Lilly's mirikizumab is first and only IL23p19 antagonist to report long-term, multi-year, sustained efficacy and safety data for both ulcerative colitis and Crohn's disease

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At three years, over 80% of patients with moderately to severely active UC who were in remission with mirikizumab sustained long-term remission and relief from disruptive symptoms, including bowel urgency

Mirikizumab also helped over 50% of patients with moderately to severely active Crohn's disease sustain long-term endoscopic remission for up to five years

INDIANAPOLIS, Oct. 28, 2024 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced results from two, multi-year, Phase 3 studies that showed patients treated with mirikizumab sustained stable, long-term remission across two types of inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn's disease. Data from the two trials – LUCENT-3 in moderately to severely active UC and VIVID-2 in moderately to severely active Crohn's disease – will be presented at the American College of Gastroenterology (ACG) Annual Meeting from October 25-30, 2024 in Philadelphia.

Mirikizumab is an interleukin-23p19 (IL23p19) antagonist that selectively binds to the p19 subunit of IL-23 and inhibits its interaction with the IL-23 receptor. Inflammation due to the overactivation of the IL-23 pathway plays a critical role in pathogenesis of UC and Crohn's disease. Inflammation from UC and Crohn's disease can lead to disruptive symptoms, including bowel urgency, that can result in decreased health-related quality of life and potentially irreversible complications for patients if left untreated. Mirikizumab is approved in the United States (U.S.) for the treatment of moderately to severely active UC in adults and is under review with the U.S. Food and Drug Administration (FDA) for moderately to severely active Crohn's disease.

"Mirikizumab is the first and only IL23p19 antagonist to report multi-year, long-term sustained efficacy data in both ulcerative colitis and Crohn's disease," said Mark Genovese, M.D., senior vice president of Lilly Immunology development. "This achievement reflects our commitment to help people with immune system conditions sustain long-standing remission and relieve disease burden."

Long-Term Data in Adults with UC
In LUCENT-3, mirikizumab helped patients with moderately to severely active UC achieve long-term outcomes, including histologic-endoscopic mucosal remission, defined as mucosal healing. Mirikizumab also provided sustained benefit across symptomatic, clinical, endoscopic and histologic endpoints for up to three years, regardless of previous failure to TNF inhibitors, tofacitinib or other biologics. Among those who achieved clinical remission with mirikizumab at one year in the LUCENT-2 study, the following results were achieved based upon observed case analysis after an additional two years of treatment (up to three years total):

- 81% of patients maintained long-term clinical remission
- 82% achieved long-term endoscopic remission
- 72% had mucosal healing
- 79% achieved corticosteroid-free clinical remission
- Patients demonstrated a sustained clinically meaningful improvement in symptom score reduction for bowel urgency (-4.72)

These results were also evaluated using a modified non-responder imputation and are presented in the About the Mirikizumab Ulcerative Colitis Program section below.

Among patients receiving mirikizumab in the LUCENT-3 study, 7.4% of patients reported a serious adverse event (AE), while 5.3% discontinued treatment due to an AE. The long-term safety profile in patients with moderately to severely active UC was consistent with the already known safety profile of mirikizumab. These data were recently published in *Inflammatory Bowel Diseases*.

Long-Term Data in Adults with Crohn's Disease
New data from patients in the Phase 2 program who enrolled into the VIVID-2 long-term extension study showed that patients with moderately to severely active Crohn's disease treated with mirikizumab maintained high rates of clinical and endoscopic remission over time. The following results were achieved based upon observed case analysis after an additional three years of treatment (up to five years total):

- 96% of patients had clinical response as measured by the Crohn's Disease Activity Index (CDAI)
- 87% were in clinical remission as measured by CDAI
- 76% had endoscopic response
- 54% of patients were in endoscopic remission

These results were also evaluated using a modified non-responder imputation and are presented in the About the Mirikizumab Crohn's Disease Program section below.

"Despite continued advances, people living with ulcerative colitis and Crohn's disease are still seeking treatments that can address difficult-to-manage symptoms such as bowel urgency, and provide lasting results over time," said Bruce Sands, M.D., M.S., Dr. Burrill B. Crohn Professor of Medicine and Chief of the Dr. Henry D. Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai. "These multi-year data show mirikizumab is a targeted therapy that can provide intestinal healing over time and improvement in key symptoms that matter most to patients."

