



NEWS RELEASE

# Marinus Pharmaceuticals Announces FDA Approval of ZTALMY® (ganaxolone) for CDKL5 Deficiency Disorder

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First and only FDA-approved treatment for seizures associated with CDKL5 deficiency disorder (CDD) in patients two years of age and older<sup>1</sup>

ZTALMY significantly reduced major motor seizure frequency in CDD patients in the pivotal Marigold trial

Rare Pediatric Disease Priority Review Voucher awarded to Marinus Pharmaceuticals by the FDA

Marinus to host conference call March 21, at 8:00 a.m. ET

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 U.S. Food and Drug Administration (FDA) has approved ZTALMY® (ganaxolone) oral suspension for the treatment of seizures associated with cyclin-dependent kinase-like 5 deficiency disorder (CDD), a rare form of genetic epilepsy, in patients two years of age and older.<sup>1</sup> ZTALMY, the first FDA approved treatment specifically in CDD, is a neuroactive steroid that acts as a positive allosteric modulator of the GABAA receptor. It is expected to be available through a designated specialty pharmacy in July 2022.

"Today is a historic milestone not only for Marinus but for CDD patients, families and caregivers who have long been navigating the unpredictable, often devastating reality of living with uncontrolled seizures," said Scott Braunstein, M.D., Chief Executive Officer of Marinus. "The approval of ZTALMY would not have been possible without the patients, caregivers and investigators who participated in the clinical trials to develop this important

new therapy. We are grateful and humbled by the opportunity to bring the first and only FDA-approved treatment for seizures associated with CDD to this community.”

CDD is a serious and rare genetic disorder characterized by early-onset, difficult-to-control seizures and severe neuro-developmental impairment.<sup>2</sup> It's caused by a mutation of the cyclin-dependent kinase-like 5 (CDKL5) gene, located on the X chromosome. The CDKL5 gene produces a protein that is important for normal brain development and function.<sup>3</sup>

“There has been a great unmet medical need for treatments that address seizures associated with CDKL5 deficiency disorder given their prominent role and profound impact on patients,” said Scott Demarest, M.D., Principal Investigator (PI) for the Marigold trial and neurologist and Clinical Director of Precision Medicine at Children's Hospital Colorado. “To date, antiseizure treatment decisions have been based on very limited clinical evidence in this patient population and the resulting outcomes underscore the need for therapies that further improve seizure control. Thanks to our research and this trial, we now have the first treatment specifically approved for seizures associated with CDKL5 deficiency disorder that was shown to have a positive benefit-risk profile.” Dr. Demarest is also PI of the International CDKL5 Clinical Research Network and Assistant Professor of Pediatrics-Neurology at the University of Colorado School of Medicine.

The approval of ZTALMY in CDD is based on data from the Phase 3 Marigold 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 ( $p=0.0036$ ). In the Marigold open label extension study, patients treated with ZTALMY for at least 12 months ( $n=48$ ) experienced a median 49.6% reduction in major motor seizure frequency. In the clinical development program, ZTALMY demonstrated efficacy, safety and tolerability with the most common adverse reactions (incidence  $>5\%$  and at least twice the rate of placebo) in the ZTALMY group being somnolence, pyrexia, salivary hypersecretion and seasonal allergy.

“As the mother of a daughter living with CDD, I've experienced first-hand the devastating impact seizures can have on these patients,” said Karen Utley, President and Co-founder of the International Foundation for CDKL5 Research. “This approval is monumental for the CDD community—bringing not only the first approved treatment option specifically for CDD patients, but renewed hope to those who have struggled to find medications that are effective in significantly reducing the number of seizures these patients experience on a daily basis.”

ZTALMY is expected to be commercially available in the U.S. in July following scheduling by the U.S. Drug Enforcement Administration. To support the CDD community, Marinus plans to launch The ZTALMY One™ Program, a comprehensive patient services program to provide assistance with product access, ongoing support to patients, caregivers and their medical teams, and financial support to eligible patients.

The FDA reviewed ZTALMY under Priority Review and granted ZTALMY orphan drug and Rare Pediatric Disease designations for the treatment of CDD. With the approval, the FDA awarded a Rare Pediatric Disease Priority Review Voucher (PRV), which Marinus plans to monetize.

## Conference Call

Marinus will host a virtual investor event on Monday, March 21, at 8:00 a.m. ET to discuss the Marinus ZTALMY Approval and its Fourth Quarter 2021 Business Update. The event will be webcast live and can be accessed under “Events & Presentations” in the Investors and Media section of the company's website at [www.marinuspharma.com](http://www.marinuspharma.com). The archived webcast will be available on the company's website beginning approximately two hours after the event.

## 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 GABAA 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 commercialization plans and the timing thereof; our expectations regarding scheduling by the U.S. Drug Enforcement Administration and the expected timing thereof; our plans to launch a patient assistance program that provides ongoing financial and product support to patients and caregivers; our expectations to monetize the PRV; our expected clinical development plans, enrollment in our clinical trials, regulatory communications and submissions and product launches for ganaxolone, and the timing thereof; our expectations and beliefs regarding the regulatory authorities with respect to our product candidates; the potential safety and efficacy of ganaxolone, as well as its therapeutic potential in a number of indications; and other statements regarding the Company's future operations, financial performance, financial position, prospects, objectives and other future events.

Forward-looking statements in this press release involve substantial risks and uncertainties that could cause our commercialization plans, 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, our ability to establish commercial infrastructure and capabilities to launch ZTALMY; physician and patient acceptance of ZTALMY; our ability to obtain adequate market access for ZTALMY; the varying interpretation of clinical data; the scheduling of ZTALMY by the U.S. Drug Enforcement Administration; our ability to

comply with the FDA's requirement for additional post-marketing studies in the required time frames; the timing of regulatory filings for our other product candidates; the potential that regulatory authorities, including the FDA and EMA, may not grant or may delay approval for our product candidates; uncertainties and delays relating to the design, enrollment, completion, and results of clinical trials; unanticipated costs and expenses; early clinical trials may not be indicative of the results in later clinical trials; clinical trial results may not support regulatory approval or further development in a specified indication or at all; actions or advice of the FDA or EMA may affect the design, initiation, timing, continuation and/or progress of clinical trials or result in the need for additional clinical trials; our ability to obtain and maintain regulatory approval for our product candidate; our ability to obtain, maintain, protect and defend intellectual property for our product candidates; the potential negative impact of third party patents on our or our collaborators' ability to commercialize ganaxolone; delays, interruptions or failures in the manufacture and supply of our product candidate; the size and growth potential of the markets for the company's product candidates, and the company's ability to service those markets; the company's cash and cash equivalents may not be sufficient to support its operating plan for as long as anticipated; the company's expectations, projections and estimates regarding expenses, future revenue, capital requirements, and the availability of and the need for additional financing; the company's ability to obtain additional funding to support its clinical development and commercialization programs; the potential for Orion to breach the collaboration or terminate the agreement in accordance with its terms; the effect of the COVID-19 pandemic on our business, the medical community, regulators and the global economy; and the availability or potential availability of alternative products or treatments for conditions targeted by us that could affect the availability or commercial potential of our product candidate. This list is not exhaustive and these and other risks are described in our periodic reports, including the annual report 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](http://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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1 ZTALMY (ganaxolone) oral suspension prescribing information. Radnor, Pennsylvania, USA. Marinus Pharmaceuticals, Inc.; March 2022.

2 Olson H et al. 2019 Pediatric Neurology

3 Jakimiec M et al. 2020 Brain Sci.

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