

Taysha (<https://www.tayshagtx.com>)

BRINGING NEW CURES TO LIFE

At Taysha Gene Therapies, we believe in a world where monogenic CNS disease can be eradicated.

And we believe that world is within our reach.

WHAT DOES TAYSHA MEAN?

Taysha is a word in the Caddo Native American language meaning “ally” or “friend,” and when translated, also means “Texas.” We are committed to being an ally to the rare disease community.

Our vision is bold, and we’ve assembled the right pieces to help make it a reality.

A new approach, based on a proven method.

Our strategy is to advance a pipeline of gene therapies that serve a population of patients who suffer from diseases with high unmet medical needs. Our proven approach bridges the gap between innovation and a potential cure.

Experts in gene therapy – and putting patients first.

We’ve reunited the top talent in gene therapy and together, we believe we can discover, develop, and commercialize novel gene therapies for both rare and large patient populations.

A pipeline built on gene therapies focused on CNS monogenic diseases.

We are advancing an extensive AAV gene therapy pipeline, with each medicine targeting the underlying biology of the specific indication. Our lead program is in development for Rett syndrome.

ABOUT

We want to do more than just treat monogenic CNS disease. We want to eradicate it.

WHO WE ARE

AT TAYSHA GENE THERAPIES, WE BELIEVE

THE PATIENT ALWAYS COMES FIRST.

This is why we are singularly focused on discovering, developing and commercializing gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), both in rare and large patient populations.

We were founded in partnership with The University of Texas Southwestern Medical Center (UT Southwestern) to develop and commercialize transformative gene therapy treatments. Together with UT Southwestern, we have created a powerful engine to develop transformative therapies with the potential to dramatically improve patients’ lives.

TAYSHA VALUES

LOVE

Do what we love and love what we do

AUDACIOUS

Think big, be courageous

EMPATHY

For each other, for patients

COLLABORATIVE

Respect each other, explore differences, unite as a team

MADE IN TEXAS

We are rooted in the heart of Dallas, not far from the iconic Spindletop oil field.

Through the generations, these hardworking explorers ultimately went on to fund the very research being conducted at UT Southwestern today.

At Taysha, we embrace the same diligent, trailblazing mindset our Texan ancestors were known for.

As the largest oil production center at the turn of the century, Spindletop fueled Texas' economy and a new breed of 'wildcatters' – the individuals who drilled new, exploratory oil wells.

UT SOUTHWESTERN PARTNERSHIP

Our partnership with UT Southwestern is different from traditional collaborations between industry and academia.

Through our partnership, we are able to leverage the collective expertise of UT Southwestern researchers, clinicians and investigators with decades of experience in conducting cutting-edge research and providing clinical care. This includes the esteemed scientists who lead the UT Southwestern Gene Therapy Program: Steven Gray, Ph.D., and Berge Minassian, M.D.

We have access to UT Southwestern's faculty, GMP viral vector manufacturing facility and integrated research and clinical care approach. Together, we believe this will enable us to advance our development programs with speed and scale.

UT Southwestern is one of the premier academic medical centers in the nation. Collectively, its faculty has earned some of the most prestigious honors in science.

6 - Nobel Prize Winners

24 - Members of the National Academy of Sciences

16 - Members of the National Academy of Medicine

14 - Howard Hughes Medical Institute Investigators

OUR TEAM

We've assembled the experts.

Our team is comprised of some of the most accomplished and knowledgeable gene therapy scientists and CNS disease experts. Together – armed with our unrelenting, patient-first focus – we are helping bring new cures to life.

LEADERSHIP TEAM

Sean Nolan

Chief Executive Officer and Board Chairman

Sean brings diverse functional expertise inclusive of commercial operations, global marketing, corporate and business development, and global manufacturing and supply chain management. Sean formerly served as CEO of AveXis.

Sukumar Nagendran, M.D.

President and Head of Research and Development

Suku brings more than 25 years of experience in gene therapy development, clinical development strategy, medical affairs, diagnostics, payer strategy and commercialization of therapeutic products; also currently advising many other gene therapy and healthcare companies. Formerly of Jaguar Gene Therapy, AveXis, Quest Diagnostics and Pfizer.

Kamran Alam, CPA, MBA

Chief Financial Officer

Finance executive with experience with follow-on financings and M&A; served as VP Finance at AveXis where he played a key role in the acquisition of AveXis by Novartis; most recently served as SVP Finance and Principal Financial Officer at Rocket Pharma.

Emily McGinnis

Chief Patient Advocacy and External Affairs Officer

Led patient advocacy and government affairs at AveXis; instrumental in the launch of Zolgensma, where she played a key role in collaborating with advocacy on newborn screening development and implementation efforts to rapidly diagnose spinal muscular atrophy patients in need of treatment.

Fred Porter, Ph.D.

Chief of Staff and Technical Operations Officer

Experienced in both academia and the biopharma industry in development of gene therapy and viral vaccine candidates with deep manufacturing experience at Novartis and most recently at BridgeBio Pharma where he was SVP of Technical Development and Manufacturing.

Sean McAuliffe

Chief Business Officer

Led the development and execution of go-to-market plan for Zolgensma; with experience at Baxter, Takeda, and most recently as US General Manager and VP of Marketing at AveXis.

Tracy M. Porter, M.Ed., SPHR

Chief People Officer

Experienced human resources executive in entrepreneurial global business environments specializing in pharmaceuticals and biotech. She most recently served as VP, Head of Human Resources at Audentes Therapeutics. Prior to Audentes, she acted as Senior Director, Organizational & Talent Development at Medivation Inc.

INDEPENDENT SCIENTIFIC ADVISORY BOARD

Professor Dr. med. Benedikt Schoser, FEAN

Associate Professor of Neurology

Friedrich-Baur-Institute

Ludwig-Maximilians-University

Munich, Germany

Prof. Dr. med. Benedikt Schoser is a trained neurologist, neurophysiologist, neurointensivist, palliative medicine doctor and muscle pathologist. He is Senior Consultant Neurologist and Co-chair of the Friedrich-Baur-Institute, Department of Neurology at the Ludwig-Maximilians-University in Munich, Germany. He became a fellow of the European Academy of Neurology (EAN) in 2017 and serves as a board member of the Educational, Rare Disease and Scientific Muscle and Neuromuscular panels of the EAN. Prof Schoser is a long-term member of the World Muscle Society (WMS) and organizes the WMS teaching course. His special interests include multisystemic neuromuscular disorders and translational research.

David P. Dimmock, M.D.

Senior Medical Director, Rady's Children's Institute for Genomic Medicine, San Diego, California

David P. Dimmock, M.D., is the Senior Medical Director of Rady Children's Institute for Genomic Medicine. Dr. Dimmock is an expert in the field of clinical genomic medicine, the Principal Investigator on multiple clinical trials of novel therapeutics in rare metabolic diseases and an author of over 100 peer-reviewed articles, publications, chapters, books and reviews. He has been an invited advisor to the U.S. Food and Drug Administration in the Office of Orphan Diseases and has overseen regulatory submissions for whole genome sequencing devices. At the Center for Disease Control, he was a member of the Planning and Organizing Committee of NeXT-StoC to develop guidance to ensure analytic quality of next-generation sequencing tests. In addition, he was a member of the National Genomics Board UK and CLIAc NGS Guidelines Forum. He is a Scientific Advisory Board member for BioMarin Pharmaceuticals.

Dr. Dimmock is a graduate from St. George's, University of London.

Gerald S. Lipshutz, M.D., M.S.

Professor-in-Residence, Departments of Surgery and Molecular and Medical Pharmacology

Surgical Director, Pancreas/Auto-Islet Transplant Program

Chair, Academic Medicine College

David Geffen School of Medicine at UCLA

Los Angeles, California

Gerald S. Lipshutz, M.D., M.S., is a Professor-in-Residence in the Departments of Surgery and Molecular and Medical Pharmacology, Surgical Director of the Pancreas/Auto-islet Transplant Program and Chairman of the Academic Medicine College at the David Geffen School of Medicine at University of California, Los Angeles. His clinical specialties and interests include liver and pancreas transplantation and gene and cell therapies for single-gene metabolic disorders of the liver. Dr. Lipshutz is a grant reviewer for the Wellcome Trust and the US National Institutes of Health where he is a standing member of the GDD study section. He is a Principal Investigator at the UCLA Lipschutz Hepatic Regenerative Medical Laboratory and for several NIH-funded and industry-sponsored studies for gene therapies. He is author of over 70 peer-reviewed articles and is an Editorial Board member of Molecular Therapy – Methods and Clinical Development and Gene Therapy.

Dr. Lipshutz earned his medical degree from the University of California, Los Angeles.

Wendy K. Chung, M.D., Ph.D.

Kennedy Family Professor of Pediatrics in Medicine

Director of Clinical Genetics, Clinical Cancer Genetics and Precision Medicine Resource, Irving Institute for Translational Research

Attending Physician, Division of Molecular Genetics, Department of Pediatrics and Medicine

Columbia University

New York, New York

Wendy K. Chung, M.D., Ph.D., is a Kennedy Family Professor of Pediatrics in Medicine, Attending Physician in the Division of Molecular Genetics, Department of Pediatrics and Medicine, and the Director of Clinical Genetics, Clinical Cancer Genetics, and Precision Medicine Resource at the Irving Institute for Translational Research, all at Columbia University. Her research interests include spinal muscular atrophy, autism, and neurogenetics. Dr Chung has authored over 500 peer-reviewed articles and 75 textbook chapters and serves on the Editorial Board of Molecular Case Studies and The American Journal of Human Genetics. Dr Chung is the Director of Clinical Research at the Simons Foundation Autism Research Initiative (SFARI) and a member of the National Academy of Medicine.

Dr. Chung earned her medical degree from Cornell University Medical College and her doctorate from Rockefeller University.

Alan Boyd, B.Sc., M.B., Ch.B., FRSB, FFLM, FRCP, FFPM

Fellow and Immediate Past-President of the Faculty of Pharmaceutical Medicine Royal College of Physicians, United Kingdom

CEO and Founder of Boyd Consultants

Consultant Pharmaceutical Physician

Fellow, Board Member, and Chair of the Specialist Advisory Committee in Pharmaceutical Medicine,

Past-President of the Faculty of Pharmaceutical Medicine

Alan Boyd, B.Sc., M.B., Ch.B., FRSB, FFLM, FRCP, FFPM, is the CEO and founder of Boyd Consultants and a fellow and Immediate Past-President of the Faculty of Pharmaceutical Medicine, Royal Colleges of Physicians, UK. Professor Boyd is also a Council Member and the Independent Clinician Trustee on the Board of the Academy of Medical Royal Colleges, UK. He is also an honorary professor at the University of Birmingham Medical School, in recognition of his expertise in medicine development. He has significant pharmaceutical industry experience and was the Head of Medical Research at AstraZeneca and the Research and Development Director at Ark Therapeutics Ltd, specializing in the development of gene therapy products.

He is a graduate in biochemistry and medicine from the University of Birmingham, UK.

Deborah Bilder, M.D.

Clinical Associate Professor of Psychiatry, Child and Adolescent Psychiatry Division

Adjunct Associate Professor, Departments of Pediatrics and Education Psychology

University of Utah

Salt Lake City, Utah

Deborah Bilder, M.D., is an Associate Professor at the University of Utah in Educational Psychology, General Pediatrics, and Child Psychiatry. Her research interests include clinical trials, medications, and biologics that target rare genetic conditions and has authored over 45 peer-reviewed articles. She is the Principal Investigator for the Utah Registry of Autism and Developmental Disabilities and Co-Principal Investigator for the Utah site of the Centers for Disease Control and Prevention's Autism and Developmental Disabilities Monitoring Network. Dr. Bilder is Co-Chair of the DAC Committee in psychiatry at the University of Utah and a consultant for the Utah Regional Education in Neurodevelopmental and Related Disabilities program. She has been awarded the Triple Board Program Teaching Award from the University of Utah Division of Child and Adolescent Psychiatry. She is a steering committee member for BioMarin Pharmaceutical Phase 3 Clinical Trial and also serves as a medical advisor for the Utah chapter of Make-a-Wish Foundation.

Dr. Bilder earned her medical degree from Vanderbilt University.

Michael W. Lawlor, M.D., Ph.D.

Professor of Pathology, Biomedical Engineering, Physiology and Cell Biology, Neurobiology, and Anatomy, Division of Pediatric Pathology

Associate Director, Neuroscience Research Center

Medical College of Wisconsin, Milwaukee, Wisconsin

Michael W. Lawlor, M.D., Ph.D., is a Professor of Pathology, Biomedical Engineering, Physiology, Cell Biology, Neurobiology, and Anatomy and the Associate Director of the Neuroscience Research Center at the Medical College of Wisconsin. He is a Board-Certified Anatomic Pathologist and Neuropathologist, and his research interests include pediatric muscle disease and gene therapy. Dr. Lawlor is an Editorial Board member of Muscle and Nerve and Journal of Neuropathology and Experimental Neurology. He is currently serving as in SAB member for Solid Biosciences in support of its gene therapy programs.

Dr. Lawlor earned his medical degree and doctorate from Loyola University School of Medicine and his residency, fellowship, and postdoctoral training was completed at Massachusetts General Hospital and Boston Children's Hospital in association with Harvard Medical School.

BOARD OF DIRECTORS

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Chief Medical Advisor

UT Southwestern Gene Therapy Program

Steven Gray, Ph.D.

Chief Scientific Advisor

UT Southwestern Gene Therapy Program

APPROACH

Our proven approach bridges the gap between innovation and potential cure.

With our gene therapy approach,

we're changing the way we speak about disease.

CREATING AN ENGINE FOR NEW THERAPIES

Gene therapies have proven to deliver transformational benefit to patients who suffer from devastating diseases. Our mission at Taysha is to build upon these advancements to eradicate monogenic CNS diseases for the thousands affected. Through our proven gene therapy strategy and our unrivaled partnership with UT Southwestern, we are creating an engine for new cures.

A PROVEN STRATEGY

The fundamental components of our approach are based on recent success in gene therapy development and commercialization: an adeno-associated virus serotype 9 (AAV9) capsid, intrathecal delivery and an efficient manufacturing process.

AAV9 Capsid

We use an AAV9 capsid to deliver therapeutic genes engineered to replace a mutated gene, enhance the expression of a silenced gene or decrease the expression of a gene. AAV9 has a unique ability to cross the blood-brain barrier, making it an ideal vector for gene therapies in the CNS, and since its discovery more than 50 years ago, AAV has been one of the most well-studied vehicles for the delivery of gene therapies.

Intrathecal Delivery

We use intrathecal administration, which directly delivers our gene therapies to the cerebrospinal fluid to facilitate optimal biodistribution and cell transduction within the central nervous system. The procedure is routinely performed in an outpatient setting, and in comparison to intravenous administration, it allows for a lower dose of the therapy.

Efficient Manufacturing

Our flexible manufacturing processes allow us to produce our gene therapy product candidates efficiently at scale. Through our partnership with UT Southwestern, we have access to a GMP-compliant manufacturing suite that utilizes a suspension HEK293 process to produce AAV9.

NEXT-GENERATION PLATFORM TECHNOLOGIES

We are developing next-generation technologies to optimize key components of our AAV-based gene therapies, including transgene regulation.

REGULATED TRANSGENE EXPRESSION USING miRARE

In a number of disorders, including Rett syndrome, the expression of a therapeutic transgene needs to be regulated. High doses of the engineered gene may be harmful, while low doses may not be effective. For disorders that require replacement of dose-sensitive genes, we have combined high-throughput microRNA (miRNA), profiling and genome mining to create miRARE, our novel miRNA target panel. This approach is designed to enable our product candidates to maintain safe transgene expression levels in the brain.

Step	Process Stage	Description	Interactions
1	Viral genome in nucleus	The transgene is introduced into the nucleus via a viral vector.	Connected to 'mRNA in cytoplasm'
2	mRNA in cytoplasm	The transgene's presence leads to the production of mRNA in the cytoplasm.	Leads to 'Translation and nuclear localization'; Interaction with 'Mature miRNAs' at step 5
3	Translation and nuclear localization	The mRNA is translated into protein, and it may also localize into the nucleus.	Results in 'Transgene drives expression of miRNAs'
4	Transgene drives expression of miRNAs	The transgene promotes the expression of multiple endogenous miRNAs.	None directly, but it's the outcome of step 3
5	Mature miRNAs regulate mRNA expression	The mature miRNAs bind to mRNA in the cytoplasm to control its expression levels.	Affects 'mRNA in cytoplasm' at step 2

PIPELINE

Thousands of patients are affected by monogenic CNS diseases.

At Taysha, we aim to address this devastating need through our pipeline of AAV-based gene therapies.

Our gene therapy candidates are designed to target the unique, underlying biology of diseases of the CNS. We are focused on advancing our lead clinical program in Rett syndrome.

Program	Indication	Discovery	Preclinical	Phase 1/2	Pivotal	Notes
TSHA-102	Regulated GRT for Rett Syndrome (REVEAL ADULT STUDY CANADA)	Yes	Yes	Yes	No	
TSHA-102	Regulated GRT for Rett Syndrome (REVEAL PEDIATRIC STUDY U.S.)	Yes	Yes	Yes	No	
TSHA-120	GRT for Giant Axonal Neuropathy	Yes	Yes	No	No	Deprioritized; seeking external strategic options
TSHA-118	GRT for CLN1 Disease	Yes	Yes	No	No	Deprioritized; seeking external strategic options
TSHA-105	GRT for SLC13A5 Deficiency	Yes	Yes	No	No	Deprioritized; seeking external strategic options

In this table, the 'Discovery', 'Preclinical', 'Phase 1/2', and 'Pivotal' columns indicate whether the program is in that stage with a "Yes" or "No".

GRT: Gene replacement therapy

We have deprioritized the company sponsored evaluation of TSHA-120 for GAN, TSHA-118 for CLN1 and TSHA-105 for SLC13A5 and are seeking external strategic options to potentially enable further program development.

TSHA-102

TSHA-102 is a self-complementary intrathecally delivered AAV9 gene transfer therapy in clinical evaluation for Rett syndrome, a neurodevelopmental disorder and one of the most common genetic causes of severe intellectual disability, characterized by rapid developmental regression and in many cases caused by heterozygous loss of function mutations in MECP2, a gene essential for neuronal and synaptic function in the brain. TSHA-102 is constructed from a neuronal specific promoter, MeP426, coupled with the miniMECP2 transgene, a truncated version of MECP2, and miRNA-Responsive Auto-Regulatory Element, or miRARE, our novel miRNA target panel, packaged in self-complementary AAV9, which enables cellular regulation of both endogenous and exogenous MECP2 expression.

PUBLICATIONS

General

Prasad, S. et al. Immune Responses and Immunosuppressive Strategies for Adeno-Associated Virus-Based Gene Therapy for Treatment of Central Nervous System Disorders: Current Knowledge and Approaches. *Human Gene Therapy*. DOI: 10.1089/hum.2022.138

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Prasad, S, et al. Accepting the Challenge: Innovative Approaches and Translational Strategies in Gene Therapy Development. Abstract/Presentation. American Society of Gene and Cell Therapy Annual Meeting 2022.

Gray, SJ. Timing of Gene Therapy Interventions: The Earlier, the Better. *Mol. Ther.* 2016 Jun; 24(6): 1017-1018

Rett

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Prasad, S, et al. Safety Assessment of High-Dose miniMECP2 AAV9 Gene-Replacement Therapy (TSHA-102) for Rett Syndrome in Rats. Abstract/Presentation. American Society of Gene and Cell Therapy Annual Meeting 2022; International Rett Syndrome Foundation Rett Syndrome Scientific Meeting 2022.

Gadalla, KKE, et al. Development of a Novel AAV Gene Therapy Cassette with Improved Safety Features and Efficacy in a Mouse Model of Rett Syndrome. *Mol Ther Methods Clin Dev.* 2017 Apr 22; 5:180-190

Sinnett, SE, et al. A New Approach for Designing a Feedback-Enabled AAV Genome Improves Therapeutic Outcomes of MiniMeCP2 Gene Transfer in Mice Modeling Rett Syndrome. Abstract 92. 2020 *Mol Ther.* Apr 28;28(4S1):47

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Sinnett, SE and Gray, SJ. Recent endeavors in MECP2 gene transfer for gene therapy of Rett syndrome. *Discov Med*. 2017 Oct; 24(132):153-159

SLC13A5

Goodspeed, K. et al. SLC13A5 Deficiency Disorder: From Genetics to Gene Therapy. *Genes* 2022; 2022 Volume: 13 Issue: 9 Pages: 1655

Bailey, L, et al. Gene Therapy Treatment in Young SLC13A5 Deficient Mice. Abstract/Presentation. American Society of Gene and Cell Therapy Annual Meeting 2022.

Yang, QZ, et al. Epilepsy and EEG Phenotype of SLC13A5 Citrate Transporter Disorder. *Child Neurol Open*. 2020 Jun 8;7:2329048X20931361

CLN1

Leal-Pardinas, F, et al. Designing a first-in-human gene replacement therapy clinical trial for CLN1. Abstract/Presentation. WORLDSymposium 2022.

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Chandra, G, et al. Cln1 gene disruption in mice reveals a common pathogenic link between two of the most lethal childhood neurodegenerative lysosomal storage disorders. *Hum Mol Genet*. 2015 Oct 1;24(19):5416-32

Koster, KP and Yoshii, A. Depalmitoylation by Palmitoyl-Protein Thioesterase 1. *Neuronal Health and Degeneration*. *Front Synaptic Neurosci*. 2019 Aug 29;11:25

Master, MC, et al. CLN1 Natural History. Abstract #260. *Molecular Genetics and Metabolism*. 2020

Schulz, A, et al. NCL diseases – Clinical Perspectives. *Biochim Biophys Acta*. 2013 Nov;1832(11):1801-06

GAN

Bailey, R, et al. Vagus Nerve Delivery of AAV9 to Treat Autonomic Nervous System Dysfunction in Giant Axonal Neuropathy. Abstract/Presentation. American Society of Gene and Cell Therapy Annual Meeting 2022.

Bharucha-Gobel D, et al. Giant axonal neuropathy: cross sectional analysis of a large natural history cohort. *Brain* 2021 awab179

Armao D, et al. Autonomic nervous system involvement in the giant axonal neuropathy (GAN) KO mouse: implications for human disease. *Clin Auton Res*. 2016 Aug;26(4):307-13

Bailey RM, et al. Development of Intrathecal AAV9 Gene Therapy for Giant Axonal Neuropathy. *Mol Ther Methods Clin Dev*. 2018 Jun 9;9:160-171

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Johnson-Kerner, BL, et al. Giant axonal neuropathy: An updated perspective on its pathology and pathogenesis. Muscle Nerve. 2014 Oct;50(4):467-76

Saade D, Gray SJ et al. Review of Safety and Interim Analysis of Efficacy in the First in Human Intrathecal Gene Transfer Trial for Giant Axonal Neuropathy. Abstract 610. Mol Ther. Apr 28;28(4S1):271

PATIENTS & CAREGIVERS

We strive to be allies to our partners in the disease advocacy community and the patient, their families and caregivers.

OUR PROMISE TO PATIENTS

At Taysha Gene Therapies, the patient is at the center of our work.

The patient, their family, caregivers and the communities we serve are the foundation for everything we do from preclinical drug development through commercialization of new treatments. We remain steadfast in our commitment to understanding the unique challenges faced by the communities we serve, keeping those stakeholders' best interests at heart as we seek to deliver impactful and life-changing therapies for monogenic CNS diseases. Our organizational decisions and activities are guided by the following principles:

OUR PATIENT GUIDING PRINCIPLES

Collaboration

Founded on the basis of collaboration, we are focused on coordination with patients, caregivers, advocacy partners, clinicians and government stakeholders.

Transparency

We are true partners to our stakeholders by providing proactive communication that is timely and informative.

Curiosity

By investing a deep-rooted understanding of the entire patient journey and disease pathway, we're able to develop the best solutions for the patient community.

Empathy

Patients and families matter most. We're fully committed to providing compassion, empathy and care beyond the product itself.

Respect

Taysha honors the privacy of patients and families by strictly adhering to policies that protect their personal and medical information.

HEALTHCARE PROFESSIONALS

We are committed to providing healthcare professionals with the information and programs that will support their efforts to treat rare, monogenic diseases of the central nervous system.

PIPELINE

5 gene therapy candidates for CNS disorders

PARTNERSHIPS

Foundational collaboration with UT Southwestern

OUR APPROACH

Our gene therapy approach builds upon proven gene therapy platforms

OUR CLINICAL TRIALS

Taysha is accelerating gene therapy research and clinical development across a broad range of monogenic CNS diseases.

For questions about Taysha programs and clinical trials please contact medinfo@tayshagtx.com

MEDICAL CONGRESSES AND EVENTS

Through participation in medical meetings and congresses, we seek to advance the understanding of disease and potential new treatment options. Explore our participation in these events here.

Past Congresses

ASGCT 24rd Annual Meeting 2021

Keynote Title: Attracting Capital and Building a Company in the Gene Therapy Space

Presenter: RA Session II, President, CEO and Founder, Taysha Gene Therapies

Session: Emerging Issues in Market Access Keynote Address

Panel Title: Working & Thriving in Industry – What You Need to Know to Prepare and Succeed

Presenter: Steven Gray, Ph.D., Associate Professor, UT Southwestern

Session: Transitioning from Academics to Industry Session

Panel Title: Learning from Experience – Case Studies of Transitions from Academia to Industry

Presenter: Fred Porter, Ph.D., Chief Technical Officer, Taysha Gene Therapies

Session: Transitioning from Academics to Industry

Panel Title: Understanding the Research Process: Being Equipped for Success

Presenter: Steven Gray, Ph.D., Associate Professor, UT Southwestern

Session: Patient Advocates' Role in Advancing Gene Therapy

17th Annual WorldSymposium 2021

Virtual Poster Presentation

Title: Co-creating a gene therapy clinical trial with GM2 gangliosidosis caregivers: A Virtual approach to patient engagement

Presenter: Kristin LaBounty Phillips, Senior Director, Community Engagement, Taysha Gene Therapies

ASGCT 23rd Annual Meeting 2020

Oral Presentations

Title: A New Approach for Designing a Feedback-Enabled AAV Genome Improves Therapeutic Outcomes of MiniMeCP2 Gene Transfer in Mice Modeling Rett Syndrome (RTT)

Presenter: Sarah E. Sinnett, Ph.D., Assistant Professor, Pediatrics, UT Southwestern Medical Center

Session: AAV Gene Delivery for CNS Disorders

Title: Intrathecal Delivery of Human Bicistronic Hexosaminidase Vector (TGTX-101) to Correct Sandhoff Disease in a Murine Model: A Dosage Study

Presenter: Alex E. Ryckman, Centre for Neuroscience Studies, Queen's University

Session: Main session, AAV Gene Delivery for CNS Disorders

Title: Direct Vagus Nerve Injection of AAV9 as a Treatment Approach for Autonomic Dysfunction in Giant Axonal Neuropathy

Presenter: Rachel M. Bailey, Ph.D., Assistant Professor, Neuroscience, UT Southwestern Medical Center

Session: New Techniques in Gene Therapy for Neurological Disorders

Poster Presentations

Title: SMRT Sequencing Allows High-Throughput Analysis of a Whole Capsid Shuffled AAV Capsid Library Following CNS Selection in Mice and NHPs

Presenter: Widler Casy, Ph.D., Postdoctoral Researcher, UT Southwestern Medical Center

Session: AAV Vectors – Virology and Vectorology

Title: Gene Replacement Therapy for SURF1-Related Leigh Syndrome Using AAV9

Presenter: Qinglan Ling, Ph.D., Postdoctoral Researcher, UT Southwestern Medical Center

Session: Neurologic Diseases

Title: A Dosage Study to Assess the Long-Term Effects of Gene Therapy for AB-Variant GM2 Gangliosidoses in a Mouse Model Using Adeno-Associated Virus Serotype 9

Presenter: Natalie M. Deschenes, Centre for Neuroscience Studies, Queen's University

Session: Main Session: Neurologic Diseases

Title: Preclinical Safety and Efficacy of AAV9 Gene Replacement Therapy for SLC6A1 Disorder

Presenter: Frances Shaffo, Ph.D., Postdoctoral Researcher, UT Southwestern Medical Center

Session: Neurologic Diseases

TAYSHA IS A RARE ALLY

Learn more about our commitment to patients and caregivers living with rare monogenic CNS disease.

(<https://tayshagtx.com/patients-caregivers/>)

EXPANDED ACCESS POLICY

Expanded Access, sometimes called Managed Access, Compassionate Use or Early Access, is a potential pathway for a patient with an immediately life-threatening condition, serious disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available.

At Taysha, we are collaborating closely with patients, caregivers, patient organizations and medical experts to conduct safe and effective clinical trials. We believe participation in well-designed clinical trials is the most ethical way to determine the safety and efficacy of investigational therapies. Clinical experience from well-controlled trials provide the highest probability of success of bringing an approved therapy to the entire patient community in a safe manner. Hence, Taysha does not offer an Expanded Access Program anywhere in the world.

If you have questions about participating in our clinical trials, please discuss with your health care provider, or contact us at: medinfo@tayshagtx.com.

We reserve the right to revise this policy at any time in accordance with the 21st Century Cures Act.

References

FDA Guidance for the Industry: Expanded Access to Investigational Drugs for Treatment Use — Questions and Answers. Updated 2017

Jarrow et al: Overview of FDA's Expanded Access Program for Investigational Drugs. Ther Innov Regul Sci. 2017 March 1; 51(2): 177–179. doi:10.1177/2168479017694850.

[21st Century Cures Act] (<https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf>)

For questions about programs and clinical trials please contact medinfo@tayshagtx.com.

CAREERS

We believe in a world where monogenic CNS disease can be eradicated. The Taysha Gene Therapies team is helping this belief become a reality.

DEEP IN THE HEART OF TAYSHA

Just like our novel gene therapies, the lifeblood of the Taysha team consists of multiple complementary components.

Whether it's on the discovery, development or commercialization front, we are singularly focused on creating gene therapies that can dramatically improve patients' lives. Regardless of their area of expertise, every member of our team is guided by this mission.

THIS IS WHAT MAKES US TAYSHA

Being an ally to the rare disease community.

Uncovering never-before-seen scientific discoveries.

Developing cutting-edge technologies and medicines.

Having a true sense for the term partnership.

Exploring uncharted territory, just like the first Texas 'wildcatters'.

But above all else, what really drives us is a desire to bring cures to patients with devastating diseases. We don't want to just treat monogenic CNS disease – we want to eradicate it.

CONTACT

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PRIVACY NOTICE

Overview

Taysha Gene Therapies, Inc. (“we”, “us”, “our”) respect your privacy. This Privacy Notice explains our practices with respect to personal data we collect and process in connection with your relationship with us. This includes information we collect through, or in association with, our website, together with all products and services we may offer from time to time via our website, or otherwise through your interactions with us (the website, products, services, collectively, the “Services”).

Please review the following to understand how we process personal data about you. By using any of our Services, whether by visiting our website or otherwise, and/or by voluntarily providing personal data to us, you acknowledge that you have read and understand the practices contained in this Privacy Notice. This Privacy Notice may be revised from time to time, so please ensure that you check this Privacy Notice periodically to remain fully informed.

What Information Do We Collect?

We collect personal data from and about you through the Services, including:

When you provide it to us directly;

Automatically through logging and analytics tools, cookies, pixel tags, and as a result of your use of and access to the Services; and

From third-party sources, including commonly used analytics platforms.

Finally, we may collect data that is not identifiable to you or otherwise associated with you, such as aggregated data, and is not personal data. To the extent this data is stored or associated with personal data, it will be treated as personal data; otherwise, the data is not subject to this notice.

Information You Share With Us

We collect personal data from you when you provide it to us, including through website forms, applying for a job with us, or contacting us with questions or comments.

For example, if you contact us for information or with questions, you must provide us with your contact information.

To apply for a job with us, you may be asked to submit your contact information and your resume through a form on the website. This information will form the job application that you submit to us in response to a job posting and will be used in our recruitment process once submitted.

Information Collected Automatically

When you browse or use the Services, we utilize commonly used logging and analytics tools, to collect information about your device, the network used to access the Services, and information about your use of the Services (such as how you navigate and move around the Services).

We also use certain technologies on the Services, including cookies and pixel tags, that allow us, our service providers, and other third parties to store information locally on your device, identify your device, track your interactions with messages we send, and track activity over time and across websites.

Information collected automatically includes the software and hardware attributes of the device you use to access the Services, unique device ID information, regional and language settings, performance data about the Services, network provider, and IP address (a number assigned to your device when you use the Internet). In addition, information is collected passively in the form of log files and third-party analytics that record website activity. For example, log file entries and analytics data are generated every time you visit a particular page on our website and track the dates and times that you use the Services, the pages you visit, the amount of time spent on specific pages, and other similar usage information, and general data (including the name of the web page from which you entered our website).

Cookies, Web Tracking, and Advertising. We use cookies and pixel tags to personalize and enhance your experience regarding our Services, to collect data about your visit to our Services, to help diagnose problems with our servers, to administer and market the Services, to permit analytics providers to gather information about your visit to the Services, and to gather broad demographic information about our users.

Information Obtained from Third Parties

We receive personal data from third parties that we have engaged to provide services to us, as well as from third parties that provide web analytics and usage information to us.

How Do We Process Personal Data?

Operational Uses

We process your personal data as part of our operations, which include:

Managing your inquiries, responding to inquiries and requests via email, and communicating with you through any newsletters or other updates; Operating, maintaining, and improving the quality of the Services and such content, products and/or services as we may make available through the Services; Recruiting activities, including assessing your qualifications and/or capability for a particular job, role, or

Task and processing pre- employment background checks; Compliance with applicable laws, regulations, rules and requests of relevant law enforcement and/or other governmental agencies; Endeavoring to protect our and our partners' rights, property, or safety, and the rights, property, and safety of our users and other third parties; and

For other purposes, as permitted or required by law.

Sharing of Personal Data

Some of the above processing involves sharing collected personal data with third parties, including service providers and other third parties.

We share personal data with our service providers, including software and Web developers, commercial email providers, security consultants, and other vendors we engage so that they may provide services to us or on our behalf;

We may share personal data we collect with certain affiliates, partners, prospective partners, and service providers in order to provide us and/or our affiliates and partners with information about the use of the Services and levels of engagement with the Services and to allow us to enter new business relationships; and

We share personal data with third parties when we believe it is required by, or necessary to comply with, applicable law.

Security

We employ reasonable physical, technical, and organizational safeguards designed to promote the security of our systems and protect the confidentiality, integrity, availability, and resilience of personal data. However, no method of safeguarding information is completely secure. While we use measures designed to protect personal data, we cannot guarantee that our safeguards will be effective or sufficient. In addition, you should be aware that Internet data transmission is not always secure, and we cannot warrant that information you transmit utilizing the Services is or will be secure.

Your Choices

You can make certain choices about how we communicate with you, and how we process certain personal data.

Cookies, Web Tracking, and Advertising

It is possible to change your browser settings to block the automatic collection of certain information. Please note that disabling or removing cookies may prevent the Services, or certain functionality on the Services, from working correctly or at all.

Other Important Information About Personal Data and the Services

Collection of Personal Data from Children

Children under 16 years of age are not permitted to use the Services, and we do not knowingly collect information from children under the age of 16. By using the Services, you represent that you are 18 years of age or older or are 16 years of age or older and have valid parental consent to do so.

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As a convenience, we may reference or provide links to third-party websites and services. When you access these third-party services, you leave our Services, and we are not responsible for, and do not control, the content, security, or privacy practices employed by any third-party websites and services. You access these third-party services at your own risk. This Privacy Notice does not apply to any third-party services; please refer to the privacy notice or policies for such third-party services for information about how they collect, use, and process personal data.

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We may, in the future, sell or otherwise transfer some or all our business, operations or assets to a third party, whether by merger, acquisition or otherwise. Personal data we obtain from or about you via the Services may be disclosed to any potential or actual third-party acquirers and may be among those assets transferred.

Do Not Track

We use analytics systems and providers that process personal data about your online activities over time and across third-party websites or online services, and these systems and providers may provide some of this information to us. We do not currently process or comply with any web browser's "do not track" signal or similar mechanisms.

Modifications and Updates to this Privacy Notice

This Privacy Notice replaces all previous disclosures we may have provided to you about our information practices with respect to the Services. We reserve the right, at any time, to modify, alter, and/or update this Privacy Notice, and any such modifications, alterations, or updates will be effective upon our posting of the revised Privacy Notice. Your continued use of the Services following our posting of any revised Privacy Notice will constitute your acknowledgement of the amended Privacy Notice.

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This Privacy Notice is subject to any agreements, including the Terms of Service that govern your use of the Services. This Privacy Notice applies regardless of the means used to access or provide information through the Services.

This Privacy Notice does not apply to information from or about you collected by any third-party services, applications, or advertisements associated with, or websites linked from, the Services. The collection or receipt of your information by such third parties is subject to their own privacy policies, statements, and practices, and under no circumstances are we responsible or liable for any third party's compliance therewith.

Additional Information and Assistance

If you have any questions or concerns about this Privacy Notice and/or how we process personal data, please contact us at:

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legal.notices@tayshagtx.com

In order to make this Privacy Notice reasonably accessible to users with disabilities, we follow the Web Content Accessibility Guidelines (WCAG 2.1). Users with disabilities may access the Services, and this Privacy Notice, using standing navigation on the website through the aid of additional software, such as screen readers.

Effective: July 30, 2021

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THE FOREGOING DOES NOT AFFECT ANY LIABILITY WHICH CANNOT BE EXCLUDED OR LIMITED UNDER APPLICABLE LAW.

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Arbitration. Any and all controversies, disputes, demands, counts, claims, or causes of action (including the interpretation and scope of this clause, and the arbitrability of the controversy, dispute, demand, count, claim, or cause of action) between you and us or our successors or assigns shall exclusively be settled through binding and confidential arbitration.

Arbitration shall be subject to the Federal Arbitration Act and not any state arbitration law. Unless otherwise agreed upon by the parties in writing, the arbitration will be conducted before one arbitrator and will be governed by the American Arbitration Association's ("AAA") Commercial Arbitration Rules and, if the arbitrator deems them applicable, the Supplementary Procedures for Consumer Related Disputes (collectively, the "Rules and Procedures"). To the fullest extent permitted by applicable law, you and we must abide by the following rules: (1) ANY CLAIMS BROUGHT BY YOU OR US MUST BE BROUGHT IN THE PARTY'S INDIVIDUAL CAPACITY, AND NOT AS A PLAINTIFF OR CLASS MEMBER IN ANY PURPORTED CLASS OR REPRESENTATIVE PROCEEDING; (2) THE ARBITRATOR MAY NOT CONSOLIDATE

MORE THAN ONE PERSON'S CLAIMS, MAY NOT OTHERWISE PRESIDE OVER ANY FORM OF A REPRESENTATIVE OR CLASS PROCEEDING, AND MAY NOT AWARD CLASS-WIDE RELIEF; (3) the arbitration shall be confidential, and neither you nor we may disclose the existence, content or results of any arbitration, except as may be required by law or for purposes of enforcement of the arbitration award; (4) the arbitrator may award any individual relief or individual remedies that are permitted by applicable law; and (5) each side pays its own attorneys' fees and expenses unless there is a statutory provision that requires the prevailing party to be paid its fees and litigation expenses, and, in such instance, the fees and costs awarded shall be determined by the applicable law.

Severability. If any provision of this Agreement shall be unlawful, void or for any reason unenforceable, then that provision shall be deemed severable from this Agreement and shall not affect the validity and enforceability of any remaining provisions. Our failure to enforce any provision of this Agreement shall not be deemed a waiver of such provision nor the right to enforce such provision.

Miscellaneous. This Agreement does not, and shall not be construed to create any partnership, joint venture, employer-employee, agency or franchisor-franchisee relationship between you and us. You may not assign, transfer or sublicense any or all of your rights or obligations under this Agreement without our express prior written consent. We may assign, transfer or sublicense any or all of our rights or obligations under this Agreement without restriction. Any heading, caption or section title contained herein is for convenience only, and in no way defines or explains any section or provision. All terms defined in the singular shall have the same meanings when used in the plural, where appropriate and unless otherwise specified. Any use of the term "including" or variations thereof in this Agreement shall be construed as if followed by the phrase "without limitation." This Agreement, including any terms and conditions incorporated herein, is the entire agreement between you and us relating to the subject matter hereof, and supersedes any and all prior or contemporaneous written or oral agreements or understandings between you and us relating to such subject matter. Notices to you (including notices of changes to this Agreement) may be made via posting to the Site or by e-mail (including in each case via links), or by regular mail. Without limitation, a printed version of this Agreement and of any notice given in electronic form shall be admissible in judicial or administrative proceedings based upon or relating to this Agreement to the same extent and subject to the same conditions as other business documents and records originally generated and maintained in printed form. We will not be responsible for any failure to fulfill any obligation due to any cause beyond our control.

