EVERYONE LIVES

TARGET ALS 2024 YEAR IN REVIEW

TARGET ALS

Dear Friend of Target ALS,

As we embark on this new year, we're taking time to reflect on the many exciting milestones that Target ALS achieved in 2024. From launching our groundbreaking Data Engine, to expanding our Global Natural History Study into Latin America, to successfully completing our $250 million capital campaign, 2024 was a testament to our values: radical collaboration, deliberate disruption, and impatient optimism in service of our mission. We successfully broke down barriers that traditionally limit scientific innovation to advance critical research that will lead to effective treatments for ALS. More important than reflection, however, we're taking stock of our impact and strategizing our next steps to continue to shape the landscape of ALS research, molding that landscape into **a world where Everyone with ALS Lives.**

At Target ALS, our scientific strategy is rooted in funding high quality science to drive results in three key areas: improving our understanding of the biology of ALS and its causes, spurring drug discovery to accelerate potential treatments from the lab to the clinic and developing biomarkers that help to diagnose and monitor disease as well as evaluate potential therapeutics in clinical trials. In 2024, we strategically allocated our grant funding to ensure balanced progress across these critical areas. We invested **38% in understanding ALS biology, 38% in drug discovery, and 24% in biomarker development** — a comprehensive approach designed to drive meaningful breakthroughs.

Because our model allows for agility, we can move as breakthroughs are made, putting muscle behind novel biological insights to rapidly advance them into therapeutic generation. For example, with the recent emergence of cryptic exons—normally excluded RNA sequences that become aberrantly included when TDP-43, a protein that regulates RNA processing, malfunctions in 97% of ALS cases—we tailored our Biomarker Consortia grants call to specifically attract projects that will further develop research into cryptic exons in ALS. By keeping our finger on the pulse of new breakthroughs, we nimbly shift focus to invest in areas that can make a major impact, not simply funding research but driving it, strategically accelerating progress in a landscape where 90% of treatments entering clinical trials fail to achieve FDA approval and expanding the drug discovery pipeline to increase the number of effective therapies.

At the same time, we understand that groundbreaking research requires more than funding. In 2024, Target ALS made major strides in both creating and expanding our Research Cores – key resources and tools that enable scientists to perform cutting-edge work. These Cores act synergistically to accelerate projects through the drug discovery pipeline. Target ALS is the only non-profit organization focused on generating large-scale multi-omic datasets from human biosamples to accelerate research and is highly regarded for our open data sharing practice. With the launch of the Target ALS Data Engine in March, researchers across the globe can now mine even larger, more comprehensive datasets at no cost, eliminating a major barrier to entry to the field. Additionally, scientists are able to request brain and spinal cord tissue and biofluids like blood, urine, and cerebrospinal fluid that the data coincides with to be shipped to their laboratories through our Longitudinal Biofluids and Human Postmortem Tissue Cores for further analysis and testing. This holistic approach gives scientists the tools they need at every stage of the research process, transforming ideas into potential treatments for ALS.

Beyond funding and enabling research, Target ALS also conducts our own research through our ALS Global Research Initiative (AGRI). Breaking down another barrier - the lack of diversity among research participants that limits our understanding of disease - AGRI programs including our Global Natural History Study and new Community Pop-Up Clinics prioritize enrolling participants from racial and ethnic backgrounds that have been traditionally underrepresented in ALS studies. This diversity is critical for identifying novel genetic risk factors, understanding environmental contributors, and uncovering new biomarkers and drug targets. In 2024, our Global

> *Without collaboration, the seemingly impossible would remain out of reach. But together — with the collective efforts of our team, the ALS community, and our supporters — we are building a world where* ***Everyone Lives****.*

Natural History Study expanded internationally to Latin America, enrolling participants at sites in Colombia and Puerto Rico and working toward onboarding a new site in Brazil. Additionally, we expanded the study to sites in South Korea and Israel, with new international sites on the horizon in 2025. Meanwhile, our first Community Pop Up Clinic in Los Angeles attracted participants from diverse backgrounds to participate in research for the first time. These programs fuel our Research Cores, providing a steady stream of new data and samples to ALS researchers worldwide working to discover the next breakthrough.

