SUPERNUS PHARMACEUTICALS, INC.

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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.
<table>
<thead>
<tr>
<th>Number</th>
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<td>99.2</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 Oxtcarbazepine 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:
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Steady-State Bioequivalence of Extended-Release, Once-Daily Trokendi XR™ (SPN-538) to Immediate-Release Topiramate (TPM-IR, Topamax®)

**Background**

The clinical use of topiramate (TPM) as a broad-spectrum antiepileptic drug (AED) is well established, with a safety profile based on extensive experience. The objective of this study was to assess the steady-state bioequivalence of once-daily SPN-538 (Trokendi XR™) versus b.i.d. TPM-IR (Topamax®) in health volunteers. The study was designed as a single-blind, randomized-sequence crossover, with TPM-IR titrated to 200 mg/day over 31 days. Topiramate concentrations were measured using a sensitive and validated method. Key findings included:

**Key Findings**

- **Bioequivalence:** The ratio of AUCs from time 0 to 24 hours for all three primary PK endpoints fell within the 80-125% limits.
- **Lower Trough Concentrations:** Once-daily SPN-538 delivered more constant plasma TPM concentrations over a 24-hour dosing period. Despite PK bioequivalence, a signal of potential convention criteria and a more rigorous measure of partial AUCs throughout a 24-hour dosing period. Slower drug absorption with SPN-538 was noted.
- **Adverse Events:** No serious adverse events were recorded. Of two subjects who discontinued due to AEs, AEs were considered study drug-related in one subject.
- **CNS/Cognitive Effects:** Most treatment-related AEs were mild to moderate, including dizziness, attention disorder, aphasia, and transient blurred vision. No deaths or other serious adverse events were reported.

**Conclusions**

At steady state, once-daily SPN-538 is bioequivalent to b.i.d. TPM-IR based on safety and efficacy. SPN-538 (Trokendi XR™, Supernus Pharmaceuticals, Inc.) is a novel extended-release formulation designed to improve tolerability and enhance adherence. This study confirms the bioequivalence of SPN-538 to TPM-IR, with potential benefits in terms of patient adherence and tolerability.

**Figure 99.2**

Exhibit 99.2
Once-Daily Trokendi XR™ (SPN-538) vs. Twice-Daily Topamax®: Impact of Nonadherence on Topiramate Concentrations

S. Brittain
EpilepsyPharmaCare, Inc., RedBall, MD

Background

Topiramate (TPM) is a widely used antiepileptic drug (AED) with an excellent safety profile. However, its discontinuation rate is high due to adverse drug reactions (ADRs) and patient nonadherence. Nonadherence results in suboptimal drug concentration, which in turn may affect the therapeutic effect. The primary objective of this study was to examine the impact of nonadherence on the plasma concentration of TPM.

Methods

A single-dose, randomized sequence (fed/fasted) crossover study (N=31) with intensive PK sampling for 168 hrs post-dose was conducted. The study aimed to compare the impact of nonadherence on TPM concentration. The study enrolled healthy adult volunteers and designed to mimic the real-world scenario of AED adherence.

Results

The plasma concentration of TPM was analyzed using a validated population PK model based on data collected in epilepsy patients (N=62) on stable maintenance TPM-IR Q12h as monotherapy or adjunctive therapy switched to identical SPN-538 QD.

Conclusions

Validated population PK model based on data collected in patients with epilepsy is highly predictive of clinical profile. Less than Company) Primary structural linear two-compartment model developed from TPM plasma concentration data for healthy volunteers. Covariates incorporated into model: Concomitant use of enzyme-inducing AEDs (EIAEDs); Body weight. Model validation Visual inspection of model graphics for goodness of fit Bootstrapping analysis of 500 datasets obtained from original data set using sampling with replacement. Nonadherence results in suboptimal drug concentration, which may affect the therapeutic effect. This study highlights the importance of adherence in achieving optimal TPM concentration and emphasizes the need for strategies to improve adherence and enhance patient satisfaction.
Pharmacokinetic Rationale for mg-to-mg Overnight Switch from Twice-Daily Immediate-Release Topiramate (TPM-IR) to Once-Daily, Extended-Release Trokend XR™ (SPN-538)

**Background**

To provide practical dosing guidance for an IR-to-ER AED switch in epilepsy, studies evaluated PK parameters of SPN-538 (Trokend XR™, Supernus) after a single mg-for-mg switch overnight from TPM-IR (Topamax®, Janssen). The objective was to determine if PK equivalence is achieved with a single mg-to-mg switch.

