fast | Dream Big.

16th Annual Global Science Summit

Welcome to FAST's 16th Annual Global Science Summit!

We are so excited to join together this weekend and celebrate all individuals living with Angelman syndrome. During the next two days, you will hear from scientists, clinicians, drug developers, regulators, and other thought leaders who all have one goal in common—to accelerate drug development for Angelman syndrome.

Our hope is that the presentations will help families understand more about Angelman syndrome and the promising treatments being developed, and will inspire researchers and pharmaceutical companies with the strength and bravery of our Angelman community.

We encourage you to take part in the many new features at this year's event: attend the community event on Friday afternoon, participate in a morning FAST Athletes workout, or book a one-on-one appointment with a specialist for personalized advice. The full schedule and details can be found in our event app.

Thank you for Dreaming Big with us!

Alana Newhouse
President, FAST

John Schlueter
Chair, FAST Board of Directors

Friday, November 10, 2023
8:30 AM – 4:20 PM

Global Science Summit
Focus on Angelman Syndrome Translational Research

Saturday, November 11, 2023
8:30 AM – 1:15 PM

Global Science Summit
Focus on Clinical Trials

Global Angelman Syndrome Registry
Come and share your Angelman syndrome journey at the Global Angelman Syndrome Registry (GASR) Lounge, situated in the Ballroom Foyer. Discover how you can start your contribution or find out what to do next. Your valuable insights are the catalyst for a brighter tomorrow for Angelman syndrome and the knowledge shared with generations to come. The GASR Lounge is made possible through the generous sponsorship of Panache Events.

WiFi Instructions
To access WiFi within the event space, please use the following network and password:

Network: FASTSummitGala
Password: dreambig

Event App
For more information, including speaker bios and a list of exhibitors, download the Global Science Summit & Gala app by following the steps below:

1. Scan the QR code below to download the “Cvent Events” app.
2. Search for “2023 FAST” to find the meeting.
3. Select/download the event.
4. To view your schedule, you will need to log in. Please use the email address you registered with.
5. You will receive a verification code in your email and/or as a text. Enter this code and you will be able to fully access your schedule.

Friday, November 10, 2023
8:30 AM – 4:20 PM

Focus on Angelman Syndrome Translational Research

8:00 AM	Breakfast	
8:30 AM	How FAST's Laser Focus Benefits Translational Efforts in Neurodevelopmental Disorders More Broadly: The View from a Large Private Research Funder	John Spiro, PhD Simons Foundation
9:00 AM	FAST's Roadmap to a Cure: A Year of Tough Setbacks and Huge Progress	Allyson Berent, DVM, DACVIM FAST
	Pillar 1	
9:50 AM	Using CRISPR activation (CRISPRa) to Upregulate the Existing Gene Copies as a Novel Therapy for the Deletion Genotype of Angelman Syndrome	Nadav Ahituv, PhD University of California, San Francisco
10:20 AM	Designing the Ultimate Backstage Pass to the Brain	Barbara Bailus, PhD Keck Graduate Institute
10:35 AM	Break	
	Pillar 2	
10:50 AM	Progress Toward ATF and CRISPR Therapies for Angelman Syndrome	David J. Segal, PhD University of California, Davis
	Pillar 3	
11:10 AM	How Microbes Regulate Gut Function in a Mouse Model of AS	Melanie Gareau, PhD University of California, Davis
11:25 AM	Stem Cells in Focus: The Role of Glia Cells in a Potential Treatment for Angelman Syndrome	Yu-Wen Alvin Huang, MD, PhD Brown University
11:45 AM	Development of a Drug that Strengthens Synaptic Connections for the Potential Treatment of Angelman Syndrome: The Role of BDNF	John Marshall, PhD Brown University