As we turn the page on 2024, we reflect with profound gratitude on the people who advance our mission every day:

- **People living with ALS and their families**, whose strength and resilience inspire us. Their stories are at the heart of everything we do, fueling our determination to deliver hope and create meaningful change.
- **The brilliant scientists and researchers** across the globe who push the boundaries of what's possible. These innovators think beyond conventional limits, exploring new ideas and forging pathways to breakthroughs that will lead to life-saving treatments.
- **You—our supporters**, whose generosity makes all of this possible. Your belief in our mission empowers us to fund groundbreaking research, foster unprecedented collaborations, and bring new treatments closer to reality.
- **Our dedicated Target ALS team**, a group of passionate professionals who embody our values of radical collaboration, deliberate disruption, and impatient optimism. Over the past year, we have thoughtfully and efficiently grown our team, ensuring that every role directly drives progress while carefully stewarding donor contributions. By building an agile and highly skilled workforce, we've maximized impact without unnecessary administrative overhead, allowing us to dedicate the majority of resources to advancing ALS research.

Without collaboration, the seemingly impossible would remain out of reach. But together—with the collective efforts of our team, the ALS community, and our supporters—we are building a world where Everyone Lives.

Thank you for being a vital part of this journey.

Dan Doctoroff
Founder, Target ALS

Manish Raisinghani
CEO, Target ALS

Research we

FUND

Target ALS has become the largest private funder of ALS research across the globe. With gratitude to the unrestricted nature of our donor funds, we have the unique ability to fund the best talent and most promising ideas anywhere in the world. In 2024, we launched several funding opportunities to fuel innovative science in our three main focus areas:

1. **Understanding the basic biology and underlying causes of ALS**, providing scientists with new ideas for transformational therapies.
2. **Accelerating drug discovery** by supporting proof-of-concept studies for new therapeutics required for advancement into clinical trials.
3. **Developing biomarkers**, critical for new diagnostics and early detection, identifying and stratifying subtypes of ALS, and monitoring disease progression.

Each grant program was strategically designed to leverage emerging biology and technology and to address areas of high unmet need. In addition, all Target ALS funding opportunities aim to encourage multi-disciplinary collaborations and attract new scientists and ideas into the field. This year, we were able to **launch six competitive funding opportunities and fund 67 projects, investing $15.5 million in grants.**

Basic Biology Consortia

Understanding ALS Biology

Six collaborative research teams have been awarded grants to explore the biology behind sporadic ALS, which makes up 90% of all ALS cases, with the goal of identifying new drug targets and biomarkers. While treatments have been developed for familial ALS, which is caused by inherited genetic mutations, less progress has been made for sporadic ALS, where there is no family history of disease. A better understanding of the disease's biology is crucial for creating treatment options for all those living with ALS. Our 2024 Basic Biology Consortia Program focused on improving our understanding of sporadic ALS by encouraging collaboration among scientists with complementary expertise. The program also promotes the use of new technologies to study ALS and invites researchers from outside the ALS field to contribute. **Target ALS received applications from 106 scientists across 76 institutions in 13 countries, and six collaborative teams were selected for funding.**

The strategy behind Target ALS grant calls

In 2024, almost 40% of our grants focused on accelerating early stage drug discovery research to deliver drug candidates for future phase I clinical trials. Funding is strategically provided to accelerate research in a landscape where **90% of treatments that enter clinical trials fail to become FDA approved.** Our grant programs are designed to fill and grow the drug discovery pipeline to increase the number of high-quality potential treatments entering - and hopefully succeeding - in clinical trials.

New Therapeutic Modalities

Drug Discovery

Recent advances in technology have unlocked new modalities to be developed for Central Nervous System (CNS) disorders - diseases that affect the brain and spinal cord. Tofersen, the first new and effective treatment for SOD1 ALS (ALS caused by a mutation in the SOD1 gene), which comprises around 2% of ALS cases, was approved by the FDA in 2023. This new type of treatment is delivered in the doctor's office by direct injection into the spinal cord once every month to allow the drug to bypass the blood-brain barrier. Tofersen reduces the levels of the mutant SOD1 gene and has shown tremendous benefit in people carrying this mutation. The success of this drug shows us that targeting known genetic mutations is both viable and effective but also highlights the need to further develop new modalities that can cross the blood-brain barrier, thereby avoiding in-clinic treatment. Launching this collaborative funding opportunity in late 2024, **Target ALS aims to support the development and optimization of these next-generation therapies** that target DNA and RNA in the CNS. We look forward to announcing the selected consortia in Spring 2025.

