Novel Drug Developments for IBD - Highlights from ECCO 2025

Ulcerative colitis and Crohn's disease are the most common chronic inflammatory bowel diseases (IBD) worldwide. Around 2 million people in Europe are currently living with diagnosed IBD, with twice as many people suffering from ulcerative colitis than Crohn's disease. In Germany, approximately 400,000 people are affected by ulcerative colitis and 250,000 people by Crohn's disease.

The exact causes of IBD are still not fully understood. Genetic, microbial and environmental factors (e.g. antibiotic intake, certain dietary and lifestyle habits) can trigger pathological immune reactions and alterations of the intestinal microbiome resulting in a damaged barrier function of the intestinal mucosa. This leads to a translocation of microorganisms into the intestinal wall and to an aberrant activation of innate immune cells so that inflammatory processes are continuously promoted.

In the last 25 years, Research & Development has done much to expand our knowledge of IBD-causing molecules. Their discovery is now the basis for targeted 'advanced therapies' that can selectively block important signalling pathways of inflammatory processes. The most important therapeutic goal is to achieve disease control with immunomodulating and anti-inflammatory drugs in order to achieve clinical remission and to improve quality of life. 'Biologics' such as tumor necrosis factor-alpha inhibitors, integrin receptor antagonists and Interleukin-12/23 inhibitors as well as 'small molecules' including Janus kinase inhibitors and sphingosine 1-phosphate receptor modulators extended therapeutic options and significantly improved IBD management.
In February 2025, 'cutting edge' results of IBD research have been presented at the 20th Congress of the European Crohn's and Colitis Organisation (ECCO 2025) in Berlin, Germany. In this Whitepaper, some novel drug classes that have already reached the late phase of clinical development are discussed in more detail. In addition, much effort is also laid to diversify the drug pool with known mode of action. Finally, improving dosing regimens of approved IBD drugs or their combinations may also help to break the 'therapeutic ceiling' often observed in patients with moderate to severe IBD.

Prof. Dr. med. Frank-Dietrich Wagner (CEO)

Charité Research Organisation GmbH has long-standing experience in the implementation of early-stage projects for new IBD drugs. In this Whitepaper, we provide an overview of approved advanced therapies for IBD currently available in the EU and present cutting-edge research activities within the IBD drug pipeline. A particular focus is on recent research into new mechanisms of action that could soon be used in the clinic for modern IBD management.

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Introduction

Inflammatory bowel diseases (IBD) comprise a group of chronic inflammatory diseases of the gastrointestinal tract such as Crohn's Disease (CD) and Ulcerative Colitis (UC), which have a number of clinical and therapeutic similarities but are clinically distinct diseases. The incidence of IBD increased over the past decade to become a *global emerging disease*. Annual incidence rates vary by geographical region with IBD estimates ranging from 10.5 to 46.14 per 100 000 in Europe, 1.37 to 1.5 per 100 000 in Asia and the Middle East, 23.67 to 39.8 per 100 000 in Oceania, 0.21 to 3.67 per 100 000 in South America, and 7.3 to 30.2 per 100 000 in North America [Caron et al., 2024].

The pathogenesis of IBD is multifactorial and still not completely elucidated. Beside a genetic predisposition, the clinical manifestation of IBD depends on the presence of several epigenetic factors (e.g., frequent exposure to antibiotics, urban environment, prevalent carnivorous diet, and for CD also smoking) resulting in a deteriorated microbiome and disruption of the intestinal epithelial barrier. Finally, this leads to a translocation of microorganisms into the intestinal wall and to an aberrant activation of innate immune cells such as neutrophils, monocytes, macrophages, dendritic cells as well as innate lymphoid cells and NK cells. Innate immune cells are the first defence against pathogens to prevent an excessive entry of intestinal microorganisms while preserving immune tolerance to resident intestinal microbiota. The aberrant activation of innate immune cells provokes the production of pro-inflammatory cytokines and activation of pro-inflammatory pathways in their target cells [Stallmach et al., 2023; Saez et al., 2023] (**Figure 1**).

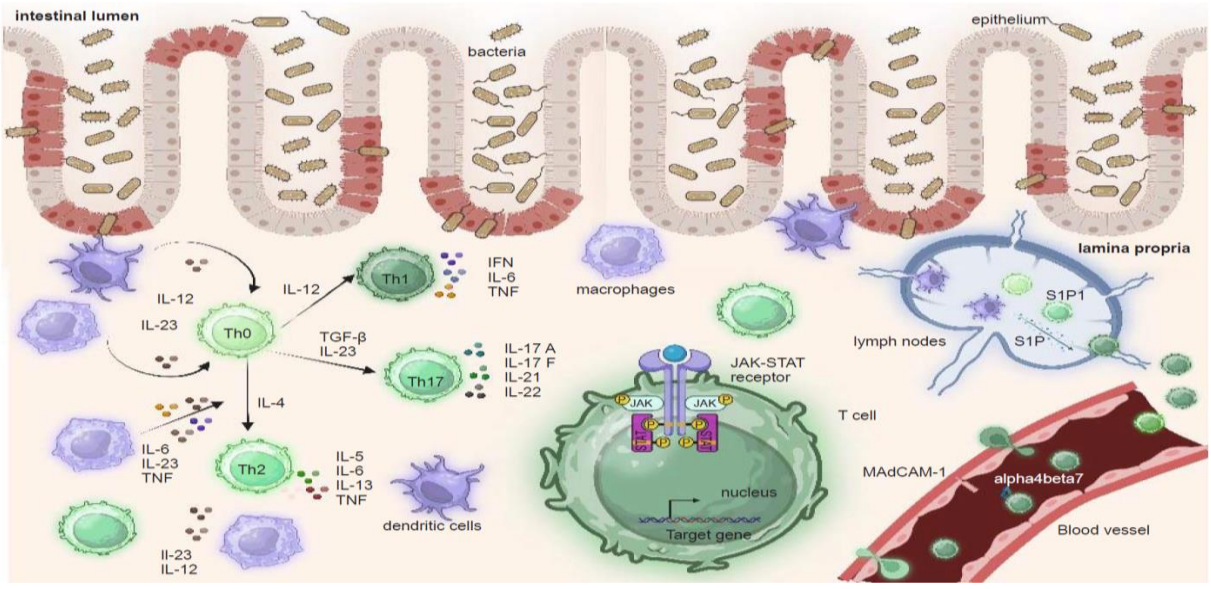

Figure 1: Clinically relevant pathways for IBD

The aberrant activation of innate immune cells provokes the production of pro-inflammatory cytokines and activation of the pro-inflammatory Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway in their target cells and increases the migration of further immune cells into the intestine. Due to a sphingosine-1 phosphate (S1P) gradient in the local lymph nodes, T cells recirculate from the intestinal tissue into the blood. Circulating T cells that express the α4ß7 integrin on their surface can interact with ligands expressed on endothelial cells such as mucosal addressin cell adhesion molecule-1 (MadCAM-1) leading to the migration of T cells into the intestine and continuous inflammation.

Source: Figure adopted from [Stallmach et al., 2023]

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Advanced Therapies for the Management of IBD

In the last 25 years, advanced therapies entered the IBD market including monoclonal antibodies ('biologics') and small molecules ('small molecules'). Biologics such as tumor necrosis factor-alpha inhibitors (TNF-alpha inhibitors), integrin receptor antagonists and Interleukin-12/23 (IL-12/13) inhibitors significantly improved IBD management. Since biologics can only be administered in the parenteral route the identification of small molecules such as Janus kinase (JAK) inhibitors and recently sphingosine 1-phosphate receptor (S1PR) modulators have reached the IBD market.

Due to their better efficacy in patients with moderate or severe IBD, advanced therapies are increasingly replacing the conventional anti-inflammatory therapies (corticosteroids, 5-aminosalicylic acid) and immunosuppressants (azathioprine, 6-mercaptopurine, methotrexate and calcineurin inhibitors). The majority of approved systemic drug classes, including advanced therapies, appear to be effective in both CD and UC, although dosages and relative efficacy may differ. In contrast, conventional therapies like 5-aminosalicylic acid (5-ASA) preparations reach the intestinal tissue from the lumen after oral or rectal administration and may be more effective in UC (superficial inflammation) than in CD (transmural inflammation). And, conventional IBD therapies are still essential treatment standards in countries where advanced therapies are currently not available.

The introduction of advanced therapies enabled an early aggressive strategy „hit early, hit hard" that is directed to prevent damage to the gastrointestinal tract caused by prolonged inflammation with consecutive irreversible stenosis, fistulisation and surgery. Prolonged untreated inflammation is also associated with the risk of complications (e.g. malignancy, thrombosis, cardiovascular diseases) and responds less frequently and less completely to drug treatment in the later course of the disease. Nevertheless, many IBD patients still experience primary non-response, secondary loss of response or adverse events limiting the overall effectiveness of current advanced therapies. For example, approximately two-thirds of anti-tumor necrosis factor (TNF) naïve patients exhibit a response after being treated with anti-TNF monoclonal antibodies, which is the most commonly used class of agents. But approximately one-third of those who initially responded subsequently become non-responders or treatment intolerant [Qiu et al., 2017]. Under well controlled conditions of a clinical trial, a 'therapeutic ceiling' is often observed in patients with moderate to severe IBD, with remission rates of only 20%–30% in induction trials [Alsoud et al., 2021]. Thus, many patients require the sequential empirical application of different drugs or drug classes or their combinations in order to break through this 'therapeutic ceiling' [Solitano et al., 2023]. In addition, the use of some advanced therapies may be limited by an unfavourable safety profile including serious infections, infusion reactions, cardiovascular events, thrombosis, and malignancies [Gordon et al., 2015]. Therefore, there remains an unmet need for novel IBD treatments that are safe and well-tolerated; and have durable efficacy. An overview of advanced therapies for IBD management that are currently available is given in **Table 1**.

