



Minerva Neurosciences Announces Outcome of Type C Meeting with FDA and Next Steps in the Development of Roluperidone

December 1, 2020

WALTHAM, Mass., Dec. 01, 2020 (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 that it has received official meeting minutes from the November 10, 2020 Type C meeting with the U.S. Food and Drug Administration (FDA) regarding development of roluperidone for treatment of negative symptoms in schizophrenia.

The objective of this meeting was to obtain FDA input regarding the roluperidone data package and its readiness to support a New Drug Application (NDA) submission. The two main topics addressed during the meeting were:

1. Readiness for submission of NDA

Minerva requested confirmation from FDA that, based on the totality of evidence, the data from the MIN-101C03 (Phase 2b) and MIN-101C07 (Phase 3) studies constitute substantial evidence of the effectiveness of the 64 milligrams (mg) dose of roluperidone for the treatment of negative symptoms in schizophrenia and would warrant review of an NDA submission.

FDA advised that the Phase 2b study is problematic because it did not use the commercial formulation of roluperidone and was conducted solely outside of the United States. In addition, FDA commented that the Phase 3 study does not appear to be capable of supporting substantial evidence of effectiveness, because neither dose of roluperidone showed a statistically significant separation from placebo at Week 12 in the intent-to-treat (ITT) analysis set. FDA cautioned that an NDA submission based on the current data from the Phase 2b and Phase 3 studies would be highly unlikely to be filed and 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 indication.

FDA acknowledged that the data from the Phase 2b and Phase 3 studies appear to show promising signals and encouraged Minerva to continue the development of roluperidone for treatment of negative symptoms in schizophrenia, which FDA confirmed is an unmet need.

Minerva recognizes FDA's comments but believes they can be addressed based on published regulatory guidance and precedents. The company has comparable pharmacokinetic data for the formulations used in Phase 2b and Phase 3 (the commercial formulation) and intends to perform a pivotal bioequivalence study to bridge the two formulations. In addition, Minerva believes the Phase 3 study has shown that US data and ex-US data are comparable, and that many precedents exist where drugs were approved by FDA based solely on ex-US data. Minerva believes that, in the Phase 3 study, results from the modified ITT (mITT) analysis set that excludes patients with implausible behavioral and physiological data from one site (17 of a total of 513 patients) address the lack of separation at Week 12.

2. FDA's consideration of both ITT and mITT data analyses from Phase 3 study

In the briefing book for the Type C meeting, Minerva highlighted that the exclusion of implausible behavioral and physiological data from 17 patients at one site forms the basis of the mITT analysis set as outlined in the Statistical Analysis Plan submitted to FDA before unblinding the study.

For the mITT analysis set, the 64 mg dose of roluperidone achieved a nominal statistically significant result (p -value ≤ 0.044) on the primary endpoint, the Marder Negative Symptoms Factor Score (NSFS) of the Positive and Negative Syndrome Scale (PANSS). The details of both the ITT and mITT results for the primary (NSFS) and key secondary endpoint, the Personal and Social Performance (PSP) total score, can be found at the end of this press release.

FDA advised that their consideration of both the mITT and ITT results would be a matter of review and that in principle all sites should be included in the primary analysis set, and FDA cannot determine at this time whether data from the referenced site should be removed without a thorough evaluation. FDA indicated that Minerva should include justification for exclusion of these data in the future NDA package and provide primary results both with and without these data.

Other matters

In addition to the two main agenda items described above, the use of the PSP total score in the label and the adequacy of the PANSS and PSP instruments and related constructs to assess the efficacy of roluperidone were also discussed. Minerva expects to provide requested literature to support the instruments' psychometric properties to FDA.

Future development of roluperidone

Minerva intends to continue development and NDA activities consistent with FDA's December 2019 draft guidance titled "Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products." Where the target indication is an unmet need such as negative symptoms in schizophrenia, the guidance allows the FDA to consider one adequate and well-controlled study and confirmatory evidence as an alternative to two adequate and well-controlled studies to establish effectiveness.