12:05 PM	Lunch	
	Pillar 4	
12:50 PM	The Novel Large Deletion Mouse Model of AS: How Can it Help us in Drug Development for Angelman Syndrome?	Xiaona Lu, MD, PhD Yale University School of Medicine
1:10 PM	How Endpoints are Used for Drug Approval	Jennifer Panagoulias, RAC FAST, ABOM
1:30 PM	Angelman Syndrome Natural History Study — How has it Benefited the Angelman Community over the Last 17 Years?	Wen-Hann Tan, MD Boston Children's Hospital
1:50 PM	Break	
2:05 PM	Understanding Critical Clinical Outcome Assessments (COAs) Used in Clinical Trials	Anjali Sadhwani, PhD Boston Children's Hospital
2:25 PM	Measuring Communication Ability in Clinical Trials: A Caregiver-Centered Approach for Angelman Syndrome	Bryce Reeve, PhD Duke University
2:45 PM	Home-Based Video Capture to Assess Function in People Living with Angelman Syndrome	Mindy Leffler, MEd Emmes Endpoint Solutions Kriszha Sheehy Emmes Endpoint Solutions
3:00 PM	Hiding in Plain Sight: Dystonia in Angelman Syndrome	Robert Carson, MD, PhD Vanderbilt University Medical Center

Friday, November 10, 2023
8:30 AM – 4:20 PM

Focus on Angelman Syndrome Translational Research
(Cont.)

3:15 PM	It's a Small World: Why FAST is Global	Alana Newhouse FAST USA Amelia Beatty FAST USA Noah Firestone FAST Canada Stephanie Azout FAST LatAm Tom Keogh FAST UK Charlotte Préstat FAST France Benedetta Sirtori FAST Italy Cesareo Goyanes FAST Spain Karolina Pospieszyńska FAST Poland Meagan Cross FAST Australia
3:30 PM	Panel Discussion	All Presenters
4:20 - 6:00 PM	Community Event	

