FDA Approves Lilly's Omvoh™ (mirikizumab-mrkz), A First-in-Class Treatment for Adults with Moderately to Severely Active Ulcerative Colitis

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Omvoh achieved primary and key secondary endpoints, including sustained clinical remission in pivotal trials

Omvoh delivered significant improvement in bowel urgency, reported by people with UC as one of the most disruptive symptoms

Lilly's first approved treatment for a type of inflammatory bowel disease

INDIANAPOLIS, Oct. 26, 2023 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that the U.S. Food and Drug Administration (FDA) has approved Omvoh™ (mirikizumab-mrkz) infusion (300 mg/15 mL)/injection (100 mg/mL), the first and only interleukin-23p19 (IL-23p19) antagonist for the treatment of moderately to severely active ulcerative colitis (UC) in adults.

Marking a significant milestone, Omvoh is the only UC treatment that selectively targets the p19 subunit of IL-23, which plays a role in inflammation related to UC.

"I see many people with ulcerative colitis who previously tried other biologic treatments, and they are still searching for an effective option that can offer rapid and lasting improvements," 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. "Today's approval represents a novel scientific advancement, providing a treatment that may offer relief from three key symptoms—stool frequency, rectal bleeding and bowel urgency—regardless of past biologic use."

The approval was based on results from the LUCENT program, which included two randomized, double-blind, placebo-controlled Phase 3 clinical trials consisting of one 12-week induction study (UC-1) and one 40-week maintenance study (UC-2) for 52 weeks of continuous treatment. All patients in the LUCENT program had past treatments, including biologic treatments, that did not work, stopped working or that they could not tolerate.

After 12 weeks of treatment with Omvoh, nearly two-thirds (65%) of patients achieved clinical response and nearly one-fourth (24%) achieved clinical remission compared to placebo (43% and 15%, for clinical response and clinical remission, respectively). Among those who achieved clinical response at 12 weeks, Omvoh demonstrated consistent efficacy across subgroups, with 51% of all patients and 45% of patients who failed prior treatment with a biologic or Janus kinase inhibitor (JAKi) achieving clinical remission at one year compared to placebo (27% and 15%, respectively). Among those who achieved clinical response at 12 weeks, one-half (50%) achieved steroid-free clinical remission at one year, compared to placebo (27%). Per a post-hoc analysis, nearly all patients (99%) who achieved clinical remission at one year were steroid-free. Patients in steroid-free clinical remission were steroid-free for at least three months prior to the end of the 52-week assessment. Among those who achieved clinical remission at 12 weeks, approximately two-thirds (66%) of patients maintained clinical remission through one year of continuous treatment compared to placebo (40%).

Rapid improvement of symptoms, such as rectal bleeding and stool frequency, were observed as early as three weeks in patients treated with Omvoh. Notably, the LUCENT trials were the first and only to use the patient-centric, Urgency Numeric Rating Scale (NRS) of 0-10, with zero being no bowel urgency and 10 being worst possible bowel urgency. At baseline, patients had a median Urgency NRS weekly average score of 7. Among patients who had an Urgency NRS weekly average score ≥3 at baseline and responded to induction therapy with Omvoh, a significantly greater proportion of patients (39%) treated with Omvoh achieved a weekly average score of 0 to 1 at one year, compared to placebo (23%).

"Bowel urgency is one of the most disruptive symptoms for patients with ulcerative colitis," said Michael Osso, president and chief executive officer, Crohn's & Colitis Foundation. "Today's approval of Omvoh offers new hope for those who have tried other therapies and still find themselves making accommodations for the uncertainty of bowel urgency-related accidents and other symptoms associated with ulcerative colitis."

Patients taking Omvoh were less likely to discontinue treatment due to adverse events (1.6% in UC-1 and 1.5% in UC-2) compared to placebo (7.2% in UC-1 and 8.3% in UC-2). The most common adverse reactions (reported in at least 2% of subjects at a higher frequency than placebo) associated with Omvoh treatment were upper respiratory infections, injection site reactions, arthralgia, rash, headache and herpes viral infection. The labeling for Omvoh contains warnings and precautions related to hypersensitivity reactions, risk of infection, tuberculosis, hepatotoxicity and immunizations. See Important Safety Information below and full Prescribing Information.

"Omvoh addresses key symptoms that matter most to patients and represents our patient-centric approach to treatment innovation," said Patrik Jonsson, Lilly executive vice president, president of Lilly Immunology and Lilly USA, and chief customer officer. "Omvoh's approval is a significant moment for Lilly's growing Immunology portfolio, and we are excited to work with the gastroenterology community to set high expectations of care for people living with ulcerative colitis."

Omvoh will be available in the United States in the coming weeks. Lilly received approval for Omvoh in Japan and the European Union this year and expects regulatory decisions in additional markets around the world in the coming months.

View the Omvoh brand logo here.

About the LUCENT Clinical Trial Program
Omvoh was studied in two, Phase 3 clinical trials which evaluated the efficacy and safety of Omvoh 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 UC-1 and maintenance UC-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 UC-1 had failed at least one biologic and 3% had failed a JAKi and 57% were biologic and JAKi-naïve.

