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Lilly's Emgality™ (galcanezumab-gnlm) Receives U.S. FDA Approval for the Preventive Treatment of Migraine in Adults

INDIANAPOLIS, September 27, 2018 – Eli Lilly and Company (NYSE: LLY) announced today that the U.S. Food and Drug Administration (FDA) has approved Emgality™ (galcanezumab-gnlm) 120 mg injection for the preventive treatment of migraine in adults.[1] Emgality offers a once-monthly, self-administered, subcutaneous injection.[1] Emgality is contraindicated in patients with serious hypersensitivity to galcanezumab-gnlm or to any of the excipients.[1]

Emgality will be available to patients shortly after approval. Patients with commercial insurance are candidates to receive Emgality for up to 12 months free as part of Lilly's patient support program (governmental beneficiaries excluded; subject to terms and conditions*). Emgality will be available for pickup at retail pharmacies.

Migraine is a disabling, neurologic disease that affects more than 30 million American adults.[2,3,4,5,6] According to the Medical Expenditures Panel Survey, the total unadjusted cost associated with migraine in the U.S. is estimated to be as high as $56 billion annually, yet migraine remains under-recognized and under-treated.[4,7,8]

"Despite the devastating impact of migraine, only about 10 percent of people living with the disease are currently taking a preventive treatment," said Christi Shaw, president, Lilly Bio-Medicines. "For more than two decades, Lilly has recognized this unmet need, and we have worked tirelessly to

develop a new option specifically designed for the prevention of migraine. With this approval, we are thrilled to offer a preventive treatment option to adults living with this disease."

The efficacy and safety of Emgality was demonstrated in two Phase 3 clinical trials in patients with episodic migraine (EVOLVE-1 and EVOLVE-2) and one Phase 3 clinical trial in patients with chronic migraine (REGAIN).

EVOLVE-1 and EVOLVE-2 were six-month, double-blind, placebo-controlled studies that enrolled adult patients with episodic migraine (defined as 4-14 migraine headache days [MHDs] per month). REGAIN was a three-month, double-blind, placebo-controlled study that enrolled adult patients with chronic migraine (defined as at least 15 headache days per month with at least 8 MHDs per month). In all three studies, patients were randomized to receive once-monthly placebo, Emgality 120 mg after an initial loading dose of 240 mg, or Emgality 240 mg. The primary endpoint was the mean change from baseline in the number of monthly MHDs over the double-blind treatment period in the intent-to-treat study population.

EVOLVE-1 (Over Months 1 to 6 - baseline migraine headache days: Emgality 9.2, placebo 9.1)[1,9]

- Mean change from baseline (days): -4.7 days (N=210) for Emgality 120 mg compared to -2.8 days (N=425) for placebo ($p<0.001$)
- At least a 50 percent reduction in MHDs in any given month on average (% responders): 62% (N=210) for Emgality 120 mg compared to 39% (N=425) for placebo ($p<0.001$)
- At least a 75 percent reduction in MHDs in any given month on average (% responders): 39% (N=210) for Emgality 120 mg compared to 19% (N=425) for placebo ($p<0.001$)
- 100 percent reduction in MHDs in any given month on average (% responders): 16% (N=210) for Emgality 120 mg compared to 6% (N=425) for placebo ($p<0.001$)

EVOLVE-2 (Over Months 1 to 6 - baseline migraine headache days: Emgality 9.1, placebo 9.2)[1,9]

- Mean change from baseline (days): -4.3 days (N=226) for Emgality 120 mg compared to -2.3 days (N=450) for placebo ($p<0.001$)
- At least a 50 percent reduction in MHDs in any given month on average (% responders): 59% (N=226) for Emgality 120 mg compared to 36% (N=450) for placebo ($p<0.001$)

- At least a 75 percent reduction in MHDs in any given month on average (% responders): 34% (N=226) for Emgality 120 mg compared to 18% (N=450) for placebo (p<0.001)
- 100 percent reduction in MHDs in any given month on average (% responders): 12% (N=226) for Emgality 120 mg compared to 6% (N=450) for placebo (p<0.001)

REGAIN (Over Months 1 to 3 - baseline migraine headache days: Emgality 19.4, placebo 19.6)[1,9]

- Mean change from baseline (days): -4.8 days (N=273) for Emgality 120 mg compared to -2.7 days (N=538) for placebo (p<0.001)
- At least a 50 percent reduction in MHDs in any given month on average (% responders): 28% (N=273) for Emgality 120 mg compared to 15% (N=538) for placebo (p<0.001)
- Emgality 120 mg was not significantly better than placebo for the proportion of patients with 75% and 100% reduction from baseline in the number of monthly MHDs over the three-month treatment period.

