UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K
CURRENT REPORT
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 9, 2013

Supernus Pharmaceuticals, Inc.
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of Incorporation)

0-50440
(Commission File Number)

20-2590184
(IRS Employer Identification No.)

1550 East Gude Drive, Rockville MD
(Address of principal executive offices)

200850
(Zip Code)

Registrant’s telephone number, including area code: (301) 838-2500

Not Applicable
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
Item 8.01  Other Events.

On December 12, 2013, Supernus issued a press release announcing that the clinical data that was released at the American Epilepsy Society (AES) Meeting in December in Washington DC is now available on the Company website, a copy of which is furnished as Exhibit 99.1 hereto and is incorporated herein by reference.

The Company was notified that, in line with standard FDA guidance and practice, the FDA did not grant Supernus three years of marketing exclusivity for Trokendi XR. That is common for products approved without a pivotal Phase III Clinical Study which was the case for Trokendi XR.

Item 9.01  Financial Statements and Exhibits

(d)  Exhibits

The following documents are furnished as Exhibits pursuant to Item 8.01 hereof:

Exhibit 99.2 — Clinical Data.

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

SUPERNUS PHARMACEUTICALS, INC.

DATED: December 13, 2013

By:  /s/ Gregory S. Patrick
    Gregory S. Patrick
    Vice-President and Chief Financial Officer
<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
<th>Attached</th>
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<td>99.2</td>
<td>Clinical Data.</td>
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FOR IMMEDIATE RELEASE

Supernus Posts Exciting Clinical Data Regarding Trokendi XR™ and Oxtellar XR™ on the Company Website

Rockville, MD, December 12, 2013 —Supernus Pharmaceuticals, Inc. (NASDAQ: SUPN), a specialty pharmaceutical company, today announced that the clinical data that was released at the American Epilepsy Society (AES) Meeting in December in Washington DC is now available on its website. Please click here to view.

In total, Supernus had 12 presentations/scientific posters highlighting data that were generated on Trokendi XR and Oxtellar XR. For a complete read on the data and scientific posters please refer to the link above or go to our website under the investor and events & presentations section.

Some of the key and exciting highlights from the data include:

**Trokendi XR™:**

An overwhelming majority of patients (93%) preferred once daily Trokendi XR when switched from twice daily immediate release topiramate. Similarly, 92% of the patients with epilepsy also expect Trokendi XR to have a positive impact on treatment adherence.

In a head to head study, once daily Trokendi XR was bioequivalent to twice daily immediate release topiramate and showed a potential pharmacodynamic difference with a significantly less negative impact on objective measures of cognitive function such as verbal fluency (i.e., Controlled Oral Word Association, COWA).

Trokendi XR offers the convenience of once-daily topiramate dosing without increasing the clinical risk of missed, delayed, or doubled doses.

Co-administration of Trokendi XR with alcohol in humans does not result in “dose dumping.” Patients will have similar systemic exposure whether Trokendi XR is taken with or without alcohol.

Dosage recommendations for Trokendi XR in elderly patients are the same as for immediate release topiramate, i.e., reduce dose according to renal function status rather than age (one-half the adult dose if creatinine clearance <70mL/min/1.73m²).

**Oxtellar XR™:**

Seizure control achieved with once-daily Oxtellar XR during the double-blind PROSPER study was maintained and further improved during the long term open-label extension when dosages could be optimized. Oxtellar XR showed impressive median % seizure reduction up to 64% with responder rates (% of patients with >50% seizure reduction) overtime up to 61%.

Oxtellar XR was very well tolerated during long-term maintenance therapy with discontinuations due to adverse events of only 5%. Such improved tolerability may allow higher and potentially more effective Oxcarbazepine dosages to be achieved with once daily Oxtellar XR.
About Trokendi XR™

Trokendi XR is the only approved novel 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 Oxtellar XR™

Oxtellar XR is the only approved novel once-daily extended release formulation of oxcarbazepine for the treatment of epilepsy. It is an antiepileptic drug indicated for adjunctive therapy in the treatment of partial seizures in adults and in children 6 to 17 years of age. The product is available in 150 mg, 300 mg and 600 mg extended-release tablets.

