**BACKGROUND**

Ulcerative colitis is a chronic inflammatory bowel disease associated with a relapsing–remitting disease course and symptoms of diarrhea, rectal bleeding, abdominal pain, and bowel urgency.

Mirikizumab is a humanized IgG4–variant monoclonal antibody that specifically binds the p19 subunit of interleukin (IL)–23.

In patients with moderately to severely active ulcerative colitis, treatment with mirikizumab was effective in induction of clinical remission at Week 12 (LUCENT-1; NCT03510867) and in maintenance of clinical remission at Week 40, corresponding to 52 weeks of continuous treatment (LUCENT-2; NCT03510868).

**KEY RESULTS**

Significantly Greater Rates of Stool Frequency Remission,Rectal Bleeding Remission, and Symptomatic Remission Were Observed With MIRI vs. PBO at 40 Weeks of Continuous Treatment

**OBJECTIVE**

To assess sustained symptom control with mirikizumab during 40 weeks of maintenance treatment (52 weeks of continuous therapy; LUCENT-2) among patients who had a clinical response to mirikizumab during the induction study (LUCENT-1).

**METHODS**

**Study Design**

- **Objectives**
  - To examine the clinical efficacy and safety of mirikizumab in patients with moderately to severely active ulcerative colitis.
- **Patient population**
  - Patients (aged ≥18 yr) with ulcerative colitis, defined as persistent or recurrent bowel symptoms for ≥8 wk and ≤6 mo, confirmed by endoscopy and/or histology.
  - Patients with a bowel inflammatory disease activity index (IBD-AI) ≥10 and ≤70, or an uncontrolled or inadequately treated prior biologic, at least 3 mo prior to screening.
- **Study Design**
  - Phase 3, double-blind, randomized, parallel–controlled factorial trial.
  - Patients were randomized to either MIRI (mirikizumab 200 mg subcutaneous [SC] every 8 wk) or placebo (PBO) at Week 12 for 32 wk.
- **Endpoints**
  - **Induction**:
    - Clinical response (CR) at Week 12: IBD-AI <10.
    - Clinical remission (CR) at Week 12: CR + no rectal bleeding.
  - **Maintenance**:
    - MIRI 200 mg SC (Maintenance: N=365)
    - PBO SC (MIRI Withdrawal: N=179)
    - MIRI 200 mg SC (PBO Withdrawal: N=176)
- **Assessments**:
  - **Clinical**
    - Bowel symptoms
    - Bowel inflammatory disease activity index
  - **Safety**
    - Adverse events
    - Laboratory tests

**RESULTS**

Baseline Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>MIRI Induction Responders</th>
<th>MIRI 200 mg SC (Maintenance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>41 (12.0)</td>
<td>43.4 (14.2)</td>
</tr>
<tr>
<td>Male</td>
<td>106 (36.1)</td>
<td>214 (56.0)</td>
</tr>
<tr>
<td>Disease activity, mean (SD)</td>
<td>6.7 (5.4)</td>
<td>6.4 (7.1)</td>
</tr>
<tr>
<td>Disease location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left-sided colitis</td>
<td>119 (36.5)</td>
<td>234 (64.1)</td>
</tr>
<tr>
<td>Proctitis</td>
<td>59 (19.0)</td>
<td>126 (32.5)</td>
</tr>
<tr>
<td>Modified Mayo Score, mean (SD)</td>
<td>6.6 (1.9)</td>
<td>6.5 (1.9)</td>
</tr>
<tr>
<td>Endoscopic Mayo subscore, moderate (mean)</td>
<td>73 (49.0)</td>
<td>130 (25.0)</td>
</tr>
<tr>
<td>Endoscopic Mayo subscore, severe (mean)</td>
<td>106 (59.2)</td>
<td>225 (46.4)</td>
</tr>
<tr>
<td>Bowel urgency severity, median (Q1, Q3)</td>
<td>6.0 (5.5, 6.0)</td>
<td>6.5 (5.5, 6.5)</td>
</tr>
<tr>
<td>Abdominal pain, mean (SD)</td>
<td>5.3 (2.0)</td>
<td>4.9 (2.4)</td>
</tr>
<tr>
<td>Baseline corticosteroids use</td>
<td>64 (38.5)</td>
<td>125 (37.0)</td>
</tr>
<tr>
<td>Immunosuppressants use</td>
<td>36 (21.0)</td>
<td>73 (21.4)</td>
</tr>
<tr>
<td>Prior biologic (or tofacitinib) failure</td>
<td>64 (38.6)</td>
<td>124 (32.7)</td>
</tr>
<tr>
<td>Prior anti-TNF failure</td>
<td>58 (34.2)</td>
<td>112 (29.7)</td>
</tr>
<tr>
<td>Prior natalizumab failure</td>
<td>23 (13.2)</td>
<td>47 (12.8)</td>
</tr>
<tr>
<td>Prior tofacitinib failure</td>
<td>8 (5.4)</td>
<td>20 (5.2)</td>
</tr>
<tr>
<td>Number of failed biologics (or tofacitinib)</td>
<td>0</td>
<td>115 (64.2)</td>
</tr>
<tr>
<td>1</td>
<td>35 (19.5)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>22 (12.0)</td>
<td></td>
</tr>
</tbody>
</table>