If you have any questions regarding this Agreement, please contact us at:

Taysha Gene Therapies, Inc.

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EFFECTIVE DATE: July 30, 2021

Monitoring and Managing Immune Responses in Taysha Gene Therapy Patients

Taysha Gene Therapies recognizes the potential for immune responses against adeno-associated viral (AAV) vectors and transgenes in their gene therapy patients. To ensure patient safety and treatment success, they employ a comprehensive approach to monitoring and managing these responses:

1. Pre-screening:

Pre-existing immunity: Patients undergo thorough testing for pre-existing antibodies against AAV vectors before receiving gene therapy. This helps identify potential risks and guide treatment decisions. (Reference: <https://www.ncbi.nlm.nih.gov/books/NBK513460/>)

2. Immunological Monitoring:

Regular blood tests: After receiving gene therapy, patients are monitored for antibody development against the AAV vector and the transgene through regular blood tests. This allows for early detection of immune responses. (Reference: https://grants.nih.gov/grants/policy/gene_therapy_20000307.htm)

3. Clinical Assessment:

Close observation: Patients are closely observed for clinical signs and symptoms suggestive of immune responses, such as fever, fatigue, injection site reactions, or changes in neurological function. (Reference: https://grants.nih.gov/grants/policy/gene_therapy_20000307.htm)

4. Management Strategies:

Immunosuppressive therapy: In case of significant antibody development or clinical symptoms, Taysha may administer immunosuppressive medications like corticosteroids to suppress the immune response and protect the transgene from destruction. (Reference: <https://pubmed.ncbi.nlm.nih.gov/31968213/>)

Dose adjustment or re-administration: For some patients, adjusting the gene therapy dose or even re-administration at a later time may be considered, depending on the severity of the immune response and individual response to immunosuppression. (Reference: <https://pubmed.ncbi.nlm.nih.gov/31968213/>)

Close All patients receiving Taysha's gene therapies require close follow-up throughout the treatment and beyond to ensure prompt identification and management of any potential immune reactions.

Challenges and Future Directions:

Balancing immune suppression: Striking the right balance between suppressing the immune response enough to protect the transgene and avoiding excessive immunosuppression that increases the risk of infections remains a challenge.

Long-term monitoring: Long-term data on the safety and efficacy of Taysha's gene therapies is still limited, and further research is needed to understand the long-term dynamics of immune responses and their potential impact on treatment outcomes.

By implementing these monitoring and management strategies, Taysha aims to ensure the safety and efficacy of their gene therapies while minimizing the risk of immune complications. As the field of gene

therapy continues to evolve, Taysha remains committed to developing innovative approaches to address and overcome immune challenges.

Additional Resources:

Taysha Gene Therapies website: <https://tayshagtx.com/>

Pipeline page on Taysha website: <https://tayshagtx.com/pipeline>

Article on GAN gene therapy and immune responses: <https://pubmed.ncbi.nlm.nih.gov/35994385/>

Target diseases for gene therapy

Taysha Gene Therapies currently focuses on central nervous system (CNS) diseases, particularly rare monogenic conditions. While they haven't publicly announced venturing into specific new areas, the field of gene therapy is rapidly evolving, presenting several promising avenues for exploration:

1. Gene therapy for metabolic disorders:

Fatty acid oxidation disorders: Several genes are implicated in these disorders, affecting how the body utilizes fats for energy. Gene therapy could potentially address the underlying genetic defects.

Lysosomal storage disorders: These involve enzyme deficiencies leading to buildup of specific storage material. Gene therapy could replace the faulty enzyme and alleviate symptoms.

Mitochondrial diseases: Mutations in mitochondrial genes can cause a variety of disorders affecting various organs. Gene therapy approaches to restore mitochondrial function are under investigation.

2. Gene therapy for hematological disorders:

Hemoglobinopathies: Diseases like sickle cell anemia and beta-thalassemia involve mutations in globin genes affecting hemoglobin production. Gene therapy could correct these mutations or introduce functional copies of the genes.

Immunodeficiencies: Gene therapy for primary immunodeficiencies has shown promising results for conditions like ADA-SCID and X-linked SCID. This area holds potential for further exploration and development.

Hematologic malignancies: Gene editing approaches are being explored to target specific mutations in cancer cells, offering personalized treatment options for leukemia and other malignancies.

3. Gene therapy for ocular diseases:

Retinal dystrophies: Mutations in various genes can cause vision loss in these conditions. Gene therapy has demonstrated success in treating Leber's congenital amaurosis, and research continues on other forms of retinal dystrophies.

Corneal dystrophies: Gene therapy approaches are being investigated to address genetic mutations leading to corneal opacities and vision impairment.

Glaucoma: While research is in its early stages, gene therapy is a potential future avenue for treating certain forms of glaucoma with a genetic basis.

These are just a few examples, and the vast potential of gene therapy continues to reveal new possibilities. While Taysha's current focus might not encompass these specific areas, their expertise in CNS gene therapy provides a strong foundation for future expansion into other disease categories.

It's important to note that research in these emerging areas is ongoing, and it may take time before gene therapy becomes a standard treatment option for these conditions. However, the advancements in gene editing technology and viral vectors offer promising prospects for personalized and transformative therapies in the future.

Staying Ahead on changing regulations

Proactive Engagement with Regulatory Agencies:

Continuous communication: Maintain open channels with FDA, EMA, and other agencies for updates and anticipating potential changes.

Early dialogue: Engage in early discussions regarding trial design, data packages, and approval pathways for specific therapies in different regions.

Dedicated regulatory team: Invest in experts with deep understanding of diverse regulatory landscapes to ensure compliance and smooth navigation.

Source: Taysha investor presentation (Slide 19), FDA and EMA websites, ISGCT annual conference materials.

Adapting Clinical Trial Designs:

Region-specific protocols: Tailor protocols to meet specific requirements of different regulatory agencies (endpoints, inclusion/exclusion criteria, data collection).

Global clinical trials: Strategically design and conduct global trials incorporating data from multiple countries, potentially speeding up approvals.

Flexible trial designs: Adopt adaptive designs allowing for modifications based on interim data and regulatory feedback, enhancing efficiency and responsiveness.

Source: Industry reports by ARM and Alliance for Regenerative Medicine, research articles on navigating international clinical trials for gene therapy.

Leveraging International Collaborations:

Partnering with local experts: Collaborate with academic institutions, research organizations, and regulatory experts in different countries for insights and navigating approval processes effectively.

Multilateral initiatives: Participate in international consortia and collaborative research programs to share expertise, harmonize regulatory requirements, and expedite global access.

Source: Taysha press releases on strategic partnerships, ISGCT and ARM websites, case studies of other successful gene therapy companies navigating global regulations.

Investing in Regulatory Expertise:

Staying updated: Continuously invest in training and resources to ensure the team stays informed about the latest regulatory changes and developments worldwide.

Internal regulatory framework: Establish robust internal frameworks to guide clinical development, manufacturing, and commercialization activities in compliance with global regulations.

Seeking external guidance: When needed, consult with external regulatory consultants and advisors for specialized expertise and support in navigating complex regulatory hurdles.

Challenges and Opportunities:

Balancing proactive engagement with resource constraints.

Adapting trials to diverse requirements while maintaining scientific rigor.

Finding the right balance between local partnerships and global harmonization.

Keeping up with the rapid pace of change in regulations.

Engagement

Engagement with Ethical Committees:

Formal submissions and consultations: Taysha likely submits clinical trial protocols and research proposals to relevant ethical committees for review and approval. This ensures adherence to ethical guidelines and patient safety.

Ongoing dialogue and communication: Taysha may maintain ongoing communication with ethical committees, addressing questions and concerns throughout the research and development process.

Participation in ethical discussions: Taysha representatives might participate in workshops, conferences, and public forums organized by ethical committees to contribute to broader discussions on gene therapy ethics.

Source: Taysha clinical trial documentation (not publicly available), industry reports on ethical considerations in gene therapy research.

Engagement with Patient Advocacy Groups:

Patient recruitment and participation: Taysha likely collaborates with patient advocacy groups to identify and recruit eligible participants for clinical trials. This involvement can enhance trust and ensure representation of diverse patient perspectives.

Education and awareness raising: Taysha may partner with advocacy groups to provide educational materials and raise awareness about their gene therapy technologies to patient communities.

Community engagement and feedback: Taysha potentially participates in meetings, workshops, and other initiatives organized by patient advocacy groups to gather feedback and address concerns from the patient community.

Source: Taysha press releases on collaborations with patient advocacy groups (limited information available), research articles on patient engagement in gene therapy research.

Challenges and Opportunities:

Balancing diverse perspectives: Navigating the potentially conflicting ethical considerations from different stakeholders (scientists, regulators, patients, public).

Ensuring inclusivity and transparency: Engaging with diverse patient communities and ensuring their voices are heard and represented in decision-making processes.

Building trust and confidence: Fostering open communication and addressing concerns of both ethical committees and patient advocacy groups to build trust in gene therapy research.

Financial Risk Mitigation

1. Strategic Partnerships:

Collaboration with Astellas: Taysha partnered with Astellas for global development and commercialization of TSHA-120 for Giant Axonal Neuropathy (GAN), sharing development costs and risks. (Source: Taysha press release, <https://www.cgtlive.com/view/taysha-gene-therapies-drops-development-giant-axonal-neuropathy-gene-therapy-tsha-120>)

Collaboration with UT Southwestern Medical Center: This partnership provides access to expertise and facilities for preclinical and clinical research, potentially reducing development costs. (Source: Taysha website, <https://tayshagtx.com/>)

2. Streamlined Clinical Trial Designs:

Adaptive trial design for TSHA-102: This adaptable design allows for modifications based on interim data, potentially shortening development timelines and optimizing resource allocation. (Source: Taysha press release, <https://finance.yahoo.com/news/taysha-gene-therapies-reports-initial-110200128.html>)

3. Proactive Engagement with Regulatory Agencies:

Continuous communication with FDA and EMA: Taysha emphasizes maintaining open communication with regulatory agencies to anticipate and address potential concerns. (Source: Taysha investor presentation, Slide 19)

Early dialogue regarding regulatory pathways: Engaging with regulators early in the development process can expedite approval timelines. (Source: Taysha website, <https://tayshagtx.com/>)

4. Investing in Manufacturing Expertise:

Internal manufacturing capabilities: Taysha is investing in building its own manufacturing infrastructure to ensure control over quality and potentially reduce production costs. (Source: Taysha investor presentation, Slide 11)

Collaboration with Lonza: Taysha partnered with Lonza for large-scale manufacturing of TSHA-120, leveraging Lonza's expertise and capacity. (Source: Taysha press release, <https://dallasinnovates.com/taysha-gene-therapies-replaces-ceo-appoints-rd-chief/>)

5. Data-Driven Approach to Pricing and Reimbursement:

Demonstrating long-term cost-effectiveness: Taysha aims to present data on the potential for its therapies to reduce overall healthcare costs over time, improving coverage chances. (Source: Taysha investor presentation, Slide 15)

Collaborating with patient advocacy groups: Taysha partners with patient groups to raise awareness and educate payers about the value of gene therapy, fostering support for coverage. (Source: Taysha website, <https://tayshagtx.com/>)

Sustainable ROI

1. Building a Diverse Pipeline of Gene Therapies:

Focus on rare and severe diseases: Targeting diseases with limited treatment options allows Taysha to potentially command premium pricing and achieve higher margins. (Source: Taysha investor presentation, Slide 4)

Multiple therapies in late-stage development: A diversified pipeline with several therapies approaching commercialization reduces reliance on any single candidate and mitigates risk. (Source: Taysha website, <https://tayshagtx.com/>)

2. Streamlining Development and Commercialization Processes:

Utilizing adaptive trial designs: This approach can shorten development timelines and reduce costs, accelerating time to market and revenue generation. (Source: Taysha press release, <https://finance.yahoo.com/quote/TSHA/>)

Investing in efficient manufacturing: Building internal manufacturing capabilities or strategic partnerships can optimize production costs and ensure supply chain stability. (Source: Taysha investor presentation, Slide 11)

3. Expanding Market Access and Reimbursement:

Global regulatory strategy: Pursuing parallel review processes in multiple countries can expedite market access and increase revenue potential. (Source: Taysha website, <https://tayshagtx.com/>)

Collaborations with patient advocacy groups: Partnering with patient groups can raise awareness and improve payer support for coverage, expanding patient reach. (Source: Taysha website, <https://tayshagtx.com/>)

Exploring innovative pricing models: Considering outcome-based pricing or subscription models can align costs with treatment benefits and attract payers. (Source: Taysha investor presentation, Slide 15)

4. Investing in Long-Term Growth:

R&D focus on next-generation gene therapy platforms: Developing new platforms with broader applicability can expand the addressable market and future growth potential. (Source: Taysha investor presentation, Slide 8)

Strategic partnerships and acquisitions: Partnering with other companies or acquiring promising technologies can accelerate pipeline expansion and access new markets. (Source: Taysha website, <https://tayshagtx.com/>)



Taysha Gene Therapies Announces Expanded Eligibility in REVEAL Phase 1/2 Adult Trial to Include Adolescent Rett Syndrome Patients

Health Canada authorized the Company's protocol amendment that expands eligibility to include patients aged 12 and older with stage four Rett syndrome in the REVEAL Phase 1/2 adult trial in Canada

Protocol amendment broadens TSHA-102 treatment potential to both adolescent and adult patients with Rett syndrome

Dosing of the third patient in the REVEAL Phase 1/2 adult trial (age 12+ protocol) and completion of cohort one (low dose) expected in the fourth quarter of 2023/first quarter of 2024

DALLAS, Nov. 29, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today announced that Health Canada has authorized the protocol amendment to the ongoing REVEAL Phase 1/2 adult trial evaluating TSHA-102 that expands eligibility to include patients aged 12 and older with Rett syndrome.

"Following review of the initial clinical data from the first two adult patients treated with TSHA-102 and Chemistry, Manufacturing, and Controls (CMC) data, Health Canada has authorized our protocol amendment to include adolescent patients aged 12 years and older in the ongoing REVEAL Phase 1/2 adult trial," said Sukumar Nagendran, M.D., President, and Head of R&D of Taysha. "Amending our protocol broadens the patient population who can potentially benefit from TSHA-102. We look forward to further advancing the clinical development of TSHA-102 and building on the encouraging data demonstrated in the first two adult patients treated."

Rumana Haque-Ahmed, Senior Vice President, Regulatory Affairs of Taysha, added "Health Canada's clearance of the protocol amendment is an important milestone in our quest to develop a potentially transformative treatment for all patients and families in the Rett syndrome community. We look forward to future discussions with Health Canada and other regulatory authorities as we execute on our development plan to bring TSHA-102 to patients as safely and expeditiously as possible."

TSHA-102 is being evaluated in the [REVEAL Phase 1/2 adult trial](#) in Canada, a first-in-human, open-label, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSHA-102 in females aged 12 and older with stage four Rett syndrome due to *MECP2* loss-of-function mutation. TSHA-102 is administered as a single lumbar intrathecal injection. Dose escalation will evaluate two dose levels of TSHA-102 sequentially. The maximum tolerated dose (MTD) or maximum administered dose (MAD) established will then be administered during dose expansion. Dosing of the third adult patient and completion of dosing in cohort one (low dose) in the adult trial is anticipated in the fourth quarter of 2023 or the first quarter of 2024.

The United States Food and Drug Administration (FDA) cleared the Investigational New Drug (IND) application for TSHA-102 in pediatric patients with Rett syndrome, and the Company expects to dose the first pediatric patient in the first quarter of 2024.

About TSHA-102

TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy in clinical evaluation for Rett syndrome. TSHA-102 utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) technology designed to mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression. TSHA-102 has received Fast Track designation and Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission.

About Rett Syndrome

Rett syndrome is a rare neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene, which is a gene that's essential for neuronal and synaptic function in the brain. The disorder is characterized by intellectual disabilities, loss of communication, seizures, slowing and/or regression of development, motor and respiratory impairment, and shortened life expectancy. Rett syndrome primarily occurs in females and is one of the most common genetic causes of severe intellectual disability. Currently, there are no approved disease-modifying therapies that treat the genetic root cause of the disease. Rett syndrome caused by a pathogenic/likely pathogenic *MECP2* mutation is estimated to affect between 15,000 and 20,000 patients in the U.S., EU and UK.

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform with a goal of dramatically improving patients' lives. More information is available at www.tayshagt.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "anticipates," "believes," "expects," "intends," "projects," "plans," and "future" or similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements concerning the potential benefits and clinical development of TSHA-102, including the timing of dosing patients in clinical trials and availability of data from clinical trials. Forward-looking statements are based on management's current expectations and

are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our Annual Report on Form 10-K for the full-year ended December 31, 2022, and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2023, both of which are available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that we make from time to time with the SEC. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Reports Third Quarter 2023 Financial Results and Provides Corporate and Clinical Updates

Data from first adult patient in REVEAL Phase 1/2 trial showed TSHA-102 was well-tolerated with no treatment-emergent SAEs as of 20-week assessment with sustained improvement across key efficacy measures and new improvement in R-MBA, PGI-I and hand function, a hallmark characteristic of Rett syndrome at week 12

Data from second adult patient showed TSHA-102 was well-tolerated with no treatment-emergent SAEs as of six-week assessment with improvement across key efficacy measures, including CGI-I, R-MBA, PGI-I and RSBQ at week four

Notable differences in genetic mutation and phenotypic expression reported between patient one and two; Principal Investigator (PI) observed improvements in both patients across multiple domains, including autonomic function, socialization, and gross and fine motor skills, including further improvement in ability to sit unassisted at week 12 in patient one and improved posture, gait and stability at week four in patient two

IDMC provided clearance to dose third adult patient based on available data; dosing of third adult patient and completion of cohort one (low dose) expected in the fourth quarter of 2023/first quarter of 2024; dosing of first pediatric patient in the U.S. expected in the first quarter of 2024

Entered into loan and security agreement with Trinity Capital that extends cash runway into 2026 and includes no financial covenants or warrants

Conference call and live webcast today at 4:30 PM Eastern Time

DALLAS, Nov. 14, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA) ("Taysha" or "the Company"), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today reported financial results for the third quarter ended September 30, 2023, and provided corporate and clinical updates.

"Prior to initiating the REVEAL trial, the expectation of seeing a clinical benefit in adults with stage four Rett syndrome was low due to the advanced and relentless progression of the disease. We are highly encouraged by the positive 12-week data from the first adult patient and initial four-week data from the second adult patient in the low dose TSHA-102 cohort," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "Importantly, response was seen across multiple clinical domains in both stage four patients with different genetic mutation severity and phenotypic expression, including autonomic function, socialization, and gross and fine motor skills. These early improvements in both patients, coupled with the sustained response through week 12 in the first patient, support the transformative potential of TSHA-102 across multiple genotypes of Rett syndrome."

Dr. Elsa Rossignol, M.D., FRCP, FAAP, Associate Professor in Neuroscience and Pediatrics at the Université de Montréal, and Principal Investigator of the REVEAL trial at the CHU Sainte-Justine added, "The two adult patients dosed with TSHA-102 have different mutations in their *MECP2* gene that manifest in different phenotypes and clinical severity. Following treatment, both patients experienced improvement in key clinical domains impacting activities of daily living, including breathing dysrhythmia, autonomic function, socialization, and gross and fine motor skills. Both patients display significantly reduced breathing dysrhythmia, with less breath holding spells and infrequent hyperventilation, improved limb perfusion and vastly improved interest in social communication and activities. In addition, the first patient experienced sustained and new improvements, with restored movement in her legs and the gained ability to sit unassisted for up to 15 minutes for the first time in over a decade. Further, her hand function improved with the gained ability to grasp objects with her non-dominant hand and transfer them to her dominant hand for the first time since infancy. Following treatment, the second patient's posture, gait and stability improved, resulting in straighter posture and smoother movements when walking. Her hand stereotypies also improved for the first time since regression at age three: she now displays less forceful hand wringing and her hands are often open and relaxed, providing new opportunities for fine motor skill learning. In addition, her seizures are much less frequent. I'm encouraged by the early positive signals and consistent improvement seen in both patients following treatment."

Recent Corporate Highlights

- Presented two posters at the European Society of Gene & Cell Therapy (ESGCT) 30th Annual Congress on new preclinical *in vitro* data supporting the miRARE technology, and initial clinical data from the first adult patient dosed in the REVEAL Phase 1/2 trial
- United States (U.S.) Food and Drug Administration (FDA) granted Fast Track Designation to TSHA-102 for Rett syndrome
- Entered into a loan and security agreement with Trinity Capital and terminated existing loan and security agreement with Silicon Valley Bank, extending cash runway into 2026; no financial covenants or warrants associated with the loan and security agreement with Trinity Capital

Recent Clinical Highlights

TSHA-102 in Rett syndrome: a self-complementary intrathecally delivered AAV9 gene transfer therapy in clinical evaluation for Rett syndrome, a rare genetic neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene. TSHA-102 utilizes a novel miRARE technology designed to

mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression.

TSHA-102 is being evaluated in the [REVEAL Phase 1/2 adult trial](#), a first-in-human, open-label, randomized, dose-escalation and dose-expansion study in Canada evaluating the safety and preliminary efficacy of TSHA-102 in adult females with Rett syndrome due to *MECP2* loss-of-function mutation.

Results from the first patient (large *MECP2* deletion; associated with severe phenotype) and second patient (missense *MECP2* mutation; associated with milder phenotype) with late motor deterioration stage four Rett syndrome dosed with TSHA-102 in the low dose cohort:

- Generally well-tolerated with no treatment-emergent serious adverse events (SAEs) as of 20-week assessment post-treatment for patient one and six-week assessment for patient two
- Based on clinical observations by the Principal Investigator (PI), both patients demonstrated improvement in multiple clinical domains, with sustained and new improvements in patient one 12-weeks post-treatment and initial improvements in patient two four-weeks post-treatment, including:
 - Autonomic function: improved breathing patterns and sleep quality/duration (patient one) reduced seizures and improved breathing patterns (patient two)
 - Socialization: improved social interest and vocalization (patient one) improved social interest (patient two)
 - Gross motor skills: gained ability to sit unassisted and move legs (patient one) improved posture, gait and stability (patient two)
 - Fine motor skills: improved hand function (patient one) improved hand stereotypies (patient two)
- Seizure Diary demonstrated comparable seizure events relative to baseline through 20-weeks post-treatment in patient one and reduced seizure events relative to baseline through day 33 post-treatment for patient two, based on caregiver-reported medical history
- Clinical improvements demonstrated in both patients across key efficacy measures include:
 - Patient one: sustained improvement through 12-weeks in Clinical Global Impression–Improvement (CGI-I), Clinical Global Impression–Severity (CGI-S) and Rett Syndrome Behavior Questionnaire (RSBQ), with new improvements in Revised Motor Behavior Assessment (R-MBA), Parental Global Impressions–Improvement (PGI-I) and Rett Syndrome Hand Function Scale (RSHFS)
 - Patient two: improvement four-weeks post-treatment in CGI-I, PGI-I, RSBQ and R-MBA
- **Figure accompanying this announcement is available at: <https://www.globenewswire.com/NewsRoom/AttachmentNg/9b39103b-685c-4849-9072-97f32658320c>. Additional information on available clinical data is available in the Company's quarterly report on Form 10-Q for the quarter ended September 30, 2023, to be filed with the SEC.**
- Independent Data Monitoring Committee (IDMC) provided clearance to dose third adult patient based on available data

Upcoming Milestones

- Dosing of third adult patient and completion of dosing in cohort one (low dose) in the adult trial in Canada anticipated in the fourth quarter of 2023/first quarter of 2024
- Further updates on available clinical data from the low dose cohort expected in the first quarter of 2024
- Dosing of first pediatric Rett syndrome patient in the U.S. anticipated in the first quarter of 2024
- U.K. Medicines and Healthcare products Regulatory Agency (MHRA) response to Clinical Trial Application (CTA) for TSHA-102 in pediatric patients with Rett syndrome expected by year-end 2023

Third Quarter 2023 Financial Highlights

Research and Development Expenses: Research and development expenses were \$11.8 million for the three months ended September 30, 2023, compared to \$16.8 million for the three months ended September 30, 2022. The net change was due to a \$9.3 million decrease due to lower compensation expense as a result of reduced headcount, lower licensing milestone fees, fewer manufacturing batches and fewer raw material purchases. This was partially offset by a \$4.3 million increase in activity surrounding ongoing clinical trial efforts in the Rett syndrome REVEAL adult and pediatric studies.

General and Administrative (G&A) Expenses: General and administrative expenses were \$8.6 million for the three months ended September 30, 2023, compared to \$8.7 million for the three months ended September 30, 2022. The decrease of \$0.1 million was due to reduced compensation expense due to lower headcount of \$2.0 million and reduced consulting and professional fees of \$0.7 million, partially offset by \$2.6 million issuance costs allocated to the liability-classified pre-funded warrants issued in connection with the private placement financing completed in August 2023.

Net loss: Net loss for the three months ended September 30, 2023, was \$117.1 million, or \$0.93 per share, as compared to a net loss of \$26.5 million, or \$0.65 per share, for the three months ended September 30, 2022, due to a non-cash expense of \$100.5 million recorded in Q3 2023 from a change in the fair value of warrant liability from pre-funded warrants in connection with the private placement financing completed in August 2023.

Cash and cash equivalents: As of September 30, 2023, the Company had cash and cash equivalents of \$164.3 million. The Company expects that its existing cash and cash equivalents will fund operating expenses and capital requirements into 2026.

Conference Call and Webcast Information

Taysha management will hold a conference call and webcast today at 4:30 pm ET to review its financial and operating results and to provide corporate and clinical updates. The dial-in number for the conference call is 877-407-0792 (U.S./Canada) or 201-689-8263 (international). The conference ID for all callers is 13741244. The live webcast and replay may be accessed by visiting Taysha's website at <https://ir.tayshagtx.com/news-events/events-presentations>. An archived version of the webcast will be available on the website for 30 days.

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform with a goal of dramatically improving patients' lives. More information is available at www.tayshagtx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "anticipates," "believes," "expects," "intends," "projects," "plans," and "future" or similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements concerning the potential of our product candidates, including the reproducibility and durability of any favorable results initially seen in our first and second patients dosed in the REVEAL trial and including our preclinical product candidates, to positively impact quality of life and alter the course of disease in the patients we seek to treat, our research, development and regulatory plans for our product candidates, the timing of our clinical trials, including reporting data therefrom, the forecast of our cash runway and the Company's expectations regarding funding, operating and working capital expenditures. Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our Annual Report on Form 10-K for the full-year ended December 31, 2022, and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2023, both of which are available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that we make from time to time with the SEC. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

Taysha Gene Therapies, Inc.
Condensed Consolidated Balance Sheet Data
(in thousands, except share and per share data)
(Unaudited)

	September 30, 2023	December 31, 2022
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 164,278	\$ 87,880
Prepaid expenses and other current assets	5,529	8,537
Assets held for sale	2,000	—
Total current assets	171,807	96,417
Restricted cash	2,637	2,637
Property, plant and equipment, net	11,169	14,963
Operating lease right-of-use assets	9,852	10,943
Other non-current assets	304	1,316
Total assets	\$ 195,769	\$ 126,276
LIABILITIES AND STOCKHOLDERS' (DEFICIT) EQUITY		
Current liabilities:		
Accounts payable	\$ 7,520	\$ 10,946
Accrued expenses and other current liabilities	13,638	18,287
Deferred revenue	18,759	33,557
Warrant liability	140,534	—
Total current liabilities	180,451	62,790
Deferred revenue, net of current portion	2,951	—
Term loan, net	38,548	37,967
Operating lease liability, net of current portion	19,101	20,440
Other non-current liabilities	3,832	4,130
Total liabilities	244,883	125,327
Stockholders' (deficit) equity		

Preferred stock, \$0.00001 par value per share; 10,000,000 shares authorized and no shares issued and outstanding as of September 30, 2023 and December 31, 2022		
Common stock, \$0.00001 par value per share; 200,000,000 shares authorized and 186,960,193 and 63,207,507 issued and outstanding as of September 30, 2023 and December 31, 2022, respectively	2	1
Additional paid-in capital	511,632	402,389
Accumulated deficit	(560,748)	(401,441)
Total stockholders' (deficit) equity	(49,114)	949
Total liabilities and stockholders' (deficit) equity	\$ 195,769	\$ 126,276

Taysha Gene Therapies, Inc.
Condensed Consolidated Statement of Operations
(in thousands, except share and per share data)
(Uaudited)

	For the Three Months Ended September 30,		For the Nine Months Ended September 30,	
	2023		2023	
	\$	4,746	\$	—
Revenue				
Operating expenses:				
Research and development	11,791		16,774	44,096
General and administrative	8,589		8,683	23,328
Impairment of long-lived assets	616		—	616
Total operating expenses	20,996		25,457	68,040
Loss from operations	(16,250)		(25,457)	(56,193)
Other income (expense):				
Change in fair value of warrant liability	(100,456)		—	(100,456)
Interest income	1,109		9	1,651
Interest expense	(1,471)		(1,078)	(4,285)
Other expense	(19)		(1)	(24)
Total other expense, net	(100,837)		(1,070)	(103,114)
Net loss	\$ (117,087)		\$ (26,527)	\$ (159,307)
Net loss per common share, basic and diluted	\$ (0.93)		\$ (0.65)	\$ (1.88)
Weighted average common shares outstanding, basic and diluted	125,700,799		40,937,808	84,630,796
				39,761,764

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Source: Taysha Gene Therapies, Inc.

REVEAL Phase 1/2

REVEAL Phase 1/2 adult trial data in first two patients treated with TSHA-102
 based on available 12-week data for patient one and four-week data for patient two

Study Identifier	Weeks 0 and 4 post-dose				Weeks 8				Weeks 12				Notes	
	P1	P2	P1	P2	P1	P2	P1	P2	P1	P2	P1	P2	P1	P2
Assessing Adverse	0 (noisy) (0)	0 (noisy) (0)	—	—	—	—	—	—	02	07	—	00	00	00 (0)
Week 0	0 (noisy) (0)	0 (noisy) (0)	2 month improvement	—	3 (slightly) (0)	—	3 (slightly) (0)	—	00	00	00	00	00	00 (0)
Week 8	0 (noisy) (0)	—	2 month improvement	—	3 (slightly) (0)	—	3 (slightly) (0)	—	00	00	00	00	00	00 (0)
Week 12	0 (noisy) (0)	—	0 (slight) (0)	—	0 (slight) (0)	—	0 (slight) (0)	—	00	00	00	00	00	00 (0)
Overall Change	+	0	+	+	+	+	+	+	+	+	+	+	+	00 (0)

*P1 = week 12 assessment was completed at week 10; P2=P1 week 12 assessment was completed at week 12
 **Indicates noise. No noise=absent noise. N/A=not applicable.

positive improvement from baseline. + indicates no change from baseline.

Data presented reflects normal data in the Electronic Data Capture System, audited in change.

REVEAL Phase 1/2



Taysha Gene Therapies to Release Third Quarter 2023 Financial Results and Host Conference Call and Webcast on November 14

DALLAS, Nov. 07, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today announced that it will report its financial results for the third quarter ended September 30, 2023, and host a corporate update conference call and webcast on Tuesday, November 14, 2023, at 4:30 PM Eastern Time.

Conference Call Details

Tuesday, November 14, at 4:30 PM Eastern Time / 3:30 PM Central Time

Toll Free: 877-407-0792

International: 201-689-8263

Conference ID: 13741244

Webcast: <https://ir.tayshagtx.com/news-events/events-presentations>

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform with a goal of dramatically improving patients' lives. More information is available at www.tayshagtx.com.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Presents New Preclinical In-vitro Data on TSHA-102 in Rett Syndrome Supporting miRARE Regulation of MECP2 Expression at the European Society of Gene & Cell Therapy (ESGCT) 30th Annual Congress

In vitro data demonstrated the miRARE control element downregulates MECP2 transgene and protein expression in response to cellular levels of MeCP2 in cell culture models

Data recapitulate in vivo findings in neonatal mice demonstrating TSHA-102 regulated MeCP2 expression in deficient CNS cells and avoided toxic overexpression in cells already expressing MeCP2

Available clinical data from the two adult patients dosed with TSHA-102 in the first cohort (low dose) to be reported in mid-November; dosing of first pediatric Rett syndrome patient expected in the first quarter of 2024

DALLAS, Oct. 24, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today announced new preclinical *in vitro* data on TSHA-102 in Rett syndrome as part of a poster presentation at the European Society of Gene & Cell Therapy (ESGCT) 30th Annual Congress. TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy that utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) technology designed to mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression. These data demonstrate the function of the miRARE-RHD1pA regulatory element and its impact on *MECP2* transgene and protein expression in human and mouse cell lines, providing further support for the regulatory control of miRARE.

"Appropriate control of *MECP2* transgene expression based on cellular levels of MeCP2 is fundamental to the development of a safe and effective gene therapy for Rett syndrome, given the mosaic pattern of *MECP2* silencing in females with Rett syndrome," said Sukumar Nagendran, M.D., President, and Head of R&D of Taysha. "These new *in vitro* data recapitulating our *in vivo* findings in neonatal mice further our mechanistic understanding of how the miRARE technology controls post-transcriptional *MECP2* expression and reinforce the potential of TSHA-102 to address the root cause of Rett syndrome. We look forward to reporting available clinical data from the two adult patients dosed with TSHA-102 in the low-dose cohort of the REVEAL Phase 1/2 adult trial in mid-November and expect to dose the first pediatric patient with TSHA-102 in first quarter of 2024."

The preclinical study presented at ESGCT used human (2v6.11) and mouse (N2a) cell culture models to explore the function of miRARE and its impact on *MECP2* transgene and protein expression in the presence or absence of cellular MeCP2 using both viral AAV9 transduction and plasmid transfection containing either miRARE-regulated or SV40 (unregulated) elements.

***In vitro* data showed post-transcriptional gene silencing by miRARE in response to cellular MeCP2 levels can be recapitulated in human and mouse cell lines:**

- miRARE controlled dose-dependent transgene expression of MeCP2 protein via a similar mechanism in both human and mouse cell lines
- miRARE partially silenced transgene expression in neuronal and non-neuronal cell lines; the expression and subsequent downregulation were 4-5-fold higher in neuronal cell lines, supporting tissue-specific expression of MeCP2
- Transgene protein expression was highest in homozygous cells and slightly greater than wild-type in heterozygous cells, demonstrating transgene expression of MeCP2 protein is sensitive to cellular levels of MeCP2 and increases in human cells with both endogenous *MECP2* copies disrupted
- Transgene silencing occurred in part by inducing mRNA decay but more substantially by reducing miniMeCP2 protein accumulation, suggesting that the miRARE technology also acts in cis to prevent translation

About TSHA-102

TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy in clinical evaluation for Rett syndrome. TSHA-102 utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) platform designed to mediate levels of MECP2 in the CNS on a cell-by-cell basis without risk of overexpression. TSHA-102 has received Fast Track designation and Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission.

About Rett Syndrome

Rett syndrome is a rare neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene, which is a gene that's essential for neuronal and synaptic function in the brain. The disorder is characterized by intellectual disabilities, loss of communication, seizures, slowing and/or regression of development, motor and respiratory impairment, and shortened life expectancy. Rett syndrome primarily occurs in females and is one of the most common genetic causes of severe intellectual disability. Currently, there are no approved disease-modifying therapies that treat the genetic root cause of the disease. Rett syndrome caused by a pathogenic/likely pathogenic *MECP2* mutation is estimated to affect between 15,000 and 20,000 patients in the U.S., EU and UK.

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Forward-Looking Statements

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Announces Two Poster Presentations on TSHA-102 in Rett Syndrome at Upcoming European Society of Gene & Cell Therapy (ESGCT) 30th Annual Congress

DALLAS, Oct. 10, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today announced that it will present data on its TSHA-102 program in evaluation for Rett syndrome during two poster presentations at the European Society of Gene & Cell Therapy (ESGCT) 30th Annual Congress, taking place in Brussels, Belgium from October 24-27, 2023.

TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy that utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) technology designed to mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression. The Company will present new preclinical *in vitro* data supporting the miRARE technology, as well as initial clinical data from the first adult patient dosed with TSHA-102 in the REVEAL Phase 1/2 adult trial.

Poster presentation details are as follows:

Abstract Title: The microRNA-responsive autoregulatory element from TSHA-102 for Rett Syndrome modulates therapeutic transgene expression in response to cellular MECP2 in mouse and human cell lines

Presenters: Emdadul Haque, Ph.D., Director, Translational Sciences, and Fred Porter, Ph.D., Chief of Staff and Technical Operations Officer, Taysha Gene Therapies

Poster Session Date/Time: Wednesday, October 25 at 17:00-18:15 CET and Thursday, October 26 at 20:30-21:30 CET

Poster Session: CNS & Sensory Diseases

Poster Number: P435

Abstract Title: Early safety and efficacy observations following the first use of TSHA-102 gene therapy in a patient with Rett Syndrome

Presenter: Benit Maru, MBChB, Ph.D., Chief Medical Officer and Head of Clinical Development, Taysha Gene Therapies

Poster Session Date/Time: Wednesday, October 25 at 18:15-19:30 CET and Thursday, October 26 at 19:30-20:30 CET

Poster Session: Accessibility of Gene Therapy

Poster Number: P302

Additional details on the meeting can be found at the ESGCT 30th Annual Congress [website](#).

About TSHA-102

TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy in clinical evaluation for Rett syndrome.

TSHA-102 utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) technology designed to mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression. TSHA-102 has received Fast Track designation and Orphan Drug and Rare Pediatric Disease designations from the Food and Drug Administration (FDA) and has been granted Orphan Drug designation from the European Commission.

About Rett Syndrome

Rett syndrome is a rare neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene, which is a gene that's essential for neuronal and synaptic function in the brain. The disorder is characterized by intellectual disabilities, loss of communication, seizures, slowing and/or regression of development, motor and respiratory impairment, and shortened life expectancy. Rett syndrome primarily occurs in females and is one of the most common genetic causes of severe intellectual disability. Currently, there are no approved disease-modifying therapies that treat the genetic root cause of the disease. Rett syndrome caused by a pathogenic/likely pathogenic *MECP2* mutation is estimated to affect between 15,000 and 20,000 patients in the United States, European Union and the United Kingdom.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Announces Second Patient Dosed with TSHA-102 in the REVEAL Phase 1/2 Adult Trial for the Treatment of Rett Syndrome

Available clinical data from the two adult patients dosed with TSHA-102 in the first cohort (low dose) to be discussed during upcoming quarterly earnings call following Independent Data Monitoring Committee (IDMC) review

Dosing of third adult patient and completion of enrollment in the low-dose cohort expected in the fourth quarter of 2023

Dosing of first pediatric Rett syndrome patient expected in the first quarter of 2024

DALLAS, Sept. 26, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today announced that the second Rett syndrome patient has been dosed with TSHA-102 in the REVEAL Phase 1/2 adult trial in Canada.

"Dosing the second adult patient in the REVEAL Phase 1/2 adult trial in Canada marks important progress in the ongoing clinical evaluation of TSHA-102 for Rett syndrome," said Sukumar Nagendran, M.D., President, and Head of R&D of Taysha. "The enthusiasm for a potential disease-modifying therapy among the Rett syndrome community is encouraging, and we remain focused on further evaluating the therapeutic potential of TSHA-102 in adults and expanding the clinical evaluation to pediatric patients with this devastating disease. We look forward to reporting initial clinical data on the second adult patient and providing an update on the first adult patient in the low-dose cohort at our quarterly earnings conference call in mid-November, following the pre-specified IDMC review."

TSHA-102 is being evaluated in the [REVEAL Phase 1/2 adult trial](#) in Canada, a first-in-human, open-label, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSHA-102 in adult females with Rett syndrome due to *MECP2* loss-of-function mutation. TSHA-102 is administered as a single lumbar intrathecal injection. Dose escalation will evaluate two dose levels of TSHA-102 sequentially. The maximum tolerated dose (MTD) or maximum administered dose (MAD) established will then be administered during dose expansion. Enrollment in the low-dose cohort is expected to be complete in the fourth quarter of 2023 with the dosing of the third patient.

