Supernus Announces P304 Phase III Data Confirming Positive Results from Previous Three Phase III Studies on SPN-812 in ADHD

March 28, 2019

- **400 mg dose reached statistical significance compared to placebo, consistent with previous Phase III studies:**
  - **Change versus baseline in ADHD Rating Scale 5, p-value = 0.0082**
  - **Effect size of 0.66**
  - **CGI-I secondary endpoint, p-value = 0.0051**
  - **Hyperactivity/Impulsivity subscale, p-value = 0.0484**
  - **Inattention subscale, p-value = 0.0042**
- **600 mg dose narrowly missed statistical significance with p-value = 0.0712**
- **SPN-812 was well-tolerated with low incidence of adverse events and low discontinuation rates consistent with previous Phase III studies**
- **Complete Phase III program consists of robust Phase III data on 100 mg, 200 mg, and 400 mg doses in more than 1,000 patients with supporting data from two Phase II studies**
- **New Drug Application (NDA) continues to be on track for 2H 2019 submission**

ROCKVILLE, Md., March 28, 2019 (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 topline results from the second Phase III study of SPN-812 in adolescents (P304) for the treatment of attention deficit hyperactivity disorder (ADHD).

P304 is the fourth clinical trial in the SPN-812 Phase III program. Positive data from three successful pivotal trials (P301, P302, and P303) were reported in December 2018.

“We are pleased with the final data confirming the positive results we announced in the previous Phase III studies on SPN-812 last year in December. We now have robust data on 100 mg, 200 mg and 400 mg doses from all four Phase III clinical trials with SPN-812 in patients with ADHD. The data are consistent in showing a clinically meaningful reduction in the symptoms of ADHD, with a favorable safety and tolerability profile,” stated Jack Khattar, President and Chief Executive Officer of Supernus Pharmaceuticals. “We are focused on putting the NDA together for submission in the second half of this year.”

About the P304 Phase III Study

The study is a randomized, double-blind, placebo controlled, multicenter, parallel group clinical trial in adolescents 12 to 17 years of age diagnosed with ADHD. Each treatment was administered orally once a day over seven weeks, including one week of titration for 400 mg and two weeks of titration for 600 mg.

A total of 297 patients were randomized across placebo and two doses of SPN-812 (400 mg/600 mg). The primary objective was to assess the effect of SPN-812 in reducing the symptoms of ADHD in adolescents 12-17 years old. The primary outcome measure was the change from baseline to the end of the study in the ADHD-RS-5 total score tested on the 600 mg followed by the 400 mg in the statistical plan. Safety and tolerability of SPN-812 were assessed by the monitoring of adverse events (AEs), 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.

P304 Phase III Topline Results

At the end of the study (EOS), SPN-812 400 mg reached statistical significance compared to placebo in the primary endpoint. Patients receiving SPN-812 400 mg had an -18.3 LS Mean change from baseline (p=0.0082) vs. LS Mean change of-13.2 from baseline for placebo at week 7. With respect to SPN-812 600 mg, the LS Mean change of -16.7 (p=0.0712) from baseline in the primary endpoint was observed at week 7.

The result, based on Mixed Model Repeated Measures (MMRM) analysis in the Intent-To-Treat (ITT) population, was consistent with the results from sensitivity analyses using Analysis of Covariance (ANCOVA) (400 mg, p=0.0191; 600 mg, p=0.1002) at week 7 (EOS) with placebo based imputation for missing data.

At the 400 mg dose, SPN-812 demonstrated statistically significant onset of action starting week 2 (p=0.0063), which continued to the end of study at week 7 (p=0.0082). At 600 mg dose, SPN-812 demonstrated statistically significant difference from placebo in the primary endpoint during the last week of titration (week 2 dosed at 400 mg, p=0.0456) and the first week of maintenance (week 3 dosed at 600 mg, p=0.0238).

Similar to the first three studies (P301, P302 and P303), at the end of the P304 study, SPN-812 400 mg reached statistical significance compared to placebo on the hyperactivity/impulsivity and inattention subscales of the ADHD-RS-5 scale with p-values of 0.0484 and 0.0042, respectively.

In addition, SPN-812 400 mg dose met the Clinical Global Impression-Improvement secondary endpoint with p-value of 0.0051 compared to placebo.

While the 600 mg dose did not reach statistical significance, it is not needed for the submission or approvability of the NDA for children and adolescents. It was included to check for a potentially higher level of efficacy, to help in identifying the maximum effective dose, and to help in designing our trials for the adult population.

Overall, the trial exhibited favorable tolerability and safety profiles consistent with the other Phase III trials with low incidence of AEs across all doses.

AEs were mild leading to low discontinuation rates of 4.0% to 5.1%. Treatment related AEs that reported at more than or equal to 5% for SPN-812 were somnolence, fatigue, decreased appetite, headache and nausea.

“In addition to the consistent and clinically meaningful efficacy data, we continue to be encouraged by the safety and tolerability of SPN-812 especially that the 600 mg dose showed a similar profile to the 400 mg dose. We believe this compelling safety profile at a wide range of doses should provide physicians with dosing flexibility,” stated Dr. Stefan Schwabe, Executive Vice President R&D and Chief Medical Officer of Supernus Pharmaceuticals.

With the completion of the P304 study, the Company now has a robust clinical data package in more than 1,000 children and adolescent patients across all three doses of SPN-812: 100 mg, 200 mg and 400 mg. The Company continues to be focused on putting together the NDA for submission to the Food and Drug Administration in the second half of this year.

Conference Call Details

The Company will hold a conference call and webcast today, March 28, 2019, 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:	9278115
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 ‘Investor Relations’.

About SPN-812

SPN-812 is a serotonin norepinephrine modulating agent (SNMA) 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 psychiatry, 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.

CONTACT:
Jack A. Khattar, President and CEO

Gregory S. Patrick, Vice President and CFO
Supernus Pharmaceuticals, Inc.
Tel: (301) 838-2591

Or

Investor Contact:
Peter Vozzo
Westwicke Partners
Office: (443) 213-0505
Mobile: (443) 377-4767
Email: peter.vozzo@westwicke.com

Source: Supernus Pharmaceuticals, Inc.