Minerva Neurosciences Provides Update from Type C Meeting with FDA and Next Steps in Preparation for Submission of a New Drug Application (NDA) for Roluperidone for the Treatment of Negative Symptoms in Schizophrenia

April 7, 2022

Company to Host Webcast Wednesday, April 13, 2022 at 11am ET

WALTHAM, Mass., April 07, 2022 (GLOBE NEWSWIRE) -- Minerva Neurosciences, Inc. (NASDAQ: NERV), a clinical-stage biopharmaceutical company developing therapies to treat central nervous system (CNS) disorders, announced today that it has received the official meeting minutes from the Type C meeting with the U.S. Food and Drug Administration (FDA) held on March 2, 2022, regarding development of roluperidone for the treatment of negative symptoms in schizophrenia.

The primary purpose of the meeting was for Minerva to seek the FDA's agreement on the use of roluperidone as monotherapy for the treatment of negative symptoms of schizophrenia in the subgroup of patients with moderate to severe negative symptoms and stable positive symptoms.

Dr. Remy Luthringer, Executive Chairman and Chief Executive Officer of Minerva Neurosciences said, “Both the patient and medical communities recognize the need for a radical new treatment to address the negative symptoms of schizophrenia. Presently, there is no approved treatment for negative symptoms in the United States. I believe roluperidone has the potential to transform the lives of people who are unable to participate in and enjoy everyday activities due to their negative symptoms. We are mindful of our responsibility to patients and would particularly like to thank Dr. Tiffany Farchione, Director, Division of Psychiatry and Dr. Billy Dunn, Director, Office of Neuroscience, and their colleagues for their support at the Type C meeting. We are committed to working with the Division and continuing an open dialogue in preparation for a potential NDA submission for roluperidone in the summer, subject to guidance from the Division.”

The Division agreed that there is an unmet need for negative symptom treatments and restated its position following the November 2020 Type C meeting in which they indicated a marketing application was highly unlikely to be filed. The Division also stated at the November 2020 meeting that, at a minimum, there would be substantial review issues due to the lack of two adequate and well-controlled trials to support efficacy claims for this novel indication. The Division acknowledged at the time that the studies appear to show promising signals and encouraged Minerva to continue the drug development program for this indication. Since the Type C meeting in November 2020, Minerva has completed the Open-label extension of the Phase 3 study and has continued to develop roluperidone as a monotherapy specifically for the treatment of negative symptoms of schizophrenia in the subgroup of patients with moderate to severe negative symptoms and stable positive symptoms.

At the recent meeting, Minerva and the Division discussed roluperidone's use as a monotherapy for negative symptoms and the Division advised that several important and substantial concerns remain including:

- the applicability of the results of the Phase 2b study (conducted in Europe) to the US population. Minerva presented data in the briefing document sent to the Division in advance of the meeting showing comparable baseline data and efficacy across both US and ex-US patients in the Phase 3 study.
- the proposed use of post hoc analyses for the primary endpoint results of the Phase 3 study. The Division added that even with the exclusion of one trial site that Minerva believes to be subject to potential data integrity issues, the overall study remains negative. For the Phase 3 study to be positive, where the truncated Hochberg procedure was used to control the overall Type I error, both roluperidone doses must be statistically significant versus placebo, which was not the case for the 32 mg dose. Minerva confirmed in post-meeting follow-up that the exclusion of one site had been prespecified in the SAP submitted to the Division in May 2020 before the unblinding of the double-blind data. Excluding the trial site with data integrity issues resulted in a nominal p-value of 0.044 on the primary endpoint for the 64 mg dose. In the Phase 2b study the 64 mg and the 32 mg doses of roluperidone achieved statistical significance versus placebo.

The Division sought reassurance that Minerva could reliably identify patients who do not need antipsychotics and how to evaluate the stability of those patients, and potential recurrence of positive symptoms of those patients, what would be considered a significant change in symptoms, how much time patients should be monitored to evaluate whether positive symptoms will recur, and what should be done if positive symptoms recur. Minerva informed the Division that it believes this patient population can be readily identified by clinicians, that this patient population presents commonly in clinical practice, that there is an unmet need for treatments for these patients and that Minerva expects that the population could be clearly characterized in product labelling.

