



Additional Pharmacological Effect

IMU-856:
Dose-Dependent Increase of
GLP-1 in Patients

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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.

IMU-856 Targets Physiological Intestinal Epithelial Regeneration and Restoration of Gut Cell Function



- Innovative oral therapeutic approach potentially applicable to a broad range of gastrointestinal disorders



- Targets physiological intestinal epithelial regeneration, including gut hormon-producing cells



- Designed to strengthen gut wall integrity and function without immunosuppression

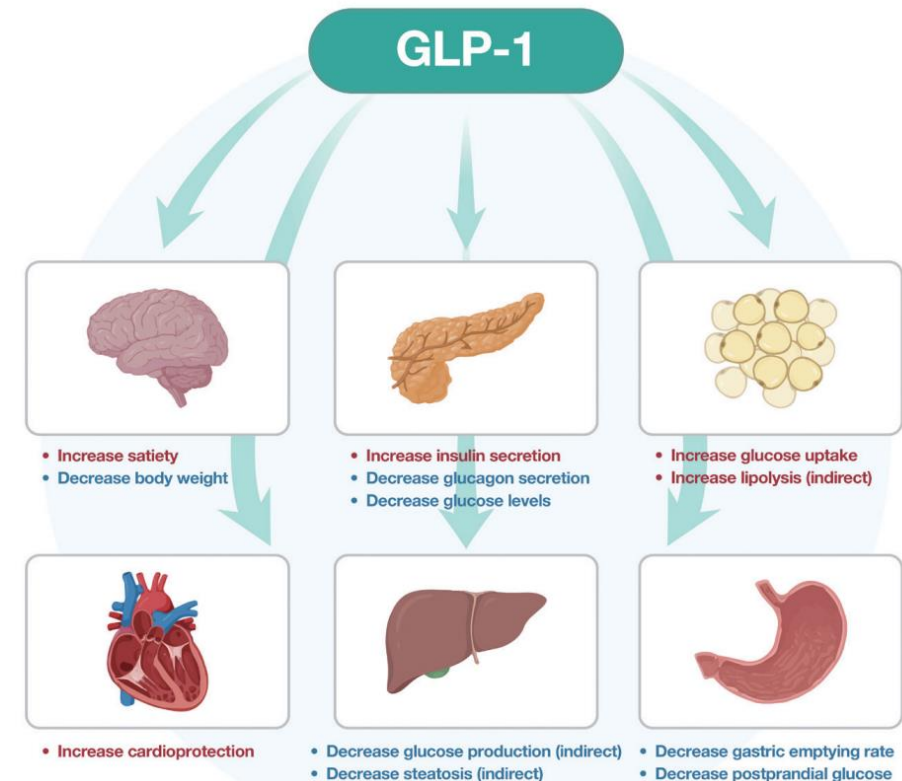
Intestinal Production of GLP-1 Mediates Effects on Body Weight



GLP-1: Glucagon-Like Peptide-1

- Peptide hormone generated through enzymatic breakdown of proglucagon
- Endocrine hormone, secreted by **enteroendocrine L-cells** located in the distal jejunum, ileum, and colon in response to **nutrient ingestion** and neuroendocrine stimulation
- Typical physiological **increase** in GLP-1 levels in healthy humans **after a meal is 2-3 times**
- GLP-1 increase leads to slow gut motility, lower food intake, increase satiety and induce insulin secretion

Main Physiologic Effects of GLP-1



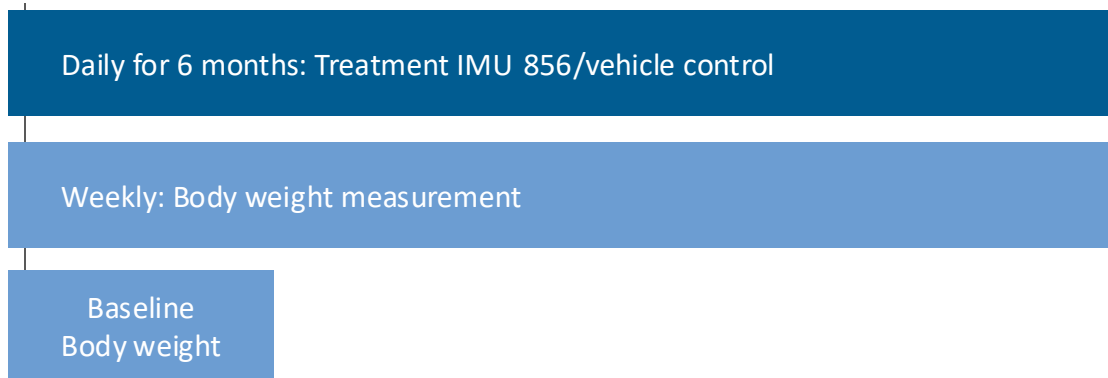
Left: Review Zheng, Z., Zong, Y., Ma, Y. et al. Sig Transduct Target Ther 9, 234 (2024); right: Jakubowska A, Roux CWL, Viljoen A. Endocrinol Metab (Seoul). 2024 Feb;39(1):12-22

