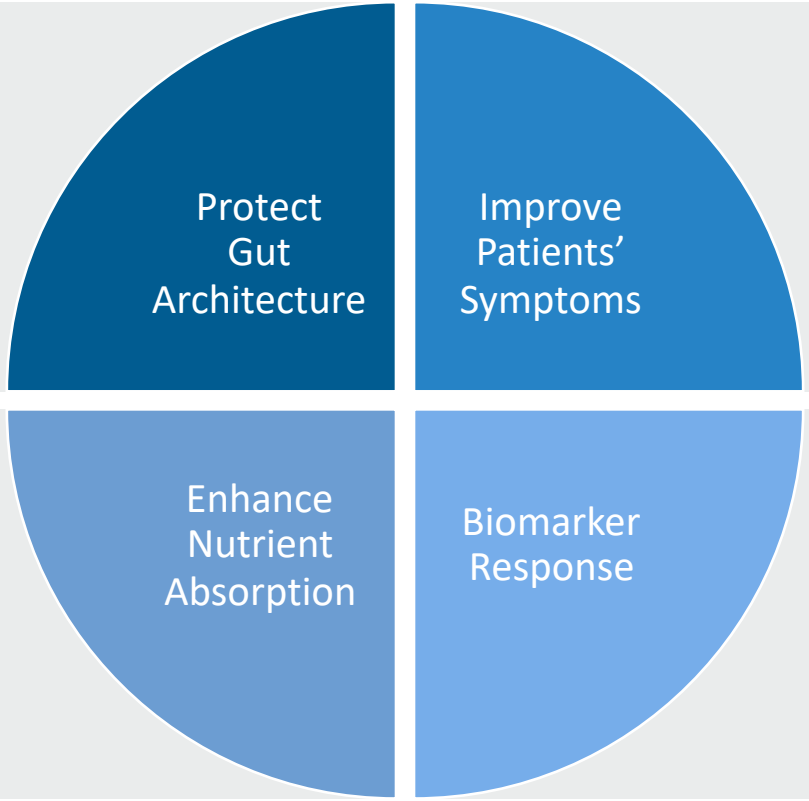
IMU-856 Shows Positive Effects in Main Four Dimensions of Clinical Outcome in Celiac Disease Patients

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



IMU-856 reduces/reverses gluten-induced symptoms reported by patients

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

IMU-856 dampens gluten-induced immune activation, as measured by IL-2, and shows positive impact on citrulline

All these effects achieved without any known suppression of the immune system

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Safety and Pharmacokinetics

Phase 1b Clinical Trial of IMU-856

Overall Summary of Treatment Emergent Adverse Events

Category	Treatment			
	IMU-856 80 mg (N=14)	IMU-856 160 mg (N=15)	All Active (N=29)	All Placebo (N=14)
Subjects with TEAEs, n (%)	13 (92.9)	13 (86.7)	26 (89.7)	10 (71.4)
Subjects with mild TEAEs, n (%)	13 (92.9)	11 (73.3)	24 (82.8)	9 (64.3)
Subjects with moderate TEAEs, n (%)	6 (42.9)	6 (40)	12 (41.4)	4 (28.6)
Subjects with severe TEAEs, n (%)	0	3 (20)	3 (10.3)	1 (7.1)
Subjects with study drug-related severe TEAEs, n (%)	0	0	0	0
Subjects with SAE, n (%)	0	2 (13.3) *	2 (6.9)	0
Subjects with TEAEs leading to withdrawal, n (%)	2 (14.3) +	1 (6.7) #	3 (10.3)	0
Number of TEAEs	79	87	166	55
Number of gluten-related TEAEs	15	17	32	15
Number of mild TEAEs	70	73	143	46
Number of moderate TEAEs	9	9	18	8
Number of severe TEAEs	0	5	5	1
Number of study drug-related severe TEAEs	0	0	0	0
Number of SAEs	0	2 *	2	0
Number of TEAEs leading to withdrawal	2 +	2 #	4	0

IMU-856 safe and well-tolerated despite a more severe patient population randomized for the active treatment groups resulting in a bias against active treatment

- No dose-dependency in adverse events
- No IMP-related severe TEAEs
- No IMP-related SAEs

* 2 SAEs: 1 subject experienced biliary colic (unrelated to IMP and Gluten challenge), 1 subject underwent elective liposuction of right and left breast; + 2 subjects with gluten sensitivity; # 2 TEAES: Biliary colic and cholelithiasis leading to study withdrawal
TEAE: Treatment-Emergent Adverse Event; SAE: Serious Adverse Event; IMP: Investigational Medicinal Product

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Disease-Related TEAEs Associated With High Number of Ongoing Active Celiac Disease Patients in IMU-856 Treatment Group

MedDRA Preferred Term	TEAEs regularly associated with celiac disease and occurring in more than 10 % of all subjects Number of subjects (%) [number of TEAEs reported]					
	IMU-856 80 mg (N=14)	IMU-856 160 mg (N=15)	Active (N=29)	Q-Marsh 3a/b/c N[1]	Placebo (N=14)	Q-Marsh 3a/b/c N[1]
Nausea	2 (14.3%) [2]	7 (46.7%) [28]	9 (31%) [30]	4	1 (7.1%) [2]	0
Diarrhea	5 (35.7%) [8]	3 (20%) [3]	8 (27.6%) [11]	5	2 (14.3%) [2]	0
Abdominal distension	4 (28.6%) [6]	3 (20%) [3]	7 (24.1%) [9]	7	1 (7.1%) [3]	0
Flatulence	3 (21.4%) [4]	0	3 (10.3%) [4]	3	0	0

- Higher incidence of celiac disease-related TEAEs in IMU-856 treatment arms derived from the high prevalence of OACD patients (Q-Marsh 3a or worse) in IMU-856 treatment arms
- Numbers of disease-related TEAEs over entire study period are independent of the improvement in disease-related symptoms shown for IMU-856 as compared to placebo during 15-day gluten challenge