**Study Features**

- **Study Medication**: TPM-IR and SPN-538.
- **Study Participants**: Adults (18-65 years) with partial-onset or primary generalized seizures.
- **Study Design**: Single-center, open-label, PK study.
- **Inclusion Criteria**: Seizures: 0-3 seizures/month (28-day period).

**Results**

- **Pharmacokinetic Parameters**:
  - Cmax: TPM-IR 5.1 ± 5.3 mg/L, SPN-538 5.2 ± 5.0 mg/L.
  - Tmax: TPM-IR 1.0 ± 1.0 h, SPN-538 5.0 ± 4.8 h.
  - FL%: TPM-IR 48%, SPN-538 34%.

- **Safety**: Adverse events were mild to moderate in severity. Only AEs reported by >1 patient: fatigue (n=2), headache (n=4) during SPN-538 administration.

**Conclusions**

- **Pharmacokinetic Equivalence**: CR-LSM (geometric least squares mean) for each treatment study populations was confirmed.
- **Adherence**: Treatment adherence was excellent (92%) with once-daily dosing to facilitate bioavailability.
- **Clinical Advantages**: Extended-release AEDs offer potential tolerability and adherence benefits.
- **Further Study**: Additional research is needed to evaluate the impact of concomitant enzyme-inducing AEDs on PK parameters.

**Acknowledgments**

The authors thank the patients and study centers for their participation. This work was funded by Supernus Pharmaceuticals, Inc.
Cognitive Effects of Extended-Release, Once-Daily Trekseni XR® (SPN-538) vs b.i.d. Immediate-Release Topiramate (TPM-IR, Topamax®) in Healthy Volunteers

**Background**

SPN-538 is a novel extended-release, once-daily topiramate formulation designed to improve cognitive function and tolerability by reducing the blood concentration peaks compared to current-release forms. The study was funded by Supernus Pharmaceuticals, Inc.

**Objectives**

1. To compare the cognitive effects and tolerability of SPN-538 to immediate-release TPM.
2. To determine if the extended-release formulation has a clinically significant impact on cognitive function.

**Study Features**

- **Population:** Healthy volunteers
- **Dosing:**
  - SPN-538 200 mg QD
  - TPM-IR Q12h
- **Duration:** 31 days (10-day main period, 21-day washout)

**Assessments**

- **Cognitive Function**
  - Controlled Oral Word Association (COWA)
- **Plasma Concentrations**
  - Plasma TPM concentrations

**Results**

- **Cognitive Function**
  - No significant differences between SPN-538 and TPM-IR in COWA scores (p > 0.05).
  - Cogntive function test was performed at the end of the dosing interval, which may explain the between-treatment difference.

- **Plasma Concentrations**
  - Most notable PK difference between products.
  - Declines in baseline causes of change scores between formulations.
  - Point estimate difference between SPN-538 and TPM-IR for AUC0-24 was 3% - relatively small difference and unlikely to account for potential cognitive tolerability difference.

**Discussion**

- **Cognitive Function**
  - Cognitive function tests were performed at the end of the dosing interval, which may explain the between-treatment difference.
  - Despite PK declines, baseline causes of change scores between formulations.

- **Plasma Concentrations**
  - Most notable PK difference between products.

**Conclusions**

- **Cognitive Function**
  - Cognitive function tests were performed at the end of the dosing interval, which may explain the between-treatment difference.
  - Despite PK declines, baseline causes of change scores between formulations.

- **Plasma Concentrations**
  - Most notable PK difference between products.

**References**

Linear and Dose Strength Equivalence of Once-Daily, Extended-Release Topiramate (Trokendi XR™, SPN-538)  

Background  
When managing patients with epilepsy, one must always consider potential patient preferences and adherence to therapy. Topiramate (TPM) is an effective add-on therapy for both partial and generalized epilepsy. The objective of this study was to confirm the equivalence of the extended-release formulation with the immediate-release formulation (Trokaire®). The study was conducted to help define the initial dose and to guide future dose adjustments. 