IMU-856: Effects on Body Weight in Preclinical Experiment and on Blood GLP-1 Levels in Celiac Disease Clinical Trial



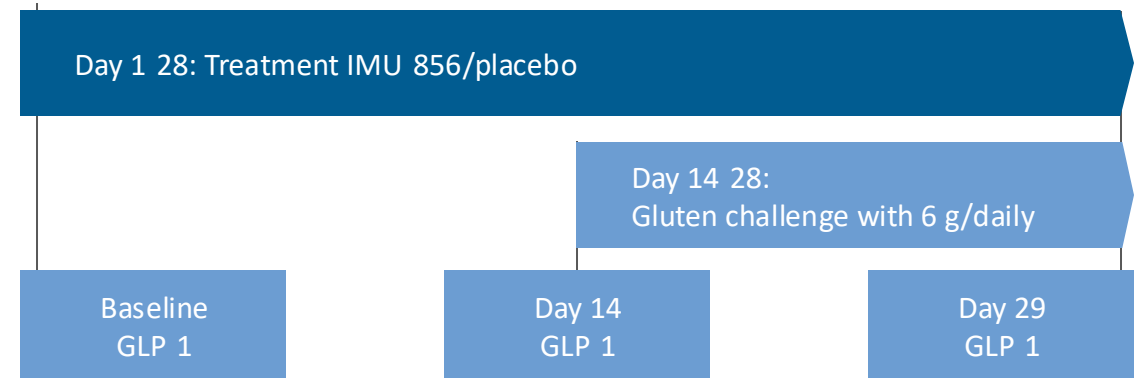
6-Months *In Vivo* Study

- Regulated GLP study^[1] to support clinical development
- Daily oral treatment of rats^[2] for 6 months
- Dosing: 0 (vehicle), 10, 25, 75 mg/kg/day of IMU-856
- Weekly body weight measurement