In Vivo Target Validation

Drug Discovery

Advancing potential therapeutics from the lab to the clinic requires rigorous animal testing to prove both the therapeutics' safety and potential to significantly modify disease. This critical step—known as *in vivo* target validation—answers two essential questions: Is the treatment safe, and does it have the potential to work effectively? However, barriers of cost and access to mouse models that accurately mimic ALS can create challenges for scientists at this stage of the drug discovery process. In 2024, Target ALS launched two *In Vivo* Target Validation grant programs, providing in-kind funding for proof-of-concept studies for promising ALS therapeutics. **Results from these studies have the potential to catapult ALS drug candidates from preclinical to clinical pipelines, creating more "shots on goal" in clinical trials.**

TDP-43 Model

In August 2024, we launched an *In Vivo* Target Validation program with Biospective, a contract research organization, to evaluate potential therapeutics in their mouse model that expresses a mutant form of human TDP-43. TDP-43 is a protein that aggregates, or clumps up, and moves from its usual location in cells in 97% of ALS cases, considered a hallmark of the disease. We experienced a high volume of high-quality proposals in response to this program. Five recipients, all from small to mid-size biotech companies, were awarded in-kind funding to support testing of their potential drugs. The data from this funded work may provide a key part of their data package submitted to FDA, significantly advancing their programs toward clinical testing. From directly targeting TDP-43 aggregates to improving function of cellular structures, **these candidate therapeutics have the potential to slow disease progression in those 97% of ALS cases.**

C9orf72 Model

In collaboration with the ALS Association, Target ALS has provided in-kind funding for proof-of-concept studies for promising therapeutics to be carried out at The Jackson Laboratory. These potential treatments will be evaluated for disease-modifying potential in mice expressing the C9orf72 genetic mutation – the most common genetic cause of ALS. The model allows scientists to test how these therapeutics interact directly with the C9orf72 DNA, RNA, and proteins and determine if they impact neurodegenerative and inflammatory processes. Target ALS funded two promising projects that will commence in early 2025, **accelerating development of novel therapeutics for C9orf72 ALS.**

Neurology Resident Grants

Drug Discovery *Biomarker Development*

Given their direct interaction with people living with ALS, clinicians and clinician scientists are uniquely positioned to drive ALS drug and biomarker development. Our Neurology Resident Grant program, launched in March 2024, aims to identify new ideas and support emerging clinician scientists as they establish themselves in the field. Through the program, three individuals have received funding to pursue innovative projects, translating research findings into practical applications that can enhance patient care and treatment outcomes. By supporting talented individuals early in their careers, this program helps nurture the next generation of researchers who have the potential to make significant, long-term contributions to ALS.

Biomarker Consortia Grants

Biomarker Development

Biomarkers are measurable characteristics or substances that provide insights into what is happening inside the body. Biomarkers of disease can indicate whether a disease is present, if it's progressing, and how treatments may affect that progression; they are essential to creating new diagnostic tools, monitoring progression of disease, and improving clinical trial design. As a disorder of the brain and spinal cord, identifying biomarkers for ALS has posed significant challenges. However, **Target ALS is committed to developing a toolkit of validated biomarkers to advance ALS research and improve patient care and outcomes.** Our Biomarker Consortia Grant Program attracted widespread appeal, with 139 scientists representing 34 collaborative projects from 17 different countries applying for funding. Five collaborative projects were selected to advance biomarkers for ALS, offering avenues to track disease progression, stratify patient populations to learn who will respond best to which treatment, and design better clinical trials to drive effective treatments to market.

About our review process

At Target ALS, we hold fairness and transparency paramount in our review process. The Target ALS Independent Review Committee (IRC) makes all research funding decisions without involvement from the organization's staff or leadership, ensuring **every application receives a fair evaluation**. What sets our approach apart from others?