Among these patients who enrolled into the VIVID-2 long-term extension study, 8.5% reported a serious AE and 1.9% discontinued treatment due to an AE. The long-term safety profile in patients with moderately to severely active Crohn's disease was consistent with the already known safety profile of mirikizumab.

Omvoh® (mirikizumab-mrkz) was approved by the FDA in October 2023 as the first IL23p19 antagonist for the treatment of moderately to severely active UC in adults and is also approved in 44 countries around the world. Lilly submitted marketing applications for mirikizumab in Crohn's disease around the globe, including in the U.S., Canada, Europe, Japan and China. Additional global regulatory submissions are planned.

Additionally, Lilly has a combination study in UC with mirikizumab and eltrekibart, a humanized monoclonal antibody that binds to the seven ligands that signal through the CXCR1 and CXCR2 chemokine receptors involved in neutrophil movement to sites of inflammation (NCT06598943). There are also ongoing studies in both UC (NCT05611671) and Crohn's disease (NCT06226883) with MORF-057, a selective oral small molecule alpha-4/beta-7 integrin inhibitor that may improve outcomes and expand treatment options for people with IBD.

Disclosure: Dr. Sands is a paid consultant for Lilly. He has not been compensated for any media work.

About the Mirikizumab Ulcerative Colitis Program
Mirikizumab was studied in two, Phase 3 clinical trials which evaluated the efficacy and safety of mirikizumab in adults with moderately to severely active ulcerative colitis (UC) and included patients who had never tried a biologic (biologic-naïve) and harder-to-treat patients who had previously taken a biologic that failed. The induction LUCENT-1 and maintenance LUCENT-2 studies were randomized, double-blind, and placebo-controlled and included those who had inadequate response, loss of response, or failed to tolerate any of the following: corticosteroids, immunomodulators (6-mercaptopurine and azathioprine), biologic therapy (TNF blocker, vedolizumab) or Janus kinase inhibitors (JAKi, tofacitinib). Additionally, 41% of patients in LUCENT-1 had failed at least one biologic, 3% had failed a JAKi and 57% were biologic and JAKi-naïve.

LUCENT-3, the ongoing long-term Phase 3 extension of LUCENT-1 and LUCENT-2 evaluated the efficacy and safety of mirikizumab in patients with UC for up to three years. Using a modified non-responder imputation analysis to handle discontinuation and missing data, among Week 52 mirikizumab remitters, 70% maintained long-term clinical remission at Week 152, and response rates for major efficacy endpoints (including endoscopic remission, histologic-endoscopic mucosal remission, corticosteroid-free remission and clinical response) ranged from 63% to 85%.

About the Mirikizumab Crohn's Disease Program
VIVID-1 was a Phase 3, randomized, double-blind, treat-through study that evaluated the safety and efficacy of mirikizumab compared with placebo and an active control (ustekinumab) in adults with moderately to severely active Crohn's disease. Patients randomized to mirikizumab were administered 900 mg of mirikizumab intravenously every four weeks from Week 0-12, then 300 mg subcutaneously every four weeks from Weeks 12-52. In this study, 49% of patients taking mirikizumab or placebo had experienced a prior biologic failure.

SERENITY, the Phase 2, multi-center, randomized, parallel-arm, double-blind, placebo-controlled trial was designed to assess the safety and efficacy of mirikizumab in patients with moderately to severely active Crohn's disease. At baseline, participants were randomized with a 2:1:1:2 allocation across four treatment arms (placebo, mirikizumab 200 mg, mirikizumab 600 mg and mirikizumab 1000 mg). The primary endpoint was endoscopic response as determined by the proportion of participants achieving at least 50% reduction from baseline on the Simple Endoscopic Score for Crohn's Disease (SES-CD) at Week 12. In May 2019, Lilly reported Phase 2 results showing more patients with moderate to severe Crohn's disease receiving mirikizumab compared with placebo achieved clinical response and remission at 12 weeks. Overall, the safety profile at 12 weeks was consistent with that of mirikizumab in studies of ulcerative colitis and with the IL23p19 class.

VIVID-2, the ongoing long-term Phase 3 extension of SERENITY and the VIVID-1 study, evaluated the efficacy and safety of mirikizumab in patients with Crohn's disease for up to five years. Using a modified non-responder imputation analysis to handle discontinuation and missing data, 61% and 44% achieved endoscopic response and endoscopic remission, respectively, at Week 156. In addition, 79% and 72% achieved clinical response and clinical remission, respectively, at Week 156.

Indications and Usage for Omvoh® (mirikizumab-mrkz) (in the United States)

Omvoh® is indicated for the treatment of moderately to severely active ulcerative colitis in adults.