[1] Number of patients with Q-Marsh score of 3a or worse experiencing respective disease-related TEAE
TEAE: Treatment-Emergent Adverse Event, OACD: ongoing active celiac disease, defined as Q-Marsh score of M3a or worse

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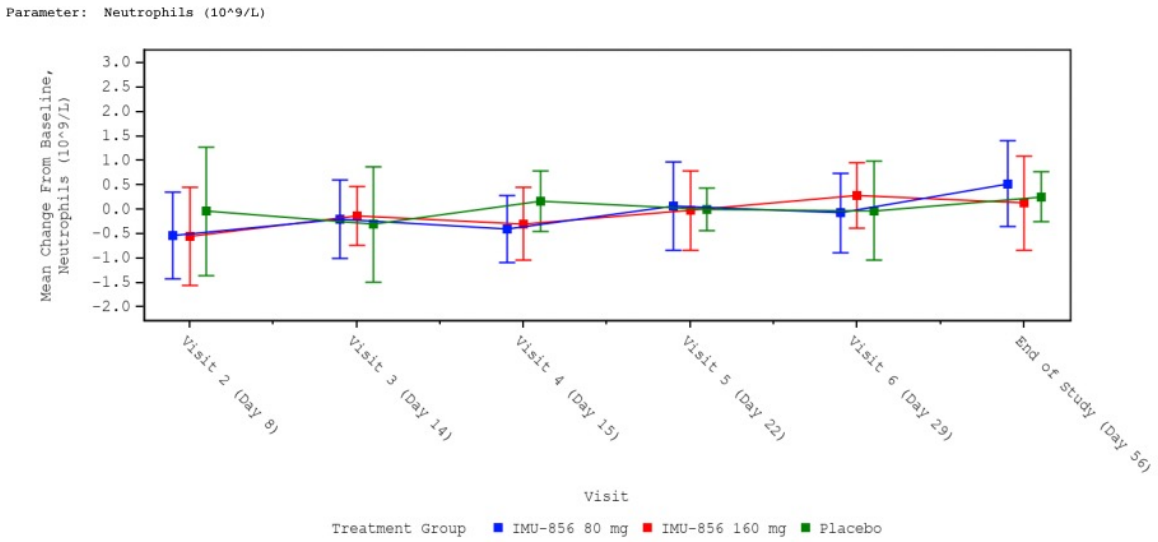
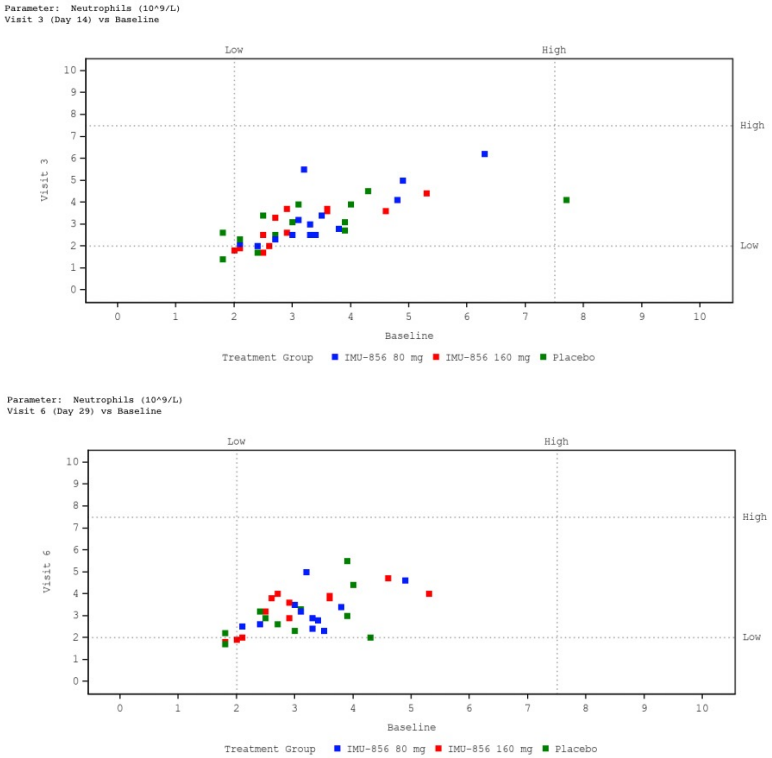
No Change in Neutrophils as Compared to Placebo