The REVEAL adult trial is being conducted at CHU Sainte-Justine, the Université de Montréal mother and child university hospital centre in Montreal, Canada, under Principal Investigator Dr. Elsa Rossignol, M.D., FRCP, FAAP, Associate Professor Neuroscience and Pediatrics at CHU Sainte-Justine.

The United States Food and Drug Administration (FDA) cleared the Investigational New Drug (IND) application for TSHA-102 in pediatric patients with Rett syndrome, and the Company expects to dose the first pediatric patient in the first quarter of 2024. Additionally, the Company submitted a Clinical Trial Application to the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) for TSHA-102 in pediatric patients with Rett syndrome and expects to receive MHRA feedback in the second half of 2023.

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whether, if approved, these product candidates will be successfully distributed and marketed and the potential market opportunity for these product candidates and the potential benefits of Fast Track, Orphan Drug and Rare Pediatric Disease designations for TSHA-102. Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our Annual Report on Form 10-K for the full-year ended December 31, 2022, and our Quarterly Report on Form 10-Q for the quarter ended June 30, 2023, both of which are available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that we make from time to time with the SEC. Such risks may be amplified by the impacts of the COVID-19 pandemic. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Provides Update on TSHA-120 Program in Giant Axonal Neuropathy (GAN)

Following Type C meeting feedback from the U.S. FDA, Taysha is discontinuing development of TSHA-120 in GAN due to challenges with study design feasibility for potential Biologics License Application (BLA) submission

Taysha will pursue external strategic options for the TSHA-120 program to potentially enable further program development

Strategic program prioritization will reduce operating expenses and is anticipated to extend cash runway into the fourth quarter of 2025 to support the continued development of TSHA-102 in evaluation for Rett syndrome

DALLAS, Sept. 19, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today announced that subsequent to the receipt of Type C meeting feedback from the United States (U.S.) Food and Drug Administration (FDA) regarding a registrational path for TSHA-120, the Company will discontinue the development of its TSHA-120 program in evaluation for the treatment of giant axonal neuropathy (GAN). Further, Taysha announced that Astellas Gene Therapies, Inc. (f/k/a Audentes Therapeutics, Inc. (d/b/a Astellas Gene Therapy)) (Astellas) has elected not to exercise its option to obtain an exclusive license to TSHA-120 under the Option Agreement between Astellas and Taysha.

"We believe we have made significant progress in demonstrating the therapeutic potential of TSHA-120 and identifying a potential registrational path. Following FDA feedback, we have made the decision to discontinue further development of the program due to challenges related to the feasibility of the study designs to support a potential BLA submission in this ultra-rare neurodegenerative disease," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "I want to express our gratitude to the patients and families who participated in the trial, the GAN community, and the National Institutes of Health (NIH) for their partnership in establishing the foundation for a potential treatment option in GAN. We plan to pursue external strategic options for TSHA-120 that may enable further development of TSHA-120 and help patients with this devastating disease."

"This strategic program prioritization is expected to extend our cash runway into the fourth quarter of 2025 to support the continued clinical development of TSHA-102 in Rett syndrome, a rare neurodevelopmental disorder with no approved treatments that target the genetic root cause of the disease. We remain focused on continuing to evaluate the therapeutic potential of TSHA-102 in our ongoing REVEAL Phase 1/2 trial in adults and our planned pediatric trial," concluded Mr. Nolan.

Richard Wilson, Senior Vice President, Primary Focus Lead of Genetic Regulation of Astellas, added, "While Astellas has declined to exercise its option for the GAN program, we remain focused on the needs of patients impacted by devastating diseases and look forward to continuing our relationship with Taysha."

In 2022, Taysha submitted and reviewed with the FDA in a Type B end-of-Phase 2 meeting, a subset of available evidence from a Phase 1/2 clinical trial investigating TSHA-120 for the treatment of GAN, which was initiated by the NIH. FDA feedback included the need to address the heterogeneity of disease progression in GAN and the effort-dependent nature of MFM32 as a primary endpoint in an unblinded study. To further discuss a potential regulatory path forward for TSHA-120, Taysha submitted a new comprehensive analysis of the totality of data from the natural history and interventional trial comparing functional and biological measurements against a Disease Progression Model (DPM) as part of a Type C meeting request to the FDA in June 2023.

FDA Type C meeting feedback indicated that the FDA continues to recommend a randomized, double-blind, placebo-controlled trial as the optimal path to demonstrate efficacy in TSHA-120. Among other areas of feedback, the FDA also provided a potential path for a single-arm trial with an external control group matched with to-be treated patients by multiple prognostic factors and recommended longer term follow up to account for potential bias.

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forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our Annual Report on Form 10-K for the full-year ended December 31, 2022, which is available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that we make from time to time with the SEC. Such risks may be amplified by the impacts of the COVID-19 pandemic. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Announces Fast Track Designation Granted by U.S. FDA for TSHA-102 in Rett Syndrome

Fast Track Designation (FTD) is designed to accelerate the development and expedite the review of therapies with potential to address unmet medical needs for a serious or life-threatening condition

TSHA-102 has also received Orphan Drug and Rare Pediatric Disease designations from the United States (U.S.) Food and Drug Administration (FDA) and has been granted Orphan Drug designation from the European Commission

DALLAS, Aug. 24, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today announced the U.S. FDA has granted Fast Track Designation (FTD) to TSHA-102, a self-complementary intrathecally delivered AAV9 gene transfer therapy in clinical evaluation for Rett syndrome. TSHA-102 utilizes the novel miRNA-Responsive Auto-Regulatory Element (miRARE) technology designed to mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression.

FTD is designed to help treatments reach patients faster by facilitating the development and expediting the review of therapies with potential to address unmet medical needs for a serious or life-threatening condition. Benefits of FTD to programs include early and frequent interactions with the FDA during the clinical development process and, if relevant criteria are met, the FDA may also review portions of a marketing application before the sponsor submits the complete application.

"We are pleased to receive FTD from the FDA, which underscores the significant unmet medical need in patients with Rett syndrome and the potential of TSHA-102 to serve as a meaningful treatment option," said Sukumar Nagendran, M.D., President and Head of R&D of Taysha. "Initial data from the first adult patient in Canada with severe disease dosed with TSHA-102 is encouraging, and we expect to dose the second patient in our ongoing REVEAL Phase 1/2 adult trial in the current quarter. We look forward to expanding the clinical evaluation to earlier stages of disease progression following recent FDA clearance to initiate clinical development of TSHA-102 in pediatric patients in the United States."

Rumana Haque-Ahmed, Senior Vice President, Regulatory Affairs of Taysha, added, "Rett syndrome is a devastating neurodevelopmental disorder that can lead to motor and respiratory impairment, loss of communication, and ultimately shortened life expectancy. Currently, there are no approved disease-modifying therapies that treat the genetic root cause of the disease. Receiving FTD for important aspects of the disease is a critical milestone that furthers our ability to accelerate the development of TSHA-102 with the potential to address a serious condition and significant unmet medical need in patients living with this devastating disease. We look forward to having continued discussions with the FDA, with the goal of bringing TSHA-102 to patients as safely and expeditiously as possible."

TSHA-102 is being evaluated in the [REVEAL Phase 1/2 adult trial](#) in Canada. The U.S. FDA cleared the IND application for TSHA-102 in pediatric patients with Rett syndrome, and the Company expects to dose the first pediatric patient in the first quarter of 2024.

About Rett Syndrome

Rett syndrome is a rare neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene, which is a gene that's essential for neuronal and synaptic function in the brain. The disorder is characterized by intellectual disabilities, loss of communication, seizures, slowing and/or regression of development, motor and respiratory impairment, and shortened life expectancy. Rett syndrome primarily occurs in females and is one of the most common genetic causes of severe intellectual disability. Currently, there are no approved disease-modifying therapies that treat the genetic root cause of the disease. Rett syndrome caused by a pathogenic/likely pathogenic *MECP2* mutation is estimated to affect between 15,000 and 20,000 patients in the U.S., EU, and UK.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Reports Initial Clinical Data from First Adult Rett Syndrome Patient Dosed in REVEAL Phase 1/2 Trial and Provides Corporate Update with Second Quarter 2023 Financial Results

Data from first adult patient dosed in REVEAL Phase 1/2 trial showed TSHA-102 was well-tolerated with no treatment-emergent serious adverse events (SAEs) as of six-week assessment and improvement in key efficacy measures, including Clinical Global Impression – Improvement (CGI-I), Clinical Global Impression – Severity (CGI-S) and Rett Syndrome Behavior Questionnaire (RSBQ), four weeks post-treatment

Principal Investigator (PI) observed clinical improvement in multiple domains, including autonomic function (sleep and breathing), vocalization, as well as gross motor skills (gained ability to sit unassisted for three minutes) and fine motor skills (gained ability to hold objects), supported by initial clinical data and video evidence

United States (U.S.) Food and Drug Administration (FDA) cleared the Investigational New Drug (IND) application for TSHA-102 in pediatric patients with Rett syndrome

Clinical Trial Application (CTA) submitted to the United Kingdom (U.K.) Medicines and Healthcare products Regulatory Agency (MHRA) for TSHA-102 in pediatric patients with Rett syndrome

Private placement financing ("PIPE") is expected to result in gross proceeds of approximately \$150 million from new and existing investors and, net proceeds from PIPE, along with existing cash and cash equivalents, extends cash runway into the third quarter of 2025

Conference call and live webcast today at 8:30 AM Eastern Time

DALLAS, Aug. 14, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today reported financial results for the second quarter ended June 30, 2023, and provided a corporate update.

"We are pleased with the progress we have made this quarter in the clinical evaluation of our two lead investigational programs. For TSHA-102 in Rett syndrome, we believe the initial safety profile and significant clinical improvements seen in the first adult patient with severe disease four weeks post-treatment reinforces the transformative potential of our gene therapy to address the root cause of Rett syndrome. Importantly, these early data indicate that the miRNA-Responsive Auto-Regulatory Element (miRARE) technology is mediating *MECP2* expression in the CNS on a cell-by-cell basis, supporting the regulatory control of miRARE. We are highly encouraged by the initial data for TSHA-102 and are focused on continuing to explore its therapeutic potential, with the dosing of the second patient expected in the third quarter. We also received FDA clearance to initiate clinical development of TSHA-102 in pediatric patients in the U.S. and have submitted a CTA to the MHRA for TSHA-102 in pediatric patients with Rett syndrome, which will expand our clinical evaluation to children with earlier stages of disease progression," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "For TSHA-120 in GAN, our new comprehensive data analysis utilizing the Disease Progression Model (DPM) was submitted to the FDA, and we plan to review the potential regulatory pathway for TSHA-120 with the Agency expected in the third quarter."

Mr. Nolan continued, "Our successful completion of a \$150 million PIPE from top-tier investors significantly bolsters our balance sheet and we believe highlights the enthusiasm for our TSHA-102 program and the early clinical readout of the first patient treated in the REVEAL trial. By extending our cash runway into the third quarter of 2025, we can focus on execution as we endeavor to deliver on key value-creating milestones."

Dr. Elsa Rossignol, M.D., FRCP, FAAP, Associate Professor Neuroscience and Pediatrics at CHU Sainte-Justine, affiliated to the Université de Montréal, and Principal Investigator of the REVEAL trial added, "The efficacy response observed following treatment with TSHA-102 in the first adult with an advanced stage of Rett syndrome is promising. Prior to treatment, the patient was in a constant state of hypertonia, had limited body movement, required constant back support, and had lost fine and gross motor function early in childhood. Following treatment, we have observed improvements in breathing patterns, vocalization and motor skills. The patient was able to sit unassisted for the first time in over a decade, and she demonstrated the ability to unclasp her hands and hold an object steadily for the first time since infancy. I believe that the patient achieving these milestones so early in treatment, coupled with the improvements in breathing patterns and quality of sleep that we have observed, are highly encouraging and support the potential of TSHA-102. I am honored to work with the Rett syndrome community and help patients and families suffering from this devastating disease."

Rett syndrome is a rare neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene. The disorder is characterized by intellectual disabilities, loss of communication, seizures, slowing and/or regression of development, motor and respiratory impairment, and shortened life expectancy. Rett syndrome caused by a pathogenic/likely pathogenic *MECP2* mutation is estimated to affect between 15,000 and 20,000 patients in the U.S., EU and UK.

Recent Corporate Highlights

\$150 million private placement financing strengthens balance sheet and, together with existing cash and cash equivalents, extends cash runway into the third quarter of 2025

- Private placement led by new investor, RA Capital Management, with participation from a large institutional investor, PBM

Capital, RTW Investments, LP, Venrock Healthcare Capital Partners, TCGX, Acuta Capital Partners, Kynam Capital Management, LP, Octagon Capital, Invus, GordonMD® Global Investments LP, and B Group Capital

- Cash runway expected to fund operational plans into the third quarter of 2025
- Net proceeds to primarily fund clinical development of TSHA-102 in Rett syndrome and provide support for program activities for TSHA-120 in GAN, working capital, and other general corporate purposes

Recent Clinical Highlights

TSHA-102 in Rett syndrome: a self-complementary intrathecally delivered AAV9 gene transfer therapy in clinical evaluation for Rett syndrome, a rare genetic neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene. TSHA-102 utilizes a novel miRARE platform designed to mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression. TSHA-102 has received Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission.

TSHA-102 is being evaluated in the [REVEAL Phase 1/2 trial](#), a first-in-human, open-label, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSHA-102 in adult females with Rett syndrome due to *MECP2* loss-of-function mutation. Primary efficacy endpoints are patient assessments by clinicians using the Clinical Global Impressions Scale – Improvement (CGI-I), Rett Syndrome Hand Function Scale, and Revised Motor Behavior Assessment (R-MBA). Secondary endpoints include patient assessments by clinicians and caregivers using the Clinical Global Impressions Scale – Severity (CGI-S), the Rett Syndrome Behavior Questionnaire (RSBQ) and other clinical assessment scales.

Results from the first adult patient dosed in cohort one (low dose) with TSHA-102 in the REVEAL Phase 1/2 trial:

- Well-tolerated safety profile with no treatment-emergent SAEs as of six-week assessment post-treatment
- The following were demonstrated in key efficacy measures four weeks post-treatment:
 - Clinical Global Impressions – Improvement (CGI-I) scale adapted to Rett syndrome, a clinician-reported assessment of overall improvement using a seven-point scale (one=“very much improved” and seven=“very much worse”), demonstrated a score of two indicating “much improved”
 - Clinical Global Impressions – Severity (CGI-S) scale, a clinician-reported assessment of overall severity of a patient’s illness using a seven-point scale, demonstrated a one-point improvement from the baseline score of six (“severely ill”) to a score of five (“markedly ill”)
 - Rett Syndrome Behavior Questionnaire (RSBQ), a 45-item questionnaire to assess Rett syndrome characteristics, demonstrated a total score improvement of 23 points from the baseline score of 52 to a score of 29
- Seizure diary demonstrated no quantifiable seizure events through week five post-treatment
- No marked changes observed four weeks post-treatment in the Revised Motor Behavior Assessment (R-MBA), a 24-question clinician-reported scale measuring disease behaviors of Rett syndrome
- Initial efficacy data and clinical observations supported by video evidence from PI six-weeks post-treatment indicate clinical improvements in multiple domains, including:
 - Autonomic function with improvements in breathing patterns and sleep quality/duration, including the normalization of night-time behavior
 - Vocalization with increased social interest
 - Gross motor skills with the gained ability to sit unassisted for three minutes
 - Fine motor skills and hand function with the gained ability to hold an object, unclasp her hands and use her fingers to touch a screen
- Further updates on available clinical data expected quarterly
- Dosing of second patient cleared by the Independent Data Monitoring Committee (IDMC) and expected in Q3 2023, with continued dosing of adult patients in second half of 2023
- U.S. FDA cleared the IND application for TSHA-102 in pediatric patients with Rett syndrome
- CTA submitted to U.K. MHRA for TSHA-102 in pediatric patients with Rett syndrome

TSHA-120 for giant axonal neuropathy (GAN): a self-complementary intrathecally delivered AAV9 gene therapy in clinical evaluation for GAN, an ultra-rare inherited genetic neurodegenerative disorder with no approved treatments. TSHA-120 has received Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission.

- At R&D Day in June 2023, Taysha provided an overview of new comprehensive data analysis and development of disease

progression model (DPM), which the Company believes has the potential to address FDA feedback regarding the heterogeneity of GAN and effort-dependent nature of MFM32 as the primary endpoint in an unblinded study

- New comprehensive data analysis utilizing the DPM submitted as meeting request to the FDA; feedback for a potential regulatory pathway for TSHA-120 expected in Q3 2023
- FDA feedback on CMC module 3 amendment concluded that the analytical data is sufficient to support the comparability of pivotal lot and release for use in clinical studies

Second Quarter 2023 Financial Highlights

Research and Development Expenses: Research and development expenses were \$19.8 million for the three months ended June 30, 2023, compared to \$23.5 million for the three months ending June 30, 2022. The \$3.7 million decrease was due to lower compensation expense as a result of reduced headcount and fewer manufacturing batches and raw material purchases.

General and Administrative Expenses: General and administrative expenses were \$6.0 million for the three months ended June 30, 2023, compared to \$9.9 million for the three months ended June 30, 2022. The decrease of \$3.9 million was due to reduced general and administrative compensation as a result of lower headcount, consulting and professional fees.

Net loss: Net loss for the three months ended June 30, 2023 was \$24.6 million or \$0.38 per share, as compared to a net loss of \$34.1 million, or \$0.85 per share, for the three months ended June 30, 2022.

Cash and cash equivalents: As of June 30, 2023, Taysha had \$45.1 million in cash and cash equivalents. Taysha expects to receive gross proceeds of \$150 million from the Private Placement, which is expected to close August 16, 2023, before deducting placement agent commissions and offering expenses. The net proceeds from the private placement, combined with the current cash and cash equivalents, are expected to fund its operational plans and capital requirements into the third quarter of 2025.

Conference Call and Webcast Information

Taysha management will hold a conference call and webcast today at 8:30 a.m. ET to review its financial and operating results and to provide a corporate update. The dial-in number for the conference call is 877-407-0792 (U.S./Canada) or 201-689-8263 (international). The conference ID for all callers is 13740092. The live webcast can be accessed here: https://viavid.webcasts.com/starthere.jsp?ei=1624983&tp_key=25b742b70a. An archived version of the webcast will be available for 30 days and can be accessed by visiting Taysha's website at <https://ir.tayshagtx.com/news-events/events-presentations>.

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform with a goal of dramatically improving patients' lives. More information is available at www.tayshagtx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "anticipates," "believes," "expects," "intends," "projects," "plans," and "future" or similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements concerning the potential of our product candidates, including the reproducibility and durability of any favorable results initially seen in our first patient dosed in the REVEAL trial and including our preclinical product candidates, to positively impact quality of life and alter the course of disease in the patients we seek to treat, our research, development and regulatory plans for our product candidates, the potential for these product candidates to receive regulatory approval from the FDA or equivalent foreign regulatory agencies, and whether, if approved, these product candidates will be successfully distributed and marketed, the potential market opportunity for these product candidates, our corporate growth plans, statements associated with the timing, size and completion of the Private Placement, the forecast of our cash runway and the Company's expectations regarding funding, operating and working capital expenditures. Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our Annual Report on Form 10-K for the full-year ended December 31, 2022, and our Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, both of which are available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that we make from time to time with the SEC. Such risks may be amplified by the impacts of the COVID-19 pandemic. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

**Taysha Gene Therapies, Inc.
Condensed Consolidated
Balance Sheet Data**
(in thousands, except share and per share data)
(Unaudited)

December 31,
June 30, 2023
2022

ASSETS

Current assets:			
Cash and cash equivalents	\$ 45,083	\$ 87,880	
Prepaid expenses and other current liabilities	9,032	8,537	
Total current assets	54,115	96,417	

Restricted cash	2,637	2,637
Property, plant and equipment, net	14,139	14,963
Operating lease right-of-use assets	10,348	10,943
Other non-current assets	304	1,316
Total assets	\$ 81,543	\$ 126,276

LIABILITIES AND STOCKHOLDERS' (DEFICIT) EQUITY

Current liabilities:			
Accounts payable	\$ 10,766	\$ 10,946	
Accrued expenses and other current liabilities	19,631	18,287	
Deferred revenue	26,909	33,557	
Total current liabilities	50,641	62,790	
Deferred revenue, net of current portion	6,212		
Term loan, net	38,354	37,967	
Operating lease liability, net of current portion	19,528	20,440	
Other non-current liabilities	3,922	4,130	
Total liabilities	118,657	125,327	

Stockholders' (deficit) equity

Preferred stock, \$0.00001 par value per share; 10,000,000 shares authorized and no shares issued and outstanding as of June 30, 2023 and December 31, 2022

Common stock, \$0.00001 par value per share; 200,000,000 shares authorized and 64,432,637 and 63,207,507 issued and outstanding as of June 30, 2023, and December 31, 2022, respectively	1	1
Additional paid-in capital	406,546	402,389
Accumulated deficit	(443,661)	(401,441)
Total stockholders' (deficit) equity	(37,114)	949
Total liabilities and stockholders' (deficit) equity	\$ 81,543	\$ 126,276

Taysha Gene Therapies, Inc.
Condensed Consolidated Statements of Operations
(in thousands, except share and per share data)
(Unaudited)

	For the three months ended June 30, 2023	For the three months ended June 30, 2022	For the six months ended June 30, 2023	For the six months ended June 30, 2022
Revenue:				
Service Revenue	\$ 2,395	\$ -	\$ 7,101	\$ -
Operating expenses:				
Research and development	19,791	23,506	32,305	61,688
General and administrative	5,988	9,867	14,739	21,336
Total operating expenses	25,779	33,373	47,044	83,024
Loss from operations	(23,384)	(33,373)	(39,943)	(83,024)
Other income (expense):				
Interest Income	223	27	542	41
Interest expense	(1,440)	(743)	(2,814)	(1,415)
Other expense	3	(3)	(5)	(11)
Total other income (expense)	(1,214)	(719)	(2,277)	(1,385)
Net loss	\$ (24,598)	\$ (34,092)	\$ (42,220)	\$ (84,409)
Net loss per common share, basic and diluted	\$ (0.38)	\$ (0.85)	\$ (0.66)	\$ (2.16)
Weighted average common shares outstanding, basic and diluted	64,244,531	40,142,403	63,755,435	39,163,996

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Announces \$150 Million Private Placement Financing

Financing led by RA Capital Management with participation from new and existing investors

Expected net proceeds, along with existing cash and cash equivalents, are expected to extend cash runway into the third quarter of 2025

DALLAS, Aug. 14, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), announced today that it has entered into a securities purchase agreement for a private placement financing (the "PIPE") that is expected to result in gross proceeds of approximately \$150 million, before deducting placement agent commissions and offering expenses. The PIPE was led by new investor, RA Capital Management, with participation from a large institutional investor, PBM Capital, RTW Investments, LP, Venrock Healthcare Capital Partners, TCGX, Acuta Capital Partners, Kynam Capital Management, LP, Octagon Capital, Invus, GordonMD® Global Investments LP, and B Group Capital.

"We are pleased by the support from this prestigious group of new and existing investors, which we believe highlights the enthusiasm of the early clinical readout of the first patient treated in our REVEAL trial and reinforces the potential of gene therapy to transform the lives of patients suffering from devastating diseases," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "We expect that the net proceeds from the PIPE, together with our existing cash and cash equivalents, will extend our cash runway into the third quarter of 2025 to primarily support the clinical development of TSHA-102 in Rett syndrome and provide support for TSHA-120 program activities in GAN, working capital and other general corporate purposes. With this capital infusion, we believe we are well positioned to continue to execute across key program milestones."

In the PIPE, Taysha is selling an aggregate of 122,412,376 shares of its common stock at a price of \$0.90 per share and, in lieu of common stock to certain investors, pre-funded warrants to purchase up to an aggregate of 44,250,978 shares of common stock at a purchase price of \$0.899 per pre-funded warrant. Each pre-funded warrant has an exercise price of \$0.001 per share of common stock and is immediately exercisable and remains exercisable until exercised in full. The PIPE is being conducted in accordance with applicable Nasdaq rules and was priced to satisfy the "Minimum Price" requirement (as defined in the Nasdaq rules). The PIPE is expected to close by August 16, 2023, subject to customary closing conditions. The pre-funded warrants will only be exercisable upon receipt of stockholder approval of an increase in the authorized shares of Taysha's common stock, which Taysha will first seek to obtain at an annual meeting of stockholders to be held by December 31, 2023.

Jefferies is acting as exclusive placement agent in the private placement.

The securities to be sold in this private placement, including the shares of common stock underlying the pre-funded warrants, have not been registered under the Securities Act of 1933, as amended, or applicable state securities laws, and may not be offered or sold in the United States except pursuant to an effective registration statement or an applicable exemption from the registration requirements. Taysha has agreed to file a registration statement with the Securities and Exchange Commission registering the resale of the shares of common stock and the shares of common stock underlying the pre-funded warrants issued in the PIPE.

This press release shall not constitute an offer to sell or the solicitation of an offer to buy any securities described herein, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of any such state or jurisdiction.

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform with a goal of dramatically improving patients' lives. More information is available at www.tayshagtx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "anticipates," "believes," "expects," "intends," "projects," "plans," and "future" or similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements related to the anticipated proceeds to be received in the proposed PIPE, expected timing of closing of the proposed PIPE and the size and completion of the proposed PIPE, the forecast of cash runway and the Company's expectations regarding funding, operating and working capital expenditures. Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our Annual Report on Form 10-K for the full-year ended December 31, 2022, and our Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, both of which are available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that we make from time to time with the SEC. Such risks may be amplified by the impacts of the COVID-19 pandemic. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Announces Positive Recommendation from Independent Data Monitoring Committee of REVEAL Phase 1/2 Trial in Rett Syndrome

Independent Data Monitoring Committee recommended REVEAL Phase 1/2 trial continuation and proceeding with dosing of second patient based on encouraging initial clinical data from the first adult with Rett syndrome dosed with investigational gene therapy TSHA-102

Initial clinical update from the first patient dosed with TSHA-102 planned for forthcoming quarterly earnings call

Dosing of second patient expected in the third quarter of 2023

DALLAS, July 31, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), announced today that the Independent Data Monitoring Committee (IDMC) recommended the continuation of the REVEAL Phase 1/2 trial and that dosing of the second patient in the first cohort can proceed. The decision follows a pre-specified IDMC review of initial clinical data from the first patient dosed with TSHA-102 following the 42-day evaluation period.

"We thank the IDMC members for their guidance and are pleased with their recommendation to continue the REVEAL Phase 1/2 trial," said Sukumar Nagendran, M.D., President and Head of R&D of Taysha. "This recommendation was based on the analysis of initial clinical data from the first adult patient with Rett syndrome to receive TSHA-102. A second patient is expected to be dosed in the third quarter of this year. We are highly encouraged by the initial clinical observations, which support the transformative potential of TSHA-102 and mark important progress in our efforts to bring a gene therapy to patients and families living with Rett syndrome. We look forward to providing an initial clinical update on the first patient at our second quarter corporate update conference call in mid-August."

The [REVEAL Phase 1/2 trial](#) is a first-in-human, open-label, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSHA-102 in adult females with Rett syndrome due to *MECP2* loss-of-function mutation. TSHA-102 is administered as a single lumbar intrathecal injection. Dose escalation will evaluate two dose levels of TSHA-102 sequentially. The maximum tolerated dose (MTD) or maximum administered dose (MAD) established will then be administered during dose expansion.

About TSHA-102

TSHA-102 is an investigational self-complementary intrathecally delivered AAV9 gene transfer therapy in clinical evaluation for Rett syndrome, a rare genetic neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene. TSHA-102 utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) platform designed to regulate cellular *MECP2* expression. TSHA-102 has received Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission. TSHA-102 is being evaluated in the first-in-human, open label, randomized, dose escalation and dose-expansion REVEAL Phase 1/2 trial for adult female patients with Rett syndrome.

About Rett Syndrome

Rett syndrome is a rare neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene, which is a gene that's essential for neuronal and synaptic function in the brain. The disorder is characterized by intellectual disabilities, loss of communication, seizures, slowing and/or regression of development, motor and respiratory impairment, and shortened life expectancy. Rett syndrome primarily occurs in females and is one of the most common genetic causes of severe intellectual disability. Currently, there are no approved disease-modifying therapies that treat the genetic root cause of the disease. Rett syndrome caused by a pathogenic/likely pathogenic *MECP2* mutation is estimated to affect between 15,000 and 20,000 patients in the U.S., EU and UK.

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could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our Annual Report on Form 10-K for the full-year ended December 31, 2022, which is available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that we make from time to time with the SEC. Such risks may be amplified by the impacts of the COVID-19 pandemic. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Provides Clinical Updates for Investigational Programs TSHA-120 in Giant Axonal Neuropathy (GAN) and TSHA-102 in Rett Syndrome at R&D Day

Company views that results of comprehensive data analysis of TSHA-120 and development of disease progression model (DPM) address U.S. Food and Drug Administration (FDA) feedback regarding the effort-dependent nature of MFM32 as primary endpoint in an unblinded study and heterogeneity of GAN; Taysha plans to review potential regulatory pathway for TSHA-120 at a formal meeting with the FDA expected in Q3 2023

New GAN analysis identified multiple functional, electrophysiological and biological measurements that demonstrate a clinically meaningful and objective measurement of TSHA-120 treatment effect on disease progression

Encouraging initial clinical observations seen in the first adult patient with Rett syndrome recently dosed with TSHA-102 in REVEAL Phase 1/2 trial; safety and efficacy update and Independent Data Monitoring Committee (IDMC) approval to dose second patient expected in early Q3 2023

Detailed updates will be presented at virtual R&D Day today at 10:00 AM ET

DALLAS, June 28, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), announced new data analyses for TSHA-120 in GAN and initial clinical observations for TSHA-102 in Rett syndrome. Taysha will host a virtual R&D Day today at 10:00 AM ET to discuss these updates. The webcast link can be accessed on the [Events and Presentations](#) section of Taysha's website.

"Late last year, the company submitted and discussed with the FDA a subset of available evidence supporting the potential therapeutic benefit and safety profile for TSHA-120 in patients with GAN, an ultra-rare disease with currently no approved treatments. FDA feedback included the need to address the heterogeneity of disease progression in GAN and the effort-dependent nature of MFM32 as a primary endpoint, considering the unblinded study design," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "Given the FDA also indicated it is open to regulatory flexibility in a controlled trial setting and willing to consider alternative study designs, we undertook an extensive analysis of the totality of data available to determine a feasible regulatory path forward for TSHA-120."

Mr. Nolan continued, "We believe the new analyses may help support an approval pathway for TSHA-120 for the treatment of GAN. Our newly developed disease progression model demonstrates predictable and homogenous disease progression in classic GAN, which in our view supports the use of natural history data as an external control. Additionally, we identified objective functional, electrophysiological and biological measurements that demonstrated a clinically meaningful treatment effect, which is also accompanied by over seven years of clinical data supporting the safety profile. We've requested a formal FDA meeting to discuss these new developments to support a potential regulatory path forward for TSHA-120. We expect the meeting to take place in the third quarter of this year."

"For our TSHA-102 program in Rett syndrome, we are encouraged by the initial clinical observations of the first adult patient recently dosed in the REVEAL Phase 1/2 trial," said Sukumar Nagendran, M.D., President, and Head of R&D. "We look forward to providing further clinical updates on the safety and efficacy observations for the first patient early in the third quarter of this year, following the required IDMC adjudication of the initial clinical data. Subsequent REVEAL trial updates will be provided quarterly, thereafter. We remain on track to submit a CTA to the UK MHRA in pediatric patients in mid-2023 and to submit an IND application to the FDA in the second half of 2023."

Key R&D Day Highlights

TSHA-120: a self-complimentary intrathecally delivered AAV9 gene therapy being evaluated in an open-label, dose-escalation, non-randomized Phase 1/2 trial for GAN, an ultra-rare inherited genetic neurodegenerative disorder with no approved treatments.

- New comprehensive data analysis enabled the development of a DPM using all available data from the largest existing GAN natural history database; DPM demonstrates a predictable and homogenous disease progression in classic GAN, which supports the potential for natural history data to serve as a suitable external control
- Given patient age and the extensive and wide-spread damage to the central nervous system as well as a length-dependent progression in the peripheral nervous system, a more positive treatment impact is expected in outcomes related to the arms compared to the legs; the longer the disease progresses, the greater the degeneration with decreasing likelihood of impacting the disease
- Relatively stable to improved sensory response amplitudes observed on nerve conduction studies, in conjunction with increased regenerative clusters on nerve biopsy, suggest sensory nerve or neuron regeneration in a progressive neurodegenerative disease
- Using natural history data as an external control, Bayesian analysis demonstrated a clinically meaningful treatment effect of TSHA-120 as measured through the slowing of disease progression observed across multiple

functional, electrophysiological and biological measures:

o **Functional endpoints:**

- Modified Friedreich's Ataxia Rating Scale (mFARS) demonstrated a 99% probability of positive treatment effect on slowing disease progression, with an estimated average treatment effect of 31%
- Motor Function Measure 32 (MFM32) Domain 3 (distal motor function – hands) demonstrated a 99% probability of positive treatment effect on slowing disease progression, with an estimated treatment effect of 28%
- Visual Acuity, as measured by Logarithm of the Minimum Angle of Resolution (LogMAR), demonstrated 100% probability of positive treatment effect on slowing disease progression, with an estimated treatment effect of 70% in the right eye and 51% in the left eye

o **Electrophysiological endpoints:**

- Analysis demonstrated a 100% probability of positive treatment effect on slowing disease progression, with an estimated treatment effect of 189% and 152% for Ulnar Sensory Nerve Action Potential (SNAP) and median SNAP amplitude, respectively, indicating disease improvement
- Compound Muscle Action Potential (CMAP) demonstrated a 94% probability of positive treatment effect on slowing disease progression, with an estimated 29% treatment effect

o **Biological Endpoints:**

- 4 out of the 5 patients that had stabilization or improvements in SNAPS had increased regenerative clusters on nerve biopsy
- Skin biopsy-nerve fiber density: 5 patients saw stabilization or increases in nerve fiber density of the skin in at least one location of the proximal or distal leg at month 12, including 3/3 in the high-dose and one in the medium-high dose

- Over seven years of long-term clinical data support the safety and tolerability profile of TSHA-120
- New data analysis will help inform discussion with the FDA regarding a regulatory path forward for TSHA-120; formal meeting with FDA expected in the third quarter of 2023

TSHA-102: a self-complementary intrathecally delivered AAV9 gene transfer therapy being evaluated in the first-in-human, open labeled, randomized dose escalation and expansion REVEAL Phase 1/2 trial for Rett syndrome, a rare genetic neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene. TSHA-102 utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) platform designed to regulate cellular *MECP2* expression.

- First patient has been dosed in the REVEAL Phase 1/2 trial in adult patients with Rett syndrome being conducted at CHU Sainte-Justine, the Université de Montréal mother and child university hospital centre in Montreal, Canada
 - o The patient was discharged from the hospital and has completed multiple follow-up visits, per the study protocol. Additional safety and efficacy updates on the first patient are expected in the early third quarter of 2023, following initial review of available safety data by the IDMC
 - o Second potential patient has been identified and will undergo screening if all protocol defined criteria are met; dosing expected to proceed pending IDMC review of available clinical data from the first patient
- CTA submission to UK MHRA in pediatric patients anticipated in mid-2023
- IND application submission to U.S. FDA expected in the second half of 2023

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform with a goal of dramatically improving patients' lives. More information is available at www.tayshagtx.com.

Forward-Looking Statements

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amplified by the impacts of the COVID-19 pandemic. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies to Host Virtual R&D Day on Lead Clinical Investigational Programs TSHA-120 in Giant Axonal Neuropathy (GAN) and TSHA-102 in Rett Syndrome

Virtual R&D Day featuring collaborator Salman Bhai, MD, and Taysha's leadership team at 10:00 AM ET on June 28, 2023

Company to provide update on new data analyses for TSHA-120 in GAN, and initial safety observations for TSHA-102 in Rett syndrome

DALLAS, June 15, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today announced it will host a virtual R&D Day on Wednesday, June 28, 2023 at 10:00 AM ET to discuss updates on TSHA-120, a self-complementary intrathecally delivered investigational AAV9 gene therapy in clinical evaluation for GAN, and TSHA-102, a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy in clinical evaluation for Rett syndrome.

The event will feature collaborator Salman Bhai, MD, Assistant Professor of Neurology at UT Southwestern Medical Center, who will discuss the disease course and biology of GAN and present new data and analyses from the ongoing natural history and interventional trial evaluating TSHA-120. In addition, Taysha leadership will provide a clinical update on the investigational TSHA-102 program, including the initial safety observations of TSHA-102 from the first patient recently dosed in the [Phase 1/2 REVEAL trial](#). The REVEAL trial is evaluating the safety and preliminary efficacy of TSHA-102 in adult females with Rett syndrome. More detailed clinical updates on the first patient will be provided in the third quarter of this year following the initial review of available safety data by the Independent Data Monitoring Committee.

A live question and answer session will follow the formal presentations. To register for the event, please click [here](#).

About Salman Bhai, MD

Dr. Bhai is an Assistant Professor in the Department of Neurology at UT Southwestern Medical Center and the Director of the Neuromuscular Center in the Institute for Exercise and Environmental Medicine at Texas Health Presbyterian Hospital Dallas. He specializes in neuromuscular disorders. Dr. Bhai earned his medical degree at Harvard Medical School. He completed his residency in neurology through Harvard Medical School at Brigham and Women's Hospital and Massachusetts General Hospital, where he also received advanced training through a fellowship in neuromuscular medicine and earned a medical education certificate. He is board certified by the American Board of Psychiatry and Neurology in neurology and neuromuscular medicine as well as by the American Board of Electrodiagnostic Medicine. He joined the UT Southwestern faculty in 2020. He is a member of the American Academy of Neurology, the Dallas County Medical Society, and the Texas Neurological Society. Dr. Bhai's clinical interests include the evaluation and treatment of neuromuscular disorders. He focuses on patients with hereditary and autoimmune neuromuscular disorders. Dr. Bhai's research focuses on understanding metabolic and mitochondrial dysfunction in muscle disorders. He is the principal investigator for multiple clinical trials in neuromuscular diseases. He serves as an organizer and a participant for European Neuromuscular Center expert workshops. He has been an invited lecturer nationally and internationally in his areas of expertise. As a clinician-scientist and educator, Dr. Bhai strives to improve the lives of patients and their families.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Announces First Patient Dosed with TSHA-102 in the REVEAL Phase 1/2 Trial Under Investigation for the Treatment of Rett Syndrome

The Phase 1/2 REVEAL trial is a first-in-human, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSHA-102 in adults with Rett syndrome

TSHA-102 utilizes novel miRARE technology, designed to regulate cellular MECP2 levels

Initial available clinical safety data from Phase 1/2 REVEAL trial will be reported at Taysha's upcoming R&D Day on June 28, 2023, at 10:00 AM Eastern Time

DALLAS, June 05, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today announced that the first patient has been dosed with TSHA-102 in the Phase 1/2 REVEAL trial evaluating the safety and preliminary efficacy of TSHA-102 in adult patients with Rett syndrome. TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy that utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) platform designed to regulate cellular MECP2 expression. The study is being conducted at CHU Sainte-Justine, the Université de Montréal mother and child university hospital centre in Montreal, Canada.

"Dosing of the first adult patient marks the beginning of clinical evaluation of TSHA-102 in the Phase 1/2 REVEAL trial, and, to our knowledge, the first time a gene therapy has ever been evaluated in a clinical setting for the treatment of Rett syndrome," said Sukumar Nagendran, M.D., President, and Head of R&D. "By targeting the regulation of gene expression on a cell-by-cell basis, we believe our miRARE technology has the ability to enable safe expression of MECP2, which may help address the risks associated with both under and overexpression resulting from the mosaic pattern of MECP2 silencing. This is a significant milestone that furthers our quest to bring a potentially transformational gene therapy to patients and families living with Rett syndrome. We look forward to sharing initial available clinical safety data from the Phase 1/2 REVEAL trial at our R&D Day on June 28, 2023."