The recommended dose for Emgality is 240 mg (two consecutive subcutaneous injections of 120 mg each) once as a loading dose, followed by monthly doses of 120 mg injected subcutaneously.[1]

The safety of Emgality was evaluated in three clinical trials that included more than 2,500 patients.[1,9] Hypersensitivity reactions (e.g., rash, urticaria and dyspnea) have been reported with Emgality in clinical studies, can occur days after administration and may be prolonged. The most common adverse reactions (incidence ≥2% for Emgality and at least 2% greater than placebo) associated with Emgality treatment (120 mg vs. placebo) were injection site reactions (18% vs. 13%). See additional Important Safety Information below.

The U.S. list price of Emgality is $575 once-monthly, or $6,900 annually.

"We know the impact high deductible and rising out-of-pocket costs have on families, and Lilly takes seriously our role in ensuring affordable access to Emgality for as many patients as possible," said Shaw. "Lilly's choice to provide Emgality for up to 12 months free to all eligible patients with commercial insurance* underscores our 25-year commitment to recognizing and addressing the need experienced by those with migraine."

Patients and healthcare professionals with questions about Emgality should contact The Lilly Answers Center at 1-800-LillyRx (1-800-545-5979) or 1-833-EMGALITY or visit www.lilly.com. Patients can also text INFO to 54559 to receive an injection how-to video and other helpful resources delivered straight to their phone.

"I have lived with migraine for more than 30 years, and I have experienced firsthand the impact it has on your life, including the ability to perform daily activities," said Jill Dehlin, chair, Patient Leadership Council, National Headache Foundation. "Those of us living with migraine have spent years hoping for new treatment options, and I am thankful for the efforts by researchers, investigators and clinical trial patients who have helped make this possible."

On September 21, 2018, the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion for Emgality for the prophylaxis of migraine in adults who have at least four migraine days per month. The CHMP positive opinion is now referred for final action to the European Commission, which grants approval in the European Union.

Indications and Usage

Emgality is a calcitonin gene-related peptide (CGRP) antagonist indicated for the preventive treatment of migraine in adults.

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 (e.g., rash, urticaria and dyspnea) have been reported with Emgality in clinical studies. 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 pen and prefilled syringe.

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***Terms and Conditions:**

Offer good for up to 12 months until 12/31/2020 if healthcare provider submits the prior authorization form or letter of medical necessity, if required, to the patient's insurance provider. $0 monthly offer for commercially insured with insurance provider coverage, subject to wholesale acquisition cost plus usual and customary pharmacy charges and a separate $4900 maximum annual cap. $0 monthly offer for commercially insured without insurance provider coverage, subject to monthly and annual cap of wholesale acquisition cost plus usual and customary pharmacy charges.

*By using the Emgality Savings Card ("Card"), you attest that you meet the eligibility criteria and will comply with the Terms and Conditions described below:

- Offer void where prohibited by law. **This offer is invalid for patients without commercial insurance coverage or those whose prescription claims are eligible to be reimbursed, in whole or in part, by any governmental program, including, without limitation, Medicaid, Medicare, Medicare Part D, Medigap, DOD, VA, TRICARE/CHAMPUS, or any state patient or pharmaceutical assistance program.** If you live in Massachusetts, the Card expires on the earlier of: (i) the expiration date of this Card (12/31/2020); (ii) the date an AB-rated generic equivalent for Emgality becomes available; or (iii) June 30, 2019, absent a change in Massachusetts state law. If you live in California, the Card expires on the earlier of: (i) the expiration date of this Card (12/31/2020) or (ii) the date an FDA-approved therapeutically equivalent for Emgality or over-the-counter product with the same active ingredients becomes available.