Saturday, November 11, 2023
8:30 AM – 1:15 PM

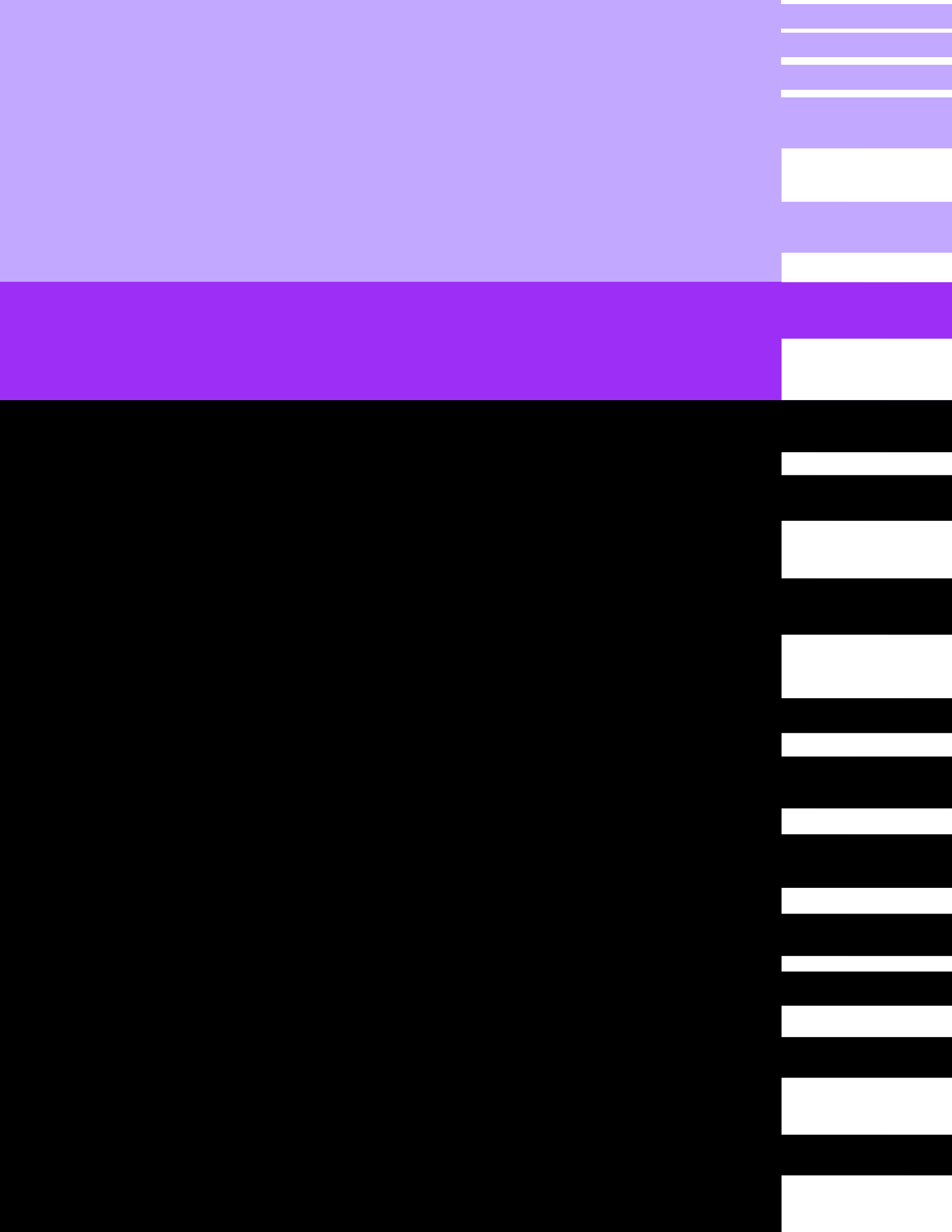
Focus on Clinical Trials

8:00 AM	Breakfast	
8:30 AM	Stronger Together: The Importance of Collaboration in Rare Disease Advocacy	Annie Kennedy Every Life Foundation
	Pillar 1	
9:05 AM	Patient Focused Drug Development	Ryan Fischer FAST
9:25 AM	GTP-220: A Gene Replacement Therapy Being Advanced for Angelman Syndrome	James M. Wilson, MD, PhD Perelman School of Medicine, University of Pennsylvania
9:55 AM	Transformatx Update: Hematopoietic Stem Cell Gene Therapy Program	Jennifer Panagoulias, RAC FAST, Transformatx Biotherapeutics
10:15 AM	Break	
	Pillar 2	
10:30 AM	Update on the GTX-102 Program for Angelman Syndrome	Kemi Olugemo, MD Ultragenyx
10:50 AM	An Update on HALOS Clinical Trial in Individuals Living with Angelman Syndrome	Rebecca Crean, PhD Ionis Pharmaceuticals

Saturday, November 11, 2023
8:30 AM – 1:15 PM

Focus on Clinical Trials
(Cont.)

11:10 AM	From Benchside to Bedside: Collaboration Leads to Acceleration for Novel Delivery of CRISPR Technology	Yong-Hui Jiang, MD, PhD Yale School of Medicine Jiangbing Zhou, PhD Yale School of Medicine Allyson Berent, DVM, DACVIM FAST Elizabeth Berry-Kravis, MD, PhD Rush University Medical Center
11:35 AM	miRNA-based *UBE3A* Unsilencing for a Potential One-Time, AAV-Mediated Gene Therapy for Angelman Syndrome	Stephanie Tagliatela Encoded Therapeutics
	Pillar 3	
11:50 AM	Clinical Development Update: NNZ-2591 as a Treatment for Angelman Syndrome	Nancy E. Jones, PhD Neuren Pharmaceuticals
12:05 PM	Updates on ALDEBARAN, a Phase 2a Trial in Angelman Syndrome	Shady Sedhom Roche Pharmaceuticals
12:20 PM	Economic Impact of AS: Results from Caregiver Survey	Elizabeth Chertavian Medicus Economics, LLC
12:30 PM	Panel Discussion	All Presenters



Angelman Syndrome (AS)
Glossary

Adeno-Associated Virus - Gene Therapy (AAV-GT)
A therapeutic approach that is done in-vivo, delivering a healthy copy of the missing or non-functional *UBE3A* gene using a viral vehicle called an Adeno-Associated Virus to carry the gene directly into the cells of the brain, called neurons.

Allele
One or two versions of a gene at a given genomic location.

Angelman Syndrome (AS)
A rare neurogenetic disorder that affects approximately 1 in 15,000 people – approximately 500,000 individuals worldwide; a single-gene disorder caused by loss of function of the *UBE3A* gene on the maternal allele located in the 15q11.2-13.1 region.

Antisense Oligonucleotides (ASO)
A therapeutic approach that uses modified RNA or DNA molecules that bind to the RNA of the *UBE3A-ATS* (*UBE3A* antisense transcript). The *UBE3A-ATS* is responsible for silencing the paternal *UBE3A* gene through a process called imprinting. In binding to the targeted antisense transcript, the ASO stops the *UBE3A-ATS* from silencing the paternal *UBE3A* gene.