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Product Class/Product	Approval Year (EMA)	Standard Dosing Regimen	Intensified Dose Regimen
TNF-alpha Inhibitors			
Infliximab* (Remicade®)	1998 for CD 2005 for UC	5mg/kgKG i.v. Wk 0, 2, 6, then every 8 Wks *OR*: from Wk 6 120mg s.c. every 2 Wks	10mg/kgKG .i.v. every 4 Wks, 120mg s.c./Wk
Adalimumab* (Humira®)	2007 for CD 2011 for UC	*CD*: 80mg s.c. Wk 0, then 40mg every 2Wks *UC*: 160mg s.c. Wk 0, 80mg Wk 2, then 40mg every 2 Wks	40mg s.c./Wk
Golimumab (Simponi®)	2013 for UC	200mg s.c. Wk 0, 100mg Wk 2, 50–100mg every 4Wks	100mg s.c. every 4Wks
Integrin Inhibitor (anti-α4β7)			
Vedolizumab (Entyvio®)	2014 for CD and UC	300 mg i.v. Wk 0, 2, 6 Then every 8 Wks 300 mg i.v. *OR* from Wk 6 onwards 108 mg every 2 Wks s.c	From Wk 6 onwards 300 mg every 4 Wks i.v.
Interleukin-12/23p40 Inhibitor			
Ustekinumab (Stelara®) Biosimilar: Otulfi®	2016 for CD 2019 for UC 2025 for CD	Weight adjusted 260 mg/ 390/520 mg, i.v. Then 90 mg every 8–12 Wks s.c.	Off-label use: 90 mg every 4–6 Wks s.c
Selective Interleukin-23p19 Inhibitors			
Risankizumab (Skyrizi®)	2022 for CD 2024 for UC	CD: 600 mg i.v. Wk 0, 4, 8, then 360 mg s.c. Wk 12 and then every 8 Wks UC: 1200 mg i.v. Wk 0, 4, 8, then 180/360 mg s.c Wk 12 then every 8 Wks	-
Mirikizumab (Omvoh®)	2023 for UC, 2025 for CD	300 mg i.v., Wk 0, 4, 8, (possibly extended - additionally Wk 12, 16, 20), then 200 mg every 4 Wks s.c.	-
Guselkumab (Tremfya®)	2025 for CD 2025 for UC	CD: 200 mg i.v. or 400 mg s.c., Wk 0, 4, 8, then 100 mg s.c. Wk 16, then every 8 Wks UC: 200 mg i.v., Wk 0, 4, 8, then 100 mg s.c. Wk 16, then every 8 Wks	CD and UC: From Wk 12 onwards 200 mg s.c., then every 4 Wks
JAK-Inhibitors			
Tofacitinib (Xeljanz®)	2018 for UC	10 mg BID p.o. for 8–16 Wks, then 5 mg BID p.o.	10 mg BID p.o. *Not recommended for patients with increased risk factors for VTE, MACE or malignancies.*
Upadacitinib (RINVOQ®)	2022 for UC 2023 for CD	UC: 45 mg QD per os for 8-16 Wks, then 15 mg QD p.o. CD: 45 mg QD p.o. for 12 Wks, then 15 mg QD p.o.	30 mg QD p.o. *Not recommended for patients > 65 years of age.*
Filgotinib (Jyseleca®)	2021 for UC	200 mg QD p.o. *Patients with risk factors for VTE, MACE or malignancies 100 mg QD p.o.*	200 mg QD p.o. *Patients with risk factors for VTE, MACE or malignancies 100 mg QD p.o.*
S1PR Inhibitors			
Ozanimod (Zeposia®)	2021 for UC	Day 1-4: 0.23 mg QD p.o. Day 5-7: 0.46 mg QD p.o. From Day 8: 0.92 mg QD p.o.	-
Etrasimod (Velsipity®)	2023 for UC	2 mg QD p.o	-

Source: Information based on SMPCs of approved IBD drugs

* Biologics for which biosimilars are available. **Abbreviations:** BID = twice daily, CD = Crohn's disease, i.v. = intravenous, JAK = Janus kinase, MACE = major cardiovascular events, p.o. = per os, QD = once daily, s.c. =subcutaneous, S1PR = Sphingosin 1 Phosphat Receptor, TNF = tumour necrosis factor, UC = ulcerative colitis, VTE = venous thromboembolic events, Wk = Week, Wks = Weeks

Table 1. Advanced therapies approved for IBD management and available on the EU market

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Advanced Combination Treatments

Many IBD patients require 'Advanced Combination Treatments' (ACT) of different or similar drug classes in order to achieve optimal disease control or to break 'therapeutic ceiling'. An ACT approach may be particularly beneficial in patients with documented medically refractory IBD and in patients with a poor prognosis, extraintestinal manifestations, or concomitant immune-mediated inflammatory diseases. [Solitano et al., 2023] (**Figure 2**).

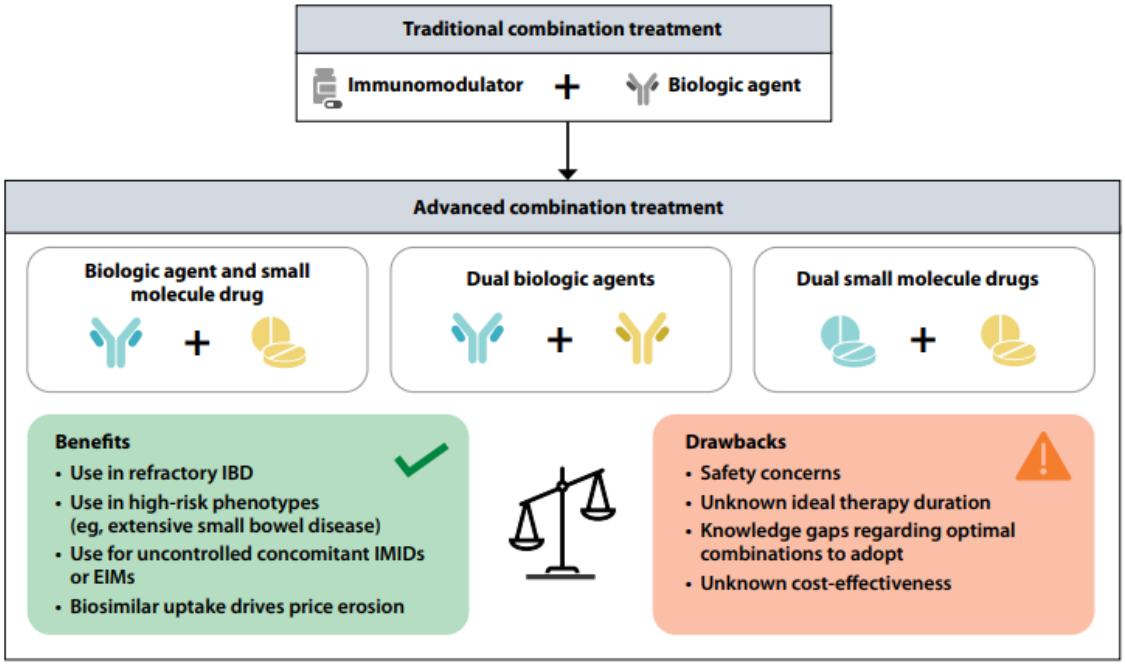

Figure 2. Traditional and advanced combination treatment: weighing benefits and drawbacks.
EIM, extraintestinal manifestation; IBD, inflammatory bowel disease; IMID, immune-mediated inflammatory disease.
Source: Figure adopted from [Solitano et al., 2023]

Highlights from ECCO 2025

The urgent medical need for more efficacious 'Advanced Therapies' for IBD with a favourable safety profile is driving big efforts in Research & Development of academia and pharma companies. The main scope is to identify novel drug classes for IBD treatment. Much effort is also laid to diversify the drug pool with known mode of action. Finally, improving dosing regimens of approved IBD drugs or the combinations thereof may also help to break 'therapeutic ceiling' in IBD. In February 2025, 'cutting edge' results of IBD research have been presented at the 20th Congress of the European Crohn's and Colitis Organisation (ECCO 2025) in Berlin, Germany. The most advanced phase 3 compounds with novel mode of action, which are the TL1A-inhibitors RO7790121 and tulisokibart and the microRNA-124 enhancer obefazimod will be discussed in more detail below. And, the promising data from one observational trial of advanced combination therapy (ACT) in patients with refractory IBD will also be presented.