The [Phase 1/2 REVEAL trial](#) is a first-in-human, open-label, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSHA-102 in adult females with Rett syndrome due to MECP2 loss-of-function mutation. Participants will receive a single lumbar intrathecal injection of TSHA-102. Dose escalation will evaluate two dose levels of TSHA-102 sequentially, with an initial dose of 5×10^{14} total vector genomes (vg) and the second dose of 1×10^{15} vg. The maximum tolerated dose (MTD) or maximum administered dose (MAD) established will then be administered during dose expansion. Per the protocol, an independent data monitoring committee will review available safety data from the first patient at approximately six weeks post-dosing to determine if the Company can proceed with dosing the second patient. Initial available clinical safety data will be reported at Taysha's upcoming R&D Day on June 28, 2023. To register for the event, please click [here](#).

Elsa Rossignol, M.D., FRCP, FAAP, Associate Professor Neuroscience and Pediatrics, and Principal Investigator of the REVEAL study added, "Based on its unique and compelling technology targeting the genetic root cause of Rett syndrome, TSHA-102 has the potential to transform care by addressing a significant unmet medical need for patients with this devastating and currently incurable disease. The dosing of the first patient in this important clinical trial represents a critical advancement in evaluating the potential of gene therapy for Rett syndrome. It is a privilege to be part of this important endeavor. In the name of all affected families, I thank Taysha for bringing this potentially transformative therapy from the bench to the bedside."

Sabrina Millson, President of Ontario Rett Syndrome Association further added, "This is a momentous day for the Rett syndrome community. As a mom to a daughter living with Rett syndrome and the president of the Ontario Rett Syndrome Association here in Canada, I know first-hand how this disease leads to debilitating symptoms, including difficulties in communication, mobility and breathing. The potential for a treatment that addresses the underlying cause of disease and slows progression or potentially prevents the onset of disease with early intervention is truly remarkable. We're pleased to collaborate with Taysha Gene Therapies in an effort to bring a gene therapy treatment that could meaningfully change the lives of patients and their caregivers."

About TSHA-102

TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy in clinical evaluation for Rett syndrome. TSHA-102 utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) platform designed to regulate cellular MECP2 expression. TSHA-102 has received Orphan Drug and Rare Pediatric Disease designations from the United States (U.S.) Food and Drug Administration (FDA) and has been granted Orphan Drug designation from the European Commission. We are advancing TSHA-102 in the REVEAL Phase 1/2 clinical trial under a CTA approved by Health Canada. A CTA submission to United Kingdom (UK) MHRA in pediatric patients with Rett syndrome is expected in mid-2023, and an Investigational New Drug (IND) application to the FDA is anticipated in the second half of 2023.

About Rett Syndrome

Rett syndrome is a rare neurodevelopmental disorder caused by mutations in the X-linked MECP2 gene, which is a gene that's essential for neuronal and synaptic function in the brain. The disorder is characterized by intellectual disabilities, loss of communication, seizures, slowing and/or regression of development, motor and respiratory impairment, and shortened life expectancy. Rett syndrome primarily occurs in females and is one of the most common genetic causes of severe intellectual disability. Currently, there are no approved disease-modifying therapies that treat the genetic root cause of the disease. Rett syndrome caused by a pathogenic/likely pathogenic MECP2 mutation is estimated to affect between 15,000 and 20,000 patients

in the U.S., EU and UK.

About Taysha Gene Therapies

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About the CHU Sainte-Justine

The Centre hospitalier universitaire Sainte-Justine is the largest mother-child hospital in Canada. A member of the Université de Montréal extended network of excellence in health (RUIS), CHU Sainte-Justine has 6759 employees, including 1770 nurses and nursing assistants; 1131 other healthcare professionals; 531 physicians, dentists and pharmacists; 931 residents and over 280 researchers; 170 volunteers; and 3 406 interns and students in a wide range of disciplines. CHU Sainte-Justine has 484 beds, including 67 at the Centre de réadaptation Marie Enfant (CRME), the only exclusively pediatric rehabilitation centre in Québec. The World Health Organization has recognized CHU Sainte-Justine as a "health-promoting hospital." chusj.org

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Presents Preclinical Data on TSHA-102 for Rett Syndrome Demonstrating Cellular Regulation of MeCP2 Expression in Key Mouse Models at the American Society of Gene and Cell Therapy 26th Annual Meeting

New preclinical data after neonatal administration in wild-type mice showed no detectable impact on survival, neurobehavioral functions and overall health, suggesting TSHA-102, engineered with novel miRARE technology, avoided toxic overexpression of MeCP2 within cells already expressing MeCP2

Data reinforce previous findings in *Mecp2^{-/-}* knockout mice demonstrating TSHA-102 regulated cellular MeCP2 levels and significantly improved survival, overall neurobehavioral function and growth

Data in neonatal mouse models highlight the potential of the miRARE technology to enable safe expression levels of MeCP2, which may address the risks associated with both under and overexpression of MeCP2 resulting from the mosaic pattern of MECP2 silencing in females with Rett syndrome

Dosing of the first adult patient with TSHA-102 in the Phase 1/2 REVEAL trial in Rett syndrome is expected in Q2 2023

DALLAS, May 19, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today presents preclinical data from neonatal mouse models on TSHA-102 for Rett syndrome, including new data in wild-type mice, at the American Society of Gene and Cell Therapy (ASGCT) 26th Annual Meeting. TSHA-102 utilizes a miniMECP2 gene and a novel miRNA-Responsive Auto-Regulatory Element (miRARE) technology designed to regulate cellular MECP2 expression. In a Taysha-sponsored study, the safety and efficacy of TSHA-102 were explored in both neonatal wild-type and *Mecp2^{-/-}* knockout mice, respectively. Preclinical in-life data on early intervention of TSHA-102 in neonatal mice suggest miRARE enables the expression of the MeCP2 protein in deficient CNS cells while preventing toxic overexpression within cells expressing normal levels of MeCP2.

"These encouraging new preclinical data in wild-type mice indicate that TSHA-102, engineered with our miRARE technology, avoided overexpression of MeCP2 within cells already expressing MeCP2, while maintaining normal survival, neurobehavioral function and overall health," said Sukumar Nagendran, M.D., President, and Head of R&D. "These new data augment previous findings in the *Mecp2^{-/-}* knockout mouse model, suggesting that TSHA-102 regulated expression of MECP2 in both normal and MECP2 deficient cells, which is critical given that Rett syndrome represents such a challenging case for human gene therapy because the therapeutic window for MECP2 transgene expression is narrow. Either MECP2 deficiency or duplication can lead to serious neurodevelopmental disease. We believe these new data from neonatal wild-type mice support the potential of miRARE to enable the optimal amount of MeCP2. This would be critical to modulating the cellular expression of MeCP2 in an appropriate, clinically relevant manner, given the mosaic pattern of MECP2 silencing characteristic of female patients with Rett syndrome."

Sarah Sinnett, Ph.D., University of Texas Southwestern Medical Center, Co-Inventor of miRARE technology, added, "TSHA-102 pairs a therapeutic gene with miRARE, all within a single vector genome. The miRARE technology was designed to mitigate the risk of MeCP2 overexpression through a post-transcriptional feedback repression mechanism. We are pleased that miRARE permitted efficacy in *Mecp2^{-/-}* mice without compromising safety in wild-type mice. Importantly, these findings could translate into clinical benefits for treating patients with Rett syndrome."

Preclinical data in neonatal wild-type mice suggest miRARE suppressed toxic overexpression after early intervention with TSHA-102:

- In wild-type mice treated with TSHA-102, new data showed no deleterious impact on survival, neurobehavioral functions and overall health, suggesting miRARE regulated expression of MeCP2 with the below results from the study:
 - No toxicity relative to vehicle treatment
 - No reduction in survival over 36-weeks
 - No treatment effect on Bird Score (a measure of Rett syndrome-like behaviors and pathologies) analysis relative to vehicle treatment
 - No impact on overall growth over the course of the study

This builds on prior preclinical data in neonatal *Mecp2^{-/-}* knockout mice showing miRARE regulated MECP2 expression levels in deficient CNS cells with early intervention of TSHA-102:

- In *Mecp2^{-/-}* knockout mice (mouse model recapitulating developmental, physiological, and behavioral features of human Rett syndrome) treated with TSHA-102 with the below results from the study:
 - 47% survived the 36-week study vs a median survival of 8.1 weeks with vehicle-treated knockout mice, representing a significant ($p < 0.0001$) >4-fold extension of their lifespan
 - Restoration of normal and faster-than-normal growth

- Aggregate Bird Score was significantly improved at several time points, with a significant delay in the onset of severe Rett syndrome-like phenotypes, including the delayed average age of onset for severe clasping from approximately 7 to 21 weeks and severely abnormal gait from approximately 8 to 20 weeks

TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy in clinical evaluation for Rett syndrome, a rare genetic neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene. TSHA-102 is currently being evaluated in the Phase 1/2 REVEAL trial in adult patients with Rett syndrome. The dosing of the first adult patient with TSHA-102 is expected in Q2 2023, with initial available clinical data, primarily on safety, anticipated thereafter in Q2 2023. TSHA-102 has received Orphan Drug and Rare Pediatric Disease designations from the U.S. Food and Drug Administration (FDA) and has been granted Orphan Drug designation from the European Commission for the treatment of Rett syndrome.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Reports First Quarter 2023 Financial Results and Provides Corporate Update

Screening completed and dosing scheduled for first potential subject in the Phase 1/2 REVEAL trial in Rett syndrome; dosing of first adult patient with TSHA-102 expected in Q2 2023; initial available Phase 1/2 clinical data, primarily on safety, expected in Q2 2023

Clinical Trial Application (CTA) submission to United Kingdom (UK) MHRA for TSHA-102 in pediatric patients with Rett syndrome expected in mid-2023; Investigational New Drug (IND) application to United States (U.S.) Food and Drug Administration (FDA) in Rett syndrome anticipated in H2 2023

New preclinical data for TSHA-102 in Rett syndrome to be presented during a poster presentation at the upcoming American Society of Gene and Cell Therapy (ASGCT) 26th Annual Meeting

R&D Day in June 2023 will overview new findings from totality of data evaluation, including comprehensive analyses of functional, biological, and electrophysiological assessments of TSHA-120 in giant axonal neuropathy (GAN), and provide an update on TSHA-102 in Rett syndrome

Formal FDA meeting request submission to discuss regulatory path forward for TSHA-120 in GAN expected in Q2 2023; formal meeting anticipated in Q3 2023

Conference call and live webcast today at 4:30 PM Eastern Time

DALLAS, May 11, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today reported financial results for the first quarter ended March 31, 2023, and provided a corporate update.

"We continue to make significant progress with our two lead clinical programs and remain on track to deliver on multiple key milestones, including the generation of first-in-human clinical data for TSHA-102 in adult patients with Rett syndrome, the submission of a CTA to the MHRA to initiate expansion of TSHA-102 in pediatric patients, the submission of an IND application to the FDA for TSHA-102, and obtaining further clarity from the FDA on the regulatory path forward for TSHA-120 in GAN," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "Screening is completed, and dosing is now scheduled for our first potential patient in the adult Rett syndrome study. For GAN, our comprehensive analyses of the totality of data for TSHA-120 continues to be encouraging and includes compelling findings with potential to further support a regulatory path forward."

Sukumar Nagendran, M.D., President, and Head of R&D added, "We plan to seek a formal meeting with the FDA to discuss the totality of findings from the functional, biological, and electrophysiological assessments of TSHA-120 in GAN, anticipated in the third quarter of this year. In the near term, we look forward to hosting an R&D Day in June where we will overview the GAN disease state and share the comprehensive analyses, as well as provide an update on our Rett program. For TSHA-102, new preclinical data supporting the efficacy and safety of TSHA-102 and the miRARE technology in Rett syndrome will be presented as part of a poster presentation at the upcoming ASGCT conference. We believe that the clinical and preclinical data generated to date across our Rett syndrome and GAN programs reinforce our gene therapy approach, and the therapeutic potential to address severe unmet needs in monogenic central nervous system disease."

Recent Corporate Highlights

TSHA-102 in Rett syndrome: a self-complementary intrathecally delivered AAV9 gene transfer therapy in clinical evaluation for Rett syndrome, a rare genetic neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene. TSHA-102 utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) platform designed to regulate cellular *MECP2* expression. TSHA-102 has received Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission.

- Phase 1/2 REVEAL trial in adult patients with Rett syndrome
 - Completed screening and scheduled dosing for first potential adult patient with dosing anticipated in Q2 2023
 - Initial available Phase 1/2 clinical data, primarily on safety, expected in Q2 2023, with planned quarterly updates on available clinical data thereafter
 - Continued dosing of adult patients with Rett syndrome in the REVEAL trial in H2 2023
- CTA submission to UK MHRA for TSHA-102 in pediatric patients with Rett syndrome anticipated in mid-2023
- IND application submission to U.S. FDA for Rett syndrome expected in H2 2023
- New preclinical data for TSHA-102 in Rett syndrome to be presented as a poster presentation at the upcoming ASGCT 26th Annual Meeting on Friday, May 19 at 12-2 PM PT; these data and available clinical data from Phase 1/2 REVEAL trial will be presented in upcoming R&D Day in June

TSHA-120 for giant axonal neuropathy (GAN): a self-complimentary intrathecally delivered AAV9 gene therapy in clinical evaluation for GAN, an ultra-rare inherited genetic neurodegenerative disorder with no approved treatments. TSHA-120 has received Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission.

- Completed CMC module 3 amendment submission detailing commercial process product manufacturing and drug comparability analysis; awaiting FDA feedback
- R&D Day in June 2023 to overview new findings from totality of data evaluation, including comprehensive analyses of functional, biological, and electrophysiological assessments of TSHA-120 in GAN
- Submission of a formal meeting request to the FDA in Q2 2023 to discuss alternative study designs, additional objective measures and regulatory path forward; formal meeting anticipated in Q3 2023

First Quarter 2023 Financial Highlights

Research and Development Expenses: Research and development expenses were \$12.5 million for the three months ended March 31, 2023, compared to \$38.2 million for the three months ending March 31, 2022. The \$25.7 million decrease was due to reduced research and development compensation as a result of lower headcount of \$10.7 million. The decrease was also due to reduced manufacturing and other raw material purchases of \$7.1 million. We also incurred \$6.4 million reduced expense in non-clinical studies related to translational and toxicology studies and \$1.5 million lower expense in other research and development activities.

General and Administrative Expenses: General and administrative expenses were \$8.8 million for the three months ended March 31, 2023, compared to \$11.5 million for the three months ended March 31, 2022. The decrease of \$2.7 million was due to reduced general and administrative compensation as a result of lower headcount and reduced consulting and professional fees.

Net loss: Net loss for the three months ended March 31, 2023 was \$17.6 million or \$0.28 per share, as compared to a net loss of \$50.3 million, or \$1.32 per share, for the three months ended March 31, 2022. The net loss for the three months ended March 31, 2023 was partially offset by revenue of \$4.7 million recognized related to the Astellas Transactions.

Cash and cash equivalents: As of March 31, 2023, Taysha had \$63.4 million in cash and cash equivalents. Taysha continues to expect that its current cash resources will support planned operating expenses and capital requirements into the first quarter of 2024.

Conference Call and Webcast Information

Taysha management will hold a conference call and webcast today at 4:30 pm ET to review its financial and operating results and to provide a corporate update. The dial-in number for the conference call is 855-327-6837 (U.S./Canada) or 631-891-4304 (international). The conference ID for all callers is 10021767. The live webcast and replay may be accessed by visiting Taysha's website at <https://ir.tayshagtx.com/news-events/events-presentations>. An archived version of the webcast will be available on the website for 30 days.

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform with a goal of dramatically improving patients' lives. More information is available at www.tayshagtx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "anticipates," "believes," "expects," "intends," "projects," "plans," and "future" or similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements concerning the potential of our product candidates, including our preclinical product candidates, to positively impact quality of life and alter the course of disease in the patients we seek to treat, our research, development and regulatory plans for our product candidates, the potential for these product candidates to receive regulatory approval from the FDA or equivalent foreign regulatory agencies, and whether, if approved, these product candidates will be successfully distributed and marketed, the potential market opportunity for these product candidates, our corporate growth plans, the forecast of our cash runway and the implementation and potential impacts of our strategic pipeline prioritization initiatives. Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our Annual Report on Form 10-K for the full-year ended December 31, 2022, which is available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that we make from time to time with the SEC. Such risks may be amplified by the impacts of the COVID-19 pandemic. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

**Taysha Gene Therapies, Inc.
Condensed Consolidated Statements of Operations
(in thousands, except share and per share data)
(Unaudited)**

For the three months ended March 31,	For the three months ended March 31,
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	2023	2022
Revenue:		
Service Revenue	\$ 4,706	\$ -
Operating expenses:		
Research and development	12,514	38,182
General and administrative	8,751	11,469
	<hr/>	<hr/>
Total operating expenses	21,265	49,651
Loss from operations	<hr/>	<hr/>
	(16,559)	(49,651)
Other income (expense):		
Interest Income	319	14
Interest expense	(1,374)	(672)
Other expense	(8)	(8)
	<hr/>	<hr/>
Total other expense	(1,063)	(666)
Net loss	<hr/>	<hr/>
	\$ (17,622)	\$ (50,317)
Net loss per common share, basic and diluted	\$ (0.28)	\$ (1.32)
Weighted average common shares outstanding, basic and diluted	63,260,905	38,174,717

Taysha Gene Therapies, Inc.
Condensed Consolidated Balance Sheet Data
(in thousands, except share and per share data)
(Uaudited)

	December 31, March 31, 2023	2022
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 63,425	\$ 87,880
Prepaid expenses and other current liabilities	8,933	8,537
Total current assets	<hr/>	<hr/>
	72,358	96,417
Restricted cash	2,637	2,637
Property, plant and equipment, net	14,642	14,963
Operating lease right-of-use assets	10,647	10,943
Other noncurrent assets	1,316	1,316
Total assets	<hr/>	<hr/>
	\$ 101,600	\$ 126,276
LIABILITIES, CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS' (DEFICIT) EQUITY		
Current liabilities:		
Accounts payable	\$ 9,002	\$ 10,946
Accrued expenses and other current liabilities	16,602	18,287
	<hr/>	<hr/>
Deferred revenue	28,851	33,557
Total current liabilities	<hr/>	<hr/>
	54,455	62,790
Term loan, net	38,161	37,967
Operating lease liability, net of current portion	19,928	20,440
Other noncurrent liabilities	4,004	4,130
Total liabilities	<hr/>	<hr/>
	116,548	125,327

Preferred stock, \$0.00001 par value per share; 10,000,000 shares authorized and no shares issued and outstanding as of March 31, 2023 and December 31, 2022

Stockholders' (deficit) equity

Common stock, \$0.00001 par value per share; 200,000,000 shares authorized and 63,473,349 and 63,207,507 issued and outstanding as of March 31, 2023 and December 31, 2022, respectively	1	1
Additional paid-in capital	404,114	402,389

Accumulated deficit	(419,063)	(401,441)
Total stockholders' (deficit) equity	(14,948)	949
Total liabilities, convertible preferred stock, and stockholders' (deficit) equity	\$ 101,600	\$ 126,276

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies to Release First Quarter 2023 Financial Results and Host Conference Call and Webcast on May 11

DALLAS, May 04, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today announced that it will report its financial results for the first quarter ended March 31, 2023, and host a corporate update conference call and webcast on Thursday, May 11, 2023, at 4:30 PM Eastern Time.

Conference Call Details

Thursday, May 11, at 4:30 PM Eastern Time / 3:30 PM Central Time

Toll Free: 855-327-6837

International: 631-891-4304

Conference ID: 10021767

<https://ir.tayshagtx.com/news-events/events-presentations>

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform with a goal of dramatically improving patients' lives. More information is available at www.tayshagtx.com.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Announces Presentation on New Preclinical Data for TSHA-102 in Rett Syndrome at Upcoming American Society of Gene and Cell Therapy 26th Annual Meeting

DALLAS, April 27, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today announced that an abstract related to its TSHA-102 program in Rett syndrome was accepted for presentation at the upcoming American Society of Gene and Cell Therapy (ASGCT) 26th Annual Meeting, taking place in Los Angeles, CA from May 16-20, 2023. The abstract includes new preclinical data from a Taysha-sponsored study for TSHA-102, a self-complementary intrathecally delivered AAV9 gene transfer therapy in clinical evaluation for Rett syndrome, a rare neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene.

Details for the presentation are as follows:

Abstract Title: A Human-Ready Regulated AAV9/miniMECP2-miRARE Gene Therapy (TSHA-102) Improves Survival, Weight, and Behavior After Intracerebroventricular (ICV) Dosing in the Neonatal Knockout Rett (RTT) Mouse Model

Presenter: Sarah Sinnett, Ph.D., University of Texas Southwestern Medical Center, Co-Inventor of miRARE technology

Poster Session Date/Time: Friday, May 19 at 12-2 PM PT

Poster Session: Friday Poster Session

Poster Number: 1365

Additional details can be found at the ASGCT 26th Annual Meeting [website](#).

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform—an engine for potential new cures—with a goal of dramatically improving patients' lives. More information is available at www.tayshagtx.com.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Reports Fourth Quarter and Full Year 2022 Financial Results and Provides Corporate Update

Initiated screening of first potential subject in Phase 1/2 REVEAL trial in Rett syndrome; dosing of first adult patient with TSHA-102 expected in H1 2023; submitted protocol amendment to allow for younger patients; initial available Phase 1/2 clinical data, primarily on safety, expected in H1 2023

Clinical Trial Application (CTA) submission to United Kingdom (UK) MHRA for TSHA-102 in pediatric patients with Rett syndrome expected in mid-2023; Investigational New Drug (IND) application to United States (U.S.) Food and Drug Administration (FDA) in Rett syndrome anticipated in H2 2023

FDA feedback for TSHA-120 in giant axonal neuropathy (GAN) suggests consideration of alternative clinical trial designs for clinically meaningful and objectively measured treatment effects; Company plans to request a formal meeting with FDA to discuss final findings from currently ongoing comprehensive data analyses and potential regulatory path forward in Q2 2023

Conference call and live webcast today at 4:30 PM Eastern Time

DALLAS, March 28, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases of the central nervous system (CNS), today reported financial results for the fourth quarter and full-year ended December 31, 2022, and provided a corporate update.

"The actions taken early this year to improve execution and expedite progress on our two lead clinical programs in Rett syndrome and GAN are having a positive effect," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "We recently initiated screening of the first potential adult subject for the REVEAL Rett syndrome trial and remain on track to dose the first patient and deliver initial available first-in-human adult data, primarily on safety, for TSHA-102 in the first half of the year. Additionally, we recently submitted a protocol amendment to allow patients as young as 15 years old to be included in the study, which we believe will further expedite enrollment. We remain on track to submit a CTA to the MHRA in mid-2023 to conduct a pediatric Rett syndrome trial, and plan to submit an IND to the FDA for Rett syndrome in the second half of 2023. For TSHA-120 in GAN, based on the constructive feedback recently received from the FDA in response to our follow up questions to the formal Type B end-of-Phase 2 meeting minutes, coupled with the positive preliminary assessment of the ongoing comprehensive data analyses, we plan to submit a formal meeting request to the Agency in the second quarter of 2023 to discuss the potential regulatory pathway forward for this ultra-rare disease with no approved treatment."

Recent Corporate Highlights

TSHA-102 in Rett syndrome: a self-complementary intrathecally delivered AAV9 gene transfer therapy in clinical evaluation for Rett syndrome, a rare inherited genetic neurodevelopmental disorder. TSHA-102 utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) platform designed to regulate cellular MECP2 expression. TSHA-102 has received Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission.

- Screening initiated for first potential adult patient with Rett syndrome for the Phase 1/2 REVEAL trial
- Submitted protocol amendment expanding enrollment eligibility to include subjects ≥ 15 years
- Dosing of the first adult patient with Rett syndrome anticipated in H1 2023
- Initial available Phase 1/2 clinical data, primarily on safety, for TSHA-102 in adult patients with Rett syndrome expected in H1 2023, with planned quarterly updates on available clinical data thereafter
- CTA submission to UK MHRA for TSHA-102 in pediatric patients with Rett syndrome anticipated in mid-2023
- IND application submission to U.S. FDA for Rett syndrome expected in H2 2023
- Continued dosing of adult patients with Rett syndrome in the REVEAL trial in H2 2023

TSHA-120 for giant axonal neuropathy (GAN): a self-complementary intrathecally delivered AAV9 gene therapy in clinical evaluation for GAN, an ultra-rare inherited genetic neurodegenerative disorder with no approved treatments. TSHA-120 has received Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission.

- Completed CMC module 3 amendment submission to FDA detailing commercial process product manufacturing and drug comparability analysis
- Receipt of FDA's response to Taysha's follow up questions to the formal Type B end-of-Phase 2 meeting minutes

- FDA clarified MFM32, the primary efficacy scale discussed at the FDA Type B end-of-Phase 2 meeting, as a relevant primary endpoint only in the setting of a randomized double blind placebo controlled trial and acknowledged Taysha's challenge in executing and enrolling such a study design due to the ultra-rare nature of GAN
- FDA is open to regulatory flexibility in a controlled trial setting and willing to consider alternative study designs utilizing objective measurements to demonstrate a relatively large treatment effect that is self-evident and clinically meaningful
- Ongoing comprehensive analyses of functional, biological and electrophysiological assessments as part of totality of data evaluation to inform future interactions with the FDA
- Submission of a formal meeting request to the FDA planned in Q2 2023

Fourth Quarter and Full-Year 2022 Financial Highlights

Research and Development Expenses: Research and development expenses were \$13.9 million for the three months ended December 31, 2022, compared to \$37.9 million for the three months ended December 31, 2021. Research and development expenses were \$91.2 million for the full year ended December 31, 2022, compared to \$131.9 million for the full year ended December 31, 2021. The \$40.7 million decrease was primarily attributable to a decrease of \$20.3 million in research and development manufacturing and other raw material purchases and a \$9.0 million decrease in license fees. The decrease in research and development expenses for the year ended December 31, 2022 was also attributable to a \$12.0 million decrease in third-party research and development fees, mainly related to non-clinical studies and toxicology studies and a \$4.7 million decrease in compensation expense as a result of lower headcount. Overall, lower research and development expenses for the year ended December 31, 2022 were partially offset by higher clinical trial expenses of \$2.4 million and higher severance expense of \$2.9 million in 2022.

General and Administrative Expenses: General and administrative expenses were \$7.3 million for the three months ended December 31, 2022, compared to \$11.8 million for the three months ended December 31, 2021. General and administrative expenses were \$37.4 million for the year ended December 31, 2022, compared to \$41.3 million for the year ended December 31, 2021. The decrease of approximately \$3.9 million was primarily attributable to \$5.0 million of lower consulting professional fees and lower compensation expenses driven by lower headcount in 2022. Lower general and administrative expenses were partially offset by \$1.1 million of severance expense.

Net loss: Net loss for the three months ended December 31, 2022 was \$55.7 million, or \$0.99 per share, as compared to a net loss of \$50.4 million, or \$1.32 per share, for the three months ended December 31, 2021. In November 2022, we recorded a \$36.4 million non-cash, non-recurring impairment charge related to the North Carolina manufacturing facility. The net loss for the three months ended December 31, 2022 was partially offset by revenue of \$2.5 million recognized related to the Astellas Transactions. Net loss for the full year ended December 31, 2022 was \$166.0 million or \$3.78 per share, as compared to a net loss of \$174.5 million, or \$4.64 per share, for the full year ended December 31, 2021.

Cash and cash equivalents: As of December 31, 2022, Taysha had \$87.9 million in cash and cash equivalents. The Company continues to expect that its current cash resources will support planned operating expenses and capital requirements into the first quarter of 2024.

Conference Call and Webcast Information

Taysha management will hold a conference call and webcast today at 4:30 pm ET to review its financial and operating results and to provide a corporate update. The dial-in number for the conference call is 877-407-0792 (U.S./Canada) or 201-689-8263 (international). The conference ID for all callers is 13736479. The live webcast and replay may be accessed by visiting Taysha's website at <https://ir.tayshagtx.com/news-events/events-presentations>. An archived version of the webcast will be available on the website for 30 days.

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform—an engine for potential new cures—with a goal of dramatically improving patients' lives. More information is available at www.tayshagtx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "anticipates," "believes," "expects," "intends," "projects," "plans," and "future" or similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements concerning the potential of TSHA-102 and TSHA-120 to positively impact quality of life and alter the course of disease in the patients we seek to treat, our research, development and regulatory plans for our product candidates, the potential for these product candidates to receive regulatory approval from the FDA or equivalent foreign regulatory agencies, and whether, if approved, these product candidates will be successfully distributed and marketed, the potential market opportunity for these product candidates, our corporate growth plans, the forecast of our cash runway. Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our Annual Report on Form 10-K for the full-year ended December 31, 2022, which is available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that we make from time to time with the SEC. Such risks may be amplified by the impacts of the COVID-19 pandemic. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

	For the three months ended		For the twelve months ended	
	December 31 2022	December 31 2021	December 31 2022	December 31 2021
Revenue:				
Service Revenue	\$ 2,502	-	\$ 2,502	\$ -
Operating expenses:				
Research and development	13,861	37,918	91,169	131,943
General and administrative	7,341	11,806	37,360	41,324
Impairment of long-lived assets	36,420	-	36,420	-
Total operating expenses	57,622	49,724	164,949	173,267
Loss from operations	(55,120)	(49,724)	(162,447)	(173,267)
Other income (expense):				
Interest Income	199	29	249	172
Interest expense	(796)	(691)	(3,798)	(1,428)
Other	(6)	-	(18)	-
Total other income (expense)	(603)	(662)	(3,567)	(1,256)
Net loss	\$ (55,723)	\$ (50,386)	\$ (166,014)	\$ (174,523)
Net loss per common share, basic and diluted	\$ (0.99)	\$ (1.32)	\$ (3.78)	\$ (4.64)
Weighted average common shares outstanding, basic and diluted	56,386,130	38,110,597	43,952,015	37,650,566

Taysha Gene Therapies, Inc.
Condensed Consolidated Balance Sheet Data
(in thousands, except share and per share data)
(Unaudited)

	December 31, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 87,880	\$ 149,103
Prepaid expenses and other current assets	8,537	10,499
Total current assets	96,417	159,602
Restricted cash	2,637	2,637
Property, plant and equipment, net	14,963	50,610
Operating lease right-of-use assets	10,943	-
Other noncurrent assets	1,316	1,107
Total assets	\$ 126,276	\$ 213,956
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	\$ 10,946	\$ 21,763
Accrued expenses and other current liabilities	18,287	29,983
Deferred revenue	33,557	-
Total current liabilities	62,790	51,746
Build-to-suit lease liability	-	25,900
Term loan, net	37,967	37,192
Operating lease liability, net of current portion	20,440	-
Other noncurrent liabilities	4,130	3,735
Total liabilities	125,327	118,573
Stockholders' equity		

Common stock, \$0.00001 par value per share; 200,000,000 shares authorized and 63,207,507 issued and outstanding as of December 31, 2022 and 38,473,945 outstanding as of December 31, 2021

Additional paid-in capital	402,389	331,032
Accumulated deficit	(401,441)	(235,649)
Total stockholders' equity	949	95,383
Total liabilities and stockholders' equity	\$ 126,276	\$ 213,956

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies to Release Fourth Quarter and Full-Year 2022 Financial Results and Host Conference Call and Webcast on March 28

DALLAS, March 15, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a patient-centric, clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic rare diseases of the central nervous system (CNS), today announced that it will report its financial results for the fourth quarter and full-year ended December 31, 2022, and host a corporate update conference call and webcast on Tuesday, March 28, 2023, at 4:30 PM Eastern Time.

Conference Call Details

Tuesday, March 28, at 4:30 PM Eastern Time / 3:30 PM Central Time

Toll Free: 877-407-0792
International: 201-689-8263
Conference ID: 13736479
Webcast: <https://ir.tayshagtx.com/news-events/events-presentations>

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform—an engine for potential new cures—with a goal of dramatically improving patients' lives. More information is available at www.tayshagtx.com.

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Source: Taysha Gene Therapies, Inc.



Taysha Gene Therapies Provides Update on TSHA-120 Program in Giant Axonal Neuropathy and a 2023 Corporate Outlook

Type B end-of-Phase 2 meeting with U.S. Food and Drug Administration (FDA) provided additional clarity for TSHA-120 for the treatment of giant axonal neuropathy (GAN) ultra-rare disease program

- FDA acknowledged MFM32 as an acceptable endpoint with a recommendation to dose additional patients in a double-blind, placebo-controlled design to support Biologics License Application (BLA) submission

Organizational and business review by new management with operational, structural and personnel changes implemented to enhance execution

Dosing of first adult patient with Rett syndrome from ongoing trial in Canada expected in H1 2023; update of initial available clinical data anticipated in H1 2023 with quarterly updates primarily on safety thereafter

Submission of Clinical Trial Application (CTA) to United Kingdom (UK) MHRA for TSHA-102 in pediatric patients with Rett syndrome expected in mid-2023

Submission of an Investigational New Drug (IND) application for TSHA-102 for Rett syndrome to FDA planned in H2 2023

Conference call and live webcast today at 4:30 PM Eastern Time

DALLAS, Jan. 31, 2023 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a patient-centric, clinical -stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic rare diseases of the central nervous system (CNS), today provided an update on the TSHA-120 program in giant axonal neuropathy (GAN) and a corporate outlook for 2023.

"We expect to deliver on several key milestones in 2023, including the generation of first-in-human adult clinical data in Rett syndrome, CTA submission to MHRA to enable initiation of our pediatric Rett syndrome program and submission of an IND for Rett syndrome in the U.S. to further expand our clinical study footprint. For our GAN program, we received the formal FDA meeting minutes and recently submitted follow up questions to clarify some of their recommendations including the feasibility of a proposed study design and the totality of evidence required for BLA submission. Their feedback will help inform next steps for the program in this ultra-rare indication with no approved treatments," said Sean P. Nolan, Chairman and Chief Executive Officer of Taysha. "I believe that the operational, structural and personnel actions recently implemented position us well to execute across our near-term milestones and deliver on our commitments to key stakeholders, especially patients."

Clinical Program Updates

TSHA-120 in GAN:

- Receipt of formal written meeting minutes from FDA in January 2023 following completion of Type B end-of-Phase 2 meeting
 - Overall approach to manufacturing of pivotal/to-be marketed product deemed appropriate pending review of a planned submission of Chemistry, Manufacturing, and Controls (CMC) data package for TSHA-120
 - FDA acknowledged MFM32 as an acceptable endpoint with a recommendation to dose additional patients in a double-blind, placebo-controlled design to support BLA submission
- Awaiting response from FDA on follow up questions the Company submitted on recommended design and totality of evidence required for BLA submission

TSHA-102 in Rett syndrome:

- Dosing of the first adult patient with Rett syndrome anticipated in H1 2023
- Initial available clinical data for TSHA-102 in the adult Rett syndrome study expected in H1 2023 with planned quarterly updates on available clinical data primarily on safety from the adult study thereafter
- Company anticipates submission of a CTA to UK MHRA for TSHA-102 in pediatric patients with Rett syndrome in mid-2023
- Company plans to submit an IND application for Rett syndrome to FDA in H2 2023

Corporate Updates

- Operational, structural and personnel changes implemented following thorough business review to enhance execution

Conference Call and Webcast Information

Taysha management will hold a conference call and webcast today at 4:30 pm ET to provide regulatory feedback from FDA on the GAN program and a corporate update. The dial-in number for the conference call is 877-407-0792 (U.S./Canada) or 201-689-8263 (international). The conference ID for all callers is 13736009. The live webcast and replay may be accessed by visiting Taysha's website at <https://ir.tayshagtx.com/news-events/events-presentations>. An archived version of the webcast will be available on the website for 30 days.

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program to build an extensive, AAV gene therapy pipeline focused on both rare and large-market indications. Together, we leverage our fully integrated platform—an engine for potential new cures—with a goal of dramatically improving patients' lives. More information is available at www.tayshagtx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "anticipates," "believes," "expects," "intends," "projects," "plans," and "future" or similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements concerning the potential of our product candidates, such as TSHA-120 and TSHA-102 and including our preclinical product candidates, to positively impact quality of life and alter the course of disease in the patients we seek to treat, our research, development and regulatory plans for our product candidates, the potential for these product candidates to receive regulatory approval from the FDA or equivalent foreign regulatory agencies, and whether, if approved, these product candidates will be successfully distributed and marketed, the potential market opportunity for these product candidates, our corporate growth plans and the impacts of our corporate operational, structural and personnel changes. Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our Annual Report on Form 10-K for the full-year ended December 31, 2021 and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, both of which are available on the SEC's website at www.sec.gov. Additional information will be made available in other filings that we make from time to time with the SEC. Such risks may be amplified by the impacts of the COVID-19 pandemic. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

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Source: Taysha Gene Therapies, Inc.



R&D Day

June 28, 2023 | 9:00 AM CT / 10:00 AM ET

Legal disclosure

FORWARD LOOKING STATEMENTS

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are subject to a number of risks, uncertainties and assumptions. Risks regarding our business are described in detail in our Securities and Exchange Commission filings, including in our Annual Report on Form 10-K for the year ended December 31, 2022. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements contained in this presentation reflect our current views with respect to future events, and we assume no obligation to update any forward-looking statements except as required by applicable law.