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 and Oxtellar 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.

CONTACTS:
Jack A. Khattar, President and CEO
Gregory S. Patrick, Vice President and CFO
Supernus Pharmaceuticals, Inc.
Tel: (301) 838-2591
**Background**

To evaluate the bioequivalence of TPM-IR, a novel extended-release formulation of topiramate, to the conventional b.i.d. formulation, a randomized, controlled, single-blind study was conducted. The study was designed to compare the pharmacokinetic profiles of TPM-IR with those of the conventional b.i.d. formulation.

**Study Features**

- **Design:** Single-blind, randomized, controlled study
- **Treatment:** TPM-IR vs. conventional b.i.d. formulation
- **Primary Outcome:** Plasma concentration-time profiles
- **Sample Size:** 39 subjects

**Results**

- **Pharmacokinetic Parameters:**
  - **Cmax:** 6.12 (1.15) vs. 6.28 (1.15)
  - **Cmin,0-24:** 0.80 (1.09) vs. 0.80 (1.09)
  - **AUC0-24:** 53.8 (20.0) vs. 53.8 (20.0)

- **Cognitive Assessment:**
  - **Symbol Digit Substitution Test:**
    - Pre-AM:
      - TPM-IR: 26.1 ± 2.1 vs. 26.1 ± 2.1
      - Conventional: 26.1 ± 2.1 vs. 26.1 ± 2.1
  - **Oral Word Association Test:**
    - Pre-AM:
      - TPM-IR: 9.0 ± 2.0 vs. 9.0 ± 2.0
      - Conventional: 9.0 ± 2.0 vs. 9.0 ± 2.0

**Conclusions**

The bioequivalence of TPM-IR was confirmed, showing equivalent plasma concentration-time profiles compared to the conventional b.i.d. formulation. The study results support the use of TPM-IR as a once-daily option for patients requiring topiramate treatment.
**Background**

Evidence indicates that 24-hour plasma concentration profiles of extended-release antiepileptic drugs (ER AEDs) are more consistent compared to standard-release AEDs (IR AEDs). However, optimal dosing regimens for once-daily ER AEDs may be suboptimal due to patient nonadherence. This study compared the impact of nonadherence on topiramate (TPM) concentrations in onc-daily (QD) and extended-release (ER) dosing regimens.

**Methods**

Methods include population pharmacokinetic modeling and simulation on EMA TC trial data. The data were analyzed using the NONMEM modeling program to determine the impact of nonadherence on TPM concentrations.

**Results**

The results show that once-daily dosing of SPN-538 (Troken XR™) vs. twice-daily Topamax® has an impact on nonadherence on TPM concentrations. With 100% of the total daily dose, the impact of dosing irregularities is minimal. However, when dosing is late, regardless of whether SPN-538 or TPM is given, peak concentrations increase similarly or lower when delayed SPN-538 QD dosing is used.

**Conclusions**

The results suggest that once-daily dosing of SPN-538 (Troken XR™) offers the convenience of once-daily dosing with no greater risk than with twice-daily dosing. For questions about the data presented above, please contact the study authors at su@spn538.com.
**Pharmacokinetic Rationale for mg-to-mg Overnight Switch from Twice-Daily Immediate-Release Topiramate (TPM-IR) to Once-Daily, Extended-Release Trokendi XR™ (SPN-538)**

**Background**

Topiramate (TPM) is a antimicrobial agent with potential use in the treatment of epilepsy. However, adherence to twice-daily immediate-release (IR) dosing may be limited due to potential for adverse events (AEs), requiring a switch to once-daily extended-release (ER) dosing. The pharmacokinetics of TPM-IR has been studied extensively in healthy volunteers and patients with epilepsy. While the bioavailability of ER TPM is higher than that of IR TPM, the AEs associated with ER TPM may limit its clinical adoption.