**CONCLUSIONS**

- A greater proportion of mirikizumab–treated patients who were induction responders achieved stable maintenance of symptomatic remission compared with placebo through 40 wk (ie, over 52 wk of continuous treatment).
- Improvement in bowel urgency continued for patients who received mirikizumab treatment for 40 wk, with patients accruing an additional 13.6 percentage point increase in bowel urgency remission during the first 8 wk of maintenance therapy.
- Sustained maintenance of remission of ulcerative colitis symptoms, including rectal bleeding, stool frequency, bowel urgency, and abdominal pain, was observed in mirikizumab–treated patients compared with placebo through 40 wk (ie, over 52 wk of continuous treatment).
Sustained Symptom Control With Mirikizumab in Patients With Moderately to Severely Active Ulcerative Colitis in the LUCENT-2 Maintenance Trial

Axel Dignass,1 Silvio Danese,2 Katsuyoshi Matsuoka,3 Marc Ferrante,4 Millie Long,5 Isabel Redondo,6 Theresa Hunter Gibble,6 Richard Moses,6 Xingyuan Li,6 Nathan Morris,6 Catherine Milch,6 Maria T. Abreu7

1Agaplesion Markus Krankenhaus, Frankfurt, Germany; 2Vita-Salute San Raffaele University - IRCCS San Raffaele Scientific Institute, Milan, Italy; 3Toho University Sakura Medical Center, Sakura, Japan; 4University Hospitals Leuven, Leuven, Belgium; 5University of North Carolina, Chapel Hill, USA; 6Eli Lilly and Company, Indianapolis, USA; 7University of Miami Miller School of Medicine, Miami, USA

Sponsored by Eli Lilly and Company
BACKGROUND AND OBJECTIVE

Background

■ Ulcerative colitis is a chronic inflammatory bowel disease associated with a relapsing-remitting disease course and symptoms of diarrhea, rectal bleeding, abdominal pain, and bowel urgency\(^1\)

■ Mirikizumab is a humanized IgG4–variant monoclonal antibody that specifically binds the p19 subunit of interleukin (IL)-23\(^2\)

■ In patients with moderately to severely active ulcerative colitis, treatment with mirikizumab was effective in induction of clinical remission at Week 12 (LUCENT-1; NCT03518086),\(^3\) and in maintenance of clinical remission at Week 40, corresponding to 52 weeks of continuous treatment (LUCENT-2; NCT03524092)\(^4\)

Objective

■ To assess sustained symptom control with mirikizumab during 40 weeks of maintenance treatment (52 weeks of continuous therapy; LUCENT-2) among patients who had a clinical response to mirikizumab during the induction study (LUCENT-1)
METHODS

Study Design

**LUCENT-1**
- Blinded Induction
  - MIRI 300 mg IV Q4W
  - PBO IV Q4W

**LUCENT-2**
- Blinded Maintenance
  - MIRI 200 mg SC Q4W (Maintenance)
  - PBO SC Q4W (MIRI Withdrawal)

**Analysis Population**
Clinical responders to induction MIRI therapy at Week 12 of LUCENT-1 who were randomized to maintenance MIRI therapy or placebo for 40 weeks (Week 52)

