ALL IN FOR A WORLD WHERE EVERYONE LIVES

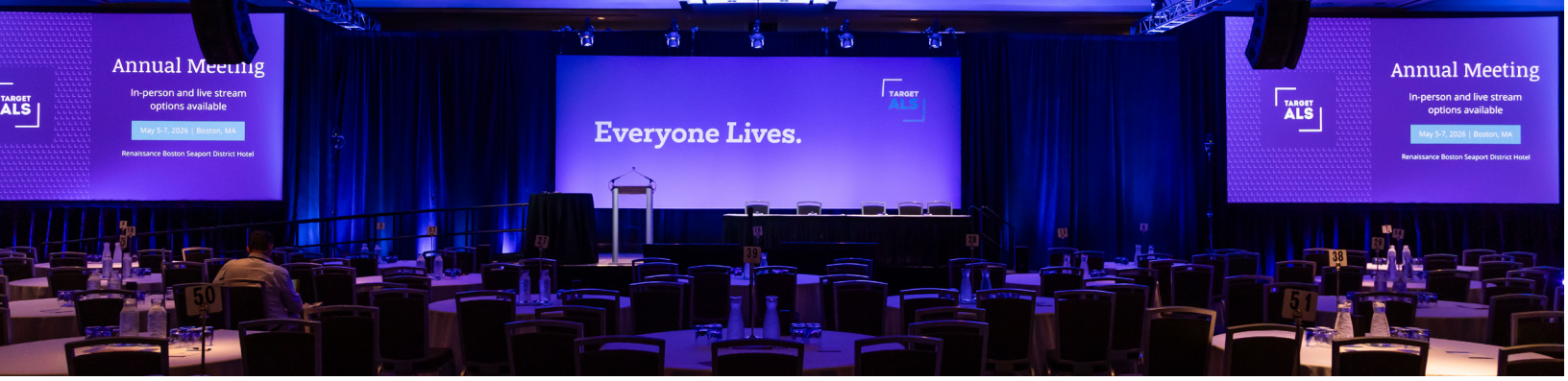
Highlights from the 2026 Target ALS Annual Meeting

TARGET ALS


Everyone Lives.
TARGET ALS


ALL IN FOR ALS RESEARCH
EVERYONE LIVES
ALL IN FOR ALS COMMUNITY

TABLE OF CONTENTS



DEAR FRIEND,

The 2026 Target ALS Annual Meeting was a powerful reminder of what is possible when urgency, collaboration, and innovation come together in pursuit of a shared goal: a world where everyone with ALS can live a long, quality life.

For some, this meeting was a familiar gathering of colleagues and friends. For many others, it was their first experience within the unique and dynamic Target ALS innovation ecosystem. The presence of both reflects the growth and evolution of a global community united by a singular mission: to accelerate effective treatments for ALS.

This year's meeting brought together every major constituency shaping the future of ALS research and drug development, including people living with ALS and their families, scientists and clinicians from academia and pharma/biotech, venture capital firms, and nonprofit organizations working on ALS as well as related neurodegenerative diseases. With more than 1,200 participants attending in person and online from 38 countries, representing over 212 academic institutions, 157 pharma/biotech and VC firms and over 47 non-profits, the meeting brought together a global community united by scientific rigor, openness, urgency, and a shared commitment to accelerating progress for people living with ALS.

Over the course of the meeting, two important trends emerged with even greater clarity.

The first is the continued expansion of expertise entering the ALS field. As scientific breakthroughs begin to crack open what once felt like an impenetrable barrier to ALS therapeutics, it is increasingly clear that solving this disease will require bold thinking and collaboration across scientific disciplines. Target ALS continues to intentionally bring experts from various scientific disciplines and other disease areas into the field, recognizing that new perspectives and approaches are essential to accelerating progress.

"The meeting brought together a global community united by scientific rigor, openness, urgency, and a shared commitment to accelerating progress for people living with ALS."

The second is the growing engagement of historically underrepresented communities worldwide. From the beginning, our global research initiatives have been built on the belief that all communities should benefit from

advances in ALS research and that more inclusive, representative datasets will lead to deeper scientific understanding and new discoveries. This work is helping create a research ecosystem that is not only more innovative, but more human and globally representative.

Throughout the meeting, there was a palpable sense of both hope and urgency.

> *"Progress will not happen overnight, but the momentum we are seeing reinforces that we are on the right path."*

Hope because meaningful progress is happening today. New therapeutic approaches rooted in a strong understanding of biology of the disease are advancing. Biomarker discoveries are opening doors that once seemed unimaginable. Science is moving forward in tangible and exciting ways.

Urgency because we know we are not yet where we need to be.

Progress will not happen overnight, but the momentum we are seeing reinforces that we are on the right path. At Target ALS, we remain committed to breaking down barriers, forging collaboration, and creating the conditions for scientists, clinicians, and industry leaders to accelerate their work as quickly as possible.

As was said during the meeting, our only competition is with ALS.

Everything we do is grounded in the belief that urgency matters, collaboration matters, and people with ALS and their families cannot wait.

Thank you for being part of this movement and for helping drive the progress highlighted throughout this report. Together, we are building a future where effective treatments for everyone living with ALS becomes a reality.

Sincerely,

MANISH RAISINGHANI, MBBS, PHD
CHIEF EXECUTIVE OFFICER
TARGET ALS

ON THE *CUTTING-EDGE*

Sharing early insights to accelerate the path forward

Our fund-enable-conduct model was borne out of a fragmented research landscape, where good ideas faced barriers to advancement and could easily slip through the cracks. Scientists were siloed, working independently within a traditional research culture that celebrated individual successes rather than collaborative efforts. The cost: time. And with a disease like ALS, time isn't something we can take for granted.

That's why Target ALS doesn't simply encourage collaboration: we insist on it. Every principal investigator funded through a Target ALS grant is required to attend our Annual Meeting and share unpublished findings from their work in front of their peers. This knowledge exchange is invaluable. Scientists receive real-time feedback from experts in the field, forge new connections with potential collaborators, and learn about novel research from across our Innovation Ecosystem.

In the decade since our founding, we haven't just shifted the culture, we've completely transformed it. Collaboration has become the preferred way of doing ALS research — a far cry from the "publish or perish" mindset and lack of industry involvement that slowed the wheels of progress.

And the presentations given at this year's Annual Meeting prove that this approach works, that the field is both expanding to include different angles and ideas and deepening in our shared expertise on the underpinnings of this disease and how we can tackle it.