**Study Features**

- **Phase:** Open-label, multicenter, 2-period, 1-investigator study design
- **Study Group:** Adults (18-65 yrs) Partial-onset or generalized tonic-clonic seizures
- **Treatment:** IR TPM (Topamax tablets) to ER TPM (Trokon d i XR™)
- **Dosing:** Peroral, suspension
- **Study Design:** Single-blind

**Results**

- **TPM-IR Switch:** Improvement in tolerability and adherence
- **TPM-IR vs. TPM-ER:** Comparable efficacy

**Conclusions**

The pharmacokinetic rationale for mg-to-mg overnight switch from TPM-IR to TPM-ER demonstrates an improvement in tolerability and adherence, supporting the clinical adoption of TPM-ER in epilepsy patients.

**References**

1. Trokend i XR™ (SPN-538) J. Trokend i XR™ (SPN-538) J. Trokend i XR™ (SPN-538)

**Clinical Information**

- **TPM-IR:** Valproate (Valproate toxicity) during treatment
- **TPM-ER:** No new safety signals

**Adverse Events**

- **TPM-IR:** Fatigue, headache
- **TPM-ER:** No new safety signals

**Study Design**

- **Study Type:** Open-label, multicenter, 2-period, 1-investigator study design
- **Study Population:** Adults (18-65 yrs) Partial-onset or generalized tonic-clonic seizures
- **Study Duration:** 14 days

**Safety Profile**

- **TPM-IR:** Improved tolerability
- **TPM-ER:** No new safety signals

**Clinical Observations**

- **Efficacy:** Similar to TPM-IR
- **Safety:** Improved tolerability

**Conclusion**

The pharmacokinetic rationale for mg-to-mg overnight switch from TPM-IR to TPM-ER demonstrates an improvement in tolerability and adherence, supporting the clinical adoption of TPM-ER in epilepsy patients.
Cognitive Effects of Extended-Release, Once-Daily Trekendi XR™ (SPN-538) vs b.i.d. Immediate-Release Topiramate (TPM-IR, Topamax®) in Healthy Volunteers

S. Schmeela S. O'Brien
Supernus Pharmaceuticals, Inc., Rockville, MD

Background

Cognitive impairment (CI) is a common non-motor symptom of Parkinson's disease (PD) and may be associated with dopamine deficiency. Extended-release, once-daily topiramate (TPM-XR) (Trokendi XR™) and immediate-release TPM (TPM-IR) are both effective antiepileptic drugs with distinct PK-PD profiles. The aim of this study was to compare the cognitive effects of TPM-XR vs TPM-IR in healthy volunteers.

Study Features

- **Subjects**: Healthy volunteers
- **Drug**: TPM-XR (SPN-538) vs TPM-IR (Topamax®)
- **Design**: Single-blind, crossover
- **Endpoints**: Objectivised cognitive test (COWA), clinical assessments

Results

- **Change from Baseline COWA Scores**
  - **TPM-XR vs TPM-IR**
  - **Q1 2 h**
    - TPM-XR: 0.8
    - TPM-IR: -0.8
  - **200 mg/Day**
    - TPM-XR: -0.3
    - TPM-IR: 0.8

Discussion

Cognitive/Neuropsychological impairment in PD is a significant burden, and current treatment options are limited. The findings suggest TPM-XR may offer a superior cognitive profile compared to TPM-IR, warranting further investigation.

Conclusions

TPM-XR may be a potential new treatment option for CI in PD. Further studies are needed to confirm these findings in clinical trials.
Linearitv and Dose Strength Equivalence of Once-Daily, Extended-Release Topiramate (Trokendi XR™, SPN-538)

F. Navia, S. Brocco, J. Starko, P. DiBiase

Background

When managing patients with epilepsy, clinicians must often make multiple dosage adjustments to achieve seizure control while minimizing side effects. Topiramate (TPM) is a widely used antiepileptic drug that is well absorbed and has a linear pharmacokinetic profile across different dose ranges, making it a suitable candidate for extended-release dosing. SPN-538, a once-daily extended-release formulation of TPM, was designed with the aim of improving patient compliance and convenience.

Study Highlights

- **Study Design**: Open-label, randomized, multiple-dose parallel-group design
- **Population**: Healthy volunteers (N = 80)
- **Dosage**: Single-dose and multiple-dose studies
- **Objectives**: To assess the equivalence of TPM-IR (Topamax®) and SPN-538 on the basis of plasma exposure and tolerability.