Study Highlights  
- Single-dose study  
- Linear dose–response  
- No unexpected safety signals  
- Dose–strength equivalence  

Results  
- The population used for the analysis included 120 subjects. 
- The mean age was 34.5 years (range, 18-81 years). 
- The mean body weight was 74.0 kg (range, 49-133 kg). 
- The mean plasma TPM concentration was 3.0 µg/mL (range, 0.5-9.0 µg/mL). 

Pharmacokinetic Parameters with 200-mg Dose Administered as Different Capsule Strengths  
- PK Parameter, 200 mg  
  - Mean a (n = 24) (n = 25) (n = 25) (n = 23)  
  - AU C0 – t  
  - AU C inf  
  - Cmax  
  - Tmax , hr  
  - t1/2  

Conclusions  
- Dose–strength equivalence  
- No unexpected safety signals  
- Linear dose–response  
- Dose–strength equivalence  

No personal views or opinions should be inferred from this study. All statements should be interpreted in the context of published data. 

E. Roers1, S. Brittain1, J. Stocks1, P. Baroldi2  
1 Supernus Pharmaceuticals, Inc., Rockville, MD; 2 formerly with Supernus 

C. Brown, J. Brittain, J. Stock, P. Baroldi 
Supernus Pharmaceuticals, Inc., Rockville, MD  

References  
Pharmacokinetics of Once-Daily, Extended-Release, Trokendi XR™ (SPN-538) in the Elderly

W. O’Neal1, S. Brittain1, J. Stocks1, J. Johnson1, P. Baroldi2
1 Supernus Pharmaceuticals, Inc., Rockville, MD; 2 formerly with Supernus Background

Agarwal is characterized by age-related functional declines affecting drug clearance are particularly common for drugs largely or primarily renally handled. Study Design

Supernus Background

An open-label, single-center, single-dose, parallel-group study. 100 mg SPN-538 under fasting conditions

Population Pharmacokinetics

Population pharmacokinetics were analyzed using NONMEM. Analysis of variance (ANOVA) model with age group as a fixed effect using natural log-transformed values. ANOVA included calculation of relative bioavailability (ANOVA) model with age group as a fixed effect using natural log-transformed values. ANOVA included calculation of post-dose. Primary PK parameters: – TPM exposure from dosing to last measurable concentration (AUC0-t) – Total TPM exposure – Maximal concentration (Cmax) – Peak plasma concentration (TPMmax) Additional PK analyses: time of observed maximum concentration (Tmax) – Apparent first-order elimination constant (kel) – Apparent first-order elimination half-life (t1/2)

Safety and tolerability

Adverse events (AEs) were mild in severity and more frequent in younger vs. older adults. No serious AEs, deaths, or discontinuations occurred during the study. Mean creatinine clearance (calculated) was 35% lower in elderly (77 mL/min) vs. younger adults. AUC: 41%-44% higher in elderly adults. 90% CIs for PK parameters fell partially outside the 80%-125% equivalence limits. Safety first-order elimination constant (kel), apparent first-order elimination half-life (t1/2).

Results

Trocend XR™ (SPN-538) in the Elderly

Mean (SD) baseline plasma concentrations of TPM max for younger and elderly patients were 1.64 (0.53) mg/L and 1.23 (0.30) mg/L, respectively. AUC0-t, AUCinf, Cmax, and TPMmax were higher in elderly vs. younger adults. Relative bioavailability (Eldeiy/Youn ger) and 90% CIs were obtained by back transformation. Creatinine clearance calculated from serum creatinine using Cockcroft-Gault equations. TPM clearance was 29% lower in elderly subjects, resulting in higher Cmax, AUC0-t, and AUCinf (30%, 41%, respectively) in elderly vs. younger adults. TPM clearance was highly correlated with creatinine clearance (calculated).

Conclusions

A single 100 mg dose of SPN-538 is bioequivalent in elderly and younger adults. Once-daily, extended-release Trokendi XR™ (SPN-538) is a valuable option for treating epilepsy in patients aged 65 years and older. No serious AEs, deaths, or discontinuations occurred during the study. Mean creatinine clearance (calculated) was 35% lower in elderly (77 mL/min) vs. younger adults. AUC: 41%-44% higher in elderly adults. 90% CIs for PK parameters fell partially outside the 80%-125% equivalence limits. Safety first-order elimination constant (kel), apparent first-order elimination half-life (t1/2).

