

## **Edison Pharmaceuticals Announces Phase 2 Positive Clinical Results for EPI-743 in Rett Syndrome**

*Head growth significantly improved in placebo-controlled trial*

Mountain View, California; September 3, 2014. Edison Pharmaceuticals today announced results of a recently completed phase 2 placebo-controlled trial in pediatric patients. Rett syndrome patients treated with EPI-743 demonstrated a statistically significant increase in head circumference. Decreased brain growth and head circumference are hallmarks of the disease.

Rett syndrome is a genetic neurodevelopmental disorder predominately affecting girls, and is usually diagnosed by 24 months of age. It is characterized by a constellation of neurological, behavioral, functional, and structural features. These include delayed development, characteristic hand wringing, seizures, impaired respiratory function, slowing of brain growth, and resultant diminished head size, as well as other neurological disorders.

The double-blind, placebo-controlled clinical trial was conducted at the General University Hospital (Azienda Ospedaliera Universitaria Senese) of Siena, Italy, a leading international Rett syndrome clinical care and research center. A total of 24 subjects, 2.5 to 8 years of age, were enrolled in the six-month trial. While the study did not meet the primary endpoint of improving the subjective Rett syndrome disease severity score, subjects treated with EPI-743 demonstrated an objective improvement in head growth. Specifically, head growth in the treatment group was 0.75 cm from baseline, compared to 0.29 cm in the placebo group ( $p=0.05$ ). In a subgroup analysis of the children with the largest head growth, improvements in oxygenation, hand function, and disease-relevant biomarkers were also recorded. These data will be submitted for publication in the near future.

The natural history of decreased head growth in girls with Rett syndrome has been quantified and is an established metric of disease. Improvement in head growth was recorded in nine of the 12 subjects in the EPI-743 treatment arm.

In this study, EPI-743 was well-tolerated with no drug-related serious adverse events or dose-limiting toxicities reported.

The rationale for the trial was to determine if EPI-743 could address putative mitochondrial/oxidative stress components of Rett syndrome.

“Given the established role of oxidative stress in the pathology of Rett syndrome, we were interested in exploring whether a mitochondrial-targeted therapeutic would result in treatment benefit,” said Joussef Hayek, MD, Professor of Child Neuropsychiatry and Principal Investigator of the study. “This study represents an important step in building a bridge between understanding the underlying pathology of Rett syndrome and discovering new treatments.”

“With the encouraging results on such an objective and meaningful endpoint, we plan to

engage with health authorities, patient foundations, and the clinical/research community in the next several months to define the next steps that may ultimately lead to new options for children with Rett syndrome and other mitochondrial diseases,” said Matthew Klein, MD MS FACS, Chief Medical Officer at Edison Pharmaceuticals, Inc.

### Rett Syndrome

Rett syndrome is a severe rare neurodevelopmental disorder affecting females almost exclusively. The disease results in slowing of brain growth, seizures, loss of motor function, loss of speech, and impaired respiratory function, as well as a characteristic hand stereotypy with progressive loss of purposeful hand function. Children with Rett syndrome also demonstrate autistic-like features, including diminished eye contact; for this reason Rett syndrome has been considered an autism spectrum disorder. Recent studies have demonstrated that Rett syndrome is characterized by high levels of systemic oxidative stress as well as alterations in mitochondrial morphology. Plasma levels of oxidative stress biomarkers have been shown to correlate with disease severity and progression. A recently published study, led by Claudio De Felice, MD, Professor of Neonatology and a co-investigator in the clinical trial, has documented the relationship between levels of oxidative stress markers in the brain and the disease in an *in vivo* disease model.

Rett syndrome affects one in every 10,000 to 15,000 live female births. The majority of cases result from a mutation in the MeCP2 gene that is carried on the X chromosome. Rett syndrome is typically diagnosed between six months and 18 months of age. Children then progress through the four stages of Rett syndrome, which are characterized by worsening neurological status and seizures. Death typically occurs prior to age 40. There is no cure for Rett syndrome and therapy is directed at management of disease symptoms.

### EPI-743

EPI-743 is an orally bioavailable small molecule being developed by Edison Pharmaceuticals for the treatment of disorders of energy metabolism. Currently EPI-743 is in phase 2 clinical development.

### **Edison Pharmaceuticals**

Edison Pharmaceuticals is focused on developing treatments for children and adults with orphan mitochondrial diseases.

### **Edison Information**

Edison Pharmaceuticals, Inc.  
350 North Bernardo Avenue  
Mountain View, CA 94043  
info@edisonpharma.com  
edisonpharma.com

