AHS 2018: Lilly's Emgality™ (galcanezumab-gnlm) Significantly Reduced Monthly Migraine Headache Days in Patients with Migraine Who Previously Failed BOTOX®* (onabotulinumtoxinA)

June 27, 2018

INDIANAPOLIS, June 27, 2018 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today results from a post-hoc analysis which demonstrated efficacy of Emgality ™ (galcanezumab-gnlm) in patients with episodic and chronic migraine who had previously failed preventive treatment with BOTOX®* (onabotulinumtoxinA). Detailed results from a post-hoc analysis of three Phase 3 studies (EVOLVE-1, EVOLVE-2 and REGAIN) will be presented as a late-breaking presentation on Saturday, June 30 at the American Headache Society (AHS) annual meeting in San Francisco.

Lilly also announced today that the intended brand name, Emgality ™, has been conditionally accepted by the U.S. Food and Drug Administration (FDA).

Emgality is a once-monthly, self-administered calcitonin gene-related peptide (CGRP) antibody currently under review by the FDA for the prevention of migraine in adults. A decision is expected by the end of September 2018.

"Despite currently available preventive options, nearly half of patients have discontinued these treatments due to side effects or lack of efficacy," said Christi Shaw, president of Lilly Bio-Medicines. "Over the last two decades, Lilly has recognized and invested in efforts to explore innovative potential treatments for primary headache disorders, including Emgality, which is specifically designed for the prevention of migraine and cluster headache."

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 Emgality (120 mg and 240 mg) in patients with episodic or chronic migraine. This post-hoc analysis evaluated patients treated in the EVOLVE-1 and EVOLVE-2 studies for six months and the REGAIN study for three months. The post-hoc 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 had previously failed BOTOX due to lack of efficacy or tolerability issues, using integrated EVOLVE-1 and EVOLVE-2 results and REGAIN results.

Analysis Results

In this subgroup analysis, patients treated with both doses of Emgality who previously failed preventive treatment with BOTOX experienced a statistically significantly greater reduction in the average number of monthly migraine headache days, and a statistically significantly greater percent (at least a 50 percent) reduction in the number of migraine headache days, compared to patients treated with placebo.

- **Average reduction in monthly migraine headache days:** 3.91 days for 120 mg and 5.27 days for 240 mg compared to 0.88 days for placebo, p≤0.03 for both dosing groups compared with placebo.
- **Mean percentages of patients with at least 50 percent reduction in monthly migraine headache days:** 41.3% for 120 mg and 47.5% for 240 mg compared to 9.4% for placebo, p≤0.02 for both dosing groups compared with placebo.

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

In this integrated analysis of patients who had previously failed treatment with BOTOX, patients treated with Emgality also had statistically significant improvements in quality of life, as measured by the Migraine-Specific Quality of Life Questionnaire (MSQ) and the Patient Global Impression of Severity (PGI-S) rating.

Emgality 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.

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 Emgality 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 Emgality 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, Emgality 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 Emgality ™
Emgality ™ (galcanezumab-gnlm) 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. Emgality 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 Emgality 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 Emgality 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 Emgality 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.

* BOTOX® is a registered trademark owned by Allergan, Inc.

[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://americanmigrainefoundation.org/understanding-migraine/identifying-treating-migraine/. Last accessed April 19, 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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