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TL1A-Inhibitors for IBD

TL1A Pathophysiology in IBD

The tumor necrosis factor-like ligand 1A (TL1A) belongs to the TNF ligand superfamily and is also known as TNF superfamily member 15 (TNFSF15). Genome-wide association studies (GWAS) have identified genetic variants in the TNFSF15 locus (encoding TL1A) and the TNFSFR25 locus (encoding Death Receptor 3, DR3) that are associated with higher susceptibility to IBD [Cordero et al., 2023]. A significant higher expression of the TL1A/DR3 system has been detected in inflamed intestinal tissue samples in IBD patients which amplifies activation of Th1 responses by synergizing with IL12, and Th17 responses by synergizing with IL23 [Bamias et al., 2003; Takedatsu et al., 2008]. Blockade of the TL1A pathway has been shown to reduce inflammatory responses while leaving baseline immunity intact, and to be beneficial in animal models of colitis and asthma [Clarke et al., 2018].

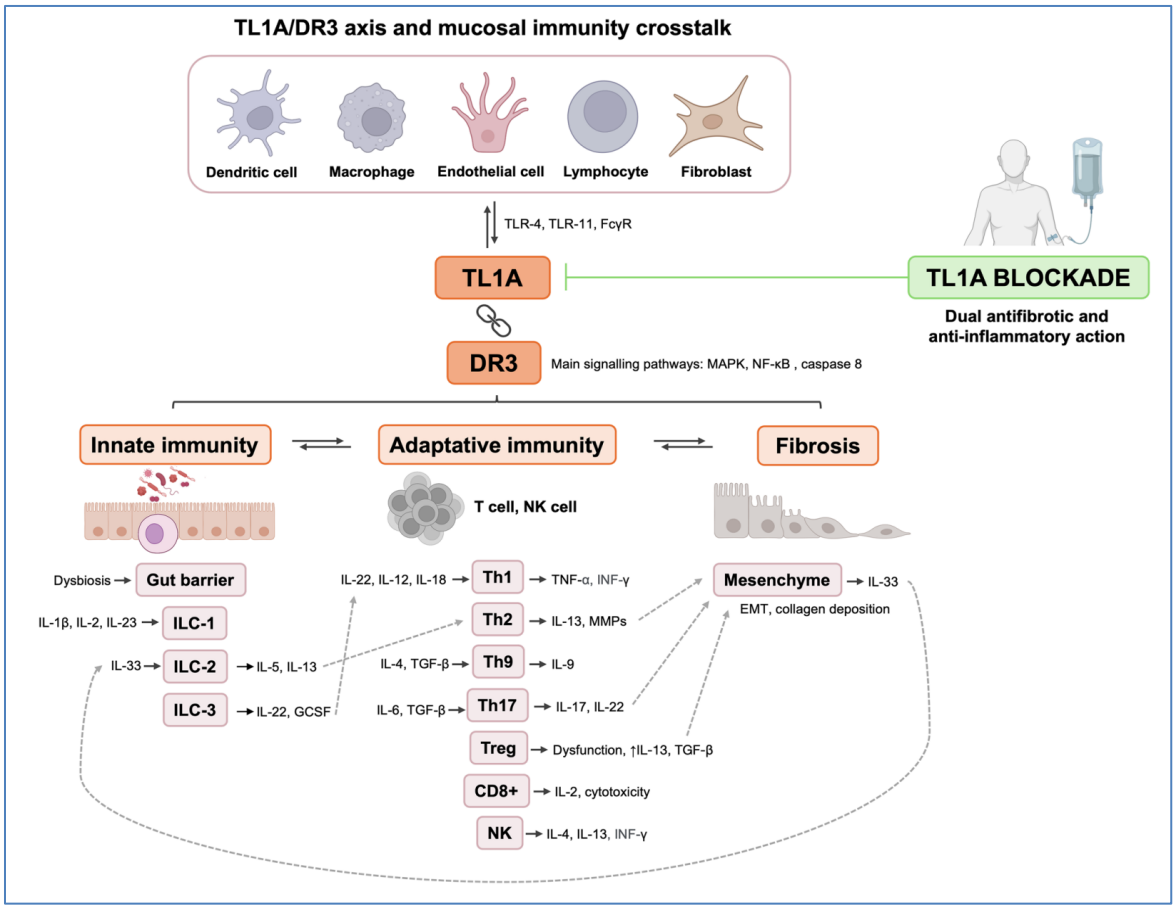

Figure 3: Crosstalk between TL1A and DR3 axis and mucosal immunity

Abbreviations: TL1A = tumor necrosis factor (TNF)-like ligand 1A, DR3 = death receptor, MAPK = mitogen-activated protein kinase, NF-κB = nuclear factor kappa-light-chain enhancer of activated B cells, ILC = innate lymphoid cells, Th = helper T cells, Treg = regulatory T cells, NK = natural killer cells, GCSF = granulocyte colony-stimulating factor, TGF-ß = transforming growth factor-beta, IFN-γ = interferon-gamma, TNF-α = tumor necrosis factor-alpha, IL = interleukin, MMP = matrix metalloproteinases

Source: Figure adopted from [Solitano et al., 2025]

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Several conditions associated with inflammation and/or the presence of gut bacteria or immune complexes may *induce* TL1A production in antigen-presenting cells like dendritic cells and macrophages but also in lymphocytes and fibroblasts. A lower *constitutive* TL1A expression has been found in endothelial cells. TL1A can be expressed as a transmembrane protein or be cleaved and secreted in a soluble form (sTL1A). By binding to its functional receptor DR3, which is expressed on activated lymphocytes, TL1A stimulates and augments mucosal effector T-cell responses. The main TL1A/DR3 signalling pathways include the activation of mitogen-activated protein kinase (MAPK), nuclear factor kappa-light-chain enhancer of activated B cells (NF-κB) and caspase 8 in various cells of the innate and adaptive immunity as well as in epithelial-mesenchymal cells. Binding of TL1A to DR3 is amplifying pathogenic interleukin signalling, inflammation and fibrosis observed in IBD [Kokkotis et al., 2022; Schweckendieck and Rogler, 2024; Solitano et al., 2025] (**Figure 3**). The inhibition of TL1A is one of the newest achievements of IBD research and seems to deliver promising clinical outcomes.

Phase 2 results of TL1A-Inhibitors presented at ECCO 2025

RO7790121 (RVT-3101, Hoffmann-La Roche) is an anti-TL1A-antibody that showed significant endoscopic improvement and favourable safety in the phase 2a TUSCANY trial [Danese et al., 2021]. The results of the subsequent phase 2b TUSCANY-2 trial (NCT04090411) in patients aged 18–75 years with moderately to severely active UC (total Mayo score ≥6, endoscopic subscore [ES] ≥2) have been reported at ECCO 2025 [Jairath et al. 2025; Allegretti et al., 2025]: Enrolled patients were randomized to receive subcutaneous doses of RO7790121 50mg, 150mg, 450mg or matched placebo monthly during the 12-week induction period, and subcutaneous doses of RO7790121 50mg, 150mg or 450mg monthly during the 40-week, treat-through maintenance period. Histologic endpoints included histologic improvement (Geboes Score [GS] ≤3.1) and remission (GS <2.1 and ES ≤1), assessed at Weeks 14 and 56. A total of 245 patients received at least one dose of RO7790121 or placebo; 228 patients completed the induction; 224 entered and 178 completed the maintenance period. Higher rates of histologic improvement and remission were observed in patients treated with RO7790121 during induction, compared with placebo, and sustained through Week 56. Similarly, a higher proportion of patients treated with RO7790121 achieved histologic-endoscopic mucosal improvement and remission, sustained through Week 56. Across the various endpoints, there was no apparent dose response [**Table 2**]. In addition, greater and earlier improvements in rectal bleeding and stool frequency were observed in patients receiving RO7790121 compared to placebo. The safety profile was reported as favourable. Due to these positive phase 2b results, RO7790121 is currently being investigated in two phase 3 studies, namely the AMETRINE-1 (NCT06589986) and AMETRINE-2 (NCT06588855) trials.

