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UPSHER-SMITH PRESENTS NEW DATA FROM YEAR-LONG, OPEN-LABEL EXTENSION STUDY OF QUDEXY™ XR (TOPIRAMATE) EXTENDED-RELEASE CAPSULES AT 68TH ANNUAL AMERICAN EPILEPSY SOCIETY MEETING

Multiple Presentations Highlight Long-Term Safety, Tolerability, and Efficacy Measures, as Adjunctive Therapy for Patients with Refractory Partial-Onset Seizures

Seattle, WA – December 8, 2014 – [Upsher-Smith Laboratories, Inc.](http://www.upsher-smith.com) (Upsher-Smith) presented findings from a year-long, open-label extension (OLE) study (PREVAIL OLE) of [Qudexy™ XR \(topiramate\) extended-release capsules](#) that demonstrated Qudexy™ XR as a generally well-tolerated adjunctive treatment option for a high proportion of patients with refractory partial-onset seizures (POS). The PREVAIL OLE study enrolled 96.8% of participants who completed the original randomized, double-blind, placebo-controlled, Phase 3 PREVAIL trial of Qudexy™ XR, a once-daily, broad-spectrum antiepileptic drug specifically engineered to deliver a smooth pharmacokinetic profile. Data from the study were presented for the first time at the 68th Annual Meeting of the American Epilepsy Society in Seattle, Washington on December 5-9, 2014.

The PREVAIL OLE study completion rate was 70%. The majority of adverse events reported were mild to moderate in severity. The median percent reduction in weekly POS frequency from the original PREVAIL trial baseline was 59% (all subjects combined) for the open-label treatment phase.

Qudexy™ XR is indicated as initial monotherapy in patients 10 years of age and older with POS or primary generalized tonic-clonic seizures. It is also approved as an adjunctive therapy in patients two years of age or older with POS, primary generalized tonic-clonic seizures, or seizures associated with Lennox-Gastaut syndrome. Qudexy™ XR and its authorized generic, Topiramate Extended-Release Capsules also from Upsher-Smith, are the only extended-release topiramate products that are FDA-approved to be administered by carefully opening the capsule and sprinkling the entire contents onto a spoonful of soft food. All strengths of Qudexy™ XR and its authorized generic may be administered by this sprinkle method. This makes them the only extended-release topiramate products approved for patients

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who experience challenges swallowing whole capsules or tablets.

“The positive findings from the year-long, open-label extension study will help clinicians who choose Qudexy™ XR for adjunctive treatment of partial-onset seizures. The results suggest that Qudexy™ XR has a favorable long-term safety and tolerability profile,” said Steve Chung, M.D., Professor of Neurology at Barrow Neurological Institute, Phoenix and trial investigator. “We are confident that this data will help clinicians make informed decisions about treatment with Qudexy™ XR.”

“Upsher-Smith is committed to the research and development of new treatments for seizure disorders and other diseases of the central nervous system,” said William Pullman, MB BS, BmedSc, PhD, FRACP, Chief Scientific Officer, Upsher-Smith. “As such, we are pleased that a high proportion of patients treated with Qudexy™ XR in the open-label extension study have seen positive results in terms of safety, tolerability, and seizure frequency measures.”

Additional PREVAIL OLE Safety and Tolerability Results

- The most common Treatment Emergent Adverse Events (TEAEs) (\geq 5% of all patients) were headache (7.6%), weight decrease (7.6%), somnolence (7.1%), dizziness (6.2%), aphasia (5.2%), and fatigue (5.2%).
- The incidence of individual neurocognitive or neuropsychiatric TEAEs newly reported during the OLE was mostly less than 3%, with the exception of aphasia (5.2%) and depression (3.8%)

Abstracts of the poster presentations can be found online at www.aesnet.org. To schedule an interview with an investigator, please contact Daina Basile at dbasile@klcpr.com.

About Upsher-Smith’s PREVAIL and PREVAIL OLE Studies

The PREVAIL OLE study was an open-label extension of PREVAIL, which was a global Phase 3 study designed to evaluate the efficacy and safety of Qudexy™ XR (USL255) as adjunctive therapy in patients with refractory partial-onset seizures (n=249) using a randomized, double-blind, placebo-controlled, parallel-group methodology. 96.8% of participants who completed PREVAIL enrolled in PREVAIL OLE (n=210). Participants underwent a 3-week, blinded-conversion phase, during which patients previously randomized to placebo in PREVAIL were titrated to 200 mg/d Qudexy™ XR, and those randomized to 200 mg/d of Qudexy™ XR in

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PREVAIL were given matching placebo. The conversion phase was followed by a 52-week open-label treatment phase. After completing 11 weeks of treatment, changes were allowed in Qudexy™ XR dosage (in 50 mg/wk increments to a maximum of 400 mg/d) and to concomitant antiepileptic drugs (AEDs).