The Division pointed out that prescribers are likely to use roluperidone in a way that differs significantly from the intended monotherapy use, noting that at this time, there are no data to show that roluperidone does not interfere with the safety or efficacy of antipsychotic medications. Minerva stated that it believes that findings from the completed Phase 2b (MIN101-C03) and Phase 3 (MIN101-C07) studies, (in which roluperidone was administered in monotherapy without concomitant use of antipsychotic medications), demonstrate continued stability of positive symptoms in patients over time. Minerva stated that the relapse rate in these trials was less than 15% of the treated population compared to relapse rates of more than 25%[1] in other trials in which patients were treated with antipsychotics. Following the meeting, Minerva submitted additional data to the Division from the Phase 2b and Phase 3 studies demonstrating that roluperidone does not interfere with the efficacy of antipsychotics in patients who suffered relapse and withdrew from the studies.

The Division confirmed that results from the pivotal bridging Bioequivalence study appear to be adequate for a future acceptable NDA submission but advised that final confirmation of this would be a matter of review and also acknowledged that Minerva's initial pediatric study plan (iPSP) dated November 28, 2017, remains in force.

Minerva continues to believe that it has conducted two adequate and well controlled studies for the intended indication, and that the data from these studies are sufficient to support a marketing application. Minerva views the concerns raised regarding the data from the Phase 2b and Phase 3 studies as those that FDA would ordinarily consider during its review of an NDA.

At the end of the meeting, the Division suggested that there may be a way to address its concerns, whether the completed studies provide substantial evidence that negative symptoms are responsive to roluperidone, concurrently with the questions about positive symptoms and coadministration with antipsychotic medication through the acquisition of additional data. The Division advised that collection of additional data could begin in parallel with Minerva's preparations for a potential marketing application and need not be deferred until a determination about submission or filing of the application has been made.

Minerva will host a webcast on Wednesday, April 13, 2022, at 11:00 ET. Joining Dr. Remy Luthringer and Geoff Race of Minerva will be Dr. Phil Harvey, Leonard M. Miller Professor of Psychiatry and Behavioral Sciences at the University of Miami Miller School of Medicine. To participate, please dial (877) 312-5845 (domestic) or (765) 507-2618 (international) and refer to conference ID 2489714.

The live webcast can be accessed under "Events and Presentations" in the Investors and Media section of Minerva's website. The archived webcast will be available on the website beginning approximately two hours after the event for 90 days.

Reference 1. Arato et al, 2002; Leucht et al 2012; Durgan et al 2016.

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 ultrahigh risk adolescents may develop full blown schizophrenia (Gomes and Grace, 2017). There are currently no treatments approved for negative symptoms of schizophrenia.

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). The medical need for treatments for this subgroup of patients is large.

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 (MIN-101), in clinical development 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. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will" and variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements in this press release include, but are not limited to, statements with respect to the clinical development of roluperidone as monotherapy for the treatment of negative symptoms of schizophrenia; the potential benefits of roluperidone as monotherapy for the treatment of negative symptoms of schizophrenia or any other indication; the adequacy and efficacy of our clinical trials and studies with roluperidone, and the sufficiency of the data from such trials and studies to support marketing application; our interpretation of the feedback from the U.S. Food and Drug Administration (FDA); the anticipated timing of New Drug Application (NDA) submission; the timing and outcomes of future interactions with U.S. and foreign regulatory bodies, including the FDA; 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 we will be able to successfully address the FDA's concerns discussed herein and whether our future interactions with the FDA will have satisfactory outcomes; whether the FDA will support and accept an NDA submission for roluperidone; whether and when, if at all, our NDA for roluperidone, if successfully submitted, will be approved by the FDA; whether roluperidone will be successfully marketed if approved; 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. Other factors that may cause our actual results to differ from those expressed or implied in the forward-looking statements in this press release are identified 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, 2021, filed with the Securities and Exchange Commission on March 1, 2022. 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 expressly disclaim any obligation to update any forward-looking statements, except as required by law.

Contact:

Investor Inquiries:
Frederick Ahlholm

Chief Financial Officer
Minerva Neurosciences, Inc.
Info@minervaneurosciences.com

Media inquiries:
Helen Shik
Principal
Shik Communications LLC
Helen@ShikCommunications.com