**Clinical Response at Week 12:**
- ≥2-point and ≥30% decrease in MMS from BL with RB = 0 or 1, or ≥1-point decrease from BL

---

a LUCENT-1 was a Phase 3, randomized, parallel-arm, double-blind, placebo-controlled induction trial of MIRI in patients with moderately to severely active ulcerative colitis

b LUCENT-2 was a Phase 3, double-blind, randomized, withdrawal maintenance study in patients who responded to MIRI induction therapy in LUCENT-1. Figure is not the full LUCENT-2 program; only the patient cohort who were MIRI responders during induction and randomized to maintenance treatment are presented here. Clinical responders to induction MIRI therapy at Week 12 of LUCENT-1 were randomized to receive maintenance MIRI therapy or PBO for 40 weeks (52 weeks of treatment). Randomization in LUCENT-2 was stratified by induction remission status, biologic failure status, baseline corticosteroid use, and region

IV=intravenous; MIRI=mirikizumab; MMS=Modified Mayo Score; Non-resp=non-responders; PBO=placebo; Q4W=every 4 weeks; R=randomization; Resp=responders; SC=subcutaneous; W=Week
Key Eligibility Criteria: LUCENT-1

- Age ≥18 and ≤80 years
- Moderately to severely active ulcerative colitis
  - Modified Mayo Score of 4-9, with an endoscopic subscore of 2-3
- Inadequate response, loss of response, or intolerance to:
  - Corticosteroids, immunomodulators, biologic therapy, or Janus kinase inhibitor for ulcerative colitis
- No previous exposure to anti–IL-12/23p40 or anti–IL-23p19 antibodies
- No previous failure of ≥3 different biologic therapies\(^a\) for ulcerative colitis

\(^a\) Regardless of mechanism of action

IL=interleukin
Assessments

- Patient-reported outcomes were recorded daily in the patient eDiary and then averaged by week:\n  - Stool frequency Mayo subscore, from 0 (stools/day normal for the patient) to 3 (≥5 stools/day more than normal)
  - Rectal bleeding Mayo subscore, from 0 (no blood) to 3 (blood alone passed)
  - Bowel urgency severity (UNRS), from 0 (no urgency) to 10 (worst possible urgency)
  - Abdominal pain NRS, from 0 (none) to 10 (worst possible pain)

- Proportion of patients achieving:
  - Stool frequency remission: Stool frequency subscore 0, or 1 with ≥1-point decrease from induction BL
  - Rectal bleeding remission: Rectal bleeding subscore 0
  - Symptomatic remission: Stool frequency and rectal bleeding remission
  - Stable maintenance of symptomatic remission: Patients in symptomatic remission for ≥7 of 9 visits from Weeks 4-36 and at Week 40 among patients in symptomatic remission and with clinical response at the end of LUCENT-1
  - Abdominal pain improvement: NRS ≥30% reduction from BL in patients with abdominal pain NRS ≥3 at induction BL
  - Bowel urgency remission: Minimal to no bowel urgency (UNRS [0,1]) in patients with bowel urgency severity UNRS ≥3 at induction BL

- Change in bowel urgency severity (UNRS) from induction BL

---

*For stool frequency and rectal bleeding, weekly assessments were calculated by averaging the 3 most recent available eDiary days in a 7-day period; for bowel urgency and abdominal pain, all available eDiary days in a 7-day period were averaged.*

BL = baseline; NRS = numeric rating scale; UNRS = Urgency Numeric Rating Scale
Statistical Analyses

- Analyses were conducted using the modified Intent-to-Treat population (patients receiving ≥1 dose of mirikizumab or placebo)
  - Excludes patients impacted by an electronic clinical outcome assessment transcription error in Poland and Turkey

- Changes from baseline were compared between treatment arms using mixed-effects model of repeated measures, including treatment, baseline value, visit, interaction of baseline value-by-visit, interaction of treatment-by-visit, prior biologic or tofacitinib failure, corticosteroid use at baseline (LUCENT-1), global region, and clinical remission status at Week 12 (LUCENT-1)

- Response rates between treatment arms were compared using Cochran-Mantel-Haenszel test adjusted for prior biologic or tofacitinib failure, corticosteroid use at baseline (LUCENT-1), global region, and clinical remission status at Week 12 (LUCENT-1)
  - Common risk difference was the difference in proportions adjusted for stratification factors, with confidence intervals calculated using the Mantel-Haenszel-Sato method
  - Missing data were handled using non-responder imputation
## RESULTS

