Lilly's REYVOW™ (lasmiditan) C-V, the First and Only Medicine in a New Class of Acute Treatment for Migraine (ditan), Now Available for Prescription

January 31, 2020

- REYVOW is a serotonin (5-HT) 1F receptor agonist (ditan)1
- 28-39% of patients achieved fast and complete elimination of migraine pain at two hours with REYVOW versus 15% and 21% with placebo across two clinical studies and three doses1
- 41-49% of patients achieved freedom from most bothersome symptom (MBS) at two hours with REYVOW versus 30% and 33% with placebo across two clinical studies and three doses1

INDIANAPOLIS, Jan. 31, 2020 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that REYVOW™ (lasmiditan) C-V 50 mg and 100 mg tablets, an oral medication for the acute treatment of migraine with or without aura in adults, is now available for prescription and will be available in pharmacies in the next few days.[1] REYVOW works differently than other acute treatments for migraine. REYVOW is a new class of acute treatment for migraine, as it is the first and only FDA-approved ditan, a 5-HT_{1F} receptor agonist, believed to act both centrally and peripherally.[1] REYVOW is available in 50 mg, 100 mg and 200 mg doses for patients, which offers dosing flexibility for physicians and other prescribers.[1]

"As a healthcare professional, I am thrilled that REYVOW is now available. In only two hours and with a single dose, REYVOW has demonstrated the chance for patients to achieve rapid and complete elimination of migraine pain and their most bothersome symptom of sensitivity to light, sensitivity to sound, or nausea,[1]" said Dr. Cori Millen, medical director of Summit Headache and Neurologic Institute. "Recent guidance issued by both the FDA and the American Headache Society raised the clinical bar by recommending migraine clinical trial efficacy demonstrates pain freedom and freedom from most bothersome symptoms, rather than just pain relief.[2,3] REYVOW is the first FDA-approved acute medicine for migraine to meet this new standard.[1]"

A migraine attack is often incapacitating and excruciating.[4-6] In the International Burden of Migraine Study, a web-based survey of 9715 adults with migraine, 79% of patients reported experiencing severe pain during a migraine attack.[4] Triptans are recommended as an acute therapy for migraine for appropriate patients by the American Headache Society.[3] However, when speaking to patients with migraine, 79% said they would be willing to try another acute treatment.[7]

"People with migraine experience attacks that can be severely burdensome, intensely painful and debilitating,[4-6]" said Michael Cobas Meyer, MD, vice president, global medical affairs, Lilly Bio-Medicines. "With a single dose, REYVOW offers the chance for quick and complete elimination of moderate to severe migraine pain in just two hours.[1] When asking people with migraine, they prioritize fast and complete elimination of pain from acute treatments.[8,9] We feel fortunate we can now provide patients with a treatment option that helps achieve that outcome."

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

The efficacy of REYVOW for the acute treatment of migraine was demonstrated in two randomized, double-blind, placebo-controlled, single-attack trials (SAMURAI and SPARTAN) of 4439 patients who took 50-mg, 100-mg, or 200-mg doses of REYVOW or placebo.[1] Pain freedom, defined as a reduction of moderate or severe headache pain to no pain at two hours, and freedom from MBS, defined as the absence of the self-identified MBS (photophobia, phonophobia, or nausea) at two hours, were the primary and secondary efficacy endpoints.[1] Across two clinical studies and three doses, 28-39% of patients achieved complete elimination of migraine pain at two hours with REYVOW compared to 15% and 21% with placebo.[1] Across two clinical studies and three doses, 41-49% of patients achieved freedom from their MBS at two hours with REYVOW versus 30% and 33% with placebo.[1]

Treatment emergent adverse events were generally mild to moderate and the most frequent included dizziness, fatigue, paresthesia (tingling or numbing sensation on the skin), sedation (sleepiness or drowsiness), nausea and/or vomiting, and muscle weakness. With new FDA guidelines in 2018 and to gain understanding about potentially centrally acting medicines' impact on patients' ability to drive, Lilly conducted two driving studies to assess REYVOW.[10] Study results showed that REYVOW may cause significant driving impairment, as all doses of REYVOW impacted study participants' ability to drive. Additionally, more sleepiness was reported at eight hours compared to placebo. Other warnings and precautions include CNS depression, serotonin syndrome and medication overuse headache.

REYVOW is a non-opioid/non-narcotic, Schedule V medication that has low abuse potential and no evidence of physical dependence. The Drug Enforcement Administration (DEA) schedules controlled substance drugs from I to V, I being the highest potential for abuse and/or dependence and V being the lowest potential for abuse and/or dependence. "We are pleased that REYVOW has received Schedule V classification from the Drug Enforcement Administration, the lowest classification," said Gudarz Davar, M.D., vice president, neurology development, Lilly Bio-Medicines. "This is consistent with our data that shows that REYVOW has a low abuse potential and no evidence of withdrawal."

Click here to learn more about REYVOW.

Lilly strives to offer a thoughtful experience across the many touchpoints patients will have with REYVOW. Patients can find out more on REYVOW.com, join our REYVOW Facebook community and download a REYVOW Savings Card.* REYVOW is conveniently packaged so patients have the option to tear off and carry a single pill.

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 continues to support addressing high deductibles and rising out-of-pocket medical costs for patients and their families. Our REYVOW Savings Card underscores Lilly's commitment to patients who live with migraine," said Patrik Jonsson, senior vice president, Eli Lilly and Company, and president, Lilly Bio-Medicines. "Lilly has devoted 25 years to researching disabling neurologic diseases. With new science comes new hope and new expectations. We are proud that with a single dose of REYVOW, people living with migraine have a chance for rapid and complete elimination of pain and their most bothersome symptom in two short hours. Everyone deserves freedom from the pain and symptoms of this crippling disease."

Click here to view the migraine fact sheet.

Click to view the REYVOW product photo and REYVOW brand logo.

Click here to learn more about REYVOW.

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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About the SAMURAI and SPARTAN Studies
SAMURAI and SPARTAN were Phase 3, randomized, double-blind, placebo-controlled trials of 4439 patients evaluating the safety and efficacy of lasmiditan administered orally (100 mg or 200 mg in SAMURAI; 50 mg, 100 mg, or 200 mg in SPARTAN) compared with placebo for the acute treatment of migraine. These studies enrolled adult patients with a history of migraine with and without aura according to the International Classification of Headache Disorders (ICHD-II) diagnostic criteria. Patients were allowed to take a rescue medication two hours after taking study drug; however, opioids, barbiturates, triptans, and ergots were not allowed within 24 hours of study drug administration. Pain freedom at two hours and freedom from most bothersome symptom at two hours in patients with moderate to severe migraine pain were the primary and secondary efficacy endpoints. The primary and secondary efficacy endpoints were conducted in patients that treated a migraine with moderate to severe pain within four hours of the onset of the attack.

***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.[11,12] More than 30 million American adults have migraine, with three times more women than men affected by migraine.[13] 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.[14,15]

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 treatments for headache disorders including REYVOW, approved by the FDA 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 broad 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 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.

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