FOR IMMEDIATE RELEASE

Study Evaluates Refractory Epilepsy Screening Tool for LGS (REST-LGS)

Deerfield, Ill. December 2, 2017 – Lundbeck today presented data at the American Epilepsy Society (AES) Annual Meeting in Washington, D.C. that demonstrates that the Refractory Epilepsy Screening Tool for LGS (REST-LGS) may help healthcare professionals identify patients who may benefit from further clinical evaluation for Lennox-Gastaut syndrome (LGS). The REST-LGS was developed by a working group of experts who care for patients with refractory epilepsy and intellectual and developmental disabilities to improve both the identification and management of patients with LGS.

"We know that LGS is one of the most challenging forms of epilepsy to diagnose, especially in older patients who often do not present the classic triad of LGS symptoms, and misdiagnosis can prevent appropriate clinical management," said Dr. Steven Wolf, study co-author and associate professor of neurology at Mount Sinai School of Medicine in New York. "Our study results suggest that the REST-LGS may be a valuable screening tool for both expert and non-expert practitioners to determine which patients should see an epileptologist for a thorough diagnostic evaluation that could lead to an LGS diagnosis."

The inter-rater reliability of the REST-LGS was measured to evaluate the validity of the tool for use in a clinical setting, and results suggest potential combinations of major and minor diagnostic criteria that may be particularly indicative of a patient with LGS.[1]

"As an epilepsy researcher, advocate and mother of a child with epilepsy, I know how important it is for people who are living with epilepsy to get an accurate diagnosis," said Danielle Boyce, study co-author and founder of Neurology Parent Professionals. "I'm encouraged by our progress in developing a tool to help identify patients who may need further evaluation to determine if they have LGS."

Lundbeck initially presented REST-LGS results at the AES Annual Meeting in December 2016. For the 2017 presentation, the study authors unblinded the data charts to determine the number or major and minor criteria that were met based upon a clinical diagnosis of LGS or drug resistant epilepsy (DRE).

About the Study

Using de-identified records of patients age 12 and older with refractory epilepsy with at least two clinic notes within the past two years, potential major and minor diagnostic criteria were evaluated on case report forms (CRFs) by two raters at two large, diverse epilepsy centers: a specialist (epileptologist or epilepsy nurse practitioner) and a non-specialist (nurse, social worker, resident or pre-medical student). The major criteria evaluated by the REST-LGS were: equal or greater than two seizure types; seizure onset is less than or equal to 12 years of age; a history of electroencephalogram (EEG) with generalized slow spike-and-wave (SSW) discharges less than 2.5 Hz; and cognitive impairment since childhood. The minor criteria evaluated were: persistent seizures despite use of greater than two antiepileptic drugs; history of vagus nerve stimulation (VNS), ketogenic diet, or epilepsy surgery; evidence of seizure-related helmet use or head or face injuries; other EEG abnormalities (e.g., multifocal spikes, generalized discharges, paroxysmal fast activity). A diagnosis of definite LGS required four major criteria to be met. The extent of the inter-rater reliability at each site was measured by Cohen's κ coefficient.

Of 200 patient records evaluated (100 at each site), most patients (81 percent to 85 percent) met one to three major criteria. At site one, moderate agreement (κ = 0.40 to 0.60) was reached between the two raters' judgements on whether patient records reflected persistent seizures despite trial of two or more anti-epileptic drugs (AEDs). At site two, both raters agreed that all patients had persistent seizures. Moderate agreement to good agreement (κ = 0.40 to 0.80) was reached among raters at each site on the following variables: two or more seizure types; seizure onset at age 12 or younger; history of EEG with generalized slow spike-wave discharges of less than 2.5 Hz; and other EEG abnormalities. At both sites, very good agreement (κ = 0.80 to 1.00) was reached on the variables of cognitive impairment since childhood and history of VNS, ketogenic diet or epilepsy surgery. At site one, very good agreement

between raters was reached on the diagnosis of definite LGS, while agreement between raters at Site two for this variable was good. At both sites, poor agreement (κ <0.20) was found on evidence of seizure-related helmet use or head or face injuries, likely driven by different interpretations of the "unavailable" responses on the CRFs.

Un-blinded data revealed the number of major and minor criteria met by each patient with LGS and DRE. Across both sites, most patients with LGS had three major criteria and two or three minor criteria. Patients with DRE met zero or one major criteria and one to two minor criteria.

About Lennox-Gastaut syndrome
LGS is a rare and severe form of epilepsy that is typically diagnosed in childhood and often persists into adulthood.[2,3] It is characterized by a classic triad of symptoms: intractable seizures (multiple types, including drop seizures), cognitive impairment and abnormal EEG with generalized slow spike-wave discharges.[3]

About Lundbeck
Lundbeck is a global pharmaceutical company specialized in psychiatric and neurological disorders. For more than 70 years, we have been at the forefront of research within neuroscience. Our key areas of research focus are depression, schizophrenia, Parkinson's disease and Alzheimer's disease.

An estimated 700 million people worldwide are living with psychiatric and neurological disorders and far too many suffer due to inadequate treatment, discrimination, a reduced number of working days, early retirement and other unnecessary consequences. Every day, we strive for improved treatment and a better life for people living with psychiatric and neurological disorders — we call this *Progress in Mind*.

Our approximately 5,000 employees in 55 countries are engaged in the entire value chain throughout research, development, manufacturing, marketing and sales. Our pipeline consists of several late-stage development programs and our products are available in more than 100 countries. We have research centers in China and Denmark and production facilities in Denmark, France and Italy. Lundbeck generated core revenue of DKK 15.6 billion in 2016 (EUR 2.1 billion; USD 2.2 billion).

In the U.S., Lundbeck employs nearly 1,000 people focused solely on accelerating therapies for brain disorders. With a special commitment to the lives of patients, families and caregivers, Lundbeck U.S. actively engages in hundreds of initiatives each year that support our patient communities, including the epilepsy community. For additional information, we encourage you to visit our corporate site at www.lundbeckus.com and connect with us on Twitter at @LundbeckUS.

CONTACT:
Rachel Vann
Lundbeck
Public Relations, Senior Manager
(224) 507-8401
rvan@lundbeck.com

References
1. Wolf S, Boyce D, et al. Refractory Epilepsy Screening Tool for Lennox-Gastaut Syndrome (REST-LGS): Improving the detection of LGS in the clinic. American Epilepsy Society Annual Meeting. 2017. Abstract 1.168.
2. Van Rijckevorsel K. Treatment of Lennox-Gastaut syndrome: Overview and recent findings. *Neuropsychiatric Disease and Treatment*. 2008;4(6):1001–1019.
3. Arzimanoglou A, French J, Blume WT, et al. Lennox-Gastaut syndrome: a consensus approach on diagnosis, assessment, management, and trial methodology. *Lancet Neurology*. 2009;8(1):82–93.