Artificial Transcription Factors/Zinc Fingers (ATF-ZF)
A therapeutic approach that consists of something called "regulatory proteins" which are comprised of modular units that are customized to stop the *UBE3A-ATS* from silencing the paternal copy of the *UBE3A* gene, so that it can be expressed in neurons.

Biomarker
A biological marker that is an objective measure of a disease state. This marker can be electrical, like EEG delta power, or molecular, like UBE3A in the cerebrospinal fluid. These markers are aimed to be measured over time so that changes can be documented biochemically or electrophysiologically.

Brain Derived Neurotrophic Factor (BDNF)
A protein that plays a crucial role in learning and memory in the brain. BDNF levels are deficient in AS and serve as a potential downstream targeted therapeutic approach.

Central Nervous System (CNS)
Brain and spinal cord.

Clinical Trial
A research study where investigators test potential ways to detect, treat or prevent a disorder.

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)
A gene editing tool that utilizes a guide RNA (gRNA) to recognize DNA or RNA and directs an enzyme to cut a targeted sequence. This therapeutic approach would work to reinstate paternal *Ube3a* by designing a CRISPR that cuts *UBE3A-ATS* allowing for paternal gene expression. It can also be used to edit a misspelling in the genome or to activate genes that are halpoinsufficient.

Delivery
The mechanism in which a therapeutic is delivered to the central nervous system of the body; delivery can include route of administration (e.g. brain, spinal cord, intravenous, etc.) and how the therapeutic reaches its target location (e.g. carrier of the therapeutic like viral vector, bone marrow stem cells, RNP, etc.).

DNA (deoxyribonucleic acid)
The molecule that carries genetic information for the development and function of an organism. DNA is made of a double helix, which is 2 linked strands that wind around each other and connect by pairs of nucleic acids or molecules and are often coded by the letters: ATCG.

Downstream Targets
A symptomatic therapeutic approach that focuses on different molecular pathways and effector proteins impacted by the missing UBE3A protein.

Dystonia
A neurological movement disorder characterized by involuntary (unintended) muscle contractions that cause slow, repetitive movements or abnormal postures.

E3 Ubiquitin Protein-Ligase Antisense Transcript (*UBE3A-ATS*)
The long, noncoding piece of RNA that blocks paternal *UBE3A* gene expression in humans.

E3 Ubiquitin Protein-Ligase Gene (*UBE3A*)
The gene that codes for the UBE3A protein in humans. *UBE3A* is located in the 15q11.2-13.1 region and is generally expressed from both the maternal and paternal alleles throughout the body, but in neurons, the cells of brain, only the maternal copy of the *UBE3A* gene is expressed. This is due to the imprinting phenomenon where the *UBE3A-ATS* is silencing the paternal *UBE3A* gene from being expressed.

Note that the human *UBE3A* gene or RNA is capitalized and italicized. The rodent *Ube3a* gene is in lower case and italicized.

E3 Ubiquitin Protein-Ligase (UBE3A)
UBE3A is the human protein coded by the *UBE3A* gene, whose loss is causal of AS. UBE3A is a protein with many functions in the human body including targeting other proteins for removal.

Note that the human UBE3A protein is capitalized but not italicized. The rodent Ube3a protein is in lower case and not italicized.

E3 Ubiquitin Protein-Ligase Antisense Transcript (*Ube3a-ATS*) Mouse
The long noncoding piece of RNA that blocks paternal *Ube3a* expression in rodent models.

E3 Ubiquitin Protein-Ligase Gene (*Ube3a*) Mouse
The gene that codes for Ube3a protein in rodents. *Ube3a* is generally expressed from both the maternal and paternal alleles throughout the body, but in neurons, the cells of the brain, only the maternal copy of the *Ube3a* gene is expressed. This is due to the imprinting phenomenon where the *Ube3a-ATS* is silencing the paternal *Ube3a* gene from being expressed.

E3 Ubiquitin Protein-Ligase Protein (Ube3a) Mouse
Ube3a is the rodent model protein coded by the *Ube3a* gene. The Ube3a protein has many of the same functions as UBE3A protein in humans. The conservation of function between humans and animals allows researchers to model AS and test therapeutic efficacy and safety.

Endpoints
Quantitative and/or qualitative measures that can be assessed in a clinical trial based on the symptoms of a disorder like communication, sleep, behaviors, motor function, etc.

