

Cosmo Announces Positive Phase 2 Study of Rifamycin 1% Topically Acting Gel, Meeting the Primary Endpoint in Distal Ulcerative Colitis and Ulcerative Proctitis

Ad hoc announcement pursuant to Art. 53 LR

- **46.2% clinical remission with rifamycin 1% topically acting gel vs 14.3% with placebo (p=0.0190).**
- **The therapy represents a new non-immune suppressive treatment modality, designed to achieve delivery to the distal colon with a novel liquid to gel delivery system, and a neutral pH.**
- **The results suggest that the anti-microbial properties of rifamycin may be positively affecting the gut microbiome and affecting host immune responses.**
- **Phase 3 planning will be informed by FDA and EMA discussions**
- **Investor call today at 4 pm CEST**

Dublin, Ireland – October 19, 2026: Cosmo N.V. (SIX: CMHC, XETRA: C43) (“Cosmo”) today announced topline results from its Phase 2 study (EUCT number: 2023-506917-23-00) of rifamycin 1% topically acting gel in patients with mildly to moderately active distal ulcerative colitis (DUC) and ulcerative proctitis. The study was designed in line with the US Food and Drug Administration (FDA) guidance on the development of drug products for ulcerative colitis.¹ The study met its primary endpoint, with a significantly greater proportion of patients treated with rifamycin 1% topically acting gel achieving clinical remission than with placebo.

Study Design

The study was a randomized, double-blind, placebo-controlled, 6-week trial in 76 patients with a diagnosis, established for at least one month, of mildly to moderately active DUC or ulcerative proctitis. All patients had a full colonoscopy with biopsy at study entry to confirm active inflammation and to exclude patients with quiescent disease, who could inflate response rates in this indication.

Patients meeting inclusion and exclusion criteria were randomized (2:1) to rifamycin 1% topically acting gel or placebo and were treated once daily for 6 consecutive weeks. The primary endpoint, defined in line with FDA guidance,¹ was the proportion of patients in clinical remission at week 6, defined as a total Mayo score of 2 or lower, rectal bleeding subscore of 0, stool frequency subscore of 0 or 1, and endoscopic subscore of 0 or 1. Clinical remission is the gold standard endpoint in ulcerative colitis and the benchmark the FDA uses to approve

new treatments. It is a demanding bar to reach: patients must be free of symptoms and show a colon free of major UC lesions on examination. Achieving remission is a meaningful outcome for patients and a strong signal of a drug's potential.

Key Findings

60 patients completed the study and comprised the primary analysis population (these were patients completing the study without major eligibility violations impacting the study results). **46.2% of patients treated with rifamycin 1% topically acting gel achieved clinical remission**, compared with 14.3% in the placebo arm (a 3.2-fold increase), with the difference between the two arms reaching statistical significance ($p = 0.0190$).

Endpoint	Rifamycin 1% topically acting gel (N=39)	Placebo (N=21)	p-value
Proportion of patients achieving clinical remission at week 6	46.2%	14.3%	0.0190

Rifamycin 1% topically acting gel was well tolerated. Drug-related adverse events were low (8), and no unexpected safety findings emerged during the study. Three serious AEs were reported during the study, none of which considered to be treatment-related.

Patients reported very high treatment satisfaction (74.3%) and expressed willingness to repeat the treatment in future (82.1%).

Analyses of secondary and exploratory endpoints are ongoing, and full results will be presented at upcoming major medical meetings or congresses.

Next Steps

Cosmo plans to discuss the results with both the FDA and EMA to inform the next stages of clinical development.

Unmet Need in DUC and Ulcerative Proctitis

Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by a relapsing disease course and significant patient burden. Distal disease involvement, including proctitis, is reported in approximately 70% of patients with UC at the time of diagnosis.² With nearly two million people living with UC in the US³ and 1.5 million in Europe,^{4,5} DUC and ulcerative



proctitis represent a substantial proportion of the UC population, potentially affecting approximately 2.4 million patients across these regions. Rectal inflammation is a major driver of symptoms and reduced quality of life in UC, yet remains inadequately controlled in many patients. Although both US and European guidelines place rectal therapy at the center of induction treatment for mild-to-moderate distal disease and proctitis, there have been no meaningful therapeutic advances in these indications in decades. This has led to both near- and long-term treatment gaps, as achieving early remission in left-sided disease prevents the spread of inflammation to the whole colon (pancolitis).