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Induction, Week 14	PBO (n=41)	50mg (n=40)	150mg (n=53)	450mg (n=82)
Histologic improvement,* %	12.2	40.0	39.6	32.9
Difference between RO7790121 and PBO, % (90% CI)	N/A	27.8 (12.1–42.8)	27.4 (12.7–40.9)	20.7 (7.5–32.1)
Histologic remission,† %	4.9	35.0	35.8	30.5
Difference between RO7790121 and PBO, % (90% CI)	N/A	30.1 (16.6–44.0)	31.0 (18.3–43.2)	25.6 (14.4–35.5)
Histologic-endoscopic mucosal improvement‡, %	4.9	30.0	32.1	25.6
Difference between RO7790121 and PBO, % (90% CI)	N/A	25.1 (12.1–38.8)	27.2 (14.8–39.3)	20.7 (9.9–30.4)
Histologic-endoscopic mucosal remission§, %	4.9	27.5	28.3	23.2
Difference between RO7790121 and PBO, % (90% CI)	N/A	22.6 (9.9–36.2)	23.4 (11.4–35.4)	18.3 (7.6–27.7)
Maintenance, Week 56[‖]	**N/A**[¶]	**50mg (n=37)**	**150mg (n=25)**	**450mg (n=26)**
Histologic improvement*, %		40.5	48.0	30.8
Histologic remission†, %		32.4	40.0	23.1
Histologic-endoscopic mucosal improvement‡, %		27.0	40.0	23.1
Histologic-endoscopic mucosal remission§, %		24.3	32.0	19.2

Data cut-off: 3 March, 2023.
n=number of participants in the analysis set with observed data or NRI and baseline Geboes score ≥2B.1, excluding participants with missing data due to medical or operational complications resulting from COVID-19.
*Histologic improvement defined as a Geboes score ≤3.1.
†Histologic remission defined as a Geboes score <2B.1.
‡Histologic-endoscopic mucosal improvement defined as a Geboes score ≤3.1 and an endoscopic subscore ≤1.
§Histologic-endoscopic mucosal remission defined as a Geboes score <2B.1 and an endoscopic subscore ≤1.
‖Analyses were conducted for all dose groups; however, maintenance efficacy results are presented only for pts receiving the same dose during the induction and maintenance periods.
¶As PBO was not administered during the maintenance period, no data for Week 56 are shown.
CI, confidence interval; COVID-19, coronavirus disease 2019; N/A, non-applicable; NRI, non-responder imputation; PBO, placebo; pts, patients.

Table 2. Summary of histologic endpoints at Week 14 and Week 56
Source: Table adopted from [Jairath et al., 2025]

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Tulisokibart (MK-7240, Merck-Prometheus Biosciences) is a monoclonal IgG1 antibody targeting TL1A that delivered positive phase 2 results in IBD patients: In the ARTEMIS-UC trial (NCT04996797), a significantly higher percentage of UC patients who received tulisokibart had clinical remission at week 12 (primary endpoint) than those who received placebo (26% vs. 1%; difference, 25 percentage points; 95% confidence interval [CI], 14 to 37; P<0.001). In addition, more patients in the tulisokibart group than in the placebo group had endoscopic improvement (37% vs. 6%; difference, 31 percentage points; 95% CI, 17 to 43; P<0.001). Endoscopic improvement was defined as an endoscopic subscore of no more than 1 with no friability. The number of adverse events was similar in the tulisokibart and placebo groups; most adverse events were mild to moderate in severity [Sands et al., 2024].

A post-hoc analysis from ARTEMIS-UC presented at ECCO 2025, reported an early and sustained improvement in patient-reported outcomes and biomarker concentrations with tulisokibart induction in patients with moderately to severely active UC [Peyrin-Biroule et al., 2025] (**Table 3**).

	Placebo N=67	Tulisikobart N=68	p-value for between-group difference
Participants with symptomatic response, n (%) (ITT)			
Week 2	27 (40.3%)	41 (60.3%)	0.0223
Week 6	31 (46.3%)	52 (76.5%)	0.0003
Week 10	38 (56.7%)	54 (79.4%)	0.0053
Week 12	33 (49.3%)	60 (88.2%)	<0.0001
Mean (SD) fecal calprotectin (µg/g)			
Baseline	1395.4 (1430.6)	1219.1 (1381.5)	n/a
Week 6	1141.0 (1020.6)	614.4 (739.3)	n/a
Week 12	977.7 (1020.7)	594.4 (926.9)	n/a
Geometric LS mean fold change from baseline in fecal calprotectin (µg/g)			
Week 6	0.81	0.34	0.0040
Week 12	0.59	0.22	0.0021
Mean (SD) hs-CRP (mg/L)			
Baseline	10.0 (13.8)	10.2 (19.2)	n/a
Week 2	9.2 (11.3)	5.0 (10.1)	n/a
Week 6	7.5 (9.9)	4.9 (8.3)	n/a
Week 10	7.8 (11.5)	5.3 (12.5)	n/a
Week 12	9.4 (13.1)	4.2 (6.1)	n/a
Geometric LS mean fold change from baseline in hs-CRP (mg/L)			
Week 2	1.01	0.58	0.0009
Week 6	0.83	0.57	0.0460
Week 10	0.79	0.52	0.0249
Week 12	0.94	0.56	0.0104

Table 3. Symptomatic response and biomarker results over time

Symptomatic response was defined as a reduction from baseline in PRO-2 score ≥ 1 point.

Estimates for the fold change and between-group difference p-values were based on Mixed Model Repeated Measures (MMRM) for logarithm of the fold change from baseline visit value, treatment visit, and treatment by visit interaction as fixed effects, and participant as random effect. ITT = intention to treat, LS =least squares, hs-CRP = high sensitivity C-reactive protein, n/a = not applicable

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Source: Table adopted from [Peyrin-Biroule et al., 2025]

A post-hoc analysis of the ARTEMIS-UC trial identified induction non-responders in both, the tulisokibart and placebo group, who were assigned to an open label 12-week re-induction treatment (intravenous tulisokibart 1000 mg, Day 1 and 500 mg, Weeks 2, 6, and 10). Non-responders were defined as patients with moderate to severe UC, who did not achieve reduction of ≥2 points and ≥30% in modified Mayo score from baseline, accompanied by a reduction ≥1 in rectal bleeding sub score or absolute rectal bleeding sub score ≤1 at week 12. Efficacy and safety were assessed following the re-induction treatment at Week 26. At Week 26, 48% and 62% of participants who received initial 12-week of tulisokibart treatment (total 24-week tulisokibart treatment) and 63% and 76% of participants who received initial 12-week placebo treatment (total 12-week tulisokibart treatment) achieved symptomatic improvement and symptomatic response, respectively. Re-induction with tulisokibart was reported as well tolerated with no serious AEs or discontinuations due to AEs and no new safety signals [Hoque et al., 2025] (**Table 4**).

Summary of Symptomatic Efficacy			
	Initial 12-Week Induction with Tulisokibart (Week 12)	**Two Tulisokibart Induction Regimens* (Week 26)**	**One Tulisokibart Regimen After No Clinical Response with Placebo (Week 26)**
Population	*n=68*	*n=21*	*n=41*
	n (%)	n (%)	n (%)
Symptomatic Response	60 (88.2)	13 (61.9)	31 (75.6)
Symptomatic Improvement	32(47.1)	10 (47.6)	26 (63.4)
Summary of Adverse Events			
	Initial 12-Week Induction with Tulisokibart (Week 12)	**Two Tulisokibart Induction Regimens* (Week 26)**	**Initial tulisokibart or placebo induction followed by tulisokibart re-induction** (Week 26)**
	n=68	*n=21*	*n=62*
	n (%)	n (%)	n (%)
Any AE	31(45.6)	5 (23.8)	23 (37.1)
Severe AE	0	0	0
Drug-related AE	3 (4.4)	1 (4.8)	1 (1.6)
Serious AE	0	0	0
Discontinued due to AE	1 (1.5)	0	0
AEs of Special Interest***			
Acute infusion reaction	0	0	0
Peri-infusion reaction	0	0	0
Infection and infestation	11 (16.2)	2 (9.5)	7 (11.3)

* Initial tulisokibart induction with no clinical response followed by tulisokibart reinduction
**Initial tulisokibart or placebo induction with no clinical response followed by tulisokibart re-induction
*** An acute infusion reaction is defined as adverse events reported within the terms of hypersensitivity MedDRA SMQ (20000214) that occurred within 1 hour after the end of study drug infusion; Peri-infusion reaction is defined as adverse events reported within the terms of hypersensitivity SMQ (20000214) that occurred within 24 hours after the end of study drug infusion. An infection is defined as those events coded under MedDRA body system of Infection and Infestation.
Symptomatic improvement is defined as rectal bleeding subscore = 0 or stool frequency subscore = 0 or 1 with a reduction of >= 1 point from baseline
Symptomatic response is defined as a reduction of PRO-2 score >= 1 point from Baseline.

Table 4. Symptomatic efficacy and adverse events after re-induction treatment
Source: Table adopted from [Hoque et al., 2025]

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In the APOLLO-CD trial (NCT05013905) tulisokibart was well tolerated and led to achievement of endoscopic response and other endpoints during a 12-week induction period and 36-week open-label extension (OLE) period in patients with moderate to severe CD [Siegel at al., 2024]. A total of 55 participants were treated in the induction period, of which 37 responders continued in the OLE (19 received tulisokibart 100 mg and 18 received tulisokibart 250 mg).

The safety results of the entire 50 weeks OLE period, were presented at ECCO 2025 [Guedelha Sabino et al., 2025]: At Week 50, 12 (63%) patients receiving 100 mg and 11 (61%) receiving 250 mg experienced non-serious infection AEs. The most common infection AEs were Urinary Tract Infection and COVID-19. There were two AEs of severe infection (bronchitis and *Clostridioides difficile*) in the 250 mg dose group. No patient discontinued treatment due to an infection AE. No dose-dependent safety signal was observed (**Table 5**).

