fast

our sole mission is a cure


Feelin' Awesome
RADIATE
POSITIVE
ENERGY

At a Glance

The Foundation for Angelman Syndrome Therapeutics (FAST) is committed to finding meaningful and transformative treatments for all individuals living with AS globally, regardless of age or genotype in order to achieve our mission of finding a cure. Angelman syndrome is not only a rare neurogenetic disorder, it is unique because it involves an imprinted gene. This unique genetic circumstance allows the pursuit of multiple pathways in which one can develop potential gene-replacement, gene-altering, gene-editing and disease modifying therapies to treat this disease.

FAST has made extraordinary advances in the pursuit of developing meaningful therapeutics for the potential treatment of Angelman syndrome and continues to fund additional research in order to expedite therapeutic development through a C.U.R.E.AS™ approach: **Collaborate, Understand, Ready, Expedite.**

Through this methodical approach, FAST is committed to accelerating all transformative therapeutics for those living with Angelman syndrome.

In order to maintain our momentum, we need to raise substantial funding to bridge the most promising translational research approaches to human clinical trials. All of our research continues to validate that a cure is attainable and we need your support to accelerate additional research.

On behalf of all those with AS and their families, thank you for learning more about FAST. We hope you will support our roadmap to a cure.

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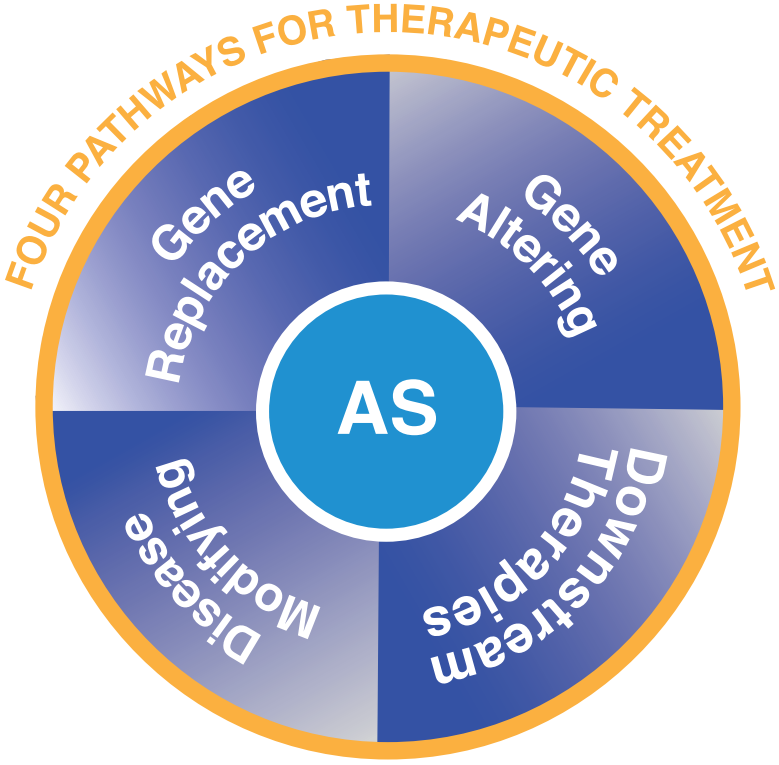
What is Angelman Syndrome?

Angelman syndrome (AS) is a rare neurogenetic disorder that affects approximately one in 15,000 people or approximately 500,000 individuals worldwide. Children and adults with AS typically do not speak verbally. They have balance issues, gross and fine motor impairments and often debiltating seizures. Some individuals never walk. Disrupted sleep cycles also can be a serious challenge to the individual and caretaker(s).

Uniqueness of Angelman Syndrome

While Angelman syndrome is not only a rare disorder, it is also unique because it involves an imprinted gene. We receive two copies of each gene, one from our mother and one from our father. Genes make proteins that perform various functions in our bodies. A small handful of our genes are imprinted, meaning only one parent's copy is making a protein. One of our imprinted genes is the *UBE3A* gene which is on chromsome 15. The copy of *UBE3A* that we receive from our mother is active in the neurons of our brain, yet the copy we receive from our father is silenced in these neurons by something called the *UBE3A-antisense*. In the rest of our body the father's copy is not silenced and is active.

If an individual is born missing the copy of the *UBE3A* gene from their mother, or the copy they get from their mother isn't functioning properly, they have Angelman syndrome. The individual still has a copy of the *UBE3A* gene from their father, but like in all of us, it is turned off, or silenced, in the neurons of the brain by this imprinting phenomenon.