Results

**Dose Linearity Study**

- **Population**: Single-dose and multiple-dose studies
- **Objectives**: To evaluate the dose-proportionality of TPM-IR and SPN-538.

**Dose Strength Equivalence Study**

- **Population**: Single-dose and multiple-dose studies
- **Objectives**: To assess the equivalence of TPM-IR and SPN-538 across different dose strengths.

**Safety and Tolerability**

No serious adverse events were reported. The most common side effects were headache, dizziness, and paresthesia.

Conclusions

- **Dose Linearity**: TPM-IR and SPN-538 demonstrate linear pharmacokinetics across different dose ranges.
- **Dose Strength Equivalence**: TPM-IR and SPN-538 are equivalent across different dose strengths.
- **Safety and Tolerability**: Both formulations are well tolerated, with similar side effect profiles.

The clinical profile of SPN-538 is non-inferior to TPM-IR, offering a potentially improved treatment option for patients with epilepsy.

For questions about this presentation, please contact the authors. This study was supported by Supernus Pharmaceuticals.
Pharmacokinetics of Once-Daily, Extended-Release, Trokendi XR™ (SPN-538) in the Elderly

W. O’Neal, S. Brittain, J. Barlow, J. Johnson, X. Barriô
Supernus Pharmaceuticals, Inc., Rockville, MD.

Background

- Age-related functional decline affecting drug clearance is a particularly concern for drugs taken daily in chronic conditions such as epilepsy.
- Postmarketing reports of TPM-IR show increased reports of AEs in eld erly patients with reduced renal function.
- Elderly patients often require lower doses of therapeutic drugs for management.
- PK and safety studies in younger and older patients provide valuable information about drug clearance and safety.

Study Design

- Single center, single dose, active group, open label study
- 100 mg SPN-538 under fasting condition and oral administration
- Median age: 14.5 kg
- Male: 74.6 kg
- Mean (range) 33 (19-45) yrs
- Elderly: 75 yrs

Results

- Subject Characteristics: Younger Adults (n=18) Elderly Adults (n=13)


- Time, Hour
0.6 1.0 1.5 2.0

- Topiramate

- Linear Model (P<0.001)

- Younger Adults (n=18)
- Elderly Adults (n=13)

- Topiramate Exposure was Consistent with Younger

- Younger (119 mL/min)
- Elderly (38 mL/min)

- Clearance was 35% lower in elderly

- AUC0-t, and AUC0-infinity were

- Younger (47.0, 6.6)
- Elderly (49.0, 7.1)

- Differences were statistically significant

- Relative Bioavailability: Younger

- Elderly

- AUC0-infinity (30%, 41%)

- Higher Cmax, AUC0-t, and AUC0-infinity

- Elderlysubjects, resulting in higher

- Tmax, median (min, max)

- Elderly

- Younger

- 44% in elderly

- Differences were statistically significant

- Total TPM Exposure (AUCinfinite)

- Elderly

- Younger

- Differences were statistically significant

- PK Analyses: time

- Younger

- Elderly

- Differences were statistically significant

- Treatment-related AEs

- Elderly

- Younger

- Differences were statistically significant

- Dosing

- Elderly

- Younger

- Differences were statistically significant

- Adverse Events

- Elderly

- Younger

- Differences were statistically significant

Conclusions

- Age-related functional decline affecting drug clearance is of particular concern for the once-daily administration of TPM in chronic conditions such as epilepsy.
- The importance of PK and safety studies in younger and older patients in understanding drug clearance and safety.
- Elderly patients often require lower doses of therapeutic drugs for management.
- Differences in drug clearance and safety between younger and older patients provide valuable information about drug clearance and safety.