Laboratory Values Over Time
Hematology – Neutrophils

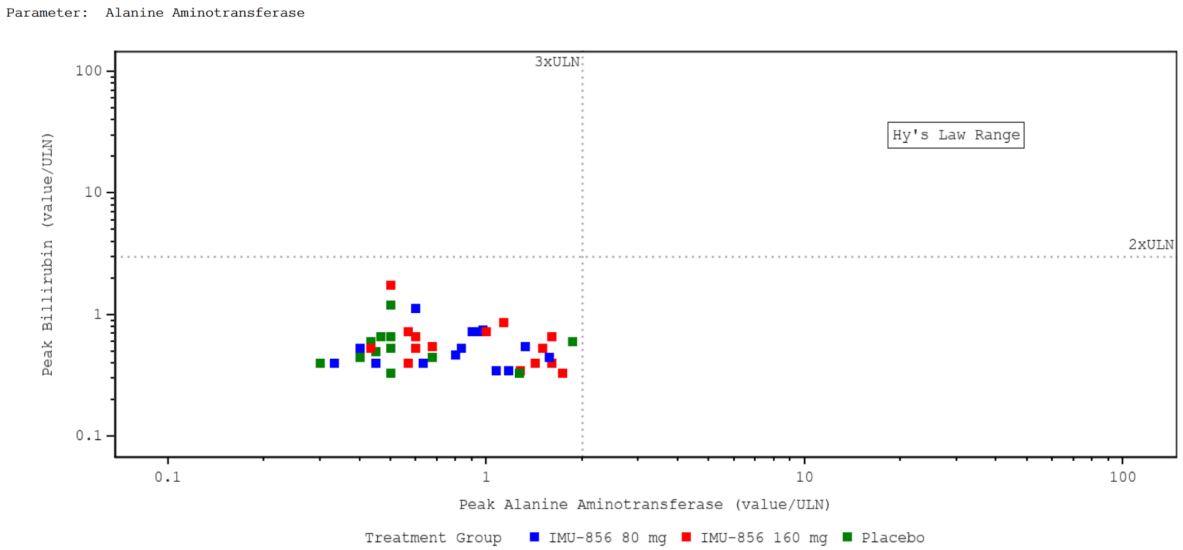


Individual Laboratory Values
Hematology – Neutrophils

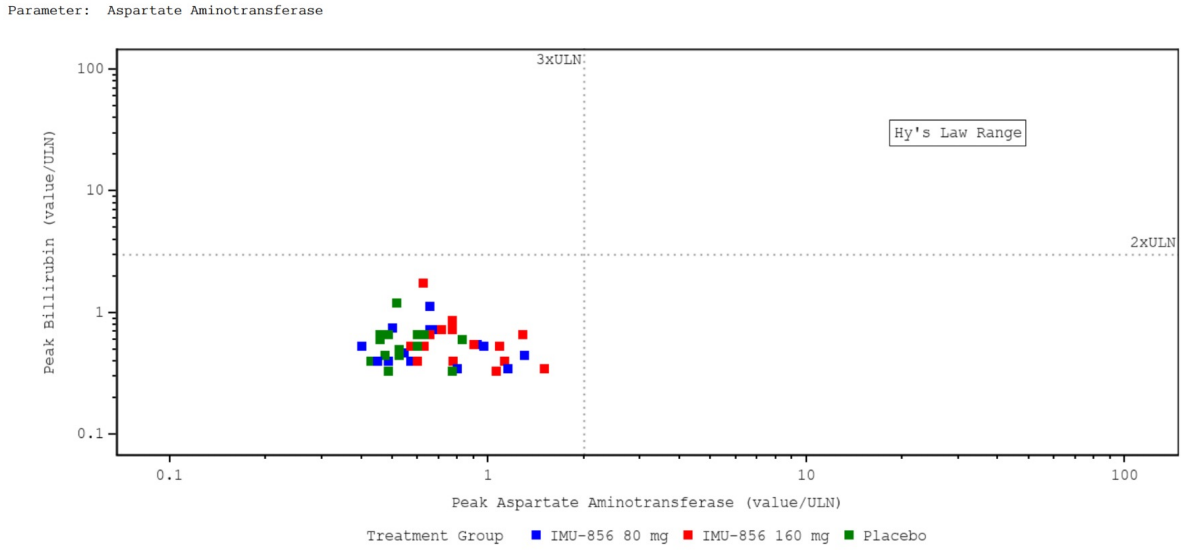


No Hy's Law Cases

Bilirubin vs. ALT Showed No Evidence of DILI Potential



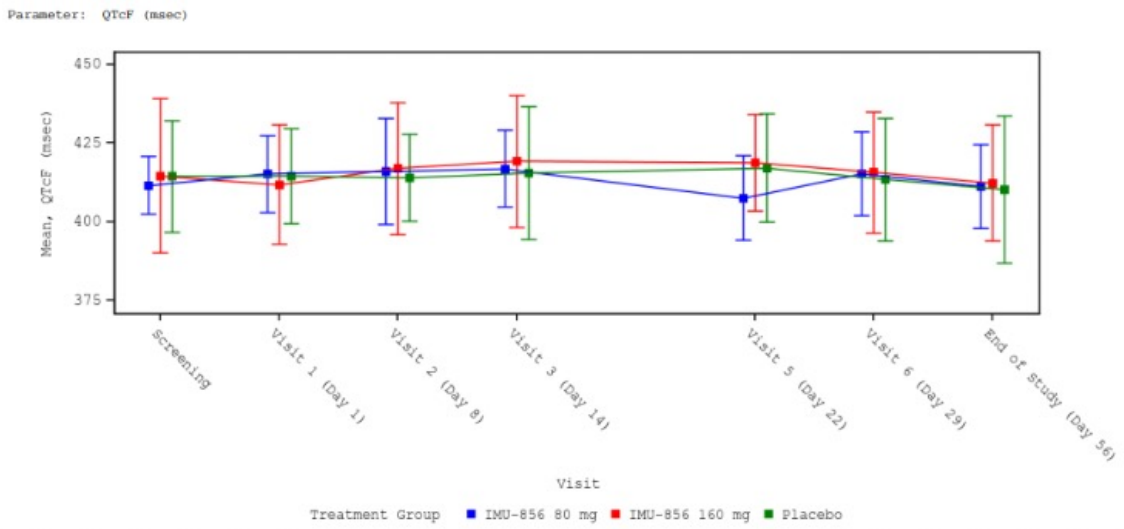
Bilirubin vs. AST Showed No Evidence of DILI Potential



