Eli Lilly and Company Statement on ICER Final Report for Acute Treatments for Migraine: Effectiveness and Value

February 28, 2020

INDIANAPOLIS, February 28, 2020 – Eli Lilly and Company shared the following statement in response to the Institute for Clinical and Economic Review (ICER) Final Report on Acute Treatments for Migraine: Effectiveness and Value.

Lilly appreciates the recognition the ICER report brings to the need for acute treatments for migraine. The FDA's approval of REYVOW (lasmiditan) C-V in October of 2019 represented the first new novel acute treatment for migraine in over 25 years. REYVOW is an important new option for doctors and patients because with a single dose it offers patients a chance at freedom from migraine pain and their most bothersome symptom (MBS; patients selected from light sensitivity, sound sensitivity and nausea) at two hours.

Lilly is disappointed that ICER's final report concludes not all novel treatments were deemed cost-effective. In clinical trials, REYVOW has shown that 28-39% of patients achieved elimination of migraine pain at two hours with REYVOW versus 15% and 21% with placebo and 41-49% of patients achieved freedom from MBS at two hours with REYVOW versus 30% and 33% with placebo across two clinical studies and three doses.[1]

This complete elimination of migraine pain at two hours aligns with what patients have prioritized, as well as what the FDA and the American Headache Society have stated new acute treatments for migraine should be measured against.[2-4] With patients in mind, it's unfortunate that the ICER analysis utilized more arbitrary efficacy endpoints that do not meet patient or key stakeholder needs to assess these new medications.

"Given important factors of efficacy, list price and dosing, Lilly firmly believes REYVOW is a cost-effective treatment option for patients with migraine," said Patrik Jonsson, senior vice president, Eli Lilly and Company, and president, Lilly Bio-Medicines. "We welcome the opportunity for additional dialogue with ICER and encourage their transparency, as Lilly wants to ensure optimal patient outcomes and access."

Lilly has concerns with the lack of transparency in ICER's process for the final report. The significant shift in their analysis from their October draft publication to the recent final report without visibility into their methodology created a situation where Lilly, patient advocacy groups, and other interested parties were not allowed to critique and respond. Unfortunately, instead of using the recommended FDA endpoints, ICER applied inconsistent methods across the treatments. The results in their final report can lead to confusion, access restrictions, and barriers for patients to obtain novel acute treatments for migraine.

Lilly continues to support addressing high deductibles and rising out of pocket medical costs for patients and their families. The out-of-pocket cost per patient will depend on their insurance. Lilly is working with insurers to offer assistance with co-pays for REYVOW and a REYVOW Savings Card is available for eligible patients at www.REYVOW.com.*

Migraine is a complex neurologic disease; no two people with migraine are the same, and no two attacks are the same. Therefore, there is no one size fits all approach to treating a migraine, and that's why patients and doctors need treatment choices. Research shows 79% of patients in a survey of 183 patients from three headache centers said they are willing to try another acute treatment.[5]

Click here to learn more about the burden and impact of migraine.

This is why innovation is essential, particularly in the treatment of migraine attacks. With new science comes new treatments and with new treatments comes new hope. REYVOW has a novel mechanism of action (MOA) as it is the first and only ditan, a 5-HT_{1F} receptor agonist, that offers patients the chance at elimination of pain and their debilitating symptoms in two hours and with a single dose. REYVOW tablets are available in pharmacies nationwide and can be prescribed at 50 mg, 100 mg and 200 mg doses for patients.

Click here to additional information about REYVOW for healthcare professionals. Click here for additional information about REYVOW for consumers.

Over the past two years, Lilly's innovation in migraine and disabling headache disorders has been unparalleled, having received three FDA approvals for treatments for two distinct headache disorders.

Lilly is committed to ensuring patients have access to much-needed medicines, and Lilly is working with insurers to do so. Lilly is offering a REYVOW Savings Card for eligible patients* to help them with their out-of-pocket costs.

"Lilly is committed to making our medicines accessible so that patients can get the right treatment at the right time. We hope REYVOW's cost effectiveness will be recognized and will have a positive impact on access so as many people with migraine as possible have a chance at the treatment outcomes they deserve and have long awaited. Everyone deserves a chance at freedom from the crippling pain and symptoms caused by migraine," said Leigh Ann Pusey, senior vice president of corporate affairs and communications at Eli Lilly and Company.

About REYVOW ™ (lasmiditan)

REYVOW is a new oral treatment that binds with high affinity to 5-HT_{1F} receptors, which may play a role in migraine, and is approved by the FDA for

the acute treatment of migraine with or without aura in adults. REYVOW is not indicated for preventive treatment of migraine. REYVOW presumably exerts its therapeutic effects by activating these receptors; however, the precise mechanism is unknown. REYVOW can be prescribed to patients in 50 mg, 100 mg and 200 mg doses.

IMPORTANT SAFETY INFORMATION FOR REYVOW

WARNINGS AND PRECAUTIONS

Driving Impairment

REYVOW may cause significant driving impairment. In a driving study, administration of single 50 mg, 100 mg, or 200 mg doses of REYVOW significantly impaired subjects' ability to drive. Additionally, more sleepiness was reported at 8 hours following a single dose of REYVOW compared to placebo. Advise patients not to engage in potentially hazardous activities requiring complete mental alertness, such as driving a motor vehicle or operating machinery, for at least 8 hours after each dose of REYVOW. Patients who cannot follow this advice should not take REYVOW. Prescribers and patients should be aware that patients may not be able to assess their own driving competence and the degree of impairment caused by REYVOW.