Who is FAST?

Foundation for Angelman Syndrome Therapeutics is run by a driven board of parents of individuals living with Angelman syndrome and professionals dedicated to curing AS through the funding of an aggressive research agenda.

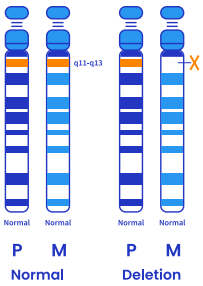
FAST operates as an impartial organization to drive collaboration and sharing across the industry (pharmaceuticals, research institutions and other global organizations) to reach a cure faster. FAST is served by two boards: the board of directors and an independent scientific advisory board. Together, we are working hard to bring practical treatment into current medical practice as quickly as possible.

FAST is committed to finding meaningful and transformative treatments for all individuals living with AS globally, regardless of age or genotype in order to achieve our mission of finding a cure.

"The stars are aligned in favor of Angelman syndrome being amenable to a really curative kind of treatment. I think FAST has transformed the landscape of Angelman research."

– Art Beaudet, M.D. National Academy of Sciences

Genotypes of Angelman Syndrome



Deletion (65-75%)

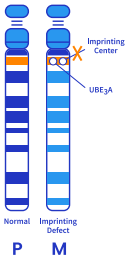
DNA (deoxyribonucleic acid) is the main component of chromosomes. It contains our unique genetic code. Most individuals with AS are missing a piece of DNA in region 15q11-13 on the maternal chromosome 15.

Mutation (5-11%)

This occurs when there is a small abnormality in the DNA of the *UBE3A* gene. A mutation can happen anywere on the gene.

Uniparental Disomy (UPD) (3-7%)

An individual with UPD has two copies of chromosome 15 from their father, instead of one each from the father and mother.



Imprinting Center Defect (ICD) (<3%)

ICD occurs when there is an abnormality in the imprinting center of the mother's copy of the 15th chromosome. The imprinting center is in the area of the chromosome that controls whether genes are turned on or off. In ICD, the *UBE3A* gene from the mother is typically present, but an abnormality in the imprinter center prevents the mother's copy of the gene from being read properly in neurons as it is "turned off".

Collaborate, Understand, Ready, Expedite

FAST's funding philosophy is focused on funding translatable therapeutics to cure Angelman syndrome (AS). This is broken down into C.U.R.E.AS™ **Collaborate, Understand, Ready and Expedite.**

Collaborate

To fast track our roadmap to a cure, we are implementing a 360º collaboration with families, researchers, pharmaceutical companies, and physicians/clinicians. We are integrating the efforts of FAST Global and the Angelman Syndrome Foundation (ASF) to share research, trial and organizational updates in order to concentrate all of our efforts to find a cure.

A-BOM ANGELMAN BIOMARKER AND OUTCOME MEASURE CONSORTIUM

A-BOM® (Angelman Syndrome Biomarker and Outcome Measure consortium). Prior to this collaboration, there were no AS-specific clinical trial assessment and measurement tools to evaluate our AS patient population. FAST continues to identify, develop and fund novel outcome measure and biomarkers to ensure success in the trials.

INSYNC-AS™ INTERNATIONAL ANGELMAN SYNDROME RESEARCH COUNCIL

Our commitment to identifying and furthering scientific advancements for various potential therapeutics led to the launch of the **INternational Angelman SYNdrome Research Council (INSYNC-AS)**. INSYNC-AS evaluates and drives research initiatives in Angelman syndrome and other similar neurodevelopmental disorders (NDDs). This enables fast tracking of all exploration by using a robust, integrated approach and tapping into the expertise of the foremost thought leaders in diverse fields.

INYNC-AS' first collaborative consortium in partnership with **Simons Foundation Autism Research Initiative (SFARI)** occurred in July 2021.

Global Science Summit, Translational Research Symposium, Pharmaceutical Updates and Gala
We gather annually as an AS community at our global science summit where we provide updates on our research programs, and pharmaceuticals update the community on their clinical programs. We connect and celebrate large and small wins within our community at our annual gala, which is the most magical evening of the year for so many.

Understand

Angelman syndrome is a rare disorder and there are multiple ways (or genotypes) in which it can manifest. It is imperative to understand how the different genotypes may benefit from different potential therapeutics. Further, we need to understand how the loss of the additional genes associated with the deletion genotype, or the duplication of the *UBE3A* antisense transcript in the UPD/ICD genotype, contribute to the unique symptoms of Angelman syndrome in that specific subgroup of the patient population. In addition, different ages may benefit from different approaches and we must ensure that we find the best therapeutic platform for every age affected by AS.

