Lilly's Galcanezumab Meets Primary Endpoint in Phase 3 Study Evaluating Galcanezumab for the Prevention of Episodic Cluster Headache

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INDIANAPOLIS, May 15, 2018 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that galcanezumab met its primary endpoint in a Phase 3 study of patients with episodic cluster headache, demonstrating statistically significant differences in the reduction of weekly cluster headache attacks compared to placebo across weeks one to three of the two-month, double-blind treatment period. A statistically significantly greater percentage of patients treated with galcanezumab also achieved at least a 50 percent reduction in weekly cluster headache attacks compared to placebo at Week 3, the gated secondary endpoint.

The observed safety and tolerability profile was consistent with previous studies that evaluated galcanezumab for the prevention of migraine. In this study, 8 percent of patients treated with galcanezumab discontinued treatment during the study compared to 21 percent of patients treated with placebo. Four percent of patients treated with galcanezumab discontinued treatment during the study due to adverse events compared to 2 percent of patients treated with placebo. Discontinuations due to lack of efficacy occurred in 2 percent of patients treated with galcanezumab, compared to 14 percent of patients treated with placebo.

"Cluster headache can be difficult to evaluate in clinical studies, which has contributed to few available treatment options for cluster headache, often considered the most severe pain one can experience," said Christi Shaw, president of Lilly Bio-Medicines. "The positive results in episodic cluster headache are truly a landmark moment—both for people living with cluster headache and for our researchers at Lilly, many of whom have spent more than two decades researching and developing innovative, non-opioid treatment options for diseases like migraine and cluster headache."

Lilly also conducted a separate Phase 3 study for patients with chronic cluster headache, which represents 10 to 15 percent of cluster headache cases.[1] This study did not meet its primary endpoint.

Based on results from the episodic cluster headache trial, Lilly is working with regulatory agencies around the world to determine the best path forward. Episodic cluster headache represents 85 to 90 percent of cluster headache cases.[1]

These studies, which evaluated a combined 343 patients, are the largest controlled preventive trials conducted in cluster headache to date.

"It is hard to articulate the devastating impact that cluster headache can have on those of us living with the disease. Many people living with cluster headache spend years searching for effective treatment options to help ease an excruciating level of pain," said Bob Wold, a patient living with cluster headache and founder of Clusterbusters, Inc. "We are very excited by these results and galcanezumab's potential as a new treatment option for people living with cluster headache, many of whom have spent years feeling ignored and alone in their struggle."

Episodic Cluster Headache Study Results

The episodic cluster headache study included a two-month treatment period comparing galcanezumab to placebo. Patients with episodic cluster headache treated with galcanezumab (300 mg once-monthly) experienced statistically significant differences in the reduction of weekly cluster headache attacks compared to patients treated with placebo across weeks one to three of the two-month, double-blind treatment period (-8.7 for galcanezumab compared to -5.2 for placebo, p=0.036), the primary endpoint of the study.

In May 2017, Lilly announced positive data from three Phase 3 studies (EVOLVE-1, EVOLVE-2 and REGAIN) evaluating galcanezumab for the treatment of chronic and episodic migraine. In these studies, galcanezumab demonstrated statistically significant reductions in the number of monthly migraine headache days compared to placebo at both studied doses (120 mg and 240 mg once-monthly).

The FDA is currently reviewing galcanezumab for the prevention of migraine in adults. A decision is expected in the third quarter of 2018.

About the Phase 3 Studies
The episodic cluster headache study was a two-month Phase 3, randomized, double-blind, placebo-controlled global trial evaluating the safety and efficacy of galcanezumab (300 mg once-monthly) administered subcutaneously compared with placebo in 106 patients with episodic cluster headache. Patients who participated in this trial had an average of 17.5 cluster headache attacks per week at baseline. The primary endpoint was the overall mean change from baseline in weekly cluster headache attack frequency across weeks one to three with galcanezumab compared with placebo.

The chronic cluster headache study was a three-month Phase 3, randomized, double-blind, placebo-controlled global trial evaluating the safety and efficacy of galcanezumab (300 mg once-monthly) administered subcutaneously compared with placebo in 237 patients with chronic cluster headache. Patients who participated in this trial had an average of 18.8 cluster headache attacks per week at baseline. The primary endpoint was the overall mean change from baseline in weekly cluster headache attack frequency during the three-month, double-blind treatment phase with galcanezumab compared with placebo. In this study, patients who completed the three-month double-blind period could choose to enter an ongoing 12-month, open-label extension phase and receive galcanezumab during that time.

About Cluster Headache
Cluster headache is an uncommon, disabling headache disorder composed of recurrent "attacks" of intense headaches on one side of the head, frequently associated with pain behind or around one eye, restlessness and agitation.[1,2] Cluster headache attacks typically last between 15 to 180 minutes, occurring near daily to multiple times daily during a cluster period.[1] It is estimated that 85 to 90 percent of cluster headache cases are classified as "episodic" with attacks occurring in periods that last from seven days to one year, separated by pain-free remission periods of one month or longer.[1] The remaining 10 to 15 percent are classified as "chronic" with attacks occurring for more than one year without a remission period, or with remission lasting less than one month.[1]

About Galcanezumab
Galcanezumab is a monoclonal antibody specifically designed to bind to and reduce the overactivity of calcitonin gene-related peptide (CGRP), which is believed to play a role in migraine and cluster headache. Galcanezumab is an investigational once-monthly, self-administered injection under evaluation for the prevention of migraine and cluster headache.

About Lilly's Commitment to Headache Disorders
For over 25 years, Lilly has been committed to helping people suffering from headache disorders, investigating more than a dozen different compounds for the treatment of migraine, cluster headache and other disabling headache disorders. These research programs have accelerated the understanding of these diseases and furthered the advancement of Lilly's comprehensive late-stage development programs studying galcanezumab for prevention of migraine and cluster headache, and lasmiditan for the acute treatment of migraine. Our goal is to make life better for people with headache disorders by offering comprehensive solutions to prevent or stop these disabling diseases. The combined clinical, academic and professional experience of our experts helps us to build our research portfolio, identify challenges for healthcare providers and pinpoint the needs of patients living with migraine and cluster headache.

About Eli Lilly and Company
Lilly is a global healthcare leader that unites caring with discovery to 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 galcanezumab as a potential treatment for patients with cluster headache and migraine and reflects Lilly's current belief. However, 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 or that galcanezumab will receive regulatory approvals. 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 undertakes no duty to update forward-looking statements to reflect events after the date of this release.

[1]Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition. *Cephalalgia.* 2013;33(9):629-808.
[2] Matharu M, Goadsby P. Trigeminal autonomic cephalgias. *Journal of Neurology, Neurosurgery, and Psychiatry*. 2002;72(Suppl II):ii19-ii26.

Refer to: Jen Dial; dial_jennifer_kay@lilly.com; 317-220-1172 (Lilly Bio-Medicines)
Kevin Hern; hern_kevin_r@lilly.com; 317-277-1838 (Investor Relations)

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