Target ALS Board Member, Alisa Doctoroff, shares her opening remarks at the 2026 Annual Meeting.

OUR APPROACH TO ALS RESEARCH

FUND

We are the largest private funder of ALS research worldwide. Our grants support both collaborative groups whose complementary expertise speeds discovery and individual emerging scientists who bring new talent and fresh perspectives into the field.

ENABLE

The best ideas in ALS research rely on more than just funding. We provide access to the tools and resources scientists need to advance their work, like brain and spinal cord tissue, biofluid samples, datasets, and more.

CONDUCT

ALS can't be solved until we have every piece of the puzzle. Through our ALS Global Research Initiative (AGRI) we're conducting comprehensive clinical studies to answer longstanding questions about the disease.

REFLECTIONS FROM THE TARGET ALS TEAM

Michael DeChellis-Marks, PhD
Manager, Scientific Programs

"After attending the Target ALS Annual Meeting for the first time, it was clear that it sets itself apart from other ALS conferences. The Annual Meeting brought together world-class researchers who were actively collaborating, in real time, within and between their consortia to continue brainstorming the next steps in ALS basic biology, biomarkers, and drug discovery. The intimacy of the Annual Meeting coupled with novel scientific findings set a strong foundation for critical, healthy, and open discussion between investigators, fellows, and stakeholders."

Read on to learn about cutting-edge research across our three funding priorities: understanding the basic biology of ALS, developing biomarkers, and advancing drug discovery.

BROADENING THE SCOPE OF ALS BASIC BIOLOGY

Investigating the Immune System

To identify effective new therapies, we must have a strong understanding of the basic biology of ALS: what's happening in the disease and why? Approximately half of our funded portfolio aims to answer those questions, analyzing ALS at every level, from RNA to proteins and single cells to systems.

ALS is a disease of the motor neurons. However, emerging research from Target ALS-funded scientists is revealing that it's not that simple; there's a complex breakdown involving the immune system, support cells, blood vessels, and even the way genes are chemically regulated. These findings collectively signal a meaningful shift in how the field understands ALS: once believed to be a bystander, the immune system may play an active role in neurodegeneration.

David Gate, PhD
Northwestern University

MEET THE SCIENTISTS REVEALING THE ROLE OF THE IMMUNE SYSTEM

David Gate, Northwestern University
New Academic Investigator

By analyzing brain and spinal cord tissue samples, Dr. Gate's research found that **neuroinflammation** is higher in the spinal cord rather than the brain. Additionally, this signal is amplified in **C9orf72 ALS** relative to **sporadic ALS**. Specifically, immune cells in the brain called **microglia** showed the most striking gene changes, indicating that their protective function is impaired in ALS.

Jack Humphrey, PhD
Icahn School of Medicine at Mount Sinai

Basic Biology Consortium

Jack Humphrey, Icahn School of Medicine at Mount Sinai
Philip Hasel, University of Edinburgh
Andrea Malaspina, The Francis Crick Institute, UCL
Rickie Patani, The Francis Crick Institute, UCL

Dr. Humphrey and his collaborators are studying how immune cells in the nervous system track with and influence survival in ALS. Taking a unique approach, the team specifically set out to study differences in genes in the brain in high, medium, or slow disease progressors. They identified two immune markers, CHIT1 and C3, that strongly track with rapid disease progression. Their dataset provides key evidence to elevate these markers as candidate biomarkers for disease progression and potential therapeutic targets.

ALS 101

NEUROINFLAMMATION is an inflammatory immune response in the brain or spinal cord that protects against infections, injuries, or toxins. However, chronic neuroinflammation can damage healthy brain tissue.

C9ORF72 ALS is the most commonly known genetic form of ALS and FTD. It's caused by a **REPEAT EXPANSION MUTATION**, where a short sequence of DNA is repeated hundreds to thousands of times, disrupting normal cellular function.

SPORADIC ALS makes up 90% of ALS cases, which have no known cause and no family history.

FAMILIAL ALS makes up the other 10% of cases with a family history of disease.

GLIAL CELLS are the support cells of the nervous system. Unlike neurons, they don't send electrical signals. They perform critical support roles by providing nutrients, removing waste, regulating immune response, and more. There are many types of glial cells, including:

MICROGLIA are the immune cells of the brain and spinal cord, responsible for defense and maintenance. They fight pathogens, clear debris, and regulate inflammation.

ASTROCYTES provide metabolic and structural support to neurons. They help maintain a balanced environment for neurons, regulate blood flow, form the blood-brain-barrier, clean up waste and more.

Basic Biology Consortium

Rita Sattler, Barrow Neurological Institute
Yuna Ayala, St. Louis University
Christopher Donnelly, University of Pittsburgh
Patrick Pirotte, Translational Genomics Research Institute
Kendall Van Keuren-Jensen, National Institute on Aging

Dr. Sattler's lab is one of the first to deeply study the impact of TDP-43 dysfunction in **glial cells**, support cells of the nervous system. They have discovered a number of abnormalities in **astrocytes** and are testing how these changes may be toxic to neighboring motor neurons.

Rita Sattler, PhD
Barrow Neurological Institute

Amanda Guise, PhD
Biogen

Industry-Led Consortium

Amanda Guise, Biogen
Paymaan Jafar-Nejad, Ionis Pharmaceuticals
Jeffrey Rothstein, Johns Hopkins University
Alyssa Coyne, Johns Hopkins University

Dr. Amanda Guise analyzed proteins within single cells, quantifying more than 1,500 proteins per motor neuron in brain and spinal cord tissue. A small pilot study revealed an increased immune response within motor neurons in tissue from people with C9 ALS compared to tissue from healthy controls. Taken together with Dr. Gate's data, inflammation is occurring both within neurons and across immune cells in the brain.

Albert La Spada, MD, PhD
University of California, Irvine

Biomarker Consortium
Albert La Spada, University of California, Irvine
Sebastian Michels, Ulm University
Wolfgang Ruf, Ulm University
Wei Li, University of California, Irvine
Arthur Cheung, TWIST Biosciences

Dr. La Spada's lab produced **epigenetic** data, chemical changes to DNA, from hundreds of blood samples from ALS cases. Their data indicate that a large number of genes are likely silenced in ALS, and the top altered genes are important for proper immune function in the brain. This discovery suggests that immune dysregulation is encoded in DNA found in the blood. It can potentially be used as a biomarker to diagnose or classify types of ALS, even in cases without a known genetic cause.

