FAST
Foundation for Angelman Syndrome Therapeutics

Roadmap to a Cure

OVERVIEW

Imagine if your child, or a loved one, could not walk or speak and had motor impairment, debilitating seizures and a sleep disorder. This is life today for many of the nearly 500,000 people living with Angelman syndrome (AS). But it doesn't have to be that way. Scientists have shown that these devastating symptoms can be reversed, and FAST (Foundation for Angelman Syndrome Therapeutics) has a plan well underway to achieve just that. We are finalizing the scientific foundational work necessary to test therapies in human clinical trials. Please take a moment to read on and learn how our Roadmap to a Cure will change the lives of people with Angelman syndrome and, potentially, millions more who have related disorders like autism and Alzheimer's disease.

Angelman syndrome is caused by a loss of function in the UBE3A gene on the maternal 15th chromosome, which prevents the body from producing enough UBE3A protein. It's a relatively simple disorder because it involves only one gene, and we have multiple options for treatment.

FAST's Roadmap is focused on three strategies to treat Angelman syndrome. AS is not a degenerative disorder, and these approaches, which have already been tested in animal models, are believed to have the potential to reverse the effects of the disorder in children, teens and adults.

Route 1
Gene Therapy

People with AS have a mutation, deletion or other defect in their *UBE3A* gene. Gene replacement therapy uses safe viruses to deliver healthy copies of the *UBE3A* gene into cells to replace the missing or underperforming gene. The goal is for the body to start making the UBE3A protein that is deficient or absent. A few gene therapy treatments have already been approved in Europe for rare disorders (e.g., Strimvelis), and many gene therapy trials are underway in the United States for a variety of disorders (e.g., Batten disease, San Filippo syndrome).

Route 2
Gene Activation Therapy

People have two sets of chromosomes – one inherited from the mother and one from the father. In a typical person, the maternally inherited *UBE3A* is active, while the copy of the gene inherited from the father is silenced in the neurons in our brains – a phenomenon known as imprinting. For individuals with Angelman syndrome, the maternal gene does not function properly. The goal of gene activation therapy is to turn on the normally silent paternal gene so there is an active copy producing the necessary UBE3A protein.

Route 3
Downstream Therapy

Downstream therapy uses drugs to treat the symptoms of Angelman syndrome and improve the quality of life for individuals with the disorder. There are many drugs that are already approved by the FDA that might be useful for treating Angleman syndrome. Finding these drugs and showing that they can be repurposed would be the fastest way to bring new treatments to the Angelman community. The U.S. Food and Drug Administration (FDA) established a Rare Disease Repurposing Database containing drugs found promising or already approved for treating rare diseases.

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So little seems to stand in the way of a cure for Angelman syndrome. The FIRE team's efforts are gaining significant attention. The Marnier-Lapostolle Foundation recently awarded a $5.8 million grant to FAST to help fund the remaining foundational laboratory tests necessary to bring the knowledge gained by FAST researchers to the next stage: human clinical trials. This gift is the largest private grant ever made to Angelman research. Inspired by a family member who has a child with the disorder, the Marnier-Lapostolle Foundation conducted an intense and highly competitive review process before investing their money in FAST. The family that created Grand Marnier founded the Marnier-Lapostolle Foundation.

Now is the time for action. FAST's Roadmap to a Cure for Angelman syndrome is bold, ambitious, and, with your help, achievable. The Roadmap costs an estimated $20 million dollars, and AS families have been challenged to raise $2 million of that investment. We are calling on everyone connected to a loved one with Angelman syndrome to support this research. Please join us by making a financial gift, spreading the word with friends and family members, and fundraising to help us cross the finish line. Your efforts will take us one step closer to making therapeutics available to those affected with AS and, ultimately, finding a cure that will free our children.

ABOUT FAST

FAST is a 501(c)(3) nonprofit research organization. Paula Evans, an Illinois mother whose daughter was diagnosed with Angelman syndrome, founded FAST in 2008. FAST raises money to fuel cutting-edge research and takes an active role in drug development to treat, and ultimately cure, the disorder.

The FAST track: from bench to bedside.
FAST is the largest non-governmental funder of Angelman syndrome research and the only organization with a detailed plan towards a cure. While others said a cure was not possible, FAST spent the past seven years strategically investing millions of dollars in research to lay the foundation for scientific breakthroughs. Recent advancements in the understanding of Angelman syndrome, made by FAST scientists, suggest finding a cure for this disorder in the near future is not only possible, it's inevitable.

Brightest minds partner in race to cure Angelman syndrome
FAST brought together a multi-disciplined team of more than two-dozen scientists from top research universities and pharmaceutical companies to join forces on a focused path to a cure. Known as the "FIRE" Consortium: FAST Integrative Research Environment, FAST's scientists know exactly what causes Angelman syndrome. They have cured the symptoms of the disorder in mice using several strategies.

To learn more about FAST's FIRE team, visit CureAngelman.org/FIRE.

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