Study endpoint: Euphoria@24h@24h

In conclusion, ITT analysis shows that SPN-538 is bioequivalent in elderly and younger adults. Once-daily, extended-release Trokendi XR™ (SPN-538) is a valuable option for treating epilepsy in patients aged 65 years and older. No serious AEs, deaths, or discontinuations occurred during the study. Mean creatinine clearance (calculated) was 35% lower in elderly (77 mL/min) vs. younger adults. AUC: 41%-44% higher in elderly adults. 90% CIs for PK parameters fell partially outside the 80%-125% equivalence limits. Safety first-order elimination constant (kel), apparent first-order elimination half-life (t1/2).

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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 an antiepileptic drug (AED) that is widely used in the management of partial-onset seizures. It is metabolized to 10-mono-hydroxy derivative (MHD), which is a more active metabolite of OXC, similar to carbamazepine. The immediate-release formulation of OXC (OXC-IR) has been shown to be efficacious in treating refractory partial-onset seizures, but it has limitations due to its short half-life, which requires multiple dosing per day. Extended-release OX C (OXC-XR) was developed to provide a more convenient dosing regimen.

**Study Design**

The study was a randomized, double-blind, placebo-controlled trial conducted at multiple centers. It included patients with refractory partial-onset seizures who were not adequately controlled with other AEDs. Patients were randomized to receive either extended-release Oxcarbazepine (OxTellar XR™) or placebo for 16 weeks, with a 4-week titration period. The primary end point was the median percent change from baseline in seizure frequency for 21 consecutive days during the 14 days following study drug receipt.

**Results**

Demographics and baseline characteristics were similar across the placebo and active treatment groups. The median seizure reduction was significantly greater in the OxTellar XR™ group compared to placebo. No new safety concerns were identified.

**Discussion**

Oxcarbazepine XR showed superior efficacy compared to placebo in the primary endpoint analysis. The study supports the use of Oxcarbazepine XR as a convenient once-daily dosage regimen with improved patient compliance.

**Conclusions**

Oxcarbazepine XR was well tolerated and showed superior efficacy compared to placebo in the treatment of refractory partial-onset seizures. It is a promising new treatment option for patients with refractory seizures who have had limited success with conventional dosing regimens.
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 Johnson1; Jordan A. Frenck2; Scott Brittain3; Dawn Leary4

1Supernus Pharmaceuticals, Inc., 2Procter & Gamble Pharmaceuticals, 3Roche Pharmaceuticals, 4Neurological Institute, New York, NY

Background

Efficacy and tolerability of oxcarbazepine (OXC) have been demonstrated in refractory partial seizures (RPS) in multiple randomized, placebo-controlled trials. However, the once-daily, extended-release (XR) formulation of OXC (Oxtellar XR™) has shown favorable tolerability in studies involving children and adults in North America. The current study evaluated the efficacy and tolerability of Oxtellar XR™ in a North American subset of patients, compared to placebo.

Methods

A randomized, double-blind, placebo-controlled study was conducted in North America (ITT population: N = 366). Patients received 1 dose of study drug, followed by a 3-week taper to 1800 mg/day in a 4-week period. Efficacy outcomes included median percentage change in 28-day seizure frequency, and tolerability outcomes included treatment-related adverse events.

Results

The median percentage change in 28-day seizure frequency was significantly lower in the Oxtellar XR™ group compared to placebo (p = 0.006). The most common adverse events reported were dizziness, headache, and nausea. Treatment-related adverse events were statistically similar between the groups.

Conclusions

Oxtellar XR™ demonstrated favorable efficacy and tolerability in North American patients with refractory partial seizures. Future studies are recommended to further evaluate the potential benefit of Oxtellar XR™ in this patient population.

References


Pharmacokinetic/Pharmacodynamic Analysis of Extended-Release Once-Daily SPN-804 (Oxtebar XR™) in Adults with Epilepsy: Correlation of MHD Concentrations and Seizure Reduction

S.T. Brittain 1; J. K. Johnson 1; P. Baroldi 2

Background

Consistency in plasma levels of antiepileptic drug is crucial for improving patient compliance and reducing the risk of seizures. The impact of antiepileptic drug (AED) concentration on patient response is a critical factor in AED selection. The current study aimed to evaluate the correlation between MHD concentrations and seizure reduction in patients with epilepsy.

