More than one-half of patients with Crohn's disease treated with Lilly's mirikizumab achieved clinical remission at one year, including patients with previous biologic failure

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Nearly one-half of patients on mirikizumab achieved endoscopic response at 52 weeks; most of these patients were also in clinical remission

INDIANAPOLIS, May 21, 2024 /PRNewswire/ -- In Eli Lilly and Company's (NYSE: LLY) pivotal Phase 3 VIVID-1 study, patients with moderately to severely active Crohn's disease, with or without previous biologic failure, achieved statistically significant and clinically meaningful improvements across multiple clinical and endoscopic endpoints at one year with mirikizumab compared to placebo. Data from this study – the first Phase 3 treat-through data reported for an IL23p19 antibody – will be presented at Digestive Disease Week® (DDW), held in Washington, D.C. from May 18-21.

"Crohn's disease is a complex condition that, if untreated, may result in irreversible damage to the digestive tract. Mirikizumab patients achieved high rates of combined clinical remission and endoscopic response, two important treatment targets that are difficult to achieve in the same patient, at one year. This is particularly impressive for patients with previous biologic failure who are generally considered hard-to-treat," 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.* "Consistent results across patient populations underscore the potential impact of mirikizumab in individuals living with this condition."

Crohn's disease is a chronic, inflammatory bowel disease associated with progressive bowel damage, disability and decreased health-related quality of life. If not adequately controlled, it may lead to complications that require hospitalization and surgical intervention. A substantial proportion of patients do not experience adequate treatment outcomes, have secondary loss of response to maintenance therapy or do not tolerate existing therapies, including biologic agents. Patients with previous biologic failure may be more difficult to treat.

As previously reported, mirikizumab achieved both co-primary endpoints and all major secondary endpoints at Week 52 compared to placebo ($p<0.000001$), including:

- Proportion of participants achieving clinical response by patient reported outcomes (PRO)** at Week 12 and clinical remission (defined as a Crohn's Disease Activity Index [CDAI] Total Score <150) at Week 52 compared to placebo
- Proportion of participants achieving clinical response by PRO at Week 12 and endoscopic response (defined as ≥50% reduction from baseline in Simple Endoscopic Score – Crohn's Disease [SES-CD] Total Score) at Week 52 compared to placebo

Consistent response rates and treatment effects were observed in patients with no prior biologic failure (bio-naïve) and harder-to-treat patients with previous biologic failure:

- 39.3% of bio-naïve and 36.7% of bio-failed patients taking mirikizumab achieved composite Week 12 PRO clinical response and Week 52 endoscopic response compared to 11.8% and 6.2% of placebo, respectively
- 47.3% of bio-naïve and 43.4% of bio-failed patients taking mirikizumab achieved composite Week 12 PRO clinical response and Week 52 clinical remission by CDAI, compared to 26.5% and 12.4% of placebo, respectively

At one year, clinical remission and endoscopic response were achieved by 54.1% and 48.4% of patients on mirikizumab, respectively. Notably, of the patients who received mirikizumab, 56.7% of bio-naïve and 51.2% of bio-failed patients achieved clinical remission at Week 52.

Patients taking mirikizumab achieved combined Week 52 clinical remission and endoscopic response at nominally statistically significant higher rates compared to patients on ustekinumab (34.4% versus 27.9%), with greater difference among those patients with previous biologic failure. At multiple time points, including Week 52, mirikizumab also achieved nominal statistical significance compared to ustekinumab in decreasing fecal calprotectin and C-reactive protein, two key biomarkers for inflammation. Superiority to ustekinumab was not achieved for endoscopic response.

Additionally, in the population with previous biologic failure, numerically greater rates were observed with mirikizumab compared to ustekinumab for endoscopic response, endoscopic remission (SES-CD total score ≤4, a ≥2-point reduction from baseline and no subscore >1 in any individual variable), and corticosteroid-free CDAI clinical remission at Week 52. These observed differences were not statistically significant.

The overall safety profile of mirikizumab in patients with moderately to severely active Crohn's disease was consistent with the known safety profile in patients with ulcerative colitis. The frequency of serious adverse events was greater in placebo than mirikizumab. The most common adverse events were COVID-19, anemia, arthralgia, headache, upper respiratory tract infection, nasopharyngitis and injection site reaction.

"After one year of treatment, more than one-half of patients treated with mirikizumab achieved clinical remission and nearly one-half achieved endoscopic response. Remarkably, the majority of patients who achieved either of these endpoints, achieved both together," said Mark Genovese, M.D., senior vice president of Lilly Immunology development. "Lilly is committed to developing innovative treatments, like mirikizumab, that may improve upon the standard of care for people impacted by inflammatory bowel disease and immune-mediated diseases."

Lilly submitted a supplemental Biologics License Application for mirikizumab in Crohn's disease to the U.S. Food and Drug Administration and European Medicines Agency this year. Additional global regulatory submissions are planned.

Lilly is committed to finding solutions to elevate care and improve treatment outcomes for people living with inflammatory bowel diseases. Lilly has

ongoing studies to evaluate the efficacy and safety of mirikizumab in other populations with Crohn's disease, including a Phase 3 study in pediatric patients (NCT05509777) and a long-term extension study of patients with moderately to severely active Crohn's disease (NCT04232553). Omvoh ™(mirikizumab-mrkz) is approved for the treatment of moderately to severely active ulcerative colitis (UC) in adults and has additional ongoing trials in UC, including a study in pediatric patients (NCT05784246) and a study to evaluate the long-term efficacy and safety of mirikizumab in adults (NCT03519945). Lilly is continuing to lead the science with an open-label UC trial studying two new endpoints in the assessment of bowel urgency with frequency and deferral time, both of which impact the quality of life for patients (NCT05767021).

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

About the VIVID-1 Clinical Trial 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.

** Clinical response by PRO is defined as ≥30% decrease in stool frequency and/or abdominal pain, and neither score worse than baseline.

Indications and Usage for Omvoh™ (mirikizumab-mrkz) (inthe 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 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.

Omvoh™ and its delivery device base are trademarks owned by Eli Lilly and Company.

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 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 and LinkedIn. P-LLY

About Digestive Disease Week®

Digestive Disease Week® (DDW) is the largest international gathering of physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA), the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT), DDW is an in-person and online meeting from May 18-21, 2024. The meeting showcases more than 5,600 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology. More information can be found at www.ddw.org.

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 Crohn's disease 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 mirikizumab will receive FDA and other additional regulatory approvals, or that it will 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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