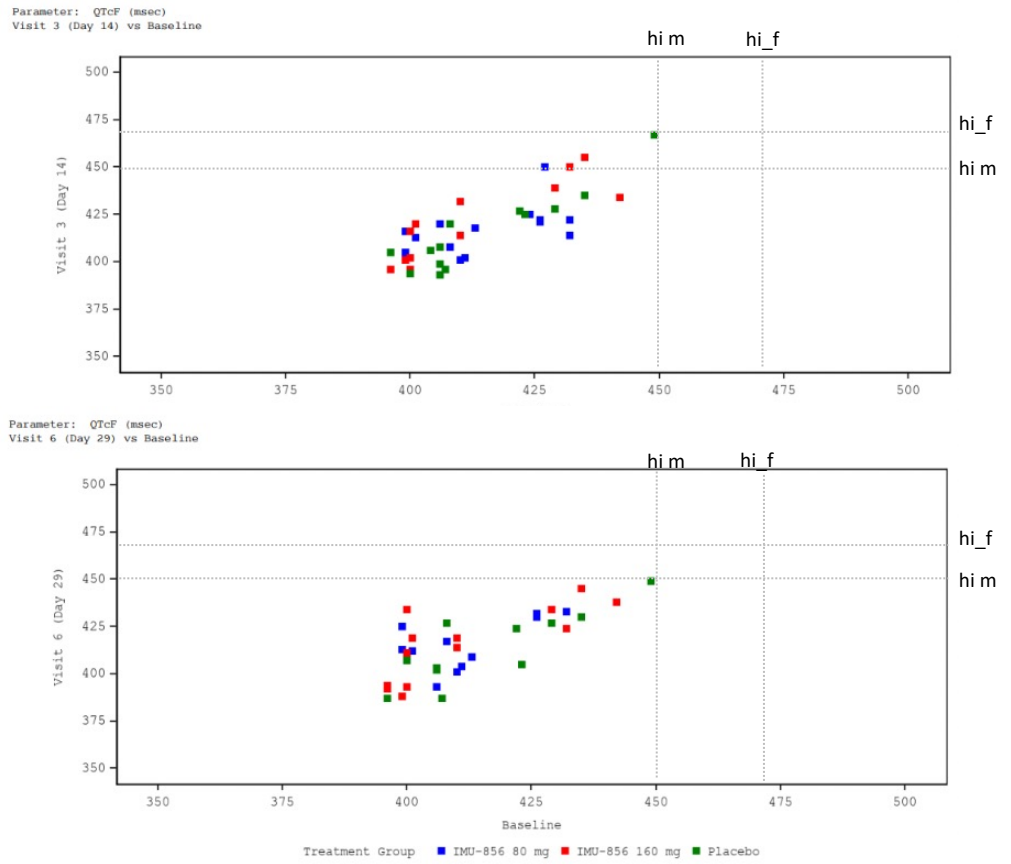
ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; DILI: drug-induced liver injury; BIL: Bilirubin; ULN: Upper Limit of Normal

No Clinically Relevant Changes of QTcF Interval

12-Lead ECGs Over Time
QTcF Interval



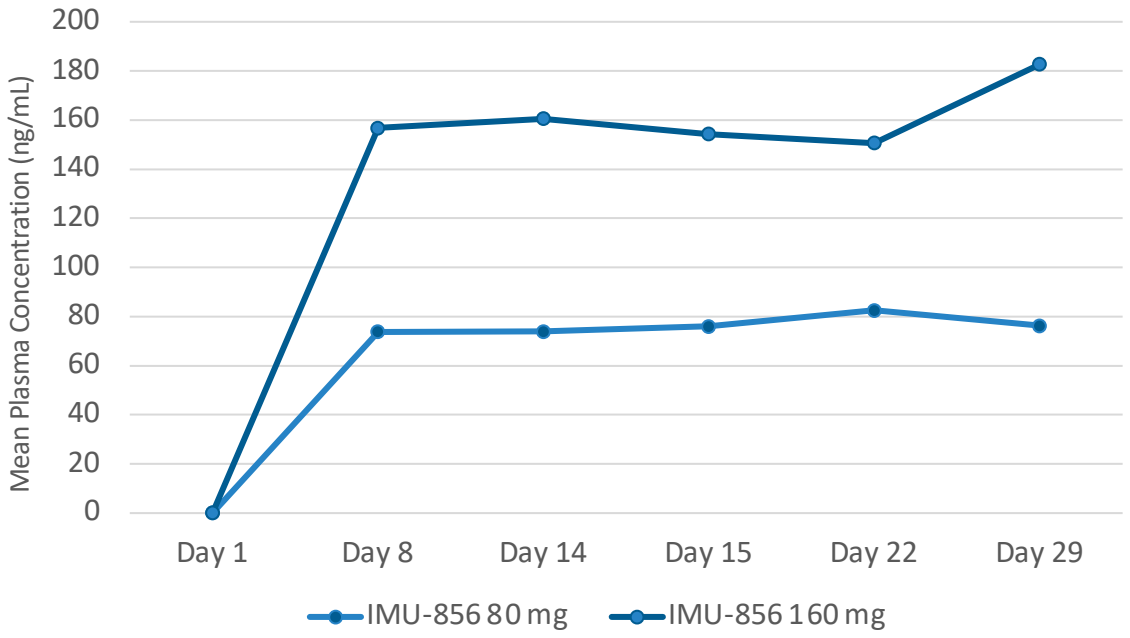
Individual 12-Lead ECGs
QTcF Interval



ECG: electrocardiogram; QTcF: Fridericia's correction formula for QT intervall

Pharmacokinetics: Trough Levels After Multiple Dosing

IMU-856 mean trough levels (ng/mL)



Day 8		
Value (Mean)	IMU-856 80 mg	IMU-856 160 mg
C_{max} (ng/mL)	354.5	765.6
T_{max} (hr)	1.9	1.5
$AUC_{0\text{-tlast}}$ (hr*ng/mL)	1568	3613

Favorable pharmacokinetics confirming data from Parts A+B in healthy human subjects with fast achievement of steady state and linear pharmacokinetics with dose-proportional increase in plasma C_{max} and AUC

Cmax: maximum plasma drug concentration; hr: hours; Tmax: time to reach maximum plasma concentration; AUC: area under the curve

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IMU-856 Shows Positive Effects in Main Four Dimensions of Clinical Outcome in Celiac Disease Patients

Final phase 1b celiac disease data consistently shows beneficial effects for IMU-856 over placebo:

- Prevents histological damage
- Consistent benefits on symptoms over placebo
- Dose-linear response for IL-2 and citrulline levels
- Enhances nutrient uptake

