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Marinus Presents Additional Data from Ganaxolone Phase 2 Trial in Refractory Status Epilepticus at the American Epilepsy Society Annual Meeting

100% of evaluable patients in target dose had no relapse during the four-week follow-up period

Independent objective EEG seizure analysis confirms target dose

Ganaxolone effective regardless of prior AED treatment and across diverse disease etiologies for RSE

KOL call and live webcast on Monday, December 9th at 7:15am ET

RADNOR, Pa., Dec. 07, 2019 (GLOBE NEWSWIRE) -- [Marinus Pharmaceuticals, Inc.](#) (Nasdaq: MRNS) ("Marinus" or "Company"), a pharmaceutical company dedicated to the development of innovative therapeutics to treat epilepsy, depression and other neuropsychiatric disorders, announced additional data from its open-label, dose-finding Phase 2 study evaluating intravenous (IV) ganaxolone in patients with refractory status epilepticus (RSE). The results were presented at the [American Epilepsy Society \(AES\) annual meeting](#) by Eugene Ramsay, M.D., Director Emeritus, Ochsner Comprehensive Epilepsy Center in New Orleans, and investigator in the study.

"We believe that the expanded data from this Phase 2 study are highly compelling and demonstrate the ability of ganaxolone to rapidly break status, maintain seizure control, and prevent progression to IV anesthetics across a diverse and severe patient population," said Scott Braunstein, M.D., Chief Executive Officer of Marinus. "These additional data provide important confirmation of our target dose through an independent analysis. Paired with our long-term follow up data that show 100% of patients in the target dose cohort have no status relapse during the 4-week follow up period, we are confident that we have identified an optimized target dose for future studies that balances safety, efficacy and durability of responses. We are on-track for an End of Phase 2 meeting with the FDA in the first quarter of 2020 and look forward to rapidly advancing this promising program to a potentially registration enabling study."

Key Presentation Highlights:

- Previously announced study results demonstrated that 100% of patients achieved the primary endpoint of preventing progression to IV anesthetics within 24 hours of treatment initiation. Additional long-term data, presented for the first time at AES, demonstrate that all evaluable patients (n=6) in the target dose cohort did not experience status relapse during the four-week follow up period.
- Efficacy and safety were consistent across disease etiologies and both nonconvulsive status epilepticus (NSCE) and convulsive status epilepticus (CSE) patients.
- Baseline patient characteristics showed that in the 17 patients enrolled in the study, 7 had RSE resulting from a vascular condition, 4 cases were caused by tumors, 2 by autoimmune disease and 2 by drug overdose/withdrawal. The underlying cause in one patient was unknown. Seven of the patients had a prior history of epilepsy.
- Patients failed a mean of 2.1 second-line IV AED with all patients failing both levetiracetam and lacosamide. All prior AEDs were given at therapeutically relevant doses, administered within recommended dosing guidelines and mean time since addition of most recent AED was 4 hours.

In addition, an independent central review of seizure EEG data as an objective diagnostic tool demonstrated a clear dose effect with the target dose level providing sustained reductions in seizure burden (greater than 80%) throughout the entire analysis window.

Cohort	No escalation to IV anesthetics within 24 hours from infusion initiation (Primary Endpoint)	Status-free at 24 hours from infusion initiation	No escalation to additional IV AEDs or IV anesthetics for status relapse at any time through the 24-hour follow-up period	No SE Relapse at any time during the 4-week follow up period
Target (713 mg/day; n=8) ¹	100% (8 of 8)	88% (7 of 8)	100% (8 of 8)	100% (6 of 6)
Medium (650 mg/day; n=4) ²	100% (4 of 4)	100% (4 of 4)	75% (3 of 4)	67% (2 of 3)
Low (500 mg/day; n=5) ³	100% (5 of 5)	100% (5 of 5)	60% (3 of 5)	50% (1 of 2)

1. One patient in the target dose cohort had status relapse at Day 1, which resolved during the ganaxolone infusion without treatment escalation, one patient discontinued early due to severe sedation on day 1 and one patient died 9 days after ganaxolone discontinuation due to bowel perforation, which was not considered to be drug related.
2. In the medium dose cohort, one patient experienced status relapse at Day 2 during taper and one patient discontinued on day 3 due to severe sedation.
3. In the low dose cohort, two patients escalated to 3rd line therapy for seizure relapse at Day 3 (one of which died 16 days after ganaxolone discontinuation due to life support withdrawal) and one patient died 22 days after ganaxolone discontinuation due to sepsis. None of the deaths were considered to be drug related.

Dr. Eugene Ramsay said, “The expanded data set presented at AES further bolsters our confidence that ganaxolone has the potential to establish a new treatment paradigm for RSE, a life-threatening condition with no approved treatments. These data build upon the previously reported remarkable efficacy, where all study participants did not need the addition of IV anesthetics. Ganaxolone provided rapid onset of efficacy, the effect of ganaxolone was sustained, and dose specific, with no relapses observed in those patients who received the target dose and who were followed for 4 weeks. Importantly, we also see that ganaxolone is effective across a population representative of the refractory status patients that we commonly see, suggesting that it can be broadly utilized regardless of the underlying cause of status. These data demonstrate that ganaxolone has the potential to revolutionize the treatment of status.”