Methods

A randomized, double-blind, placebo-controlled study was conducted to evaluate the safety and efficacy of SPN-804, an extended-release oxcarbazepine formulation. The study included 166 patients with refractory partial-onset seizures. MHD concentrations were derived by inspection of the individual predicted (patient-specific) concentration-time profile. PK variables were derived for each subject at each visit for which the maximum effect size, C50, is the concentration producing 50% of Emax, and is the shape factor; was fixed to a series of values and the shape was kept fixed to a sigmoidal Emax model. MHD Cmin values as low as 10 mg/L were significantly linked to clinical improvement.

Results

A single representative value for Cmin was calculated for each patient in the PK analysis dataset by taking the median across visits. Results of this analysis were applied to the analysis of pharmacodynamic (PD) data, i.e., percent change (PCH) in 28-day profile for that visit. A single value was calculated for each patient in the PK analysis dataset by taking the median across visits. Results of this analysis were applied to the analysis of pharmacodynamic (PD) data, i.e., percent change (PCH) in 28-day profile for that visit.

Conclusions

The study provided evidence that MHD concentrations are predictive of seizure reduction. The correlation between MHD concentrations and seizure reduction is crucial for improving patient response and compliance. Further studies are needed to confirm these findings and explore the implications for clinical practice.

Figure 1: Plot of Individual MHD Cmin Estimated from Population PK Model and Median Seizure Reduction

Figure 2: Median Percent Seizure Reduction by MHD Concentration at Baseline
Long-Term, Open-Label Safety and Tolerability Study of Oxtear XR™, A Novel Once-Daily, Extended-Release Oxcarbazepine Formulation, as Adjunctive Therapy in Patients with Refractory Partial-Onset Seizures

**Background**

Oxcarbazepine (OXC) is a commonly used antiepileptic medication. However, patient adherence may be limited by adverse effects and the need for multiple daily dosing. Oxtear XR™ is a novel, once-daily extended-release oxcarbazepine formulation designed to improve patient adherence and tolerability.

**Study Design**

The study included an open-label extension phase following a double-blind, placebo-controlled trial. Patients were switched to Oxtear XR™ after a period of force-titrated dosing in the double-blind trial. The open-label extension phase evaluated tolerability and safety with optimized dosing.

**Results**

- **Seizure Frequency Reduction**
  - Median percentage reduction in seizure frequency from baseline: 28-39%.*
- **Side Effects**
  - Headache: 15%
  - Diplopia: 9%
  - Nausea: 7%
  - Vomiting: 6%
  - Somnolence: 6%
  - Balance disorder: 5%
  - Upper respiratory tract infection: 5%

*Improvement following addition of Oxtear XR™.

**Conclusions**

Oxtear XR™ was well tolerated during long-term maintenance therapy. Improved tolerability with once-daily Oxtear XR™ may allow higher and more effective OXC dosages to be achieved. Once-daily Oxtear XR™ may be a suitable alternative to OXC-IR when tolerability is a concern.
Effect of Alcohol on Bioavailability of Extended-Release, Once-Daily SPN-538 (Troked X R™) in Healthy Adult Males

S. Schwabe, J. Dodds, S. Brittain
Supernus Pharmaceuticals, Inc., Ballston, NY

**Background**

Extended-release oral medications may contain excipients that are soluble in alcohol but not water. The oral availability of such oral extended-release medications may be influenced by alcohol consumption. This study assessed the effect of alcohol on once-daily extended-release SPN-538 (Troked X R™) in healthy male volunteers.

**Methods**

Healthy male volunteers (21-55 years) were randomized to receive a single 200 mg SPN-538 capsule with 0%, 4%, 20%, or 40% alcohol. Disolution profiles were compared in dilute HCl solutions containing 0-40% alcohol. Primary endpoints were peak plasma concentration (Cmax), area under the curve from time 0 to infinity (AUCinf), area under the concentration-time curve from time 0 to infinity (AUC0 inf), and time to peak plasma concentration (Tmax).

**Results**

Pharmacokinetic parameters, including Cmax, AUC0-t, AUC0-inf, and Tmax, did not change significantly with increasing alcohol doses. The elimination phases suggested no effect of alcohol on TPM absorption or elimination if SPN-538 is co-administered with alcohol.

**Conclusions**

Alcohol slightly decreased primary exposure parameters (AUC0-inf, AUC0-t, Cmax). Mean t1/2 and median Tmax were similar for all alcohol doses. The effect of alcohol on bioavailability of 200 mg SPN-538 is minimal.