This presentation includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. All of the market data used in this prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

Introduction

SEAN NOLAN

Board Chairman and Chief Executive Officer

Agenda

Topic	Presenter
Introduction	Sean Nolan
TSHA-120 Program Overview and History	Sukumar Nagendran, MD
GAN Disease Overview and New Clinical Data Update	Salman Bhai, MD
Regulatory Path Forward for TSHA-120	Sukumar Nagendran, MD
Rett Disease Overview and New Clinical Data Update	Azhar Rana, MD
Q&A and Closing Remarks	Sean Nolan

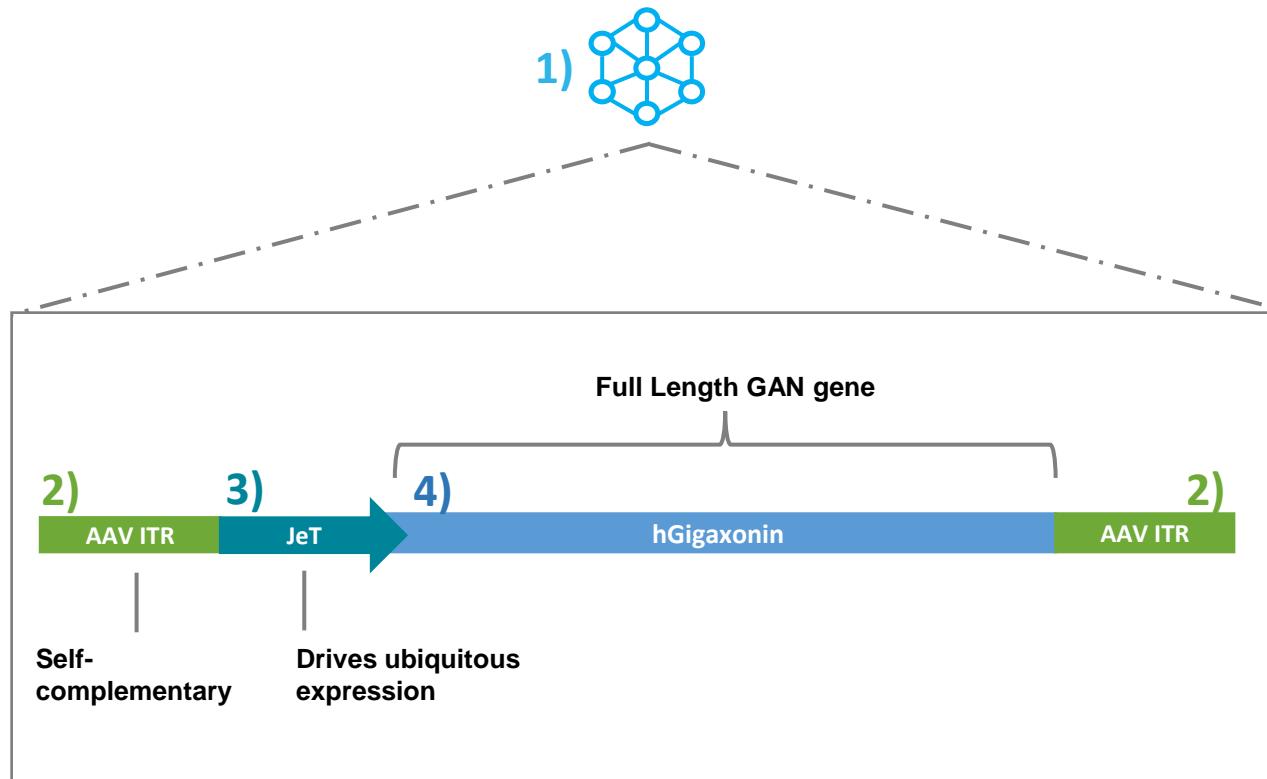
Program Overview and History: TSHA-120, an Investigational Gene Therapy for GAN

SUKU NAGENDRAN, MD

President and Head of R&D



TSHA-120 construct design aims to address the root cause of giant axonal neuropathy (GAN)



TSHA-120

- 1) AAV9 viral vector with engineered transgene encoding the human gigaxonin protein
- 2) Self-complementary inverted terminal repeats (ITR) for rapid activation and stable expression
- 3) JeT promoter drives ubiquitous expression
- 4) Designed to deliver a codon optimized, functional copy of the GAN gene with optimal tropism for rapid expression

NIH initiated a natural history (NH) basket study in 2012 that included GAN

Study design

- Clinical and Molecular Manifestations of Neuromuscular and Neurogenetic Disorders of Childhood
- Diagnostic and prospective longitudinal natural history study
- Data collected over a period of 10 years
- n=5650*; of which 53 have a genetic diagnosis of GAN
- Aged 3-21 years

Main outcome measures

- Diagnose and characterize patients with neuromuscular and neurogenetic disorders with congenital or pediatric onset and study the natural history and underlying disease mechanism
- Identify and develop effective outcome measures for use in future clinical trials

*The full study was a genetic, nerve and muscle disorder basket natural history study

Clinical Trial: NCT01568658

This study presents the largest collection of GAN NH data in world

Natural history data of first 45 GAN patients published in *Brain*

Cross-sectional baseline data from GAN patients in the NH study served as the external control for the Phase 1/2 clinical trial evaluating TSJA-120 for the treatment of GAN

- 45 subjects (3-21 years) with genetically confirmed GAN
- Mean age of symptom onset for the full cohort is 2.9 years

doi:10.1093/brain/awab179 BRAIN 2021; 144; 3239–3250 | 3239

BRAIN
ORIGINAL ARTICLE



Giant axonal neuropathy: cross-sectional analysis of a large natural history cohort

Diana X. Bharucha-Goebel,^{1,2} Gina Norato,³ Dimah Saade,¹ Eduardo Paredes,¹ Victoria Biancavilla,⁴ Sandra Donkervoort,¹ Rupleen Kaur,¹ Tanya Lehky,⁵ Margaret Fink,¹ Diane Armao,^{6,7} Steven J. Gray,⁸ Melissa Waite,⁴ Sarah Debs,¹ Gilberto Averion,¹ Ying Hu,¹ Wadih M. Zein,⁹ A. Reghan Foley,¹ Minal Jain⁴ and Carsten G. Bönnemann¹

Giant axonal neuropathy (GAN) is an ultra-rare autosomal recessive, progressive neurodegenerative disease with early childhood onset that presents as a prominent sensorimotor neuropathy and commonly progresses to affect both the PNS and CNS. The disease is caused by biallelic mutations in the GAN gene located on 16q23.2, leading to loss of functional gigaxonin, a substrate specific ubiquitin ligase adapter protein necessary for the regulation of intermediate filament turnover. Here, we report on cross-sectional data from the first study visit of a prospectively collected natural history study of 45 individuals, age range 3–21 years with genetically confirmed GAN to describe and cross-correlate baseline clinical and functional cohort characteristics. We review causative variants distributed throughout the GAN gene in this cohort and identify a recurrent founder mutation in individuals with GAN of Mexican descent as well as cases of recurrent uniparental isodisomy. Through cross-correlational analysis of measures of strength, motor function and electrophysiological markers of disease severity, we identified the Motor Function Measure 32 to have the strongest correlation across measures and age in individuals with GAN. We analysed the Motor Function Measure 32 scores as they correspond to age and ambulatory status. Importantly, we identified and characterized a subcohort of individuals with a milder form of GAN and with a presentation similar to Charcot–Marie–Tooth disease. Such a clinical presentation is distinct from the classic presentation of GAN, and we demonstrate how the two groups diverge in performance on the Motor Function Measure 32 and other functional motor scales. We further present data on the first systematic clinical analysis of autonomic impairment in GAN as performed on a subset of the natural history cohort. Our cohort of individuals with genetically confirmed GAN is the largest reported to date and highlights the clinical heterogeneity and the unique phenotypic and functional characteristics of GAN in relation to disease state. The present work is designed to serve as a foundation for a prospective natural history study and functions in concert with the ongoing gene therapy trial for children with GAN.

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Phase 1/2 dose-escalating interventional study began enrolling in 2015

Study design	<ul style="list-style-type: none">• Open-label, dose-escalation, non-randomized, single-center interventional Phase 1/2 trial• Safety, tolerability and efficacy of TSHA-120 in participants with GAN• Up to 15 years follow up (84.5 months longitudinal follow-up as of 03, May 2023)• n=14 (up to 21 subjects, 14 enrolled)
Dose cohorts	<ul style="list-style-type: none">• Low: 1.0×10^{13} total vg ($n=2$)• Medium-low: 3.5×10^{13} ($n=4$)• Medium-high: 5.3×10^{13} total vg ($n=5$)• High: 1.0×10^{14} total vg ($n=3$)
Key inclusion criteria	<ul style="list-style-type: none">• Genetic confirmation of GAN• 3 years of age and older
Route of administration	<ul style="list-style-type: none">• Delivered intrathecally
Main outcome measures (12 months)	<ul style="list-style-type: none">• Safety of the vector• Safety and tolerability of gene transfer in patients with null mutations receiving immunosuppression• Motor function (e.g., <i>MFM</i>, <i>FARS</i>, <i>NIS</i>, <i>myometry</i>, <i>timed motor functions</i>)• Electrophysiologic assessment (nerve conduction) of sensory-motor nerves• Neuropathology in peripheral nerve biopsies (e.g., <i>superficial radial nerve</i>, <i>skin biopsies</i>)• Examination of cerebrospinal fluid to monitor for inflammatory markers• Assessment of vector shedding

Clinical Trial: NCT02362438

Historical overview of recent interactions with the FDA

December 2022-February 2023	January 2023-Present	Next Steps
Type B End-of-Phase 2 Meeting	Totality of Data Analysis	FDA Interactions
<ul style="list-style-type: none">Presented FDA with a subset of available evidence suggesting favorable benefit/risk profile of TSHA-120Significant emphasis placed on MFM32 as primary endpointFDA suggested a double-blind placebo-controlled study given “effort dependent” endpoint and the heterogeneity of disease progression in GANSubsequent feedback from FDA highlighted openness to an alternate study design that's “well controlled” and demonstrates significant impact on clinically meaningful, objective endpoints	<ul style="list-style-type: none">Taysha obtained all available data from 7+ years of the interventional trial and 10+ years of from the natural history study and initiated comprehensive analysisDeveloped a disease progression model (DPM)* to serve as external control demonstrating a predictable and homogenous disease progressionNew data analysis reinforces a clinically meaningful treatment effect*: <ul style="list-style-type: none">Functional Measures: MFM32, mFARS, LogMARElectrophysiological Measures: SNAP, CMAPBiological Measures: Nerve biopsies	<ul style="list-style-type: none">Taysha anticipates formal FDA meeting in Q3 2023In this meeting, Taysha plans to address FDA's previous feedback and present updated analysis to align on path forward

*The DPM models classic GAN only



GAN Disease Overview and New Clinical Data

SALMAN BHAI, MD

Assistant Professor of Neurology at UTSW and Director of the
Neuromuscular Center at the Institute for Exercise and Environmental
Medicine



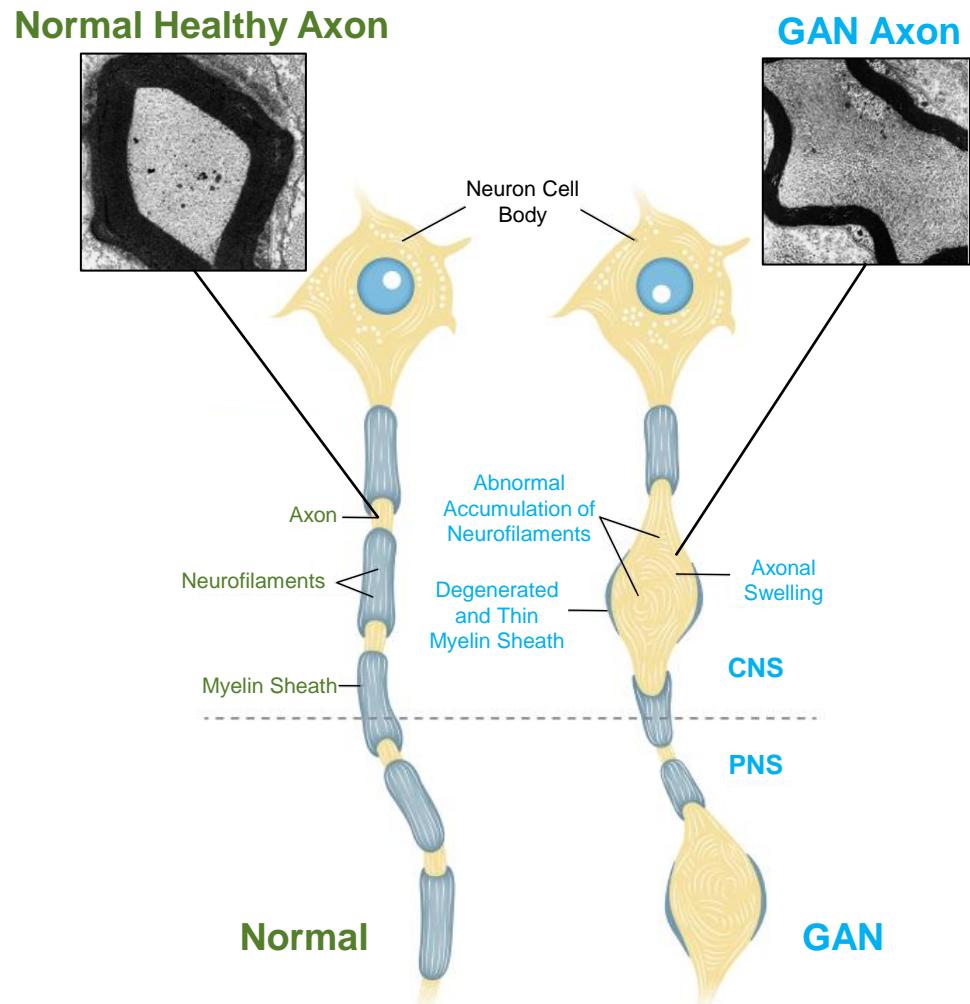
Giant axonal neuropathy (GAN) disease overview

- GAN is an ultra-rare, autosomal recessive, progressive neurodegenerative disease that impacts the central, peripheral and autonomic nervous systems
- Biallelic variants in the GAN gene result in deficiency or complete loss-of-function of gigaxonin and the accumulation of intermediate filaments (IF)
- Accumulation of IF in axons (morphologically "giant" axons) causes neurodegeneration
 - Length-dependent progressive sensory motor axonal neuropathy
 - Progressive cerebellar ataxia

Disease progression:

- Patients with classical phenotype are clinically identified due to delayed developmental milestones between 2 and 3 years of age and tightly curled hair
- A highly predictable decline in balance and distal muscle strength typically leading to loss of ambulation by age 10
- Disease progresses with unsteady gait, limb ataxia, distal muscle weakness in arms and legs, followed by proximal muscle weakness, intellectual disability, and death by the third decade of life, often due to respiratory failure
- Progressive optic nerve atrophy seen early on results in increasing deterioration of visual acuity

No treatments are currently approved; current treatments are palliative only



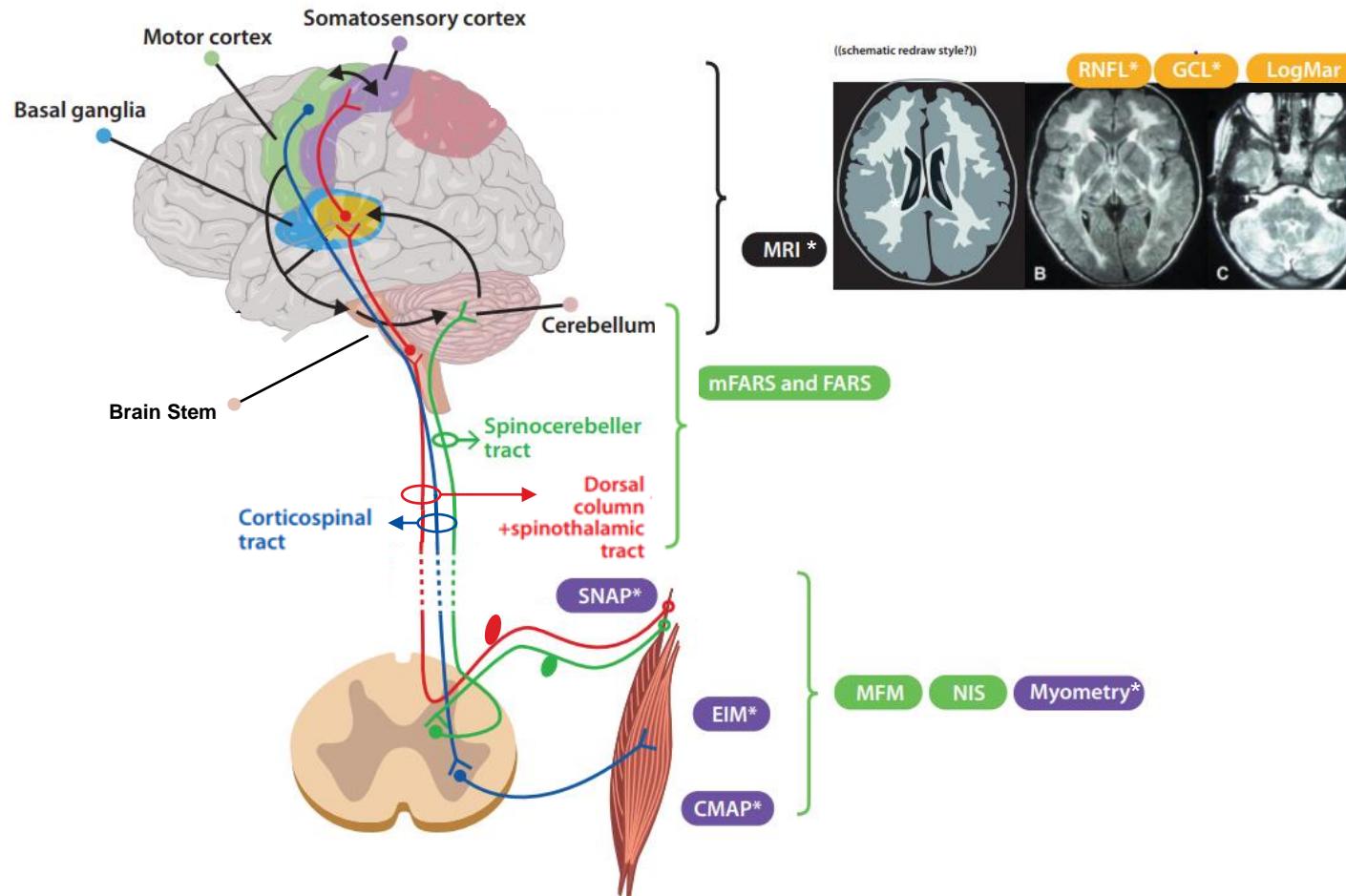
Source: Bharucha-Goebel DX et al. Giant axonal neuropathy: cross-sectional analysis of a large natural history cohort. *Brain*. 2021;144(10):3239-3250.

Opal P. GAN-Related Neurodegeneration. 2003 Jan 9 [Updated 2021 Oct 14]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1136/>

MedlinePlus (2021) Giant Axonal Neuropathy. 2022:01 January 2022. Available from: <https://medlineplus.gov/genetics/condition/giant-axonal-neuropathy/>

Integrated, multisystem assessment of GAN

SNAP – Sensory Nerve Action Potential; **CMAP** – Compound Muscle Action Potential; **EIM** – Electrical Impedance Myography; **LogMAR** – Logarithm of the Minimum Angle of Resolution; **FARS**-Friedreich Ataxia Rating Scale; **GCL** – Ganglion cell layer; **mFARS** – modified FARS; **NIS** – Neuropsychological Impairment Scale; **RNFL** – retinal nerve fiber layer



Key

Functional Outcomes

PNS Clinical Data

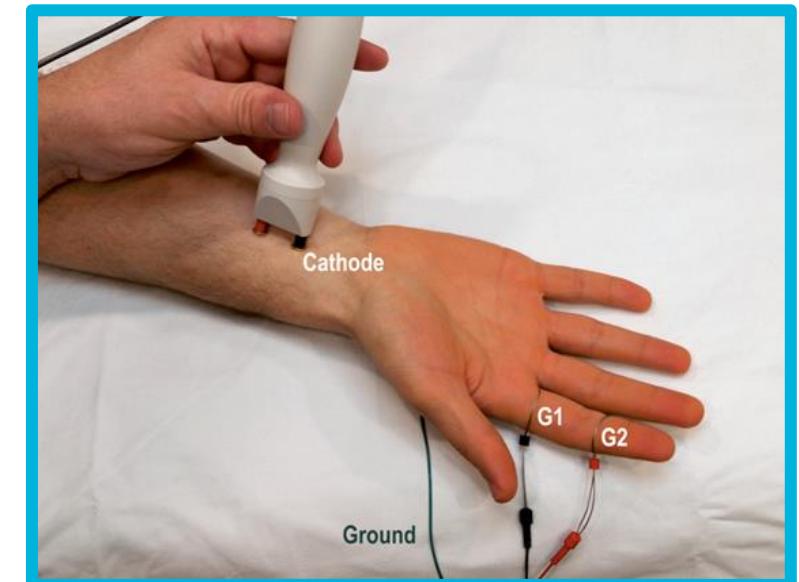
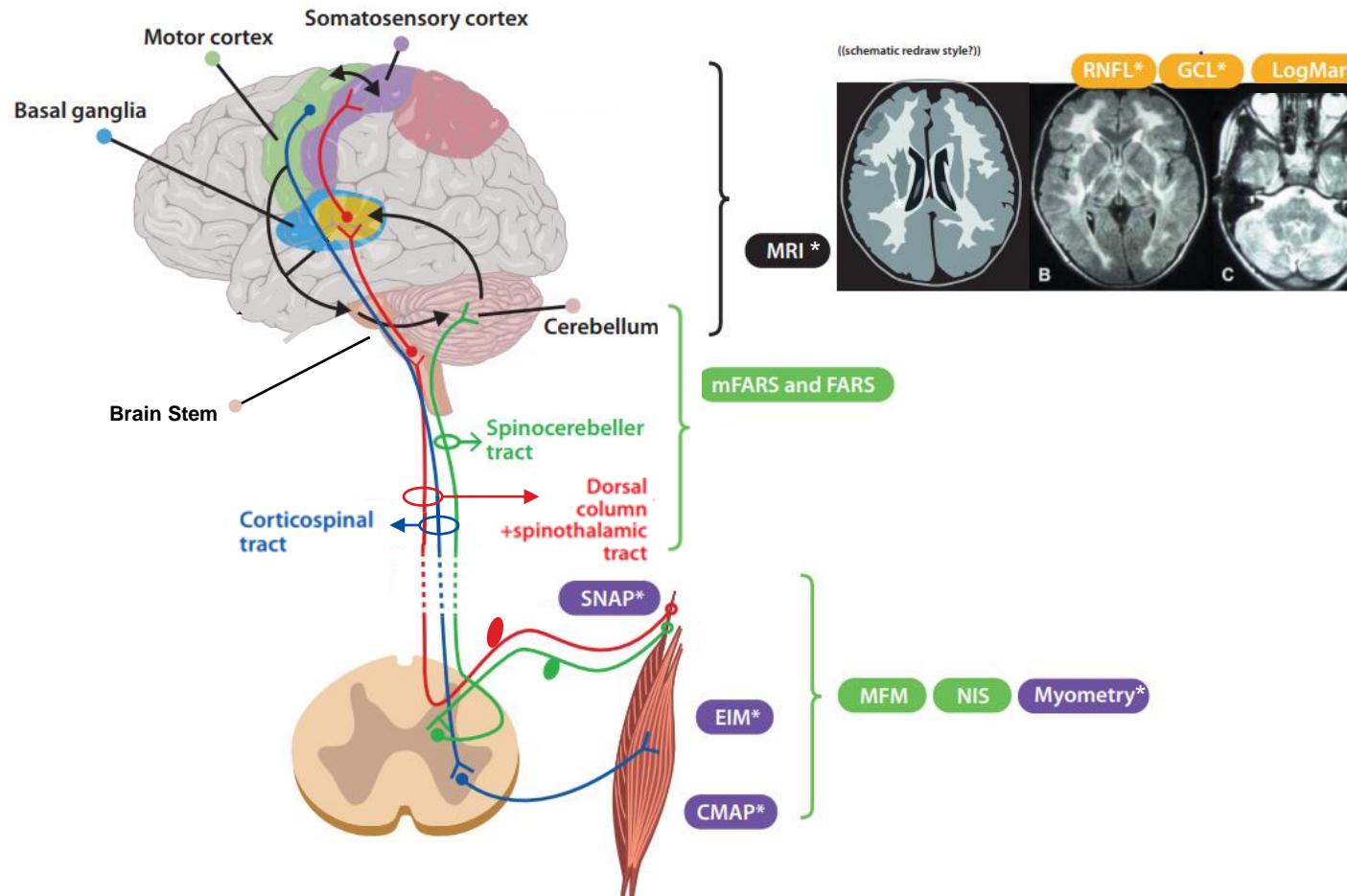
Ophthalmology

CNS Clinical Data

*Objective Measures

Integrated, multisystem assessment of GAN

SNAP – Sensory Nerve Action Potential; **CMAP** – Compound Muscle Action Potential; **EIM** – Electrical Impedance Myography; **LogMAR** – Logarithm of the Minimum Angle of Resolution; **FARS**-Friedreich Ataxia Rating Scale; **GCL** – Ganglion cell layer; **mFARS** – modified FARS; **NIS** – Neuropsychological Impairment Scale; **RNFL** – retinal nerve fiber layer



T
Source: David C. Preston, Barbara Shapiro Electromyography and Neuromuscular Disorders: Clinical Electrophysiologic Correlations. 2. Elsevier. 2005.

New disease progression model (DPM) supports the use of natural history data as external control

Activities of Daily Living

Clinical Functional Endpoints

MFM32, mFARS, LogMAR



Electrophysiological Endpoints

SNAP, CMAP

(not subject to effort dependency)



Biological Endpoints

visual acuity, nerve biopsies

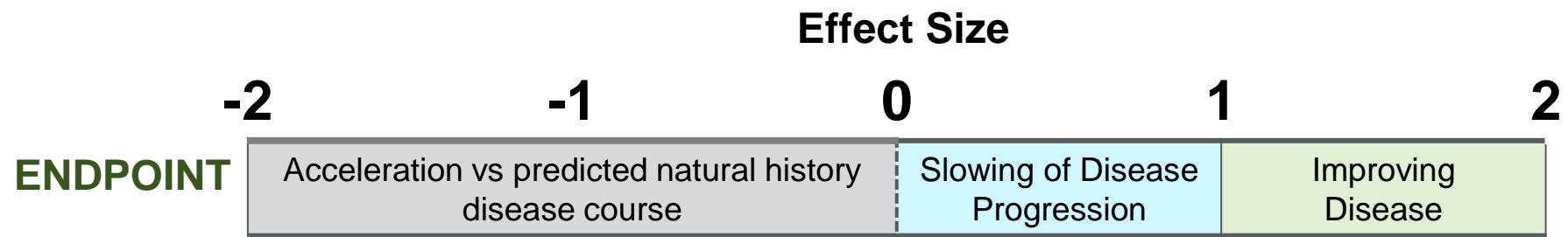
(not subject to effort dependency)

Bayesian DPM establishes a predictable disease course – this enables Taysha to address FDA's concerns in the context of an ultra-rare disease

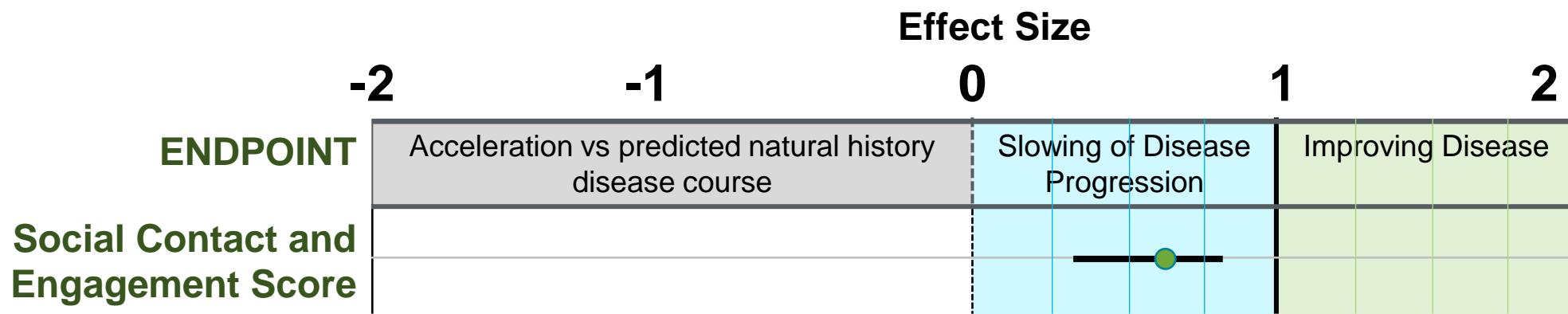
1. Benefits over Patient as Own Control (PAOC): shows homogeneity and monotonicity of disease and can account for limited pre-treatment data
2. DPM confidently estimates a treatment effect across many biological and clinical functional endpoints
3. DPM accepted by regulatory agencies in interventional studies of rare diseases and small patient populations, per FDA's recently published guidance¹



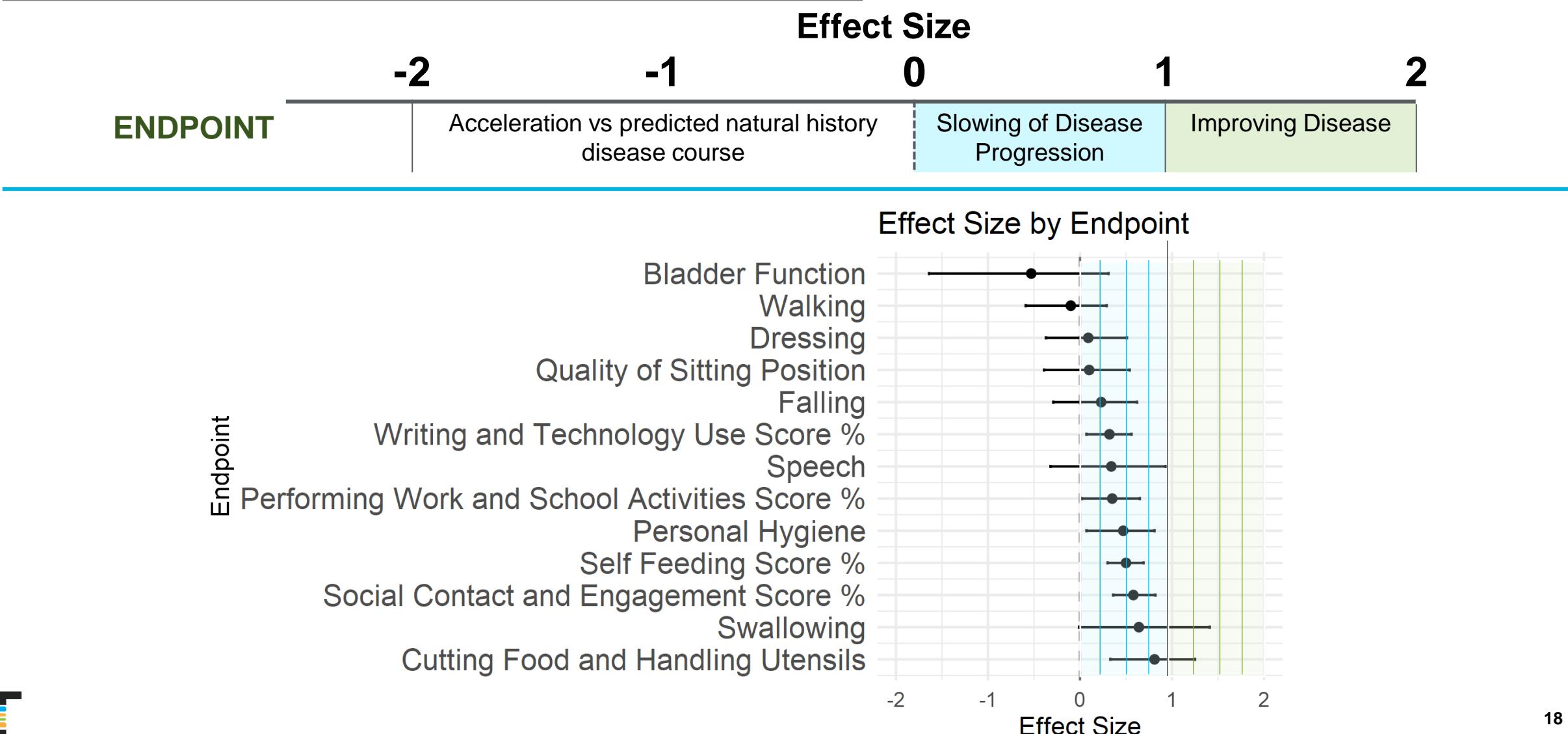
Measuring effect size



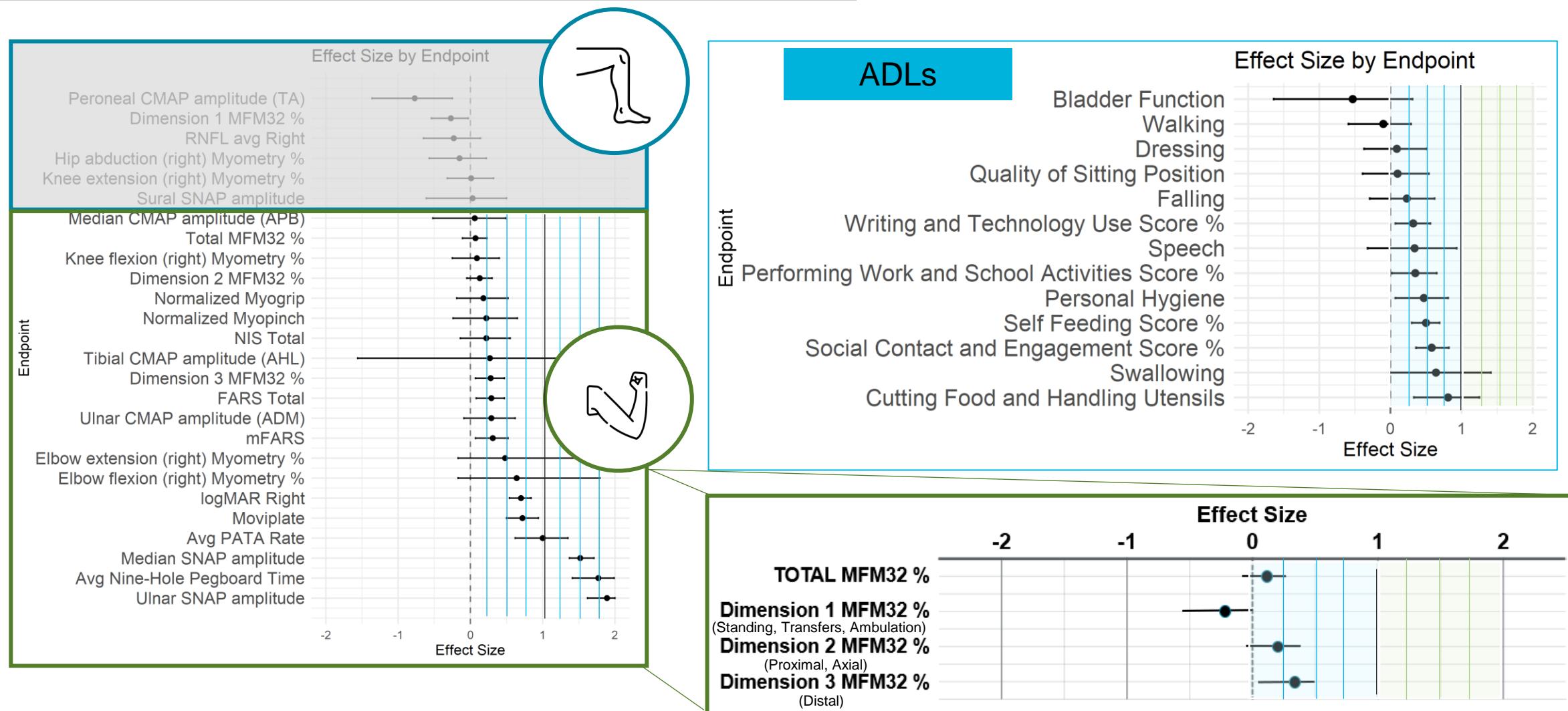
Measuring effect size



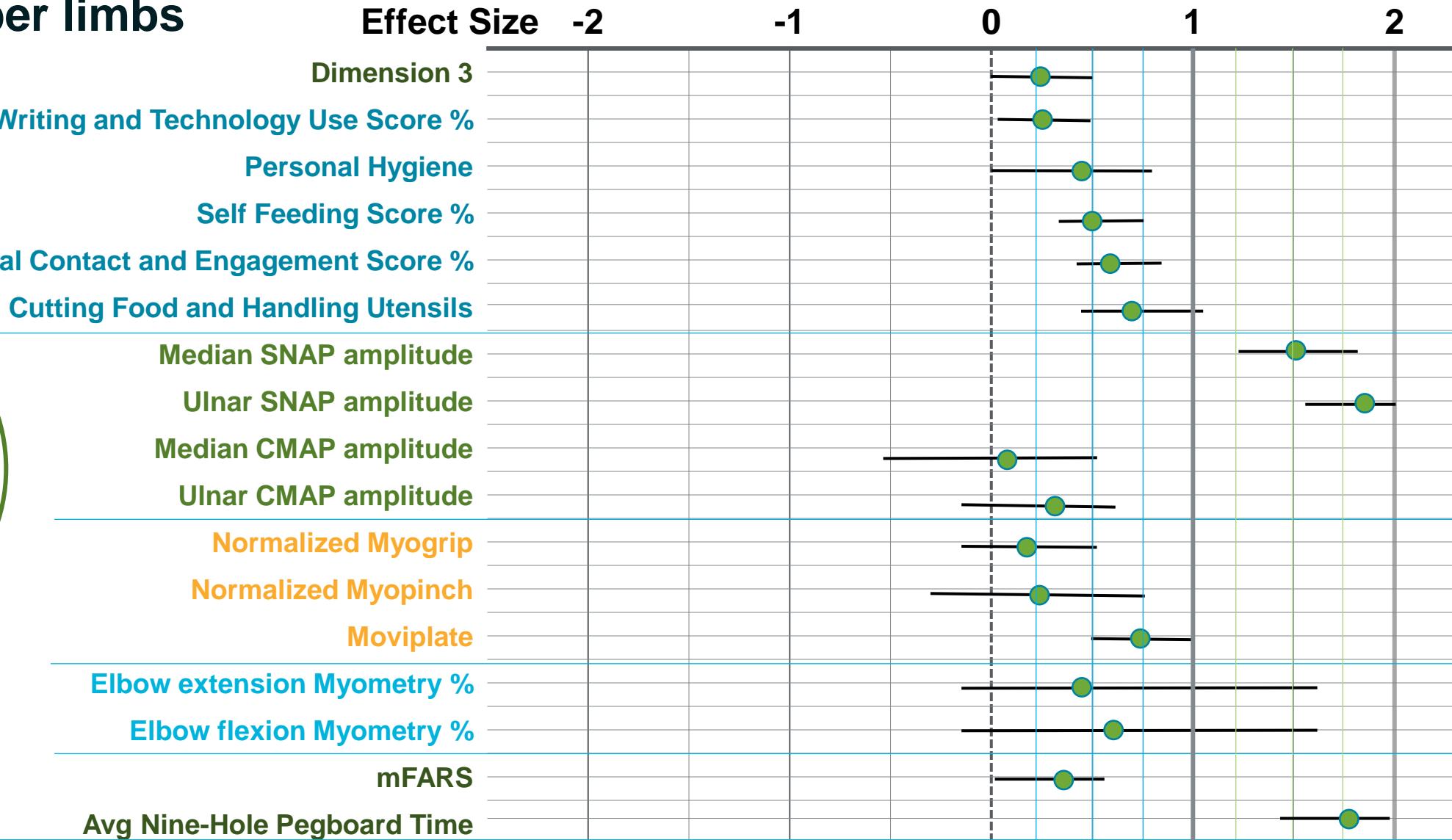
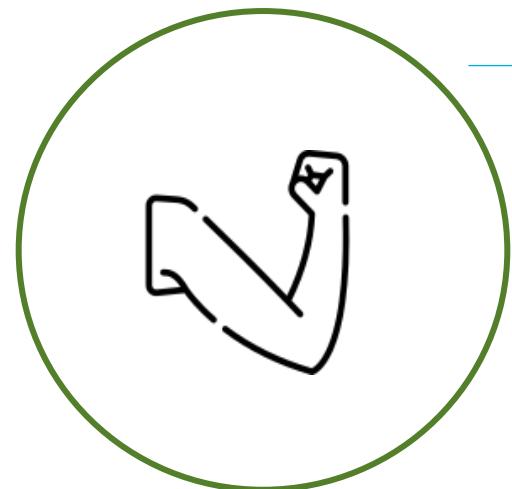
Understanding observed effect size on patients' Activities of Daily Living (ADL)



Majority of endpoint measures are consistent with a slowing of the rate of disease progression post-dosing with TSHA-120, compared to DPM



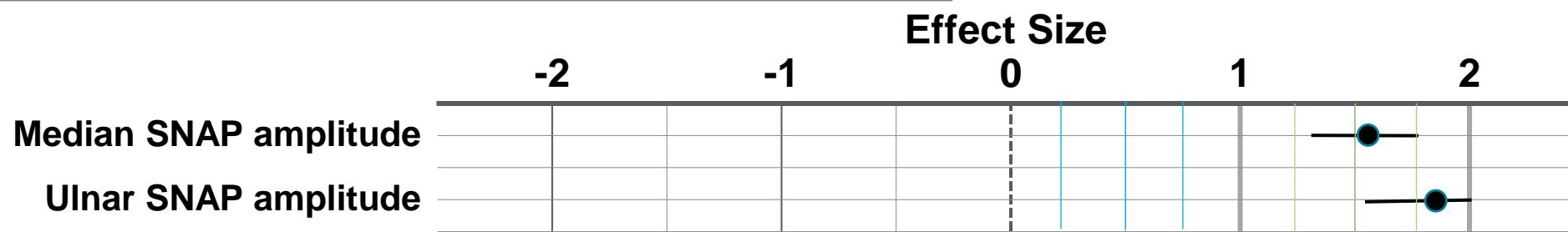
Moderate to robust treatment effects observed in categories related to personal independence and self-care, particularly activities involving the use of the upper limbs



Source: Company data –
preliminary data, subject to change

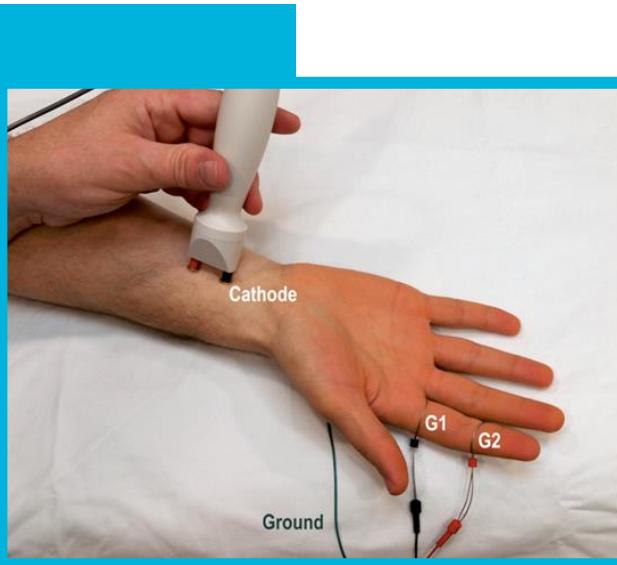
Results suggest direct and real benefit to patients with ancillary reduction of caregiver burden anticipated

Restoration of sensory nerve action potential (SNAP) and increased regenerative clusters on nerve biopsy



5 patients experienced a gain in nerve conduction amplitude post treatment, suggesting neuroregeneration

4 of the 5 patients that had stabilization or improvements in SNAPs had increased regenerative clusters on nerve biopsy



Nerve conduction study of sensory nerves revealed that most interventional study participants were at an advanced state of the disease when first treated with TSHA-120 and had abnormal SNAP responses at baseline

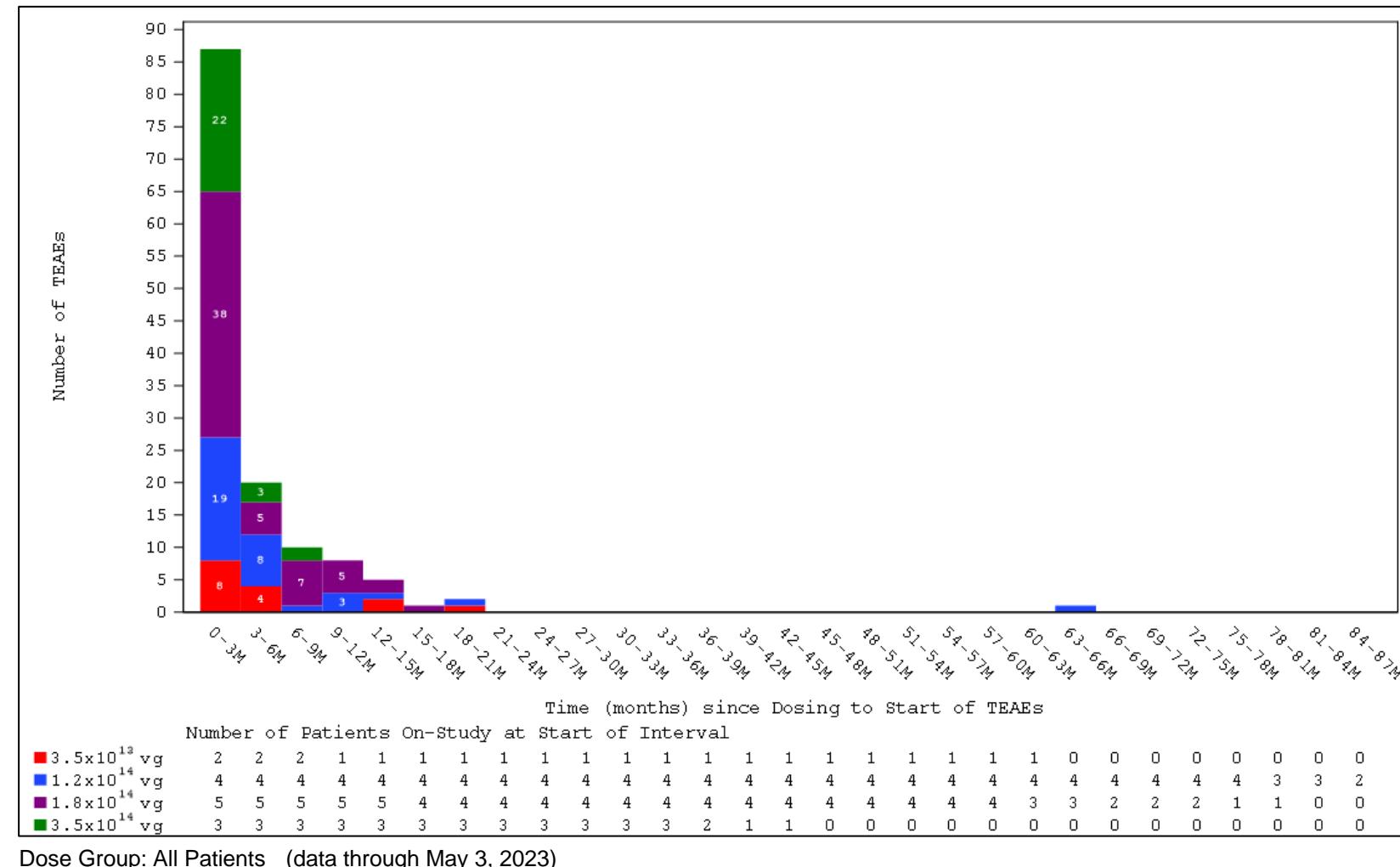


Source: Company data – preliminary data, subject to change

David C. Preston, Barbara Shapiro Electromyography and Neuromuscular Disorders: Clinical Electrophysiologic Correlations. 2. Elsevier. 2005.