- The IRC is comprised of **experts across scientific disciplines** reflecting the evolving nature of ALS research. By design, to ensure a balanced perspective, the committee has 50% representation from each constituency, academia and the pharma/biotech industry.
- To avoid any possible conflicts of interest, **no member of the IRC can apply for or receive Target ALS funding** for their own work.
- Members on the IRC abide by a comprehensive **conflict of interest policy** and are under a **confidentiality agreement**.
- We do not prescribe the number of grants that can be awarded in each funding cycle, **allowing the IRC to select the best applications for funding** without external limits.

Members of the Target ALS IRC at the 2024 Annual Meeting

Featured Projects

Targeting the CCDC146 Gene for Therapeutic Benefit - A Consortia Approach

Through our Basic Biology Consortia Program, Dr. Johnathan Cooper-Knock (University of Sheffield, UK), Eran Hornstein (Weizmann Institute, Israel), Ophir Shalem (University of Pennsylvania, USA), and Mike Snyder (Stanford University, USA) have been collaborating for the past two years to enable the study of multiple genes or genetic mutations simultaneously within the same experiment. By using a unique combination of high-powered genetic analyses with cutting-edge lab techniques, the team expects to identify several candidate drug targets. Our Basic Biology programs encourage exploratory research like this to better understand disease biology and generate new targets for potential treatments. Through this work, the team identified that the CCDC146 gene is linked to motor neuron death in ALS. The group then created an antisense oligonucleotide (ASO), a small piece of DNA or RNA that can block formation of harmful proteins, designed for CCDC146. **Importantly, this ASO isn't limited to providing benefit for one form of ALS - the team's preliminary work indicates it has the potential to become a therapy for C9orf72 ALS and sporadic ALS.** Due to their outstanding achievements and the high impact of their work, the Target ALS Independent Review Committee (IRC) unanimously awarded the team a third year of funding to allow them to dive deeper into the biology of CCDC146 in ALS and validate potential new treatment avenues.

Dr. Cooper-Knock presenting at the Target ALS Annual Meeting.

> *If we find a genetic change, we know it's a driver of the disease. It's not a consequence of disease. And that's really exciting because if we can correct that upstream driver,* ***then potentially we've got a therapy.***"

Dr. Johnathan Cooper-Knock, MD, PhD
Clinician Scientist, University of Sheffield

Biomarker Milestone Achieved - Target Identification

Exciting progress is being made toward the development of the first-ever diagnostic biomarker for ALS. Funded by Target ALS, a consortium of labs led by Pietro Fratta (University College London, UK), Michael Ward (NINDS/NIH, USA), Mercedes Prudencio, and Len Petrucelli (Mayo Clinic, USA) have been collaborating to detect cryptic peptides, abnormal protein fragments produced in ALS. **The consortium published the first body of work demonstrating the ability to detect cryptic peptides** in cerebrospinal fluid (or CSF, the fluid that bathes the brain and spinal cord) in February 2024. Leveraging the expertise of the consortium's industry partner, BioMarin, the group is developing a highly sensitive test to detect these cryptic peptides in the CSF and blood of people at risk for ALS. This work is the translational extension of the original fundamental biology observation by Phil Wong (Johns Hopkins University, USA) and his colleagues in 2015 that was funded by Target ALS.

Why is this so important? First, **detecting cryptic peptides could lead to diagnosing ALS in its earliest stages** — possibly even before symptoms appear. ALS is currently classified as a diagnosis of exclusion, meaning there is no definitive test for ALS and the clinician has to rule out other potential causes for the symptoms. This results in delayed diagnosis when symptoms are already advanced. Currently, the average life expectancy for a person with ALS after symptoms appear is just two to five years. Early detection and diagnosis offer the opportunity to explore treatment options and improve quality of life, providing critical time to individuals with ALS and families.

Secondly, the ability to detect these cryptic peptides could improve drug discovery efforts. In clinical trials, pharma and biotech companies must prove to the FDA that their candidate therapeutics are both safe and effectively treat disease. Biomarkers are critical to providing the FDA with definitive proof that a therapy works. If the consortium is successful, **detection of cryptic peptides will transform how clinical trials are designed**.

