September 29, 2016

Ganaxolone Reduces Seizures in Females with PCDH19 Pediatric Epilepsy

Positive Results from First Ever Proof-of-Concept Clinical Study in Children with the Rare Genetic Mutation of PCDH19

RADNOR, Pa., Sept. 29, 2016 (GLOBE NEWSWIRE) -- Marinus Pharmaceuticals, Inc. (Nasdaq:MRNS), a biopharmaceutical company dedicated to the development of innovative therapeutics to treat epilepsy and neuropsychiatric disorders, today announced top-line results from a Phase 2 exploratory open-label clinical trial evaluating ganaxolone, its CNS-selective $GABA_A$ modulator, in females with PCDH19 pediatric epilepsy. In the trial, ganaxolone reduced seizure frequency from baseline in the majority of patients enrolled in the study and was generally safe and well tolerated. PCDH19 pediatric epilepsy is a rare, serious epilepsy characterized by early-onset cluster seizures, cognitive and sensory impairment, and behavioral disturbances, with no approved treatments. In 2015, the U.S. Food and Drug Administration granted Orphan Drug Designation to ganaxolone for the treatment of PCDH19.

Top-Line Results:

- 64% (7 of 11) of patients showed a seizure reduction compared to baseline.
  - 57% (4 of the 7 patients) showed a reduction of greater than 50% compared to baseline.
- 73% (8 of 11) of patients showed an increase in seizure-free days.
- 73% (8 of 11) of patients showed CGI-I (Clinical Global Impression of Improvement) scores of very much improved, much improved or minimally improved at their last visit when administered by the parent/caregiver, which correlated with overall seizure reduction and participation in the study extension.
- Consistent with earlier studies, ganaxolone was generally safe and well tolerated. The most common drug-related adverse event was somnolence.

Michael G. Chez, M.D., a pediatric neurologist at Sutter Medical Center in Sacramento, California, and an investigator in the Phase 2 trial, commented, "The benefit that ganaxolone provided in reducing seizures is clinically meaningful for these difficult-to-treat patients with a severe, rare epilepsy. Children with PCDH19 epilepsy are faced with many comorbidities that impact the quality of life for them and their families. In addition to seizure reduction, the patients that I treated with ganaxolone displayed improved behavior and cognitive skills during treatment. A drug that can lessen seizure burden and behavioral comorbidities caused by this disease would be welcomed by patients, their families and the medical community."

The open-label Phase 2 exploratory study enrolled 11 female children between 4 and 15 years of age at seven sites in the United States and one site in Italy. Enrolled patients had a confirmed PCDH19 genetic mutation and uncontrolled seizures despite antiepileptic pharmacotherapy. Ganaxolone was studied as an adjunctive treatment, administered as either oral liquid suspension or capsules, for 26 weeks after establishing up to 12 weeks of baseline seizure frequency. The primary efficacy measure was the percent change in seizure frequency per 28 days relative to the baseline. Secondary measures included percent increase in seizure free days from baseline and evaluation of the safety and tolerability of ganaxolone as adjunctive therapy.

The following table summarizes selected key efficacy measures for each patient:

Patient	% Reduction in Seizure Frequency from Baseline	% Increase in Seizure Free Days from Baseline
1	100.0%	22.5%
2	72.8%	852.8%
3	69.5%	31.6%
4	53.8%	4.9%
5	26.6%	27.4%
6	18.7%	7.5%
7	2.6%	32.2%

8	(3.5%)	9.2%
9	(140%)	(2.9%)
10	(256%)	(9.7%)
11	(1031%)*	(89.5%)

*Seizure calendar data not verified with caregiver

A majority of patients experienced reduced seizures during ganaxolone treatment and elected to enter the study extension following completion of 26-weeks of ganaxolone treatment. All patients that experienced reduced seizures also experienced an increased number of seizure-free days. Ganaxolone was generally safe and well tolerated with somnolence (4/11), headache (3/11), seizure (3/11) and fatigue (3/11) reported as the most common drug related adverse events. Three adverse events were reported as serious (one patient with rash and two patients with seizures). Of the five patients who discontinued the study, two patients discontinued due to lack of efficacy and three due to an adverse event. Further data will be presented in future publications and medical meetings.

Albena Patroneva, M.D., Chief Medical Officer of Marinus Pharmaceuticals, commented, "I am excited by the positive signal seen in this first proof-of-concept clinical study in females with the rare genetic mutation of PCDH19. This clinical trial confirms that the PCDH19 mutation affects every child differently with respect to severity and frequency of seizures and comorbidities. The knowledge gained from this study will be invaluable in informing our overarching pediatric plan for ganaxolone. We are now enrolling patients with other pediatric genetic epilepsies who we believe are underserved by current approved therapeutic options and who may benefit from ganaxolone treatment."

Marinus has expanded enrollment in this clinical trial to include patients with CDKL5, Lennox-Gastaut Syndrome and other pediatric genetic epilepsies. Data from these additional patient populations will be available in 2017 and, along with interactions with regulatory agencies, will inform the Company's future pediatric orphan clinical development strategy.

About PCDH19 Pediatric Epilepsy

PCDH19 pediatric epilepsy is a serious and rare epileptic syndrome that predominantly affects females. The condition, which is caused by an inherited mutation of the protocadherin 19 (PCDH19) gene, located on the X chromosome, is characterized by early-onset and highly variable cluster seizures, cognitive and sensory impairment, and behavioral disturbances. The PCDH19 gene encodes a protein, protocadherin 19, which is part of a family of molecules supporting the communication between cells in the central nervous system. In case of mutation, protocadherin 19 may be malformed, reduced in its functions or not produced at all. The abnormal expression of protocadherin 19 is associated with highly variable seizures, cognitive impairment and behavioral or social disorders with autistic traits. Currently, there are no approved therapies for PCDH19 pediatric epilepsy. No previous formal clinical trials have been conducted in this population.

About Ganaxolone

Ganaxolone is a CNS-selective $GABA_A$ modulator 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. Ganaxolone acts on a well-characterized synaptic and extrasynaptic $GABA_A$ target known for anti-seizure and anti-anxiety activity. Ganaxolone has been studied in more than 1,300 subjects, both pediatric and adult, at therapeutically relevant dose levels and treatment regimens for up to two years. In these studies, ganaxolone was generally safe and well tolerated, with the most commonly reported adverse events of somnolence, dizziness and fatigue.

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 CNS-selective $GABA_A$ modulator that acts on a well-characterized target in the brain known to have both anti-seizure 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. Ganaxolone IV is in a Phase 1 clinical trial to treat status epilepticus. Ganaxolone IV is complemented by its oral dose forms, providing the potential for IV-to-oral continuation therapy for patients transitioning from acute care to outpatient settings. Ganaxolone capsule and liquid is being studied in orphan pediatric indications with comorbidities in seizures and behavior disorders — PCDH19, CDKL5, Lennox-Gastaut Syndrome, and Fragile X Syndrome. For more information visit 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 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, and other matters, including the development of formulations of ganaxolone, 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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