To learn more about the original PREVAIL study, see www.clinicaltrials.gov ([NCT01142193](https://clinicaltrials.gov/ct2/show/study/NCT01142193)). Additional information concerning the open-label extension study, PREVAIL OLE, can be found by searching [NCT0119086](https://clinicaltrials.gov/ct2/show/study/NCT0119086) at www.clinicaltrials.gov or by contacting Upsher-Smith Medical Affairs at 1-800-654-2299.

About Epilepsy

Epilepsy is a medical condition that is characterized by recurrent seizures. More than two million people in the U.S. are estimated to be affected by epilepsy, with about 150,000 new cases of epilepsy diagnosed each year.¹ Epilepsy can be associated with profound physical, psychological and social consequences that negatively impact people's lives.

About Upsher-Smith

Upsher-Smith Laboratories, Inc., founded in 1919, is a growing pharmaceutical company dedicated to its mission of *Advancing Pharmacotherapy. Improving Life™*. With capabilities ranging from early-stage research to delivering on-market products, Upsher-Smith is committed to offering quality products that enable people to live life to its greatest potential. Upsher-Smith's approach to product development and partnering has resulted in a broad range of both branded and generic therapeutic solutions to address patients' needs. The Company has a particular focus on developing therapies for people living with central nervous system (CNS) conditions, such as seizure disorders, and has a robust pipeline of promising CNS compounds in various stages of development. For more information, visit www.upsher-smith.com.

IMPORTANT SAFETY INFORMATION

Do not take Qudexy™ XR or Topiramate Extended-Release Capsules if you have metabolic acidosis and are also taking metformin (e.g., Glucophage®).

Qudexy XR and Topiramate Extended-Release Capsules can cause serious side effects including: Eye problems. Serious eye problems include blurred vision, sudden decrease in vision with or without eye pain and redness, and a blockage of fluid that may cause increased

pressure in the eye (secondary angle closure glaucoma). **Decreased sweating and increased body temperature (fever).** People, especially children, should be watched for signs of decreased sweating and fever, especially in hot temperatures. Some people may need to be hospitalized for this condition. **Increased acid level in your blood (metabolic acidosis).** This may or may not cause symptoms. Symptoms may include feeling tired, decreased appetite, change in heartbeat, or trouble thinking clearly. If left untreated, metabolic acidosis can cause brittle or soft bones (osteoporosis, osteomalacia, osteopenia), kidney stones, can slow the rate of growth in children, and may harm your baby if you are pregnant. **High blood ammonia levels.** High ammonia in the blood can affect mental activities, slow alertness, cause tiredness, or cause vomiting. This can also happen when Qudexy XR or Topiramate Extended-Release Capsules are taken with a medicine called valproic acid (e.g., Depakene[®] and Depakote[®]). **Kidney stones.** Drink plenty of fluids when taking Qudexy XR or Topiramate Extended-Release Capsules to decrease your chances of getting kidney stones. **Low body temperature.** Taking Qudexy XR or Topiramate Extended-Release Capsules when you are also taking valproic acid may cause a drop in body temperature to less than 95°F, tiredness, confusion, or coma. **Effects on thinking and alertness.** Qudexy XR and Topiramate Extended-Release Capsules may affect how you think, and can cause confusion, and problems with concentration, attention, memory, or speech. Qudexy XR and Topiramate Extended-Release Capsules may cause depression or mood problems, tiredness, and sleepiness. **Dizziness or loss of muscle coordination.** Call your healthcare provider right away if you have any of the above symptoms.

Like other antiepileptic drugs, Qudexy XR and Topiramate Extended-Release Capsules may cause suicidal thoughts or actions in a very small number of people, about 1 in 500. Before you take Qudexy XR or Topiramate Extended-Release Capsules, tell your healthcare provider if you have or have had depression, mood problems, or suicidal thoughts or behavior. Call a healthcare provider right away if you have thoughts about suicide or dying; have attempted to commit suicide; have new or worsening depression or anxiety; feel agitated or restless; experience panic attacks, trouble sleeping (insomnia), or new or worsening irritability; feel or act aggressive, angry, or violent; act on dangerous impulses; have an extreme increase in activity and talking (mania); or experience other unusual changes in behavior or mood.

