Supernus Announces Positive Results from Two Phase III Studies For SPN-812 in Children with ADHD

December 6, 2018

- ***Each study, P301 and P303, met primary endpoint with robust statistical significance***
- ***Each study showed efficacy on both hyperactivity/impulsivity and inattention subscales with statistical significance***
- ***P301 study showed statistically significant onset of action as early as week 1 on both treatment doses***
- ***SPN-812 was well-tolerated with low incidence of adverse events and low discontinuation rates***
- ***Conference call and webcast to discuss results at 9:00 a.m. ET today, December 6, 2018***

ROCKVILLE, Md., Dec. 06, 2018 (GLOBE NEWSWIRE) -- Supernus Pharmaceuticals, Inc. (NASDAQ:SUPN), a pharmaceutical company focused on developing and commercializing products for the treatment of central nervous system diseases, today announced positive topline results from each of two pivotal Phase III studies of SPN-812 in children for the treatment of attention deficit hyperactivity disorder (ADHD).

Both trials were successful in achieving the primary endpoint, with SPN-812, at daily doses of 100 mg and 200 mg in study P301 and 200 mg and 400 mg in study P303. Robust statistical significance in improvement in the symptoms of ADHD from baseline to end of study as measured by the ADHD Rating Scale-5 was achieved. Both active doses in each study were well tolerated.

The Company expects to announce topline data from study P302, the first adolescent Phase III trial of SPN-812, by the end of December 2018. Topline data from the second adolescent Phase III trial, P304, are expected by the end of the first quarter of 2019. The Company expects to submit a New Drug Application (NDA) for SPN-812 in the second half of 2019, and to launch it, pending U.S. Food and Drug Administration (FDA) approval, in the second half of 2020.

“These are very exciting data demonstrating the important role we believe SPN-812 can play in treating patients with ADHD,” stated Jack Khattar, President and Chief Executive Officer of Supernus Pharmaceuticals. “We believe these data from the two pivotal Phase III studies, which are consistent with the Phase IIb data, demonstrate that SPN-812 is a well-differentiated novel non-stimulant treatment option for many children with ADHD.”

About the P301 and P303 Studies

Both studies are randomized, double-blind, placebo controlled, multicenter, parallel group clinical trials in children 6 to 11 years of age diagnosed with ADHD. Each treatment was administered orally once a day over five weeks in study P301 and seven weeks in study P302, after the titration phase.

A total of 477 patients were randomized in the P301 study across placebo and two doses of SPN-812 (100mg/200mg). A total of 313 patients were randomized in the P303 study across placebo and two doses of SPN-812 (200mg/400mg). The primary objective of both studies was to assess the effect of SPN-812 in reducing the symptoms of ADHD in children. The primary outcome measure was the change from baseline to the end of the study in the ADHD-RS-5 total score. Safety and tolerability of SPN-812 were assessed by the monitoring of adverse events, clinical laboratory tests, vital signs, ECGs, suicidality and physical examinations. Patients who completed the study were offered the opportunity to continue into an open-label phase that is currently on-going.

Topline Results

P301 Study

At the end of the study, SPN-812 100 mg and 200 mg doses reached statistical significance compared to placebo in the primary endpoint. Patients receiving SPN-812 100 mg and 200 mg had a -16.6 point change ($p=0.0004$) and a –17.7 point change ($p<0.0001$) from baseline, respectively, in the primary endpoint vs. -10.9 for placebo at week 6.

This primary result based on Mixed Model Repeated Measures (MMRM) analysis in the Intent-To-Treat (ITT) population was confirmed by sensitivity analyses using Analysis of Covariance (ANCOVA) (100 mg, $p=0.0008$; 200 mg, $p<0.0001$). With respect to the effect size, patients receiving SPN-812 100 mg and 200 mg had an effect size of 0.54 and 0.57, respectively, within the range of 0.46 to 0.63 in the Phase IIb study results.

The study demonstrated fast onset of action, reaching statistical significance for 100 mg and 200 mg doses as early as week 1 with p- values of 0.0004 and 0.0244, respectively. Statistical significance was maintained on a weekly basis through the end of the trial at week 6.

In addition, at the end of the study, SPN-812 100 mg and 200 mg reached statistical significance compared to placebo on the hyperactivity/impulsivity and inattention subscales of the ADHD-RS-5 scale with p- values ranging from <0.0001 to 0.0026.

Finally, SPN-812 100 mg and 200 mg met all secondary endpoints, including the important analysis of the Clinical Global Impression Improvement (CGI-I) secondary endpoint, with p- values of 0.002 and <0.0001, respectively, compared to placebo.