Target ALS is at the forefront of the funding community, accelerating this area of research. Pietro Fratta's lab is exploring cryptic peptides, not only as biomarkers, but as drug targets. They recently published research in Science, the leading scientific journal, demonstrating potential for targeting cryptic peptides using a personalized medicine approach with support from our Research Cores and funding. By accelerating breakthroughs like these, **Target ALS is driving science toward a future where ALS is no longer a terminal diagnosis, but a manageable condition where people can live long, quality lives**.

"In the vast majority of patients with ALS, a critical protein known as TDP-43 moves from its normal location in the nucleus of brain cells into the periphery of cells. This mis-positioning of TDP-43 causes many problems with the function of brain cells, and correcting TDP-43 function is the target of many drug therapies currently in development. However, we currently cannot monitor the location or function of TDP-43 in living people, hindering the development of effective new therapies for patients with ALS. **Our Target ALS-funded consortia discovered that cells with TDP-43 dysfunction make abnormal proteins that can be detected with sensitive assays.** *Current efforts by the consortia focus on developing clinically-robust assays of these abnormal proteins to enable the first clinical-grade biomarkers of TDP-43 function."*

Dr. Michael Ward, MD, PhD
Principal Investigator, NINDS/NIH

Conference Spotlight

The Target ALS Scientific Programs team joined global leaders in research and innovation at the International Symposium on ALS/MND in Montreal, Canada in December. The team presented a poster on Target ALS's Global Natural History Study and Longitudinal Biofluids Core, while also acknowledging innovative work from global ALS scientists that has been catalyzed by Target ALS support. With over 16 presentations and posters acknowledging Target ALS at the Symposium, we're proud of the critical role we're playing in transforming the field and accelerating the path to effective treatments for ALS.

Target ALS team members Laura Dugom (Clinical Research Scientist), Amy Easton, Ph.D. (Senior Director of Scientific Programs), and Ellen Guss, Ph.D. (Scientific Programs Coordinator), at the Symposium.

Target ALS team member Laura Dugom presents the Target ALS Global Natural History Study and Longitudinal Biofluid Study at the poster session.

For example, in a session focused on antisense and siRNA-based therapeutic strategies, Target ALS was noted as a supporter of five out of the seven therapeutics in development. Target ALS is also supporting the development of other disiRNA and ASO therapeutics beyond the list presented in this session at the Symposium.

ASO & siRNA Therapeutics in Development	STMN2	TDP43	CHCHD10	UNC13A	PIKFYVE	C9ORF72 ANTISENSE TRANSCRIPT	CCDC146
Supported by Target ALS	✓	✓		✓		✓	✓

By fostering radical collaboration and breaking down barriers to research, Target ALS is paving the way for breakthroughs that could dramatically impact the ALS landscape.

Research we

ENABLE

Target ALS Research Cores: Empowering Global ALS Discovery

Target ALS is breaking down barriers to ALS research by providing no-strings-attached access to critical tools and resources through our innovative Research Cores. Addressing issues like resource scarcity, lack of standardization, and high costs that traditionally hinder progress in ALS research, the Cores are designed to accelerate drug discovery and biomarker development.

Target ALS Data Engine

In March 2024, Target ALS launched our revolutionary Data Engine, designed to accelerate breakthroughs in biomarker and drug discovery for ALS. Created in collaboration with DNAstack and Verily, the Data Engine hosts comprehensive data collections from Target ALS's Research Cores, including the Postmortem Tissue Core, Longitudinal Biofluids Core, and Stem Cell Core, facilitating multi-omic analysis (computational scientific analysis in which researchers integrate information about all of the DNA, RNA, or protein in individual cells or samples) to discover ALS biomarkers and therapeutic targets. New data is uploaded to the Engine every 4-6 months, ensuring all samples collected from the ALS community through our Cores can have a near-immediate impact on ALS research.

True to our mission, the Data Engine breaks down barriers by providing no-strings-attached access to all data. Additionally, researchers retain full rights to any intellectual property stemming from their discoveries. Since the launch, 250 scientists worldwide have already accessed the Data Engine, underscoring the significant need for this resource.

