Marinus Pharmaceuticals Announces Publication in The Lancet Neurology of ZTALMY® (ganaxolone) Phase 3 Marigold Trial Results

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Results demonstrate safety and efficacy of ZTALMY, first FDA-approved treatment for seizures associated with CDKL5 deficiency disorder in patients two years and older

RADNOR, Pa.--(BUSINESS WIRE)--Marinus Pharmaceuticals, Inc. (Nasdaq:MRNS), a pharmaceutical company dedicated to the development of innovative therapeutics to treat seizure disorders, today announced that The Lancet Neurology has published results from the pivotal Phase 3 Marigold trial of ZTALMY® (ganaxolone) for the treatment of seizures associated with CDKL5 deficiency disorder (CDD). The paper, “Efficacy and safety of ganaxolone in patients with CDKL5 deficiency disorder: a randomized, double-blind, placebo-controlled, Phase 3 trial,” can be accessed on The Lancet Neurology website, here. This was the first double-blind placebo-controlled study providing evidence of efficacy in CDD-associated seizures.

“The publication of these data highlights the importance of bringing new treatments to people affected by very refractory epilepsy, including the CDKL5 deficiency disorder community, and adds to the growing body of clinical research data currently available,” said Dr. Elia M. Pestana Knight, M.D., a Principal Investigator for the Marigold trial and pediatric epileptologist at the Cleveland Clinic Neurological Institute. “The results demonstrate that ZTALMY was effective in treating seizures associated with CDKL5 deficiency disorder and provides physicians with a novel medication for the management of this difficult to treat patient population.” Dr. Pestana Knight is a member of Marinus’ Scientific Advisory Board. She joined the Board after the completion of the Marigold randomized trial.

The paper presents the results of the Phase 3 Marigold trial, a double-blind placebo-controlled trial in which 101 patients were randomized and individuals treated with ZTALMY showed a median 30.7% reduction in 28-day major
motor seizure frequency, compared to a median 6.9% reduction for those receiving placebo, achieving the trial’s primary endpoint (p=0.0036). ZTALMY was generally well-tolerated and showed a safety profile consistent with previous clinical trials, with the most frequent adverse event being somnolence.

“We are pleased to have results from the Marigold trial published in The Lancet Neurology, a highly ranked peer-reviewed journal, at this inflection point for Marinus,” said Alex Aimetti, Senior Vice President of Scientific Affairs, Marinus Pharmaceuticals. “These trial results exemplify our confidence in the unique mechanism of action of ganaxolone to benefit CDD patients with uncontrolled seizures, and we will continue to explore its potential across a range of seizure disorders.”

About CDKL5 Deficiency Disorder

CDKL5 deficiency disorder (CDD) is a serious and rare genetic disorder that is caused by a mutation of the cyclin-dependent kinase-like 5 (CDKL5) gene, located on the X chromosome. CDD is characterized by early-onset, difficult-to-control seizures and severe neurodevelopmental impairment.

About ZTALMY® (ganaxolone) oral suspension

ZTALMY® is the first and only FDA-approved treatment indicated specifically for seizures associated with cyclin-dependent kinase-like 5 deficiency disorder (CDD) in patients two years of age and older. ZTALMY, a neuroactive steroid that acts as a positive allosteric modulator of the GABA<sub>A</sub> receptor, is taken three times daily. It is expected to be available in July following scheduling by the U.S. Drug Enforcement Administration.

Indication and Usage

ZTALMY is indicated for the treatment of seizures associated with cyclin-dependent kinase like 5 (CDKL5) deficiency disorder (CDD) in patients 2 years of age and older.

Important Safety Information

Warnings and Precautions

Somnolence and Sedation: ZTALMY can cause somnolence and sedation. In a clinical study somnolence and sedation appeared early during treatment and were generally dose related. Other CNS depressants, including opioids, antidepressants, and alcohol, could potentiate these effects. Monitor patients for these effects and advise them not to drive or operate machinery until they have gained sufficient experience on ZTALMY to gauge whether it adversely affects their ability to drive or operate machinery.
Suicidal Behavior and Ideation: Antiepileptic drugs (AEDs), including ZTALMY, increase the risk of suicidal thoughts or behavior. Monitor patients taking ZTALMY for the emergence or worsening of depression, suicidal thoughts or behavior, or any unusual changes in mood or behavior. Advise patients, caregivers, and their families to be alert for these behavioral changes and report behaviors of concern immediately to healthcare providers. When considering ZTALMY, or any other AED, balance the risk of suicidal thoughts or behaviors with the risk of untreated illness. If these symptoms emerge during treatment, consider whether it may be related to the AED or the underlying illness.