Before taking Qudexy XR or Topiramate Extended-Release Capsules, tell your healthcare provider about any other medical conditions, including if you have had depression, mood problems, or suicidal thoughts or behavior; have kidney problems, kidney stones, or are getting kidney dialysis; have a history of metabolic acidosis (too much acid in the blood); have liver problems; have weak, brittle or soft bones (osteomalacia, osteoporosis, osteopenia, or decreased bone density); have lung or breathing problems; have eye problems, especially glaucoma; have diarrhea; have a growth problem; are on a diet high in fat and low in carbohydrates, which is called a ketogenic diet; are having surgery; are pregnant or plan to become pregnant; or if you are breastfeeding. The medicine in Qudexy XR and in Topiramate Extended-Release Capsules (topiramate) passes into your breast milk. It is not known if the

medicine, topiramate, that passes into breast milk can harm your baby. Talk to your healthcare provider about the best way to feed your baby if you take Qudexy XR or Topiramate Extended-Release Capsules.

Qudexy XR and Topiramate Extended-Release Capsules can harm your unborn baby. All women of childbearing age should talk to their healthcare providers about possible alternative treatments. If you take Qudexy XR or Topiramate Extended-Release Capsules during pregnancy, your baby has a higher risk for birth defects called cleft lip and cleft palate. These defects can begin early in pregnancy, even before you know you are pregnant. If the decision is made to use Qudexy XR or Topiramate Extended-Release Capsules, you should use effective birth control (contraception) unless you are planning to become pregnant. Tell your healthcare provider right away if you become pregnant while taking Qudexy XR or Topiramate Extended-Release Capsules.

The most common side effects include tingling of the arms and legs (paresthesia), irregular movements of the eyes (nystagmus), loss of appetite, nausea or indigestion, a change in the way foods taste, diarrhea, weight loss, nervousness, and upper respiratory tract infection. These are not all the possible side effects of Qudexy XR and Topiramate Extended-Release Capsules. For more information, ask your healthcare provider or pharmacist.

Tell your healthcare provider about any other medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Qudexy XR or Topiramate Extended-Release Capsules and other medicines may affect each other causing side effects. Especially tell your healthcare provider if you take metformin (e.g., Glucophage); valproic acid (e.g., Depakene or Depakote); any medicines that impair or decrease your thinking, concentration, or muscle coordination; birth control pills; medicines used to prevent seizures; or any other carbonic anhydrase inhibitors. Qudexy XR or Topiramate Extended-Release Capsules may make your birth control pills less effective.

Do not stop Qudexy XR or Topiramate Extended-Release Capsules without first talking to a healthcare provider. If you have epilepsy and you stop taking Qudexy XR or Topiramate Extended-Release Capsules suddenly, you may have seizures that do not stop. Your healthcare provider will tell you how to stop taking Qudexy XR or Topiramate Extended-Release Capsules slowly.

Do not drink alcohol while taking Qudexy XR or Topiramate Extended-Release Capsules. Qudexy XR or Topiramate Extended-Release Capsules and alcohol can cause serious side effects such as severe sleepiness and dizziness and an increase in seizures.

Do not drive a car, swim, climb, or operate heavy machinery until you know how Qudexy XR or Topiramate Extended-Release Capsules affects you. Qudexy XR or Topiramate Extended-Release Capsules can slow your thinking and motor skills, and may affect vision. Even when taking Qudexy XR or Topiramate Extended-Release Capsules, some patients with epilepsy will continue to have unpredictable seizures.

If you are unable to swallow Qudexy XR or Topiramate Extended-Release Capsules whole, the medicine may be sprinkled on a spoonful of soft food like applesauce. Do not store the food and medicine mixture to use later or crush or chew the food and medicine mixture before swallowing.

This safety information is not all-inclusive. For additional important information, talk to your healthcare provider and read the [Medication Guide](#) for Qudexy XR and Topiramate Extended-Release Capsules. You can also visit www.upsheer-smith.com or call 1-888-650-3789.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see full Prescribing Information at www.QudexyXR.com.

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Reference

1. Epilepsy.com. Available at: <http://www.epilepsy.com/learn/epilepsy-statistics>. Accessed November 5, 2014.