Baseline<sup>a</sup> Demographics and Disease Characteristics (1/2)

<table>
<thead>
<tr>
<th></th>
<th>MIRI Induction Responders</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PBO SC (N=179)</td>
</tr>
<tr>
<td>Age, years, mean (SD)</td>
<td>41.2 (12.8)</td>
</tr>
<tr>
<td>Male</td>
<td>104 (58.1)</td>
</tr>
<tr>
<td>Disease duration, years, mean (SD)</td>
<td>6.7 (5.6)</td>
</tr>
<tr>
<td>Disease location</td>
<td></td>
</tr>
<tr>
<td>Left-sided colitis</td>
<td>119 (66.5)</td>
</tr>
<tr>
<td>Pancolitis</td>
<td>59 (33.0)</td>
</tr>
<tr>
<td>Modified Mayo Score, mean (SD)</td>
<td>6.6 (1.2)</td>
</tr>
<tr>
<td>Endoscopic Mayo subscore, moderate [score 2]</td>
<td>73 (40.8)</td>
</tr>
<tr>
<td>Endoscopic Mayo subscore, severe [score 3]</td>
<td>106 (59.2)</td>
</tr>
<tr>
<td>Bowel urgency severity, median (Q1, Q3)</td>
<td>6.0 (5.0, 8.0)</td>
</tr>
<tr>
<td>Abdominal pain NRS, mean (SD)</td>
<td>5.3 (2.2)</td>
</tr>
</tbody>
</table>

Data are presented as n (%) unless stated otherwise

<sup>a</sup> Refers to induction BL (Week 0 of LUCENT-1)

BL=baseline; MIRI=mirikizumab; NRS=numeric rating scale; PBO=placebo; Q=quartile; SC=subcutaneous; SD=standard deviation
## RESULTS

**Baseline\(^a\) Demographics and Disease Characteristics (2/2)**

<table>
<thead>
<tr>
<th></th>
<th>MIRI Induction Responders</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PBO SC (N=179)</td>
<td>MIRI 200 mg SC (N=365)</td>
<td></td>
</tr>
<tr>
<td><strong>Baseline corticosteroid use</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>68 (38.0)</td>
<td>135 (37.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Immunomodulator use</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>39 (21.8)</td>
<td>78 (21.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Prior biologic (or tofacitinib) failure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>64 (35.8)</td>
<td>128 (35.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Prior anti-TNF failure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>58 (32.4)</td>
<td>112 (30.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Prior vedolizumab failure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>23 (12.8)</td>
<td>47 (12.9)</td>
<td></td>
</tr>
<tr>
<td><strong>Prior tofacitinib failure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8 (4.5)</td>
<td>8 (2.2)</td>
<td></td>
</tr>
<tr>
<td><strong>Number of failed biologics (or tofacitinib)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>115 (64.2)</td>
<td>237 (64.9)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>35 (19.6)</td>
<td>77 (21.1)</td>
<td></td>
</tr>
<tr>
<td>≥2</td>
<td>29 (16.2)</td>
<td>51 (14.0)</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as n (%) unless stated otherwise

\(^a\) Refers to induction BL (Week 0 of LUCENT-1)

*BL=baseline; MIRI=mirikizumab; PBO=placebo; SC=subcutaneous; TNF=tumor necrosis factor*
Significantly Greater Rates of Stool Frequency Remission, Rectal Bleeding Remission, and Symptomatic Remission Were Observed With MIRI vs. PBO at 40 Weeks of Continuous Treatment

- Common risk difference for MIRI vs. PBO (95% CI)
- CI=confidence interval; MIRI=mirikizumab; NRI=non-responder imputation; PBO=placebo; SC=subcutaneous
Remission Rates Were Sustained Through 40 Weeks of Continuous Treatment With MIRI vs. PBO

Mean (SD) stool frequency Mayo subscore at Week 0: 0.87 (0.77) for PBO SC, 0.81 (0.73) for MIRI 200 mg SC

Mean (SD) rectal bleeding Mayo subscore at Week 0: 0.17 (0.38) for PBO SC, 0.13 (0.34) for MIRI 200 mg SC