Enzyme Replacement Therapy (ERT)
A therapeutic approach replacing the missing or nonfunctional UBE3A protein in the brain.

Food & Drug Administration (FDA)
A government agency in the USA that is responsible for protecting the public's health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products (like cell and gene therapies), medical devices, food supply, cosmetics, etc.

Gamma-Aminobutyric Acid (GABA)
Gamma-aminobutyric acid (GABA) is an inhibitory neurotransmitter in the brain that plays a crucial role in regulating brain activity. GABA's primary function is to inhibit or reduce the excessive firing of neurons, which can lead to overstimulation and conditions like anxiety, stress, and even seizures.

Gene
A segment of DNA that can code for a specific protein. When genes are missing or letters are misspelled, this can lead to a nonfunctional or nonexistent protein.

Gene Editing
A technology that allows one to change or edit parts of the genome, either the DNA or the RNA. This can be used to create tools that mimic genetic disorders, and can also be used to correct certain genetic disorders. This results in either the removal of existing DNA or RNA or the insertion or replacement of DNA or RNA.

Gene Therapy (GT)
A therapeutic approach that involves introducing, modifying or replacing specific genes within target cells with the goal of correcting or compensating for a genetic condition, resulting in the absence or loss of function of a gene.

Genome
A complete set of an organism's genetic material, including all of its genes. This serves as a genetic blueprint or instruction manual for the growth, development, functioning, and reproduction of that organism; the genome is encoded in the DNA (deoxyribonucleic acid) of an organism's cells.

Genotype
Refers to the specific genetic makeup or combination of genes that an individual organism possesses. AS has 5 genotypes: Deletion, Mutation, UPD, ICD, and Mosaic.

Global Angelman Syndrome Registry (GASR)
A registry that assists pharmaceutical companies in understanding the scope of AS based on the data contributed by those who know the patients best: caregivers.

Hematopoietic Stem Cell - Gene Therapy (HSC-GT)
A therapeutic approach where a patient's own bone marrow stem cells are removed from the body, modified ex vivo, or outside the body, and returned to the body with a replaced copy of the missing or nonfunctional gene; in this case *UBE3A*. Once they are injected back into the patient they go to the bone marrow and populate that space with the goal of being released into the system continuously to supply the body with a healthy copy. These cells are able to cross from the blood to the brain, which is called crossing the blood brain barrier. Once they cross the blood brain barrier they become a cell type called microglia and secrete the UBE3A protein throughout the brain for neurons to use.

Imprinting
The process by which only one copy of a gene in an individual (either maternal or paternal) is expressed, while the other copy is suppressed or "silenced."

Induced Pluripotent Stem Cells (iPSCs)
iPSCs are derived from mature cells in the body, like skin or blood, and can be reprogrammed back into very young cells enabling them to grow into a determined cell type, like neurons. This allows them to be used as tools for testing and research purposes.

International Angelman Syndrome Research Council (INSYNC)
A council that brings together world experts in and outside of the Angelman syndrome space to help support advancing AS drug development, ensuring all research avenues are identified, de-risking novel therapeutic platforms, and encouraging collaborative efforts.

Investigational New Drug-Enabling (IND-enabling)
A key milestone prior to clinical testing in humans where various safety, toxicology, pharmacology, and pharmacokinetic properties are determined. These studies help define the properties and de-risk the appropriate therapeutic candidates for a clinical trial.

Maternal
Genetic traits or factors inherited from the mother's genetics or allele. *UBE3A* is only expressed from the maternal allele in neurons and the paternal copy is silenced due to the *UBE3A-ATS*.

Methylation
Methylation is a chemical modification of DNA that can affect gene expression. Methylation testing is a common type of diagnostic testing in AS used to determine if *UBE3A* is abnormally methylated. If the methylation test is abnormal, expected genotypes include deletion, UPD, and ICD. If it is normal, a mutation genotype may still be possible after testing the sequency of the *UBE3A* gene.

Mouse Model (AS Mouse)
The mouse is the foremost mammalian model for studying human disease. Several mouse models of AS exist, which have been able to recapitulate many of the symptoms like balance disorders, anxiety, learning and memory challenges, motor dysfunction, increased seizure susceptibility, and an abnormal EEG.

