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Lilly's Galcanezumab Significantly Reduces Number of Migraine Headache Days for Patients with Migraine: New Results Presented at AHS

INDIANAPOLIS, June 10, 2017 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today positive results from three Phase 3 studies of galcanezumab, an investigational treatment for the prevention of episodic and chronic migraine, including late-breaking data on several key secondary endpoints for galcanezumab compared to placebo at both studied doses. Detailed results from these studies (EVOLVE-1, EVOLVE-2 and REGAIN) will be presented today at the American Headache Society (AHS) annual scientific meeting in Boston.

"The detailed Phase 3 results presented today represent a crucial step forward for the millions of patients living with migraine who have not yet tried, or found, an effective preventive therapy," said Christi Shaw, president of Lilly Bio-Medicines. "Following more than 25 years of research in migraine, Lilly is excited to help usher in a new era of preventive migraine therapies that may substantially improve the current standard of care for people living with migraine."

The observed safety and tolerability profile was consistent with findings from previous studies of galcanezumab. In these three studies, the most commonly-reported adverse events were injection site reactions.

Based on these results, Lilly will submit a Biologics License Application to the U.S. Food and Drug Administration (FDA) for galcanezumab in the second half of 2017, followed by submissions to other regulatory agencies around the world.

EVOLVE-1 and EVOLVE-2 Study Results

In both studies, over the six-month treatment period, patients with episodic migraine treated with galcanezumab 120 mg and 240 mg doses experienced a statistically significantly greater decrease in the average number of monthly migraine headache days compared to patients treated with placebo, with statistically significant improvements observed at each month starting at one month of treatment.

A statistically significantly greater percentage of patients treated with both doses of galcanezumab achieved at least a 50 percent, 75 percent and 100 percent reduction in the number of migraine headache days compared to placebo over the six-month treatment period, in both studies after multiplicity adjustment.

EVOLVE-1:

- | At least a 50 percent reduction: 62.3% for 120 mg and 60.9% for 240 mg compared to 38.6% for placebo, $p < 0.001$ for both dosing groups
- | At least a 75 percent reduction: 38.8% for 120 mg and 38.5% for 240 mg compared to 19.3% for placebo, $p < 0.001$ for both dosing groups
- | 100 percent reduction: 15.6% for 120 mg and 14.6% for 240 mg compared to 6.2% for placebo, $p < 0.001$ for both dosing groups

EVOLVE-2:

- | At least a 50 percent reduction: 59.3% for 120 mg and 56.5% for 240 mg compared to 36.0% for placebo, $p < 0.001$ for both dosing groups
- | At least a 75 percent reduction: 33.5% for 120 mg and 34.3% for 240 mg compared to 17.8% for placebo, $p < 0.001$ for both dosing groups
- | 100 percent reduction: 11.5% for 120 mg and 13.8% for 240 mg compared to 5.7% for placebo, $p < 0.001$ for both dosing groups

Patients treated with galcanezumab in both studies also had a statistically significantly greater reduction of monthly migraine headache days with acute medication use compared to placebo over the six-month treatment period after multiplicity adjustment.

- | EVOLVE-1: An average reduction of 4.0 days for 120 mg and 3.8 days for 240 mg compared to 2.15 days for placebo, $p < 0.001$ for both dosing groups

- EVOLVE-2: An average reduction of 3.7 days for 120 mg and 3.6 days for 240 mg compared to 1.85 days for placebo, $p < 0.001$ for both dosing groups

Patients treated with both doses of galcanezumab also saw statistically significant improvement in physical function compared to placebo over the six-month treatment period, as measured by both the Role Function-Restrictive (RF-R) domain score of the Migraine-Specific Quality of Life Questionnaire (MSQ) and the Patient Global Impression of Severity (PGI-S) rating after multiplicity adjustment.

REGAIN Study Results

Over the three-month treatment period, patients with chronic migraine treated with galcanezumab 120 mg and 240 mg doses experienced a statistically significantly greater decrease in the average number of monthly migraine headache days compared to patients treated with placebo. Statistically significant improvements for both doses of galcanezumab were observed at each month starting at one month of treatment.

A statistically significantly greater percentage of patients also achieved at least a 50 percent reduction in the number of migraine headache days compared to placebo over the three-month treatment period (27.6% for 120 mg and 27.5% for 240 mg compared to 15.4% for placebo, $p < 0.001$ for both dosing groups) after multiplicity adjustment.

Compared with placebo over the three-month treatment period, a statistically significantly higher percentage of patients treated with the 240 mg dose of galcanezumab achieved at least a 75 percent reduction in the number of migraine headache days (8.8% compared to 4.5% for placebo, $p < 0.001$) after multiplicity adjustment. Patients treated with the 240 mg dose of galcanezumab also achieved a statistically significantly greater reduction in the number of monthly migraine headache days with acute medication use compared to placebo over the three-month treatment period (an average of 4.3 days compared to 2.2 days for placebo, $p < 0.001$) after multiplicity adjustment.

Patients treated with 240 mg of galcanezumab also saw statistically significant improvement in physical function compared to placebo over the three-month treatment period, as measured by both the RF-R domain score of the MSQ and PGI-S rating after multiplicity adjustment.

Lilly will submit these findings for publication in peer-reviewed journals in the coming year.

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 1,773 patients with episodic migraine (858 patients in EVOLVE-1 and 915 patients in EVOLVE-2). 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 1,113 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 disabling neurological disease characterized by recurrent episodes of severe headache, and is often accompanied by other symptoms including nausea, vomiting, sensitivity to light and sound, and changes in vision.^{i ii} More than 38 million Americans have migraine, with three times more women affected by migraine compared to men.ⁱⁱⁱ Of the approximately 40 percent of patients suffering from migraine for whom prevention is appropriate, only 13 percent are currently receiving therapy.^{iv v vi} Results from the Second International Burden of Migraine study show that side effects of treatment play a role in this disconnect, with up to 53 percent of respondents discontinuing migraine prevention therapy because of side effects.^{vii} According to the Migraine Research Foundation, healthcare and lost productivity costs associated with migraine are estimated to be as high as \$36 billion annually in the U.S., yet it remains under-recognized and under-treated.^{3,7}

About Lilly in Migraine

Lilly has been committed to helping people suffering from migraine for over 25 years, investigating more than a dozen different compounds for the treatment of 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 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 this disabling disease. 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.

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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 chronic and episodic migraine and cluster headache, 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.

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iii Migraine facts. Migraine Research Foundation website. <http://migraineresearchfoundation.org/about-migraine/migraine-facts/>. Accessed May 24, 2017.

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