ALS 101

EPIGENETICS is the study of changes that act like "on" and "off" switches for genes, influencing gene activity without altering the actual DNA sequence.

DIVE DEEPER: SCAN TO WATCH

We interviewed Dr. La Spada about his consortium's work to transform how ALS is diagnosed and monitored. Scan the QR code to learn more about this biomarker discovery project.

Drs. Michels, Li, and La Spada listen to a question about their work from session moderator and Target ALS Independent Review Committee (IRC) member Dr. Biljana Djukic.

Lindsay Goodman, PhD
Baylor College of Medicine

Lindsay Goodman, Baylor College of Medicine
Springboard Fellow

When neurons are under stress, they generate toxic **lipid** byproducts that normally get handed off to glial cells to clean up. In ALS and **Frontotemporal Dementia (FTD)**, this cleanup system is disrupted. Dr. Goodman is studying whether the proteins Tau and TDP-43 in **glial cells** make lipid damage worse. The potential impact is twofold: first, her work could point to new lipid-based biomarkers, and second, it could reveal glial lipid droplets as a potential therapeutic target.

ALS 101

LIPIDS are organic molecules that perform functions like regulating what goes in and out of cells, energy storage, and more. Under stress, the breakdown of lipids can create harmful, toxic byproducts.

FRONTOTEMPORAL DEMENTIA (FTD) is a neurodegenerative disease that affects the brain's frontal and temporal lobes, leading to changes in behavior, personality, and language. FTD and ALS are closely related, and some people develop symptoms of both diseases. Both conditions share the C9orf72 gene mutation as their most common cause and involve the buildup of abnormal TDP-43 protein.

Target ALS Springboard Fellows Lindsay Goodman, Chloe Lopez-Lee, and Julie Smeyers participate in a Q&A session following their presentations moderated by Target ALS IRC member Dr. Martha Bhattacharya.

Chloe Lopez-Lee, Icahn School of Medicine at Mount Sinai
Springboard Fellow

People with ALS often experience **blood-brain barrier** leaks and inflammation in the cells lining blood vessels, signs that the immune system and vascular system are tightly linked in the disease process. A rare genetic variant in a gene called CREB3 appears to strengthen vascular health and lower ALS risk. Dr. Lopez-Lee is evaluating whether boosting CREB3 protein levels can restore healthy immune and vascular function. She's also identifying additional vascular proteins that provide resilience. Her work could lead to development of new treatments that strengthen the brain's vascular system and reduce damage.

Chloe Lopez-Lee, PhD
Icahn School of Medicine at Mount Sinai

The **BLOOD-BRAIN BARRIER** is a protective layer of tightly packed cells that lines the blood vessels in the brain and spinal cord. It acts like a security gate, allowing essential nutrients through while blocking harmful substances, such as toxins or germs. While it protects the brain, it also makes it difficult for medications to pass through, a major challenge for diseases like ALS.

Key Takeaway

Taken together, these projects provide a strong argument. The immune system may not merely be a responder to neurodegeneration, but a potential contributor and even initiator — one whose earliest actions in the nervous system may set ALS in motion. This reframing carries profound implications for therapy development — pointing researchers away from motor-neuron-only targets and toward strategies that restore immune balance, protect vascular integrity, and address the broad cellular environment in which motor neurons live and die.

POSTER SESSION

Sparking conversation and collaboration

Poster sessions have long offered an opportunity for scientists to talk about the details of research directly with the investigator doing the work. At the Annual Meeting, this unique forum allows academic investigators, industry scientists, representatives from venture capital, and fellows from across our global Innovation Ecosystem to network and discuss new hypotheses and findings.

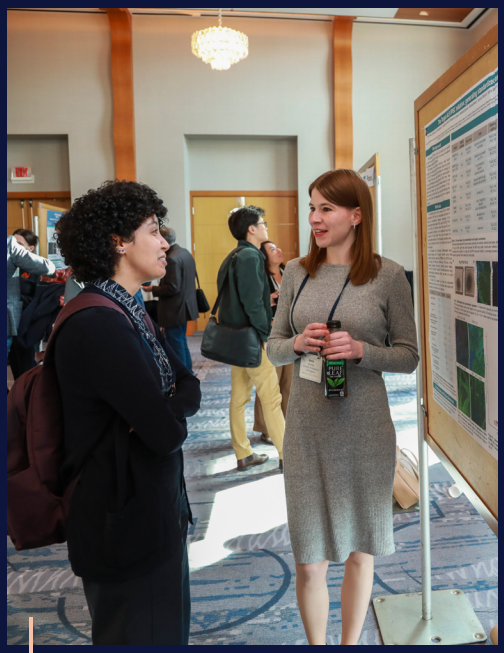
This year's session included 44 poster presentations, many sharing progress on work supported by Target ALS via our Research Cores and Data Engine. Top scientists presented new findings from basic disease biology research to the development of research tools, biomarker discovery, and therapeutics just entering the clinic, generating a collective energy and excitement about the future of the field.

Many of this year's posters feature work supported by Target ALS' Research Cores, demonstrating the breadth of support across our fund-enable-conduct model.

DIVE DEEPER: SCAN TO SEE THE POSTERS

Check out a selection of the poster presentations in detail by scanning the QR code.

Laura Dugom, Associate Director of Clinical Research at Target ALS, presents a poster on the ALS Global Research Initiative (AGRI), the largest and most inclusive clinical research effort for ALS worldwide, to Dan Doctoroff, Founder and Chair of Target ALS.



A more intimate format than the plenary session, the poster session allows for meaningful exchanges.

Hosted during the opening reception, the poster session is a popular forum for networking and forging new connections as the meeting kicked off.

FROM BENCH TO BEDSIDE

Fueling the drug discovery pipeline

About a third of our funded portfolio is focused on drug discovery: projects aiming to bring effective therapies into the clinic. To date, 13 clinical trials have been launched from research supported by Target ALS.

We expect that number to grow as we continue taking bold bets on science with high potential and advancing work rooted in fundamental ALS biology through the drug discovery pipeline.

