



AAN 2018: Lilly's Galcanezumab Significantly Reduced Monthly Migraine Headache Days in Patients with Migraine Who Previously Failed to Respond to Multiple Preventive Therapies

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INDIANAPOLIS, April 24, 2018 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today results from a post-hoc subgroup analysis which demonstrated efficacy of galcanezumab in patients with episodic and chronic migraine who previously failed to respond to two or more preventive therapies. Detailed results from a new subgroup analysis of three Phase 3 studies (EVOLVE-1, EVOLVE-2 and REGAIN) evaluating galcanezumab will be presented today as part of the "Best of Headache" platform session at the American Academy of Neurology (AAN) annual meeting in Los Angeles.



As previously reported, in these Phase 3 studies, the most commonly-reported adverse events were injection site reactions.

The U.S. Food and Drug Administration (FDA) is reviewing galcanezumab for the prevention of migraine in adults. A decision is expected in the third quarter of 2018.

"Despite available options, research has shown nearly half of patients with migraine discontinue a newly-prescribed preventive therapy within sixty days of prescription, often due to side effects or lack of efficacy," said Christi Shaw, president of Lilly Bio-Medicines. "The research presented today on galcanezumab validates Lilly's decades-long effort to bring a new therapy to market that has the potential to help people experience more migraine-free days, regardless of past preventive therapy use."

Analysis Design

EVOLVE-1, EVOLVE-2 and REGAIN were Phase 3, randomized, double-blind, placebo-controlled studies that evaluated the efficacy of two doses of galcanezumab (120 mg and 240 mg) in patients with episodic or chronic migraine. This subgroup analysis evaluated patients treated in the EVOLVE-1 and EVOLVE-2 studies for six months and the REGAIN study for three months. The subgroup analysis reviewed the mean change from baseline in the number of monthly migraine headache days and the proportion of patients with at least a 50 percent reduction in number of monthly migraine headache days in patients who previously failed two or more preventive therapies, using integrated EVOLVE-1 and EVOLVE-2 results and REGAIN results.

Analysis Results

In this subgroup analysis, patients treated with both doses of galcanezumab who previously failed two or more preventive therapies experienced a statistically significant reduction in the average number of monthly migraine headache days, and at least a 50 percent reduction in the number of migraine headache days, compared to patients treated with placebo.

- EVOLVE-1/ EVOLVE-2 (as evaluated over six months) for patients who failed at least 2 prior preventive medications (N=172):
 - **Average reduction in monthly migraine headache days:** 3.45 days for 120 mg and 3.85 days for 240 mg compared to 0.81 days for placebo, $p < 0.001$ for both dosing groups compared with placebo.
 - **Mean percentages of patients with at least 50 percent reduction in monthly migraine headache days:** 54.6% for 120 mg and 61.2% for 240 mg compared to 26.2% for placebo, $p < 0.001$ for both dosing groups compared with placebo.

- **REGAIN (as evaluated over three months) for patients who failed at least 2 prior preventive medications (N=323):**
 - **Average reduction in monthly migraine headache days:** 5.91 days for 120 mg and 3.30 days for 240 mg compared to 1.44 days for placebo, $p < 0.01$ for both dosing groups compared with placebo.
 - **Mean percentages of patients with at least 50 percent reduction in monthly migraine headache days:** 30.4% for 120 mg and 18.3% for 240 mg compared to 9.7% for placebo, $p < 0.05$ for both dosing groups compared with placebo.

Galcanezumab represents the first of three investigational, non-opioid treatments in development as part of Lilly's overall pain portfolio. The portfolio also includes lasmiditan for the acute treatment of migraine and tanezumab, developed in partnership with Pfizer, for the treatment of osteoarthritis pain, chronic low back pain and cancer pain.

Lilly also is evaluating galcanezumab for the treatment of cluster headache with Phase 3 trial results expected in the second quarter of 2018.

About the EVOLVE-1 and EVOLVE-2 Studies

EVOLVE-1 and EVOLVE-2 are six-month Phase 3, randomized, double-blind, placebo-controlled global trials evaluating the safety and efficacy of two doses of galcanezumab administered subcutaneously (120 mg or 240 mg once-monthly, following a 240 mg starting dose) compared with placebo in patients with episodic migraine. To be eligible for the trials, patients must have experienced between four and 14 migraine headache days per month. Patients that participated in these trials had an average of 9.1 migraine headache days per month at baseline. The primary endpoint was the mean change from baseline in monthly migraine headache days over the six-month, double-blind treatment phase.

About the REGAIN Study

REGAIN is a three-month Phase 3, randomized, double-blind, placebo-controlled global trial evaluating the safety and efficacy of two doses of galcanezumab administered subcutaneously (120 mg or 240 mg once-monthly, following a 240 mg starting dose) compared with placebo in patients with chronic migraine. To be eligible for the trial, patients must have experienced at least 15 headache days per month, of which at least eight met criteria for migraine. Patients that participated in the trial had an average of 19.4 migraine headache days per month at baseline. The primary endpoint was the mean change from baseline in monthly migraine headache days over the three-month, double-blind treatment phase. In REGAIN, galcanezumab was further evaluated for an additional nine months of an open-label extension phase following the three-month, double-blind treatment phase.

About Migraine

Migraine is a neurological disease characterized by recurrent episodes of severe headache accompanied by other symptoms including nausea, vomiting, sensitivity to light and sound, and changes in vision.^{[1],[2]} More than 36 million Americans have migraine, with three times more women affected by migraine compared to men.^[3] According to the Medical Expenditures Panel Survey, total annual healthcare costs associated with migraine are estimated to be as high as \$56 billion annually in the United States, yet it remains under-recognized and under-treated.^[4]

About Lilly in Migraine

For over 25 years, Lilly has been committed to helping people suffering from migraine, investigating more than a dozen different compounds for the treatment of migraine and disabling headache disorders. These research programs have accelerated understanding of this disease and advanced the development 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 migraine by offering comprehensive solutions to prevent or stop disabling migraine attacks. 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 Galcanezumab

Galcanezumab is a monoclonal antibody specifically designed to bind to and inhibit the activity 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 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 migraine and cluster headache; lasmiditan as a potential treatment for patients with migraine; and tanezumab as a potential treatment for patients with osteoarthritis pain, chronic low back pain, and cancer pain; 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, that galcanezumab will achieve its primary study endpoints or 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 Katsarava Z, Buse D, Manack A, et al. Defining the differences between episodic migraine and chronic migraine. *Current Pain Headache Reports*. 2012;16:86.

² Blumenfeld AM, Payne KA, Varon SF, et al. Disability, HRQOL, and resource use amongst chronic and episodic migraineurs. Results from the International Burden of Migraine Study (IBMS). *Cephalalgia* 2011;31:301.

³ Identifying and treating migraine. American Migraine Foundation website. <https://americanmigraine.org/understanding-migraine/identifying-treating-migraine/>. Last accessed March 28, 2018.

⁴ Raval AD, Shah A. National trends in direct health care expenditures among US adults with migraine: 2004 to 2013. *Journal of Pain*. 2017;57:60.

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