Aquestive Therapeutics Announces U.S. Food and Drug Administration (FDA) Approval for SYMPAZAN™ (clobazam) Oral Film

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- SYMPAZAN is the first and only FDA-approved oral film formulation of clobazam, a benzodiazepine approved for adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in patients 2 years of age or older(1)
- SYMPAZAN is delivered via Aquestive's proprietary PharmFilm® technology
- Aquestive is on track to launch SYMPAZAN in November 2018

WARREN, N.J., Nov. 2, 2018 /PRNewswire/ -- Aquestive Therapeutics, Inc. (NASDAQ: AQST), a specialty pharmaceutical company, today announced that the U.S. Food and Drug Administration (FDA) approved SYMPAZAN ™ (clobazam) oral film for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in patients 2 years of age or older.[1] SYMPAZAN is the first and only oral film FDA-approved to treat seizures associated with LGS. Previously, clobazam was marketed as ONFI® and offered in two formulations – either tablet or oral suspension.[2]

"Aquestive Therapeutics is pleased to bring SYMPAZAN to the LGS community," said Keith J. Kendall, Chief Executive Officer of Aquestive Therapeutics. "Treating LGS can be difficult; patients may have a hard time swallowing oral medications. We're optimistic SYMPAZAN can help address unmet medical needs and be an important treatment option for this patient population."

LGS is a severe form of epilepsy that begins in early childhood and is characterized by multiple types of seizures and intellectual disability.[3] LGS patients often have difficulty swallowing pills and large volume suspensions due to physical limitations, behavioral or cognitive impact.[4,5] Challenges with treatment administration can lead to uncertain and inconsistent dosing, and increase the burden of care, particularly for patients that may be combative or resistant to treatment. [5-8]

Since FDA approval in 2011, clobazam tablets and oral suspension (brand name ONFI®) have been a trusted adjunctive treatment for LGS. In a Phase 3, randomized, double-blind, placebo-controlled study of 238 LGS patients, clobazam tablets significantly reduced the frequency of drop seizures (which involve falls) compared to baseline by 41 percent (low dose) to 68 percent (high dose) vs. 12 percent for placebo ($p<0.05$ for all doses vs. placebo).[2,9] Please see more Important Safety Information below, including the Boxed Warning on the risks associated with concomitant use of opioids.

"Many LGS patients have a hard time swallowing pills and suspensions. This can make administering medication hard for caregivers," says Christina SanInocencio, Executive Director of the LGS Foundation. "We believe SYMPAZAN will be welcomed by patients and caregivers impacted by LGS and searching for treatment solutions."

SYMPAZAN is a formulation based on Aquestive's proven PharmFilm® technology. Multiple pharmacokinetic studies were conducted to compare SYMPAZAN with ONFI. Based on the studies, SYMPAZAN oral film was demonstrated to be bioequivalent to clobazam tablets and have comparable safety profiles.[1] Aquestive's clinical development of SYMPAZAN followed the 505(b)(2) regulatory pathway.

"SYMPAZAN is the beginning of a meaningful CNS franchise for Aquestive," Kendall says. "We are actively working to advance more redesigned, proprietary treatments that can offer meaningful improvements for patients and caregivers who live with epilepsy and other complex conditions."

Aquestive plans to commercialize SYMPAZAN in November, and has engaged Ashfield Healthcare, a company specializing in commercialization services, to build and train a highly qualified, national sales force. The sales force will focus on pediatric neurologists and epileptologists.

SYMPAZAN oral film is berry flavored and offered in 5 mg, 10 mg, and 20 mg dosages to meet a range of LGS patient and caregiver needs.[1]

About Aquestive Therapeutics
Aquestive Therapeutics is a specialty pharmaceutical company committed to identifying, developing and commercializing differentiated products to address unmet medical needs. Aquestive Therapeutics has a late-stage proprietary product pipeline focused on the treatment of CNS diseases, and is working to advance orally-administered complex molecules that it believes can be alternatives to invasively-administered standard of care therapies. As the leader in developing and delivering drugs via its PharmFilm® technology, Aquestive Therapeutics also collaborates with pharmaceutical partners to bring new molecules to market in differentiated and highly-marketable dosage forms.

IMPORTANT SAFETY INFORMATION
BOXED WARNING: RISKS FROM CONCOMITANT USE WITH OPIOIDS

Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death.

- Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.

CONTRAINDICATIONS
SYMPAZAN is contraindicated in patients with a history of hypersensitivity to the drug or its ingredients. Hypersensitivity reactions have included serious dermatological reactions.

WARNINGS AND PRECAUTIONS
Potentiation of Sedation from Concomitant Use with Central Nervous System (CNS) Depressants
SYMPAZAN has a CNS depressant effect. Caution patients and/or caregivers against simultaneous use with other CNS depressants or alcohol as the effects of other CNS depressants or alcohol may be potentiated.