Important Safety Information for Omvoh (mirikizumab-mrkz)

CONTRAINDICATIONS - Omvoh is contraindicated in patients with a history of serious hypersensitivity reaction to mirikizumab-mrkz or any of the excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions
Serious hypersensitivity reactions, including anaphylaxis during intravenous infusion, have been reported with Omvoh administration. Infusion-related hypersensitivity reactions, including mucocutaneous erythema and pruritus, were reported during induction. If a severe hypersensitivity reaction occurs, discontinue Omvoh immediately and initiate appropriate treatment.

Infections
Omvoh may increase the risk of infection. Do not initiate treatment with Omvoh in patients with a clinically important active infection until the infection resolves or is adequately treated. In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing Omvoh. Instruct patients to seek medical advice if signs or symptoms of clinically important acute or chronic infection occur. If a serious infection develops or an infection is not responding to standard therapy, monitor the patient closely and do not administer Omvoh until the infection resolves.

Tuberculosis
Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with Omvoh. Do not administer Omvoh to patients with active TB infection. Initiate treatment of latent TB prior to administering Omvoh. Consider anti-TB therapy prior to initiation of Omvoh in patients with a history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor patients for signs and symptoms of active TB during and after Omvoh treatment. In clinical trials, subjects were excluded if they had evidence of active TB, a history of active TB, or were diagnosed with latent TB at

screening.

Hepatotoxicity
Drug-induced liver injury in conjunction with pruritus was reported in a clinical trial patient following a longer than recommended induction regimen. Omvoh was discontinued. Liver test abnormalities eventually returned to baseline. Evaluate liver enzymes and bilirubin at baseline and for at least 24 weeks of treatment. Monitor thereafter according to routine patient management. Consider other treatment options in patients with evidence of liver cirrhosis. Prompt investigation of the cause of liver enzyme elevation is recommended to identify potential cases of drug-induced liver injury. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded. Instruct patients to seek immediate medical attention if they experience symptoms suggestive of hepatic dysfunction.

Immunizations
Avoid use of live vaccines in patients treated with Omvoh. Medications that interact with the immune system may increase the risk of infection following administration of live vaccines. Prior to initiating therapy, complete all age-appropriate vaccinations according to current immunization guidelines. No data are available on the response to live or non-live vaccines in patients treated with Omvoh.

ADVERSE REACTIONS
Most common adverse reactions (≥2%) associated with Omvoh treatment are upper respiratory tract infections and arthralgia during induction, and upper respiratory tract infections, injection site reactions, arthralgia, rash, headache, and herpes viral infection during maintenance.

During induction, Omvoh is available as a single dose vial for intravenous infusion containing 300 mg/15 mL that is administered in a healthcare facility. During maintenance, Omvoh is available as a one-time use prefilled pen or syringe with 100 mg/mL for subcutaneous injections. See Prescribing Information for dosing information.

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Please click for Prescribing Information and Medication Guide for Omvoh. Please click for Instructions for Use included with the device.

About Omvoh®
Omvoh® (mirikizumab-mrkz) is an interleukin-23p19 antagonist indicated for the treatment of moderately to severely active ulcerative colitis in adults. Omvoh selectively targets the p19 subunit of IL-23 and inhibits the IL-23 pathway. Inflammation due to over-activation of the IL-23 pathway plays a critical role in the pathogenesis of ulcerative colitis. Treatment of ulcerative colitis with Omvoh starts with 300-mg IV infusions, once every four weeks for a total of three infusions, and transitions to two, 100-mg subcutaneous injections every four weeks during maintenance treatment.

About Lilly
Lilly is a medicine company turning science into healing to make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help tens of millions of people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges: redefining diabetes care; treating obesity and curtailing its most devastating long-term effects; advancing the fight against Alzheimer's disease; providing solutions to some of the most debilitating immune system disorders; and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit Lilly.com and Lilly.com/news, or follow us on Facebook, Instagram and LinkedIn. P-LLY

Cautionary Statement Regarding Forward-Looking Statements
This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about mirikizumab as a potential treatment for people with moderately to severely active ulcerative colitis and Crohn's disease and the timeline for future readouts, presentations, and other milestones relating to mirikizumab and its clinical trials, and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date, that mirikizumab will prove to be a safe and effective treatment for Crohn's disease, that mirikizumab will receive regulatory approval, or that Lilly will execute its strategy as expected. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

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