Aimed to restore a healthy gut

- Regenerates bowel architecture
- Normalizes bowel permeability

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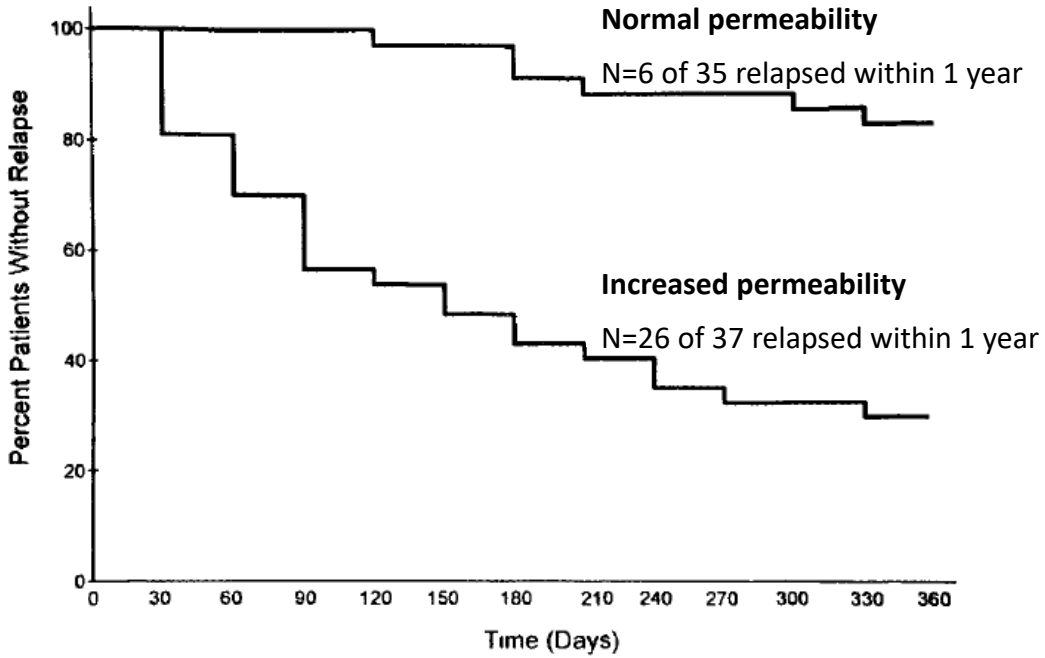
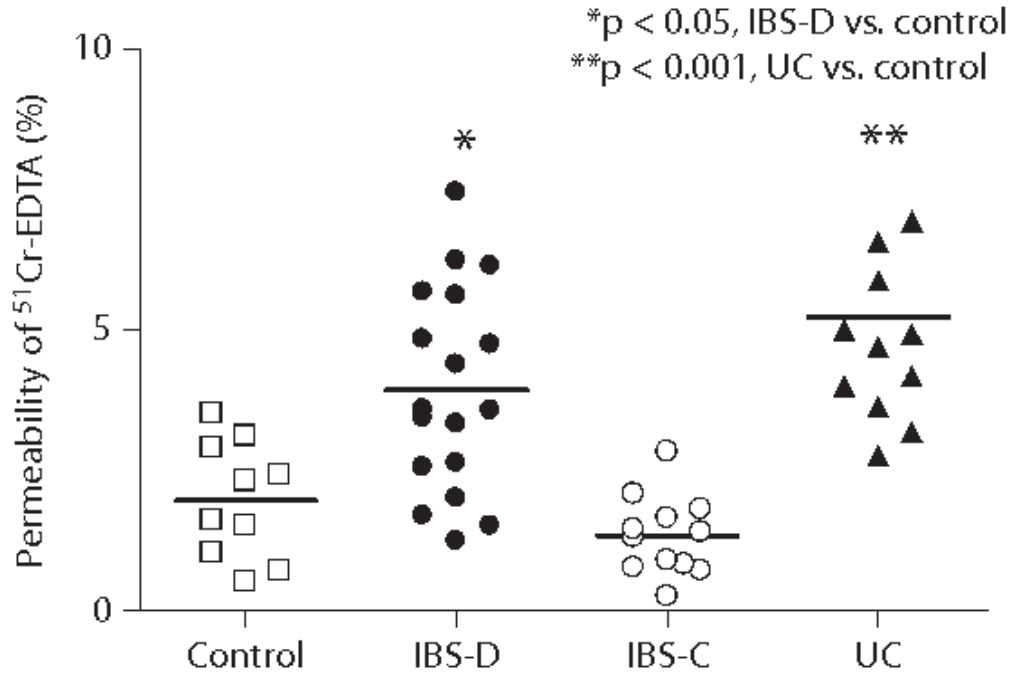
Intestinal Barrier Function is a Therapeutic Target Beyond Celiac Disease

Compromised intestinal barrier function has been associated not only with celiac disease but with a number of disease states, both intestinal and systemic

Crohn's disease: low bowel permeability has better probability to maintain patients in remission[1]

