UPSHER-SMITH PRESENTS FAVORABLE PHARMACOKINETIC DATA ON ONCE-DAILY USL255 (EXTENDED-RELEASE TOPIRAMATE)

Findings Presented at 30th International Epilepsy Congress

Maple Grove, MN – June 24, 2013 – Upsher-Smith Laboratories, Inc., (Upsher-Smith) today announced the presentation of Phase I data supporting dose-proportional pharmacokinetics, consistent drug levels, and favorable tolerability of its investigational drug, USL255 (extended-release topiramate), across a wide range of doses in healthy subjects. USL255 is specifically engineered to provide convenient once-daily dosing and reduce fluctuations in plasma topiramate levels observed with currently available treatment options. These findings were presented at the 30th International Epilepsy Congress (IEC) in Montreal, Canada, June 23-27, 2013.

USL255 is a proprietary, extended-release formulation of topiramate being developed by Upsher-Smith for the management of epilepsy in adults.

“Maintenance of stable antiepileptic drug plasma concentrations to prevent seizures is an important consideration in the management of patients with epilepsy,” said James Cloyd, PharmD, Professor and Lawrence C. Weaver Endowed Chair-Orphan Drug Development, Department of Experimental and Clinical Pharmacology, College of Pharmacy, University of Minnesota. “Second-generation, extended-release antiepileptic drug formulations aim to reduce the frequency of dosing, thereby increasing patient compliance, while at the same time lowering the risk of adverse events related to peak drug concentrations.”

The abstract of the poster presentation, USL255, Extended-Release Topiramate, Demonstrates Dose-Proportional Pharmacokinetics and Tolerability over a Wide Dosing Range in Healthy Subjects, can be found online at www.epilepsymontreal2013.org.

-more-
About the Study

The data presented at IEC 2013 evaluated USL255 in two single-dose, Phase 1 studies in healthy subjects: 1) an open-label, 5-way crossover study of USL255 at dosage strengths of 25 - 400 mg in 30 subjects; 2) a randomized, placebo-controlled, double-blind, ascending, maximum tolerated dose study where 40 subjects received 600, 800, 1000, 1200, or 1400 mg of USL255. Post-hoc analyses evaluated dose proportionality and variability of AUC and C_{max} across the entire dosing range (25 – 1400 mg). USL255 demonstrated dose proportionality in AUC from 25 - 1400 mg; C_{max} was proportional to dose from 50 – 1400 mg. Across the dosing range, consistent plasma topiramate exposure was observed with low inter-subject variability.

In healthy subjects, single doses of USL255 were reported to be well tolerated, as measured by investigator-reported adverse events, electrocardiograms, and evaluation of clinical laboratory tests and vital sign measurements obtained throughout the studies.

About PREVAIL

Upsher-Smith recently announced the successful completion of its global Phase III (PREVAIL) clinical trial for USL255 and that its New Drug Application for USL255 has been accepted for review by the U.S. Food and Drug Administration (FDA).

The PREVAIL trial was a randomized, multicenter, double-blind, placebo-controlled, parallel-group study designed to evaluate the efficacy and safety of USL255 as adjunctive therapy in patients with refractory partial-onset seizures (POS). Preliminary findings from the Phase III trial will be submitted for presentation at the 2013 Annual Meeting of the American Epilepsy Society, December 6-10 in Washington, D.C.

PREVAIL was conducted under a Special Protocol Assessment (SPA) agreement with the FDA. More information about the trial is available at www.clinicaltrials.gov (NCT01142193).

An open-label extension study to evaluate the safety of USL255 as adjunctive therapy in patients with refractory POS who had participated in PREVAIL is ongoing. The open-label extension study can be found by searching NCT01191086 on www.clinicaltrials.gov.

About Epilepsy

Epilepsy is a medical condition that causes seizures affecting a variety of cognitive and physical functions. More than two million people in the U.S. are estimated to be affected by epilepsy with about 200,000 new cases of epilepsy diagnosed each year.¹ For many people
with epilepsy, medication will prevent seizures if taken regularly, but some people continue to have seizures.\(^1\) As many as two out of three patients treated for epilepsy have seizures that are refractory to therapy, either because they have incomplete control of their seizures or they experience treatment-related side effects that interfere with their quality of life.\(^2\)

**Upsher-Smith’s Epilepsy Pipeline**

Upsher-Smith’s clinical development pipeline includes three investigational drugs that are being studied for the management of epilepsy. USL255 is an investigational once-daily, extended-release topiramate for the management of epilepsy. The pipeline also includes USL261, an investigational intranasal midazolam for the rescue treatment of seizures in patients who require control of intermittent bouts of increased seizure activity, often called seizure clusters, which is the subject of an ongoing international Phase III clinical trial (ARTEMIS1) with an open-label safety extension study. In addition, USL260 (tonabersat) is in early clinical development as a potential first-in-class neuronal gap junction modulator.

**About Upsher-Smith**

Upsher-Smith, founded in 1919, is an independent and privately-owned specialty pharmaceutical company headquartered in Maple Grove, Minnesota that focuses on product growth and innovation for branded and generic pharmaceuticals. Upsher-Smith has a particular focus on developing therapies to assist people suffering from central nervous system diseases, and also markets products relating to cardiology, dermatology, and women’s health. For more information, visit [www.upsher-smith.com](http://www.upsher-smith.com).

### References