Withdrawal of Antiepileptic Drugs: As with most AEDs, withdraw ZTALMY gradually to minimize the risk of increased seizure frequency and status epilepticus. If withdrawal is needed because of a serious adverse event, rapid discontinuation can be considered.

Adverse Reactions

The most common adverse reactions (incidence of at least 5% and at least twice the rate of placebo) were somnolence, pyrexia, salivary hypersecretion, and seasonal allergy.

Drug Interactions

Cytochrome P450 inducers will decrease ganaxolone exposure. Avoid concomitant use with strong or moderate CYP3A4 inducers; if unavoidable, consider a dosage increase of ZTALMY, but do not exceed the maximum recommended dosage.

Use In Specific Populations

Pregnancy: Use caution when ZTALMY is administered to pregnant women as there are no adequate data on the developmental risk associated with use in pregnant women. In animal studies, developmental adverse effects were observed following exposure during organogenesis or throughout gestation and lactation.

Lactation: ZTALMY is excreted in human milk at concentrations resulting in a dose to the breastfed infant of 1% maternal dose. The effects of ZTALMY on milk production and the breastfed infant are unknown.

Hepatic Impairment: Monitor patients with hepatic impairment for the incidence of adverse reactions. Patients with hepatic impairment may require a reduced dosage of ZTALMY.

Drug Abuse and Dependence
ZTALMY contains ganaxolone (controlled substance schedule to be determined after review by the Drug Enforcement Administration.) Advise patients of the potential for abuse and dependence. It is recommended that ZTALMY be tapered according to the dosage recommendations unless symptoms warrant immediate discontinuation.

**Full Prescribing Information for ZTALMY® is available here.**

**About Marinus Pharmaceuticals**

Marinus is a pharmaceutical company dedicated to the development of innovative therapeutics to treat seizure disorders. Ganaxolone is a neuroactive steroid GABAA receptor modulator that acts on a well-characterized target in the brain known to have anti-seizure effects. It is being developed in IV and oral dose formulations intended to maximize therapeutic reach to adult and pediatric patient populations in both acute and chronic care settings. For more information visit [www.marinuspharma.com](http://www.marinuspharma.com).

**Forward-Looking Statements**

To the extent that statements contained in this press release are not descriptions of historical facts regarding Marinus, they are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Words such as "may", "will", "expect", "anticipate", "estimate", "intend", "believe", and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. Examples of forward-looking statements contained in this press release include, among others, statements regarding our expected clinical development plans, enrollment in our clinical trials, regulatory communications and submissions; product launches for ganaxolone, and the timing thereof; our continued explorations of ganaxolone across a range of seizure disorders; our expectations in ganaxolone's unique mechanism of action to benefit patients with seizure disorders; our expectation regarding ZTALMY's availability; and other statements regarding the Company's future operations, financial performance, financial position, prospects, objectives and other future event.

Forward-looking statements in this press release involve substantial risks and uncertainties that could cause our clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, uncertainties and delays relating to the design, enrollment, completion, and results of clinical trials; uncertainties regarding future development of ganaxolone across a number of rare seizure disorders; the scheduling of ZTALMY by the U.S. Drug Enforcement Administration; our ability to commercialize ZTALMY; delays, interruptions or failures in the manufacture and supply of ZTALMY; unanticipated costs and expenses; and the company's cash and cash
equivalents may not be sufficient to support its operating plan for as long as anticipated. This list is not exhaustive and these and other risks are described in our periodic reports, including our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, filed with or furnished to the Securities and Exchange Commission and available at www.sec.gov. Any forward-looking statements that we make in this press release speak only as of the date of this press release. We assume no obligation to update forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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