New England Journal of Medicine Publishes Positive Phase 3 Data for Emgality® (galcanezumab-gnlm) in Episodic Cluster Headache

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INDIANAPOLIS, July 11, 2019 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that the *New England Journal of Medicine* published positive Phase 3 study results of Emgality® (galcanezumab-gnlm) for the treatment of episodic cluster headache.[1] In this study, Emgality reduced the frequency of weekly cluster headache attacks across Weeks 1 to 3 compared to placebo.[1]The U.S. Food and Drug Administration (FDA) approval of Emgality for the treatment of episodic cluster headache in adults in June 2019 was based on these results.

"Cluster headache is one of the most severe primary headache disorders, with excruciatingly painful recurrent headache attacks and remarkably limited treatment options," said Peter Goadsby, M.D., PhD, Professor of Neurology at King's College London and lead author of the *New England Journal of Medicine* paper. "Publication of these results with Emgality, showing a reduction in the frequency of attacks caused by this debilitating neurologic disorder, is encouraging for both patients and physicians."

The study enrolled 106 patients who were randomized 1:1 to receive either 300 mg Emgality (via three 100 mg subcutaneous monthly injections) or placebo. Prior to enrollment, patients averaged 17.8 weekly cluster headache attacks in the Emgality arm (n=49) and 17.3 attacks in the placebo arm (n=57).[1] Results showed that patients taking Emgality had an average reduction of 8.7 weekly cluster headache attacks across Weeks 1 to 3 compared to a 5.2 average reduction in attacks for placebo (p=0.036). Additionally, 71.4% of patients treated with Emgality had their weekly cluster headache attack frequency reduced by 50% or more at Week 3, the key secondary endpoint, compared to 52.6% of placebo-treated patients (p=0.046).[1]

"People with episodic cluster headache describe attacks as the most excruciating pain they have ever known. Despite the severity of this disease, there has been limited innovation to help treat cluster headache," said Gudarz Davar, M.D., vice president, Neurology Development, Lilly Bio-Medicines.[2] "We are pleased that the results published in the *New England Journal of Medicine* showed over 70% of patients taking Emgality cut their number of weekly cluster headache attacks at least in half at Week 3."

Overall, the safety profile observed in patients with episodic cluster headache treated with Emgality 300 mg monthly is consistent with the safety profile in patients with migraine treated with Emgality 120 mg monthly.[1] Two Emgality-treated patients discontinued double-blind treatment during the episodic cluster headache study because of adverse events.[1]

Cluster headache is a disabling primary headache disorder.[3] People with episodic cluster headache represent 85 to 90 percent of cluster headache prevalence, with approximately 250,000 adults living with this disease in the U.S.[3,4] Cluster headache, although severely crippling, is challenging to diagnose because of limited awareness and, for some, may take five years or more to diagnose on average.[5]

About Emgality
Emgality is a monoclonal antibody that selectively binds to calcitonin gene-related peptide (CGRP) and was approved by the FDA in September 2018 for the preventive treatment of migraine in adults and in June 2019 for the treatment of episodic cluster headache in adults. Emgality was also approved in Europe in November 2018 for the prophylaxis of migraine in adults who have at least four migraine days per month.

Indications and Usage for Emgality (galcanezumab-gnlm) Injection
Emgality is a calcitonin gene-related peptide (CGRP) antagonist indicated in adults for the:

- preventive treatment of migraine
- treatment of episodic cluster headache

Important Safety Information

Contraindications
Emgality is contraindicated in patients with serious hypersensitivity to galcanezumab-gnlm or to any of the excipients.

Warnings and Precautions
Hypersensitivity Reactions
Hypersensitivity reactions, including anaphylaxis, angioedema, dyspnea, urticaria, and rash, have been reported with Emgality. If a serious or severe hypersensitivity reaction occurs, discontinue administration of Emgality and initiate appropriate therapy. Hypersensitivity reactions can occur days after administration and may be prolonged.

Adverse Reactions
The most common adverse reactions (incidence ≥2% and at least 2% greater than placebo) in Emgality clinical studies were injection site reactions.

Please see Full Prescribing Information, including Patient Information, for Emgality. See Instructions for Use included with the device.

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About the Phase 3 Study of Emgality in Cluster Headache
The Phase 3 study was a randomized, double-blind, placebo-controlled trial conducted at 35 sites in Europe and North America to assess the safety and efficacy of Emgality 300 mg subcutaneously each month, for two months, for the treatment of episodic cluster headache.[1]

In the study, 106 adult patients (18 to 65 years old) with episodic cluster headache, as determined by the ICHD-3-beta diagnostic criteria, were enrolled and randomly assigned to receive Emgality 300 mg (n=49) subcutaneously or placebo (n=57) subcutaneously once monthly for two months. Patients were allowed to use certain specified acute/abortive cluster headache treatments, including triptans, oxygen, acetaminophen, and NSAIDs during the study. The study's primary endpoint was the mean change from baseline in weekly cluster headache attack frequency across Weeks 1 to 3. The key secondary endpoint was the proportion of participants achieving a reduction from baseline of 50% or more in weekly cluster headache attack frequency at Week 3.[1]

About Cluster Headache
Cluster headache is a disabling primary headache disorder characterized by severe pain with recurrent 'attacks' of intense headaches which occur in cyclical patterns on one side of the head, frequently associated with pain behind or around one eye, restlessness and agitation.[3] During a cluster period, attacks can last 15 to 180 minutes and occur from once every other day to eight times a day for more than half of the time during a cluster period.[3] Episodic cluster headache is the most common form of the disease, affecting 85 to 90 percent of people with the disorder.[3,4] In episodic cluster headache, attacks occur in series lasting for weeks or months (so-called cluster periods) separated by remission periods of at least three months.[3]

About Lilly's Commitment to Headache Disorders
For over 25 years, Lilly has been committed to helping people affected by headache disorders, investigating more than a dozen different compounds for the treatment of migraine and cluster headache. These research programs have accelerated our understanding of these diseases and furthered the advancement of our comprehensive late-stage development programs studying galcanezumab-gnlm, approved by the U.S. Food and Drug Administration for the preventive treatment of migraine in adults and the treatment of episodic cluster headache in adults, and lasmiditan, an investigational drug currently under review by the U.S. Food and Drug Administration for the acute treatment of migraine with or without aura in adults. Our goal is to apply our combined clinical, academic and professional experience to build a research portfolio that delivers comprehensive solutions and addresses the needs of people affected by these disabling neurologic diseases.

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 upon 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 (galcanezumab-gnlm) as a preventive treatment for patients with migraine and as a treatment for patients with episodic cluster headache and lasmiditan as a potential acute treatment for patients with 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 Emgality 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 undertakes no duty to update forward-looking statements to reflect events after the date of this release.

References:

[1] Goadsby PJ, Dodick DW, Leone M, Trial of galcanezumab in prevention of episodic cluster headache. *New England Journal of Medicine.* 2019;382(2).

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[3] Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition. *Cephalalgia*. 2018;38(1):1-211.

[4] Data on File. Lilly USA, LLC. DOF-GZ-US-0068.

[5] Rozen TD, Fishman RS. Cluster headache in the United States of America: demographics, clinical characteristics, triggers, suicidality, and personal burden. *Headache.* 2012 Jan; 52(1): 99-113.

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