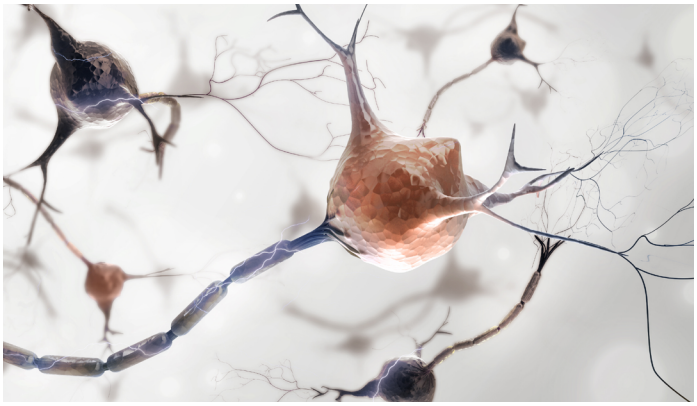
HIGH RISK, HIGH REWARD: USHERING NEW IDEAS INTO THE CLINIC

The Annual Meeting Moment: QurAlis Presents New Data from ANQUR Study

The standout moment of the meeting was when QurAlis presented new interim data from their Phase 1/2 ANQUR clinical trial. Their drug candidate, QRL-201, is an **antisense oligonucleotide (ASO)** therapy intended to restore Stathmin-2, a protein vital to structural integrity of neurons and proper muscle innervation. Chief Executive Officer Kasper Roet walked attendees through the interim analysis, which demonstrated two positive effects in a small cohort of people with sporadic ALS:

1. Slowing of disease progression on the **ALS Functional Rating Scale–Revised (ALSFRS-R)**
2. Reductions in **neurofilament** levels

In addition, the analysis shed light on the dynamics of neurofilaments in blood and **cerebrospinal fluid (CSF)**, showing earliest changes in CSF and later changes in blood. By sharing these insights publicly, QurAlis offered meaningful guidance for optimizing clinical trial design to peers across the field.



ALS 101

ANTISENSE OLIGONUCLEOTIDES (ASOS) are small pieces of genetic material designed to bind to RNA in cells for therapeutic benefit. By attaching to specific RNA sequences, ASOs can block or change how certain genes are used, either reducing harmful proteins or increasing production of helpful ones.

The **ALS FUNCTIONAL RATING SCALE-REVISED (ALSFRS-R)** is the global standard questionnaire used by neurologists and researchers to assess and track progression in people with ALS.

NEUROFILAMENTS are structural proteins in neurons. In ALS, as motor neurons degenerate, neurofilaments are released into the blood and cerebrospinal fluid (CSF), the fluid that surrounds the brain and spinal cord. Neurofilaments are now an accepted biomarker for ALS, as their levels indicate the extent of motor neuron death in disease.

Kasper Roet, PhD
QurAlis

KEY TAKEAWAY

In 2020, Target ALS funded a consortium led by QurAlis to study Stathmin-2 as a drug target. Two years later, they launched the ANQUR clinical trial. Today, they're sharing that their treatment is demonstrating a positive effect on disease progression.

What does this teach us? First, our model helped to accelerate a process that traditionally takes a decade or more. And, second, research rooted in strong fundamental biology has the potential to make a real impact on disease.

DIVE DEEPER: SCAN TO WATCH

We interviewed Dr. Kasper Roet about the new data presented about the ANQUR clinical trial. Scan the QR code to watch now.

On the Starting Block: Trace Neuroscience Prepares for Phase I

Terry Fang (Trace Neuroscience) presented on their ASO treatment aimed at restoring UNC13A, a protein critical to **neurotransmitter** release. Citing meaningful advances towards the clinic, the company plans to launch a Phase I clinical trial later this year. Like QurAlis, Trace represents another early-stage investment by Target ALS in an ASO-based startup — a reflection of our continued commitment to backing high-potential therapeutic approaches from the ground up.

Terry Fang, PhD
Trace Neuroscience

KEY TAKEAWAY

While both QurAlis and Trace have employed an ASO strategy, their targets, Stathmin-2 and UNC13A, represent distinct biology important to motor neuron health. Therefore, if successful, the two therapies are likely to benefit patients in meaningfully different and potentially complementary ways. Looking ahead, we can envision a suite of effective treatments that work together to provide people with ALS long, quality lives.

After each presentation, audience members are invited to ask questions and provide feedback, creating real-time dialogue and sparking new collaborations.

ALS 101

NEUROTRANSMITTERS are chemicals released by neurons to send messages to other neurons, muscles, or glands, helping you move your muscles, react to your environment, and more.

Like ASOs, **SMALL INTERFERING RNAs (siRNAs)** are small pieces of genetic material designed to bind to RNA in cells for therapeutic benefit. While both tools have similar effects, they have different structures, are active in different locations in cells, and work via different mechanisms.

Making (Anti) Sense of C9: Targeting the Most Common Genetic Cause

The most common genetic cause of ALS is a mutation in the C9orf72 gene, accountable for up to 40% of familial ALS cases. Since the identification of this mutation in 2011, scientists have explored different avenues to tackle it. One approach aims to target the buildup of toxic RNA.

To create proteins, DNA is read and transcribed into molecules called RNA, which are then translated to proteins. During this process, two RNA strands are created, called the sense and antisense strands. In C9 ALS, the sense and anti-sense strands are not formed properly, as they are created from the repeat expansion in the DNA.

Buildup of these aberrant strands of RNA can be toxic. But which strand is responsible for that toxicity? Sense or antisense? Which strand should we target?

Drs. Jeffrey Rothstein (Johns Hopkins), Alyssa Coyne (Johns Hopkins), Amanda Guise (Biogen), and Paymaan Jafar-Nejad (Ionis Pharmaceuticals) have come together to answer these questions.

After earlier work developing an ASO targeting the sense strand wasn't successful, the team pivoted to focus on the antisense strand. They developed new antisense ASOs, which have demonstrated encouraging preclinical data. Repeat dosing was effective and well-tolerated in cell and animal models.

Key Takeaway

The C9 mutation is not only responsible for the majority of genetic ALS cases, but also causes another neurodegenerative disease called Frontotemporal Dementia (FTD). After trial and error, this consortium is making headway with a treatment that may have a major impact on ALS and beyond.

Aaron Gitler, PhD
Stanford University

DIVE DEEPER: SCAN TO WATCH

In this interview, Dr. Aaron Gitler, a collaborator on the Trace Neuroscience project, shares how Target ALS's model advances research from foundational discoveries to potential therapies. Scan the QR code to watch now.

Maximizing Impact: A Dual-Action Approach for ASOs

ASOs hold immense promise as treatment strategies for ALS and many other diseases. However, scientists still face hurdles in maximizing the impact of these molecules. Drs. Evangelos Kiskinis (Northwestern University), Jonathan Watts (UMass Chan Medical School), and Damon Wang and Joseph Klim (NuCyRNA Therapeutics) are developing a novel technology that combines an ASO with small interfering RNAs (siRNAs), allowing a single drug to tackle two targets. In animal models, this dual-targeting technology provided the unique flexibility to address more than one aspect of disease biology simultaneously and was both a safer and more effective alternative to ASOs alone.