Natural History Study (NHS)
An observational clinical study that aims to conduct a prospective, longitudinal natural history study of children and adults with Angelman syndrome using investigator-observed and parent-reported outcome measures to obtain data that will be useful for future clinical trials.

Neurodevelopmental Disorders (NDD)
A group of conditions in which the development of the brain is different from that of neurotypical individuals. This can impact language, emotions, behavior, learning, memory, motor, milestones, and more.

Novel
An adjective that describes something that is new and unique to the research field, for example, a delivery method or therapy.

Observational Clinical Study
A type of clinical study in which participants are identified, observed, and assessed for biomedical or health outcomes. Usually there is no drug introduced into this type of clinical trial.

Observer-Reported Communication Ability Measure (ORCA)
A caregiver reported outcome measure that separates communication into three main concepts: expressive, receptive and pragmatic communication. This measure was developed by FAST in collaboration with Duke University for AS specifically and is now being advanced for 14 other rare NDDs. The ORCA is now being assessed in all active clinical trials for AS and is the first validated endpoint specially developed for the AS population.

Organoids
Three-dimensional tissue cultures that are derived from stem cells. Organoids are self-organized cultures that can be crafted to replicate much of the complexity of an organ to characterize and test various therapeutic approaches. For AS, brain cortical organoids have been developed for every genotype.

Outcome Measures
A measure, or test, to determine if a treatment or therapeutic has an effect. Typically, this assessment is collected before a treatment/therapeutic for baseline results, then re-administered after the intervention to measure for changes due to intervention.

Paternal
Genetic traits or factors inherited from the father's genetics or allele. *UBE3A* is only expressed from the maternal allele in neurons and the paternal copy is silenced due to the *UBE3A-ATS*.

Phenotype
An individual's observable characteristics resulting from their genotype. In AS this can be their ability to walk, talk, sleep, have seizures, etc.

Pillar 1
Pillar of FAST's strategic roadmap which focuses on replacing the missing or non-functional maternal copy of the *UBE3A* gene or protein in neurons of the brain. This includes therapeutic platforms like AAV-GT, HSC-GT, ERT, etc.

Pillar 2
Pillar of FAST's strategic roadmap which focuses on activating the silent copy of the paternal *UBE3A* gene in the brain. This includes therapeutic approaches like ASOs, CRISPR, ATF-ZF, miRNA, etc.

Pillar 3
Pillar of FAST's strategic roadmap which focuses on different molecular pathways and effector proteins impacted by the missing UBE3A protein. These drugs generally aim to improve the communication of neurons at the synapse (junction between the two neurons).

Pillar 4
Pillar of FAST's strategic roadmap which focuses on work supporting necessary research tools, clinical developments, and community efforts to prepare for AS clinical trials and drug approvals. This includes the development of a clinical trial training centers, newborn screening efforts, advancing endpoints and biomarkers, and driving policy and visibility globally.

Pre-Clinical
Refers to any research investigating a potential therapeutic approach prior to clinical assessment in humans.

Rescue
Refers to a technique or experimental approach aimed at restoring or improving a specific biological function or phenotype that is disrupted in a genetic or disease model.

Ribonucleic Acid (RNA)
Ribonucleic acids are the nucleic acids present in all living cells that contain the instruction to make proteins. These molecules are present in a majority of living organisms and are made up of nucleotides, which are sugars attached to bases including the letters: AGUC. RNA is essential for most biological functions and is generally made based on the DNA sequences in the genome through something called transcription. RNA contains the instruction to make proteins.

RNA Interference (RNAi)
A natural cellular process that regulates gene expression. RNAi occurs when small RNA molecules inhibit the expression of a particular gene(s).

Scientific Advisory Board (SAB)
A group of FAST volunteers made up of scientists and clinicians who review grants, advise on new scientific ideas, and support ongoing programs in academia and industry.