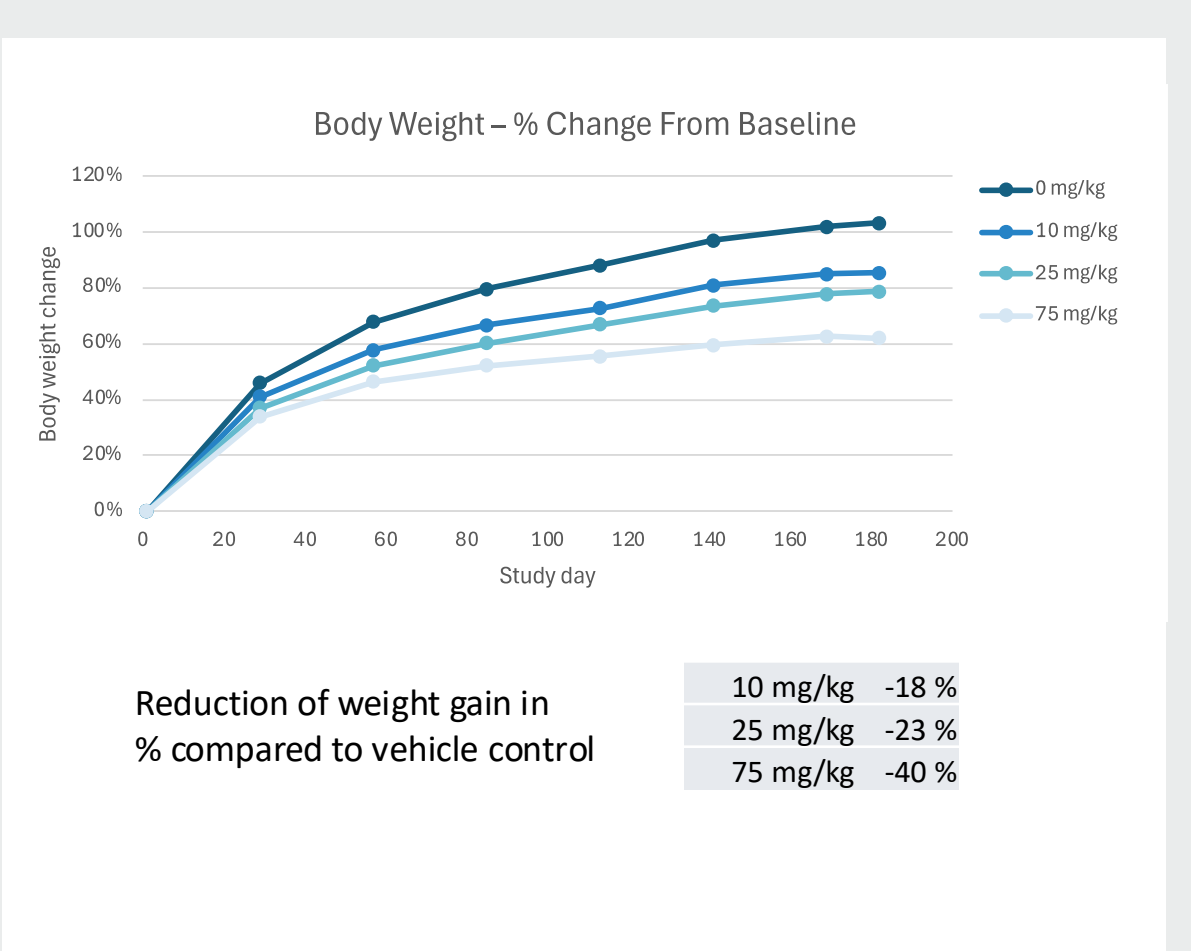
Phase 1b Clinical Trial of IMU-856

- Designed to explore effects of gluten challenge in a celiac disease patient population
- Total of 43 patients enrolled (IMU-856: N=29)
- Dosing: 80 and 160 mg QD of IMU-856, or placebo
- Double-blind treatment period of 28 days, 13 days without and 15 days with 6 g daily gluten challenge
- Patients measured post hoc for plasma GLP-1 concentrations



[1] according to ICH M3(R2) [2] Wistar Han rats / GLP-1: glucagon-like peptide-1; GLP: Good Laboratory Practice; QD: quaque die = once-daily; ICH: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