Ulcerative proctitis represents a significant unmet medical need. Historically excluded from most advanced-therapy development programs, patients with isolated disease have limited evidence-based treatment options for their condition.

Moreover, despite a growing body of evidence demonstrating the importance of the microbiome in UC pathogenesis, prior studies have not shown a clear benefit of antibiotic therapy in resolving UC symptoms and inflammation.⁶ As a result, there remains a significant need for safe, effective, and topically acting therapies designed to address the unique biology and symptom burden of DUC and ulcerative proctitis.

Rifamycin 1% topically acting gel targets the intestinal microbial environment believed to drive and sustain mucosal inflammation in the disease. Moreover, it has anti-inflammatory properties, as demonstrated by several pharmacological studies.⁶⁻¹⁰ These attributes are combined with precision local delivery, strong mucosal adherence, and a neutral pH formulation, enabled by Cosmo's proprietary technology, which transforms a liquid enema into a bio-adhesive gel upon administration. This allows targeted delivery of the active drug directly to the distal colon and rectum, where inflammation occurs, while minimizing systemic exposure and side effects.

Physician Commentary

Professor David Rubin, Joseph B. Kirsner Professor of Medicine and Director of the Inflammatory Bowel Disease Center at the University of Chicago Medicine, said:

"Previously available topical therapies for distal UC or isolated proctitis have been inadequate due to limited efficacy and poor tolerability. The results of this rifamycin formulation are very positive, and combine both the novel treatment effect of rifamycin as well as a unique and attractive delivery system that I believe will be greatly appreciated by patients. The results of this anti-microbial treatment are also provocative and warrant further study of the potential for targeting the gut microbiome effectively in UC."

Professor Simon Travis, Professor of Clinical Gastroenterology, University of Oxford, and former President of the European Crohn's and Colitis Organization (ECCO), who



contributed to the study design, said: *"The Phase 2 results are particularly encouraging and demonstrate a clear benefit using the same rigorous efficacy criteria typically applied in the Phase 3 trials that support approval. Beyond the efficacy findings, the programme is notable for evaluating a novel gel formulation designed for target delivery and retention in the distal colon. If approved, rifamycin 1% could become the first antibiotic approved for ulcerative colitis, an advance that could redefine how we manage patients with distal disease and proctitis."*

Management Commentary

Giovanni Di Napoli, Chief Executive Officer of Cosmo, said: *"These results validate our patient-centric approach to solving day-to-day clinical challenges. Rifamycin 1% topically acting gel is our answer to the question the UC community has been asking for forty years: how do we treat local disease without suppressing the immune system? It embodies what defines Cosmo: innovative formulation, end-to-end in-house development, and the rapid translation of science from preclinical models. For the approximately 2.4 million patients in the US and Europe affected by DUC and ulcerative proctitis, rifamycin 1% topically acting gel has the potential to establish a new treatment paradigm. Patients don't want to wait, and neither do we: we will discuss these data regulatory agencies and move into Phase 3 as fast as regulators allow."*

Investor Call

Cosmo's management will host a conference call with investors and analysts today at 4:00 pm CEST to discuss the Phase 2 results.

Conference Call

Participants may call the following numbers, 10 – 15 minutes before conference start

Switzerland / Europe:	+41 (0) 58 310 50 00	Other international numbers available HERE
United Kingdom:	+44 (0) 203 059 58 63	
United States:	+1 (1) 631 570 56 13	
HD Web Phone™:	Click Here	

Webcast link: <https://event.choruscall.com/mediaframe/webcast.html?webcastid=Yi060EX3>



About Cosmo

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Financial calendar

Jefferies Global Healthcare Conference, London

November 16-19, 2026

Berenberg European Conference, Windsor

November 30-December 3, 2026

For further information, please contact:

investor.relations@cosmohc.com

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References

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