	12-Week Induction	**OLE (Week 14 to Week 50**	
	Tulisokibart 1000 mg baseline -> Tulisokibart 500 mg Weeks 2, 6, and 10 (n=55)	Tulisokibart 100 mg (Q4W) (n=19)	Tulisokibart 250 mg (Q4W) (n=18)
	n (%)	n (%)	n (%)
Any infection AE	25 (45.5)	12 (63)	11 (61)
Severe Infection AEs	0	0	2 (11)
Serious Infection AEs	2 (4)	0	0
Discontinued due to Infection AEs	0	0	0
Drug-Related Infection AEs	1 (2)	0	0
Most Common Infection AEs (>10% in a treatment group)			
Urinary Tract Infection	5 (9)	3 (16)	2 (11)
COVID-19	6 (11)	2 (11)	2 (11)
Upper Respiratory Tract Infection	1 (2)	3 (16)	1 (6)
Bronchitis	1 (2)	0	2 (11)
Clostridioides difficile	0	0	2 (11)
Influenza	1 (2)	2 (11)	0

Table 5. Infection AEs during the 12-week induction and OLE periods of tulisokibart treatment
Source: [Guedelha Sabino et al., 2025]

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MicroRNA-124 Enhancer for IBD

Obefazimod (formerly ABX464, Abbvie) is a novel small molecule with anti-inflammatory properties that selectively upregulates the expression of microRNA-124 (miR-124) in activated macrophages and Th17 cells involved in the pathogenesis of IBD. Upregulation of miR-124 in activated macrophages or Th17 cells reduces the secretion of inflammatory cytokines via the suppression of STAT3 (signal transducers and activators of transcription 3) signalling resulting in lower Th17 proliferation. Upregulation of miR-124 in macrophages also reduces the production of MCP1 (monocyte chemoattractant protein 1), leading to reduced neutrophil recruitment and initiation of tissue repair by M1 to M2 trans-differentiation of resident macrophages [Tazi et al., 2021] (**Figure 4**).

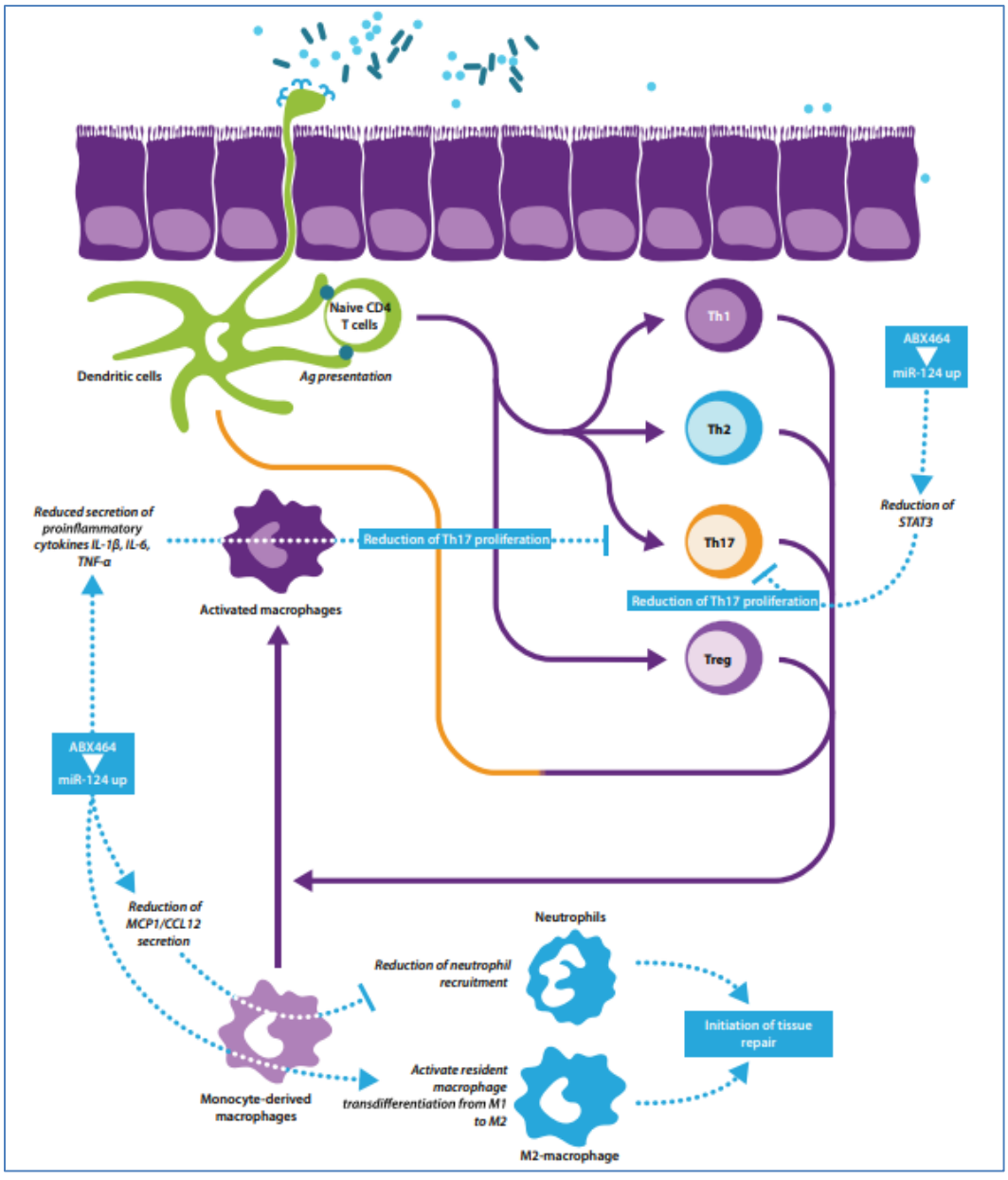

Figure 4. Mode of action of ABX464 in the control of the intestinal immune system homeostasis
Source: Figure adopted from [Tazi et al., 2021]

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Obefazimod was originally designed as anti-HIV drug. Preclinical data, obtained in a mouse model of dextran sulphate sodium (DSS)-induced colitis, demonstrated a strong and long-lasting reduction of intestinal inflammation under treatment with ABX464. In particular, ABX464 reduced the colonic production of the inflammatory cytokines IL-6 and TNFα as well as that of the monocyte chemoattractant protein-1 (MCP-1). Moreover, RNA profiling analysis revealed the capacity of ABX464 to induce the expression of IL-22, a cytokine involved in colitis tissue repair. These results supported the clinical development of ABX464 as therapy for patients with IBD [Chebli et al., 2017].

Obefazimod demonstrated efficacy and safety in patients with moderate to severe active UC at Week 8 in two phase 2b double-blind, placebo-controlled induction trials and in their subsequent open-label maintenance (OLM) trials [Vermeire et al., 2021-2022-2023]. At ECCO 2025, newly analysed data were presented demonstrating that increased proportions of patients experienced clinically meaningful improvements in endoscopic, histologic and combined histologic-endoscopic outcomes at the end of the induction trial (corresponding to baseline of OLM), and at Weeks 48 and 96 of the OLM study [Magro et al., 2025] (**Table 6**). Two phase 3 trials, ABTECT-1 (NCT05507203) and ABTECT-2 (NCT05507216), are now evaluating the efficacy and safety of obefazimod given at 25 or 50 mg QD in inducing clinical remission in 612 patients each with moderate to severe active UC.

Efficacy Endpoint, %, (n)		Data as observed		Non responder imputation*	
	Baseline of Open-Label Study [1**] (N=217)	Week 48 (N=176)	Week 96 (N=129)	Week 48 (N=217)	Week 96 (N=217)
Endoscopic improvement [2]	48.8 (106)	72.7 (128)	77.5 (100)	61.3 (133)	59.0 (128)
Histologic improvement [3]	59.0 (128)	85.2 (150)	89.1 (115)	69.6 (151)	54.8 (119)
Endoscopic remission [4]	10.6 (23)	39.2 (69)	50.4 (65)	33.2 (72)	35.9 (78)
Histologic remission [5]	11.1 (24)	18.2 (32)	24.0 (31)	14.7 (32)	15.2 (33)
HEMI [6]	39.2 (85)	69.3 (122)	74.4 (96)	56.2 (122)	45.6 (99)
HEMR [7]	1.8 (4)	9.1 (16)	17.1 (22)	7.4 (16)	10.6 (23)

1: OLM baseline used induction week 16 and/or week 8 result
2: Endoscopic improvement: endoscopic sub-score ≤1
3: Histological improvement: Neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations or granulation tissue according to the Geboes grading system (ie, Geboes histologic score ≤3.1)
4: Endoscopic remission: endoscopic sub-score = 0
5: Histological remission: Absence of neutrophils in the epithelial crypts or lamina propria and no increase in eosinophils, no crypt destruction, and no erosions, ulcerations, or granulation tissue, according to the Geboes grading system (ie, Geboes histologic score <2.0)
6: Histo-endoscopic mucosal improvement (HEMI): A combination of histologic improvement (ie, Geboes histologic score ≤ 3.1) and endoscopic improvement (Mayo endoscopy subscore of 0 or 1 with no friability)
7: Histo-endoscopic mucosal remission (HEMR): Absence of neutrophils in the epithelial crypts or lamina propria and no increase in eosinophils, no crypt destruction, and no erosions, ulcerations, or granulation tissue, according to the Geboes grading system (ie, Geboes histologic score <2.0) and Mayo endoscopy subscore of 0).
*: non-responder imputation was used for patients missing either endoscopy data and/or histology data. At OLM baseline, W48 and W96, there were 9, 6, and 26 patients with endoscopy data, respectively, who were imputed as non-responders due to missing histology data.
**: There were 16 weeks of treatment prior to entering the 96-week OLM study; OLM baseline data includes 55 patients that received placebo during the induction period and were switched to 50mg QD in the OLM.

