Supplementary Material

Supplementary table 1. The international BUX-3 study group investigators

Centre	Investigator
Germany	
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Latvia	
Pauls Stradiņš University, Riga	Juris Pokrotnieks
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Daugavpils Regional Hospital, Daugavpils	Glebs Delmans
Lithuania	
Lithuanian University of Health Sciences, Kaunas	Laimas Jonaitis

Vilnius University Hospital Santariskiu Clinics, Vilnius	Gintautas Radziunas

Supplementary table 2. Independent ethics committee approvals of the protocol

Independent ethics committees	Date of approval of protocol
Ethik-Kommission der Universität zu Lübeck, Lübeck, Germany	26 May 2015
Egészségügyi Tudományos Tanács, Klinikai Farmakológiai Etikai Bizottság, Budapest, Hungary	13 July 2015
Ethics Committee for Clinical Research at Paula Stradina University Hospital, Riga, Latvia	01 July 2015
Lithuanian Bioethics Committee, Vilnius, Lithuania	08 September 2015

Supplementary table 3. Clinical Activity Index

CAI was calculated according to Rachmilewitz et al.[13] as the sum of the scores of seven variables:	
Variable	**Score**
Number of stools, weekly[a]	
<18	0
18 to 35	1
36 to 60	2
>60	3
Blood in or on the stools, weekly[a]	
0 to 1 stools	0
≤30% of all stools	2
>30% of all stools	4
Abdominal pain/cramps, weekly[a]	
None (0–3 points)	0
Mild (4–10 points)	1
Moderate (11–17 points)	2
Severe (18–21 points)	3
General wellbeing, weekly[a]	
Good (0–3 points)	0
Average (4–10 points)	1
Poor (11–17 points)	2

Very poor (18–21 points)	3
Temperature/fever as a result of UC[b]	
≤38 °C	0
>38 °C	3
Extraintestinal manifestations[b]	
None	0
Iritis	3
Erythema nodosum	3
Arthritis	3
Laboratory findings[c]	
ESR ≤50 mm and Hb ≥100 g/L	0
ESR >50 mm, but ≤100 mm in first hour	1
ESR >100 mm in first hour	2
Hb <100 g/L	4

The primary endpoint of clinical remission was defined as CAI ≤4, with stool frequency <18/week and the absence of rectal bleeding. Clinical improvement was defined as a decrease of ≥3 from baseline to Week 8. [a]Self-reported in patient diary. [b]Assessed via clinical examination. [c]ESR assessed at local laboratories, Hb assessed at the central laboratory. CAI, Clinical Activity Index; ESR, erythrocyte sedimentation rate; Hb, haemoglobin; UC, ulcerative colitis.

Supplementary table 4. Modified Disease Activity Index

mDAI was calculated according to Sutherland et al.[14] and Sandborn et al.[15] as the sum of the scores of four variables:	
Variable	**Score**
Number of stools, daily[a]	
Normal	0
1 to 2 more than normal	1
3 to 4 more than normal	2
>4 more than normal	3
Rectal bleeding, weekly[a]	
None	0
Streaks of blood	1
Obvious blood	2
Mostly blood	3
Mucosal appearance[b, c]	
Normal	0
Erythema, decreased vascular pattern, minimal granularity	1
Marked erythema, friability, granularity, absent vascular pattern, bleeding on minimal trauma, no ulcerations	2
Ulceration, spontaneous bleeding	3
Physician's rating of disease activity[d]	
Normal	0

Mild	1
Moderate	2
Severe	3

The secondary endpoint of clinical remission was defined as an mDAI stool frequency subscore of ≤1 and a rectal bleeding subscore of 0 at Week 8. [a]Self-reported in patient diary. [b]Assessed via endoscopy. [c]To increase stringency, patients showing any mucosal friability were assigned the mucosal appearance subscore of ≥2. Friability was defined as contact bleeding. [d]Assessed via clinical examination. mDAI, modified Disease Activity Index.

Supplementary table 5. Endoscopic Index

EI was calculated according to Rachmilewitz et al.[13] as the sum of the scores of four variables:	
Variable	**Score**
Granulation scattering reflected light	
No	0
Yes	2
Vascular pattern	
Normal	0
Faded/disturbed	1
Completely absent	2
Vulnerability of mucosa	
None	0
Slightly increased (contact bleeding)	2
Greatly increased (spontaneous bleeding)	4
Mucosal damage (mucus, fibrin, exudate, erosions, ulcers)	
None	0
Slight (<10 ulcers/10 cm mucosa)	2
Pronounced (≥10 ulcers/10 cm mucosa)	4

Endoscopic remission was defined as an EI score of <4. Endoscopic improvement was defined as an EI score decrease of ≥1 from baseline to Week 8. EI, Endoscopic Index.

