



November 6, 2013

## Supernus Announces Release of Exciting New Clinical Data on Trokendi XR(TM)

ROCKVILLE, Md., Nov. 6, 2013 (GLOBE NEWSWIRE) -- Supernus Pharmaceuticals, Inc. (Nasdaq:SUPN), a specialty pharmaceutical company, today announced that new clinical data will be released at the American Epilepsy Society (AES) Meeting this coming December in Washington DC.

The first abstract titled "Cognitive Effects of Extended-Release, Once-Daily Trokendi XR™ vs b.i.d. Immediate-Release Topiramate (TPM-IR, Topamax®) in Healthy Volunteers" will be presented at the meeting on December 7, 2013 followed by several other abstracts.

### COGNITIVE EFFECTS OF EXTENDED-RELEASE, ONCE-DAILY TROKENDI XR™ VS B.I.D. IMMEDIATE-RELEASE TOPIRAMATE (TPM-IR, TOPAMAX®) IN HEALTHY VOLUNTEERS

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#### RATIONALE:

Dose-management strategies (slow titration, low doses) improve the tolerability of TPM, a potent, broad-spectrum AED that can cause distinctive cognitive symptoms (e.g., word-finding difficulty). Neuropsychometric tests have shown significant negative changes, especially in verbal fluency, in a relatively small subset of patients receiving TPM-IR. SPN-538 (Trokendi XR, Supernus Pharmaceuticals, Inc.) is a novel extended-release, once-daily capsule formulation of TPM that may improve tolerability and adherence. In a crossover study in healthy volunteers establishing bioequivalence of once-daily SPN-538 to b.i.d. TPM-IR (200 mg/day), effects of treatments on cognitive function were compared.

#### METHODS:

Design: Single-blind, randomized-sequence, crossover study in healthy adults. Treatments: b.i.d. TPM-IR and once-daily SPN-538 (AM, active drug; PM, matching placebo) force-titrated in 50-mg weekly increments over 4 wks to 200 mg/day for 10 days; 32-day washout between periods. Cognitive tests (verbal fluency: Controlled Oral Word Association, COWA; processing speed: Digit Symbol Substitution Test, DSST) performed before the AM dose on Days 1 (baseline); 8 (50 mg/day), 15 (100 mg/day), 22 (150 mg/day), 31 (200 mg/day), and 38 (washout). Between-treatment comparisons were evaluated by fitting a repeated measures linear mixed model with fixed effects for treatment, sequence, period, day, and treatment by day.

#### RESULTS:

In the per-protocol analysis of all subjects with data (TPM-IR, n=39; SPN-538, n=34), COWA change scores favored once-daily SPN-538 over b.i.d. TPM-IR at all test points; differences were significant at 50 (P=0.05) and 100 mg/day (P=0.0002) and for the entire treatment period (P=0.005). Subjects with moderate/severe (> 1 SD) negative COWA changes: TPM-IR, 42%; SPN-538, 12%. Similar patterns for DSST changes did not reach statistical significance.

#### CONCLUSIONS:

Based on the per-protocol analysis of COWA change scores, the concentration-time profile of once-daily SPN-538 was associated with significantly less negative impact on COWA despite PK bioequivalence to b.i.d. TPM-IR on all standard PK parameters, similar  $C_{avg0-24}$  (SPN-538, 6.1 µg/mL; TPM-IR, 6.3 µg/mL), and nearly identical mean TPM concentrations (5.6 µg/mL) when cognitive function tests were performed 18 (SPN-538) and 10 (TPM-IR) hrs after  $T_{max}$ . Once-daily SPN-538 produces more consistent TPM plasma concentrations (14% difference,  $P < 0.001$ , in peak-trough fluctuation) due to a markedly slower absorption rate (24-fold difference vs TPM-IR). COWA, known to be highly sensitive to specific effects of TPM, may be sensitive to differences in rates at which TPM concentrations increase/change. Further work to confirm these findings as well as elucidate their potential clinical significance is warranted. Funded by Supernus Pharmaceuticals, Inc.

All abstracts are now available on the AES website, [www.aesnet.org](http://www.aesnet.org) by conducting an "Abstract Search" for "Trokendi XR".

· **Cognitive Effects of Extended-Release, Once-Daily Trokendi XR™ vs b.i.d. Immediate-Release Topiramate (TPM-IR, Topamax®) in Healthy Volunteers**

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· **Linearity and Dose Strength Equivalence of Once-Daily, Extended-Release Topiramate (Trokendi XR™, SPN-838)**

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· **Steady-State Bioequivalence of Extended-Release, Once-Daily Trokendi XR™ (SPN-838) to Immediate-Release Topiramate (TPM-IR, Topamax®)**

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· **Pharmacokinetic Rationale for mg-for-mg Overnight Switch from Twice-Daily Immediate-Release Topiramate (TPM-IR) to Once-Daily, Extended-Release Trokendi XR™ (SPN-838)**

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· **Once-Daily Trokendi XR™ (SPN-838) vs. Twice-Daily Topamax®: Impact of Nonadherence on Topiramate Concentrations**

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· **Pharmacokinetics of Once-Daily, Extended-Release Trokendi XR™ (SPN-838) in the Elderly**

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"We are looking forward to presenting these exciting new data on Trokendi XR at the AES meeting. The product was launched in August of this year and is off to a solid start since its launch with positive feedback from the market confirming its unique benefits to epilepsy patients," said Jack Khattar, President & CEO, of Supernus.

## About Trokendi XR™

Trokendi XR is the only approved once-daily extended release formulation of topiramate for the treatment of epilepsy. Trokendi XR is an antiepileptic drug indicated for initial monotherapy in patients 10 years of age and older with partial onset or primary generalized tonic-clonic seizures; adjunctive therapy in patients 6 years of age and older with partial onset or primary generalized tonic-clonic seizures; and adjunctive therapy in patients 6 years of age and older with seizures associated with Lennox-Gastaut syndrome. The product is available in 25mg, 50mg, 100mg and 200mg extended-release capsules.

For full prescribing and safety information, [click here](#).

## About Supernus Pharmaceuticals, Inc.

Supernus Pharmaceuticals, Inc. is a specialty pharmaceutical company focused on developing and commercializing products for the treatment of central nervous system, or CNS, diseases. The Company has two marketed products for epilepsy, Oxtellar XR™ (extended-release oxcarbazepine) and Trokendi XR™ (extended-release topiramate). The Company is also developing several product candidates in psychiatry to address large market opportunities in ADHD, including ADHD patients with impulsive aggression. These product candidates include SPN-810 for impulsive aggression in ADHD and SPN-812 for ADHD.

## Forward-Looking Statements

This press release contains forward-looking statements regarding clinical data and the potential for Trokendi XR to treat epilepsy. Actual results may differ materially from those in these forward-looking statements as a result of various factors, including, but not limited to, risks regarding the company's ability to commercialize the product successfully, whether physicians will prescribe and patients will use the product, and competition in the market. For a further description of these and other risks facing the Company, please see the risk factors described in the Company's Annual Report Form 10-K that was filed with the United States Securities and Exchange Commission on March 15, 2013 and under the caption "Risk Factors" and the updates to these risk factors in the Company's quarterly report form 10-Q that was filed with the Commission on August 15, 2013. Forward-looking statements speak only as of the date of this press release, and the company undertakes no obligation to update or revise these statements, except as may be required by law.

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