Evangelos Kiskinis, PhD
Northwestern University

KEY TAKEAWAY

> This drug design would enable combination treatment in a single molecule, allowing for less frequent dosing and a greater, longer lasting benefit for patients. By investing in next generation technology, we are advancing a new wave of safer, more effective potential treatments for ALS.

DIVE DEEPER: SCAN TO WATCH

Watch Dr. Evangelos Kiskinis describe why now is the most exciting time in ALS research.

Dr. Morwena LaTouche and her collaborators participate in the Q&A session following their presentations, moderated by Target ALS Independent Review Committee member Dr. Choya Yoon.

BACK TO THE BASICS: FROM FUNDAMENTALS TO THE FINISH LINE

Unraveling TDP-43: Small Molecules That Pack a Punch

Drs. Morwena Latouche (Paris Brain Institute), Emanuele Buratti (International Centre for Genetic Engineering & Biotechnology), Jean-Christophe Cintrat (Commissariat à l'énergie Atomique et aux Énergies Alternatives), and Olivier Sperandio (Institut Pasteur) are working together to counteract **TDP-43** aggregation. Leveraging artificial intelligence to conduct rapid screens, paired with expertise in structural biology and chemistry, the consortium has identified small molecules that can break apart toxic TDP-43 clumps. Early experiments in cell models demonstrate that their lead candidate successfully disaggregates these clumps and improves related harmful effects. With this encouraging data, the consortium recently filed a patent application on their lead candidate and plans to perform pre-clinical evaluations necessary to move into human testing.

Restoring the Relationship Between Tankyrase and TDP-43

Leeanne McGurk (University of Dundee), a Target ALS New Academic Investigator, is studying the interaction between the proteins Tankyrase and TDP-43. Her research has found that Tankyrase prevents TDP-43 from binding to RNA. Without this ability, TDP-43 behaves abnormally, as seen in the majority of ALS cases, ultimately driving motor neuron damage. Dr. McGurk aims to restore normal interaction between Tankyrase and TDP-43. She's in the early stages of developing compounds that inhibit Tankyrase from binding to TDP-43 to restore normal function.

ALS 101

TDP-43 is an essential protein that normally regulates RNA processing in the nucleus of cells. In 97% of ALS cases, TDP-43 moves out of the nucleus, losing its normal function, and forms toxic aggregates. This dysfunction is known as a hallmark of ALS, but is also seen in up to 50% of FTD cases and 25-50% of Alzheimer's Disease cases.

Key Takeaway

Both of these projects began by asking fundamental questions about the hallmark of ALS: TDP-43 pathology. By supporting these investigators' early stage work on basic biology, their research has evolved into drug discovery programs developing potential treatments for one of ALS' most common culprits.

AI AND ML: THE FUTURE OF TARGET DISCOVERY AND DRUG DEVELOPMENT

From the desk of Dr. Amy Easton

Amy Easton, PhD
VP, Scientific Programs
Target ALS

The convergence of artificial intelligence and biomedical research is bringing new hope to the ALS community, offering the potential to identify novel therapeutic targets and accelerate drug development in a disease where time is everything. AI and ML now enable the rapid virtual design and testing of thousands of new molecules and the simulation of their interactions with therapeutic targets.

Leading pharmaceutical companies are investing heavily in these tools. Roche has built the largest announced GPU footprint of any pharmaceutical company, embedding accelerated computing into the core of how it discovers and develops new therapies. Eli Lilly partnered with NVIDIA to build a powerful AI supercomputer for medicine discovery and launched its TuneLab platform, backed by over $1 billion in proprietary research data, to give biotech companies access to its AI-enabled drug discovery models.

These topics and more were covered at this year's Annual Meeting. We had the honor of sponsoring a roundtable moderated by Puneet Batra of Ember AI with Alexander McCampbell, Global Head of Research for Rare Disease at Roche, Kristina Kitko of Lilly Ventures, and Ajamete Kaykas, CXO of insitro. While all three companies are betting on AI, with insitro as one of the early Bay Area pioneers for new target discovery, all panelists conveyed a healthy dose of caution with regard to an immediate transformation of the industry. They shared optimism on the current impact of AI on drug discovery operations, but felt it would take five more years to see the impact of AI on improving efficiencies of clinical trials in the future.

Novel target discovery will always require benchwork to validate the target, though in silico models may become more prominent. One of the key takeaways from the researchers was clear — curation of high-quality clinical datasets representing diverse patient populations is needed to unlock the power of AI-based modeling of disease progression and patient stratification.

Alexander McCampbell, Kristina Kitko, and Ajamete Kaykas discuss the application of AI/ML technologies to ALS research, moderated by Puneet Batra.

DIVE DEEPER: SCAN TO WATCH

Interested in learning more about AI/ML for ALS?

Watch the full roundtable discussion with these experts by scanning the QR code.

DIVE DEEPER: SCAN TO WATCH

We asked Dr. Ajamete Kaykas how platforms like Target ALS's Data Engine are spurring the use of AI and ML to advance research. Scan the QR code to watch now.

CRACKING THE CODE

Developing TDP-43 biomarkers

Biomarkers are measurable indicators that tell us what's happening inside the body. For example, blood pressure is a biomarker for heart health. In ALS, we're lacking a suite of biomarkers to diagnose the disease, track its progression, and stratify patient populations — critical information for early intervention, evaluating the efficacy of new drugs, and pairing the right treatments to the right patients.

Since TDP-43 pathology is seen in 97% of ALS cases, it's a desirable target for biomarker development. We've brought together scientists from different scientific disciplines and disease areas to crack the code on TDP-43 biomarkers. At the Annual Meeting, Wednesday's biomarker session was one of the most dynamic, with several groups sharing both breakthroughs and hard-won lessons in measuring TDP-43.

Len Petrucelli, PhD
University of Miami

Clarifying the Cryptic: Developing Tools to Detect Cryptic Peptides

Drs. Michael Ward (National Institute of Neurological Disorders and Stroke), Pietro Fratta (University College London) and Len Petrucelli (University of Miami) have been working together to advance **cryptic peptide** biomarkers. Their work confirms that a cryptic peptide called HDGFL2 appears in brain and spinal cord tissue with TDP-43 pathology, indicating its potential as a specific biomarker for disease. However, detecting and measuring cryptic peptides has proven difficult. A new collaboration between Dr. Petrucelli and Dr. Nicholas Ashton (Banner Sun Health Research Institute) yielded a notable advancement: they have developed an ultra-sensitive test that successfully detects the HDGFL2 cryptic peptide in CSF. Critically, the test has demonstrated the ability to distinguish people with ALS from healthy controls.