Table 6. Histologic and combined histologic outcomes at baseline and during the OLE periods of obefazimod
Source: Table adopted from [Magro et al., 2025]

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Advanced combination therapy (ACT) in patients with refractory IBD

A prospective, single-centre observational study was conducted, including all patients diagnosed with UC or CD starting treatment with ACT from March to August 2024. Clinical and biological response and remission were assessed at week 16 and the last available (final) visit. Clinical response was defined as a decrease ≥3 points from baseline Harvey-Bradshaw Index (HBI) in CD or baseline Partial Mayo Score (pMS) in UC. Clinical remission was considered as HBI ≤4 or pMs of 0-1. Biological response was determined as a ≥50% decrease from baseline C-reactive protein (CRP) and faecal calprotectin (FC) and remission as a CRP<5 mg/dL and FC <250 mg/Kg.

A total of 20 patients were included, 70% (14/20) diagnosed with UC. The most frequent combination was vedolizumab with upadactitinib with 25% (5/20). 65% of patients achieved clinical response and 20% reached clinical remission at week 16. At the end of follow-up, 80% achieved clinical response and 65% clinical remission (**Figure 5A**). At week 16, 45% and 20% of patients achieved biological response and remission, respectively. At the end of follow-up, 65% were in biological response and 45% in biological remission (**Figure 5B**). The results demonstrate adequate clinical and biological response in patients treated with ACT, with good safety profile. Nevertheless, to confirm these results further large prospective trials are needed [Gallardo et al., 2025].

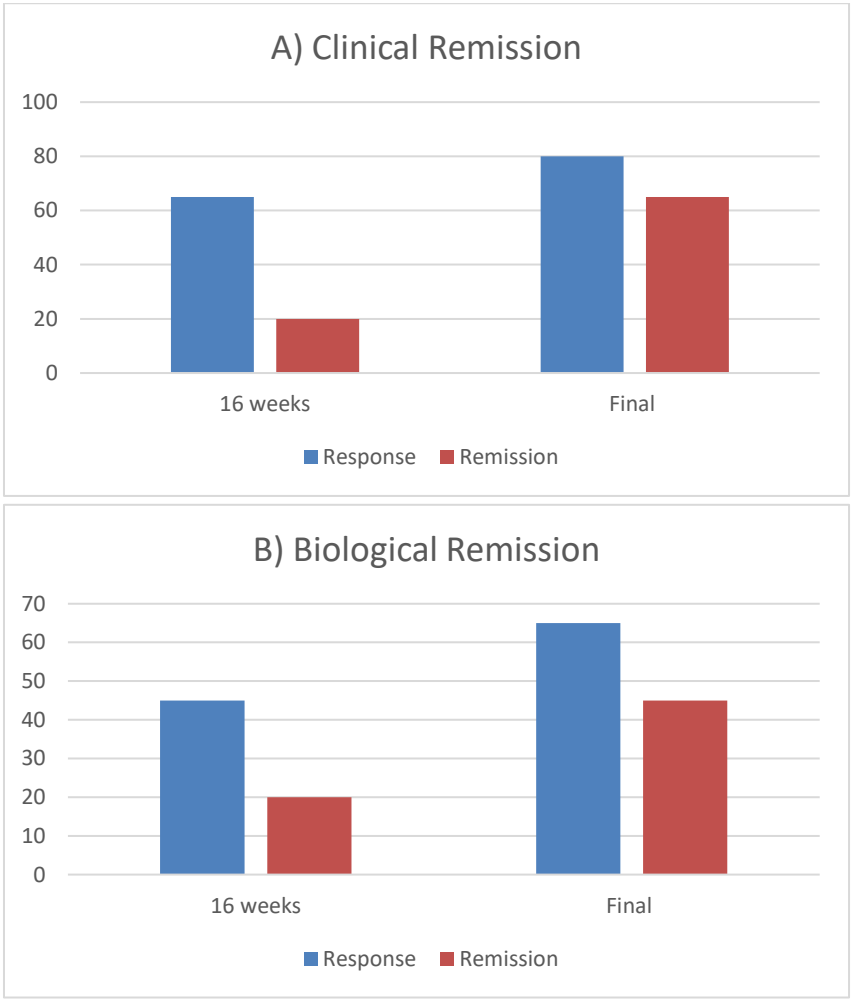

Figure 5. Percentage of patients in Clinical Remission (A) and Biological Remission (B)
Source: Figure adopted from [Gallardo et al., 2025].

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IBD Drug Pipeline

Based on a thorough review of the clinical trial projects currently in phases 2 and 3 published on CLINICALTRIALS.GOV and the publicly available literature, the current IBD drug candidates with known or novel mode of action are summarised in **Tables 7 and 8**, respectively.

Product /Product Class	Indication (EMA)	Development Phase/NTC (clinialtrials.gov)
Anti-Integrins		
ABBV-382/ anti-α4β7	CD	Phase 2/NCT06548542, SCE: AUG-2028
MORF-057/ anti-α4β7	CD, UC	Phase 2: CD/ NCT06226883, SCE: JUN-2028 Phase 2: UC/ NCT05611671, SCE: AUG-2026
GS-1427/ anti-α4β7	UC	Phase 2: NCT06290934, SCE: FEB-2027
PN-943 / GI-restricted anti-α4β7	UC	Phase 2: NCT04504383, completed 2023
Carotegrast methyl (AJM300)/ anti-α4	UC	Phase 3: NCT03531892, completed 2023
Interleukin-Inhibitors		
Dupilumab/ anti-IL-4R	UC	Phase 2: NCT05731128, SCE: FEB-2026
GSK1070806/ anti-IL-18	CD	Phase 2: NCT03681067, completed 2020
Icotrokinra (JNJ-77242113)/ oral anti-IL-23R	UC	Phase 2: NCT06049017, SCE: JAN-2026
Lutikizumab (ABT-981)/ anti-IL-1α/β	CD, UC	Phase 2: CD/ NCT06548542, SCE: AUG-2028 Phase 2: UC/ NCT06257875, SCE: April 2028
Olamkicept (TJ301)/ anti-IL-6R	UC	Phase 2: NCT03235752, completed 2020
Picankibart (IBI112)/ anti-IL-23	UC	Phase 2: NCT05377580, SCE: SEP-2025
JAK-Inhibitors/TYK-Inhibitors		
Brepocitinib (PF-06700841)/ JAK1+TYK2 inhib.	CD, UC	Phase 2: CD/ NCT03395184, completed 2023 Phase 2: UC/ NCT02958865, completed 2021
Deucravacitinib (BMS-986165)/TYK2 inhib.	CD/UC	Phase 2/ NCT04877990, completed 2023
Oncostellae (OST-122) / JAK3+TYK+ARK5 inhib.	UC	Phase 2/ NCT04353791, completed 2022
Ritlecitinib (PF-06651600)/JAK3+TEC inhib.	CD, UC	Phase 2: CD/ NCT03395184, completed 2023 Phase 2: UC/ NCT02958865, completed 2021
VTX958/ TYK2 inhib.	CD	Phase 2: NCT05688852, terminated 2024
Zasocitinib (TAK-279) / TYK2 inhib.	CD, UC	Phase 2: CD/ NCT06233461, SCE: JUL-2027 Phase 2: CD or UC/ NCT06764615, SCE: 2029
Ivarmacitinib (SHR0302) / JAK1 inhib.	CD, UC	Phase 2: CD/ NCT03677648, completed 2021 Phase 3: UC/ NCT05181137, SCE: MAR-2025
S1PR Modulators		
Amiselimod (MT-1303) / S1PR1 modulator	UC	Phase 2: NCT04857112, SCE: SEP-2024
Icanbelimod (CBP-307) / S1PR1 modulator	UC	Phase 2: NCT04700449, completed 2022
Tamuzimod (VTX002) / S1PR1 modulator	UC	Phase 2: NCT05156125, SCE: AUG-2026
Etrasimod/ S1PR1, S1PR4, S1PR5 modulator	CD	Phase 3: NCT04173273, SCE: AUG-2029
Ozanimod/ S1PR1 + S1PR5 modulator	CD	Phase 2/3: NCT05470985, completed 2024
Combination Treatments		
Infliximab + Ustekinumab/ anti-TNF + anti IL-12/23p40	UC	Phase 2: NCT06453317, SCE: JUN-2028
Golimumab + Guselkumab (JNJ-78934804)/ anti-TNF + anti-IL-23	CD, UC	Phase 2: CD/ NCT05242471, SCE: NOV2029 Phase 2: UC/ NCT05242484, SCE: MAR-2029
Risankizumab + Lutikizumab/ anti-IL-23 + anti-IL-1α/β	CD	Phase 2: NCT06548542, SCE: AUG-2028
Risankizumab + ABBV-382/ anti-IL-23 + anti-integrin α4β7	CD	Phase 2: NCT06548542, SCE: AUG-2028
Vedolizumab + Upadacitinib/ anti-α4β7 + JAK1 inhibitor	CD	Phase 3: NCT06227910, SCE: AUG-2028
Abbreviations: ARK5 = AMPK-related protein kinase 5, CD = Crohn's Disease, IL = Interleukin, JAK = Janus kinase, SCE = Study Completion Expected, S1PR = Sphingosin 1 Phosphat Receptor, TEC = Tyrosine Kinase Expressed in hepatocellular Carcinoma, TNF = tumour necrosis factor, TYK2 = Tyrosine Kinase 2, UC = Ulcerative Colitis		

