AAN 2019: Two New Analyses of Lasmiditan Phase 3 Studies Measured Onset of Effect and the Effect of Lasmiditan in Patients with Prior Triptan Experience

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- The lasmiditan Phase 3 program encompassed more than 4,000 patients and 20,000 migraine attacks[1,2,3]

INDIANAPOLIS, May 8, 2019 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced new data and post-hoc analyses for lasmiditan, an investigational, oral, first-in-class molecule for the acute treatment of migraine, being presented at the Annual Meeting of the American Academy of Neurology (AAN) taking place in Philadelphia from May 4-10, 2019. The presentations include pooled analyses from the Phase 3 SAMURAI and SPARTAN studies. The first analysis, presented on Monday, May 6, reviewed data on the early onset of effect of lasmiditan for several key outcomes. The second analysis, being presented today, shared data on the effect of lasmiditan in patients who took a triptan within the three months prior to study participation. In addition to these new analyses, Lilly presented interim results from the Phase 3, one-year, open-label extension study of lasmiditan (GLADIATOR), on Sunday, May 5, that showed results on measures of safety and efficacy were generally consistent with observations from the SAMURAI and SPARTAN studies.

Lasmiditan is a centrally-penetrant, selective serotonin 5-HT_{1F} agonist that is structurally and mechanistically distinct from other approved migraine therapies and lacks vasoconstrictive activity. It is the first and only molecule in the "ditan" class under evaluation by the U.S. Food and Drug Administration (FDA) for the acute treatment of migraine in adults.

"Migraine remains one of the most debilitating neurologic diseases, impacting more than 30 million adults in the U.S. The ability to quickly stop migraine attacks continues to be an important objective in advancing the acute treatment of this serious disorder. These new analyses showed that lasmiditan may provide rapid relief from a migraine attack and may be an effective option for people who have tried triptans. The data presented from the lasmiditan Phase 3 program included more than 4,000 patients and treatment of over 20,000 migraine attacks. This research represents Lilly's commitment to helping people across the spectrum of the disease," said Gudarz Davar, M.D., vice president, Neurology Development, Lilly Bio-Medicines.

Onset of Efficacy Findings from the Phase 3 SAMURAI and SPARTAN Studies

A pooled analysis of these Phase 3 studies was conducted to determine the onset of improvement in migraine symptoms after taking lasmiditan (50 mg, 100 mg or 200 mg) versus placebo. Rates of pain relief, and freedom from most bothersome symptom (MBS; patient selected from nausea, photophobia which is sensitivity to light, or phonophobia, which is sensitivity to sound) were both higher and statistically significant starting as early as 30 minutes post-dose in the lasmiditan 100 mg and 200 mg treated groups ($p<0.05$) when compared with placebo. The 200 mg lasmiditan treated group also achieved higher and statistically significant rates of freedom from photophobia and phonophobia than placebo starting as early as 30 minutes post-dose ($p<0.05$).[1] The primary endpoint of freedom from pain was statistically significant for both the 100 mg and 200 mg doses starting at 60 minutes ($p<0.05$ and $p<0.001$, respectively).[1]

These results were presented on Monday, May 6, in an oral presentation (**S17.007**) from 1:00 PM – 3:00 PM.

Response to Lasmiditan Based on Prior Experience with Triptan Therapy from the Phase 3 SAMURAI and SPARTAN Studies

To assess the effect of prior triptan exposure on lasmiditan efficacy, a post-hoc analysis of the pooled Phase 3 studies was conducted on patients who reported taking triptans within three months of trial enrollment. At baseline, patients rated themselves as either having a good, poor, or no response to triptans within the three months prior to study participation. The results showed that patients taking lasmiditan experienced higher rates of freedom from pain, freedom from MBS and pain relief versus placebo, regardless of prior experience with triptans.[2]

The data is being presented in a poster presentation (**P4.10-022**) from 11:30 AM – 6:30 PM today.

