Lilly's Mirikizumab Met Primary Endpoint and Key Secondary Endpoints in Phase 2 Study, Including Reductions of Gastrointestinal Lesions

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The safety and efficacy data from the induction period of the Phase 2 trial encourage Lilly to initiate a Phase 3 trial for mirikizumab for the treatment of Crohn's disease later this year

INDIANAPOLIS, May 21, 2019 /PRNewswire/ -- In an oral presentation from the Digestive Disease Week medical conference in San Diego, California today, Eli Lilly and Company (NYSE: LLY) announced new safety and efficacy data for mirikizumab in patients with moderately- to severely active Crohn's disease. Patients treated with mirikizumab in the SERENITY Phase 2 study achieved significant reductions in clinical and endoscopic measures of disease activity at 12 weeks compared to placebo. The maintenance phase of this study is ongoing.

In this study, patients with moderately- to severely active Crohn's disease were randomized to receive either placebo or one of three doses of mirikizumab, which is an investigational antibody that targets the p19 subunit of interleukin 23. The primary endpoint evaluated mirikizumab versus placebo on endoscopic response, which was defined as a 50 percent reduction from baseline in the severity of each patient's disease, as measured by the Simple Endoscopic Score for Crohn's Disease (SES-CD)[1]. Secondary endpoints included clinical remission as measured by Patient Reported Outcomes (PRO remission), endoscopic remission, and safety.

At 12 weeks, treatment with mirikizumab achieved the following results:

- **Endoscopic response**: Rates of endoscopic response, which was defined as a 50 percent reduction from baseline in the severity of each patient's disease, as measured by the Simple Endoscopic Score for Crohn's Disease (SES-CD), were significantly greater for patients receiving all mirikizumab doses compared to placebo: 25.8 percent, 37.5 percent, and 43.8 percent of patients in the 200 mg, 600 mg, and 1000 mg groups, respectively, achieved response compared to 10.9 percent of placebo patients.
- **Endoscopic remission**: Endoscopic remission, which was defined as an ileal-colonic SES-CD score of less than 4, an isolated ileal SES-CD score of less than 2, and no subscore greater than 1, was achieved in 6.5 percent, 15.6 percent and 20.3 percent of patients treated with mirikizumab 200 mg, 600 mg and 1000 mg respectively, versus 1.6 percent of patients treated with placebo.
- **PRO remission**: PRO remission, which was defined as an average daily stool frequency of less than or equal to 2.5 and abdominal pain less than or equal to 1, was achieved in 12.9 percent, 28.1 percent and 21.9 percent of patients treated with mirikizumab 200 mg, 600 mg and 1000 mg, respectively, compared to 6.3 percent of patients treated with placebo.
- **Safety assessment:** Across the 3 mirikizumab treatment groups, 5 patients (4 percent) reported one or more serious adverse event (SAE), and 81 patients (64 percent) reported one or more treatment emergent adverse event (TEAE) during the induction phase of the trial. The most commonly reported TEAEs were headache, weight gain, and nasopharyngitis. Among the placebo group, 7 patients (11 percent) reported one or more SAE, and 45 patients (70 percent) reported one or more TEAE.

Bruce E. Sands, MD, MS, Dr. Burrill B. Crohn Professor of Medicine, Chief of the Dr. Henry D. Janowitz Division of Gastroenterology at the Icahn School of Medicine at Mount Sinai and lead investigator of the study, said "Mirikizimab may have the potential to be a valuable addition to the available treatment options for Crohn's disease because of the endoscopic and symptomatic responses seen in this trial across all doses."

Lotus Mallbris, M.D., Ph.D., vice president of immunology development at Lilly, said "Following last year's presentation of positive Phase 2 results for mirikizumab for the treatment of moderate- to severe ulcerative colitis, we are excited to return to DDW to present more positive data for mirikizumab in patients with chronic, inflammatory gastrointestinal conditions. As we continue to advance the science of gastroenterology, we are hopeful that mirikizumab helps us raise the standard and make remission possible for people living with immune-mediated diseases like Crohn's disease. Physicians want objective signs of improvement to be able to convey to patients that they are getting better, and data from this study suggest mirikizumab may address this need. We look forward to initiating Phase 3 trials to further evaluate mirikizumab's benefit-risk profile for the treatment of Crohn's disease."

About Mirikizumab

Mirikizumab is an investigational monoclonal antibody that binds to the p19 subunit of interleukin 23. Mirikizumab is being studied for the treatment of immune diseases, including psoriasis, ulcerative colitis and Crohn's disease.

About Crohn's Disease

Crohn's disease, which is a form of inflammatory bowel disease (IBD), is a chronic immune-mediated condition of the gastrointestinal (GI) tract. Crohn's most commonly affects the end of the small bowel (the ileum) and the beginning of the colon, but it may affect any part of the GI tract, from the

mouth to the anus. IBD, which is inclusive of Crohn's disease and ulcerative colitis, affects 10 million people worldwide.

About the Mirikizumab Phase 2 Trial in Crohn's Disease
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 (mirikizumab 200 mg, mirikizumab 600 mg, mirikizumab 1000 mg, and placebo). The primary endpoint measured endoscopic response as determined by the proportion of participants achieving 50 percent reduction from baseline on the Simple Endoscopic Score for Crohn's Disease (SES-CD) at Week 12. Secondary endpoints included clinical remission as measured by Patient Reported Outcomes (PRO remission), endoscopic remission, and safety.

About Lilly in Immunology
Lilly is bringing our heritage of championing groundbreaking, novel science to immunology and is driven to change what's possible for people living with autoimmune diseases. There are still significant unmet needs, as well as personal and societal costs, for people living with a variety of autoimmune diseases and our goal is to minimize the burden of disease. Lilly is investing in leading-edge clinical approaches across our immunology portfolio in hopes of transforming the autoimmune disease treatment experience. We've built a deep pipeline and are focused on advancing cutting-edge science to find new treatments that offer meaningful improvements to support the people and the communities we serve.

About Eli Lilly and Company
Lilly is a global healthcare leader that unites caring with discovery to create medicines that make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com and www.lilly.com/newsroom/social-channels. P-LLY

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 moderately- to severely active Crohn's disease and moderate- to severe ulcerative colitis, and reflects Lilly's current belief. As with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with the results to date, that mirikizumab will receive additional regulatory approvals, or be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertake no duty to update forward-looking statements to reflect events after the date of this release.

[1] "The Simple Endoscopic Score for Crohn's Disease (SES-CD) assesses the size of mucosal ulcers, the [area of the] ulcerated surface, the endoscopic extension and the presence of stenosis," which in Crohn's disease is the pathological narrowing of the gastrointestinal tract. http://www.igibdscores.it/en/info-sescd.html Accessed, May 17, 2019.

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