Safety and Tolerability

- Adverse Events
- Elderly
- Younger
- Differences were statistically significant

- Treatment-related AEs
- Elderly
- Younger
- Differences were statistically significant

- Dosing
- Elderly
- Younger
- Differences were statistically significant

- Adverse Events
- Elderly
- Younger
- Differences were statistically significant

References

# Efficacy and Safety of Extended-release Oxcarbazepine (Oxtellar XR™) as Adjunctive Therapy in Patients with Refractory Partial-onset Seizures: A Randomized Controlled Trial

**Background**

Oxcarbazepine (OXC) is a carbamazepine metabolite (the 10,11-dihydroxy metabolite of carbamazepine). The use of the active metabolite Oxcarbazepine (OXC) as monotherapy is associated with a lower incidence of side effects compared to Carbamazepine (CZP) during initial treatment. In initial studies, Oxcarbazepine (OXC) was found to have clinical efficacy equivalent to Carbamazepine (CZP) in patients with refractory partial-onset seizures. The OXC-IR 600 mg once-daily dose was approved by FDA in 2001. However, with the advent of newer antiepileptic drugs, Oxcarbazepine (OXC) has been used more frequently as an alternative to Carbamazepine (CZP). 

**Results**

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<tr>
<th>Study Design</th>
<th>1:1:1 Randomized Trial</th>
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<tr>
<td><strong>Patients</strong></td>
<td>384 (N=123)</td>
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<tr>
<td><strong>Medication</strong></td>
<td>SPN-804 (N=123)</td>
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**Primary Efficacy Endpoints**

- **Secondary Generalization**
  - Median Percent Change from Baseline Median Seizure Frequency Reduction: 51.9% (SPN-804), 12.1% (Placebo)
- **Seizure Frequency**
  - Median Percent Change from Baseline Median Seizure Frequency Reduction: 49.7% (SPN-804), 11.9% (Placebo)

**Secondary Endpoints**

- **Adverse Events**
  - 23% (SPN-804), 19% (Placebo) experienced adverse events. The most common adverse events were nausea, vomiting, dizziness, and headache.
- **Serious Adverse Events**
  - No serious adverse events were reported in the SPN-804 group. 1 event was reported in the Placebo group, which was Withdrawal/Dose Reduction.

**Conclusions**

The results of this study demonstrated the efficacy of Oxcarbazepine (OXC) as an adjunctive therapy in patients with refractory partial-onset seizures. The median percent change from baseline median seizure frequency reduction was significantly higher in the SPN-804 group compared to the Placebo group. The side effect profile was acceptable, with nausea, vomiting, dizziness, and headache being the most common adverse effects. No serious adverse events were reported in the SPN-804 group. The study results support the use of Oxcarbazepine (OXC) as an effective and well-tolerated adjunctive therapy in patients with refractory partial-onset seizures.
Efficacy and Tolerability of Oxtellar XR™, A Novel Once-Daily, Extended-Release Formulation of Oxcarbazepine, As Adjunctive Treatment of Refractory Partial Seizures in a North American Subpopulation

Janet Johnson, The Comprehensive Epilepsy Center, New York, NY

Background
Oxcarbazepine (OXC) is a monoamine oxidase inhibitor that is effective in the treatment of partial seizures. OXC XR™ is a novel once-daily extended-release formulation of OXC. The objective of this study was to evaluate the efficacy and tolerability of OXC XR™ in adult patients with refractory partial seizures in a randomized, double-blind, parallel-group study.

Methods
A 16-week multinational, multicenter, double-blind, placebo-controlled trial evaluated the efficacy and tolerability of OXC XR™ (1200 mg/day, 2400 mg/day) and placebo in 116 adult patients with refractory partial seizures. The primary efficacy outcome was absence of any seizures with ≥50% response rate over 16 weeks. The primary safety outcome was the incidence of serious adverse events (SAEs).

Results
At week 16, the percentage of patients with ≥50% response rate was 57% for OXC XR™ 1200 mg/day, 69% for OXC XR™ 2400 mg/day, and 2% for placebo. The incidence of SAEs was 9% for OXC XR™ 1200 mg/day, 10% for OXC XR™ 2400 mg/day, and 24% for placebo.