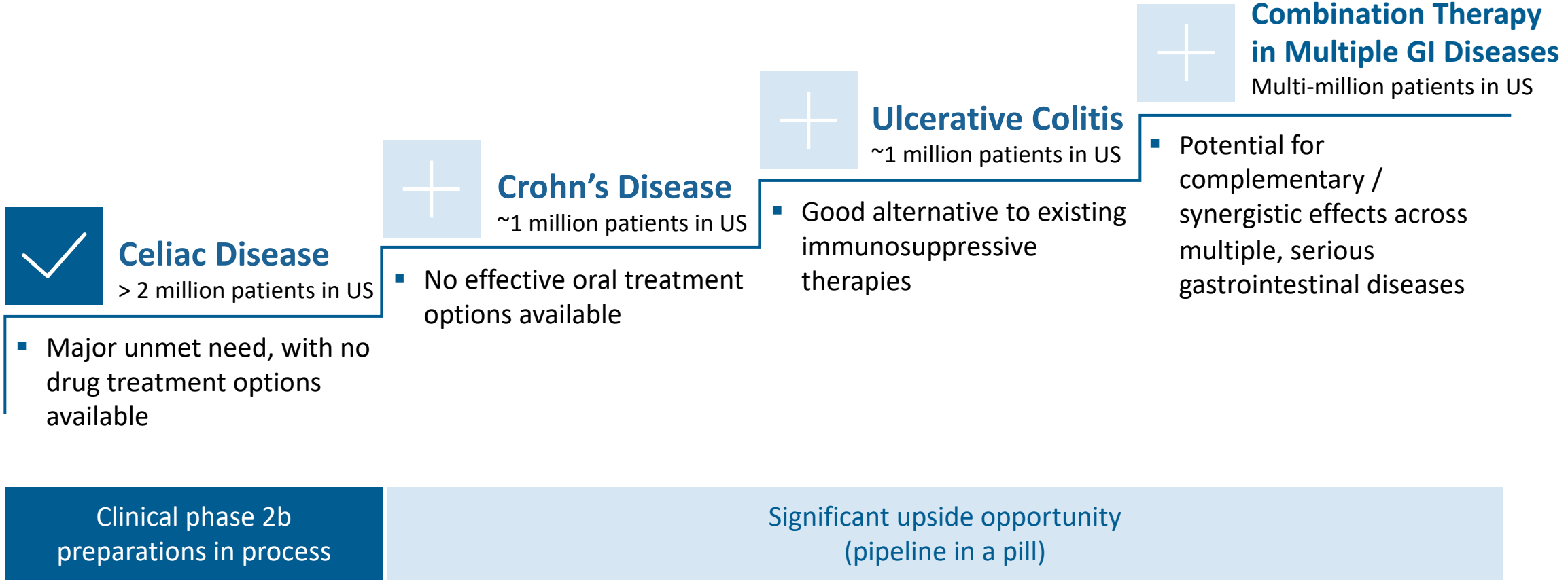


IBS-D: bowel permeability is similar to IBD[2]



[1] Wyatt et al. Lancet 341/8858, P1437-1439, 1993 [2] Gecse et al., Digestion. 2012;85(1):40-6
IBS-D: irritable bowel syndrome with diarrhea; IBS-C: irritable bowel syndrome with constipation; IBD: inflammatory bowel disease; UC: ulcerative colitis

IMU-856 Could Elevate the Standard-of-Care Across Multiple Gastrointestinal Diseases With Histologic Damage



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IMU-856 Could Become a Game Changer for the Treatment of Gastrointestinal Disorders

- IMU-856 is poised to be a **potential paradigm shift** in how to treat gastrointestinal diseases.
- Dozens of endpoints were investigated in this small exploratory trial and all demonstrated that **IMU-856 has a beneficial effect** in the treated celiac disease patients.
- Immunic is **preparing clinical phase 2b testing** of IMU-856 in ongoing active celiac disease.
- IMU-856 has the potential for broad development where renewal of the gut wall is important; **multiple indications** are under evaluation.

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Q&A Session

Phase 1b Clinical Trial of IMU-856

Thank You!

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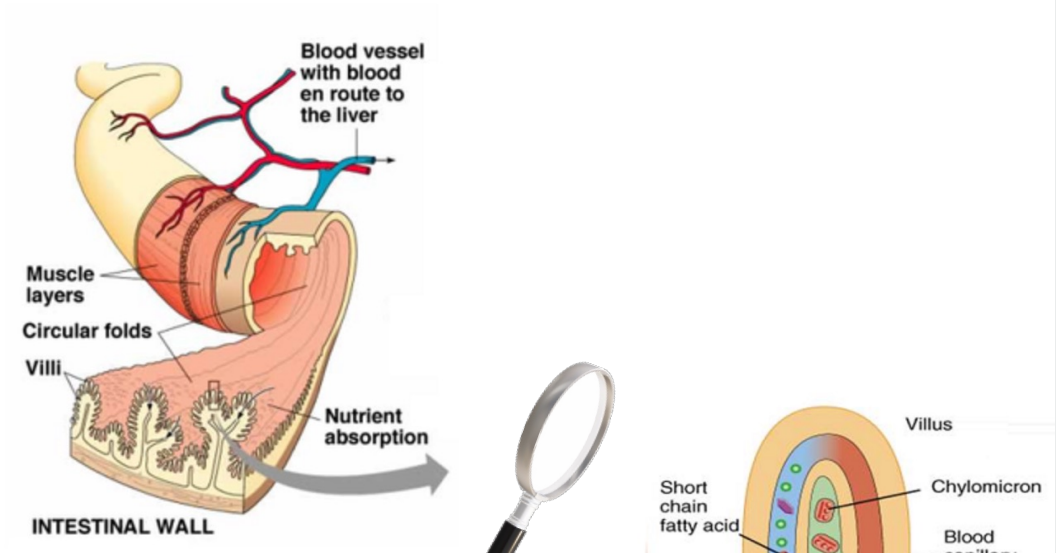
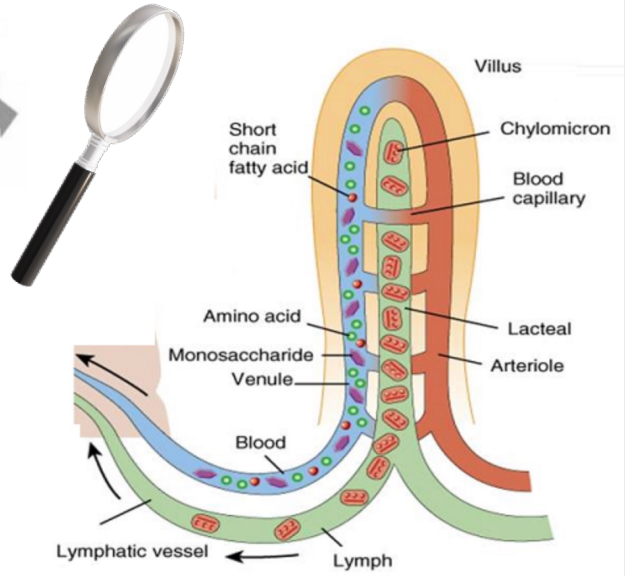
Appendix