Postmortem Tissue Core

The Target ALS Postmortem Tissue Core provides high-quality human postmortem brain and spinal cord tissue and associated clinical data to academic and industry researchers worldwide, aiming to deepen our understanding of ALS and spur drug discovery. Over the last 10 years, we have provided samples to over 300 laboratories, facilitating hundreds of research projects. **We maintain the largest postmortem tissue biobank with ALS cases in the world, with over 50,000 brain and spinal cord tissue samples banked at six geographically distributed sites.** In 2024, expert pathologists from the University of Edinburgh joined the Core as the first international site, dramatically expanding our biobank, which currently holds frozen and preserved tissue from a total of 532 donors with ALS and frontotemporal dementia (FTD), a related neurodegenerative disease, and healthy controls.

Longitudinal Biofluids Core

Our Longitudinal Biofluids Core aims to create and make available the most comprehensive collection of biofluids (cerebrospinal fluid, blood, and urine) from people with ALS and healthy controls to support development of biomarkers and treatments for ALS. Collected over time via our Global Natural History Study (GNHS), these biofluids, which are well-characterized with associated clinical demographic and epidemiological information, are critical to improving our understanding of ALS and how it progresses. **In February 2024, we officially launched distribution of these biofluids to the global ALS research community.** To date, our Independent Review Committee (IRC) has reviewed 29 unique requests, 19 of which were approved and 12 biofluid requests have been shipped to research teams across the globe. Two of these shipments were sent to researchers who are already demonstrating success in their experiments with the first round of samples received. We prioritize efficiency; turnaround time from request to receipt of samples can be as short as 12 days, an unprecedented pace compared to other repositories.

The Core is led by our expanding Biofluid Consortium, which includes 14 global ALS clinics to advance our understanding of ALS across genetically and ethnically diverse populations. In 2024, we activated the first international site in Bogotá, Colombia, with 10 participants already enrolled. In addition to the physical biofluids, researchers can access a wealth of data through our Data Engine, including clinical and demographic information, genome sequencing files and metadata, longitudinal speech data, and measures of respiratory function. Datasets from each category can be linked by Neuroguid (a compliant way to deidentify a participant's information), allowing researchers to integrate data across categories for a more comprehensive analysis.

Learn more about how our GNHS supports this core in the Research We Conduct section on page 16.

An equity lens

ALS affects people of all backgrounds, yet previous research studies and clinical trials have predominantly included around 93% Caucasian participants. This means that other ethnicities and races have been underrepresented, which is a crucial gap in understanding genetic risk factors for ALS. Target ALS's Longitudinal Biofluids Core and Data Engine address this gap by providing access to biofluids and data from participants in our Global Natural History Study, which expanded to sites in Latin America and Asia in 2024.

At Target ALS, our vision is a world where Everyone Lives. To make that vision a reality, we will continue to expand our research footprint across the globe and in underrepresented communities, ensuring treatment options are developed for everyone who lives with this disease.

Stem Cell Core

Stem cell models are an invaluable resource for researchers to study disease mechanisms and test new therapeutics. Through our Stem Cell Core, we provide access to a range of induced pluripotent stem cell (iPSC) lines from people with ALS and controls. iPSCs are made from skin or blood cells from a donor and maintain the donor's genetic information. During ALS research, iPSCs from a donor with ALS can be turned into disease-relevant cell types, like motor neurons or nervous system immune cells called microglia and astrocytes. Researchers can use these cells to study which biological factors contribute to ALS and test candidate drugs to help predict whether they would be beneficial. Historically, scientists have not had access to human stem cells. Instead, they used animal models and other cell-based models that are quite biologically different from human nervous system cells, contributing to lack of drug efficacy in clinical trials due to misleading results. Because human motor neurons allow investigators to test drugs in the exact cell type that exists in people, iPSCs are a critical resource for understanding the disease and testing therapeutics.