P303 Study

At the end of the study, SPN-812 200 mg and 400 mg doses reached statistical significance compared to placebo in the primary endpoint. Patients receiving SPN-812 200 mg and 400 mg had a -17.6 point change (p=0.0038) and a –17.5 point change (p=0.0063) from baseline, respectively, in the primary endpoint vs. -11.7 for placebo at week 8.

This primary result based on Mixed Model Repeated Measures (MMRM) analysis in the ITT population was confirmed by sensitivity analyses using Analysis of Covariance (ANCOVA) (200 mg, p=0.0058; 400 mg, p<0.0121). With respect to the effect size, patients receiving 200 mg and 400 mg had an effect size of 0.46 and 0.49, respectively, within the range of 0.46 to 0.63 in the Phase IIb study results.

Onset of action for SPN-812 showed clear differences compared to placebo starting by week 1, reaching statistical significance at week 5, which was sustained through the rest of the trial.

Similar to the P301 study, at the end of the P303 study, SPN-812 200 mg and 400 mg reached statistical significance compared to placebo on the hyperactivity/impulsivity and inattention subscales of the ADHD-RS-5 scale with p- values ranging from 0.0020 to 0.0248.

In addition, SPN-812 200 mg and 400 mg met the CGI-I secondary endpoint with p- values of 0.0028 and 0.0099, respectively, compared to placebo.

Safety and tolerability

Overall, both trials exhibited favorable tolerability and safety profiles with low incidence of adverse events (AEs) across all doses. AEs were mild leading to low discontinuation rates due to AEs of 2.2% to 4.8%. Treatment related AEs that reported at more than or equal to 5% for SPN-812 were somnolence, headache, decreased appetite, fatigue, and upper abdominal pain.

“Considering the strong efficacy and robust statistical significance on the primary endpoint, and several other key measures, coupled with a fast onset of action and a favorable tolerability and safety profile, we believe the data from these two pediatric Phase III trials for SPN-812 point to a well-differentiated ADHD product,” stated Dr. Stefan Schwabe, Executive Vice President R&D, Chief Medical Officer of Supernus Pharmaceuticals.

Conference Call Details

The Company will hold a conference call and webcast today, December 6, 2018, at 9:00 a.m. ET to discuss these topline results. The call will be hosted by Jack Khattar, President and Chief Executive Officer, Dr. Stefan Schwabe, Executive Vice President R&D and Chief Medical Officer, and Greg Patrick, Vice President and Chief Financial Officer. Presentation slides will be available via this webcast link approximately 30 minutes prior to the call. A question and answer session with the Supernus management team will follow the Company’s remarks.

Please refer to the information below for conference call dial-in information and webcast registration. Callers should dial in approximately 10 minutes prior to the start of the call.

Conference dial-in:	(877) 288-1043
International dial-in:	(970) 315-0267
Conference ID:	8685367
Conference Call Name:	Supernus Pharmaceuticals SPN-812 Phase III Topline Results
Webcast link:	Click here

Following the live call, a replay will be available on the company's website, www.supernus.com, under ‘Investors’.

About SPN-812

SPN-812 is a norepinephrine reuptake inhibitor with selective serotonin modulation activity that Supernus is developing as a novel non-stimulant for the treatment of ADHD. Based on data generated to date, the Company believes SPN-812 could be a well-differentiated ADHD treatment compared to other non-stimulant treatments for ADHD due to its different pharmacological and pharmacokinetic profile. The active ingredient in SPN-812, viloxazine hydrochloride, has an extensive safety record in Europe, where it was previously marketed for many years as an antidepressant.

About Supernus Pharmaceuticals, Inc.

Supernus Pharmaceuticals, Inc. is a pharmaceutical company focused on developing and commercializing products for the treatment of central nervous system (CNS) diseases. The Company currently markets Trokendi XR® (extended-release topiramate) for the prophylaxis of migraine and the treatment of epilepsy, and Oxtellar XR® (extended-release oxcarbazepine) for the treatment of epilepsy. The Company is also developing several product candidates to address large market opportunities in the CNS market, including SPN-810 for the treatment of Impulsive Aggression in ADHD

patients, SPN-812 for the treatment of ADHD and SPN-604 for the treatment of bipolar disorder.

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 ability to successfully complete the development of its product candidates including SPN-812, obtain regulatory approval and commercially market them; 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; the Company's ability to increase its net revenue; 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 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; the Company's ability to protect its intellectual property 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; 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; 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; 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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