Supernus Announces Promising Interim Data from Ongoing Open-Label Phase 2a Study of SPN-817 in Epilepsy

May 23, 2024

SPN-817 is a novel, first-in-class highly selective acetylcholinesterase (AChE) inhibitor for epilepsy

Company to host webcast today at 4:30 p.m. ET to discuss the interim data

ROCKVILLE, Md., May 23, 2024 (GLOBE NEWSWIRE) -- Supernus Pharmaceuticals, Inc. (Nasdaq: SUPN), a biopharmaceutical company focused on developing and commercializing products for the treatment of central nervous system (CNS) diseases, today announced data from the planned interim analysis of the exploratory open-label Phase 2a clinical study of SPN-817 for treatment-resistant seizures. The study is examining the safety and tolerability of SPN-817 as adjunctive therapy in adult patients with treatment-resistant seizures, as well as finding effective doses in various treatment-resistant seizure types. The interim analysis is as of May 1, 2024, and is based on 41 enrolled subjects, of which 19 completed the maintenance period. Of these 19 subjects, 16 subjects had focal seizures.

Summary of the Interim Data

- 75% median focal seizure reduction at the 3mg to 4mg twice daily doses in the maintenance period.
- 86% median focal seizure reduction at the 3mg to 4mg twice daily doses in the open label extension period.
- Responder analysis across all doses in maintenance period:
  - 81% of subjects with focal seizures had 30% or more seizure reduction.
  - 63% of subjects with focal seizures had 50% or more seizure reduction.
  - 19% of subjects with focal seizures had 75% or more seizure reduction.
- Median focal seizure reduction with more severe subjects (greater than 11.3 mean baseline number of seizures per 28-day period):
  - 74% in the maintenance period.
  - 86% in the open label extension period.
- Median seizure reduction in subjects with three or more other anti-seizure medications (ASMs):
  - 70% in the maintenance period.
  - 60% in the open-label extension period.
- Responder analysis in subjects across all doses with three or more ASMs in maintenance period:
  - 100% of subjects with focal seizures had 30% or more seizure reduction.
  - 82% of subjects with focal seizures had 50% or more seizure reduction.
  - 27% of subjects with focal seizures had 75% or more seizure reduction.
- Overall focal seizure reduction (all doses, 1mg to 4mg twice daily):
  - 58% median seizure reduction in the maintenance period.
  - 38% median seizure reduction in the open label extension period.
- Assessment by Epitrack®, a validated cognitive screening tool that is designed for patients with epilepsy, indicated that 83% of twelve subjects from whom data are available, was equally split into those who showed improvement and those who had no change in cognitive function.
- SPN-817 was safe and had acceptable tolerability with a discontinuation rate due to adverse events (AEs) of 22% in the titration period and 2.4% in the maintenance period.
- Most common AEs related to the drug were consistent with the known profile of acetylcholinesterase inhibitors and included nausea, diarrhea, headache, dizziness, and decreased appetite. Additional AEs such as fatigue, insomnia, vomiting, blurred vision, somnolence, and irritability were observed.

“This planned interim analysis of our Phase 2a clinical study provides early, yet what seems to be strong evidence, of the clinical utility of SPN-817 in epilepsy. In addition, the data provide important insights for the design of the upcoming Phase 2b clinical study that we plan on initiating before year end 2024,” said Jack Khattar, President and CEO of Supernus. “We will continue to analyze the valuable information provided on safety and tolerability of SPN-817 and the effective dose range in subjects. We will extend the current Phase 2a study to explore potential approaches that we have identified to further improve the tolerability during titration. Full topline results from the Phase 2a study excluding this new extension period are still on track to report in the second half of 2024. We believe SPN-817 could provide a novel, differentiated treatment option for this hard-to-treat and underserved patient population by currently available therapies.”

Webcast Details

A live webcast with presentation slides will be available via this webcast link or in the Events & Presentations section of the Company's Investor Relations website at www.supernus.com/investors. Following management's prepared remarks and discussion of the interim trial results, the call will open for questions.

Participants may also pre-register any time before the call here. Once registration is completed, participants will be provided a dial-in number with a personalized conference code to access the call. Please dial in 15 minutes prior to the start time.

Following the live call, a replay will be available on the Company's Investor Relations website at www.supernus.com/investors. The webcast will be available on the Company's website for 60 days following the live call.