Table 7. IBD drug candidates with known Mode of Action

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Product /Product Class	Indication (EMA)	Development Phase/NTC (clinialtrials.gov)
Anti-TL1A		
Duvakitug (TEV-48574)	CD, UC	Phase 2: NCT05499130, completed 2024 Phase 2: NCT05668013, SCE: MAR-2031
RO7790121 (RVT-3101)	CD, UC	Phase 3: CD/ NCT06819891, SCE: 2028 Phase 3: CD/ NCT06819878, SCE: 2033 Phase 3: UC/ NCT06589986, SCE: 2029 Phase 3: UC/ NCT06588855, SCE: 2029
Tulisokibart (MK-7240)	CD, UC	Phase 3: CD/ NCT06430801, SCE: 2029 Phase 3: CD/ NCT06651281, SCE: 2037 Phase 3: UC/ NCT06052059, SCE: 2029 Phase 3: UC/ NCT06651281, SCE: 2037
Other mode of action		
Aldesleukin (ILT-101) / IL-2R agonist	CD, UC	Phase 2: CD/ NCT04263831, SCE: DEC-2025 Phase 2: UC/ NCT02200445, completed 2021
Amelenodor (NX-13) / NLRX1 agonist	UC	Phase 2: NCT05785715, SCE: DEC-2025
AZD7798 /anti-CCR9	CD	Phase 2: NCT06450197, SCE: 2027
GLPG3970/ SIK2/3 inhibitor	UC	Phase 2: NCT04577794, completed 2021
Leiolizumab (ALTB-268) /ICE; PSGL1 agonist antibody	UC	Phase 2: NCT06109441, SCE: 2026
Mufemilast (Hemay005) / anti-PDE4	UC	Phase 2: NCT05486104, completed 2024
Obefazimod (ABX464)/ micro RNA-124 enhancer	CD, UC	Phase 2: CD/ NCT06456593, SCE: APR-2028 Phase 3: UC/ NCT05507216, SCE: Q2-2025 Phase 3: UC/ NCT05507203, SCE: Q2-2025 Phase 3: UC/ NCT05535946, SCE: JAN-2030
Olamkicept (TJ301)	UC	Phase 2: UC/ NCT03235752, completed 2020
PL-8177/ melanocortin 1 receptor agonist	UC	Phase 2: NCT05466890, SCE: Q2-2025 (Active, not recruiting)
Rosnilimab (ANB030) / PD-1 depleter and agonist	UC	Phase 2: NCT06127043, SCE: MAY-2026
SPH3127/ renin inhibitor	UC	Phase2: NCT05770609, SCE: FEB-2025 Phase 2: NCT05019742, SCE: DEC-2025
Tilpisertib Fosmecarbil (GS-5290)/ potent serine/threonine kinase inhibitor	UC	Phase 2: NCT06029972, SCE: MAY-2025
Usnoflast (ZYIL1) / NLRP3 inflammasome inhibitor	UC	Phase 2: NCT06398808, completed 2024
Vixarelimab /oncostatin M R inhibitor	UC	Phase 2: NCT06137183, SCE: SEP-2026 (Active, not recruiting)
Vorinostat/ HDAC inhibitor *followed by* Ustekinumab/ anti IL-12/23p40	CD	Phase 2: NCT03167437, SCE: JUN-2026
Bacterial and/or anti-bacterial therapy		
VE202/ Live Biotherapeutic Product	UC	Phase 2: NCT05370885, SCE: NOV-2025
Nifuroxazide/ antimicrobiotic	UC	Phase 2-3: NCT05988528, SCE: NOV-2028
RHB-104/ anti-MAP therapy	CD	Phase 3: NCT03009396, completed 2019
Abbreviations: CD = Crohn's Disease, ICE = immune checkpoint enhancer, IL = Interleukin, MAP = *Mycobacterium avium subspecies paratuberculosis,* NLRX1 = nucleotide-binding oligomerization domain, leucine rich repeat containing X1, PSGL1 =P-selectin glycoprotein ligand-1, SCE = Study Completion Expected, UC = Ulcerative Colitis		

Table 8. IBD drug candidates with novel Mode of Action

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Early Phase IBD product olamkicept

Interleukin-6 (IL-6) is a major immunomodulatory cytokine which uses distinct signalling modes to exert physiological functions in immune homeostasis and inflammation, and to promote the pathogenesis of diverse diseases [Jostock et al., 2001; Drucker et al., 2010; Wagner et al., 2024] (**Figure 5**):

- *Classical IL-6 signalling* involves the binding of IL-6 to the membrane-bound IL-6 receptor α-subunit (mIL-6R) which leads to dimerization and activation of the signal transducing glycoprotein 130 (gp130) expressed by almost all cells. Whereas gp130 is expressed on all cells of the body, the expression of mIL-6R is restricted to hepatocytes, neutrophils, macrophages and some lymphocyte subpopulations. Therefore, the classical IL-6 signal pathway is restricted to these cells. Classic signalling via mIL-6R and gp130 has homeostatic, protective and acute inflammatory functions

- *IL-6 trans-signalling* involves complexes of IL-6 and the soluble form of IL-6 receptor (sIL-6R) which signal via membrane-bound gp130. The major protease involved in the shedding of sIL-6R during inflammation is the membrane-bound metalloproteinase ADAM17 (a disintegrin and metalloproteinase 17). Cells that express gp130 but not mIL-6R are not responsive to IL-6, but they become responsive to IL-6 in the presence of sIL-6R. This switch to IL-6 trans-signalling has emerged as the predominant pathway by which IL-6 promotes pathogenetic signalling through the JAK/STAT pathways in inflammatory and neoplastic diseases. By using the designer protein sgp130Fc, Jostock and co-workers could demonstrate that soluble gp130 (sgp130) is the natural inhibitor of soluble IL-6R trans-signalling responses. sgp130Fc specifically blocks only IL-6 signalling via the sIL-6R, but not via the membrane bound IL-6R.

- *Cluster IL-6 signalling* involves a transmitter cell which presents preformed IL-6–mIL-6R complexes to activate gp130 subunits on target cells.

Olamkicept (also known as FE 999301 or TJ301) is a *first-in-class* selective IL-6 soluble receptor (sIL-6R) antagonist currently under development by Ferring in collaboration with I-Mab. It is a soluble gp130-Fc-fusion-protein formed by fusing 2 complete extracellular domains of gp130 to human IgG1 Fc [Tenhumberg et al., 2008; Waetzig et al., 2010]. Olamkicept mimics the natural trans-signalling inhibitor sgp130, but with a higher binding affinity and, consequently, a stronger inhibitory activity. Therefore, it selectively inhibits IL-6 trans-signalling by neutralising the soluble IL-6/soluble IL-6R complex without inhibition of classic IL-6 signalling. The selective inhibition of IL-6 trans-signalling induces apoptosis of aberrant T-cells involved in multiple inflammatory diseases. Therefore, olamkicept is being developed for IBD and other immune disorders.