Approximately seven years of long-term clinical data support safety and tolerability of TSHA-120, with no significant safety issues

- No dose-limiting toxicity
- Some evidence of asymptomatic cerebrospinal fluid pleocytosis
- Well-tolerated at multiple doses and safely dosed in the presence of neutralizing antibodies
- No signs of significant acute or subacute inflammation, no sudden sensory changes and no drug-related or persisting transaminitis
- All serious adverse events (SAEs) were deemed unrelated or unlikely to be related to TSHA-120 other than one event of Pyrexia(Gr1, resolved within 4 days)



New data analysis shows an overall impact of treatment on both objective biological and clinically relevant endpoints

GAN is a disorder of the CNS (leukodystrophy) and PNS (CMT)

Combination of weakness and ataxia support clinical relevance of MFM32 and mFARS

Disease Progression Model shows homogeneity of disease progression

The DPM supports the use of NH data as external control

Clinician reported and functional outcomes are supported by objective clinical and biological data unsusceptible to bias

Peripheral nerve regeneration supported by SNAPs and regenerative clusters in a dose-dependent manner

Biological Data + Clinical Data + Clinician Reported and Functional Outcomes

Patients' Activities of Daily Living

We believe in the transformative potential of TSHA-120 to bring meaningful change to patients and families impacted by this ultra-rare disease with no approved treatments.

Regulatory Path Forward for GAN

SUKU NAGENDRAN, MD

President and Head of R&D



Company position: existing data supports approval of TSHA-120 for the treatment of GAN

High unmet need	<ul style="list-style-type: none">GAN is a devastating ultra-rare disease with no approved treatments
Robust dataset	<ul style="list-style-type: none">Robust natural history and interventional study datasets represent a significant percentage of the known patient population
DPM enables external control	<ul style="list-style-type: none">DPM demonstrates monotonicity and homogenous disease progression – supports potential for NH to serve as a suitable external control
Promising new data and analysis	<ul style="list-style-type: none">New analysis demonstrates weakness and ataxia are major sources of disability in GANMultiple objective and clinically meaningful endpoints identified to demonstrate efficacy<ul style="list-style-type: none">Functional: mFARS, MFM32, LogMAR<ul style="list-style-type: none"><i>mFARS recently served as basis for approval of Friedreich's ataxia drug</i>Electrophysiological: SNAP, CMAPBiological: visual acuity, nerve biopsies
Established safety	<ul style="list-style-type: none">Approximately 7 years of safety data

Patients need treatment options

The benefit of treatment outweighs the risk in this devastating disease, where there are no approved treatments.



Program Overview and Update: TSHA-102, an Investigational Gene Therapy for Rett Syndrome

AZHAR RANA, MD

Head of Medical Affairs



Rett syndrome is a devastating rare neurological disorder with high unmet medical need

- Rett syndrome is a rare neurological disorder caused by mutations in the X-linked *MECP2* gene
 - *MECP2* regulates the expression of many genes involved in normal brain function and mutations lead to impaired brain development and function
- Disorder causes intellectual disabilities, loss of communication abilities, seizures, slowing and/or regression of development, motor and respiratory impairment and shortened life expectancy
- No approved disease-modifying therapies exist that treat the genetic root cause of the disease
- Estimated prevalence of typical Rett syndrome caused by a *MECP2* mutation is between 15,000 and 20,000 (U.S., EU+UK)
- Rett syndrome occurs worldwide in 1 of every 10,000 female births¹



STAGE I

6-18 months (typical)
≤6 months (early)
Developmental Arrest
Symptom Onset

Infants are generally described as having normal development until approximately 6 to 18 months of age



STAGE II

1-4 years
Rapid Deterioration Symptom progression-regression

Hallmark Rett symptoms appear:
Hand wringing or squeeze, clapping, rubbing, washing, or hand to mouth movements



STAGE III

4-10 years
Pseudo stationary Symptoms stabilize/improve

After a period of rapid deterioration neurological symptoms stabilize, with some even showing slight improvements

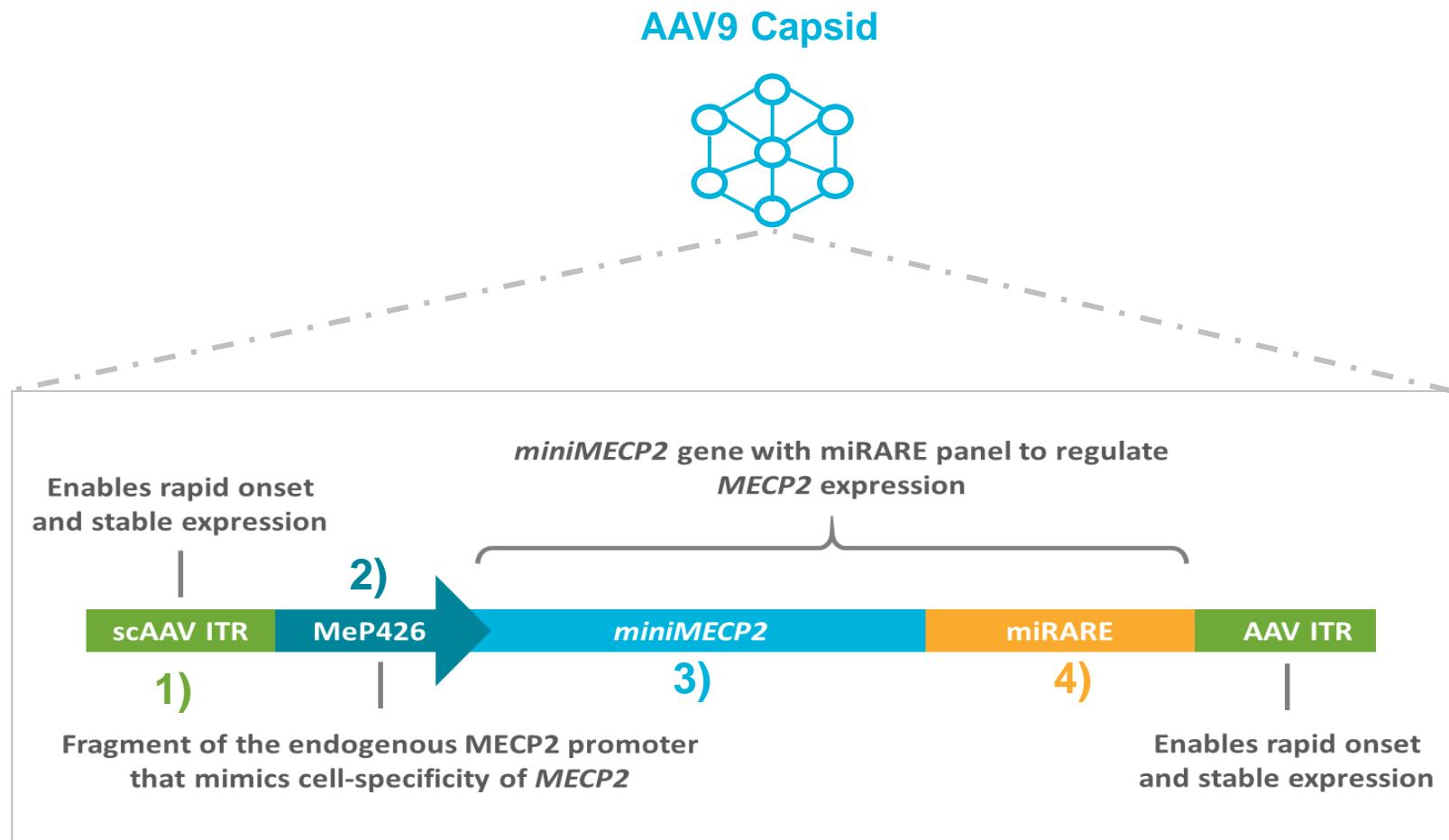


STAGE IV

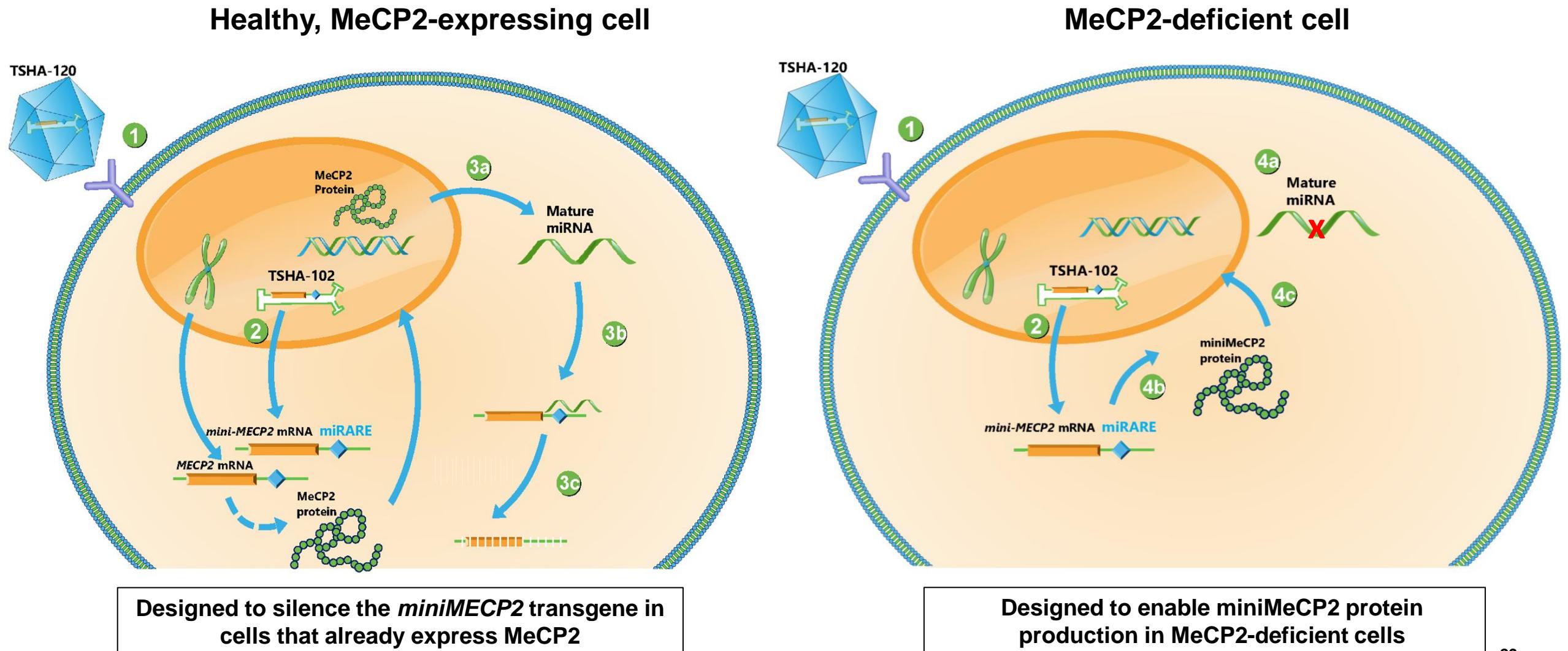
>10 years
Late Motor Deterioration Muscle wasting with age

85-90% of affected people may experience growth failure and muscle wasting that worsens with age

TSHA-102 construct designed to regulate cellular *MECP2* expression



TSHA-102 utilizes a novel miRARE technology to mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression



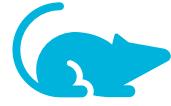
Robust pre-clinical data supports the safety and efficacy for TSHA-102 across animal species



Mice

Pharmacology and tolerability studies

- Conducted in *Mecp2^{-/-}* knockout (KO) mice and wild-type (WT) mice



Rats

Toxicology and biodistribution studies

- Conducted in Sprague Dawley rats up to ~6 months post-administration
- Three dose levels up to 4x starting clinical dose were evaluated



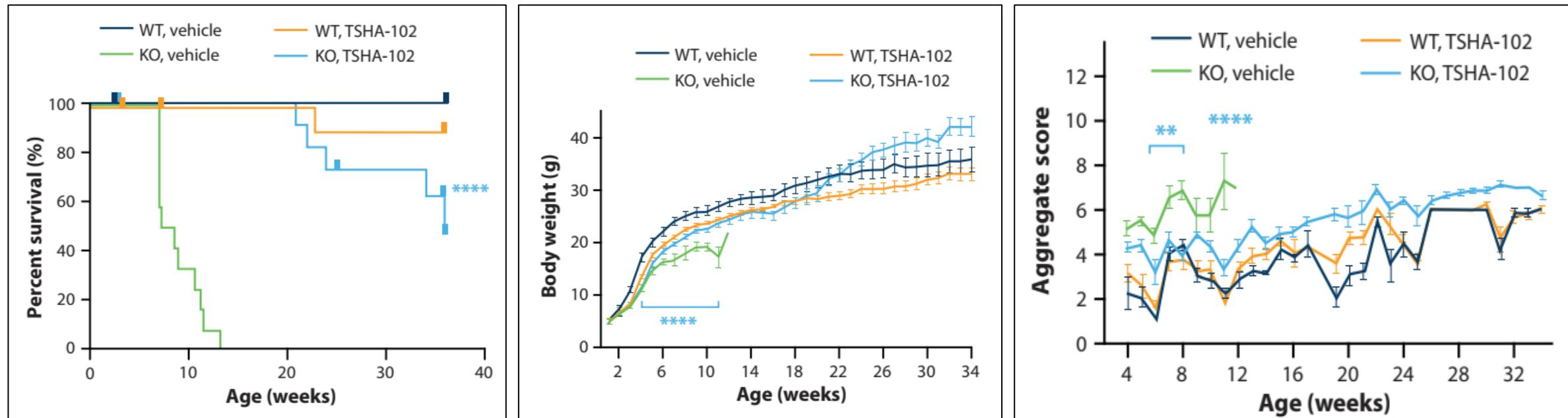
Non-Human Primates

Toxicology and biodistribution studies

- Conducted in cynomolgus monkeys up to 6 months post-administration
- Three dose levels up to 4x starting clinical dose were evaluated

TSHA-102 improved survival, weight and behavior in neonatal *Mecp2*^{-/-} knockout mice with no impact on wild-type mice

Neonatal mouse efficacy study – 45 pups treated with TSHA-102 (8.8×10^{10} vg) or vehicle via ICV at P2



TSHA-102 extended survival of KO mice, no reduction on WT

- 47% KO mice survived the 36-week study vs a median survival of 8.1 weeks with vehicle-treated KO mice
- Significant ($p < 0.0001$) >4-fold lifespan extension

Normalization of body weight following TSHA-102 in KO mice, no impact on WT

- TSHA-102 restored normal and faster-than-normal growth in KO mice ($p < 0.05$ vs vehicle-treated KO mice)

Early sustained improvement in Rett-like phenotypes in KO mice following TSHA-102, no impact on WT

- Average age of onset for severe clasping from approximately 7 to 21 weeks in KO mice
- Severely abnormal gait from approximately 8 to 20 weeks in KO mice

Neonatal data reinforce the ‘Goldilocks’ potential of the miRARE technology to enable the optimal amount of MeCP2

Regulated *MECP2* expression in deficient CNS cells

Supported by significant improvements in survival, overall neurobehavioral function and growth in *Mecp2^{-/-}* knockout mice

Avoided toxic overexpression in cells already expressing MeCP2

Supported by no deleterious impact on survival, neurobehavioral functions and overall health in wild-type mice

miRARE technology may address the risks associated with both under and overexpression of MeCP2 resulting from the mosaic pattern of *MECP2* silencing in females with Rett syndrome



TSHA-102 REVEAL Phase 1/2 trial in adults with Rett syndrome

Study design	<ul style="list-style-type: none">Open-label, dose-escalation, randomized, multi-center Phase 1/2 trial (the REVEAL study)Safety and preliminary efficacy
Study location	Canada (CHU Sainte-Justine)
Key inclusion criteria	<ul style="list-style-type: none">Adult females with pathogenic confirmation of <i>MECP2</i> mutation
Intervention	<ul style="list-style-type: none">Cohort one: 5×10^{14} total vector genomes (vg)Cohort two: 1×10^{15} total vector genomes (vg)
Route of Administration	<ul style="list-style-type: none">Intrathecal route of administration

NCT05606614



The first adult patient was dosed with TSCHA-102 at CHU Sainte-Justine, in Montreal, Canada, under Dr. Rossignol, principal investigator.

IDMC will review available clinical data from the first patient at approximately 6 weeks post-dosing.

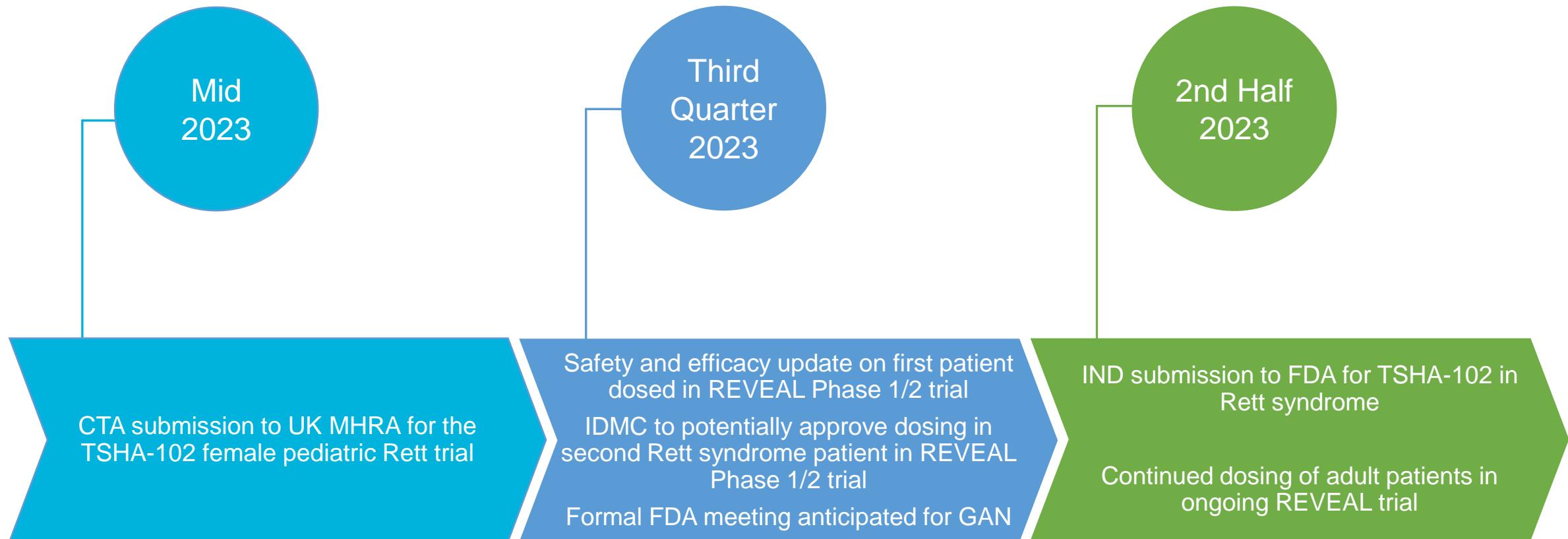
Closing Remarks

SEAN NOLAN

Board Chairman and Chief Executive Officer



Focused on achieving anticipated near-term milestones and building long-term value





Q&A



Code of Business Conduct and Ethics

HOW TO BE A COMPLIANT #RAREALLY

October 2023

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“

At Taysha Gene Therapies, we are driven by our mission to eradicate monogenic CNS disease. We're held to a high set of standards knowing there are patients, families and communities at the center of every decision we make who are counting on us. That's why we must actively work to build a culture of integrity and accountability that enables each of us to always be and do our best.

We are committed to creating an environment where employees feel empowered to do their best work for patients – and where everyone is treated with respect and valued for their contributions. Our Code of Business Conduct and Ethics reflects this commitment. Each of us is responsible for understanding the Code.

As Taysha employees, we must always hold ourselves accountable to these standards because being a Rare Ally to the patient community starts with doing right by ourselves. I hope you take pride in the important work you do on behalf of the patients we serve. Thank you for being an important part of the Taysha journey.

- Sean P. Nolan, Chief Executive Officer and Board Chairman

”

The Why

About the Code

Taysha Gene Therapies, Inc. (“**Taysha**”) is committed to creating an environment where we can do our best work while maintaining the highest standards of business conduct and ethics.

This Code of Business Conduct and Ethics (the “**Code**”) reflects the business practices and principles of behavior that support this commitment.

We expect every director, officer and employee (collectively, “**Personnel**”) to read and understand the Code and its application to the performance of their business responsibilities.



What is it?

The Code of Business Conduct and Ethics is a set of expectations written in plain language. These expectations guide employees on the basics of operating in a public company within a highly regulated industry.

How can the Code help you?

- **Conduct yourself honestly and ethically**
- **Uphold our values and protect our reputation**
- **Understand what Taysha expects of its employees**
- **Comply with laws, regulations and standards that apply to Taysha**
- **Understand where to go for assistance or guidance**



Make Values-Based Decisions

- The Code addresses conduct that is particularly important to proper dealings with the people and entities with whom we interact but reflects only a part of our commitment.
- Where there is no stated guideline in the Code or otherwise, **it is the responsibility of Personnel to apply common sense**, together with the highest personal ethical standards, in making values-based business decisions.
- It is our policy to promote high standards of integrity by conducting our affairs in an honest and ethical manner. The integrity and reputation of Taysha depends on the honesty, fairness and integrity brought to the job by each person associated with us. **Unyielding personal integrity is the foundation of our corporate integrity.**

Legal Compliance – The Basics

**1**

Obey the law. This is the foundation of the Code.

- We expect you to understand the legal and regulatory requirements applicable to your business unit and area of responsibility.
- This isn't a memory exam. You aren't expected to recite the law, rules and regulations, but we do want you to know when to seek advice from others. If you have a question about legal compliance, you are responsible for seeking an answer from your manager or from the Compliance Officer.

2

Mirror image of Rule # 1 – Disregard of the law will not be tolerated.

- Violation of laws, rules and regulations of any country may subject an individual, as well as Taysha, to civil and/or criminal penalties.
- You should be aware that conduct and records, including emails, are subject to internal and external audits and to discovery by third parties in the event of a government investigation or civil litigation. It is in everyone's best interests to know and comply with our legal obligations.

Insider Trading



Personnel who have access to confidential (or “inside”) information are not permitted to use or share that information for stock trading purposes or for any other purpose except to conduct our business.



All non-public information about Taysha or about companies with which we do business **is considered confidential information**.

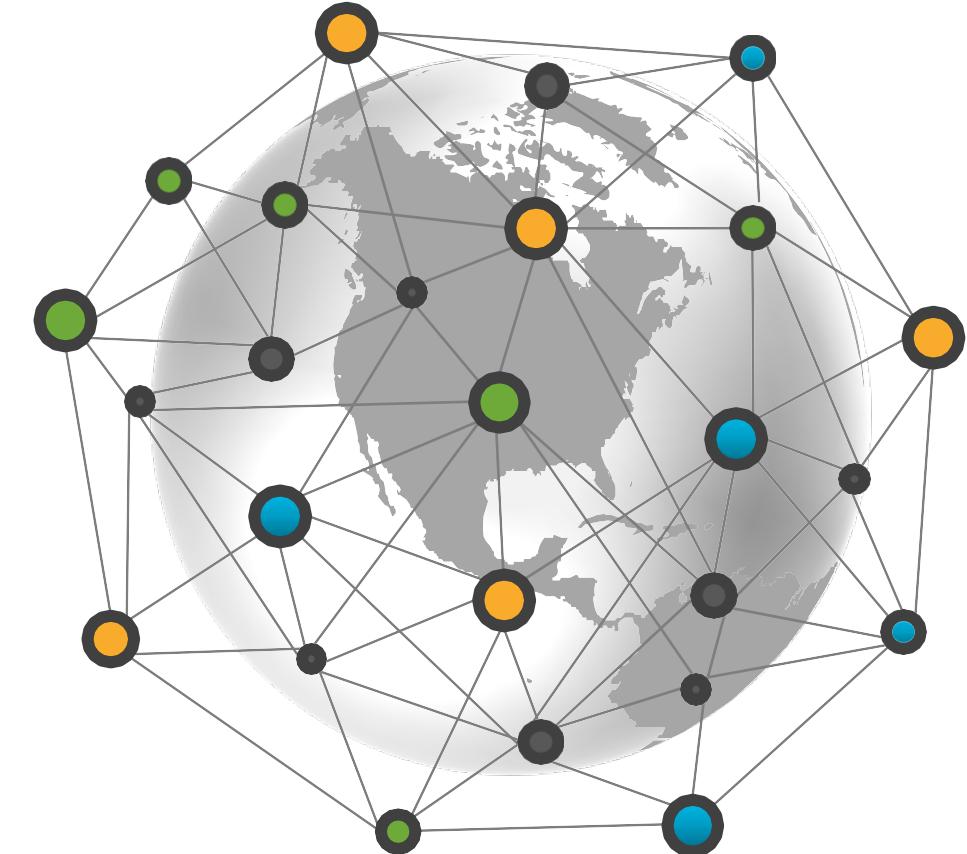


To use **material non-public information** in connection with buying or selling securities, including “tipping” others who might make an investment decision based on this information, **is not only unethical, but also illegal**. You must exercise the utmost care when handling material inside information.



International Business Laws

- Our Personnel are expected to comply with the applicable laws in all countries to which they travel, in which they operate and where we otherwise do business, including laws prohibiting bribery, corruption or the conduct of business with specified individuals, companies or countries.
- The fact that, in some countries, certain laws are not enforced or that violation of those laws is not subject to public criticism is not an excuse for noncompliance.
- We expect our Personnel to comply with U.S. laws, rules and regulations governing the conduct of business by its citizens and corporations outside the U.S.



Anti-Corruption



We expect compliance with the Foreign Corrupt Practices Act (the “FCPA”), which prohibits directly or indirectly giving anything of value to a government official to obtain or retain business or favorable treatment and requires the maintenance of accurate books of account, with all Taysha transactions being properly recorded.



We have adopted a separate Anti-Corruption Policy, which provides guidance regarding compliance with the FCPA, as well as rules regarding interactions and dealings with foreign and U.S. government officials and private persons (including customers).



If you have any question as to whether an activity is restricted or prohibited, please ask before taking any action, including giving any verbal assurances that may be regulated by international laws.

Antitrust Laws



Antitrust laws protect the competitive process and generally prohibit:

- Agreements with competitors that harm competition or customers, including price fixing and allocations of customers, territories or contracts
- Agreements that establish or fix the price at which a customer may resell a product
- The acquisition or maintenance of a monopoly or attempted monopoly through anti-competitive conduct



Do not exchange information such as our strategies and identification of local business partnerships with competitors

- Regardless of how innocent or casual the exchange may be
- Regardless of the setting, whether business or social

Antitrust law violations may include criminal penalties and potential fines and damages of millions of dollars, which may be tripled under certain circumstances.

Seek guidance from your supervisor or the Compliance Officer to understand the requirements of antitrust and unfair competition laws of the various jurisdictions where we do business.

The How

How We Operate

- We deal fairly with our stakeholders
- We identify and resolve conflicts of interest
- We do not provide gifts or entertainment
- We maintain confidentiality and participate ethically on social media
- We maintain corporate books and records with the highest financial integrity



Fair Dealing



You are expected to deal fairly with our partners, suppliers, and employees and anyone else with whom you have contact while performing your job



We strive to outperform our competition fairly and honestly



Our advantage is our products, not unethical or illegal business practices



Proprietary and trade secret information obtained improperly or inducing improper disclosure of confidential information from past or present employees of other companies is prohibited, even if motivated by an intention to advance our interests, is prohibited



Conflicts of Interest

Our goal is to uphold the best interests of Taysha

To do so means avoiding conflicts of interest or potential conflicts

- Between the best interests of Taysha and your personal interests
- Including those of your significant others and immediate family

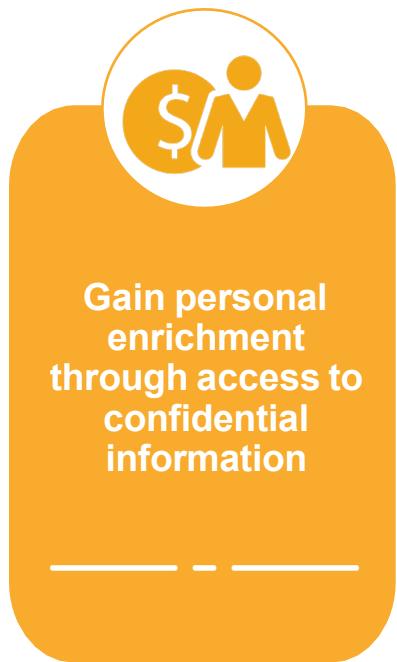


Conflicts of Interest

A conflict of interest can arise when Personnel:



Have a financial interest that could affect their judgment



Gain personal enrichment through access to confidential information



Conduct personal business (such as personal charitable work) on Taysha time or using Taysha resources



Misuse their position at Taysha in a way that results in personal gain



Have a personal interest, direct or indirect, in any supplier or customer

Conflicts of Interest and Affiliations

If you choose to participate in activities related to the diseases in which Taysha is conducting research, the following rules apply:

- Clarify your participation is (1) unrelated to your employment with Taysha and (2) not based on a desire that the organization will recommend Taysha for business opportunities because of your participation.
- If you are donating funds to an organization, the donations must be a personal contribution not be reimbursed by Taysha.
- If you play a decision-making role in an organization (e.g., member of the Board of Directors), avoid situations in which a potential for conflict of interest exists between your role within the organization and your employment with Taysha or Taysha's business interests.
 - For instance, if the organization must decide which gene therapy companies will participate in an event, you should recuse yourself from participating in the discussion and the decision.
 - You should also ensure that your participation in the management or activities of an organization does not imply and is not perceived as a promise or a commitment that Taysha will provide funding for the organization's causes.

Taysha takes pride in having Personnel who are dedicated to serving their communities outside of their employment.

Taysha Personnel should be aware, however, of potential conflicts of interest that may arise with healthcare-related organizations whose activities intersect with those of Taysha.

What To Do About Conflicts



- Questions or reporting of an actual or potential conflict should be directed to your supervisor or the Compliance Officer
- A supervisor may not on their own authorize conflict of interest matters or make determinations as to whether a problematic conflict of interest exists
- Instead, your supervisor must seek approval of the Compliance Officer after providing a full description of the activity
- If the supervisor is involved in the potential or actual conflict, you should discuss the matter directly with the Compliance Officer
- Officers and directors may seek authorizations and determinations from the Audit Committee of our Board of Directors

Gifts and Entertainment

Offering or providing anything of value with the intent of obtaining an improper business advantage or facilitating approvals from government officials is strictly prohibited.

- As a normal business courtesy, meals may be provided if they are modest and provided only on an occasional basis.
- Educational items or other materials that advance disease or treatment education and which do not have independent value to the recipient may be provided with the prior approval of the Compliance Officer or in accordance with written Taysha policy
- Entertainment and/or recreation (such as tickets to a game or the theater or a round of golf) may not be provided.

Personnel should not accept gifts or entertainment that may reasonably be deemed to affect their judgment or actions in the performance of their duties.

- **Could reasonably be deemed to affect judgment:** A vendor sending a food basket at the holidays to your home address, for instance.
- **Unlikely to affect judgment:** The same vendor sending a food basket to the office that is then shared with all employees in the employee kitchen.

This policy applies to our transactions everywhere in the world, even where a different practice is widely considered “a way of doing business.”

- Our partners, suppliers, contributors, consumers and the public at large should know that our judgment is not for sale.

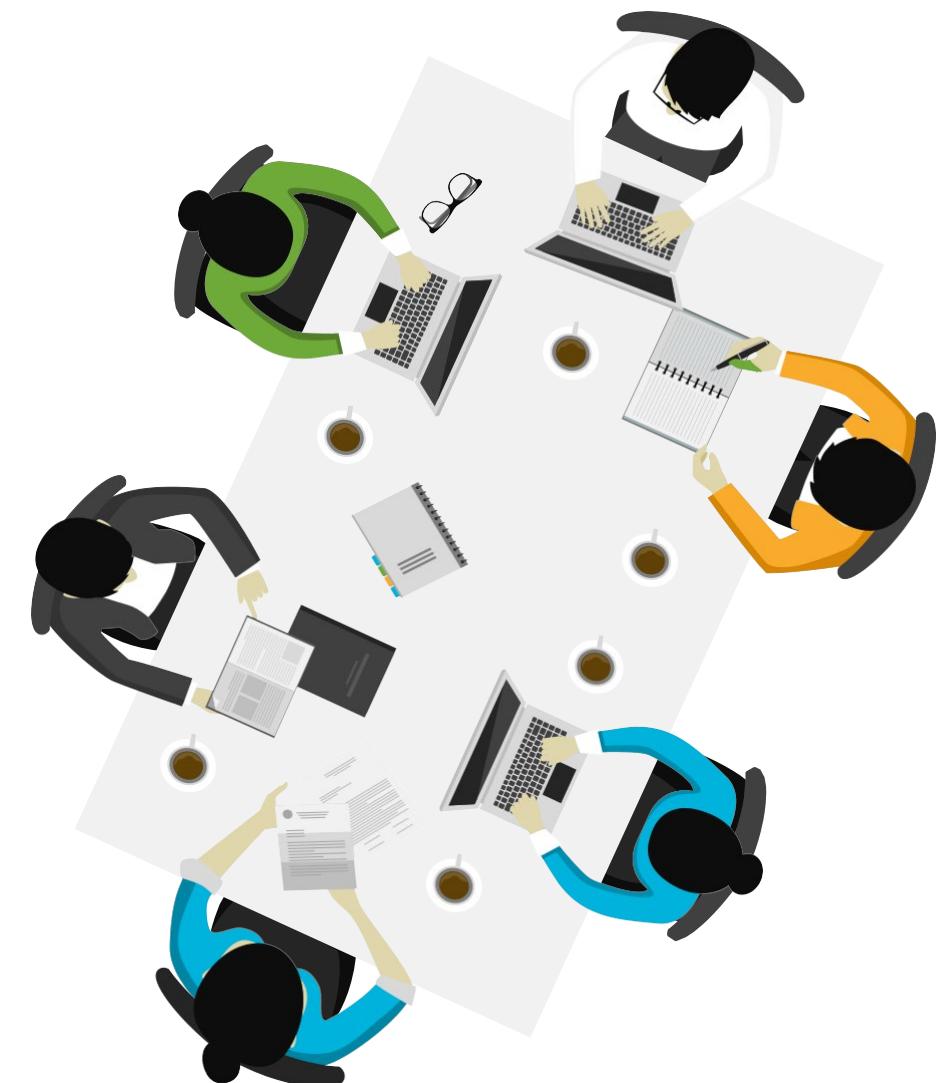
Confidentiality

- If we share with you information that is confidential, we expect you to keep it confidential.
- If you aren't sure if something is confidential, ask your supervisor, but you should assume everything is confidential unless you hear otherwise.
- This includes financials, strategy and plans, scientific and technical data, **details and results of our studies and clinical trials**, information about our product candidates, Personnel information, and legal disputes.



Maintaining Confidentiality

- If you learn non-public information when interacting with other companies or organizations, treat it as proprietary and keep it confidential. This includes possibly a time when we may have an interest in, or be involved with, another company.
- You may not disclose any confidential information or proprietary information learned in the course of your employment to anyone **until that information is disclosed via approved channels such as a press release, an SEC filing, or a formal communication from a member of Taysha management.**
- Unauthorized use or distribution of this information could be illegal and result in civil liability and criminal penalties.