ALS 101

CRYPTIC PEPTIDES are small protein fragments that are not generated under normal cellular conditions. When TDP-43 malfunctions in ALS, it forfeits its normal role of regulating RNA. This leads to errors in protein production, including the creation of cryptic peptides. Because they are only generated under these circumstances, these fragments could offer a method to measure TDP-43.

EXTRACELLULAR VESICLES (EVs) are particles released by cells that carry pieces of the cell's internal material, like proteins, RNA, and more, to communicate with other cells. They are potential windows to track what's happening inside cells in disease.

Nicholas Ashton, PhD
Banner Sun Health Research Institute

Marta Garcia Montojo, PhD
Twilight Bioscience

DIVE DEEPER: SCAN TO WATCH

Watch this interview with Dr. Nicholas Ashton to learn more about how he's bringing his expertise from Alzheimer's Disease biomarker development to ALS.

A Window Inside the Cell: Tracking TDP-43 via Extracellular Vesicles

A consortium including Drs. Erez Eitan (NeuroDex, Inc.), Marta Garcia Montojo (Twilight Bioscience), Alain Prochiantz (BrainEver), and Avindra Nath (NINDS) is investigating whether **extracellular vesicles (EVs)** can provide insight into TDP-43 dysfunction. By analyzing EVs derived from the brain, the consortium was able to detect elevated levels of TDP-43 in ALS samples relative to healthy controls.

Communication Breakdown: Monitoring Loss of Synaptic Function

Perhaps the most compelling presentation came from Drs. Philip Van Damme (KU Leuven), Rosa Rademakers (VIB), and Koen Poesen (KU Leuven), who are investigating the proteins that enable and support **synapses**. The team observed elevated synaptic proteins called SV2A and VAMP2 in CSF from people with ALS, suggesting that the proteins are lost in the course of the disease. Additionally, the team found a corresponding decrease in SV2A in imaging of the brain region responsible for motor function. The imaging measures correlated with ALSFRS-R scores, with the decreased signal linked to higher disease progression. Supported by both fluid and imaging-based techniques, these striking findings shed light on synaptic function and could be a valuable early biomarker of disease onset.

ALS 101

SYNAPSES are the junctions between neurons and other neurons, muscles, or glands. They're critical communication points, acting as bridges for impulses to travel across.

Philip Van Damme, MD, PhD
KU Leuven

Key Takeaway

Building tools to effectively track TDP-43, either directly or through indirect approaches like detecting cryptic peptides or analyzing EVs, offers scientists a clearer picture of what's happening inside the body in the majority of ALS cases. Further, TDP-43 dysfunction isn't unique to ALS; it's seen in up to 50% of FTD cases and 25-50% of Alzheimer's Disease cases. The bottom line: the tools we're developing could improve diagnosis, monitoring, and care across neurodegenerative disease.

DIVE DEEPER: SCAN TO WATCH

Interested in learning more about biomarkers?

Watch the roundtable discussion featuring Danielle Graham (Biogen), Nicholas Ashton (Banner Sun Health Research Institute), and Michael Benatar (University of Miami), moderated by Toby Ferguson (Target ALS Board of Directors, Alnylam Pharmaceuticals), breaking down the challenges of ALS biomarker development and recent advances in the field.

Conversation flows during breaks throughout the meeting, scheduled to ensure participants have time to network and connect.

ADDRESSING UNMET NEED

Special initiatives uniquely positioned for success

We're transforming the ALS research landscape by supporting the best ideas and unlocking new insights into ALS. As the field evolves, we recognize that significant gaps remain in our understanding of the genetics and biology of the disease. And it's our responsibility as the leading ALS research nonprofit in the world to address these gaps. Our leadership team makes strategic decisions to satisfy areas of unmet need and explore new frontiers of scientific inquiry so that we can find effective treatments for all forms of ALS.

In 2025, we set out to fill a gap in our collective understanding of the genetic architecture of ALS. At this year's Annual Meeting, the two powerhouse consortia we brought together to tackle this challenge presented early advances in their research to understand the role of genetics in disease.

BUILDING THE BIOLOGICAL ROADMAP: DECIPHERING THE COMPLEXITIES OF C9 ALS

In 2011, Dr. Rosa Rademakers (VIB) and her team first identified the repeat expansion mutation in C9orf72 as a major genetic driver of ALS and FTD. However, since this breakthrough, scientists have been stymied by the complexity of this mutation and the wide-ranging differences in how the disease presents across people who carry it. We've learned that repeat expansion length varies between individuals, across generations of families, and even between blood and brain samples

Rosa Rademakers, PhD
VIB

DIVE DEEPER: SCAN TO WATCH

Watch Dr. Rosa Rademakers discuss her journey from discovering the C9orf72 mutation as the leading genetic cause of ALS and FTD to her work unraveling its complexity.

from the same individual. While the target is in our sights, these complexities have led to several failed clinical trials.

To accelerate therapeutic development, we brought together a powerhouse collaboration led by Dr. Rademakers with colleagues Renzo Mancuso (VIB), Marka Van Blitterswijk (Mayo Clinic, Florida), and Adrian Isaacs (University College London). This team's complementary expertise across ALS and FTD, genetics and molecular biology of the C9orf72 repeat expansion, and deep technical knowledge uniquely positions them to determine the genetic drivers of neurodegeneration in C9 ALS and FTD.

In their presentation, the team described initial work in brain and spinal cord tissue to study repeat expansion length and genetic risk factors underlying whether or not a person carrying this mutation expresses disease and how that disease presents. They also shared historical and recent data indicating that proteins produced from this mutated section of DNA are toxic. However, given the failures of the clinical trials targeting these proteins, the team proposed that many other toxic factors are likely to come into play. They hypothesize that C9 factors may be early toxic factors, while TDP-43-related phenomena cause toxicity later on in the disease. The session generated lively discussion and debate, underscoring the importance of this work to advancing the field.

KEY TAKEAWAY

The repeat expansion in C9orf72 is the most commonly known genetic cause of both ALS and FTD. It's a major priority to address this cause, but scientists have struggled to crack the code. This consortium's efforts aim to unravel the complexities of this mutation, building a biological roadmap for the broader scientific community to better understand and develop treatments for C9.

