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UPSHER-SMITH PRESENTS DATA CHARACTERIZING THE PHARMACOKINETICS AND SAFETY/TOLERABILITY OF INVESTIGATIONAL MIDAZOLAM NASAL SPRAY (USL261) IN PEDIATRIC PARTICIPANTS WITH EPILEPSY

Findings Presented at the 45th Annual Meeting of the Child Neurology Society

VANCOUVER, British Columbia – October 28, 2016 – Upsher-Smith Laboratories, Inc., today announced that data from a Phase 1 study of USL261 (midazolam nasal spray) in pediatric participants with epilepsy were presented at the 45th Annual Meeting of the Child Neurology Society (CNS) in Vancouver, British Columbia, October 26-29, 2016. The results demonstrated that USL261, administered as single doses of 1.25 mg, 2.5 mg or 5 mg, was rapidly absorbed (median T_{max} of approximately 15 minutes) and no dose-dependent differences in maximum plasma concentration were observed. The findings support the continued development of USL261 in this population.

USL261 is a novel, investigational midazolam formulation, specifically designed for intranasal delivery, being developed for the rescue treatment of seizures in patients who require control of intermittent bouts of increased seizure activity, such as seizure clusters or acute repetitive seizures. It is intended to be delivered intranasally, without active inhalation by the patient. USL261 has been granted orphan drug designation and fast track designation for this use by the Food and Drug Administration (FDA).

"Upsher-Smith is pleased to debut these Phase I clinical trial results at this year's Child Neurology Society meeting," said William Pullman, MB, BS, BMedSc, PhD, FRACP, Chief Scientific Officer and Biotech Research Institute Division President, Upsher-Smith. "Pediatric patients and their caregivers currently have few options for treating bouts of increased seizure activity. This study of intranasal midazolam, in patients from ages two to 13 years with epilepsy, showed a desirable pharmacokinetic profile, which supports the continued development of USL261 in this important patient population."

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About the Study

The Phase I study examined the pharmacokinetics and safety/tolerability of USL261 in pediatric participants with epilepsy (2-13 years of age; n=36). The open-label, multicenter, inpatient study consisted of single doses of USL261 (1.25 mg, 2.5 mg or 5 mg) based on body weight. Pharmacokinetic parameters were calculated for midazolam and its metabolite (1-hydroxymidazolam). Safety and tolerability assessments included treatment-emergent adverse events (TEAEs), clinical laboratory evaluations, vital sign measurements and nasal examinations.

In the study, mean maximum observed plasma concentration (C_{max}) and median time to peak plasma concentration (T_{max}) were similar for midazolam across dose groups (~35 ng/mL and ~15 minutes, respectively), whereas area under the concentration time curve (AUC) values were higher in the 5 mg group versus the 1.25 or 2.5 mg groups. C_{max} and AUC values for 1-hydroxymidazolam were similar across cohorts. The most common TEAEs were somnolence and product taste abnormal.

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 Seizure Clusters

Seizure clusters, also referred to as acute repetitive seizures, seizure flurries, crescendo seizures, cluster seizures, or bouts of increased seizure activity, consist of multiple seizures which occur over a relatively brief period of time with a pattern distinguishable from the patient's usual seizure pattern.[2]

Reports of seizure cluster prevalence vary depending on the population evaluated. Seizure clusters have been associated with poor seizure control.[3] In a study conducted in a tertiary epilepsy center in patients with a broad range of seizure control, the prevalence of seizure clusters was close to 30%.[3] The number of patients with epilepsy in the United States who experience seizure clusters has been estimated to be 152,000.[4,5,6,7]

About Upsher-Smith

Upsher-Smith Laboratories, Inc., founded in 1919, is a growing, fully integrated pharmaceutical company dedicated to its mission of delivering high-value, high-quality therapies and solutions which measurably improve individuals' lives. As a family-owned pharmaceutical company, we are able to adapt and thrive in a dynamic healthcare environment. Our world is constantly evolving, and we are continually adapting to the ever-changing needs of patients, physicians, pharmacists, and healthcare organizations. Where there is a need, we will work to deliver solutions that simplify access to treatment, deliver better health outcomes, and enhance life. Upsher-Smith has a particular focus on developing therapies for people living with central nervous system (CNS) conditions, such as seizure disorders. For more information, visit www.upsher-smith.com.

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References

1. Epilepsy.com. Available at: http://www.epilepsy.com/learn/epilepsy-statistics. Accessed October 11, 2016.
2. Dreifuss FE, Rosman NP, Cloyd JC, et al. A comparison of rectal diazepam gel and placebo for acute repetitive seizures. *N Engl J Med*. 1998;338:1869-75.
3. Haut SR, Shinnar S, and Moshe SL. Seizure Clustering: Risks and Outcomes. *Epilepsia.* 2005;46(1):146-149.
4. Kobau R, Zahran H, Thurman DJ, et al. Epilepsy Surveillance Among Adults – 19 States, Behavioral Risk Factor Surveillance System, 2005. *MMWR.* 2008;57:SS-6.
5. Kwan P, Brodie MJ. Early Identification of Refractory Epilepsy. *N Engl J Med.* 2000;342:314-319.
6. Berg AT, Vickrey BG, Testa FM, et al. How long does it take for epilepsy to become intractable? A prospective investigation. *Annals of Neurology*. 2006;60:73-79.
7. Haut SR, Lipton RB, LeValley AJ, et al. Identifying seizure clusters in patients with epilepsy. *Neurology*. 2005 October 25;65(8):1313-1315.