Central Nervous System Depression

REYVOW may cause central nervous system (CNS) depression, including dizziness and sedation. Because of the potential for REYVOW to cause sedation, other cognitive and/or neuropsychiatric adverse reactions, and driving impairment, REYVOW should be used with caution if used in combination with alcohol or other CNS depressants. Patients should be warned against driving and other activities requiring complete mental alertness for at least 8 hours after REYVOW is taken.

Serotonin Syndrome

In clinical trials, reactions consistent with serotonin syndrome were reported in patients treated with REYVOW who were not taking any other drugs associated with serotonin syndrome. Serotonin syndrome may also occur with REYVOW during coadministration with serotonergic drugs [e.g., selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and monoamine oxidase (MAO) inhibitors]. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular signs (e.g., hyperreflexia, incoordination), and/or gastrointestinal signs and symptoms (e.g., nausea, vomiting, diarrhea). The onset of symptoms usually occurs within minutes to hours of receiving a new or a greater dose of a serotonergic medication. Discontinue REYVOW if serotonin syndrome is suspected.

Medication Overuse Headache

Overuse of acute migraine drugs (e.g., ergotamines, triptans, opioids, or a combination of drugs for 10 or more days per month) may lead to exacerbation of headache (i.e., medication overuse headache). Medication overuse headache may present as migraine-like daily headaches or as a marked increase in frequency of migraine attacks. Detoxification of patients including withdrawal of the overused drugs and treatment of withdrawal symptoms (which often includes a transient worsening of headache) may be necessary.

ADVERSE REACTIONS

The most common adverse reactions associated with REYVOW (≥2% and greater than placebo in clinical studies) were dizziness, fatigue, paresthesia, sedation, nausea and/or vomiting, and muscle weakness.

DRUG ABUSE AND DEPENDENCE

REYVOW contains lasmiditan, a Schedule V controlled substance.

Abuse

In a human abuse potential study in recreational poly-drug users (n=58), single oral therapeutic doses (100 mg and 200 mg) and a supratherapeutic dose (400 mg) of REYVOW were compared to alprazolam (2 mg) (C-IV) and placebo. With all doses of REYVOW, subjects reported statistically significantly higher "drug liking" scores than placebo, indicating that REYVOW has abuse potential. Subjects who received REYVOW reported statistically significantly lower "drug liking" scores than alprazolam. Euphoric mood occurred to a similar extent with REYVOW 200 mg, REYVOW 400 mg, and alprazolam 2 mg (43-49%). A feeling of relaxation was noted in more subjects on alprazolam (22.6%) than with any dose of REYVOW (7-11%). Phase 2 and 3 studies indicate that, at therapeutic doses, REYVOW produced adverse events of euphoria and hallucinations to a greater extent than placebo. However, these events occur at a low frequency (about 1% of patients). Evaluate patients for risk of drug abuse and observe them for signs of lasmiditan misuse or abuse.

Dependence

Physical withdrawal was not observed in healthy subjects following abrupt cessation after 7 daily doses of lasmiditan 200 mg or 400 mg.

See Full Prescribing Information and Medication Guide.

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***Terms and Conditions:**

Offer good until 12/31/2021 for up to 12 months of REYVOW. Patients with commercial drug insurance may be able to pay as little as $0 for their first fill of REYVOW. For the 2nd and subsequent fills, patients must have coverage for REYVOW through their commercial drug insurance plan to continue to pay as little as $0 per fill. Offer subject to a monthly savings of wholesale acquisition cost plus usual and customary pharmacy charges and a separate $3,000 maximum annual savings. Participation in the program requires a valid patient HIPAA authorization. Patient is responsible for any applicable taxes, fees, or amounts exceeding monthly or annual caps. This offer is invalid for patients without commercial drug insurance 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. Offer

void where prohibited by law and subject to change or discontinue without notice. Card activation is required. Subject to additional terms and conditions, which can be found at REYVOW.com/savings.

Patients and healthcare professionals with questions about REYVOW should contact 1-833-REYVOW1 (1-833-739-8691), visit www.REYVOW.com or connect with us on Facebook.

About Migraine
Migraine is a severely disabling neurologic disease characterized by recurrent episodes of moderate to severe headache accompanied by other symptoms including nausea, sensitivity to light, and sensitivity to sound.6,7 More than 30 million American adults have migraine, with three times more women than men affected by migraine.8 Migraine is often incapacitating, leading to high personal, societal and economic burden. According to the Medical Expenditures Panel Survey, total annual healthcare costs associated with migraine are estimated to be as high as $56 billion in the United States, yet it remains under-recognized and under-treated.[9,10]

About Eli Lilly and Company
Lilly is a global health care leader that unites caring with discovery to create medicines that 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 lilly.com and lilly.com/newsroom. P-LLY

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about REYVOW (lasmiditan) as an 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. These forward-looking statements are based on the company's current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Commercialization and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with: the company's ability to effectively commercialize REYVOW in the U.S.; delays or problems in the supply or manufacture of REYVOW; obtaining and maintaining appropriate pricing and reimbursement for REYVOW; complying with applicable U.S. regulatory requirements; and other risks and uncertainties affecting the company. 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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