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Marinus Provides Business Outlook for 2017

Several Data Milestones Anticipated With Ganaxolone

RADNOR, Pa., Jan. 05, 2017 (GLOBE NEWSWIRE) -- Marinus Pharmaceuticals, Inc. (Nasdaq:MRNS), a biopharmaceutical company dedicated to the development of innovative therapeutics to treat epilepsy and neuropsychiatric disorders, today provided a business overview to outline the clinical status of its CNS-selective $GABA_A$ modulator, ganaxolone, and an overview of near-term value-creating milestones expected in 2017.

Near-term Clinical Value Catalysts

- Initiate Phase 2 study in women with postpartum depression (PPD) in 1H 2017
- Initiate Phase 2 study in patients with refractory status epilepticus (RSE) in 1H 2017
- Report top-line data from patients with orphan, genetic disorders in mid-2017
- Report data from PPD patients in 2H 2017
- Report data from RSE patients in 2H 2017

"We have put in place a targeted strategy to unlock the value of our ganaxolone franchise," commented Christopher M. Cashman, chief executive officer of Marinus Pharmaceuticals. "We enter 2017 focused and optimistic about our prospects for the clinical advancement of ganaxolone in patients suffering from seizures and depression."

Clinical Development Overview

Marinus is developing ganaxolone to treat adults and children suffering from acute and chronic neuropsychiatric conditions where there is a mechanistic rationale for ganaxolone to provide a benefit. Ganaxolone is a one-carbon analog of a naturally occurring neurosteroid, allopregnanolone (allo), and based on pre-clinical and clinical studies conducted to date, has exhibited anxiolytic, anti-seizure and anesthetic activity by virtue of its $GABA_A$ receptor modulating properties.

Postpartum Depression (PPD)

Marinus is preparing to initiate a Phase 2 double-blind, placebo-controlled, multi-center, dose-finding study to evaluate the safety, efficacy and pharmacokinetics of ganaxolone in women with PPD. Marinus plans to evaluate dosing regimens utilizing its intravenous (IV) and oral dose forms, which will inform dosing for the pivotal studies in PPD.

PPD is a mood disorder that affects about 15% of women within the first year of childbirth. Common symptoms include feelings of extreme sadness, hopelessness, suicidal ideation, anxiety, and fatigue. PPD is thought to be linked to the rapid fluctuations in the levels of reproductive hormones and allo after childbirth. Treatment with ganaxolone may provide benefit to women suffering from PPD.

Marinus plans to initiate this Phase 2 clinical trial in women with PPD in the first half of 2017 and expects to announce data from the initial patient cohort(s) in the second half of 2017.

Refractory Status Epilepticus (RSE)

Marinus is preparing to commence a Phase 2 open-label, multi-center study to evaluate the safety, tolerability, efficacy, and pharmacokinetics of ganaxolone IV as adjunctive therapy in patients with various stages of status epilepticus (SE) who have failed first-line benzodiazepine treatment.

SE is a life-threatening occurrence within the spectrum of epileptic disorders and is characterized by the manifestation of continuous or intermittent seizures lasting more than five minutes in duration without full recovery. If SE is not treated immediately, prolonged seizure activity can result in permanent neuronal damage and contributes to the high rates of morbidity and mortality. In RSE, certain synaptic $GABA_A$ receptors are internalized, thereby making them unavailable and limiting the effectiveness of drugs that target these receptors, such as benzodiazepines. Ganaxolone modulates both synaptic and extrasynaptic $GABA_A$ receptors, allowing a therapeutic pathway for situations where synaptic $GABA_A$ receptors are unavailable.

Marinus plans to initiate this Phase 2 clinical trial in patients with RSE in the first half of 2017 and expects to announce data in the second half of 2017. The study results will be used to inform dosing for the pivotal program in RSE.

Orphan, Genetic Disorders

Ganaxolone is currently being evaluated in an ongoing Phase 2 open-label exploratory study as a treatment for orphan, genetic epilepsies. In addition to seizures, children with genetic epilepsies typically suffer from cognitive impairment and behavioral disorders. In clinical studies, ganaxolone has shown both anti-seizure as well as anti-anxiety activity. This dual benefit has the potential to address both the seizures and behavioral co-morbidities associated with a variety of orphan, genetic disorders.

The ongoing multi-cohort study is designed to enroll up to 10 patients each with CDKL5 disorder, Lennox Gastaut Syndrome (LGS) and PCDH19 pediatric epilepsy. Marinus completed the PCDH19 cohort in the study and previously announced that ganaxolone reduced seizure frequency from baseline in the majority of patients enrolled in the study and was generally safe and well tolerated. The study is actively recruiting CDKL5 and LGS patients. Marinus expects to complete enrollment and report top-line data from these cohorts in mid-2017.

The results from the CDKL5 and LGS cohorts will be evaluated alongside the completed PCDH19 cohort and Fragile X Syndrome (FXS) Phase 2 study. Based on clinical data, anticipated regulatory pathway, program risk assessments and commercial considerations, Marinus plans to prioritize one or more indications for advancement to later-stage clinical trials. Marinus anticipates announcing its strategy for orphan, genetic disorders in the second half of 2017.

Expanded Profiling of Ganaxolone

Through continued pre-clinical and clinical development, Marinus has identified additional key properties in the profile of ganaxolone.

Synergistic Activity with Benzodiazepines

In a preclinical benzodiazepine refractory rat model of SE, the combination of ganaxolone and diazepam administered intravenously produced a synergistic effect in blocking pilocarpine-induced seizures in rats. Ganaxolone and diazepam plasma levels were identical when measured both alone and in combination, indicating that neither drug affected the pharmacokinetic disposition of the other. These data may have clinical implications on the treatment and dosing of ganaxolone in patients with SE who are or have been treated with benzodiazepines.

Sedative and Anesthetic Activity of Ganaxolone IV

In a Phase 1 clinical study evaluating the safety, pharmacokinetics, and pharmacodynamics activity of ganaxolone IV, a Bispectral Index Score (BIS) was used to measure the level of consciousness by algorithmic analysis of the patient's electroencephalogram. The data showed that healthy volunteers who received a high bolus dose of ganaxolone IV achieved a sedative and anesthetic BIS range of 40-60. These additional properties of ganaxolone IV may be further explored clinically in patients with SE.

Anxiolytic Activity of Ganaxolone

The anxiolytic effects of ganaxolone were seen in a Phase 2 placebo-controlled study in children with FXS who had high anxiety at baseline. In the study, anxious FXS patients (identified as those patients with a Pediatric Anxiety Rating Score ≥13) treated with ganaxolone showed improvements in anxiety and hyperactivity across multiple measurement scales. These anxiety benefits could be instrumental, not only in the continued development of ganaxolone for FXS patients, but for other indications that Marinus is pursuing where anxiety is a common feature of the disease, such as PPD and orphan, genetic epilepsies.

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. Marinus is currently evaluating ganaxolone in orphan indications for the treatment of genetic seizure and behavior disorders, and preparing to initiate Phase 2 studies in status epilepticus, an orphan indication, and postpartum depression. 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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