While iPSC models are extremely important for diseases like ALS and have been made available through several initiatives, research efforts have been plagued with difficulties reproducing results across laboratories because of complicated protocols for generating disease-relevant cells and the large impact of genetic variation on experimental outcomes. **To tackle this major obstacle, Target ALS assembled an international consortium of iPSC experts in 2024, aiming to provide robust ALS iPSC resources globally**. The goal is to create new iPSC lines from skin cells donated by people with ALS carrying one of the following more commonly identified genetic mutations that cause ALS: C9orf72, FUS, SOD1, and TARDBP (TDP-43). With the help of technical experts at Jackson Labs, perfect isogenic control lines will be created from the donor line. Isogenic control lines are genetic equivalents to donor lines except for a singular replacement of the mutated gene with the healthy gene. Pairing the donor line with an isogenic control line allows researchers to compare results in ALS versus healthy cells. Then, the lines will be edited further to express genes that facilitate differentiation of the iPSCs into motor neurons in a reproducible fashion. These types of lines are very rare, expensive, and technically challenging to produce. Aligned with our mission to break down barriers, we plan to share the iPSCs, cell type generation protocols, and data with researchers worldwide through the Stem Cell Core, providing academic and industry labs to access high-quality research tools to study ALS.

Multiplying Impact: Research Cores Propel Breakthroughs

In 2024, the Postmortem Tissue Core facilitated groundbreaking work led by Dr. Moses Leavens from the McLaughlin Research Institute for Biomedical Sciences. By using a technique called RT-QuIC, researchers were able to detect abnormal protein clumps called SOD1 aggregates in postmortem tissue from ALS cases. These clumps were previously thought to only appear in people with ALS caused by SOD1 gene mutations, which account for just 2% of all ALS cases. However, this study found that these aggregates also appear in people with sporadic ALS, which comprises 90% of ALS cases where there is no family history of disease, and in people with ALS caused by a mutation in the C9orf72 gene, the most common genetic cause of ALS. **This finding suggests that diagnostic methods developed for specific types of ALS could potentially translate to other forms that currently lack effective tools for diagnosis and treatment.** The researchers are now testing this method in biofluids of people living with ALS from the Target ALS Longitudinal Biofluids Core. This work exemplifies the critical impact of our Postmortem Tissue Core and how the synergy between our Cores advances discovery of new diagnosis tools and potential treatment for all forms of ALS.