CI=confidence interval; MIRI=mirikizumab; NRI=non-responder imputation; PBO=placebo; SC=subcutaneous
Improvement in Bowel Urgency Was Sustained Through 40 Weeks of Continuous Treatment With MIRI vs. PBO

**Bowel Urgency Severity UNRS Score**

- **LSM difference (95% CI)**
  - at Week 40: -1.06 (-1.51 to -0.61)

**Change From Baseline, LSM (SE), MMRM**

- **Weeks**: 0, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40
- **PBO SC (MIRI Withdrawal: N=179)**
- **MIRI 200 mg SC (Maintenance: N=365)**

**Bowel Urgency Remission**

- **Common risk difference (95% CI)**
  - at Week 40: 18.1 (9.8-26.4)

**Patients, % (95% CI), NRI**

- **Weeks**: 0, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40
- **PBO SC (MIRI Withdrawal: N=172)**
- **MIRI 200 mg SC (Maintenance: N=336)**

*In patients with Bowel Urgency NRS ≥3 at BL (LUCENT-1)

* p<0.05; ** p<0.01; *** p<0.001 vs. PBO

**BL=baseline; CI=confidence interval; LSM=least squares mean; MIRI=mirikizumab; MMRM=mixed-effect model of repeated measures; NRI=non-responder imputation; PBO=placebo; SC=subcutaneous; SE=standard error; UNRS=Urgency Numeric Rating Scale**
Improvement in Abdominal Pain Was Sustained Through 40 Weeks of Continuous Treatment With MIRI vs. PBO

* p<0.05; ** p<0.01; *** p<0.001 vs. PBO

In patients with Abdominal Pain NRS ≥3 at BL (LUCENT-1)

BL=baseline; CI=confidence interval; MIRI=mirikizumab; NRI=non-responder imputation; NRS=numeric rating scale; PBO=placebo; SC=subcutaneous
CONCLUSIONS

- A greater proportion of mirikizumab-treated patients who were induction responders achieved stable maintenance of symptomatic remission compared with placebo through 40 weeks (ie, over 52 weeks of continuous treatment).

- Improvement in bowel urgency continued for patients who received mirikizumab treatment for 40 weeks, with patients accruing an additional 13.6-percentage point increase in bowel urgency remission during the first 8 weeks of maintenance therapy.

- Sustained maintenance of remission of ulcerative colitis symptoms, including rectal bleeding, stool frequency, bowel urgency, and abdominal pain, was observed in mirikizumab-treated patients compared with placebo through 40 weeks (ie, over 52 weeks of continuous treatment).
REFERENCES