Adrian Isaacs, PhD
University College London

This presentation sparked the liveliest Q&A session of the meeting, with several scientists approaching the microphones set up around the room to ask questions and offer feedback. This energy and interest underscores the importance of this work.

FAMILY TIES: ONE MUTATION LEADS TO VASTLY DIFFERENT OUTCOMES

A collaboration led by geneticist Juliana Acosta-Uribe (UC, Santa Barbara) with Kenneth Kosik (UC, Santa Barbara) and David Aguillón (University of Antioquia) aims to understand why members of large multi-generational families carrying the same mutation have different clinical trajectories. In 2022, the group published the results of a large-scale genomic study in which they identified an extended family carrying a specific mutation in the TARDBP gene. This mutation is one of many causes of the TDP-43 dysfunction we see in 97% of ALS cases and around 50% of FTD cases. Since then, four additional families with the same mutation have been discovered in the Colombian population. Upon evaluation of at least 50 individuals from these families, the research team observed significant variability in how the mutation is expressed. Remarkably, some family members develop symptoms of ALS or FTD, and others experience healthy aging. By analyzing clinical assessments and biofluids collected over time, along with brain and spinal cord tissue and stem cell models from these family members, the scientists plan to determine the genetic and molecular factors that lead to these varied clinical presentations. At the Annual Meeting, the team shared data highlighting changes in genes implicated by TDP-43 dysfunction long before the TDP-43 aggregates, indicating other factors may influence disease onset.

Juliana Acosta-Uribe, MD, PhD
University of California, Santa Barbara

DIVE DEEPER: SCAN TO WATCH

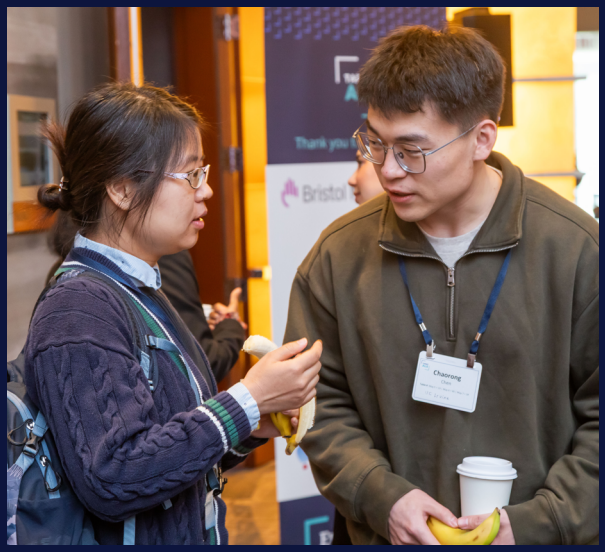
Watch Dr. Juliana Acosta-Uribe explain how tracking a genetic mutation across large families in Colombia may reveal new insights into ALS and FTD.

Key Takeaway

This study is uniquely positioned to reveal novel insights about ALS by studying an identical mutation expressed among family members living in northern Colombia. Researchers can better understand the effect of both environmental and biological factors contributing to the disease and potentially better inform biomarker and drug development.


ALL IN
FOR ALS
RESEARCH


Everyone Lives.



CONVENING THE RESEARCH CORES

Enabling the best ideas in ALS research

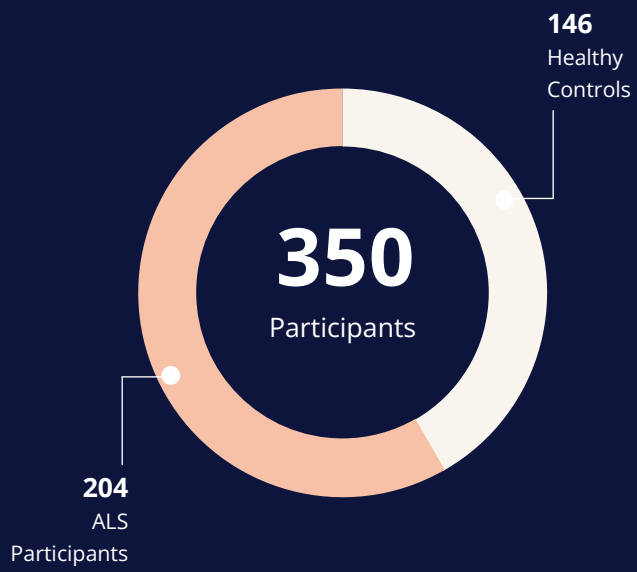
The best ideas in ALS research require more than just funding. We launched our Research Cores to create, collect, and provide expedited access to critical tools and resources like data, biosamples, stem cells, and more. Historically, these resources were difficult to access, cost-prohibitive, and lacked consistent quality, creating barriers for scientists worldwide from pursuing their ideas on ALS. To date, we've enabled more than 1,950 projects across the globe with no-strings-attached support.

While the focus of the Annual Meeting is our funded research portfolio, before the main event begins, we convene with the principal investigators and coordinators who lead our Research Cores focused on biosamples. While previous Core Days focused on building and expanding these resources, this year's gathering marked an inflection point: our biofluid and tissue repositories and the datasets generated from them have now grown large enough to support analyses that can help answer longstanding questions about ALS.

Longitudinal Biofluids Core: Powered by the Global Natural History Study

We are building the most comprehensive and inclusive biofluid repository for ALS, designed to accelerate the discovery and validation of biomarkers. Powered by our Global Natural History Study (GNHS), the Core includes cerebrospinal fluid, blood, and urine collected over time from participants with ALS and healthy controls across international sites. Scientists across the globe can request these precious samples to advance their research.

BIOFLUIDS BY THE NUMBERS



Because we control the collection of samples end-to-end, they're paired with detailed clinical, demographic, and epidemiologic information, at-home digital health measures, and multi-omic datasets. As the GNHS matures, this data is primed for analysis.

We partnered with digital health companies Aural Analytics and ZEPHYRx, which enable at-home testing for measuring speech and breathing, respectively, in study participants with ALS. These sub-studies have been completed, and researchers can now analyze the data from these efforts to identify potential biomarkers of disease progression.

By working with populations historically underrepresented in ALS research, we're building datasets that will help us put pieces of the ALS puzzle together. Our sites in Colombia and Puerto Rico have already supported the growth of a large Hispanic cohort of participants, and these sites can now analyze their own ethnic groups. We can finally examine trends in disease progression and whether it varies by country. Plus, our partnership with international sites provides a pathway to validate state-of-the-art scales and launch clinical trials in parts of the world where that wasn't previously possible.