"We thank FDA for their constructive approach and comments related to the development of roluperidone and their recognition of the significant unmet medical need which exists for patients and their families," said Dr. Remy Luthringer, Executive Chairman and Chief Executive Officer. "As a priority, we plan to communicate with FDA regarding their comments about the Phase 2b study, and continue to move forward with the clinical pharmacology, non-clinical, and CMC work needed to support an NDA submission. Following completion of the open label extension of the Phase 3 study, we expect to request a pre-NDA meeting with FDA to discuss the NDA submission plans based on the clinical efficacy and safety data. Minerva plans to share

additional information as it becomes available.”

Roluperidone Phase 3: ITT and mITT NSFS & PSP total score change from baseline scores and p-values						
Timepoint	Intent-to-Treat			Modified Intent-to-Treat (Excluding patients from 1 site)		
	Placebo (N=172)	64 mg Roluperidone (N=171)	p-value	Placebo (N=167)	64 mg Roluperidone (N=162)	p-value
Primary Endpoint: Marder Negative Symptoms Factor Score						
Week 2	-1.6 (0.22)	-1.9 (0.22)	NS	-1.6 (0.22)	-1.9 (0.22)	0.311
Week 4	-2.0 (0.26)	-2.9 (0.26)	0.007	-2.0 (0.26)	-3.0 (0.27)	0.005
Week 8	-2.9 (0.30)	-3.8 (0.32)	0.027	-2.9 (0.31)	-3.9 (0.32)	0.021
Week 12	-3.5 (0.34)	-4.3 (0.38)	0.064	-3.5 (0.35)	-4.5 (0.35)	0.044
Key Secondary Endpoint: Personal and Social Performance Total Score						
Week 4	1.3 (0.56)	3.2 (0.56)	0.005	1.2 (0.58)	3.3 (0.59)	0.004
Week 8	2.8 (0.66)	4.8 (0.66)	0.019	2.8 (0.68)	4.9 (0.68)	0.014
Week 12	3.9 (0.73)	6.1 (0.73)	0.021	3.8 (0.75)	6.2 (0.77)	0.017

About Minerva Neurosciences:

Minerva’s portfolio of compounds includes: roluperidone (MIN-101), in clinical development for schizophrenia; a potential royalty stream from seltorexant (MIN-202 or JNJ-42847922), in clinical development for insomnia and 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.

Forward-Looking Safe Harbor Statement

This press release contains forward-looking statements. 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, without limitation, statements herein with respect to Minerva’s ability to successfully address FDA’s concerns regarding the data package of roluperidone (MIN-101) and its suitability to support NDA filing or approval; Minerva’s interpretations of FDA regulatory guidance documents and precedents the likelihood of establishing bioequivalence between the formulations of roluperidone used in the Phase 2 and Phase 3 studies or the comparability of roluperidone’s US data and ex-US data; Minerva’s ability to justify exclusion of data from the Phase 3 study’s primary analysis set ; whether the mITT analysis set addresses the lack of statistical separation at Week 12 in the ITT set; Minerva’s ability to address FDA’s comments regarding the adequacy of the PANSS and PSP instruments; the conduct of clinical pharmacology, non-clinical, CMC and other work needed to support NDA submission; the completion of the open label extension of the Phase 3 study; Minerva’s plan to request a pre-NDA meeting with FDA ; the clinical and therapeutic potential of roluperidone; the likelihood of future sales and a royalty stream from seltorexant; the timing and outcomes of future interactions with U.S. and foreign regulatory bodies; 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 will advance further in the clinical trials process and whether and when, if at all, it will receive final approval from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies and for which indications; failure to obtain regulatory approval in additional international jurisdictions preventing us from marketing our product candidates in such jurisdictions; 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; risks and uncertainties arising as a result of the ongoing COVID-19 pandemic; 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 September 30, 2020, filed with the Securities and Exchange Commission on November 2, 2020. 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.

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