FAST Funding to Understand All Genotypes

Texas A&M AgriLife Research Creation & characterization of deletion pig model. **Texas A&M Agrilife Research** Scott Dindot, Ph.D.	Yale University Creation of large deletion mouse model, with and without *ube3a*. **Yale University** Yong-Hui Jiang, M.D., Ph.D.
University of South Florida Creation & characterization of deletion rat model. **University of South Florida** Kevin Nash, Ph.D. and Edwin Weeber, Ph.D. UC Davis University of California **University of California/Davis** David Segal, Ph.D. and Jill Silverman, Ph.D.	NC State University Creation of a gene insertion platform to unlock the ability to rescue expression of *UBE3A* and 10 neighboring protein coding genes lost in deletion genotypes. Creation of a landing pad and organioids for ICD/UPD genotypes. **North Carolina State University** Albert Keung, Ph.D.
Yale University Creation of induced pluripotent stem cell (iPSC) lines for all genotypes. **Yale University** Yong-Hui Jiang, M.D., Ph.D.	NC State University Creation of organoid (mini-brain) to evaluate the impact of other genes in large deletion genotype and UPD/ICD and mosaic genotype. **North Carolina State University** Albert Keung, Ph.D.

Ready

In early 2020, FAST funded $1.25 million for the formation of a dedicated lab at University of California, Davis to provide a stable infrastructure to support rapid testing of numerous therapeutic candidates for the potential treatment of Angelman syndrome. This infrastructure maintains AS cell lines and rodent model colonies at the university to keep their focus on identifying and evaluating potential therapeutics for the treatment of Angelman syndrome. Multiple pharmaceutical companies have potentially promising therapeutics for the treatment of AS. However, they do not have the R&D capabilities or expertise in the models to accurately access the tools necessary to properly evaluate these drugs for this population. This collaborative infrastructure provides those services and identifies potential therapeutics that warrant further development toward potential human success in trials, not in clinics.

Infrastructure: Devoted FAST lab at the University of California, Davis

Expedite

Due to the etiology of AS, we can explore multiple strategies, in the most thorough and robust way, that have the potential to treat the disorder at its root cause or through numerous downstream targeted approaches.

FAST launched GeneTx Biotherapeutics to be singularly focused on the development of a potentially safe and effective antisense oligonucleotide (ASO) for the treatment of AS.

December 2017: GeneTx licensed the rights to the intellectual properties of this specific discovery from the Texas A&M Agrilife Research and advanced this program to IND-enabling studies and a phase 1/2 clinical trial.

August 2019: GeneTx and Ultragenyx Pharmaceutical Inc. partnered in the development program of an intrathecally administered ASO called GTX-102, an investigational treatment for Angelman syndrome. Ultragenyx received an exclusive option to acquire GeneTx.

February 2020: GeneTx initiated the Phase 1/2 clinical trial exploring the safety and tolerability of GTX-102, the first potentially disease-modifying drug for AS.

May 2021: Clearance received from Health Canada to begin enrolling the Phase 1/2 study of GTX-102 in AS pediatric patients in Canada.

June 2021: Clearance received from MHRA (Medicines and Healthcare Regulatory Agency) to begin enrolling the Phase 1/2 study of GTX-102 in AS pediatric patient in the UK.

September 2021: Clearance received from FDA in dosing naive pediatric patients in Phase 1/2 study of GTX-102 in the US.

October 2021: Clearance received from Health Canada to begin dosing naive pediatric patients in Phase 1/2 study of GTX-102 in Canada.

In order to ensure we are ready for FDA approval of therapeutics, we need to have the right outcome measures demonstrating a specific therapy is effective for the disorder and is making a meaningful difference in the lives of patients. Our work with ABOM enabled our caretakers to support the creation of a novel outcome assessment tool **Observer Reported Measure of Communication Ability (ORCA®)**. GeneTx and FAST piloted **Actimyo®** which measures patients' movements and has been qualified by European Medical Agency (EMA) for Duchenne Muscular Dystrophy.

> **"Curing Angelman syndrome is not impossible, which means it's possible."**
>
> *– Allyson Berent, FAST Chief Science Officer*

FAST Facts

Since 2008, FAST has funded numerous research grants, dedicated scientific labs, biomarker and endpoint measure developments to find meaningful and tranformative therapeutics for those living with Angelman syndrome.