Social Media



Social media can reach a diverse and inclusive audience. But in a highly regulated industry like ours, caution is advised when considering your participation in social media. Here are helpful guideposts:

- Never post patient identifiable information
- Do not reference content related to specific pipeline products or scientific research on social media unless the use and reference has been approved by Legal
- Maintain the confidentiality of Taysha's trade secrets, non-public or confidential information, including the development of processes, products, know-how and technology
- Never post internal reports, policies, procedures, attorney-client privileged information or other internal business-related confidential communications
- Harassment, and threats of violence or similar inappropriate or unlawful conduct will not be tolerated, and may result in disciplinary action up to and including termination

Social Media



Social media can mean many things.

At Taysha we consider it includes all means of communicating or posting information or content of any sort on the Internet

- This covers your own or someone else's:
 - Blog, journal or diary
 - Personal web site
 - Social networking or affinity web site
 - Web bulletin board or a chat room, whether associated or affiliated with Taysha
 - Any other form of electronic communication

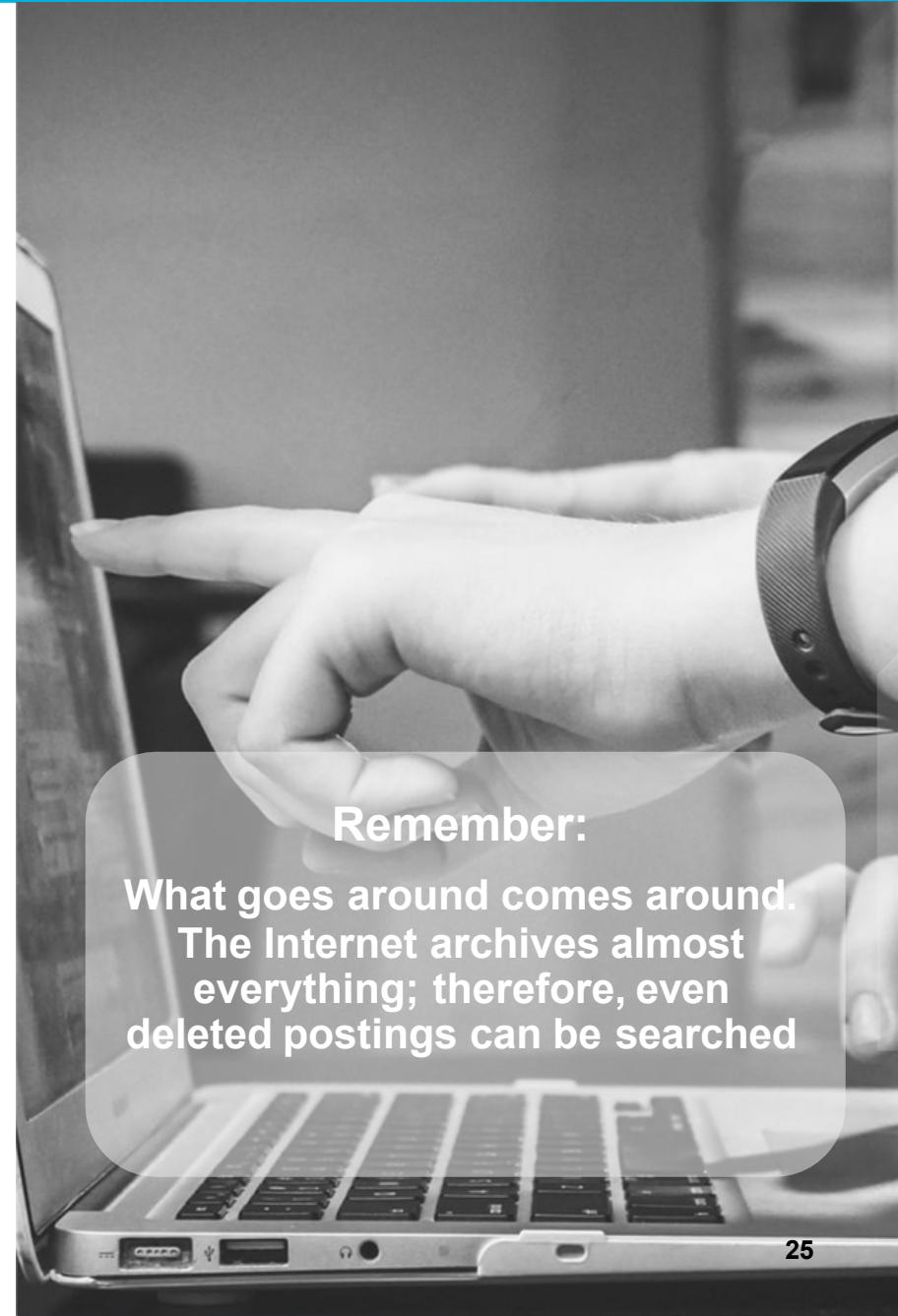


Social Media



**Keeping in mind the restrictions stated previously,
if you do post to social media, remember:**

- Express your personal opinions – do not represent yourself as a spokesperson for Taysha.
- If Taysha as a company is a subject of the content you are creating, be clear and open about the fact that you are an employee and your views do not represent those of Taysha, fellow employees, or people working on behalf of Taysha.
- Make sure you are always honest and accurate when posting information or news, and if you make a mistake, correct it quickly.
- Never post any information or rumors that you know to be false about Taysha, fellow employees or other people working on behalf of Taysha or competitors.
- Refrain from using social media while on work time or on equipment we provide unless it is work-related as authorized by your manager or consistent with Taysha policy.



Remember:

**What goes around comes around.
The Internet archives almost
everything; therefore, even
deleted postings can be searched**

Corporate Books and Records



The integrity of our records and public disclosure depends upon the validity, accuracy and completeness of the information supporting the entries in our books of account.



Therefore, our corporate and business records should be completed accurately and honestly.



The making of false or misleading entries, whether they relate to financial results or otherwise, is strictly prohibited.



Financial Integrity

Do not knowingly take or authorize any action that would cause our financial records or financial disclosure to fail to comply with the rules and regulations of the SEC or other applicable laws, rules and regulations

Do not knowingly make (or cause or encourage any other person to make) any false or misleading statement in any of our SEC reports or knowingly omit (or cause or encourage any other person to omit) any information necessary to make the disclosure in any of our SEC reports accurate in all material respects

Cooperate fully with our accounting and audit teams, as well as our independent public accountants and counsel, respond honestly to their questions and provide them with complete and accurate information

Any employee who becomes aware of any departure from these standards has a responsibility to report his or her knowledge promptly to a supervisor, the Compliance Officer, the Audit Committee or one of the other compliance resources described below or in accordance with the provisions of the Company's Open-Door Policy for Reporting Complaints Regarding Accounting and Auditing Matters

The Rest

Reporting Possible Violations

- It is your responsibility to report suspected or actual violations of the Code by others. Please do so promptly to your compliance resource (described in subsequent slides) with a specific description of the violation that you believe has occurred and any information you have about the persons involved and the time of the violation.
- Supervisors report complaints or observations of Code violations promptly to the Compliance Officer. Contact the Compliance Officer directly if you believe your supervisor has not taken appropriate action.
- Please do not conduct any preliminary investigation unless authorized to do so by the Compliance Officer.
- Your cooperation in the investigation will be expected. It is our policy to employ a fair process by which to determine violations of the Code.
- If any investigation indicates a violation of the Code has occurred, we will take such action as we believe to be appropriate under the circumstances. This may include disciplinary action up to, and including, termination of an employee if responsible for a Code violation. In appropriate cases this may also include civil action or referral for criminal prosecution. Appropriate action may also be taken to deter any future Code violations.
- If your concern involves potential misconduct by another person and relates to questionable accounting or auditing matters at the Company, you should report that violation to the Compliance Officer pursuant to the Company's Accounting and Auditing Whistleblower Policy.

Compliance Resources



Kamran Alam, CPA, MBA
Chief Financial Officer

Questions

- Your Supervisor is your appropriate first contact
- Our Compliance Officer is Kamran Alam
 - Phone: (773) 562-0560
 - Email: kalam@tayshagtx.com
- You may also email compliance@tayshagtx.com for clarifications or questions regarding the Code

Reporting Resources

- To report a potential Code violation, you may call the Compliance Hotline at:

877-346-8073

- You may also report a potential Code violation using the web form found by clicking here: [**Compliance Hotline Web Form**](#)
- You may call or access the hotline web form anonymously, but this can make it hard to follow-up on details necessary to investigate the matter. Your access will be kept strictly confidential within the objectives of the Code.
 - The Compliance Officer shall promptly inform the Audit Committee of any complaints or observations of compliance violations of the Code including those that involve accounting, internal accounting controls or auditing concerns.
 - The Audit Committee shall be responsible for supervising and overseeing the inquiry and any investigation that is undertaken.



Protection

No Retaliation

When you report potential violations of the Code, you should do so without fear of any form of retaliation. We will take prompt disciplinary action against any employee who retaliates against you, which may include termination of employment.

Taysha will not tolerate any form of intimidation or retaliation by an officer, employee, contractor, subcontract, or agent of Taysha against any employee because of any good faith act taken by the employee under the Code.



The Law vs. Internal Processes

It is a federal crime for anyone to retaliate intentionally against any person who provides truthful information to a law enforcement official concerning a possible violation of any federal law.

Please note, however, that no protection from internal disciplinary procedures is available to those who make malicious or unfounded allegations, and particularly if they persist with making them after they have been fully considered and found to be without merit.



With the approval of the audit committee of the Board of Directors, Taysha reserves the right to amend, alter or terminate this Code of Business Conduct and Ethics at anytime for any reason. The most current version of the Code can be found on the Investor Relations section of Taysha's website.

This document is not an employment contract between Taysha and any of its employees, officers or directors and does not alter Taysha's at-will employment policy.



TAYSHA GENE THERAPIES, INC.
CORPORATE GOVERNANCE GUIDELINES
AMENDED AND RESTATED AS OF APRIL 18, 2022

The Board of Directors (the “*Board*”) of Taysha Gene Therapies, Inc. (the “*Company*”) has established the following guidelines for the Board’s conduct and operation. These guidelines are designed to give directors and management a flexible framework for effectively pursuing the Company’s objectives for the benefit of its stockholders. That is why these guidelines should be interpreted in the context of all applicable laws, the Company’s organizational documents, and other policies.

I. BOARD COMPOSITION AND SELECTION

A. Size of the Board. The Board will establish the number of directors in accordance with the certificate of incorporation and bylaws of the Company. The Board will periodically review the appropriate Board size, which may vary to accommodate the availability of suitable candidates and the Company’s needs.

B. Independence of Directors. The Board will have a majority of independent directors, subject to any exceptions permitted by the applicable listing standards of the stock exchange that lists the Company’s capital stock. To determine independence, the Board will consider the definition of independence in the applicable listing standards, and other factors that will contribute to effective oversight and decision-making.

At times required by the rules of the Securities and Exchange Commission or listing standards of the exchange that lists the Company’s capital stock (the “*Exchange*”) and based on information provided by Board members and advice of counsel, the Board or the Nominating and Corporate Governance Committee will affirmatively determine director independence. In accordance with applicable rules and Company policies, the Board will confirm that each director designated as independent has no other relationships to the Company (either directly or with an organization in which the director is a partner, stockholder or officer or is financially interested) that may interfere with the director’s ability to exercise independent judgment in carrying out his or her responsibilities as a director. Directors may be asked from time to time to leave a Board meeting when the Board is considering a transaction in which the director (or another organization in which the director is a director or officer) has a financial or other interest.

The Audit Committee shall review and approve any proposed related party transactions in compliance with the Company’s Related Person Transaction Policy and Exchange rules.

C. Management Directors. The Board anticipates that the Chief Executive Officer will serve on the Board. The Board also anticipates that other members of management who can assist the Board in fulfilling its responsibilities based on their experience and role at the Company may serve on the Board.

D. Board Leadership. The Board may select a chairperson of the Board in the manner and on the criteria that the Board deems appropriate. In the event that the Company does not have an independent chairperson of the Board, the independent directors will designate a lead independent director. The name of the chairperson or lead independent director will be listed in the Company's proxy statement. The independent chairperson or lead independent director will be responsible for coordinating the activities of the independent directors. In addition to the duties of all Board members, the specific responsibilities of the independent chairperson or lead independent director are to:

- work with the Chief Executive Officer to develop and approve an appropriate Board meeting schedule;
- work with the Chief Executive Officer to develop and approve Board meeting agendas;
- provide the Chief Executive Officer feedback on the quality, quantity, and timeliness of the information provided to the Board;
- develop the agenda and moderate executive sessions of the independent members of the Board;
- preside over Board meetings when the Chief Executive Officer is not present or when Board or Chief Executive Officer performance or compensation is discussed;
- act as principal liaison between the independent members of the Board and Chief Executive Officer;
- convene meetings of the independent directors as appropriate;
- be available for consultation and direct communication with stockholders as deemed appropriate; and
- perform other duties as the Board may determine from time to time.

E. Selection of Directors. The Board will be responsible for nominating members for election to the Board by the Company's stockholders. The Board is also responsible for filling any vacancies on the Board unless the vacancy is filled by the stockholders. The Nominating and Corporate Governance Committee is responsible for identifying, reviewing, evaluating, and recommending candidates to serve as directors of the Company, in accordance with its charter and consistent with the criteria listed below.

The Company's Secretary will be notified of all persons proposed to serve as potential candidates for nomination to the Board. For nominations of potential candidates made other than by the Board, the stockholder or other person making such nomination must comply with the Company's Bylaws, including without limitation, submission of the information or other materials required with respect to proposed nominees. Each potential candidate must provide a list of references and agree (i) to be interviewed by members of the Nominating and Corporate Governance Committee or other directors in the discretion of the Nominating and Corporate

Governance Committee, and (ii) to a background check or other review of the qualifications of a proposed nominee by the Company. Prior to nomination of any potential candidate by the Board, each member of the Board will have an opportunity to meet with the candidate. Upon request, any candidate nominated will agree in writing to comply with these Corporate Governance Guidelines and all other policies and procedures of the Company applicable to the Board.

F. Board Membership Criteria. The Board will determine the appropriate characteristics, skills, and experience for the Board as a whole and for its individual members. The Board considers recommendations for nominees from the Nominating and Corporate Governance Committee. The Board will consider the minimum general criteria below, and may add any specific additional criteria with respect to specific searches, in selecting candidates and existing directors for serving on the Board. An acceptable candidate may not fully satisfy all of the criteria, but is expected to satisfy nearly all of them. The Board believes that candidates for director should have certain minimum qualifications, including the highest personal integrity and ethics, the ability to read and understand basic financial statements, and being older than 21.

In considering candidates recommended by the Nominating and Corporate Governance Committee, the Board intends to consider other factors, such as:

- relevant expertise to our current and planned operations to offer advice and guidance to management,
- sufficient time to devote to the affairs of the Company,
- excellence in his or her field,
- the ability to exercise sound business judgment, and
- the commitment to rigorously represent the long-term interests of the Company's stockholders.

The Board reviews candidates for director nomination in the context of the current composition of the Board, our operating requirements, and the long-term interests of our stockholders. In conducting this assessment, the Board considers diversity (including gender, racial and ethnic diversity), age, skills, and other factors that it deems appropriate to maintain a balance of knowledge, experience, and capability on the Board. For incumbent directors, the Board reviews those directors' overall service to the Company during their term, including the number of meetings attended, level of participation, quality of performance, and any other relationships and transactions that might impair the directors' independence. In the case of new director candidates, the Board also determines whether the nominee must be independent for purposes of the stock exchange that lists the Company's capital stock.

G. Changes in Board Membership Criteria. The Board wishes to maintain members who can productively contribute to the success of the Company. From time to time, the Board, in its discretion, may change the criteria for Board membership. When this occurs, the Board will evaluate existing members according to the new criteria. The Board may ask a director who no

longer meets the complete criteria for board membership to adjust his or her committee assignments or resign from the Board.

H. Term Limits. The Board does not believe it should limit the number of terms for which an individual may serve as a director. Directors who have served on the Board for an extended period of time are able to provide continuity and valuable insight into our operations and prospects because of their experience and understanding of our history, policies, and objectives. The Board believes that it can ensure that it continues to evolve and adopt new ideas and viewpoints through the director nomination process in these guidelines. The director nomination process achieves what term limits seek to accomplish.

I. Limits on Board Memberships. Directors should advise the chairperson of the Nominating and Corporate Governance Committee before accepting an invitation to serve on the Board or committee of another company. The Board recognizes that a director's ability to fulfill his or her responsibilities as a director can be impaired if he or she serves on multiple other boards or board committees. Service on boards and board committees of other companies should be consistent with our conflict-of-interest policies.

J. Retirement Age. The Board believes that it is inappropriate to have a retirement age for directors.

K. Directors Who Change Their Job Responsibility. A director who retires or materially changes his or her present job (other than an ordinary course promotion) should notify the Board and the Nominating and Corporate Governance Committee. While the Board does not believe any director who retires or materially changes his or her present job should necessarily leave the Board, there should be an opportunity for the Nominating and Corporate Governance Committee to review their qualifications under these circumstances.

II. ROLE OF THE BOARD OF DIRECTORS

The primary responsibilities of the Board are oversight and strategic guidance to senior management. A director's responsibility is to fulfill his or her fiduciary duties of care and loyalty, and otherwise to exercise his or her business judgment in the best interests of the Company and its stockholders. Board service requires significant time and attention. More specifically, the Board has responsibilities to review, approve, and monitor fundamental financial and business strategies, assess our major risks, and consider ways to address those risks, select and oversee management, and establish and oversee processes to maintain our integrity. To fulfill their duties, directors must prepare for meetings and discussions with management, participate in Board meetings, review relevant materials, and serve on committees. The Company expects directors to maintain an attitude of constructive involvement and oversight, ask relevant and incisive questions, and demand honest and accurate answers. Directors must act with integrity and demonstrate a commitment to the Company, our values, business, and long-term stockholder value.

III. DIRECTOR ORIENTATION AND EDUCATION

The Nominating and Corporate Governance Committee may implement an orientation process for directors that includes background material on our policies and procedures, meetings with senior management, and visits to our facilities. We may also offer continuing education

programs to assist the directors in maintaining the level of expertise necessary to perform their duties.

IV. DIRECTOR COMPENSATION

The Compensation Committee will review and recommend to the Board the type and amount of director compensation for Board and committee service for non-management directors in accordance with applicable legal and regulatory guidelines. Compensation for non-management directors and committee members should be designed to be aligned with the long-term interests of the stockholders and consistent with market practices of similarly situated companies. In determining compensation, the Board will consider the impact on the director's independence and objectivity.

V. BOARD MEETINGS

A. Number of Meetings. The Board expects to have at least four regular Board meetings each year. The Board may also take action from time to time by unanimous written consent.

B. Attendance and Preparation. We expect our Board members to prepare for, attend and participate in all meetings of the Board and committees on which they serve. Directors should notify the Company's Secretary when he or she will be absent from a meeting. Directors are also encouraged to attend the Company's annual meeting of stockholders. We will provide directors with appropriate materials before the meeting, except in unusual or exigent circumstances.

C. Agenda. The Chief Executive Officer and chairperson or lead independent director will create a schedule of topics to be discussed during the year and an agenda for each Board meeting. Each Board member is encouraged to suggest topics for the agenda at any time, and each Board member is free to raise subjects that are not on the agenda.

D. Executive Session. The independent non-management directors of the Board will meet periodically in executive session but no less than two times per year or whatever minimum has been set by applicable listing standards. Executive session discussions may include any topics decided by the attendees.

E. Committee Reports. At each regular Board meeting, if requested by the Board, each committee will present a brief summary of the principal subjects discussed, any conclusions reached, and the final actions of the committee. The chairperson of the appropriate committee will present the report. Minutes of committee meetings will be available to any director.

VI. BOARD COMMITTEES

A. Number of Committees; Independence of Members. The Board will constitute and maintain an Audit Committee, a Compensation Committee, and a Nominating and Corporate Governance Committee. Only independent directors may serve on the Audit Committee, the Compensation Committee, and the Nominating and Corporate Governance Committee. The Board may form, merge, or dissolve additional committees, as it deems appropriate.

B. Committee Functions and Charters. All standing committees will have a written charter that describes the committee's responsibilities. Unless otherwise directed by the Board, any new committee formed by the Board will develop a written charter delineating its responsibilities. Each committee will periodically review its charter and recommend any proposed charter changes to the Board.

C. Board Committee Membership. The Nominating and Corporate Governance Committee oversees the Board's committee structure and operations, including authority to delegate to subcommittees and committee reporting to the Board. The Nominating and Corporate Governance Committee will annually recommend to the Board each committee's chairperson and membership. In making those recommendations, the Nominating and Corporate Governance Committee will consider the interests, independence, and experience of the directors and the independence and experience requirements of the stock exchange that lists our stock, the rules and regulations of the Securities and Exchange Commission, and applicable law.

D. Committee Meetings and Agenda. Each committee chairperson, in consultation with that committee's members, will determine the processes frequency, length, and agenda for each committee meeting and the appropriate attendees in light of that committee's charter, the authority delegated by the Board to that committee, and the legal, regulatory, accounting and governance principles applicable to that committee's functions.

VII. BOARD ACCESS TO MANAGEMENT; USE OF OUTSIDE ADVISORS

Board members will have access to Company management, subject to such processes as deemed appropriate by the Nominating and Corporate Governance Committee. Board members are expected to use their judgment to ensure that this contact is not distracting to our operations or to management's duties and responsibilities.

The Board and each committee will have the power to hire, at the expense of the Company, independent legal, financial, or other advisors that they may deem necessary, without consulting or obtaining the advanced approval of any officer.

VIII. CHIEF EXECUTIVE OFFICER EVALUATION

The Board, based on recommendations from the Compensation Committee, will annually review the Chief Executive Officer's performance. The Board will evaluate performance based on objective criteria, including how well the business achieves long-term strategic objectives and successfully develops management. The Compensation Committee and Board will use this evaluation when considering the compensation of the Chief Executive Officer.

IX. SUCCESSION PLANNING

The Nominating and Corporate Governance Committee should develop and periodically review with the Chief Executive Officer a plan with respect to executive officers' succession and recommend to the Board appropriate individuals who might fill those positions. The Chief Executive Officer should also recommend and evaluate potential successors. The Chief Executive Officer will also review any development plans for those potential successors.

X. BOARD ASSESSMENT

The Nominating and Corporate Governance Committee will periodically review, discuss, and assess the performance of the Board and the committees. The Nominating and Corporate Governance Committee may also consider and assess the independence of directors. The Nominating and Corporate Governance Committee should provide the results of these evaluations to the Board for further discussion as appropriate.

XI. BOARD RESPONSIBILITIES

A director should discharge his or her duties, including duties as a member of any committee on which he or she serves, in good faith and in a manner the director reasonably believes to be in the best interests of the Company and its stockholders. Board members will comply with the laws and requirements of the Exchange and other applicable regulatory agencies and with all policies and guidelines of the Company, including without limitation, the Company's Code of Business Conduct.

Each director is expected to disclose promptly to the Board and respond promptly and accurately to periodic questionnaires or other inquiries from the Company regarding any existing or proposed relationships with the Company, including compensation and stock ownership, which could affect the independence of the director. Each director will also promptly inform the Board of any material change in such information, to the extent not already known by the Board.

Board members are expected to devote sufficient time and attention to prepare for, attend and participate in Board meetings and meetings of committees on which they serve, including advance review of meeting materials that may be circulated prior to each meeting

Directors have an obligation to protect and keep confidential all of our non-public information unless the Company has authorized public disclosure or unless otherwise required by applicable law. Confidential information includes all non-public information entrusted to or obtained by a director by reason of his or her position on the Board. This includes information regarding our strategy, business, finances, and operations, and will include minutes, reports, and materials of the Board and committees, and other documents identified as confidential by the Company. The obligations described above continue even after service on the Board has ended.

Directors may not use such confidential information for personal benefit or to benefit other persons or entities other than the Company. Unless authorized by the Company or applicable law, directors will refrain from disclosing confidential information to anyone outside the Company, especially anyone affiliated with any entity or person that employs the director or has sponsored the director's election to the Board. These obligations continue even after service on the Board has ended. Any questions or concerns about potential disclosures should be directed to the Company's Chief Financial Officer, who then may communicate with the Chief Executive Officer or the Nominating and Corporate Governance Committee regarding the potential disclosures.

XII. REVIEW OF GOVERNANCE GUIDELINES

The Nominating and Corporate Governance Committee will periodically review and assess the adequacy of these guidelines and recommend any proposed changes to the Board for approval.

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TAYSHA GENE THERAPIES, INC.

CHARTER OF THE AUDIT COMMITTEE OF THE BOARD OF DIRECTORS

AMENDED AND RESTATED AS OF APRIL 18, 2022

I. PURPOSE

The primary purpose of the Audit Committee (the “*Committee*”) of the Board of Directors (the “*Board*”) of Taysha Gene Therapies, Inc. (the “*Company*”) shall be to act on behalf of the Board in fulfilling the Board’s oversight responsibilities with respect to (i) the Company’s corporate accounting and financial reporting processes, systems of internal control over financial reporting and audits of financial statements, systems of disclosure controls and procedures, as well as the quality and integrity of the Company’s financial statements and reports, (ii) the qualifications, independence and performance of the registered public accounting firm or firms engaged by the Company (the “*Auditors*”), (iii) review of any reports or other disclosure required by the applicable rules and regulations of the Securities and Exchange Commission (the “*SEC*”) to be included in the Company’s annual proxy statement and periodic reports within the scope of authority outlined herein and (iv) the performance of the Company’s internal audit function, if any. The Committee may also provide oversight assistance in connection with the Company’s legal, regulatory and ethical compliance programs as established by management and the Board.

The policy of the Committee, in discharging these obligations, shall be to maintain and foster an open avenue of communication among the Committee, the Auditors and the Company’s financial management, and, if any, the Company’s internal auditors.

II. COMPOSITION

The Committee shall consist of at least three (3) members of the Board. The members of the Committee shall satisfy (i) the independence and financial literacy requirements imposed by the SEC and The Nasdaq Stock Market LLC (“*Nasdaq*”), including any phase-in periods permitted by such requirements, as applicable to Committee members as in effect from time to time, when and as required by the SEC and Nasdaq, and (ii) any other qualifications determined by the Board or the Nominating and Corporate Governance Committee of the Board from time to time. At least one member of the Committee shall satisfy the applicable financial sophistication requirements and any other requirements, each as in effect from time to time, for accounting or related financial management expertise when and as required by the SEC or any stock exchange on which any of the Company’s capital stock is listed. The members of the Committee shall be appointed by and serve at the discretion of the Board. Resignation or removal of a Committee member from the Board for any reason shall automatically constitute resignation or removal, as applicable, from the Committee. Vacancies occurring on the Committee shall be filled by the Board. The Committee’s chairperson shall be appointed by the Board, or if the Board does not do so, the Committee members shall elect a chairperson by vote of a majority of the full Committee.

III. OPERATING PRINCIPLES AND PROCESSES

In fulfilling its functions and responsibilities, the Committee should give due consideration to the following operating principles and processes:

A. Communication. Regular and meaningful contact with the Board, members of senior management and independent professional advisors to the Board and its various committees, as applicable, shall be encouraged as a means of strengthening the Committee's knowledge of relevant current and prospective corporate accounting, financial reporting and internal control issues.

B. Meeting Agendas. Committee meeting agendas shall be the responsibility of the chairperson of the Committee with input from the Committee members and other members of the Board, as well as, to the extent deemed appropriate, by the chairperson of the Board, from members of senior management and outside advisors.

C. Information Needs. The Committee members shall communicate to the Chief Executive Officer, or his or her designees, the Committee's expectations, and the nature, timing and extent of any specific information or other supporting materials requested by the Committee for its meetings and deliberations.

D. Committee Education. Developing with management and participating in a process for systematic review of important accounting and financial reporting issues and trends in accounting, financial reporting and internal control practices that could potentially impact the Company shall be encouraged to enhance the effectiveness of the Committee.

IV. MEETINGS AND MINUTES

The Committee shall meet at least quarterly and hold such special meetings as its members shall deem necessary or appropriate. Any member of the Committee or the Board may call a meeting of the Committee. Unless otherwise directed by the Committee, each regularly scheduled meeting will conclude with an executive session of the Committee absent members of management.

Minutes of each meeting of the Committee shall be prepared and distributed to each director of the Company and the Secretary of the Company promptly after each meeting. The chairperson of the Committee shall report to the Board from time to time, or whenever so requested by the Board.

V. AUTHORITY

Each member of the Committee shall have full access to all books, records, facilities and personnel of the Company as deemed necessary or appropriate by any member of the Committee to discharge his or her responsibilities hereunder. The Committee shall have authority to appoint, determine compensation for (at the Company's expense), retain and oversee the Auditors (as set forth in Section 10A(m)(2) of the Securities Exchange Act of 1934, as amended, and the rules thereunder (the "*Exchange Act*")) and otherwise to fulfill its responsibilities under this charter. The Committee shall have authority to retain and determine compensation for, at the expense of

the Company, special legal, accounting or other advisors, experts or consultants as it deems necessary or appropriate in the performance of its duties under this charter, including any studies or investigations. The Committee shall also have authority to pay, at the expense of the Company, ordinary administrative expenses that, as determined by the Committee, are necessary or appropriate in carrying out its duties, unless prohibited by Nasdaq listing rules or applicable law. The Committee shall have authority to request that any of the Company's personnel, counsel, accountants (including the Auditors) or investment bankers, or any other consultant or advisor to the Company attend any meeting of the Committee or meet with any member of the Committee or any of its special, outside legal, accounting or other, advisors or consultants.

The Committee may form and delegate authority to one or more subcommittees as appropriate, to the extent consistent with the Company's amended and restated certificate of incorporation, amended and restated bylaws (the "**Bylaws**"), Corporate Governance Guidelines, Nasdaq rules and other applicable law. Delegation by the Committee to any subcommittee shall not limit or restrict the Committee on any matter so delegated, and, unless the Committee alters or terminates such delegation, any action by the Committee on any matter so delegated shall not limit or restrict future action by such subcommittee on such matters. The operation of the Committee shall be subject to the Bylaws of the Company as in effect from time to time and Section 141 of the Delaware General Corporation Law (or any successor section). The approval of this charter by the Board shall be construed as a delegation of authority to the Committee with respect to the responsibilities set forth herein.

VI. RESPONSIBILITIES

The Committee's responsibility is one of oversight. The members of the Committee are not employees of the Company, and they do not perform, or represent that they perform, the functions of management or the Auditors. The Committee relies on the expertise and knowledge of management, the internal auditor (if any) and the Auditors in carrying out its oversight responsibilities. Management is responsible for preparing accurate and complete financial statements in accordance with generally accepted accounting principles ("**GAAP**"), preparing periodic reports and establishing and maintaining appropriate accounting principles and financial reporting policies and satisfactory internal control over financial reporting. The Auditors are responsible for auditing the Company's annual financial statements and management's assessment of the Company's internal control over financial reporting as well as reviewing the Company's quarterly financial statements. It is not the responsibility of the Committee to prepare or certify the Company's financial statements, guarantee the audits or reports of the Auditors or ensure that the financial statements or periodic reports are complete and accurate, conform to GAAP or otherwise comply with applicable laws.

The Committee shall oversee the Company's financial reporting process on behalf of the Board, and shall have direct responsibility for the appointment, compensation, retention and oversight of the work of the Auditors and any other registered public accounting firm engaged for the purpose of performing other review or attest services for the Company. The Auditors and each such other registered public accounting firm shall report directly and be accountable to the Committee. The Committee's functions and procedures should remain flexible to address changing circumstances most effectively. To implement the Committee's purpose and policy, the Committee shall be charged with the following functions and responsibilities with the understanding, however,

that the Committee may supplement or deviate from these activities as appropriate under the circumstances (except as otherwise required by applicable laws or requirements of any stock exchange on which any of the Company's capital stock may be listed):

A. Evaluation and Retention of Auditors. To evaluate the performance of the Auditors, to assess their qualifications (including their internal quality control procedures and any material issues raised by that firm's most recent internal quality control review or any investigations by regulatory authorities) and to determine whether to retain, or to terminate, the engagement of the existing Auditors, or to appoint and engage a different independent registered public accounting firm, which retention shall be subject only to ratification by the Company's stockholders (if the Committee or the Board elects to submit such retention for ratification by the stockholders).

B. Communication Prior to Engagement. Prior to engagement of any prospective Auditors, to review a written disclosure by the prospective Auditors of all relationships between the prospective Auditors, or their affiliates, and the Company, or persons in financial oversight roles at the Company, that may reasonably be thought to bear on independence, and to discuss with the prospective Auditors the potential effects of such relationships on the independence of the prospective Auditors, consistent with Ethics and Independence Rule 3526, *Communication with Audit Committees Concerning Independence* (or any successor rule, "**Rule 3526**"), of the Public Company Accounting Oversight Board (United States) (the "**PCAOB**").

C. Approval of Audit Engagements. To determine and approve engagements of the Auditors, prior to commencement of such engagements, to perform all proposed audit, review and attest services, including the scope of and plans for the audit, the adequacy of staffing, the compensation to be paid by the Company to the Auditors and the negotiation and execution, on behalf of the Company, of the Auditors' engagement letters; such approval may be pursuant to preapproval policies and procedures established by the Committee consistent with applicable laws and rules, including the delegation of preapproval authority to the chairman of the Committee so long as any such preapproval decisions are presented to the full Committee at the next scheduled meeting.

D. Approval of Non-Audit Services. To determine and approve engagements of the Auditors prior to commencement of such engagements (unless in compliance with exceptions available under applicable laws and rules related to immaterial aggregate amounts of services), to perform any proposed permissible non-audit services, including the scope of the service and the compensation to be paid therefor by the Company; such approval may be pursuant to preapproval policies and procedures established by the Committee consistent with applicable laws and rules, including the delegation of preapproval authority to the chairman of the Committee so long as any such preapproval decisions are presented to the full Committee at the next scheduled meeting.

E. Audit Partner Rotation. To monitor the rotation of the partners of the Auditors on the Company's audit engagement team as required by applicable laws and rules, and to consider periodically and, if deemed appropriate, adopt a policy regarding rotation of auditing firms.

F. Auditor Independence. At least annually, consistent with Rule 3526, (i) to receive and review (a) written disclosures from the Auditors delineating all relationships between the

Auditors, or their affiliates, and the Company, or persons in financial oversight roles at the Company, that may reasonably be thought to bear on independence and (b) a letter from the Auditors affirming their independence, (ii) to consider and discuss with the Auditors any potential effects of any such relationships on the independence of the Auditors as well as any compensation or services that could affect the Auditors' objectivity and independence, and (iii) to assess and otherwise take appropriate action to oversee the independence of the Auditors.

G. Former Employees of Auditors. To consider and, if deemed appropriate, adopt policies regarding Committee preapproval of employment by the Company of individuals employed or formerly employed by the Auditors and engaged on the Company's account.

H. Annual Audit Results. To review with management and the Auditors, (i) the results of the annual audit, including the Auditors' assessment of the quality of the Company's accounting principles and practices, (ii) the Auditors' views about qualitative aspects of the Company's significant accounting practices, (iii) the reasonableness of significant judgments and estimates (including material changes in estimates and analyses of the effects of alternative GAAP methods on the financial statements), (iv) all misstatements identified during the audit (other than those the Auditors believe to be trivial), (v) the adequacy of the disclosures in the financial statements, and (vi) any other matters required to be communicated to the Committee by the Auditors under the standards of the PCAOB.

I. Auditor Communications. At least annually, to discuss with the Auditors the matters required to be discussed by Auditing Standard No. 1301, *Communications with Audit Committees*, as amended, as adopted by the PCAOB (including any successor rule adopted by the PCAOB).

J. Audited Financial Statement Review; Annual Report on Form 10-K. To review with management and the Auditors, as appropriate, upon completion of the audit, (i) the Company's financial statements and any disclosure from the Company's Chief Executive Officer and Chief Financial Officer to be made in connection with the certification of the Company's Annual Report on Form 10-K to be filed with the SEC, prior to public disclosure of such financial information, if practicable, or filing with the SEC of the Company's Annual Report on Form 10-K, and to recommend whether such financial statements should be so included and (ii) other relevant reports or financial information submitted by the Company to any governmental body or the public, including relevant reports rendered by the Auditors (or summaries thereof).

K. Quarterly Results and Reports on Form 10-Q. To review with management and the Auditors, as appropriate, (i) the results of the Auditors' review of the Company's quarterly financial statements and any disclosure from the Company's Chief Executive Officer and Chief Financial Officer to be made in connection with the certification of the Company's quarterly reports filed with the SEC, prior to public disclosure of quarterly financial information, if practicable, or filing with the SEC of the Company's Quarterly Report on Form 10-Q, and any other matters required to be communicated to the Committee by the Auditors under the standards of the PCAOB and (ii) other relevant reports or financial information submitted by the Company to any governmental body or the public, including relevant reports rendered by the Auditors (or summaries thereof).

L. Management's Discussion and Analysis and Risk Factors. To review with management and the Auditors, as appropriate, the Company's disclosures contained under the captions "*Management's Discussion and Analysis of Financial Condition and Results of Operations*" and "*Risk Factors*" in its periodic reports and other filings to be filed with the SEC.

M. Press Releases. To review with management and the Auditors, to the extent appropriate, earnings press releases, as well as the substance of financial information and earnings guidance provided to analysts and ratings agencies (including, without limitation, reviewing any pro forma or non-GAAP information), which discussions may be general discussions of the type of information to be disclosed or the type of presentation to be made.

N. Accounting Principles and Policies. To review with management and the Auditors, as appropriate, significant issues that arise regarding accounting principles and financial statement presentation, including critical accounting policies and practices, alternative accounting policies available under GAAP related to material items discussed with management, the potential impact on the Company's financial statements of off-balance sheet structures and any other significant reporting issues and judgments, significant regulatory, legal and accounting initiatives or developments that may have a material impact on the Company's financial statements, compliance programs and policies if, in the judgment of the Committee, such review is necessary or appropriate.

O. Risk Assessment and Management. To review and discuss with management and the Auditors, as appropriate, (i) the Company's guidelines and policies with respect to financial risk management and financial risk assessment, including the Company's major financial risk exposures and the steps taken by management to monitor and control these exposures and (ii) management risks relating to data privacy, technology and information security, including cyber security and back-up of information systems, the steps the Company has taken to monitor and control such exposures and major legislative and regulatory developments that could materially impact the Company's privacy and data security risk exposure.

P. Management Cooperation with Audit. To evaluate the cooperation received by the Auditors during their audit examination, including any significant difficulties encountered during the audit or any restrictions on the scope of their activities or access to required records, data and information and, whether or not resolved, significant disagreements with management and management's response, if any.

Q. Management Letters. To review with the Auditors and, if appropriate, management, any "management" or "internal control" letter issued or, to the extent practicable, proposed to be issued by the Auditors and management's response, if any, to such letter, as well as any additional material written communications between the Auditors and management.

R. National Office Communications. To review with the Auditors, as appropriate, communications between the audit team and the Auditors' national office with respect to accounting or auditing issues presented by the engagement.

S. Disagreements Between Auditors and Management. To review with management and the Auditors, or any other registered public accounting firm engaged to perform

review or attest services, any conflicts or disagreements between management and the Auditors, or such other accounting firm, whether or not resolved, regarding financial reporting, accounting practices or policies or other matters, that individually or in the aggregate could be significant to the Company’s financial statements or the Auditors’ report, and to resolve any conflicts or disagreements regarding financial reporting.

T. Internal Control over Financial Reporting; Disclosure Controls. To (i) confer with management and the Auditors, as appropriate, regarding the scope, adequacy, and effectiveness of internal control over financial reporting and the Company’s disclosure controls and procedures, including any significant deficiencies, significant changes in internal controls and the adequacy and effectiveness of the Company’s information and cyber security policies and the internal controls regarding information security, (ii) confer with management and the Auditors, as appropriate, regarding the responsibilities, budget and staff of the internal audit function (if any) and review of the appointment or replacement of the senior internal audit executive or manager and (iii) obtain reports on significant findings and recommendations with respect to internal controls over financial reporting, together with management responses and any special audit steps adopted in light of any material control deficiencies.

U. Separate Sessions. Periodically, to meet in separate sessions with the Auditors, the internal auditors, if any, or other personnel responsible for the internal audit function, as applicable and appropriate, and management to discuss any matters that the Committee, the Auditors, the internal auditors, if any, or other personnel responsible for the internal audit function, or management believe should be discussed privately with the Committee.

