Minerva Neurosciences Announces Positive Top Line Results in Phase 2b Clinical Trial With Seltorexant (MIN-202) in Treatment of Depressed Patients With an Inadequate Response to SSRIs and SNRIs

May 13, 2019

- ***Potential first-in-class, oral specific orexin-$_2$ inhibitor demonstrates statistically significant improvement in MADRS scores at 6 weeks compared to placebo***
- ***Well tolerated, with adverse events similar to or lower than the rate observed in the placebo group***
- ***Improves depressive symptoms and sleep function, thus differentiating seltorexant from current therapies***
- ***Demonstrates improvement in symptoms of MDD patients not adequately treated by SSRIs and/or SNRIs, a significant unmet need***
- ***Data support ongoing development of seltorexant in MDD***

WALTHAM, Mass., May 13, 2019 (GLOBE NEWSWIRE) -- Minerva Neurosciences, Inc. (NASDAQ: NERV), a clinical-stage biopharmaceutical company focused on the development of therapies to treat central nervous system (CNS) disorders, today announced positive results from a Phase 2b clinical trial of seltorexant (MIN-202) as adjunctive therapy to antidepressants in adult patients with major depressive disorder (MDD) who have responded inadequately to selective serotonin reuptake inhibitors (SSRIs) and/or serotonin-norepinephrine reuptake inhibitors (SNRIs).

In this dose finding study, the 20 milligram (mg) dose of seltorexant, under co-development with Janssen Pharmaceutica NV, showed a statistically significant improvement in the MADRS (Montgomery-Asberg Depression Rating Scale) score compared to placebo. The least squares mean (LS mean) difference from placebo of the change in MADRS total score at the end of week 6 was 3.1 for the 20 mg dose of seltorexant, and the 2-sided p-value was 0.083, which is below the pre-specified 2-sided type I error level of 0.1.

After three weeks of treatment, seltorexant at the 20 mg dose also showed a statistically significant improvement over placebo, highlighting its ability to improve mood symptoms over a short period of time. In addition, a key secondary outcome measure, which was based on patient stratification according to baseline insomnia severity index (ISI), showed an even greater difference from placebo for the seltorexant 20 mg arm in patients with clinically significant insomnia (ISI ≥ 15) with LS mean difference versus placebo of 4.9 on the MADRS total score and a 2-sided p-value of 0.050 compared to the overall patient population in this trial.

The 40 mg dose, to which further enrollment was stopped following the interim analysis, showed an improvement in the MADRS total score versus placebo at the end of week 6 but did not reach statistical significance. Results for the 10 mg dose were not interpretable due to the small sample size of patients assigned to this dose.

Seltorexant was well tolerated, and adverse events recorded were similar to those observed in previous studies and similar to or lower than the rate observed in the placebo group.

“Results of this study represent the first clinical observation in a large, late-stage study that a selective orexin molecule can achieve a positive effect as an adjunctive treatment in patients with MDD who have an inadequate response to SSRIs and SNRIs,” said Dr. Remy Luthringer, Executive Chairman and Chief Executive Officer of Minerva. “These findings, if confirmed in Phase 3 studies, point to a completely novel approach which would give hope to patients and to the professionals who treat them for a potential new treatment for MDD with an improved safety profile compared to existing therapies. Around 60%-70% of patients diagnosed and treated with first-line therapies, including SSRIs and/or SNRIs, do not experience adequate treatment response, and seltorexant potentially represents a unique opportunity to improve treatment response rates safely in most of these patients.”

Dr. Luthringer added, “The top line results from a separate Phase 2b trial of seltorexant in insomnia, now completely enrolled, are expected to be announced later this quarter and will add to the body of clinical data with seltorexant in insomnia and MDD.”

About the Phase 2b study (aMDD2001)

The multicenter, double-blind, randomized, parallel-group, placebo-controlled, 6-week adaptive dose-finding study consisted of three phases: a screening phase lasting up to 4 weeks, a 6-week double-blind treatment phase and a 2-week post-treatment follow-up phase. In total, 287 adult patients were enrolled at 84 clinical sites in the U.S., Europe and Japan. The study was powered for a 2-sided type I error level of 0.100. The objectives of the study were to evaluate which dose(s) of seltorexant shows a statistically significant difference from placebo on mood using the MADRS scale after 6 weeks of treatment, to assess the influence of insomnia on the observed effects on mood, and to further evaluate the overall safety and tolerability of seltorexant.

At commencement of study enrollment, subjects were randomly assigned to receive 1 of 3 treatments in a 2:1:1 ratio of seltorexant to placebo (20 mg, 40 mg). After a pre-planned interim analysis (IA), subjects were randomly assigned to receive 1 of 3 treatments in a 3:3:1 ratio of seltorexant to placebo (10 mg, 20 mg). The randomization was stratified by region (U.S., Europe, and Japan) and by baseline insomnia status (insomnia severity index, or ISI, score ≥15 versus <15). A mixed model for repeated measures (MMRM) analysis was preplanned (analysis of response by each dose, compared to placebo).