Representatives from the Target ALS Longitudinal Biofluids and Postmortem Tissue Cores come together at the Annual Meeting.

18
Sites targeted

42,000+
Vials of biofluid samples collected

17
Biofluids requests already fulfilled in 2026 (versus 20 total in 2025)

Postmortem Tissue Core: A Direct View of ALS in the Brain and Spinal Cord

Our Postmortem Tissue Core provides scientists with access to one of the largest and most comprehensive repositories of brain and spinal cord tissues worldwide. These tissues, paired with de-identified clinical and genomic data, offer a direct window into the cellular and molecular structures and pathways affected in ALS.

Beyond expanding the Core, we're taking on new initiatives, developing tools, and generating datasets to accelerate target and biomarker identification for ALS.

Analyzing 200 cases from the Core, Dr. Panos Roussos (Mount Sinai School of Medicine) is leading a significant effort to produce the most comprehensive single-cell dataset to date for ALS. This work will profile tens of thousands of individual cells from brain and spinal cord tissues in ALS, FTD, and healthy controls, offering an exceptionally granular view at changes within cells in disease. Unlike existing datasets that examine mixed populations of cells together, single-cell analyses can pinpoint disease associated changes within individual cell types, creating new opportunities to better understand disease mechanisms and potentially uncover new therapeutic targets.

TDP-43 aggregates can only be seen in postmortem brain and spinal cord tissue on a slide under a microscope. In an effort to democratize access to these tissues, we're conducting a large-scale effort to create slides of postmortem tissue, perform staining so that the TDP-43 aggregates are visible, digitize the slides, and create an AI-driven image algorithm to support analysis. To date, digitized images for 247 cases are currently available on the Target ALS Data Engine. This resource will help scientists analyze the hallmark of ALS, TDP-43 dysfunction, at the molecular level, informing our understanding of disease and its progression.

REFLECTIONS FROM THE TARGET ALS TEAM

Marina Selenica, MS
Core Project Manager

"Our Postmortem Tissue Core provides scientists access to one of the largest and most comprehensive repositories of brain and spinal cord tissue worldwide. We are also prioritizing dual enrollment across our GNHS and Postmortem studies to capture a clinical snapshot during life that can be directly linked to postmortem tissue after death, creating an even richer biorepository. Our annual Cores Day enables collaborative discussion to identify opportunities and ensure we are advancing science faster than ALS progresses."

The Target ALS Science Team celebrates ALS Awareness Month by posing for a photo for our "All In For ALS Awareness" campaign.

Members of the Target ALS Biofluids and Postmortem Tissue Cores join our ALS Awareness Month campaign.

REFLECTIONS FROM THE TARGET ALS TEAM

Laura Dugom, MPH
Associate Director, Clinical Research

"Progress shared during Cores Day underscored the growing impact of the GNHS and Postmortem Tissue Core as a foundation for ALS discovery. With each participant, visit, and data point collected, these resources become increasingly powerful and an even richer platform for understanding disease biology, identifying biomarkers, and advancing the development of future therapies. This convening serves as a forum for scientific leadership, bringing together experts across disciplines to identify emerging opportunities and ensuring the research we conduct continues to drive innovation in ALS research and therapeutic development."

FROM OUR FOUNDER

For a long time, ALS was something that haunted my family.

My father died from ALS in 2002. Years later, my uncle was diagnosed with the disease and passed as well. Through both experiences, I came to understand not only the devastation of ALS, but also the widespread belief that it was impossible to solve.

I have never accepted that.

ALS has taken a great deal from me personally. In the past year, I have lost my voice. I have lost the ability to eat most foods. My hands and arms have weakened, and my neck muscles have deteriorated. But I adapt. I use eye gaze technology to communicate. I use a feeding tube to eat. I can still control my wheelchair.

And despite everything, I remain optimistic.

My family gives me joy. This community gives me hope. Seeing so many people — researchers, donors, families, caregivers, and advocates — commit themselves to changing the future of ALS strengthens my resolve every single day

When we founded Target ALS, we did so because we believed the problem was not a lack of brilliant scientists or promising ideas. The problem was that the system was not designed to move fast enough. Researchers worked in silos. Data was not shared openly. Too many barriers stood between discovery and treatment.

So we chose a different path. A path rooted in collaboration, urgency, and action.

> *"Science alone does not push movements forward.*
>
> ***People do."***

We believed that if you bring the best minds together, remove barriers, and create an environment where people can work collectively toward a shared goal, progress will accelerate.

And it has.

At this year's Target ALS Annual Meeting, I could see real progress in ALS research. New discoveries are happening faster. Companies are entering the field with renewed urgency. Researchers are collaborating in ways that simply did not exist years ago. **What once felt unimaginable now feels possible.**

But science alone does not push movements forward. People do.

Every person involved in this mission matters. Some will donate. Others will participate in research studies. Some will advocate, raise awareness, tell stories, or bring new people into this community. Others will simply refuse to accept hopelessness.

All of that matters.

ALS continues to take so much from so many families. That is why urgency matters. It is why we push forward every day at Target ALS with determination, focus, and optimism about what lies ahead.

I believe we are closer than we have ever been to a world where Everyone Lives.

Thank you for believing in this mission and for helping make this progress possible.

With gratitude,

DAN DOCTOROFF
FOUNDER AND CHAIR
TARGET ALS

The Annual Meeting is the cornerstone of Target ALS. It is where collaboration, partnership, urgency, and discovery come together in pursuit of a common goal: a world where everyone with ALS lives.

This gathering is made possible by the researchers, clinicians, academic institutions, pharmaceutical and biotech companies, venture capital firms, and nonprofit organizations that make up our Innovation Ecosystem. But it is also made possible by you.

You who support this work. You who give. You who advocate. You who champion our mission and believe in what is possible.

Because of you, we continue to build momentum. Because of you, we can move faster, think bigger, and do more than ever before. Every breakthrough, every collaboration, and every step forward is fueled by your partnership.

Thank you for making this work possible. We are closer than we have ever been before. And together, we are going to figure this out. Together, we are going to solve ALS.

Thank you.

Thank you to our leading corporate partners, Alnylam, Biogen, Bristol Myers Squibb, Eli Lilly and Company, and Shionogi, for their generous sponsorship of the 2026 Annual Meeting.

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THANK YOU FOR BEING ALL IN

TARGET ALS