Marinus Pharmaceuticals, Inc. Logo

Marinus Pharmaceuticals Phase 2 Clinical Trial Data Show Long-term Effectiveness of Ganaxolone in Reducing Seizure Frequency in CDKL5 Deficiency Disorder Patients

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Predictive biomarker also identified in PCDH19-related pediatric epilepsy

RADNOR, Pa., Dec. 04, 2018 (GLOBE NEWSWIRE) -- Marinus Pharmaceuticals, Inc. (Nasdaq:MRNS) (the "Company", "Marinus"), a biopharmaceutical company dedicated to the development of innovative therapeutics to treat epilepsy and neuropsychiatric disorders, today announced that ganaxolone data from its Phase 2 clinical trial in pediatric genetic epilepsies, CDKL5 Deficiency Disorder (CDD) and PCDH19-related pediatric epilepsy (PCDH19 epilepsy) were presented at the American Epilepsy Society (AES) Annual Meeting in New Orleans on December 2 and 3, 2018.

In the CDD cohort of patients, ganaxolone showed sustained, long-term effectiveness in treating children with CDD, a refractory form of pediatric epilepsy with no currently approved treatments. This is the first time a treatment has demonstrated long-term effectiveness in reducing seizure frequency in CDD.

Data from the cohort of patients with PCDH19 epilepsy identified preliminary evidence of a predictive clinical biomarker showing a significant treatment effect of ganaxolone in biomarker-positive patients.

"Both CDD and PCDH19 epilepsy are serious genetic conditions that cause early onset and difficult-to-control seizures in young children, particularly girls," said Christopher M. Cashman, chief executive officer of Marinus. "Our hope in sharing this research is to advance the understanding and treatment of rare pediatric genetic epilepsies. Current anti-epilepsy drugs show limited or temporary relief in controlling the frequency or duration of seizures."

In the CDD cohort, four patients with a 54 percent average reduction in seizure frequency at the six-month primary endpoint were included in the open label extension phase of the study to evaluate the long-term effectiveness of ganaxolone. Average seizure frequency for these patients has continued to improve, now to a 66 percent reduction. One patient experienced a robust and durable seizure reduction of 85 to 90 percent and another patient dramatically improved from a 38 percent reduction at the six-month mark to 87 percent reduction at 18-month mark. Two patients noted mild increases in seizure frequency at 12 or 18-month marks relative to six months, yet both remain improved from baseline with clinically meaningful seizure reductions (37 to 45 percent) at or beyond 12 months.

For reference, existing antiepileptic drugs (AEDs) and the ketogenic diet used in treating CDD offer limited and short-lived benefits in seizure reduction such that their effectiveness after 12 months of use degrades to only one-third of that seen at three months (Müller et al.).

"Based on these encouraging data," commented Cashman, "Marinus Pharmaceuticals has recently initiated the first global randomized, placebo-controlled pivotal Phase 3 study in children with CDD to further investigate ganaxolone's effectiveness in treating CDD."

In the PCDH19 epilepsy cohort, 11 patients with a confirmed PCDH19 mutation were enrolled at six centers in the United States and Italy and received oral ganaxolone daily for up to 26 weeks. A post-treatment analysis comparing the baseline plasma neurosteroid levels of the 11 patients revealed a significant association between the level of endogenous neurosteroid allopregnanolone-sulfate (Allo-S) and response to ganaxolone treatment. The seven patients who were positive for this biomarker showed significant improvement, with a median reduction in seizure frequency of 54 percent. The four who were negative for the biomarker showed a median 247 percent increase in seizure frequency.

"Having a clinical biomarker that could identify beforehand those patients with PCDH19 epilepsy that would respond to treatment with ganaxolone could be a game-changer in this refractory form of pediatric epilepsy," concluded Cashman. "Marinus Pharmaceuticals is evaluating the next steps needed to follow up on these encouraging results."

About CDKL5 Deficiency Disorder (CDD)

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 neuro-developmental impairment. Most children affected by CDD cannot walk, talk, or feed themselves, and many are confined to wheelchairs, dependent on others for everything. Currently, there are no approved therapies for CDD.

About PCDH19-related Epilepsy

Protocadherin 19 (PCDH19)-related epilepsy is a serious and rare epileptic syndrome characterized by highly variable early-onset cluster seizures with comorbid cognitive and behavioral disturbances with or without intellectual disability. About 1 in 10 girls who begin having seizures before the age of 5 has PCDH19 related epilepsy. The features of PCDH19-related epilepsy can overlap or look similar to the features in Dravet Syndrome. It is estimated that there are approximately 1,500 children with PCDH19 related epilepsy in the United States.

About Ganaxolone

Marinus's investigational drug, ganaxolone, is designed to provide anti-seizure activity by calming the brain and restoring its electrical balance. Ganaxolone's method of action is different from existing epilepsy and anti-depressant medications, binding to unique $GABA_A$ receptors. In clinical trials to date, ganaxolone has shown to be safe and well-tolerated, and effective in reducing seizures and anxiety in various patient populations.

About Marinus Pharmaceuticals

Marinus Pharmaceuticals, Inc. is a biopharmaceutical 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 neuropsychiatric disorders. 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 three different dose forms (IV, capsule and liquid) intended to maximize therapeutic reach to adult and pediatric patient populations in both acute and chronic care settings. Marinus has initiated the first ever pivotal study in children with CDD, a rare form of epilepsy, and is currently conducting studies in patients with postpartum depression and 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 trial testing schedule and milestones, the ability to complete enrollment in our clinical trials, 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 trials, the timing of the clinical trials, enrollment in clinical trials, availability of data from ongoing clinical trials, expectations for regulatory approvals, the attainment of clinical trial 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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