Seltorexant and the Major Depressive Disorder (MDD) landscape

Major Depressive Disorder (MDD) is one of the most commonly encountered mental disorders, with a prevalence rate in the United States of 4.7%. Globally, more than 300 million people of all ages suffer from depression. Depression is the leading cause of disability worldwide and is a major

contributor to the overall global burden of disease. It is associated with significant comorbid medical conditions that include diabetes, hypertension and cardiovascular disease, and there is an increased risk of early mortality in patients with MDD.

Among those patients suffering from MDD disorders, some do not respond adequately to either SSRIs or SNRIs. Inadequate response to these pharmacological treatments is a major challenge to worldwide public health. Although it is widely considered that current intervention benefits approximately 60% of MDD patients, only about 30% to 40% of patients show full remission of their symptoms as defined by the MacArthur criteria (for example, a 17-item Hamilton Depression Rating Scale (HDRS) score < 8).

To overcome the lack of adequate response, the use of atypical antipsychotics as adjunctive therapy for the management of patients with an inadequate response to standard of care has become one of the most widely used therapeutic strategies. Use of adjunctive atypical antipsychotics for MDD is associated with significant side effects such as weight gain, akathisia, and sedation. Several other approaches have been evaluated but, in most cases, with non-conclusive results.

Innovative approaches are needed to improve current response rates to existing treatments. The orexin system is viewed as a pivotal system in the brain and its effects classically include promotion of feeding, maintaining homeostasis, arousal, modulation of sleep-wake circadian cycles and motivation. These functions are mediated via two orexin receptors, ORX_1 and ORX_2.

Seltorexant is the most advanced specific ORX_2 molecule in clinical development with antagonistic activity when binding to its receptor. Seltorexant is currently being developed in two indications, specifically insomnia without associated psychiatric disorders and MDD in patients who have an inadequate response to SSRIs and SNRIs. Previous clinical trials have indicated that seltorexant might be useful in both indications.

About Seltorexant (MIN-202)

Seltorexant is a selective orexin-$_2$ receptor antagonist under co-development by Janssen Pharmaceutica NV and Minerva as adjunctive therapy for MDD and for the treatment of insomnia disorder. The orexin system in the brain is involved in the control of several key functions, including metabolism, stress response and wakefulness. This system promotes arousal (wakefulness) and is hypothesized to play a role in excessive arousal, which occurs in subsets of patients with mood disorders, and to have clinical utility in the treatment of such patients.

About Minerva Neurosciences

Minerva Neurosciences, Inc. is a clinical-stage biopharmaceutical company focused on the development and commercialization of a portfolio of product candidates to treat CNS diseases. Minerva's proprietary compounds include: roluperidone (MIN-101), in clinical development for schizophrenia; seltorexant (MIN-202 or JNJ-42847922), in clinical development for insomnia and MDD; MIN-117, in clinical development for major depressive disorder (MDD); and MIN-301, in pre-clinical development for Parkinson's disease. Minerva's common stock is listed on the NASDAQ Global Market under the symbol "NERV." For more information, please visit www.minervaneurosciences.com.

About the Minerva & Janssen collaboration

Minerva is developing seltorexant with Janssen Pharmaceutica, a Johnson & Johnson company. Under the terms of the collaboration, Minerva has exclusive commercialization rights to seltorexant and other orexin molecules for the treatment of insomnia and all other indications including MDD in the Minerva Territory (EU, Iceland, Lichtenstein, Switzerland & Norway). Royalties on sales outside of the Minerva Territory are payable by Janssen. Minerva pays royalties on sales (excluding sales of products for the treatment of insomnia) within the Minerva Territory.

Minerva has no financial obligations for development costs until completion of the Phase 2b development milestone. Minerva has strategic control of matters relating to the clinical development of seltorexant for insomnia.

Forward-Looking Safe Harbor Statement

This press release contains forward-looking statements which are subject to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts, reflect management's expectations as of the date of this press release, and involve certain risks and uncertainties. Forward-looking statements include statements herein with respect to the timing and scope of current clinical trials and results of clinical trials with roluperidone, seltorexant, MIN-117 and MIN-301; the timing and scope of future clinical trials and results of clinical trials with these compounds; the clinical and therapeutic potential of these compounds; our ability to successfully develop and commercialize our therapeutic products; the sufficiency of our current cash position to fund our operations; and management's ability to successfully achieve its goals. These forward-looking statements are based on our current expectations and may differ materially from actual results due to a variety of factors including, without limitation, whether roluperidone, seltorexant, MIN-117 and MIN-301 will advance further in the clinical trials process and whether and when, if at all, they will receive final approval from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies and for which indications; whether any of our therapeutic products will be successfully marketed if approved; whether any of our therapeutic product discovery and development efforts will be successful; management's ability to successfully achieve its goals; our ability to raise additional capital to fund our operations on terms acceptable to us; and general economic conditions. These and other potential risks and uncertainties that could cause actual results to differ from the results predicted are more fully detailed under the caption "Risk Factors" in our filings with the Securities and Exchange Commission, including our Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, filed with the Securities and Exchange Commission on May 6, 2019. Copies of reports filed with the SEC are posted on our website at www.minervaneurosciences.com. The forward-looking statements in this press release are based on information available to us as of the date hereof, and we disclaim any obligation to update any forward-looking statements, except as required by law.

Contact:

William B. Boni
VP, Investor Relations/
Corp. Communications
Minerva Neurosciences, Inc.
(617) 600-7376

Source: Minerva Neurosciences, Inc