In a 6-Months *In Vivo* Study, IMU-856 Dose-Dependently Reduced Weight Gain

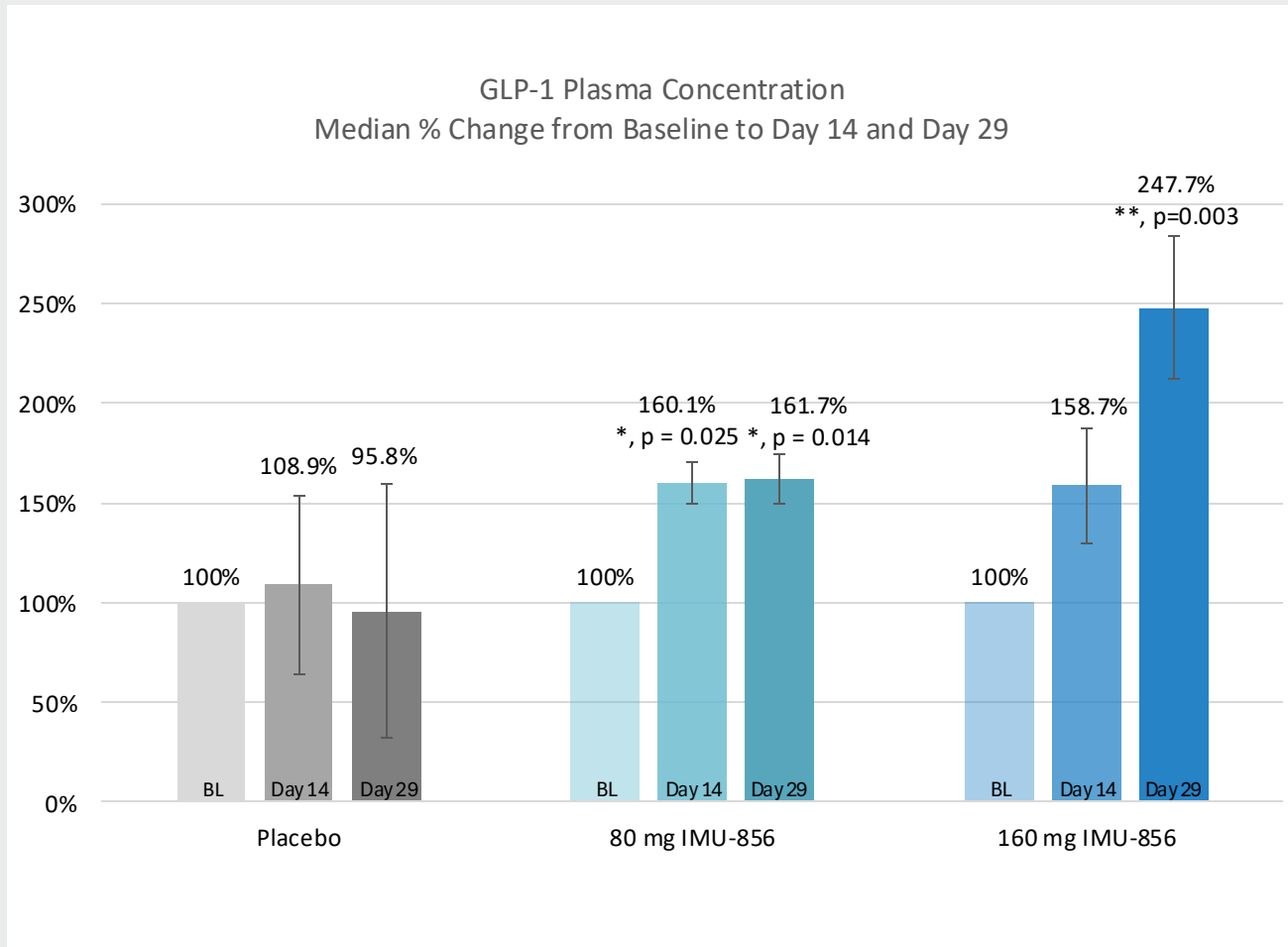


- Dose-dependent effect on body weight gain
- Linked to reduced food consumption
- Effect in both males and females
- No effect on general health condition

→ **IMU-856 reduced body weight gain in a dose-dependent fashion up to -40 % compared to vehicle control**

Reduced body weight gain observed in 6-month toxicology study. Rats were 7-8 weeks old at study start and were expected to gain weight over the course of the study. Data show less weight gain in IMU-856 treated animals in connection with reduced food consumption.

Confirmation of Effects as Part of Phase 1b Clinical Trial: IMU-856 Dose-Dependently Increased GLP-1 in Celiac Disease Patients



GLP-1: glucagon-like peptide-1; BL: baseline

28-day phase 1b clinical trial of IMU-856 in celiac disease

- Patients measured for plasma GLP-1 concentrations: N=11 (placebo), N=13 (80 mg IMU-856), N=13 (160 mg IMU-856)
- Baseline: Day 1, N=37 over all arms
- Day 14: before start of challenge, N=36
- Day 29: after last treatment on Day 28, N=32
- Morning baseline levels under fasting conditions

- **Dose-dependent increase of endogenous GLP-1 levels of up to 2.5 times versus placebo control**
- **Typical physiological increase in GLP-1 levels in healthy humans after a meal is also 2-3 times**