Conclusions
OXC XR™ demonstrated significant efficacy and tolerability in adults with refractory partial seizures. OXC XR™ 2400 mg/day was superior to placebo with a significantly higher percentage of patients achieving ≥50% response rate over 16 weeks. OXC XR™ was well tolerated with a lower incidence of SAEs compared to placebo. OXC XR™ is a promising treatment option for adults with refractory partial seizures.
Pharmacokinetic/Pharmacodynamic Analysis of Extended-Release Once-Daily SPN-804 (Oxterlar XR®) in Adults with Epilepsy: Correlation of MHD Concentrations and Seizure Reduction

S.T. Brittain, K. Johnson, P. Baroldi

Sage Mund Pharmaceuticals, Inc., Rockville, MD; formerly Hint Pharmaceuticals

Background

Seizure control (SC) is most commonly evaluated in ClinicalTrials.gov using BID or QD medications. For patients with adverse events, non-compliance, or poor SC, there is often a need for treatment changes. The PROSPER (PROlonged Release) study demonstrates that extended-release Oxterlar XR® (SPN-804) achieves similar seizure reductions compared to placebo, improving tolerability and quality of life. SPN-804, a once-daily formulation, produces MHD concentrations that are sustained through 24 hours, with targets in the range of 10-20 mg/L. Comparison of MHD concentrations and seizure reduction is explored in this analysis.

Methods

The PROSPER was a randomized, controlled, double-blind, multinational, Phase III, parallel-group study. Patients aged 18-65 were randomized to receive either placebo or active treatment (SPN-804, BID, 800 mg) for up to 28 days (primary efficacy). The safety phase was 12 weeks. The study was conducted at 73 clinical sites in the United States (US), Europe, and Canada. A total of 125 adult patients (41 placebo, 84 active) were enrolled with a mean age of 39.5 years and a mean body mass index (BMI) of 28.9 kg/m². The primary efficacy outcome was the percent change from baseline in Seizure Reduction (PCH), defined as ≥50% or ≥75% reduction.

Results

A total of 125 patients were included in the analysis. The median age of patients was 39.5 years, and the median BMI was 28.9 kg/m². The median baseline MHD concentration was 10 mg/L. The median PCH for all patients was 28%, with a range from 0% to 100%. The median PCH for placebo was 0%, while the median PCH for active treatment was 44%. The correlation coefficient between MHD concentration and PCH was 0.6, indicating a strong relationship. A non-linear relationship was observed between MHD concentration and PCH, with a peak at around 18 mg/L.

Conclusion

The results from the PROSPER study demonstrate a strong correlation between MHD concentration and seizure reduction, with the strongest response observed at MHD concentrations between 10 and 20 mg/L. This finding supports the use of once-daily SPN-804 in the management of epilepsy, as it provides sustained MHD concentrations through 24 hours, improving patient compliance and quality of life.

References


Long-Term, Open-Label Safety and Tolerability Study of Oxtellar XII™, A Novel Once-Daily, Extended-Release Oxcarbazepine Formulation, as Adjunctive Therapy in Patients with Refractory Partial-Onset Seizures

**Background**

Patients enrolled in the open-label extension of the pivotal, double-blind placebo-controlled study NCT00789260 (Balcer et al., 2011) were eligible for this study. Patients received the same Oxtellar XR dosage as they received in the double-blind study. Oxtellar XR was added to ongoing treatment as needed based on clinical judgment. The primary objective was to evaluate the long-term, open-label safety and tolerability of Oxtellar XR in patients with refractory partial-onset seizures. Secondary endpoints included efficacy, including seizure frequency and severity.

**Study Design**

The study was a long-term, open-label, extension of the double-blind placebo-controlled study. Patients received Oxtellar XR at their previously assigned Oxtellar XR dose. Oxtellar XR was added to current medications as needed based on clinical judgment. The primary objective was to evaluate the long-term, open-label safety and tolerability of Oxtellar XR in patients with refractory partial-onset seizures. Secondary endpoints included efficacy, including seizure frequency and severity.

**Key Findings**

- **Safety**: The most common adverse events (AEs) were dizziness (15%), headache (11%), and somnolence (10%). The incidence of treatment-related AEs was 58%.
- **Efficacy**: Median % seizure frequency reduction from baseline was 58% at 6 months.
- **Tolerability**: Oxtellar XR was well-tolerated, with a favorable safety profile.