Trial Design

The Phase 2 RSE proof-of-concept clinical trial was an open-label, efficacy, safety and PK, dose-finding study conducted at 8 sites in the U.S. The study enrolled 17 medically heterogeneous patients that received an infusion of IV ganaxolone (adjunctive to second line standard of care AED) for up to 96 hours followed by a taper. The three dose groups studied were a low dose (500 mg/day), medium dose (650 mg/day) and target dose (713 mg/day). RSE patients enrolled into the study had failed a mean of 2.1 second line IV AEDs. The primary endpoint for the study was prevention of progression to third line IV anesthetics within the first 24 hours post treatment initiation. Secondary endpoints included safety, tolerability and other efficacy analyses.

KOL Breakfast and Live Webcast

Marinus will host a KOL breakfast meeting and webcast on Monday, December 9th from 7:15am to 8:30am ET which will feature presentations by Michael A. Rogawski, M.D., Ph.D., University of California, Davis, a key opinion leader in the field of neurosteroids, as well as Joe Hulihan, M.D., Chief Medical Officer of Marinus. Members of the Company’s management team will also present further information on its recently completed Phase 2 trial of ganaxolone in RSE. The breakfast will be held at the Royal Sonesta Harbor Court, 550 Light Street Baltimore, MD and is intended for institutional investors and sell-side analysts. Please [RSVP](#) in advance if you plan to attend, as space is limited. The live webcast and replay of the event will be accessible [here](#), and is also available on the Investors page of the Company’s website <https://www.marinuspharma.com/investors>.

About RSE

Status epilepticus (SE) is a rare epileptic seizure of prolonged duration, lasting more than five minutes for convulsive seizures or 30 minutes for non-convulsive. It is believed to affect approximately 75,000 patients in the U.S. each year. SE is a true medical emergency that can cause permanent damage to the brain and even death if not quickly brought under control. SE is first treated with IV benzodiazepines then IV anti-epileptic drugs. Patients that fail second line treatment with IV AEDs, are considered to be in refractory status epilepticus (RSE). There are currently no indicated treatments for refractory RSE. The primary treatment goals of clinicians treating SE are; to stop the patient from seizing immediately, assess and resolve the underlying medical condition, and move the patient towards discharge from the hospital as quickly as possible.

About Ganaxolone

Ganaxolone, a positive allosteric modulator of GABA_A, is being developed in three different dose forms (intravenous, capsule and liquid) intended to maximize therapeutic reach to adult and pediatric patient populations in both acute and chronic care settings. Unlike benzodiazepines, ganaxolone exhibits anti-seizure and anti-anxiety activity via its effects on synaptic and extrasynaptic GABA_A receptors. Ganaxolone has been studied in more than 1,600 subjects, both pediatric and adult, at therapeutically relevant dose levels and treatment regimens for up to four years. In these studies, ganaxolone was generally safe and well-tolerated. The most commonly reported adverse events were somnolence, dizziness and fatigue.

About Marinus Pharmaceuticals

Marinus Pharmaceuticals, Inc. is a pharmaceutical company dedicated to the development of ganaxolone, which offers a new mechanism of action, demonstrated efficacy and safety, and convenient dosing to improve the lives of patients suffering from epilepsy and depression. Ganaxolone is a positive allosteric modulator of GABA_A that acts on a well-characterized target in the brain known to have anti-seizure, anti-depressant and anti-anxiety effects. Ganaxolone is being developed in IV and oral dose forms intended to maximize therapeutic reach to adult and pediatric patient populations in both acute and chronic care settings. Marinus is conducting the first ever pivotal studies in children with CDKL5 deficiency disorder and PCDH19-related epilepsy and has recently released top-line data from Phase 2 studies in women with postpartum depression and patients with refractory status epilepticus. For more information visit www.marinuspharma.com. Please follow us on Twitter: @MarinusPharma.

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 interpretation of preclinical studies, development plans for our product candidate, including the development of dose forms, the clinical study testing schedule and milestones, the ability to complete enrollment in our clinical studies, interpretation of scientific basis for ganaxolone use, timing for availability and release of data, the safety, potential efficacy and therapeutic potential of our product candidate and our expectation regarding the sufficiency of our working capital. Forward-looking statements in this 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, the uncertainties inherent in the conduct of future clinical studies, the timing of the clinical studies, enrollment in clinical studies, availability of data from ongoing clinical studies, expectations for regulatory approvals, the attainment of clinical study results that will be supportive of regulatory approvals, and other matters, including the development of formulations of ganaxolone, and the availability or potential availability of alternative products or treatments for conditions targeted by the Company that could affect the availability or commercial potential of our drug candidates. Marinus undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the Company in general, see filings Marinus has made with the Securities and Exchange Commission.

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