Available only in the US and Puerto Rico for residents of the US and Puerto Rico. By accepting this offer, you agree that if you are required to do so under the terms of your insurance coverage for this prescription or are otherwise required to do so by law, you should notify your insurance carrier of your redemption of this Card. This offer is not valid with any other program, discount, incentive, or similar offer involving Emgality. It is prohibited for any person to sell, purchase, or trade; or to offer to sell, purchase, or trade; or to counterfeit this Card. This offer may be terminated, rescinded, revoked, or amended by Lilly USA, LLC, at any time **without notice. This Card is not health insurance. This Card expires on 12/31/2020.**

About the EVOLVE-1 and EVOLVE-2 Studies[1]

EVOLVE-1 and EVOLVE-2 were six-month, double-blind, placebo-controlled studies that enrolled a total of 1773 adult patients with episodic migraine (defined as 4-14 migraine headache days per month). Participants were randomized to once-monthly placebo, Emgality 120 mg after an initial loading dose of 240 mg, or Emgality 240 mg. The studies excluded patients on any other migraine preventive treatment, patients with medication overuse headache, patients with electrocardiogram abnormalities compatible with an acute cardiovascular event and patients with a history of stroke, myocardial infarction, unstable angina, percutaneous coronary intervention, coronary artery bypass grafting, deep vein thrombosis, or pulmonary embolism within 6 months of screening. For each study, the primary endpoint was the mean change from baseline in the number of monthly MHDs over Months 1 to 6 in the intent-to-treat study population. Emgality is approved as a 120 mg injection. Emgality 240 mg is not an approved dose.

About the REGAIN Study[1]

REGAIN was a 3-month, double-blind, placebo-controlled study that enrolled 1113 adult patients with chronic migraine (defined as ≥15 headache days per month with ≥8 migraine days per month). Participants were randomized to receive once-monthly placebo, Emgality 120 mg after an initial loading dose of 240 mg, or Emgality 240 mg. A subset of patients (15%) continued one concomitant migraine preventive medication. Patients were excluded if they had electrocardiogram abnormalities compatible with an acute cardiovascular event and patients with a history of stroke, myocardial infarction, unstable angina, percutaneous coronary intervention, coronary artery bypass grafting, deep vein thrombosis, or pulmonary embolism within 6 months of screening. The primary endpoint was the mean change from baseline in the number of monthly MHDs over the 3-month treatment period. Emgality is approved as a 120 mg injection. Emgality 240 mg is not an approved dose.

About Migraine

Migraine is a disabling, neurologic disease characterized by recurrent episodes of severe headache accompanied by other symptoms including nausea, vomiting, sensitivity to light and sound, and changes in vision.[2,3] More than 30 million American adults have migraine, with three times more women affected by migraine compared to men.[4,5,6,10] According to the Medical Expenditures Panel Survey, the total unadjusted cost associated with migraine in the U.S. is estimated to be as high as $56 billion annually, yet migraine remains under-recognized and under-treated.[4,7,8]

About Emgality

Emgality is a humanized monoclonal antibody that binds to calcitonin gene-related peptide (CGRP) and blocks its binding to the receptor. Emgality offers a once-monthly, self-administered, subcutaneous injection.

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 Emgality (galcanezumab-gnlm) as a preventive 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.

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[1] Emgality Prescribing Information, 2018.

[2] Katsarava Z, Buse D, Manack A, et al. Defining the differences between episodic migraine and chronic migraine. *Current Pain Headache Reports*. 2012;16:86.
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[5] Data on File. Lilly USA, LLC. DOF-GZ-US-0028.
[6] US Census Bureau. Quick Facts. https://www.census.gov/quickfacts/fact/table/US/PST045217 . Updated September 23, 2018. Last accessed September 24, 2018.
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[9] Data on File. Lilly USA, LLC. DOF-GZ-US-0002.
[10] Migraine: Symptoms and causes. Mayo Clinic. https://www.mayoclinic.org/diseasesconditions/migraine-headache/symptoms-causes/syc-20360201. Updated May 31, 2018. Last accessed September 23, 2018.

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