March 19, 2013 – Upsher-Smith Laboratories, Inc. (Upsher-Smith) today announced that Phase I data for USL261 (intranasal midazolam) in healthy volunteers were presented at the Annual American Academy of Neurology (AAN) Meeting in San Diego, CA. The results demonstrated that maximum midazolam plasma concentrations were rapidly achieved (10-15 min) after dosing with USL261. USL261 also demonstrated increased absorption with an improved bioavailability compared to an equivalent dose of injectable midazolam delivered intranasally. Single doses of USL261 up to 7.5 mg were generally well tolerated.

USL261 is a novel, investigational formulation of the benzodiazepine midazolam, delivered intranasally for the rescue treatment of seizures in patients who require control of intermittent bouts of increased seizure activity, often called seizure clusters or acute repetitive seizures. It is intended to be administered by a caregiver without active inhalation by the patient. USL261 is the subject of the ongoing, global Phase III ARTEMIS1 (Acute Rescue Therapy in Epilepsy with Midazolam Intranasal Spray) trial. Additionally, there is an ongoing long-term, open-label safety study for patients who successfully complete the ARTEMIS1 trial. More information about these studies can be found at http://www.clinicaltrials.gov (NCT01390220/NCT01529034).

Commented Barry Gidal, PharmD, RPH, Professor of Pharmacy and Neurology/Division Chair, University of Wisconsin, “The data presented at AAN from the development program for USL261 support the safety profile and favorable pharmacokinetics/pharmacodynamics of USL261 in healthy volunteers. These findings support the further development of USL261 for seizure rescue in patients with intermittent bouts of increased seizure activity, a population for which few treatment options are currently available.”

USL261 (Intranasal Midazolam) Data
USL261 data presented at AAN 2013 examined the pharmacokinetics, pharmacodynamics, safety, and tolerability of USL261 in healthy volunteers. In this study, increasing USL261 doses
corresponded with an apparent linear increase in midazolam exposure, with all doses demonstrating rapid time to maximal plasma concentration (10 – 15 min). Researchers concluded that USL261 dosed up to 7.5 mg was generally well tolerated and did not result in excessive or prolonged sedation or psychomotor impairment. Further, when compared with an equivalent dose of injectable midazolam delivered intranasally, USL261 demonstrated improved midazolam bioavailability with similar pharmacodynamic effects and safety/tolerability profiles.

Abstracts of the poster presentations can be found online at: http://www.aan.com

- Safety and Pharmacodynamics of USL261, a Novel Formulation of Midazolam Optimized for Intranasal Administration
  P02.211. Session P02: Epilepsy: Novel Therapeutics and Basic Science
- Pharmacokinetics of USL261, a Novel Formulation of Intranasal Midazolam
  P02.212. Session P02: Epilepsy: Novel Therapeutics and Basic Science

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

About Seizure Clusters

Seizure clusters, also referred to as acute repetitive seizures or increased bouts of seizure activity, are multiple seizures which occur over a relatively brief period of time with a pattern distinguishable from the usual seizure pattern.² Typically, there is recovery between seizures.³

Reports of seizure cluster prevalence vary, but it has been estimated that approximately 22% of the intractable epilepsy population (approximately 152,000 people) experience them.⁴,⁵,⁶,⁷

Seizure emergencies, such as repetitive seizures and seizure clusters, are serious medical events requiring immediate treatment to reduce the risk of morbidity and mortality.⁸,⁹ Inadequate treatment of seizure clusters may potentially impact the safety of an epilepsy patient, may result in emergency room visits, and/or may evolve into status epilepticus, a potentially life-threatening condition.¹⁰,¹¹,¹² Benzodiazepines are the treatment of choice for management of acute seizures.² Prehospital treatment with benzodiazepines has been shown to reduce seizure activity significantly compared with seizures that remain untreated until the patient reaches the emergency department; however, currently available options are underused.²,⁸,¹³ It is important to treat seizure emergencies early for many reasons, including findings that patients treated within 30 minutes of seizure onset are more responsive to first-line treatment.¹⁴

Market research has shown that patients and caregivers would prefer a rescue medication for seizure clusters that could be administered in any setting and that provides effective and rapid seizure termination in an easy-to-use, non-invasive form of administration.¹⁵ Physicians, much like patients and caregivers, have expressed interest in a non-invasive rescue therapy for use outside of the hospital.¹⁶
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, branded-generic and generic pharmaceuticals. Upsher-Smith has a particular focus on providing therapies to assist people suffering from central nervous system diseases (including epilepsy, Parkinson's disease, and Alzheimer's disease) and also markets products relating to cardiology, dermatology, and women’s health. For more information, visit www.upsher-smith.com.

References