About SPN-817 *(huperzine A)*

SPN-817 represents a novel mechanism of action (MOA) for an anticonvulsant. SPN-817 is a novel synthetic form of huperzine A, whose MOA includes potent acetylcholinesterase inhibition, with pharmacological activities in CNS conditions such as epilepsy. The development will initially focus on the drug's anticonvulsant activity, which has been shown in preclinical models to be effective for the treatment of partial seizures and Dravet Syndrome. SPN-817 has received Orphan Drug designation for both Dravet Syndrome and Lennox-Gastaut Syndrome from the U.S. Food and Drug Administration (FDA). We are focused on completing and optimizing the synthesis process of the synthetic drug as well as developing a novel dosage form. Given the potency of SPN-817, a novel extended-release oral dosage form is critical to the success of this program because initial studies with the immediate-release formulations of non-synthetic SPN-817 have shown serious dose-limiting, side effects. An open-label Phase 2a clinical study of SPN-817 in adult patients with treatment-resistant seizures is ongoing.

About the Phase 2a Clinical Study

The study is a Phase 2a multicenter, three-phase, long-term open-label study assessing the safety and tolerability of SPN-817 in adults 18-70 years of age with treatment resistant seizures, as well as assessing efficacy. The screening period is up to 8 weeks in duration. For eligible participants, treatment period is 20 weeks in duration followed by an option open-label extension period which is up to 52 weeks in duration. The primary outcome measure is incidence of AEs and AEs leading to discontinuation. Key secondary outcome measures include: 1) Percent Change from Baseline (PCB) in quantifiable motor seizure frequency per 28 days throughout SPN-817 dosing during maintenance period and open-label extension, 2) Treatment response defined as ≥30%, ≥50%, and ≥75% reduction in quantifiable motor seizure frequency per 28 days relative to the baseline period, 3) Change from baseline in Clinical Global Impression-Severity (CGI-S) scores, and 4) Change from baseline in cognitive profile as assessed by EpiTrack®.

About Supernus Pharmaceuticals, Inc.

Supernus Pharmaceuticals is a biopharmaceutical company focused on developing and commercializing products for the treatment of central nervous system (CNS) diseases.

Our diverse neuroscience portfolio includes approved treatments for epilepsy, migraine, ADHD, hypomobility in Parkinson's disease (PD), cervical dystonia, chronic sialorrhea, dyskinesia in PD patients receiving levodopa-based therapy, and drug-induced extrapyramidal reactions in adult patients. We are developing a broad range of novel CNS product candidates including new potential treatments for hypomobility in PD, epilepsy, depression, and other CNS disorders.

For more information, please visit www.supernus.com.

Forward Looking Statements
This press release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements do not convey historical information but relate to predicted or potential future events that are based upon management's current expectations. These statements are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. In addition to the factors mentioned in this press release, such risks and uncertainties include, but are not limited to, the Company's reporting on preliminary and partial interim data from an exploratory open label clinical study on SPN-817, the Company's ability to sustain and increase its profitability; the Company's ability to raise sufficient capital to fully implement its corporate strategy; the implementation of the Company's corporate strategy; the Company's future financial performance and projected expenditures; the Company's ability to increase the number of prescriptions written for each of its products and the products of its subsidiaries; the Company's ability to increase its net revenue; the Company's ability to commercialize its products and the products of its subsidiaries; the Company's ability to enter into future collaborations with pharmaceutical companies and academic institutions or to obtain funding from government agencies; the Company's ability to conduct and progress product research and development activities, including the timing and progress of the Company's clinical trials, and projected expenditures; the Company's ability to receive, and the timing of any receipt of, regulatory approvals to develop and commercialize the Company's product candidates including SPN-817; the Company's ability to protect its intellectual property and the intellectual property of its subsidiaries and operate its business without infringing upon the intellectual property rights of others; the Company's expectations regarding federal, state and foreign regulatory requirements; the therapeutic benefits, effectiveness and safety of the Company's product candidates including SPN-817; the accuracy of the Company's estimates of the size and characteristics of the markets that may be addressed by its product candidates; the Company's ability to increase its manufacturing capabilities for its products and product candidates including SPN-817; the Company's projected markets and growth in markets; the Company's product formulations and patient needs and potential funding sources; the Company's staffing needs; the Company's ability to increase the number of prescriptions written for each of its products and the products of its subsidiaries; the Company's ability to increase its net revenue from its products and the products of its subsidiaries; and other risk factors set forth from time to time in the Company's filings with the Securities and Exchange Commission made pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended. The Company undertakes no obligation to update the information in this press release to reflect events or circumstances after the date hereof or to reflect the occurrence of anticipated or unanticipated events.

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