Phase 1b Clinical Trial of IMU-856

Pathophysiology of Malabsorption in Celiac Disease





- The small intestine measures approximately 6 m in length
- The surface area of the small intestine is significantly **enhanced by the presence of villi and microvilli by up to 600-fold**
- One of the main functions of villi is to absorb nutrients from the lumen in the small intestine whereas crypt cells are generally regarded as secretory[1]
- Villous atrophy leads to a reduction of the absorptive area and therefore to malabsorption

[1] Kiela PR, Ghishan FK. Best Pract Res Clin Gastroenterol. 2016 Apr;30(2):145-59
Figures: https://biology-igcse.weebly.com/absorption-ndash-function-of-the-small-intestine-and-significance-of-villi.html

Patient Demographics

Parameter		IMU-856 80 mg (N=14)	IMU-856 160 mg (N=15)	All Active (N=29)	All Placebo (N=14)
Mean age (years)		43.1	40.9	42.0	43.4
Female N (%)		8 (57.1)	10 (66.7)	18 (62.1)	11 (78.6)
Race N (%)	White	14 (100)	15 (100)	29 (100)	14 (100)
	Other	0	0	0	0
Mean height (cm)		173.86	169.53	171.62	167.19
Mean weight (kg)		81.62	74.23	77.80	73.51
Seronegative N(%)		14 (100)	15 (100)	29 (100)	14 (100)
Time since diagnosis (mean, years)		7.7	10.7	9.3	10.6

Villous Height Results Stratified by Baseline Disease Severity

Baseline Disease Severity (Q-Marsh)	Baseline Disease Severity by Treatment Arm (Q-Marsh)	N[1]	Baseline Villous Height[1] (in µm)	Mean Absolute Change to Day 29 (in µm)	Mean Relative Change to Day 29
Q-Marsh Score M0-M2	Placebo pooled (M0-M2)	10 (11)	383.6	-56.6	-14.4%
	IMU-856 pooled (M0-M2)	10 (12)	388.6	-32.5	-8.3%
Q-Marsh Score M3a/b/c	Placebo pooled (M3a/b/c)	1 (3)	352.0	-97.0	-27.6%
	IMU-856 pooled (M3a/b/c)	14 (17)	321.4	-14.1	-3.2%

Beneficial effects of IMU-856 on villous height not related to baseline disease severity

Categories of Q-Marsh categorized by Vh:Cd are: M0 (≥2,8), M1 (≥2,8 with IEL), M2 (2.0-2.79), M3a (1.2-1.99), M3b (0.5-1.19) and M3c (0.0-0.49)
[1] The number of patients displayed is the number of patients for which Baseline and Day 29 histology data are available (Disease Analysis Set), and (in parentheses) the number of total patients (including 8 patients that discontinued before Day 29). Baseline data and data for mean absolute and relative change include only patients in the Disease Analysis Set (N=35); Vh:Cd: Villous height:Crypt depth; IEL: intraepithelial lymphocytes

IMU-856 Shows Signal Preventing Histological Damage During Two-Week, 6 g Gluten Challenge (Vh:Cd)

Absolute change in Vh:Cd between Baseline and Day 29				
	IMU-856 80 mg (N=11) Mean (SD)	IMU-856 160 mg (N=13) Mean (SD)	All Active (N=24) Mean (SD)	All Placebo (N=11) Mean (SD)
Absolute Change Vh:Cd	-0.19 (0.29)	-0.28 (0.41)	-0.24 (0.36)	-0.43 (0.31)

Gluten Challenge for 15 days with 6 g daily. Central pathology laboratory: Jilab Inc. Tampere, Finland
Exploratory post-hoc statistical analysis; EGD: esophagogastroduodenoscopy; Vh:Cd: Villous height:Crypt depth; SD: standard deviation

Patient Reported Outcomes: Celiac Disease Symptom Diary (CDSD)

CDSD Version 2.1©

Description

- The CDSD is a daily patient reported outcome measurement assessing the presence or absence of a broad range of symptoms typical for celiac disease
- Phase 1b trial of IMU-856:
  - On Day 1: CDSD Questionnaire must have been completed twice, once in the morning before first IMP administration to get a baseline value (patients tick how they felt during the past 24 hours before IMP administration) and once in the evening
  - On Day 2-29: questionnaire is filled out daily at the same time each day in the evening

Five symptoms:

- Diarrhea
- Abdominal pain
- Bloating
- Nausea
- Tiredness

Worst score during the past 24 hours:

1 = none
2 = mild
3 = moderate
4 = severe
5 = very severe

CDSD Version 2.1© ImmunogenX LLC; IMP: Investigational Medicinal Product

IMU-856 Shows Signal Protecting Against Acute Gluten-Induced Symptoms on First Day of Gluten Challenge

Mean change from last day before gluten challenge to first day of gluten challenge				
Symptom	IMU-856 80 mg (N=13) Mean (SD)	IMU-856 160 mg (N=13) Mean (SD)	All Active (N=26) Mean (SD)	All Placebo (N=12) Mean (SD)
Nausea	0.2 (0.69)	0.7 (1.03)	0.4 (0.90)	0.8 (1.22)
Abdominal pain	0.5 (0.78)	0.4 (0.87)	0.5 (0.81)	0.8 (1.06)
Diarrhea	0.5 (0.97)	0.6 (1.12)	0.6 (1.03)	0.8 (1.36)

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

IMU-856 Shows Signal Protecting Against Chronic Gluten-Induced Symptoms

	Mean change from Day 13 to Day 14			Mean change from Day 14 to Day 29		
	N	Bloating Mean (SD)	Tiredness Mean (SD)	N	Bloating Mean (SD)	Tiredness Mean (SD)
IMU-856 80 mg	13	0.3 (0.85)	0.2 (0.60)	9	-0.4 (1.01)	-0.1 (0.33)
IMU-856 160 mg	13	0.5 (0.88)	0.5 (0.66)	11	-0.5 (1.04)	-0.5 (1.04)
All Active	26	0.4 (0.85)	0.3 (0.63)	20	-0.5 (1.00)	-0.3 (0.80)
All Placebo	12	0.5 (0.67)	0.8 (1.14)	8	0.1 (0.83)	0.1 (0.64)

