Experimental gene therapy targets Duchenne muscular dystrophy

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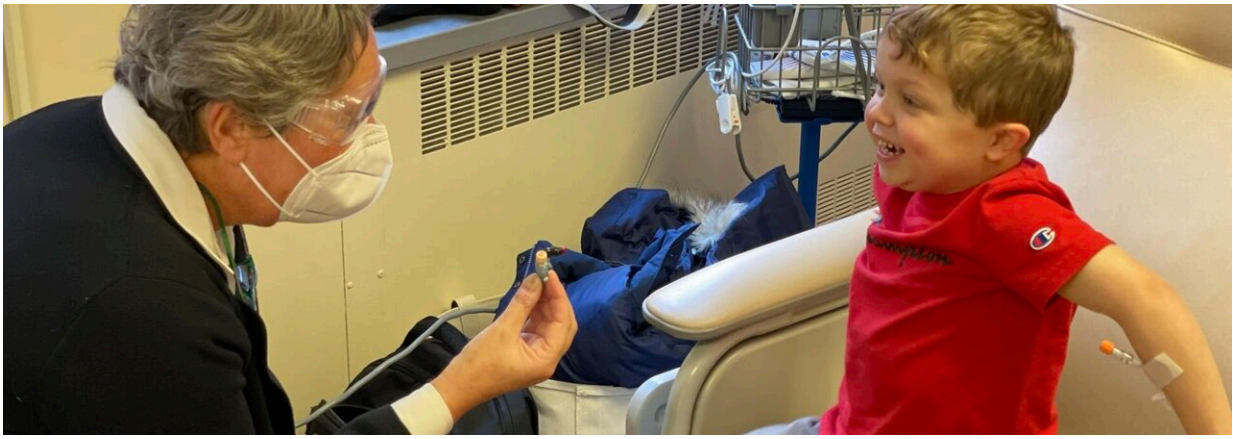

Credit: University of Rochester Medical Center

Children in Rochester were recently among the first in the nation to receive an experimental treatment for Duchenne muscular dystrophy (DMD). The study is part of an accelerating trend of clinical trials involving gene therapies that could transform how we treat a number of devastating childhood neurological disorders.

Emma Ciafaloni, M.D., a neuromuscular neurologist with the University of Rochester Medical Center (URMC) Department of Neurology and Golisano Children's Hospital, is leading the Rochester study site. URMC was recently one of the first three sites in the nation to start dosing patients in a phase 3 placebo-controlled clinical trial for a gene therapy

being developed by Sarepta Therapeutics for children with DMD. The international study will soon add additional sites in North America, Europe, and Asia. Ciafaloni served as the chair of the independent Data Safety and Monitoring Board for the company's early phase clinical trials of the therapy.

DMD is a condition found almost exclusively in boys and is characterized by muscle weakness, the symptoms of which often appear at a young age and progress rapidly leading to significant disability. Children with DMD typically end up in a wheelchair by age 9 or 10 because of weakness in their legs. The symptoms eventually spread to the heart and muscles responsible for breathing, and the disease is often fatal by the time the individual reaches their 20s or early 30s. An estimated 12,000 people in the U.S. suffer from the disease.

The muscle weakness associated with DMD occurs due to a genetic defect in muscle cells that impairs the production of dystrophin, an important muscle building protein that is largely absent in people with the disease. The new treatment consists of a single infusion that, via an associated adenovirus, delivers into muscle cells a separate and potentially functional "micro" version of the dystrophin gene that takes over production of the protein.

The study is the latest in a number of new gene therapies for pediatric neurological disorders that are in the developmental pipeline and have the potential to transform care and significantly reduce the burden of disease. This includes a gene therapy for spinal muscular atrophy (SMA) that was approved by the FDA in 2019. Ciafaloni was involved in the clinical trials that led to the therapy's approval and some of the first children to receive the therapy in the U.S. were patients of the UR Medicine Pediatric Neuromuscular Medicine Program. Last year, it was announced that URMC would be the lead study site for an experimental gene therapy for CNL5 Batten disease, a rare and fatal disorder that first

appears in childhood. This study is being led by pediatric neurologist Jonathan Mink, M.D., Ph.D.

In many childhood neurological disorders, spotting the disease before symptoms appear is critical for these new therapies to be effective. Ciafaloni is currently working to get Duchene added to the New York State Newborn Screening Program, a panel of medical tests that screen newborns for 50 different disorders, primarily genetic, that can be more effectively treated if identified earlier. DMD strikes early in life and the target age for the new study is 4–7 years old. In 2018, Ciafaloni, along with others in the medical community and families, successfully convinced the state to add SMA to the list of newborn tests.

Provided by University of Rochester Medical Center