Long-Term Safety and Efficacy of Lasmiditan Over One Year: GLADIATOR Interim Results

Interim results were also shared from the Phase 3, prospective, randomized, open-label GLADIATOR study which enrolled patients who had

previously participated in the single-attack SAMURAI and SPARTAN studies. Patients were randomized 1:1 to receive lasmiditan 100 mg or 200 mg over 12 months, with a median duration of time in study of 288 days for these interim results. At the time of interim analysis, 1,978 patients had received at least one dose of lasmiditan and 19,058 acute migraine attacks had been treated.[3]

The most frequent treatment-emergent adverse events (TEAEs) (≥2%) were dizziness (18.6%), somnolence (sleepiness or drowsiness; 8.5%), paresthesia (tingling or numb sensation on the skin; 6.8%), fatigue (5.5%), nausea (4.7%) and asthenia (physical weakness or lack of energy; 2.0%). The incidence and types of TEAEs were similar to those in the SAMURAI and SPARTAN studies.[3]

The lasmiditan efficacy results from this interim analysis, defined as achieving freedom from pain and freedom from MBS, also appeared similar to the results from the SAMURAI and SPARTAN studies and were consistent across sequential three-month quarters of the study.[3]

These data were presented in a poster presentation (**P1.10-021)** on Sunday, May 5 from 11:30 AM – 6:30 PM.

About Lasmiditan
Lasmiditan is an investigational, oral, first-in-class molecule under evaluation for the acute treatment of migraine in adults. Lasmiditan selectively targets 5-HT_{1F} receptors expressed in the trigeminal pathway and has been designed for the acute treatment of migraine without vasoconstrictive activity.

About the SAMURAI Study
SAMURAI is a Phase 3, randomized, double-blind, placebo-controlled U.S. trial evaluating the safety and efficacy of two doses of lasmiditan administered orally (100 mg or 200 mg) compared with placebo for the acute treatment of migraine. To be eligible for the trial, patients were required to have at least moderate migraine disability (as measured by a Migraine Disability Assessment Score (MIDAS) ≥ 11). Patients who participated in the trial had an average of more than five migraine attacks per month at baseline. The primary endpoint of the study was comparison of the percentage of patients in the lasmiditan 200 mg and placebo groups who were migraine pain-free at two hours following the first dose. The key secondary endpoint of the study was comparison of the percentage of patients in the lasmiditan 200 mg and placebo groups who were free of their most bothersome symptoms (MBS) (nausea, sensitivity to sound or sensitivity to light) at two hours following the first dose.

About the SPARTAN Study
SPARTAN is a Phase 3, randomized, double-blind, placebo-controlled global trial evaluating the safety and efficacy of three doses of lasmiditan administered orally (50 mg, 100 mg or 200 mg) compared with placebo for the acute treatment of migraine. To be eligible for this trial, patients were required to have at least moderate migraine disability (as measured by a Migraine Disability Assessment Score [MIDAS] ≥ 11). Patients who participated in the trial had an average of more than five migraine attacks per month at baseline. SPARTAN did not exclude patients with known coronary artery disease. The primary endpoint of the study was comparison of the percentage of patients in the lasmiditan 200 mg and placebo groups who were migraine pain-free at two hours following the first dose. The key secondary endpoint of the study was comparison of the percentage of patients in the lasmiditan 200 mg and placebo groups who were free of their most bothersome symptoms (MBS) (nausea, sensitivity to sound or sensitivity to light) at two hours following the first dose.

About the GLADIATOR Study
GLADIATOR is a comprehensive, long-term, open-label Phase 3 study of lasmiditan for the acute treatment of migraine, enrolling patients who have previously participated in the Phase 3, placebo-controlled, single-attack lasmiditan studies (SAMURAI and SPARTAN). The study enrolled 1872 patients who were randomized 1:1 to receive either lasmiditan 100 mg or 200 mg for up to 12 months. The primary outcome measure is the proportion of patients and the proportion of attacks associated with any adverse event and with specific adverse events. A secondary outcome measure is the proportion of migraine attacks treated with lasmiditan 100 mg and with lasmiditan 200 mg which respond at two hours, calculated for each three-month period.

About Migraine
Migraine is a 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.[4,5] More than 30 million U.S. adults have migraine, with three times more women affected by migraine compared to men.[6] 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.[7]

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 currently under Priority Review for 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 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 lasmiditan as a potential acute treatment for patients with migraine, and Emgality as a preventive treatment of migraine and a potential treatment for episodic cluster headache in adults, 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 lasmiditan will receive regulatory approval. 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:

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7. 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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