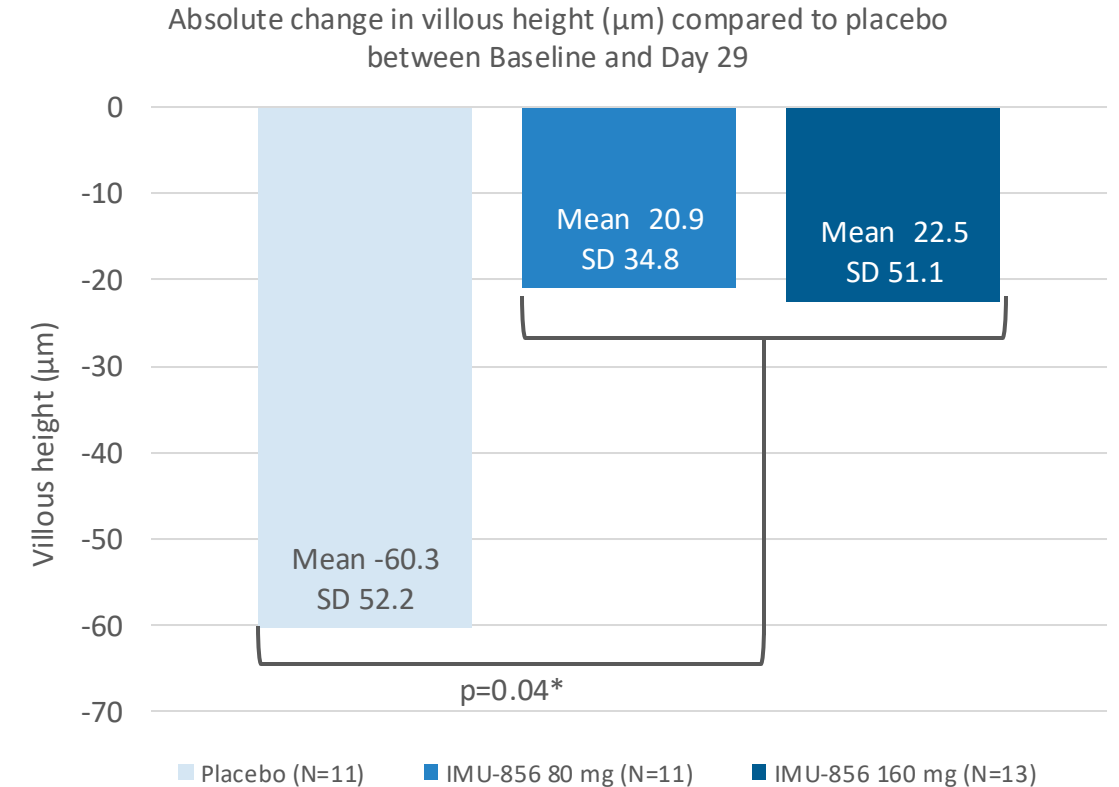
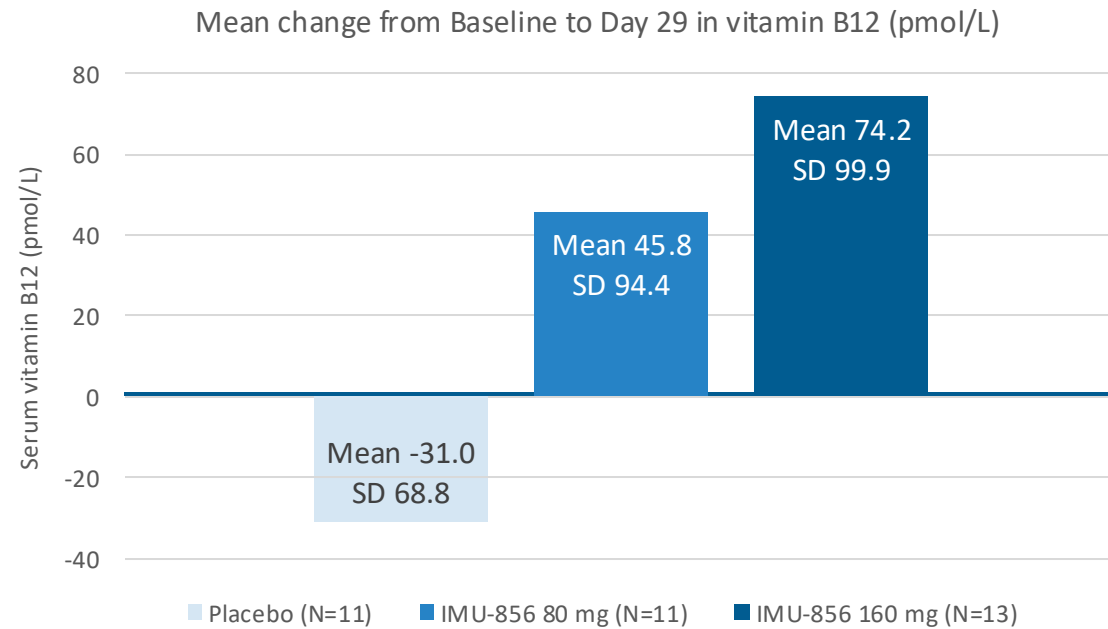
IMU-856 Demonstrated Functional Improvement of Gut Epithelial Cells in Phase 1b Clinical Trial in Celiac Disease Patients