Supplementary table 6. Histological Index

HI was calculated according to Riley et al.[16] The severity (none [0], mild [1], moderate [2], severe [3]) of the following variables was assessed in a semi-quantitative way:

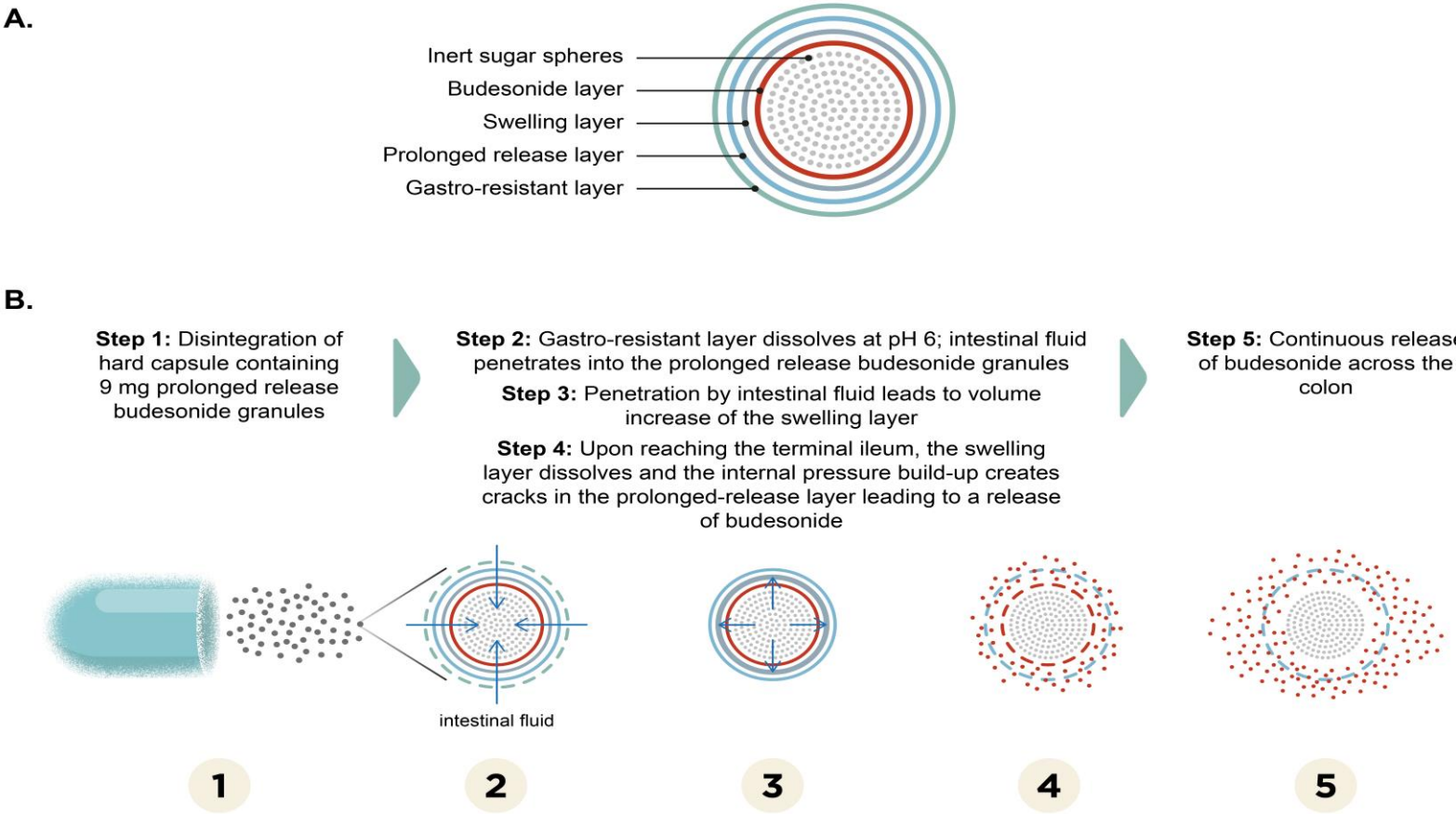
- Acute inflammatory cell infiltrate (polymorphonuclear neutrophil leucocytes in the lamina propria)
- Crypt abscesses
- Mucin depletion
- Surface epithelial integrity
- Chronic inflammatory cell infiltrate (round cells in the lamina propria)
- Crypt architectural irregularities

On this basis, the degree of mucosal inflammation was classified separately for the bowel segments biopsied and for the overall evaluation by the central pathologist using the following scale:

Variable	**Score**
No signs of UC	0
Remission	1
Mild activity	2
Moderate activity	3
Severe activity	4

Histological remission was defined as an HI of ≤1, which signifies a complete absence of neutrophils in the lamina propria and epithelium, no crypt abscesses, no mucin depletion, normal surface epithelial integrity, no or mild round cells in the lamina propria or epithelium, mild-to-moderate crypt architectural irregularities and no erosions or ulcers. Histological improvement was defined as a decreased HI of ≥1 from baseline scores of 2, 3 or 4 at Week 8. HI, Histological Index; UC, ulcerative colitis.

Supplementary Fig 1



Supplementary Fig 2