V. Correspondence with Regulators. To consider and review with management, the Auditors, outside counsel, as appropriate, and any special counsel, separate accounting firm or other consultants and advisors as the Committee deems appropriate, any correspondence with regulators or governmental agencies and any published reports that raise material issues regarding the Company’s financial statements or accounting policies.

W. Complaint Procedures. To establish procedures, when and as required by applicable laws and rules, for the receipt, retention and treatment of complaints received by the Company regarding accounting, internal accounting controls or auditing matters and the confidential and anonymous submission by employees of concerns regarding questionable accounting or auditing matters, including under the Company’s “Whistleblower Policy for Accounting and Auditing Matters.”

X. Engagement of Registered Public Accounting Firms. To determine and approve engagements of any registered public accounting firm (in addition to the Auditors), prior to commencement of such engagements, to perform any other review or attest service, including the compensation to be paid by the Company to such firm, which approval may be pursuant to preapproval policies and procedures, including the delegation of preapproval authority to the chairman of the Committee, so long as any such preapproval decisions are presented to the full Committee at the next scheduled meeting.

Y. Ethical Compliance. To review the results of management's efforts to monitor compliance with the Company's programs and policies designed to ensure adherence to applicable laws and rules, as well as to its Code of Business Conduct and Ethics.

Z. Investigations. To investigate any matter brought to the attention of the Committee within the scope of its duties if, in the judgment of the Committee, such investigation is necessary or appropriate.

AA. Proxy Report. To oversee the preparation of the report of the Committee required by the rules of the SEC to be included in the Company's annual proxy statement.

BB. Insurance Coverage. The Committee shall have the authority to review and establish appropriate insurance coverage for the Company's directors and officers.

CC. Report to Board. To report to the Board material issues that arise regarding the quality or integrity of the Company's financial statements, the Company's compliance with legal or regulatory requirements, the performance or independence of the Auditors, the performance of the Company's internal audit function (as applicable) or such other matters as the Committee deems appropriate from time to time or whenever it shall be called upon to do so.

DD. Internal Control Report. To obtain and review, at least annually, a report by the Auditors describing that firm's internal quality control procedures, any material issues raised by the firm's most recent internal quality control review or peer review or by any inquiry or investigation within the preceding five years by governmental or professional authorities with respect to one or more independent audits performed by the firm, as well as any steps taken to address the issues raised.

EE. Annual Charter Review. To review and assess the adequacy of this charter annually and recommend any proposed changes to the Board for approval.

FF. Review Related Person Transactions and Policy. To review, consider, approve or ratify "Related Person Transactions" pursuant to the Company's Related Person Transactions Policy (the "**Related Persons Transactions Policy**") duly adopted by the Board, and to review and assess the adequacy of the Related Persons Transactions Policy annually and recommend any proposed changes to the Board for approval.

GG. Other Legal and Finance Matters. To review, (i) with the Company's counsel, legal compliance and legal matters that could have a significant impact on the Company's financial statements and (ii) with management, the Company's finance function, including its budget, organization and quality of personnel.

HH. General Authority. To perform such other functions and to have such powers as may be necessary or appropriate in the discharge of any of the foregoing.

VII. PUBLICATION

The Company shall make this charter freely available to stockholders on request and, provided that the Company is subject to the periodic reporting requirements of the Exchange Act, shall publish it on the Company's website.

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TAYSHA GENE THERAPIES, INC.

**CHARTER OF THE COMPENSATION COMMITTEE OF
THE BOARD OF DIRECTORS**

I. PURPOSE

The primary purpose of the Compensation Committee (the “*Committee*”) of the Board of Directors (the “*Board*”) of Taysha Gene Therapies, Inc. (the “*Company*”) shall be to act on behalf of the Board in fulfilling the Board’s oversight responsibilities with respect to the Company’s compensation policies, plans and programs, and to review and determine (or recommend to the Board for approval) the compensation to be paid to the Company’s executive officers and directors. In addition, the Committee shall (i) review and discuss with management the Company’s disclosures contained under the caption “*Compensation Discussion and Analysis*” (“*CD&A*”), when and as required by applicable rules and regulations of the Securities and Exchange Commission (the “*SEC*”) in effect from time to time, for use in any of the Company’s annual reports on Form 10-K, registration statements, proxy statements or information statements filed with the SEC and (ii) prepare and review the Committee report on executive compensation included in the Company’s annual proxy statement in accordance with applicable rules and regulations of the SEC in effect from time to time.

The term “compensation” shall include salary, long-term incentives, bonuses, perquisites, equity incentives, severance arrangements, retirement benefits and other related benefits and benefit plans. The term “executive officer” means any “officer” as defined in Rule 16a-1(f) under the Securities Exchange Act of 1934, as amended (the “*Exchange Act*”).

The policy of the Committee shall be to maintain an overall compensation structure designed to attract, retain and motivate management and other employees by providing appropriate levels of risk and reward in proportion to individual contribution and performance.

II. COMPOSITION

The Committee shall consist of at least two (2) members of the Board. All members of the Committee shall satisfy, as determined by the Board, (i) the independence requirements imposed by The Nasdaq Stock Market LLC (“*Nasdaq*”) applicable to compensation committee members, as in effect from time to time, when and as required, including any phase-in periods permitted by these requirements, (ii) any other qualifications determined by the Board or the Nominating and Corporate Governance Committee from time to time, (iii) the “non-employee director” standard within the meaning of Rule 16b-3 promulgated under the Exchange Act and (iv) any other requirements imposed by applicable law.

Any subsequent determination that any member of the Committee does not qualify as a “non-employee director” will not invalidate any previous actions by the Committee, except to the extent required by law or determined to be appropriate to satisfy regulatory standards.

The members of the Committee shall be appointed by and serve at the discretion of the Board. Vacancies occurring on the Committee shall be filled by the Board. The Committee's chairperson shall be appointed by the Board, or if the Board does not do so, the Committee members shall designate a chairperson by vote of a majority of the full Committee.

III. MEETINGS AND MINUTES

The Committee shall hold such regular or special meetings as its members shall deem necessary or appropriate, but in no event shall it meet less than annually. Any member of the Committee or the Board may call a meeting of the Committee.

Minutes of each meeting of the Committee shall be prepared and distributed to each director of the Company and the Secretary of the Company promptly after each meeting. The chairperson of the Committee shall report to the Board from time to time and whenever requested to do so by the Board.

IV. AUTHORITY

Each member of the Committee shall have full access to all books, records, facilities and personnel of the Company as deemed necessary or appropriate by any member of the Committee to discharge his or her responsibilities hereunder, including human resources personnel preparing the CD&A for inclusion in the Company's filings with the SEC when and as required.

The Committee shall have authority to pay, at the expense of the Company, ordinary administrative expenses that the Committee deems necessary or appropriate in carrying out its duties, unless prohibited by Nasdaq listing rules or applicable law. Except as limited by applicable law, rules and regulations, the Committee shall have authority to request that any of the Company's personnel, counsel, accountants or investment bankers, or any other consultant or advisor to the Company, attend any meeting of the Committee or meet with any member of the Committee or any of its Compensation Consultants.

The Committee may form and delegate authority to subcommittees as appropriate (but only to the extent consistent with the Company's amended and restated certificate of incorporation, amended and restated bylaws (the "*Bylaws*"), Corporate Governance Guidelines (as defined below), rules of Nasdaq and other applicable law), including, but not limited to a subcommittee composed of one or more members of the Board or officers of the Company to grant stock awards under the Company's equity incentive plans to persons who are not then subject to Section 16 of the Exchange Act. Without limiting the generality of the foregoing, the Committee may form and delegate authority to a committee composed solely of employees of the Company to serve as an administrative and/or investment committee, with fiduciary responsibilities under the Employee Retirement Income Security Act of 1974 ("*ERISA*"), with respect to one or more Company plans that are subject to ERISA. Delegation by the Committee to any subcommittee shall not limit or restrict the Committee on any matter so delegated, and, unless the Committee alters or terminates such delegation, any action by the Committee on any matter so delegated shall not limit or restrict future action by such subcommittee on such matters. The operation of the Committee shall be subject to the Bylaws as in effect from time to time and Section 141 of the Delaware General Corporation Law (or any successor section). The approval

of this charter by the Board shall be construed as a delegation of authority to the Committee with respect to the responsibilities set forth herein.

V. RESPONSIBILITIES

To implement the Committee's purpose, the Committee shall have the following responsibilities. The Committee may supplement and deviate from these activities as appropriate under the circumstances (except as otherwise required by applicable law or the requirements of any stock exchange on which any of the Company's capital stock is then listed):

A. Overall Compensation Strategy. The Committee shall review, modify (as needed) and approve, or review and recommend, as applicable, the overall compensation strategy and policies for the Company, including:

- reviewing and approving, or reviewing and recommending to the Board for approval, annual corporate goals and objectives relevant to the compensation of the Company's Chief Executive Officer (the "*CEO*") and, to the extent applicable, other executive officers and senior management, as appropriate;
- evaluating and approving, or recommending to the Board for approval, the Company's performance against corporate goals and objectives;
- evaluating and approving, or recommending to the Board for approval, the compensation plans and programs advisable for the Company, as well as evaluating and approving, or recommending to the Board for approval, the modification or termination of existing plans and programs;
- establishing policies with respect to equity compensation arrangements with the objective of appropriately balancing the perceived value of equity compensation and the dilutive and other costs of that compensation to the Company;
- reviewing compensation practices and trends to assess the adequacy and competitiveness of the Company's executive compensation programs among comparable companies in the Company's industry; however, the Committee shall exercise independent judgment in determining the appropriate levels and types of compensation to be paid or awarded to executives and in recommending to the full Board the appropriate levels and types of compensation to be paid or awarded to non-employee members of the Board;
- reviewing and approving the terms of any employment agreements, severance arrangements, change-of-control protections and any other compensatory arrangements (including, without limitation, perquisites and any other form of compensation) for the Company's executive officers and other senior management, as appropriate, which includes the ability to adopt, amend and terminate such agreements or arrangements, and to delegate authority to the Company's CEO and any other executive officer to approve and adopt employment agreements or arrangements;
- reviewing and approving any compensation arrangement for any executive officer involving any subsidiary, special purpose or similar entity, taking into account the

potential for conflicts of interest in such arrangements and whether the arrangement has the potential to benefit the Company;

- monitoring the Company's compliance with the requirements of the Sarbanes Oxley Act of 2002 relating to loans to officers and directors and with all other applicable laws affecting employee compensation and benefits;
- reviewing the Company's practices and policies of employee compensation as they relate to risk management and risk-taking incentives, to determine whether such compensation policies and practices are reasonably likely to have a material adverse effect on the Company;
- review and consider the results of any advisory vote on executive compensation if required by Section 14A of the Exchange Act and the rules and regulations promulgated thereunder; and
- evaluating the efficacy of the Company's compensation policy and strategy in achieving expected benefits to the Company and otherwise furthering the Committee's policies.

B. Compensation of Chief Executive Officer. The Committee shall determine and approve, or review and recommend to the Board for approval, the compensation and other terms of employment of the Company's CEO and shall evaluate the CEO's performance in light of relevant corporate goals and objectives, taking into account, among other things, the policies of the Committee and the CEO's performance in:

- fostering a corporate culture that promotes the highest level of innovation, integrity and the highest ethical standards;
- developing and executing the Company's long-term strategic plan and conducting the business of the Company in a manner appropriate to enhance long-term stockholder value;
- achieving specified corporate goals and objectives; and
- achieving other individual or corporate goals and objectives deemed relevant to the CEO as established by the Committee.

In determining any long-term incentive component of the CEO's compensation, the Committee should seek to achieve an appropriate level of risk and reward, taking into consideration the Company's long-term performance, need for a sustainable pipeline of products and relative stockholder return, the potential benefits and costs to the Company of the award, the value of similar incentive awards given to chief executive officers of comparable companies, the awards given to the CEO in past years and such other criteria as the Committee deems advisable. Based on its evaluation, the Committee shall determine and approve, or recommend to the Board for determination and approval, the compensation and other terms of employment of the CEO. The CEO may not be present during the voting or deliberations regarding his or her compensation.

C. Compensation of Other Officers and Senior Management. The Committee shall evaluate and approve, or recommend to the Board for approval, the achievement of individual performance goals and objectives of the Company's other officers (as that term is defined in Section 16 of the Exchange Act and Rule 16a-1 thereunder) and other senior management, as appropriate, that are established annually by the CEO. The Committee shall determine and approve, or review and recommend to the Board for approval, all elements of the compensation and other terms of employment of these executive officers and other senior management, as appropriate, taking into consideration the person's success in achieving his or her individual performance goals and objectives and the corporate goals and objectives deemed relevant to the person as established by the Committee or the Board, as appropriate, and in fostering a corporate culture that promotes the highest level of innovation, integrity and the highest ethical standards. In evaluating and determining, or making recommendations regarding, officer compensation, the Committee may, at its sole discretion, give consideration to the recommendations of the CEO.

D. Market Data. The Committee shall review industry and market appropriate compensation practices and trends to assess the adequacy and competitiveness of the Company's executive compensation programs among comparable companies as well as the appropriateness of such programs.

E. Compensation of Directors. The Committee shall review and recommend to the Board the type and amount of compensation to be paid or awarded to non-employee Board members, including any consulting, retainer, meeting, committee and committee chair fees, as well as equity awards.

F. Selection of Compensation Consultants, Legal Counsel and Other Advisors. The Committee shall have the authority to obtain, at the expense of the Company, advice and assistance from internal or external legal, accounting or other advisors, experts and consultants (collectively, "**Compensation Consultants**") as the Committee deems necessary or appropriate for carrying out its duties under this charter. The Committee shall have direct responsibility for the appointment, compensation and oversight of the work of Compensation Consultants. Such Compensation Consultants shall report directly, and be accountable, to the Committee. The Committee may retain, or receive advise from, Compensation Consultants only after assessing the independence of such person in accordance with Nasdaq Listing Rule 5605(d)(3) or the requirements of any stock exchange on which any of the Company's capital stock is listed. However, nothing in this provision requires that any Compensation Consultants be independent. The Committee need not conduct this independence assessment with respect to: (a) the Company's in-house legal counsel; or (b) any Compensation Consultant whose role is limited to (i) consulting on any broad-based plan that does not discriminate in scope, terms or operation in favor of executive officers or directors of the Company and that is available generally to all salaried employees or (ii) providing information that either is not customized for a particular company or that is customized based on parameters that are not developed by the Compensation Consultant and about which the Compensation Consultant does not provide advice. The Committee shall have sole authority to approve the reasonable fees and the other terms and conditions of such engagement, including authority to terminate the engagement. The Company must provide for appropriate funding, as determined by the Committee, for payment of reasonable compensation to any such Compensation Consultant retained by the Committee.

Nothing in this provision requires the Committee to implement or act consistently with the advice or recommendations of any Compensation Consultant or affects the ability or obligation of the Committee to exercise its own judgment in fulfillment of its duties.

G. Administration of Benefit Plans. The Committee shall have full power and authority to adopt, amend and terminate the Company's stock option plans, stock appreciation rights plans, pension and profit sharing plans, incentive plans, stock bonus plans, stock purchase plans, bonus plans, deferred compensation plans and sub-plans thereof, severance plans and similar programs, including perquisites pertaining to executive officers, as the Committee deems appropriate or as otherwise required under such plans. The Committee shall have full power and authority to administer these plans, establish guidelines, interpret plan documents, select participants, approve grants and awards, approve modifications to awards, and exercise such other power and authority as may be permitted or required under such plans. Notwithstanding anything to the contrary, the Board shall retain the right to act on all such matters without limiting the Committee's authority, subject to compliance with applicable laws and regulations.

H. Compensation Discussion and Analysis. When and as required by applicable rules and regulations of the SEC in effect from time to time, the Committee shall review and discuss with management the Company's disclosures contained under the caption "*Compensation Discussion and Analysis*" for use in any of the Company's annual reports on Form 10-K, registration statements, proxy statements or information statements and determine whether to recommendation to the Board that the CD&A be approved for inclusion in the Company's annual reports on Form 10-K, registration statements, proxy statements or information statements.

I. Compensation Proposals. The Committee shall provide recommendations to the Board on compensation related proposals to be considered at the Company's annual meeting of stockholders, including the frequency of advisory votes on executive compensation.

J. Conflict of Interest Disclosure. The Committee shall review and discuss with management any conflicts of interest raised by the work of a Compensation Consultant retained by the Committee or management and how such conflict is being addressed, and prepare any necessary disclosure in the Company's annual proxy statement in accordance with applicable SEC rules and regulations.

K. Committee Report. The Committee shall prepare and review the Committee report on executive compensation to be included in the Company's annual proxy statement in accordance with applicable SEC rules and regulations.

L. Clawback Policies. Approve, modify (or recommend to the Board for approval or modification) and oversee and the Company's compensation clawback or similar policies, including, when required, a clawback policy that complies with the requirements of the SEC and Nasdaq listing standards.

M. Charter. The Committee shall review and assess the adequacy of this charter annually and shall recommend any proposed changes to the Board for its consideration.

N. General Authority. The Committee shall perform such other functions and have such other powers as may be necessary or appropriate in the discharge of any of the foregoing.

VI. PUBLICATION

The Company shall make this charter freely available to stockholders on request and, provided that the Company is subject to the periodic reporting requirements of the Exchange Act, shall publish it on the Company's website.

* * * *

TAYSHA GENE THERAPIES, INC.

CHARTER OF THE NOMINATING AND CORPORATE GOVERNANCE COMMITTEE OF THE BOARD OF DIRECTORS

AMENDED AND RESTATED AS OF APRIL 18, 2022

I. PURPOSE

The primary purpose of the Nominating and Corporate Governance Committee (the “*Committee*”) of the Board of Directors (the “*Board*”) of Taysha Gene Therapies, Inc. (the “*Company*”) shall be to: (i) oversee aspects of the Company’s corporate governance functions on behalf of the Board; (ii) make recommendations to the Board regarding corporate governance issues; (iii) identify and evaluate candidates to serve as directors of the Company, consistent with the criteria approved by the Board, (iv) review and evaluate the performance of the Board; (v) serve as a focal point for communication between director candidates, non-committee directors and the Company’s management; (vi) make recommendations to the Board regarding the selection and approval of candidates to serve as nominees for director to be submitted to a stockholder vote at the annual meeting of stockholders; and (vii) make other recommendations to the Board regarding affairs relating to the directors of the Company.

II. COMPOSITION

The Committee shall consist of at least two (2) members of the Board. The members of the Committee shall satisfy the independence requirements imposed by any stock exchange on which any of the Company’s capital stock is listed, including any phase-in periods permitted by such requirements. The members of the Committee shall be appointed by and serve at the discretion of the Board. Vacancies occurring on the Committee shall be filled by the Board. The Committee’s chairperson shall be appointed by the Board, or if the Board does not do so, the Committee members shall designate a chairperson by vote of a majority of the full Committee.

III. MEETINGS AND MINUTES

The Committee shall hold such regular or special meetings as its members shall deem necessary or appropriate, but in no event shall it meet less than annually. Any member of the Committee or the Board may call a meeting of the Committee.

Minutes of each meeting of the Committee shall be prepared and distributed to each director of the Company and the Secretary of the Company after each meeting. The chairperson of the Committee shall report to the Board from time to time or whenever so requested by the Board.

IV. AUTHORITY

Each member of the Committee shall have full access to all books, records, facilities and personnel of the Company as deemed necessary or appropriate by any member of the Committee to discharge his or her responsibilities hereunder. The Committee shall have access to and shall

communicate with the Board, chairpersons of the committees of the Board, members of senior management and independent professional advisors to the Board and its various committees, as applicable. The Committee shall have the authority to obtain, at the expense of the Company, taking into account budgetary constraints then facing the Company and strategic priorities, advice and assistance from internal or external legal, accounting or other advisors, experts and consultants as the Committee deems necessary or appropriate for carrying out its duties under this charter. The Committee shall have the authority to retain and terminate executive search firms to help identify director candidates. The Committee shall have the authority to approve fees, costs and other terms of engagement of such outside resources and shall be directly responsible for the oversight of such outside resources. The Committee shall also have authority to pay, at the expense of the Company, ordinary administrative expenses that, as determined by the Committee, are necessary or appropriate in carrying out its duties, unless prohibited by Nasdaq listing rules or applicable law. The Committee shall have authority to request that any of the Company's personnel, counsel, accountants or investment bankers, or any other consultant or advisor to the Company, attend any meeting of the Committee or meet with any member of the Committee or any of its special, outside legal, accounting or other, advisors or consultants.

The Committee may form and delegate authority to one or more subcommittees as appropriate, but only to the extent consistent with the Company's amended and restated certificate of incorporation, amended and restated bylaws (the "**Bylaws**"), Corporate Governance Guidelines (as defined below), rules of The Nasdaq Stock Market LLC and other applicable law. Delegation by the Committee to any subcommittee shall not limit or restrict the Committee on any matter so delegated, and, unless the Committee alters or terminates such delegation, any action by the Committee on any matter so delegated shall not limit or restrict future action by such subcommittee on such matters. The operation of the Committee shall be subject to the Bylaws as in effect from time to time and Section 141 of the Delaware General Corporation Law (or any successor section). The approval of this charter shall be construed as a delegation of authority to the Committee with respect to the responsibilities set forth herein.

V. RESPONSIBILITIES

To implement the Committee's purpose, the Committee shall have the following responsibilities. The Committee may reasonably supplement and deviate from these activities as appropriate under the circumstances (except as otherwise required by applicable law or the requirements of any stock exchange on which any of the Company's capital stock is then listed):

A. Director Nominations. The Committee shall identify and evaluate candidates to serve on the Company's Board consistent with the criteria approved by the Board, including consideration of the potential conflicts of interest as well as applicable independence and other requirements as set forth in the Company's Corporate Governance Guidelines, as in effect from time to time (the "**Corporate Governance Guidelines**"). The Committee shall also have responsibility for reviewing, evaluating and considering the recommendation for nomination of incumbent directors for re-election to the Board, as well as monitoring the size of the Board. The Committee shall also recommend to the Board for selection, candidates to the Board to serve as nominees for director for the annual meeting of stockholders. The Committee shall also have the power and authority to consider recommendations for Board nominees and proposals submitted by the Company's stockholders, to recommend to the Board appropriate action on any such proposal or recommendation and to make any disclosures required by Nasdaq listing rules and

applicable law in the course of exercising its authority. The Committee shall recommend nominees to the Board at an appropriate time: (a) prior to each annual meeting of stockholders at which directors are to be elected or re-elected; and (b) after a vacancy arises on the Board or a director advises the Board of his or her intention to resign.

B. Board Assessment. The Committee shall periodically review, discuss and assess the performance of the Board, including Board committees, seeking input from senior management, the full Board and others. The assessment shall include evaluation of the Board's contribution as a whole and the Board's effectiveness in serving the best interests of the Company and its stockholders, specific areas in which the Board and/or management believe contributions could be improved, and overall Board composition and makeup. The factors to be considered shall include whether the directors, both individually and collectively, can and do provide the integrity, experience, judgment, commitment, skills and expertise appropriate for the Company. The Committee shall also consider and assess the independence of directors, including whether a majority of the Board continue to be independent from management in both fact and appearance, as well as within the meaning prescribed by any stock exchange on which any of the Company's capital stock is then listed. The results of these reviews shall be provided to the Board for further discussion as appropriate.

C. Board Committee Membership. The Committee oversees the Board's committee structure and operations. The Committee, after due consideration of the interests, independence and experience of the individual directors and the independence and experience requirements set forth in the listing standards of any stock exchange on which the Company's capital stock is listed, the rules and regulations of the Securities and Exchange Commission and applicable law, shall make recommendations to the entire Board regarding the appointment of directors to serve as members of each committee and committee chairmen.

D. Stockholder Communications. The Committee shall periodically review and make recommendations to the Board regarding the Company's process for stockholder communications with the Board, and make such recommendations to the Board with respect thereto as the Committee deems appropriate.

E. Director Education. The Committee may implement an orientation process for directors that includes background material on the Company's policies and procedures and expectations as to directors and committee member duties and responsibilities, meetings with senior management and visits to the Company's facilities. The Committee shall also recommend to the Board such plan or program as it may deem appropriate for the continuing education of directors.

F. Corporate Governance Guidelines and Principles. The Committee shall periodically review and assess the Corporate Governance Guidelines and the Code of Business Conduct and Ethics, and shall recommend any changes deemed appropriate to the Board for its consideration.

G. Management Succession. The Committee shall develop and periodically review with the Company's Chief Executive Officer the plans for succession for the Company's executive officers, as it sees fit, and make recommendations to the Board with respect to the selection of appropriate individuals to succeed to these positions.

H. Procedures for Information Dissemination. The Committee shall periodically review the processes and procedures used by the Company to provide information to the Board and its committees and make recommendations to the Board and management for improvement as appropriate. The Committee should consider, among other factors, the reporting channels through which the Board and its committees receive information and the level of access to outside advisors where necessary or appropriate, as well as the procedures for providing accurate, relevant and appropriately detailed information to the Board and its committees on a timely basis.

I. Ethical Compliance. The Committee shall review the results of management's efforts to monitor compliance with the Company's programs and policies designed to ensure adherence to applicable laws and rules, as well as to its Code of Business Conduct and Ethics.

J. Insider Trading Policy and Risk Assessment. The Committee shall review, and recommend that the Board consider and approve, any changes to the Company's Insider Trading Policy. The Committee shall also oversee and review with management the Company's major legal compliance risk exposures and the steps management has taken to monitor or mitigate such exposures, including the Company's procedures and any related policies with respect to risk assessment and risk management.

K. Leadership Structure. The Committee shall consider the Board's leadership structure, including the separation of the chairperson and Chief Executive Officer roles and/or appointment of a lead independent director of the Board, either permanently or for specific purposes, and make such recommendations to the Board with respect thereto as the Committee deems appropriate. The Committee shall also review and discuss the narrative disclosure regarding the Board leadership structure and role in risk oversight to be included in any public filing in response to the requirements of Item 407(h) of Regulation S-K (or any successor disclosure item).

L. Committee Self-Assessment; Charter. The Committee shall review, discuss and assess its own performance at least annually. The Committee shall also review and assess the adequacy of this charter annually, including the Committee's role and responsibilities outlined herein, and shall recommend any proposed changes to the Board for its consideration.

M. Report to the Board. The Committee, through the Committee's chairperson, shall regularly report to the Board regarding the Committee's actions, or whenever so requested by the Board.

N. General Authority. The Committee shall perform such other functions and have such other powers as may be necessary or appropriate in the discharge of the foregoing.

VI. PUBLICATION

The Company shall make this charter freely available to stockholders on request and, provided that the Company is subject to the periodic reporting requirements of the Securities Exchange Act of 1934, as amended, shall publish it on the Company's website.

* * * *

Nasdaq Spotlight: Taysha Gene Therapies

In this special Nasdaq interview for Black History Month, the host, Christine Lee, speaks with R.A. Session II, President, Founder, and CEO of Tasha Gene Therapies. Tasha Gene Therapies, founded in 2019, aims to eradicate monogenic CNS diseases, particularly for pediatric patients, using gene therapy. The company's mission is driven by the curative potential of gene therapy.

The conversation delves into Tasha Gene Therapies' commitment to advancing Black health and wellness. R.A. emphasizes the importance of global thinking in drug development, ensuring diverse representation in clinical trials, and addressing the burden of diseases that affect everyone, regardless of ethnicity.

The term "Taisha" in the Caddo Native American language means ally or friend, reflecting the importance of having allies in one's life. R.A. acknowledges the impact of mentors and allies throughout his career, providing opportunities and support that contributed to his success.

On the topic of diversity and inclusivity within Tasha Gene Therapies, R.A. highlights the company's commitment to hiring the best people for the job, fostering a management team with around 40% women and significant ethnic diversity. He encourages expanding networks for greater inclusivity.

R.A. emphasizes the need for the biotech sector to mirror the diversity of the patients it serves, advocating for equitable access to healthcare and innovative medicines. The interview concludes with a call for organizations, including Nasdaq, to promote diversity at all levels, ensuring that companies and clinical trials reflect the global population they serve.

Taysha Gene Therapies Rett Syndrome Community November 2022 Update

In this YouTube video transcript, Chelsea Carbocus, the leader of the patient advocacy team at Tasia Gene Therapies, provides an overview of their investigational gene therapy approach for Rett syndrome. The presentation emphasizes the importance of patient perspectives in shaping their clinical trials. Chelsea introduces the company's focus on developing gene therapies for rare monogenic diseases of the central nervous system, particularly Rett syndrome.

Kristen Phillips, head of patient experience, discusses insights gathered from caregivers of adults with Rett syndrome, detailing the impact of symptoms on quality of life. The information obtained influenced the design of the clinical trial protocol, with key endpoints selected based on caregivers' desired improvements.

Dr. Suyash Prasad, Tasia's chief medical officer, explains the science behind their gene therapy program for Rett syndrome. He describes the gene therapy's goal to replace the missing protein (MeCP2) using a viral vector. Dr. Prasad introduces the "Reveal" study, a multi-center phase one-two clinical trial in adult females with Rett syndrome. The study aims to assess safety and efficacy, with two separate doses and a randomized approach.

Dr. Prasad outlines the potential benefits and risks of the study, highlighting the commitment required from participants. He also discusses eligibility criteria and the study's operational logistics. Tasia plans to expand trials to pediatric females and males with Rett syndrome, aiming to address the significant unmet need in the community.

The presentation concludes with gratitude towards patient advocacy groups, colleagues, and the Rett community for their collaboration. Chelsea encourages further engagement, providing an email address for inquiries and expressing Tasia's commitment to integrating patient feedback throughout the research program.

Taysha Gene Therapies: Putting Patients at the Center

representatives from Taysha Gene Therapies discuss the company's focus on developing gene therapy treatments for rare and severe neurological diseases, particularly in children. The speakers introduce Taysha's approach, mentioning their use of AAV9 capsid, HEK-293 mammalian cell suspension, and intrathecal delivery across their programs. They highlight their collaboration with the University of Texas Southwestern for early proof-of-concept work and discuss their three main program franchises: neurodegenerative diseases, neurodevelopmental diseases (including Angelman syndrome), and genetic epilepsies.

The transcript provides an overview of Taysha's portfolio, mentioning ongoing clinical trials and plans to share data on various programs. The focus then shifts to Angelman syndrome, where Taysha has two approaches – one involving gene replacement therapy and the other using an shRNA approach to knock down ATS transcripts. The speakers discuss the design of these approaches and emphasize their commitment to collaboration with advocacy groups like the Foundation for Angelman Syndrome Therapeutics (FAST).

The presentation concludes with a discussion on Taysha's patient-centric guiding principles, emphasizing collaboration, transparent communication, curiosity, empathy, and respect. The company expresses gratitude for the partnerships with advocacy groups and the Angelman community, highlighting their intent to work closely with these communities to advance gene therapy programs. The transcript also includes a portion where Emily, a representative from Taysha, discusses their approach to collaboration with patient advocacy groups and the importance of understanding patient needs and developing educational resources together.

NTSAD GM2 Breakout | Taysha Gene Therapies

Suyash Prasad, introduces himself as a pediatrician turned clinical researcher in rare pediatric metabolic and neurological diseases. He is the Chief Medical Officer and Head of Research and Development at Tasher Gene Therapies, a company based in Dallas, Texas, focusing on AAV9 gene therapy for treating rare and severe neurological diseases.

Tasher has a broad portfolio with 26 programs, and Prasad specifically discusses their approach to treating GM2 gangliosidosis, a rare genetic disorder. The gene therapy, named Tasha 101, aims to replace the missing enzyme (beta-hexosaminidase) responsible for the disease by introducing DNA coding for the alpha and beta subunits into the patient's cells. The therapy uses the AAV9 vector, which has demonstrated safety in other gene therapy approaches.

Preclinical data, including studies on mice, indicates a reduction in GM2 ganglioside accumulation, improved survival rates, and functional outcomes after Tasha 101 administration. The company collaborates with UT Southwestern for gene therapy expertise and has a patient-focused approach to clinical development, incorporating insights from patient surveys and focus groups.

Tasha has initiated a clinical trial in Canada for patients under 12 months old, focusing on early diagnosis and treatment. They plan to open a study in the U.S. later, with ongoing efforts to involve the international patient community. The company aims to share preliminary clinical data by the end of the year.

During the Q&A, Prasad addresses questions about potential multiple dosing, emphasizing the goal of one-time administration. He also distinguishes Tasha's gene replacement therapy from CRISPR-Cas9 and other genetic medicine approaches, highlighting the clinical precedent for gene replacement therapies. The speaker expresses openness to learning from the Canadian study and making adjustments for the U.S. study in collaboration with the FDA.

RA Session, Taysha Gene Therapy Discusses FOXG1 Syndrome

In the YouTube video transcript, the speaker discusses their initial surprise and positive impression when meeting with the Foxy One Foundation and the parents associated with it. The organization's understanding of the biology, unmet medical needs, disease progression, and epidemiology impressed the speaker. They highlight the professionalism of the group, mentioning that their positive impression extended to investors, collaborators, and friends in the industry.

The speaker emphasizes the importance of understanding the biology of a disease and having an animal model for testing potential therapeutics. They commend Foxy One Foundation for achieving these milestones in a relatively short period, stating that such progress typically takes patient advocacy groups decades. The focus is on early diagnosis and treatment, with an optimistic view of potential reversibility in neurodevelopmental diseases like FoxG1.

The speaker draws parallels with their experience in gene therapy for SMA (Spinal Muscular Atrophy) and expresses the desire to apply similar curative approaches to diseases like FoxG1. They discuss the challenges of overexpression and toxicity in gene therapy, using the example of Rett syndrome's 15-year research journey.

FoxG1 is compared to diseases like Angelman and Fragile X, and the speaker explains their approach to guard against overexpression-associated toxicity using genotypic tools. They express confidence in using their existing target panel for FoxG1, saving time in research and development.

The ultimate goal, as stated by the speaker, is to eradicate monogenic CNS diseases. They acknowledge the harshness of the term "eradicate" but argue that these diseases are similarly harsh. The speaker envisions a future where diseases like FoxG1 are eliminated from public awareness, likening it to the disappearance of polio.

The speaker shares a personal goal of making genetic diseases seem inconsequential to future generations, imagining a scenario where individuals casually mention having had a genetic disease but not dwelling on it. The overall tone is optimistic about the potential of gene therapy to revolutionize the treatment of various genetic diseases, including FoxG1.

Professional:

Overview

Taysha Gene Therapies is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we hope to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program to quickly and efficiently build an extensive, AAV gene therapy pipeline focused on both rare and large-market indications. Together, we leverage our fully integrated platform—an engine for new cures—to dramatically improve patients' lives.

Website

<http://www.tayshagtx.com>

Industry

Biotechnology

Company size

51-200 employees

[79 associated members](#) LinkedIn members who've listed Taysha Gene Therapies as their current workplace on their profile.

Headquarters

Dallas, TX

Founded

2020

Specialties

Gene Therapy, Central Nervous System, and Molecular Biology



Taysha Gene Therapies Announces First Pediatric Patient Dosed with TSHA-102 in REVEAL Phase 1/2 Pediatric Trial in Rett Syndrome

January 10, 2024

| Source: [Taysha Gene](#)[Follow](#)

08:00 ET

[Therapies, Inc.](#)

Initiation of REVEAL pediatric trial in the U.S. broadens the clinical evaluation of TSHA-102 to female patients 5-8 years old with stage three Rett syndrome

MHRA authorized the CTA for TSHA-102 in pediatric patients with Rett syndrome, enabling expansion of ongoing U.S. REVEAL pediatric trial into the U.K.

TSHA-102 clinical program now includes broad evaluation across pediatric, adolescent and adult patients in three countries including the U.S., U.K. and Canada

Initial safety and efficacy data for cohort one (low dose, n = 3) in the REVEAL pediatric trial expected in mid-2024

DALLAS, Jan. 10, 2024 (GLOBE NEWSWIRE) -- Taysha Gene Therapies, Inc. (Nasdaq: TSHA), a clinical-stage gene therapy company focused on developing and commercializing AAV-based gene therapies for the treatment of monogenic diseases

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Taysha Gene Therapies Announces First Pediatric Patie...



(MHRA) has authorized the Clinical Trial Application (CTA) for TSHA-102 in pediatric patients, enabling expansion of the ongoing U.S. REVEAL pediatric trial into the U.K.

TSHA-102 is a self-complementary intrathecally delivered AAV9 investigational gene transfer therapy that utilizes a novel miRNA-Responsive Auto-Regulatory Element (miRARE) technology designed to mediate levels of *MECP2* in the CNS on a cell-by-cell basis without risk of overexpression. Initial dosing in the REVEAL Phase 1/2 pediatric trial took place at RUSH University Medical Center in Chicago under Principal Investigator Elizabeth Berry-Kravis, M.D., Ph.D., Professor of Pediatrics, Neurology and Anatomy/Cell Biology at RUSH University Medical Center.

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“Dosing the first pediatric patient with Rett syndrome marks an important step forward in our efforts to broaden the clinical

evaluation of TSHA-102 to younger patients with earlier stages of Rett syndrome. We are pleased with our progress on expanding the study of TSHA-102 across a broad population of ages and stages of Rett syndrome to bring a potentially transformative

treatment option to all patients and families suffering from this devastating disease,” said Sukumar Nagendran, M.D., President, and Head of R&D of Taysha. “The pediatric trial will build on our ongoing REVEAL adolescent and adult trial, where early data demonstrated improvements across multiple clinical domains in

adult patients with the most advanced stage of disease. We also plan to expand our U.S. pediatric trial into the U.K. following the recent acceptance of our CTA by the MHRA.”

Elizabeth Berry-Kravis, M.D., Ph.D., Professor of Pediatrics, Neurology and Anatomy/Cell Biology, and Principal Investigator of the REVEAL pediatric trial added, “Designed as a one-time, disease-modifying treatment with the ability to mediate *MECP2* expression on a cell-by-cell basis, TSHA-102 holds the potential

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Caregivers in the clinic.

The [REVEAL Phase 1/2 pediatric trial](#) is an open-label, randomized, dose-escalation and dose-expansion study evaluating the safety and preliminary efficacy of TSZA-102 in pediatric females with Rett syndrome due to *MECP2* loss-of-function mutation in the U.S. and U.K. TSZA-102 is administered as a single lumbar intrathecal injection. Part A of the study will focus on determining Maximum Administered Dose (MAD) and Maximum Tolerated Dose (MTD) in at least six patients (three per dose) aged 5-8 years old. Part B will evaluate TSZA-102 at the MAD or MTD in two age cohorts (5-8 years and 3-5 years). The Company expects to complete dosing in cohort one (low dose) of the pediatric trial and report initial safety and efficacy data in mid-2024.

TSZA-102 is also being evaluated in the ongoing first-in-human [REVEAL Phase 1/2 adolescent and adult trial](#) in females aged 12 and older with Rett syndrome in Canada. The Company previously reported initial clinical data from the first two adult patients dosed with TSZA-102. Further updates on available clinical data from the low dose cohort in the REVEAL adolescent and adult trial are expected in the first quarter of 2024. TSZA-102 has received Fast Track designation and Orphan Drug and Rare Pediatric Disease designations from the FDA and has been granted Orphan Drug designation from the European Commission.

About Rett Syndrome

Rett syndrome is a rare neurodevelopmental disorder caused by mutations in the X-linked *MECP2* gene, which is a gene that's essential for neuronal and synaptic function in the brain. The disorder is characterized by intellectual disabilities, loss of communication, seizures, slowing and/or regression of development, motor and respiratory impairment, and shortened

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15,000 and 20,000 patients in the U.S., EU and U.K.

About Taysha Gene Therapies

Taysha Gene Therapies (Nasdaq: TSHA) is on a mission to eradicate monogenic CNS disease. With a singular focus on developing curative medicines, we aim to rapidly translate our treatments from bench to bedside. We have combined our team's proven experience in gene therapy drug development and commercialization with the world-class UT Southwestern Gene Therapy Program. Together, we leverage our fully integrated platform with a goal of dramatically improving patients' lives. More information is available at www.tayshagtx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "anticipates," "believes," "expects," "intends," "projects," "plans," and "future" or similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements concerning the potential benefits and clinical development of TSHA-102, including the timing of dosing patients in clinical trials and availability of data from clinical trials. Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our Annual Report on Form 10-K for the full-year

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