Improved Uptake of Actively Transported Essential Nutrient Vitamin B12



Protected Against Gluten-Induced Decrease in Villous Height

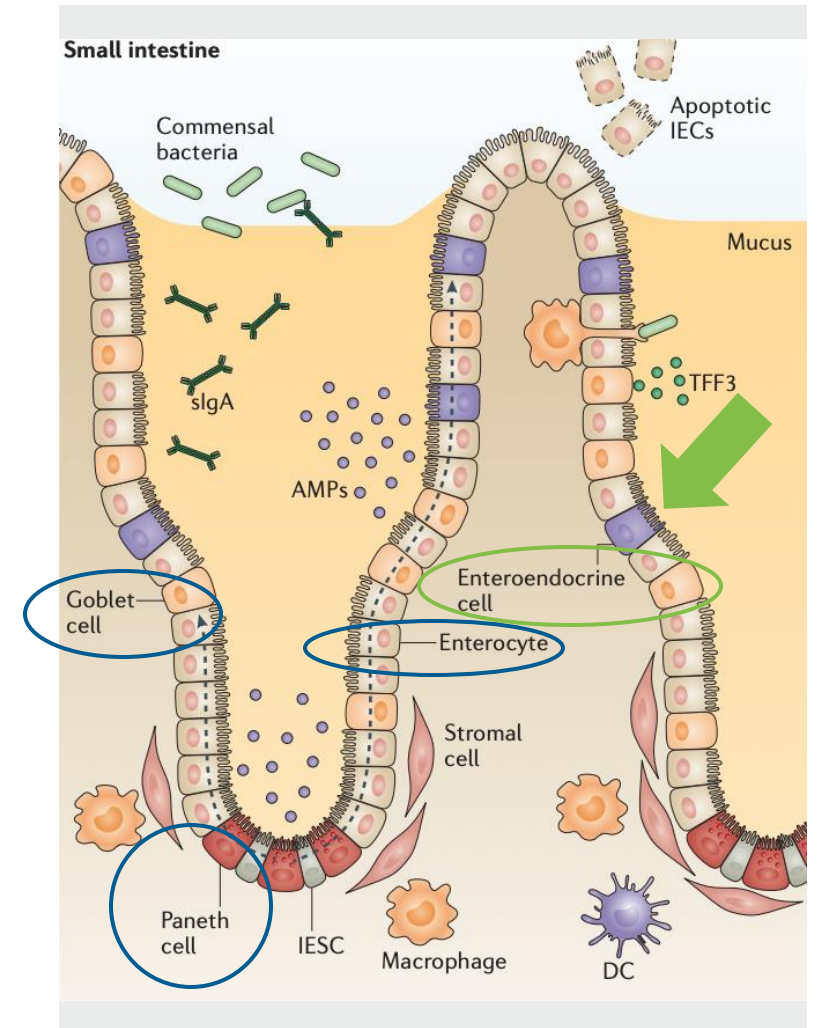
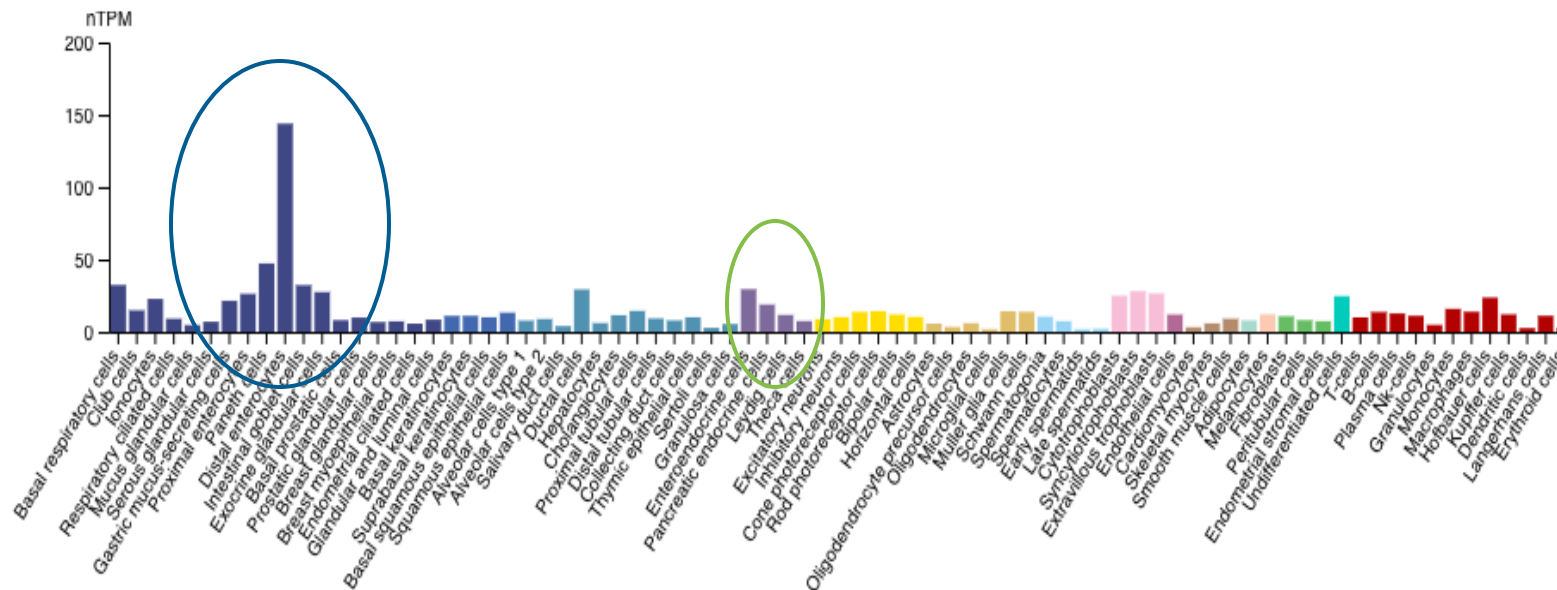


