Minerva Neurosciences Receives Complete Response Letter from FDA for New Drug Application for Roluperidone for the Treatment of Negative Symptoms in Patients with Schizophrenia

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BURLINGTON, Mass., Feb. 27, 2024 (GLOBE NEWSWIRE) -- Minerva Neurosciences, Inc. (Nasdaq: NERV), a clinical-stage biopharmaceutical company focused on the development of therapies to treat central nervous system disorders, announced today that the U.S. Food and Drug Administration (FDA) has issued a Complete Response Letter (CRL) to the Company's New Drug Application (NDA) for roluperidone for the treatment of negative symptoms in patients with schizophrenia.

In the CRL, the FDA cited the following clinical deficiencies:

1. Although one study (MIN-101C03) demonstrated statistical significance on the primary efficacy endpoint, it is insufficient on its own to establish substantial evidence of effectiveness.

2. The NDA submission lacks data on concomitant antipsychotic administration.

3. The NDA submission lacks data needed to establish that the change in negative symptoms of schizophrenia with roluperidone treatment was clinically meaningful.

4. The submitted safety database included an inadequate number of subjects exposed to roluperidone at the proposed dose (64 mg) for at least 12 months.

To address these deficiencies, the FDA stated that Minerva must submit at least one additional positive, adequate, and well-controlled study to support the safety and effectiveness of roluperidone for the treatment of negative symptoms. Minerva must also provide additional data to demonstrate the safety and efficacy of roluperidone co-administered with antipsychotic medications, to support that observed effect on negative symptoms with roluperidone treatment corresponds to a clinically meaningful change, and to demonstrate the long-term safety of the proposed dose.

In addition to the clinical deficiencies described above, the FDA also provided comments on, among other items, clinical pharmacology, product quality, biopharmaceutics, and nonclinical issues.

"We are disappointed that the FDA has not approved roluperidone and will request a meeting to discuss the issues raised and attempt to address FDA's feedback," said Dr. Remy Luthringer, Executive Chairman and Chief Executive Officer of Minerva. "There is a critical need for a treatment for the negative symptoms of schizophrenia. We believe that roluperidone is a safe and effective therapy for negative symptoms of schizophrenia and we will review FDA's feedback and consider our potential paths forward, including continuing to work closely with the FDA and providing any additional information as needed, with the goal of bringing this much needed therapy to patients and physicians."

About roluperidone

Roluperidone has been shown to block serotonin, sigma and α-adrenergic receptors that are all involved in the regulation of important brain functions, including mood, cognition, sleep, and anxiety.

Roluperidone was designed to avoid a direct blockade of dopaminergic receptors (the key pharmacological target for first- and second-generation antipsychotics), while maintaining blockade of a specific subtype of serotonin receptor called 5-HT_{2A} (an additional key target of second-generation antipsychotics) as well as additional pharmacological targets (sigma$_2$ and adrenergic-α_{1A}).

About Schizophrenia and Negative Symptoms
Schizophrenia is a chronic, severe, and debilitating type of mental illness characterized by distortions in thinking, perception, emotions, language, sense of self and behavior. Schizophrenia affects 20 million people worldwide. (World Health Organization).

Negative symptoms can cause individuals with schizophrenia to withdraw from society, become disinterested or unable to complete tasks or feel pleasure. Negative symptoms are characterized by five constructs: blunted affect, alogia, avolition, anhedonia, and asociality (Marder and Galderisi, 2017).

Negative symptoms are the main cause of the poor functional outcome of patients suffering from schizophrenia (Harvey et al., 2020) and may also be one of the main reasons ultra-high risk adolescents may develop full blown schizophrenia (Gomes and Grace, 2017). There are currently no treatments approved for negative symptoms of schizophrenia in the US.

Minerva believes that research continues to emerge indicating that there is a large subgroup of patients with schizophrenia who have moderate to severe primary negative symptoms and minimal positive symptoms (Galderisi 2021) and have a low risk of worsening of positive symptoms even in the absence of antipsychotic treatments (Harrow 2013; Moilanen 2016; Murray 2016; Wils 2017; Wunderink 2013; Landolt 2016).

About Minerva Neurosciences

Minerva Neurosciences, Inc. (Nasdaq: NERV) is a clinical-stage biopharmaceutical company focused on developing product candidates to treat central nervous system (CNS) diseases. Our goal is to transform the lives of patients with improved therapeutic options. Minerva's portfolio of

compounds includes roluperidone, for negative symptoms of schizophrenia, and MIN-301, for Parkinson's disease. For more information, please visit our website.

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, but are not limited to, statements herein with respect to roluperidone's potential as a safe and effective therapy for the treatment of negative symptoms of schizophrenia and critical need for such treatment; expectations concerning Minerva's ability to remediate or otherwise resolve deficiencies identified in the CRL; expectations concerning meeting request with the FDA and the outcome thereof; Minerva's plans to discuss next steps and timing for resolution of deficiencies identified in the CRL; and general expectations concerning decisions of regulatory bodies, including the FDA, and the timing thereof. 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, risks associated with developing biopharmaceutical product candidates; uncertainties associated with regulatory processes, including the content and timing of decisions by the FDA; Minerva's ability to address FDA's feedback and timing thereof; management's ability to successfully execute on its plans; Minerva's ability to raise additional capital to fund its operations and corporate objectives on terms acceptable to Minerva; general economic conditions; and other factors that are described under the caption "Risk Factors" in our filings with the Securities and Exchange Commission, including our Annual Report on Form 10-K for the year ended December 31, 2023, filed with the Securities and Exchange Commission on February 22, 2024. Copies of reports filed with the SEC are posted on our website at http://ir.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.

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