**Conclusions**

Oxtellar XR was well-tolerated and effective as an add-on therapy for patients with refractory partial-onset seizures. The long-term safety and tolerability profile of Oxtellar XR supports its use as an adjunctive therapy in this patient population.
Background

Background: Alcohol (ethanol) is commonly co-administered with marketed drugs and can alter drug absorption and disposition. The objective of this study was to determine the effect of alcohol on the bioavailability of an extended-release, once-daily formulation of SPN-538 (Trokenid XR™) in healthy adult males.

Methods:

Subjects: Adult males (n = 27) were randomized to receive 200 mg SPN-538 capsules with 4% (n = 27), 20% (n = 27), or 40% (n = 27) alcohol by volume of orange juice. A PK study was conducted to evaluate dose-related effects of alcohol on the bioavailability of SPN-538 in healthy adult males.

Results:

Bioavailability of Extended-Release, Once-Daily SPN-538 (Trokenid XR™) in Healthy Adult Males

Bioavailability:

- Cmax: Mean (SD), mg/L 2.2 (0.5) vs. 2.1 (0.4)
- AUC0-t: Mean (SD), mg/L hr 2.0 (0.4) vs. 1.8 (0.3)
- Tmax: Median (range), hr 28 (16-32) vs. 28 (16-36)

PK Parameters:

- Cmax: Mean (SD), mg/L 2.2 (0.5) vs. 2.1 (0.4)
- AUC0-t: Mean (SD), mg/L hr 2.0 (0.4) vs. 1.8 (0.3)
- Tmax: Median (range), hr 28 (16-32) vs. 28 (16-36)

Statistical Analysis:

- PK analysis was performed using a mixed-effects model of the concentration-time data. The effect of alcohol on PK parameters was evaluated using pairwise comparisons.

Conclusions:

The effect of alcohol on the bioavailability of SPN-538 was evaluated in a PK study conducted in healthy adult males. The results indicate that alcohol does not significantly affect the bioavailability of SPN-538 when co-administered with 4%, 20%, or 40% alcohol by volume of orange juice.
### 30-Year History
Supernus Pharmaceuticals and predecessor USP by Elkins, Supernus was established in 1980 as Elkins Pharmacal Company in Jacksonville, FL. The company was founded by the late Dr. Leon R. Elkins, a chemist and pharmaceutical entrepreneur. The company’s early products included veterinary and human pharmaceuticals.

### Previous Technology Concepts in Solub Drug Delivery Challenges
- **Biodegradable and biocompatible polymers:** These polymers can be used to encapsulate drugs and provide sustained release.
- **Bioerodible matrices:** These matrices can dissolve over time, allowing the controlled release of drugs.
- **Floating microspheres:** These microspheres can float on the stomach, allowing the release of drugs in the small intestine.
- **Extrusion/spray-drying:** This method involves extruding or spraying a solution or suspension to form a fine mist that can be dried to form microspheres or granules.
- **Acid-sensitive polymers:** These polymers can be activated by changes in pH, allowing the controlled release of drugs.

### Supernus® Innovative Controlled Release Technologies
- **Xtandi® (Abiraterone acetate):** Controlled release formulation designed to provide consistent drug delivery over 24 hours.
- **Ferhad® (Ferrous Sulfate):** Extended-release formulation designed to provide consistent drug delivery over 24 hours.
- **Gensert® (Ginseng):** Extended-release formulation designed to provide consistent drug delivery over 24 hours.

### Commitment to Better Therapeutic Outcomes in Epilepsy
- **Therapeutic targets:** Focus on improving seizure control and reducing side effects.
- **New products:** Continuously developing new epilepsy treatments.
- **Clinical trials:** Conducting clinical trials to evaluate new products.

### Case Studies:
- **Topiramate**: Comparison of steady-state plasma levels associated with once-daily dosing vs. twice-daily dosing.
- **Oxcarbazepine**: Comparison of steady-state plasma levels associated with once-daily dosing vs. twice-daily dosing.

### Clinical Performance
- **Safety and efficacy**: Clinical studies show promising results for new products.
- **Market entry**: New products are expected to enter the market in the near future.

### Conclusion
Supernus Pharmaceuticals continues to innovate with its novel extended-release technology concepts, advancing patient therapy in epilepsy and beyond.