SD: standard deviation

SIRT6 Target Is Highly Expressed in Gut Epithelial Cells



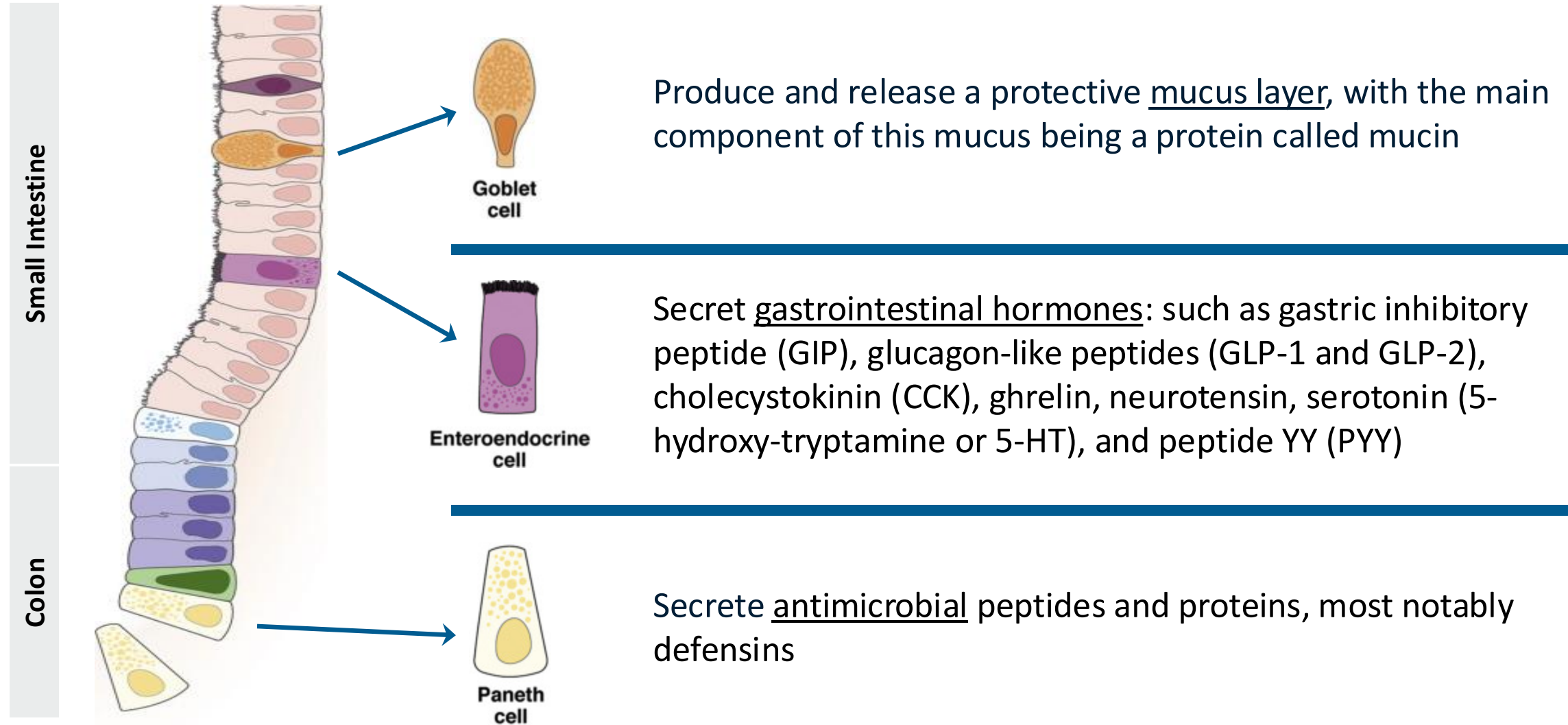
Highest mRNA Expressions in Paneth Cells, Enterocytes, Goblet Cells and Enteroendocrine Cells such as L-Cells