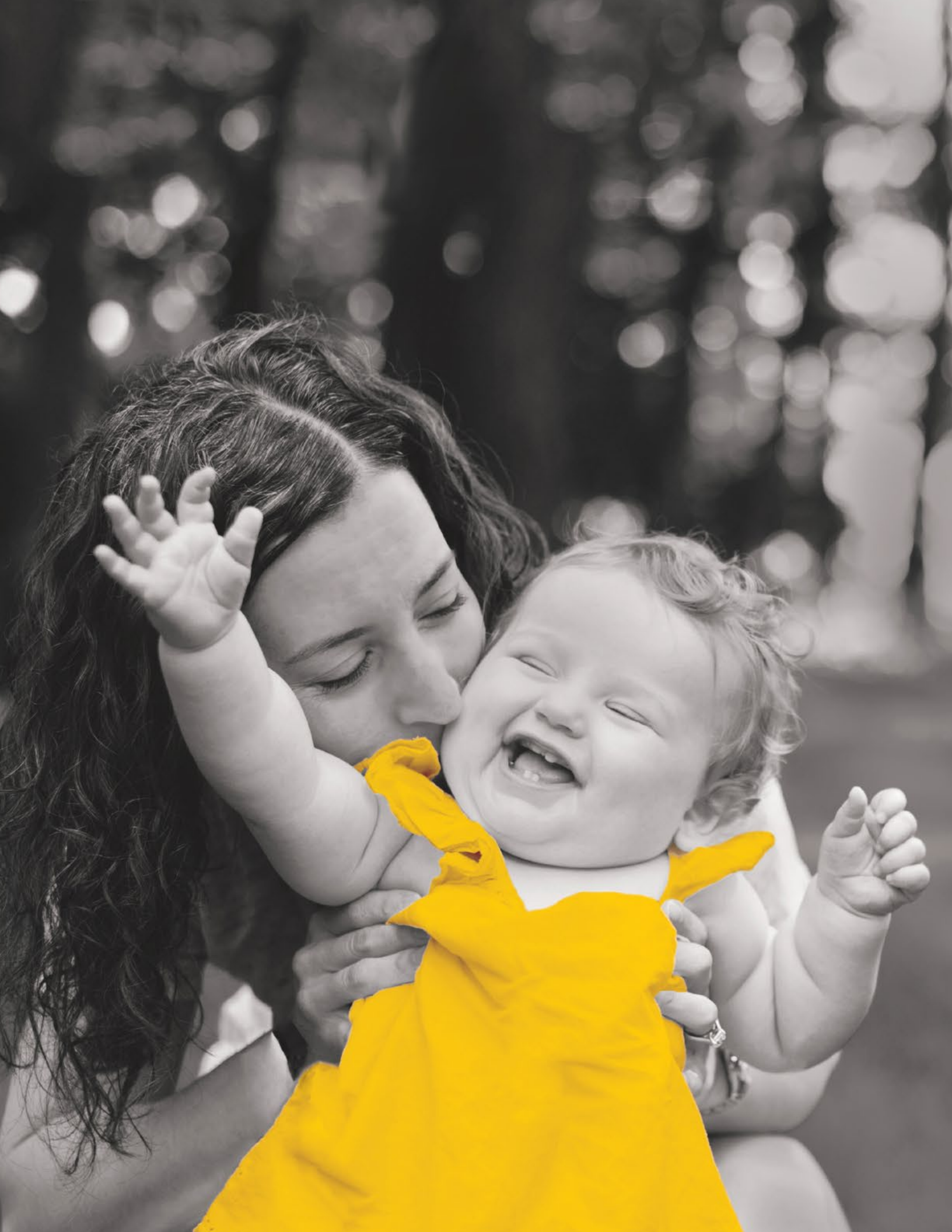
Synapse
A neuronal junction, which is the site of electric nerve impulse communication between two neurons or between a neuron and a muscle cell. This junction is impacted in AS.