ABBREVIATIONS

BL=baseline; CI=confidence interval; IV=intravenous; LSM=least squares mean; MIRI=mirikizumab; MMRM=mixed-effects model of repeated measures; MMS=Modified Mayo Score; Non-resp=non-responders; NRI=non-responder imputation; NRS=numeric rating scale; PBO=placebo; Q=quartile; Q4W=every 4 weeks; R=randomization; Resp=responders; SC=subcutaneous; SD=standard deviation; SE=standard error; TNF=tumor necrosis factor; UNRS=Urgency Numeric Rating Scale; W=Week
A. Dignass has received consulting fees from: AbbVie, Abivax, Amgen, Arena Pharmaceuticals, Bristol Myers Squibb (Celgene), Celltrion, Dr. Falk Pharma, Eli Lilly and Company, Ferring Pharmaceuticals, Fresenius Kabi, Galapagos, Gilead Sciences, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Pharmacosmos, Roche, Sandoz/Hexal, Takeda, Tillotts Pharma AG, and Vifor Pharma; has received lecture fees or honoraria from: AbbVie, Amgen, Bristol Myers Squibb, Dr. Falk Pharma, Ferring Pharmaceuticals, Galapagos, High5Md, Janssen, Materia, Merck Sharp & Dohme, Pfizer, Sandoz, Takeda, Tillotts Pharma AG, and Vifor Pharma; and manuscript preparation fees from: Dr. Falk Pharma, Janssen, Takeda, and Thieme; S. Danese has received consulting fees from: AbbVie, Janssen, Takeda, and Thieme; and manuscript preparation fees from: Dr. Falk Pharma, Janssen, Takeda, and Thieme; K. Matsuoka has received fees for grants and/or contracts from: AbbVie, EA Pharma, JIMRO, Kissei Pharmaceutical, Kyowa Kyorin, Mitsubishi Tanabe, Mochida Pharmaceutical, and Zeria Pharmaceutical Nippon; and manuscript preparation fees from: Eli Lilly and Company; M. Ferrante has received fees for grants and/or contracts from: AbbVie, Amgen, Biogen, Janssen Cilag, Pfizer, Takeda, and Viatris; consulting fees from: AbbVie, Boehringer Ingelheim, Celltrion, Eli Lilly and Company, Janssen Cilag, Medtronic, Merck Sharp & Dohme, Pfizer, Regeneron, Sandoz, Takeda, and Thermo Fisher Scientific; lecture fees or honoraria from: AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celltrion, Dr. Falk Pharma, Eli Lilly and Company, Ferring Pharmaceuticals, Gilead Sciences, Hospira, Inotrem, Janssen, Johnson & Johnson, Merck Sharp & Dohme, Mundipharma, Mylan, Pfizer, Roche, Sandoz Sublimity, Takeda, TiGenix, UCB Pharma, and Vifor Pharma; and lecture fees from: AbbVie, Amgen, Ferring Pharmaceuticals, Gilead Sciences, Janssen, Mylan, Pfizer, and Takeda; K. Matsuoka has received fees for grants and/or contracts from: AbbVie, EA Pharma, JIMRO, Kissei Pharmaceutical, Kyowa Kyorin, Mitsubishi Tanabe, Mochida Pharmaceutical, and Zeria Pharmaceutical Nippon; and manuscript preparation fees from: Eli Lilly and Company; M. Ferrante has received fees for grants and/or contracts from: AbbVie, Amgen, Biogen, Janssen Cilag, Pfizer, Takeda, and Viatris; consulting fees from: AbbVie, Boehringer Ingelheim, Celltrion, Eli Lilly and Company, Janssen Cilag, Medtronic, Merck Sharp & Dohme, Pfizer, Regeneron, Sandoz, Takeda, and Thermo Fisher Scientific; lecture fees or honoraria from: AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celltrion, Dr. Falk Pharma, Eli Lilly and Company, Ferring Pharmaceuticals, Gilead Sciences, Janssen, Lamepro, Medtronic, Merck Sharp & Dohme, Mylan, Pfizer, Samsung Bioepis, Sandoz, Takeda, and Thermo Fisher Scientific; M. Long has received consulting fees from: AbbVie, Bristol Myers Squibb, Calibr, Eli Lilly and Company, Genentech, Janssen, Pfizer, Prometheus Biosciences, Roche, Takeda, TARGET PharmaSolutions, and TheraVance Biopharma; and is on the Board of Trustees of: American College of Gastroenterology; I. Redondo, T. Hunter Gibble, R. Moses, X. Li, and N. Morris are employees and shareholders of: Eli Lilly and Company; C. Milch is a former employee of: Eli Lilly and Company; M. T. Abreu has received fees for grants and/or contracts from: Pfizer, Prometheus Biosciences, and Takeda; consulting fees from: AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, Eli Lilly and Company, Gilead Sciences, Janssen, Microba Life Sciences, Prometheus Biosciences, UCB Pharma, and WebMD; lectures fees from: Alimentiv, Intellisphere LLC (HCP Live Institutional Perspectives in GI), Janssen, Prime CME, and Takeda; support to attend meetings from: AbbVie, Alimentiv, Arena Pharmaceuticals, Bristol Myers Squibb, Eli Lilly and Company, Gilead Sciences, Intellisphere LLC (HCP Live Institutional Perspectives in GI), Janssen, Microba Life Sciences, Prime CME, Prometheus Biosciences, Takeda, UCB Pharma, and WebMD; data safety monitoring fees from: AbbVie, Arena Pharmaceuticals, Bristol Myers Squibb, Eli Lilly and Company, and Gilead Sciences; and is on the advisory board of: Janssen, Microba Life Sciences, Prometheus Biosciences, UCB Pharma, and WebMD

Medical writing assistance was provided by Serina Stretton PhD, CMPP, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company