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FOR IMMEDIATE RELEASE

GROUNDBREAKING 30-YEAR STUDY IDENTIFIES CRITICAL NEED OF DISEASE-MODIFYING THERAPIES FOR MAPLE SYRUP URINE DISEASE (MSUD)

STRASBURG, PA- A new study analyzes 30 years of patient data and details the clinical course of 184 individuals with genetically diverse forms of Maple Syrup Urine Disease (MSUD), which is among the most volatile and dangerous inherited metabolic disorders. Researchers collected data on survival, hospitalization rates, metabolic crises, liver transplantation, and cognitive outcome. This represents the largest systematic study of MSUD, with regard to both cohort size and the duration of clinical follow up. The study was a broad collaborative effort led by clinicians and researchers at the Clinic for Special Children (CSC) and will appear in *Molecular Genetics and Metabolism.*

Before the CSC's inception, one in three children born with MSUD died from neurological complications of the disease before 10 years of age, and the majority of survivors were permanently disabled. Three decades of innovation and clinical care by the CSC team have increased survival from 63% to 95% while hospitalization rates have decreased from 7 to just 0.25 hospital days per patient per year. Specific advances in management include new prescription formulas for children and adults as well as elective liver transplantation, a collaboration with the Hillman Center for Pediatric Transplantation (UPMC Children's Hospital of Pittsburgh) that has been 100% successful for 93 individuals transplanted since 2003.

Treatment of MSUD requires close monitoring of blood amino acid levels. A total of 13,589 amino acid profiles were generated by CSC's on-site clinical laboratory and the data were analyzed to determine the overall effectiveness of treatment. The authors conclude that although stringent dietary therapy maintains blood amino acid

concentrations within acceptable limits, it is challenging to implement, especially for individuals older than 10 years of age, and does not fully prevent the cognitive and psychiatric disabilities caused by MSUD.

Eighty-two (82) MSUD patients underwent IQ testing, with higher IQ scores correlating by age with younger patients. On average, MSUD patients scored 23% lower on IQ testing than their unaffected siblings and, as compared to the general population, the prevalence of affective illness (depression, anxiety, and panic disorder) was much higher among both MSUD patients and their unaffected siblings. Based on these observations, the authors conclude that despite advances in clinical care, MSUD remains a morbid and potentially fatal disorder, and there remains a critical unmet need for safer and more effective disease-modifying interventions, including gene replacement or editing therapies.

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The research was conducted by a team including the study's first author Kevin A. Strauss from the Clinic for Special Children, Strasburg, PA; senior author D. Holmes Morton from the Clinic for Special Children, Strasburg, PA and Central Pennsylvania Clinic, Belleville, PA; Vincent J. Carson, Karlla W. Brigatti, Millie E. Young, Lauren E. Bowser, Donna L. Robinson, Christine Hendrickson, Erik G. Puffenberger, Katie B. Williams, Keturah Beiler, Ashlin Rodrigues, KaLynn Loeven, and Adam D. Heaps from the Clinic for Special Children, Strasburg, PA, Kyle Soltys, Diana A. Shellmer, and George V. Mazariegos from the Hillman Center for Pediatric Transplantation, Children's Hospital of University of Pittsburgh School of Medicine, Pittsburgh, PA, Cora M. Taylor and Barbara Haas-Givler at Geisinger Autism & Developmental Medicine Institute, Lewisburg, PA, Stephanie Chopko from Department of Pediatrics, Nemours Alfred I. duPont Hospital for Children, Wilmington, DE and Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA, Jennifer Hailey and Zachary Radcliff from Wellspan Philhaven, Mount Gretna, PA, and Emilie R. Muelly from Department of Internal Medicine, Kaiser Permanente Medical Center, Santa Clara, CA.

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About the Clinic for Special Children

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The Clinic for Special Children (CSC) is a non-profit organization located in Strasburg, PA, which provides primary pediatric care and advanced laboratory services to those who suffer from genetic or other complex medical disorders. Founded in 1989, the organization provides services to over 1,050 active patients and is recognized as a world-leader in translational and precision medicine. The organization is primarily supported through community fundraising events and donations. For more information, please visit www.ClinicforSpecialChildren.org