~500,000 Individuals globally with Angelman syndrome

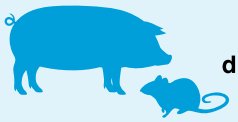
23+
AS Therapeutic Programs in the pipeline toward human clinical trials

FAST
launched in 2008

FAST
has invested over **$25 million** to help bring transformative therapeutics to humans living with AS

20+ FAST
Laboratories funded to understand the etiology and identify treatment options for AS

9 Gene therapy/disease modification based programs funded to support drug development options for AS



$3M+
directed to create novel animal models of AS

We move fast!

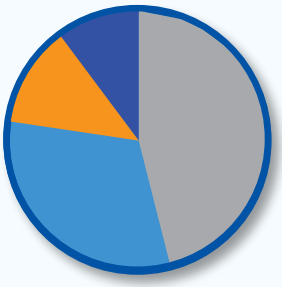
- **2008 FAST** launches with the mission to cure AS
- **2012 FAST** funds human clinical trial on minocycline for the treatment of AS
- **2013 FAST** launches the FIRE (FAST Integrative Research Environment) initiative to identify and characterize treatments for AS through a collaborative research consortium
- **2014 FAST** funds the creation of 2 novel animal models of AS
- **2015 FAST** launches the first medical research grade global AS registry to prepare for clinical trials
- **2016 FAST** FAST receives the largest grant to AS given to date of $5.8 million for a 24 month translational research initiative
- **2017 FAST** launches the for-profit GeneTx Biotherapeutics to develop an antisense oligonucleotide (ASO) program for AS
- **2020 FAST** establishes an infrastructure with a dedicated UC Davis Laboratory
- **2020 FAST** funded GeneTx launches Phase 1/2 Clinical Trial
- **2021 FAST** invests $1M into ABOM
- **2021 FAST** launches INSYNC-AS (International Angelman Syndrome Research Council)

Transparency in Funding

- Program Expenses | 94%
- Fundraising Expenses | 4%
- G&A Expenses | 2%

* Based on 2019 990 filings.

Strategic Spending C.U.R.E.AS™



- Collaborate | 10.49%
- Uncover | 47.49%
- Ready | 29.32%
- Expedite | 12.68%

The Company You Keep

If the old adage “the company you keep is a reflection of who you are, or who you want to be” is true, then FAST is in good company.

Ovid Therapeutics · Disruptive Enterprises · Roche · Biogen · PTC Therapeutics · A-BOM Angelman Syndrome · Taysha Gene Therapies · UC Davis University of California · ultragenyx pharmaceutical · Sarepta Therapeutics · stridebio · The University of North Carolina at Chapel Hill · genetx · Amicus Therapeutics · ORCA Observer-Reported Communication Ability Measure · neuren pharmaceuticals · AskBio · Penn · exicure · IPSEN Innovation for patient care · Exegenesis Bio · Genentech

Drug Development Pipeline

* Timelines based on public disclosure ** Up to date as of September 2021 Those **bolded** above are supported and/or funded by FAST to accelerate to clinical trials.

Roadmap to a Cure

Since its founding in 2008, FAST has awarded over $25M in grants that have focused on funding our C.U.R.E.AS™ approach. FAST has made extraordinary advances in pursuit of developing meaningful therapeutics for those living with Angelman syndrome. In order to accelerator our speed, advance our current pipeline through IND and add to our research pipeline will require raising substantial funding. We want to ensure we have the ability to move the needle for each program if more human clinical candidates seem to be incredibly promising.

C.U.R.E.AS™	Funded to date
Collaborate - 360° collaboration with families, researchers, pharmaceuticals, physicians/clinics, FAST Global and ASF sharing research, trial and organization updates in order to promote, engage and encourage the AS community.	**$2.61M**
Understand - Investigate, identify and fund research opportunities leading to Investigational New Drugs (IND) enabling studies and discovery of differentiation across genotypes and manifestation of symptoms.	**$12.27M**
Ready - As a foundation establish an infrastructure to drive and fund thorough and promising initiatives toward reaching our mission of a cure for AS. Establish and maintain an enduring framework to ensure preparedness for new and ongoing research and transformative therapeutics.	**$7.53M**
Expedite - Accelerate promising research toward clinical trials for all genotypes and all age groups to drive biomarker outcome measurements and endpoints.	**$3.25M**
TOTAL	**$25.66M**

You can make a difference today and be part of a CURE.

FAST was founded on the sole mission of finding a cure for AS. The research we fund makes a cure not only possible, but probable. We hope you will support our efforts by providing life-changing funding.

cureangelman.org