Somnolence or Sedation
SYMPAZAN causes dose-related somnolence and sedation, which generally begins within the first month of treatment and may diminish with continued treatment. Monitor patients for somnolence and sedation, particularly with concomitant use of other CNS depressants. Caution patients against engaging in hazardous activities requiring mental alertness, i.e., operating dangerous machinery or motor vehicles, until the effect of SYMPAZAN is known.

Withdrawal Symptoms
Abrupt discontinuation of SYMPAZAN should be avoided. The risk of withdrawal symptoms is greater with higher doses. Withdraw SYMPAZAN gradually to minimize the risk of precipitating seizures, seizure exacerbation, or status epilepticus.

Serious Dermatological Reactions
Serious skin reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported with clobazam in both children and adults. Discontinue SYMPAZAN at the first sign of rash, unless the rash is clearly not drug-related.

Physical and Psychological Dependence
Patients with a history of substance abuse should be under careful surveillance when receiving SYMPAZAN.

Suicidal Behavior and Ideation
AEDs, including SYMPAZAN, increase the risk of suicidal thoughts or behavior in patients. Patients treated with SYMPAZAN should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Inform patients, their caregivers, and families of the increased risk of suicidal thoughts and behaviors. Advise them to be alert for and report immediately to healthcare providers any emergence or worsening signs and symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts of self-harm.

ADVERSE REACTIONS
Adverse reactions (≥10% and more frequently than placebo) included constipation, somnolence or sedation, pyrexia, lethargy, and drooling.

DRUG INTERACTIONS
The concomitant use of benzodiazepines and opioids increases the risk of respiratory depression. Limit dosage and duration of concomitant use of benzodiazepines and opioids and follow patients closely for respiratory depression and sedation. Concomitant use of SYMPAZAN with other CNS depressants, including alcohol, may increase the risk of sedation and somnolence. Caution patients and/or caregivers against simultaneous use with other CNS depressants or alcohol, as effects of other CNS depressants or alcohol may be potentiated.
Hormonal contraceptives that are metabolized by CYP3A4; effectiveness may be diminished when given with SYMPAZAN. Additional non-hormonal forms of contraception are recommended when using SYMPAZAN. Dose adjustment may be necessary of drugs metabolized by CYP2D6 and of SYMPAZAN when co-administered with strong CYP2C19 inhibitors (e.g., fluconazole, fluvoxamine, ticlopidine).

USE IN SPECIFIC POPULATIONS
Pregnancy and Lactation: SYMPAZAN may cause fetal harm and should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus. Infants born to mothers who have taken benzodiazepines during the later stages of pregnancy can develop dependence, withdrawal syndrome and symptoms suggestive of floppy infant syndrome. SYMPAZAN is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from SYMPAZAN, discontinue nursing or discontinue the drug. Encourage patients to call the toll-free number 1-888-233-2334 to enroll in the Pregnancy Registry or visit http://www.aedpregnancyregistry.org/.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please click here to see full Prescribing Information, including Boxed Warning.

Forward-Looking Statement
This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995.

Words such as "anticipate," "believe," "could," "estimate," "expects," "intend," "may," "plan," "potential," "project," "will," "would," or the negative of those terms, and similar expressions, are intended to identify forward-looking statements. Such statements include, but are not limited to, statements about regulatory approvals and pathways, clinical trial timing and plans, the achievement of clinical and commercial milestones, future financial and operating results, business strategies, market opportunities, financing, and other statements that are not historical facts.

These forward-looking statements are based on our current expectations and beliefs and are subject to a number of risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. Such risks and uncertainties include, but are not limited to, risks associated with the Company's development work, including any delays or changes to the timing, cost and success of our product development activities and clinical trials; the risks of delays in FDA approval of our drug candidates or failure to receive approval; the risks inherent in commercializing a new product (including technology risks, financial risks, market risks and implementation risks and regulatory limitations); development of our sales and marketing capabilities; the rate and degree of market acceptance of our product candidates; the success of any competing products; the size and growth of our product markets; the effectiveness and safety of our product candidates; risks associated with intellectual property rights and infringement; unexpected patent developments; and other risks and uncertainties affecting the Company including those described in the "Risk Factors" section included in our Registration Statement on Form S-1 declared effective by the SEC on July 24, 2018. As with any pharmaceutical product candidate under development, there are significant risks with respect to the development, regulatory approval and commercialization of new products. Given these uncertainties, you should not place undue reliance on these forward-looking statements, which speak only as of the date made. All subsequent forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by this cautionary statement. We assume no obligation to update our forward-looking statements after the date of this press release whether as a result of new information, future events or otherwise, except as may be required under applicable law.

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