Assessed via Celiac Disease Symptom Diary (CDSD). Day 13: Last day before Gluten Challenge. Day 14: First Day of Gluten Challenge. Day 29: First Day after Completion of Gluten Challenge; SD: standard deviation

Patient Reported Outcomes: Impact Of Celiac Disease Symptom Questionnaire (ICDSQ©)

Description

- Questionnaire is assessed weekly and suggested as complement to the Celiac Disease Symptom Diary (CDSD)[1]:

▪ Schedule of assessment phase 1b trial of IMU-856:	– Baseline (Day 1) – Visit 2 (day 8) – Visit 3 (Day 14)	– Visit 5 (Day 22) – Visit 6 (Day 29)/ETV

- The ICDSQ is designed to measure the impact of symptoms on overall quality of life and includes 14 questions on four domains:

4 Domains:

- Daily activities (4 questions)
- Social activities (3 questions)
- Emotional well-being (5 questions)
- Physical activities (2 questions)

Affected by celiac disease symptoms over past 7 days:

1 = not at all
2 = a little
3 = moderately
4 = very much
5 = completely

ICDSQ © ImmunogenX LLC
[1] Canestaro WJ et al., Aliment Pharmacol Ther 2016; 44: 313–331; ETV: Early Termination Visit

IMU-856 Ameliorates Negative Gluten-Induced Impact on Daily Activities

Daily Activities, Mean Change						
	Baseline to Day 14		Day 14 to Day 22		Day 14 to Day 29	
	N	Mean Change Mean (SD)	N	Mean Change Mean (SD)	N	Mean Change Mean (SD)
IMU-856 80 mg	14	0.089 (0.362)	11	0.091 (0.573)	10	0.000 (0.425)
IMU-856 160 mg	13	-0.058 (0.341)	13	0.250 (0.468)	13	0.231 (0.484)
All Active	27	0.019 (0.353)	24	0.177 (0.513)	23	0.130 (0.464)
All Placebo	14	-0.054 (0.175)	11	0.364 (0.466)	11	0.455 (0.740)

Assessed via Impact of Celiac Disease Symptom Questionnaire (ICDSQ). Day 14: First Day of Gluten Challenge. Day 29: First Day after Completion of Gluten Challenge
Questions on Daily Activities assess the impact of celiac disease symptoms on day-to day life, quality of sleep, interference with work (including housework, paid and unpaid work, home maintenance and studying); SD: standard deviation

IMU-856 Non-Inferior to Placebo Regarding Negative Gluten-Induced Impact on Social Activities

Social Activities, Mean Change						
	Baseline to Day 14		Day 14 to Day 22		Day 14 to Day 29	
	N	Mean Change Mean (SD)	N	Mean Change Mean (SD)	N	Mean Change Mean (SD)
IMU-856 80 mg	14	-0.095 (0.275)	11	0.182 (0.721)	10	-0.033 (0.246)
IMU-856 160 mg	13	-0.128 (0.442)	13	0.103 (0.285)	13	0.179 (0.376)
All Active	27	-0.111 (0.358)	24	0.139 (0.519)	23	0.087 (0.337)
All Placebo	14	0.024 (0.514)	11	-0.121 (0.402)	11	0.091 (0.397)

Assessed via Impact Of Celiac Disease Symptom Questionnaire (ICDSQ). Day 14: First Day of Gluten Challenge. Day 29: First Day after Completion of Gluten Challenge
Questions on Social Activities assess the impact of celiac disease symptoms on the ability to participate and enjoy social activities (social events, meeting family and friends etc.); SD: standard deviation

IMU-856 Ameliorates Negative Gluten-Induced Impact on Emotional Well-Being

Emotional Well-Being, Mean Change						
	Baseline to Day 14		Day 14 to Day 22		Day 14 to Day 29	
	N	Mean Change Mean (SD)	N	Mean Change Mean (SD)	N	Mean Change Mean (SD)
IMU-856 80 mg	14	-0.014 (0.183)	11	0.105 (0.294)	9	-0.044 (0.088)
IMU-856 160 mg	13	0.000 (0.082)	13	0.092 (0.194)	13	0.092 (0.253)
All Active	27	-0.007 (0.141)	24	0.098 (0.239)	22	0.036 (0.211)
All Placebo	14	-0.114 (0.170)	11	0.055 (0.270)	11	0.164 (0.427)

Assessed via Impact Of Celiac Disease Symptom Questionnaire (ICDSQ). Day 14: First Day of Gluten Challenge. Day 29: First Day after Completion of Gluten Challenge
Questions on Emotional Well-Being assess whether the patient feels embarassed, anxious, sad, angry or annoyed because of celiac disease symptoms; SD: standard deviation

IMU-856 Ameliorates Negative Gluten-Induced Impact on Physical Activities

Physical Activities, Mean Change						
	Baseline to Day 14		Day 14 to Day 22		Day 14 to Day 29	
	N	Mean Change Mean (SD)	N	Mean Change Mean (SD)	N	Mean Change Mean (SD)
IMU-856 80 mg	14	0.11 (0.289)	11	-0.09 (0.302)	9	-0.11 (0.333)
IMU-856 160 mg	13	0.00 (0.000)	13	0.31 (0.435)	13	0.35 (0.427)
All Active	27	0.06 (0.212)	24	0.13 (0.423)	22	0.16 (0.447)
All Placebo	14	0.00 (0.000)	11	0.18 (0.405)	11	0.23 (0.518)

Assessed via Impact Of Celiac Disease Symptom Questionnaire (ICDSQ). Day 14: First Day of Gluten Challenge. Day 29: First Day after Completion of Gluten Challenge
Questions on Physical Activities assess the impact of celiac disease symptoms on the ability to participate and enjoy activities (exercise, sport, walking etc.); SD: standard deviation