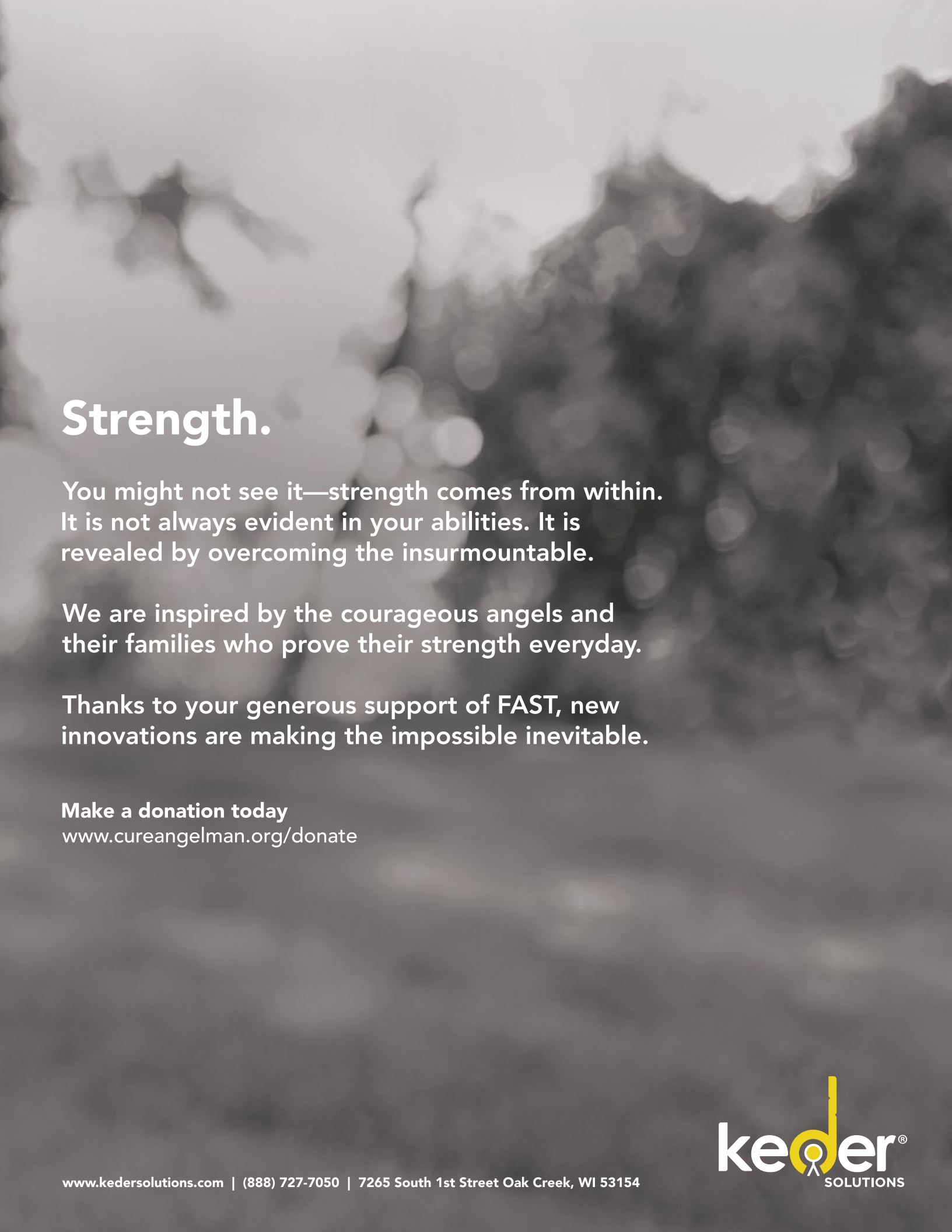
Translational Research
The process of turning observations in the laboratory, clinic, and community into interventions that improve the health of individuals.

Upregulate
A term used in genetics and molecular biology to describe the process of increasing the expression or activity of a gene or protein.

Vector
A delivery system or carrier used to transport therapeutic agents, such as gene therapies, vaccines, or other medical treatments, to their intended target within a patient's body. Terms you might hear are Adeno-associated Virus Vector or Lentiviral Vector.

Wildtype (WT)
When animal models are designed, the WT genotype refers to an animal without any mutated genes. The phenotype of a WT mouse is considered to be "typical" functioning and can be used as a comparison group for animals with the mutated gene, or the AS model.





Strength.

You might not see it—strength comes from within. It is not always evident in your abilities. It is revealed by overcoming the insurmountable.

We are inspired by the courageous angels and their families who prove their strength everyday.

Thanks to your generous support of FAST, new innovations are making the impossible inevitable.

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Going beyond every day.™

Ultragenyx is proud to sponsor the 2023 FAST Global Science Summit & Gala and support FAST's ongoing work with the Angelman community.

Together, we will continue to Dream Big and transform the lives of people living with Angelman syndrome.

To learn more visit **Ultragenyx.com**

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Notes

Notes

A Special Thank You

To all of our partners, thank you for your generosity and commitment to advancing therapeutics for our loved ones living with Angelman syndrome.

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