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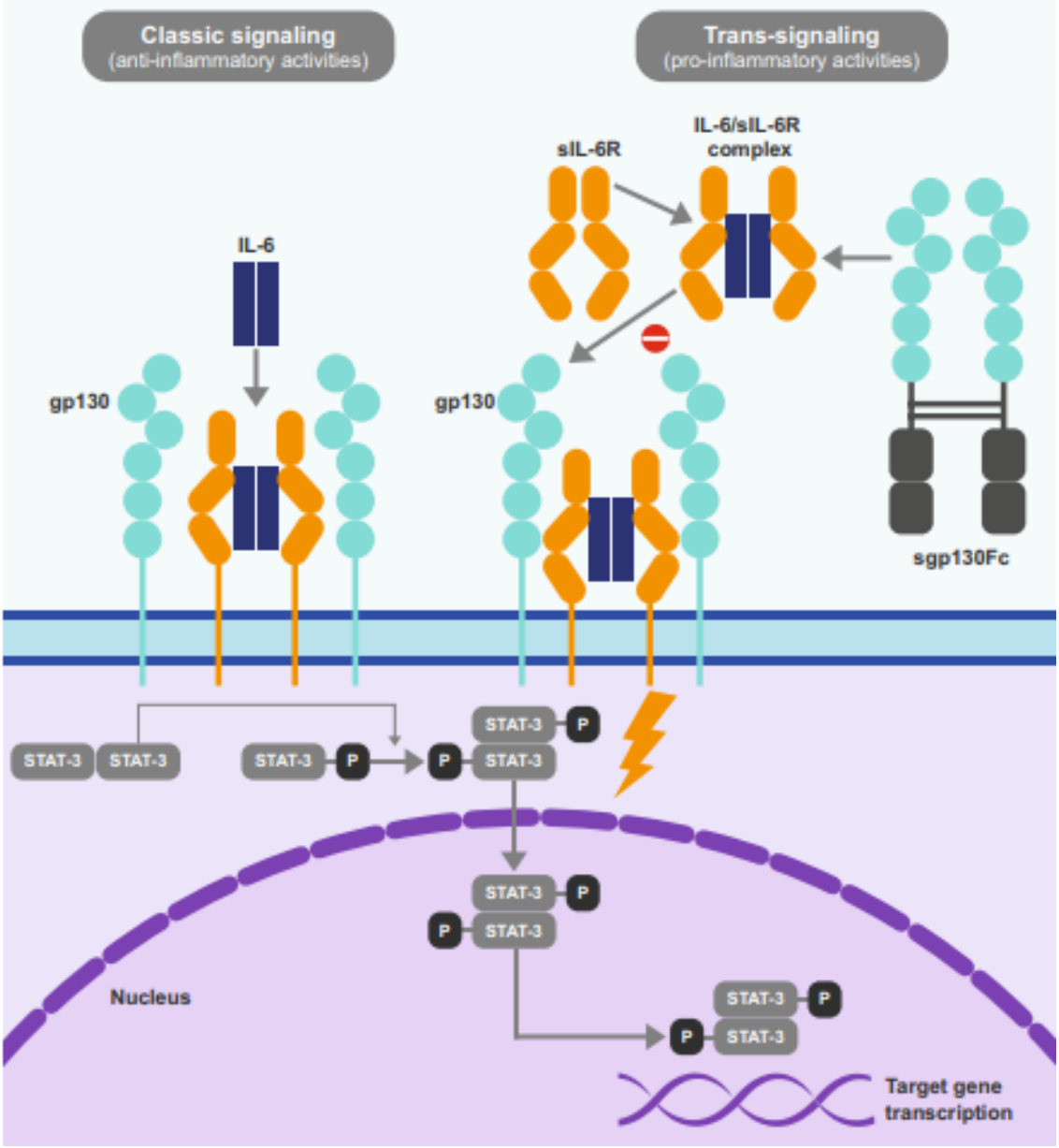

Figure 5. IL-6 classic signalling and trans-signalling.

IL-6 trans-signalling is specifically blocked by sgp130. sgp130 only binds the IL-6/sIL-6R complex and cannot bind to IL-6 alone. It therefore does not influence classical IL-6 signalling.

Abbreviations: IL-6, interleukin-6; P, phosphorylation: STAT3, signal transducer and activator of transcription-3

Source: Figure adopted from [Wagner et al., 2024]

Olamkicept has been shown to be safe when administered as single intravenous (IV) infusions at doses up to 750 mg in healthy subjects and in patients with Crohn's disease and as multiple IV infusions of up to 600 mg in healthy subjects (weekly for 4 weeks) and in patients with moderate to severe ulcerative colitis (once every 2 weeks for 12 weeks), as evaluated in two phase 1 trials (Trial 000067 and Trial 000115) conducted in Germany [Wagner et al., 2024] and two phase 2 trials conducted in Europe (Germany) and in Asia (China, Taiwan, and South Korea) [Schreiber et al., 2021; Zhang et al., 2023].

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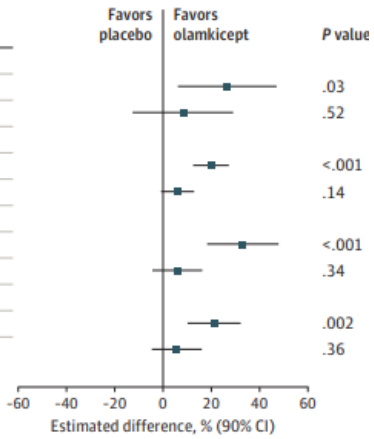
In the phase 2a open-label induction trial conducted in Germany (FUTURE, EudraCT 2016-000205-36), 16 patients with moderate to severely active IBD received 7 infusions of olamkicept 600 mg over 12 weeks. Olamkicept was well tolerated and induced clinical response in 44% and clinical remission in 19% of patients. Clinical effectiveness coincided with target inhibition (reduction of phosphorylated STAT3) and marked transcriptional changes in the inflamed mucosa. An olamkicept-specific transcriptional signature, distinguishable from remission signatures of anti–tumor necrosis factor (infliximab) or anti-integrin (vedolizumab) therapies was identified [Schreiber et al., 2021].

	No./total No. (%)		Estimated difference, % (90% CI)
	Olamkicept	Placebo	
Clinical response at wk 12			
600 mg vs placebo	17/29 (58.6)	10/29 (34.5)	26.6 (6.2 to 47.1)
300 mg vs placebo	13/30 (43.3)	10/29 (34.5)	8.3 (-12.6 to 29.1)
Clinical remission at wk 12			
600 mg vs placebo	6/29 (20.7)	0/29	19.9 (12.5 to 27.3)
300 mg vs placebo	2/30 (6.7)	0/29	6.1 (-0.8 to 12.9)
Mucosal healing at wk 12			
600 mg vs placebo	10/29 (34.5)	1/29 (3.4)	33.1 (18.3 to 47.9)
300 mg vs placebo	3/30 (10.0)	1/29 (3.4)	6.0 (-4.4 to 16.3)
Remission per modified Mayo score at wk 12			
600 mg vs placebo	7/29 (24.1)	1/29 (3.4)	21.2 (10.2 to 32.2)
300 mg vs placebo	3/30 (10.0)	1/29 (3.4)	5.7 (-4.6 to 16.1)



Clinical response at week 12 was defined as a decrease of 3 or greater and of 30% or greater from baseline in total Mayo score, including a decrease of 1 or greater from baseline in rectal bleeding subscore or of 1 or less1 in rectal bleeding subscore. Clinical remission at week 12 was defined as a total Mayo score of 2 or less, no individual subscore greater than 1, and a rectal bleeding subscore of 0. Mucosal healing at week 12 was defined as a Mayo endoscopic subscore of 0 or 1. Remission per modified Mayo score (ie, total Mayo score excluding Physician's Global Assessment subscore) at week 12 was defined as a stool frequency subscore of 1 or less, a rectal bleeding subscore of 0, and an endoscopy subscore of 0 or 1. The 90% CI and *P* value for treatment difference were derived from a logistic regression model adjusted for treatment group, randomization stratification factors, and total Mayo score at baseline as covariates. The numbers of patients were based on the full analysis set, consisting of all randomized patients with at least 1 postbaseline 9-point partial Mayo score value, and patients with missing outcomes were imputed as nonresponders (4 patients in the olamkicept 600-mg group, 3 in the 300-mg group, and 8 patients in the placebo group).

Figure 6. Primary end point and selected secondary end points in the phase 2b trial of olamkicept in patients with active ulcerative colitis
Source: Figure adopted from [Zhang et al., 2023]

In the randomized, double-blind phase 2b trial (NCT03235752), 91 patients with active ulcerative colitis and an inadequate response to conventional therapy received biweekly intravenous infusions with olamkicept 600 mg, olamkicept 300 mg, and placebo resulting in clinical response rates of 58.6%, 43.3%, and 34.5%, respectively, at 12 weeks. Only the difference between 600 mg and placebo was statistically significant. Exposure-response analysis of data from this trial indicate higher probability of patients achieving clinical efficacy with higher exposure of olamkicept, hence the need for further evaluations at dose levels above 600 mg [Zhang et al., 2023] (**Figure 6**). A subsequent phase 1c trial (NCT06298032) investigated the safety, tolerability, immunogenicity and pharmacokinetics of olamkicept higher doses (up to 2400 mg) in healthy subjects to support the clinical development program for IBD. In part A (single IV infusion) and part B (repeated IV infusions), 24 healthy volunteers each were exposed to olamkicept or placebo. The study was completed in November 2024; and results are expected to be made available in due course.

Concluding Remarks

- Comprehensive and effective IBD care integrates pharmacological therapies, surgical interventions and tailored lifestyle modifications to holistically address individual patient needs.

- Current treatment options for IBD consist of conventional therapies including corticosteroids, aminosalicylates, immunomodulators and 'Advanced Therapies' including biologic agents (anti-TNF agents, anti-integrins, anti-interleukins), and small molecules such as JAK inhibitors and S1PR modulators.

- Emerging therapies for IBD, including TL1A inhibitors and microRNA-124 enhancer, offer novel targeted approaches to mitigate inflammation, expanding therapeutic options for patients with IBD.

- Combinations of 'Advanced Therapies' of different or similar drug classes may improve disease control and break through 'therapeutic ceiling'. This is of particular importance in patients with refractory IBD or in patients with a poor prognosis, extraintestinal manifestations, or concomitant immune-mediated inflammatory diseases.

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