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

Main Secretory Epithelial Cells of the Bowel Epithelium

All Have Been Shown to Express SIRT6 Target



Meyer AR, Brown ME, McGrath PS, Dempsey PJ. Cell Mol Gastroenterol Hepatol. 2022;13(3):843-856 / SIRT: sirtuin

IMU-856: A Novel Mechanism Offering Potential to Go Beyond Existing GLP-1, GLP-2, GIP Mimetics



SIRT6 Targeting Approach IMU-856

- **Functional improvement** of enteroendocrine and other epithelial cells through increasing physiologic cell regeneration in gut wall
- Secretion of the **physiological GLP-1** protein and possible increase of secretion of **multiple incretins** (currently being investigated)
- Improvement of gut barrier and functionality in general
- **Oral** administration, small molecule



Incretin Mimetics GLP-1, GLP-2, GIP

- Providing **synthetic peptides** that mimic the natural hormones secreted by enteroendocrine cells
- Targets **one or two target incretins** only (at this point)
- **Injectable**, peptide

SIRT: sirtuin; GLP: glucagon-like peptide; GIP: glucose-dependent insulin-tropic polypeptide

Obesity Market Expected to Reach More Than \$170 Billion Globally by 2031^[1]



Unmet Needs Still Exist to Address This Growing Medical Challenge

- Obesity and overweight are among the fastest growing and most prevalent chronic human conditions in the world affecting ~2.5 billion adults worldwide^[2]
- The economic impact of obesity and overweight in the United States is estimated to be \$706 billion, increasing to \$2.6 trillion by 2060^[3]
- GLP-1 receptor agonist class has revolutionized obesity treatment but there are still **unmet needs for novel mode of actions, oral administration**, increased tolerability and greater efficacy
- Current drugs in development are mainly peptidomimetics – with challenges in oral administration

[1] GlobalData Pharma DECODED, Feb. 11th 2025 "Obesity: Seven-Market Drug Forecast and Market Analysis – Update" [2] <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight#:~:text=In%202022%2C%202.5%20billion%20adults%20aged%2018%20years%20and%20older,1990%20to%2020%25%20in%202022>
[3] <https://data.worldobesity.org/economic-impact-new/countries/US.pdf>

IMU-856's GLP-1 Effect: Summary and Outlook



- Dose-dependent reduction of body weight gain of up to -40 % observed in preclinical study
- Dose-dependent increase of endogenous GLP-1 levels of up to 2.5 times versus placebo observed in celiac disease phase 1b clinical trial
- Typical physiological increase in GLP-1 levels in healthy humans after a meal is also 2-3 times
- IMU-856 may offer potential as an oral option for weight management; potential for immediate phase 1b or phase 2 clinical testing
- IMU-856 offers benefits as an easy-to-use, once-daily, oral small molecule



IMU-856/GLP-1

Q&A Session

Thank You!



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