Summary – Edison Pharma EPI-743 Clinical Trial Meeting
Presented by ***Guy Miller, MD, PhD, CEO of Edison Pharmaceuticals & Greg Enns, MD, Lucille Packard Children's Hospital at Stanford University***

Introduction

In September (2012), Edison Pharmaceuticals announced positive results of their Phase 2A clinical trial of EPI-743 for children with Leigh syndrome conducted in Rome, Italy. All children treated showed reversal of disease progression. Following this unprecedented news, the results were published online in the September 10, 2012, publication of the *Molecular Genetics and Metabolism* journal. At the same time, Edison announced that EPI-743 had received orphan drug status from the European Medicines Agency (the European regulatory agency akin to the FDA in the United States).

Background

Generally, several studies are required before a drug can be approved by the US or European regulatory agencies for public availability: Phase 1 (initial phase to test for safety); Phase 2A (to demonstrate in an unequivocal manner that the drug meets a specific threshold for efficacy and safety); Phase 2B (a double-blind trial with control group); and Phase 3 (a broader group sample).

For the EPI-743 Phase 2A trial, ten (10) children in Rome, Italy with Leigh syndrome were treated for 180 days. All ten subjects responded favorably. After 90 days all subjects demonstrated arrest and reversal of the disease; after 180 days the reversal persisted in all but one subject. In this one patient, treatment was discontinued by the choice of the patient's parents and the patient reverted to his original status. All patients also had a normalization of disease-relevant biomarkers. An extension phase of this trial that includes the original 10 enrolled patients is ongoing. Based on the findings of this Phase 2A trial, Edison Pharmaceuticals plans to conduct a Phase 2B trial—the next step in the process for drug approval. The trial will enroll 30 (or more) children at four different sites in the US. In the Phase 2B trial, children will randomly be placed into one of two groups. One group will receive EPI-743 for 6 months; the other group will receive a placebo for 6 months. Importantly, parents, patients, and physicians are blinded, meaning they do not know which children are receiving EPI-743 and which are receiving placebo. Following six months, all children in the placebo group will receive EPI-743 for six months. The children who received EPI-743 initially will continue to receive EPI-743 for six additional months.

To determine the effectiveness of EPI-743 as compared to placebo, the following will be measured:

- disease progression based on the Newcastle Pediatric Mitochondrial Disease Scale
- neurologic and neuromuscular function
- respiratory function
- quality of life
- number of hospitalizations and admissions to the intensive care unit

Brain imaging, including MRI's, will also be obtained to study response to therapy. Safety will be followed using laboratory studies and electrocardiograms.

While EPI-743 has been well tolerated and shown to be safe and effective in the children treated to date, surveillance continues. Worldwide there have been over 125 patients (children and adults) who have been treated with EPI-743 with only one serious side effect possibly related to EPI-743.

P**hase 2B Trial** Criteria for participation in the Phase 2B EPI-743 trial will be posted on clinicaltrials.gov and are briefly as follows:

- Age between 1 and 12 years;
- MRI findings consistent with Leigh syndrome
- Moderate degree of disease severity based on Newcastle score with evidence of disease progression in the past year;
- Parental consent;
- Access to a treatment center (Akron Children's Hospital, Ohio; Lucille Packard Children's Hospital, California; Baylor University, Texas; Seattle Children's Hospital, Seattle, WA)
  - *Note: Travel funds are being established to assist patients and families*

Complete details, including full exclusion and inclusion criteria may be found at www.clinicaltrials.gov

Children enrolled in the trial are not allowed to take Coenzyme Q10, vitamin E, alpha lipoic acid and/or vitamin C within two weeks prior to enrollment and for the duration of trial. In addition, potential enrollees must not be allergic to sesame oil. Children with end-stage kidney disease, severe liver disease or who are ventilator dependent are excluded from this trial at this time.

What can parents and patients do?

Adult patients, parents of affected children and families are encouraged to:

a) Enroll in the North American Mitochondrial Disease Registry http://rarediseasesnetwork.epi.usf.edu/NAMDC/register/index.htm ;
b) Contact a participating site (listed below) if your child has Leigh Syndrome;

c) Share the information from www.clinicaltrials.gov and related EPI-743 publication abstracts from www.pubmed.gov with your physician.

MitoAction, UMDF, Edison Pharmaceuticals and physicians around the world stress the value of participating in the NAMDC registry. As protocols become available for additional trials for EPI-743 (or other new treatments), those who are on the registry are likely to be the first to be able to enter the trials. Patient databases and registries follow strict patient privacy guidelines and are offered at no cost to the patient. Likewise, for patients who qualify and enroll in an EPI-743 trial, there is no cost to the patient.

The Future
Adult patients and children with other mitochondrial disorders are encouraged to participate by taking the action steps outlined above. It is our collective hope that by galvanizing the mitochondrial disease community, we can assist in enrollment of at least 30 children with Leigh syndrome by January 2013; consequently, we remain optimistic that additional trials and options for more patients will become available in late 2013. The success of EPI-743 brings hope to the entire Mito community**!**

Additional Information about Participating Centers:

AKRON CHILDREN'S HOSPITAL
Investigator: Bruce Cohen, MD, FAAN
Director of Pediatric Neurology; Professor of Pediatrics
1 Perkins Square
Akron, OH 44308-1062
Site Coordinator: Hilary Wolf
Phone: 330-543-3193
Fax: 330-543-3166
Email: hwolf@chmca.org
Hospital Study Line: 330-543-5012 (Voicemail, will be transferred to Hilary on the next business day.)
Hospital Information:
One Perkins Square
Akron, Ohio 44308
Website : www.akronchildrens.org

LUCILE PACKARD CHILDREN'S HOSPITAL -STANFORD
Investigator: Gregory M. Enns, MB ChB
Associate Professor and Director of Biochemical and Genetics Program
Phone: (650) 498-5798
Greg.enns@stanford.edu
Site Coordinator: Katherine Connors, MPH
Sr. Clinical Research Coordinator
Spectrum Child Health - Genetics
Stanford University School of Medicine
300 Pasteur Drive, H-315 (Rm A071)
Stanford, CA 94305-5208
Tel: 650-736-8166
Fax: 650-498-4555
kconnors@stanford.edu

BAYLOR COLLEGE OF MEDICINE
Investigator: Fernando Scaglia, M.D.
Department of Molecular and Human Genetics
Phone: (832) 822-4280
E-mail: fscaglia@bcm.edu

Baylor College of Medicine
One Baylor Plaza, MS BCM225
Houston, TX, 77030

Site Coordinator:
Catherine Loffredo, BSN, RN, CCRP

Research Nurse

Department of Molecular and Human Genetics

Baylor College of Medicine

Texas Children's Hospital

6701 Fannin CC 1560

Houston, TX 77030

email: catherine.loffredo@bcm.edu
832-822-4276 (office)

832-825-1515 (fax)

Seattle Children's Hospital
Investigator: Russell Saneto, DO, PhD
Professor, Neurology
Seattle Children's Hospital
4800 Sandpoint Way NE, MS B 5552
Seattle, WA 98105
Email: russ.saneto@seattlechildrens.org
Site Coordinator:
Laurie Guidry, RNC, BSN
Research Nurse Coordinator, Dept. of Neurology
Seattle Children's Hospital
4800 Sandpoint Way NE, MS B 5552
Seattle, WA 98105
Email: laurie.guidry@seattlechildrens.org
(Phone) 206-987-0058
For more information:
www.edisonpharma.com
www.umdf.org/epi743
www.mitoaction.org/epi743

For more information, please visit our EPI-743 page