- UC-1 was a 12-week induction study (n=1,279) that was followed by UC-2, a 40-week maintenance study (n=581), for a total of 52 weeks of continuous therapy. In UC-1, patients were randomized 3:1 to receive Omvoh (300 mg) IV or placebo IV every 4 weeks for 12 weeks. Patients who achieved clinical response at Week 12 with Omvoh in UC-1 were re-randomized 2:1 to receive Omvoh (200 mg) subcutaneous injection or placebo subcutaneous injection every 4 weeks for another 40 weeks in UC-2.
- The primary endpoint of UC-1 and UC-2 was clinical remission at Week 12 and Week 52, respectively. The secondary endpoints of UC-1 were clinical response, endoscopic improvement, and histologic-endoscopic mucosal improvement (HEMI) at 12 weeks. The secondary endpoints of UC-2 were endoscopic improvement, maintenance of clinical remission in subjects who achieved clinical remission at 12 weeks, corticosteroid-free clinical remission, HEMI and bowel urgency improvement (defined as patients achieving a weekly average urgency NRS of 0 to 1) at 40 weeks (a total of 52 weeks of treatment).
- Omvoh achieved primary and key secondary endpoints, including sustained clinical remission in pivotal trials.
- Of patients treated with Omvoh at 12 weeks in UC-1:
    - 24% achieved clinical remission compared to 15% of placebo (n=191/795 vs, n=39/267)
    - 65% achieved a clinical response compared to 43% of placebo (n=514/795 vs, n=116/267)
    - 34% achieved endoscopic improvement compared to 21% of placebo (n=274/795 vs, n=56/267)
    - 25% achieved histologic-endoscopic mucosal improvement compared to 14% of placebo (n=200/795 vs, n=38/267)
- Of patients treated with Omvoh at 40 weeks (a total of 52 weeks of treatment) in UC-2:
    - 51% achieved clinical remission compared to 27% of placebo (n=171/337 vs, n=45/169)
        - In a post-hoc analysis, 99% (n=169/171) of patients who achieved clinical remission at one year of treatment were steroid-free for at least the previous 12 weeks.
    - 50% achieved corticosteroid-free clinical remission compared to 27% of placebo (n=169/337 vs, n=45/169). Patients in steroid-free remission stopped using corticosteroids for at least the previous 12 weeks prior to the one-year assessment.
    - 58% achieved endoscopic improvement compared to 30% of placebo (n=195/337 vs, n=50/169)
    - 66% achieved maintenance of clinical remission in patients who achieved clinical remission at Week 12 compared to 40% of placebo (n=84/128 vs, n=25/62)
    - 43% achieved histologic-endoscopic mucosal improvement compared to 22% of placebo (n=145/337 vs, n=37/169)
- Bowel urgency was assessed during UC-1 and UC-2 with an Urgency Numeric Rating Scale (NRS) of 0 to 10. Among patients who had an Urgency NRS weekly average score ≥3 at baseline and responded to induction therapy with Omvoh in UC-1, a significantly greater proportion of subjects treated with Omvoh achieved an Urgency NRS weekly average score of 0 to 1 (39% [n=119/307] versus 23% [n=37/160]) at Week 40 in UC-2. Urgency NRS weekly average scores of 0 to 1 were also observed in a greater proportion of subjects treated with Omvoh compared to placebo at 12 weeks in UC-1.
- Decreases in rectal bleeding and stool frequency subscores were observed as early as three weeks in subjects treated with Omvoh compared to placebo.
- Adverse reactions were reported in at least 2% of subjects at a higher frequency than placebo during induction and maintenance trials:
    - Induction
        - 8% of patients taking Omvoh (n=72/958) experienced upper respiratory infections versus 6% on placebo (n=20/321) in UC-1
        - 2% of patients taking Omvoh (n=20/958) experienced arthralgia versus 1% on placebo (n=4/321) in UC-2
    - Maintenance
        - 14% of patients taking Omvoh (n=53/389) experienced upper respiratory infections versus 12% on placebo (n=23/192)
        - 9% of patients taking Omvoh (n=34/389) experienced injection-site reactions versus 4% on placebo (n=8/192)
        - 7% of patients taking Omvoh (n=26/389) experienced arthralgia versus 4% on placebo (n=8/192)
        - 4% of patients taking Omvoh (n=16/389) experienced rash versus 1% on placebo (n=2/192)
        - 4% of patients taking Omvoh (n=16/389) experienced headache versus 1% on placebo (n=2/192)
        - 2% of patients taking Omvoh (n=9/389) experienced herpes viral infection versus 1% on placebo (n=1/192)

Lilly is committed to helping people access the medicines they are prescribed and will work with insurers, health systems and providers to help enable patient access to Omvoh. Lilly will offer an Omvoh savings card for people who qualify. Patients or healthcare professionals with questions about Omvoh can visit www.Omvoh.com or call The Lilly Answers Center at 1-800-LillyRx (1-800-545-5979).

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.

MR HCP ISI UC APP

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 UC. Treatment with Omvoh starts with 300-mg IV infusions, once a week every four weeks for a total of three infusions, and transitions to two, 100-mg subcutaneous self-injections every four weeks during maintenance treatment.

About Lilly
Lilly unites caring with discovery to create medicines that make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help more than 51 million 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, Twitter and LinkedIn. P-LLY

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

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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 Omvoh as a treatment for people with moderately to severely active ulcerative colitis 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, or that Omvoh will receive additional regulatory approvals, or be commercially successful. 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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