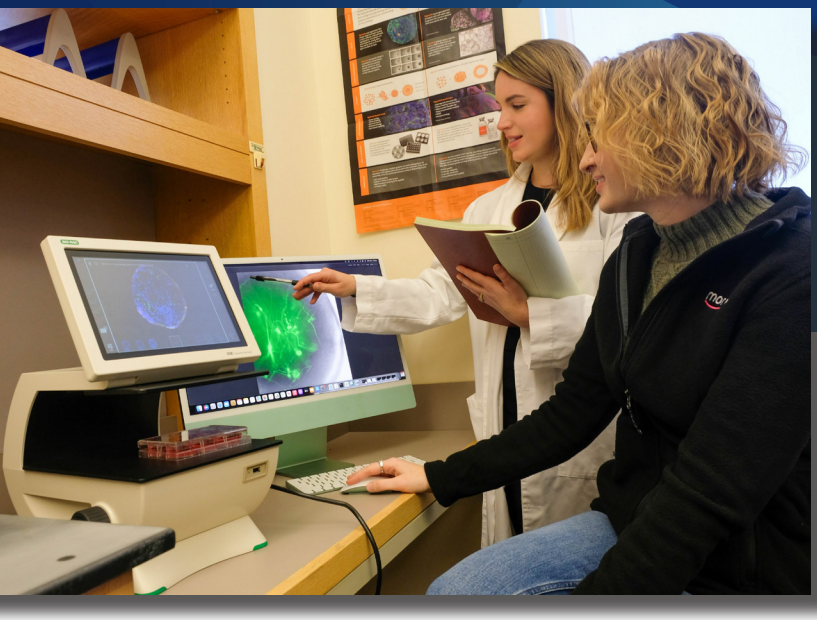
Animal Models Core

Our Animal Models Core breaks down barriers to animal model access through three mechanisms to facilitate cutting-edge ALS preclinical research: funds to test potential therapeutics in animal models at contract research organizations (CROs), support to develop new mouse models, and generation and integration of multi-omic datasets from animal models into the Data Engine. Testing potential drugs in animal models is often required before a drug can enter clinical trials to prove its safety and potential benefit. However, many companies either have no animal facility or lack the ability to license and breed ALS mouse models. Target ALS provides these groups an option to apply for funding at an accredited CRO to do this work for them. In 2024, we launched a collaboration with the CRO Biospective, prosecuting the first funding call for an animal model that mimics TDP-43 pathology that occurs in 97% of people with ALS. Biospective has deeply characterized the animal model and has identified study endpoints that are expected to translate from the mouse to human.

Reagents Core

We offer a range of high-quality antibodies for ALS research through our Reagents Core. Scientists use these antibodies to detect and study mutant proteins associated with ALS. In 2024, we announced the availability of a new validated phosphorylated TDP-43 (pTDP-43) antibody in collaboration with Dr. Len Petrucelli and the Developmental Studies Hybridoma Bank (DSHB). pTDP-43 aggregates are a defining feature in approximately 97% of ALS cases, making it one of the most crucial biomarkers for understanding this devastating disease. Despite its importance, research into pTDP-43 has been hampered by one significant barrier: the lack of reliable, widely accessible antibodies that can accurately detect these aggregates. Historically, these antibodies have been either too expensive or too difficult to obtain, leaving many researchers unable to properly visualize and study this critical element of ALS pathology. Recognizing this challenge, we worked with renowned ALS expert Dr. Len Petrucelli and DSHB to distribute a validated antibody that recognizes human pTDP-43. This antibody allows academic and industry researchers around the world to visualize pTDP-43 aggregates in human cells, mouse models, and postmortem human tissue, accelerating the path toward potential treatments. **In just one month, our first batch of this antibody was exhausted through requests from researchers worldwide, emphasizing the critical need among the ALS scientific community.** We are currently working with our partners to triple the amount of antibody available in early 2025.

Research Core Spotlights



Dr. Kathryn Morelli, PhD, and Abby Kirch, PhD student, working in the Morelli Lab at University of Vermont.

Democratizing ALS Research

At Target ALS, we understand that our mission is urgent; we seek opportunities to propel ALS research rapidly forward, breaking down the barriers that have traditionally limited scientific progress. That is why we offer no-strings-attached access to all of our Research Cores. **Scientists from both academia and industry can benefit from these essential tools and resources at little to no cost and retain all intellectual property from their discoveries.** As the field evolves, we launch new services to meet the needs of the ALS scientific community head on. Through our Research Cores, Target ALS is empowering researchers worldwide to make faster, more impactful strides toward effective treatments for ALS.

Dr. Kathryn Morelli received a Springboard Fellowship from Target ALS in 2023, facilitating her transition from a postdoctoral fellowship to her current independent faculty appointment at University of Vermont. While Springboard Fellows receive grant funding to support their work, equally important, they receive a six-year period of no-cost and no-strings-attached access to our Research Cores, enabling continued development of their ideas and commitment to ALS research.

I utilized the Target ALS Stem Cell Core to engineer, evaluate, and compare spinal cord organoids derived from various forms of familial ALS. These organoids were critical for modeling disease-specific phenotypes and testing therapeutic interventions.

Additionally, I accessed the Reagents Core, acquiring the Rabbit Polyclonal TDP-43 Antibody and the C9orf72 Poly(GP) Monoclonal Antibody. These reagents were used as key output measures to assess the efficacy of a novel therapeutic candidate targeting C9-ALS, applied in both mouse models and organoid systems.

I am sincerely grateful for access to the Target ALS Research Cores, which were instrumental in advancing this research. *The resources provided by the Stem Cell Core and the Reagents Core greatly supported the development and evaluation of disease models and therapeutic approaches for ALS. Thank you for enabling these critical studies."*

Dr. Kathryn Morelli, PhD
Assistant Professor, University of Vermont

> **Target ALS runs a very tight ship, so I have trusted this resource implicitly.**

Cooper Penner
MD-PhD Candidate, University of Pennsylvania, speaking about the Target ALS Data Engine

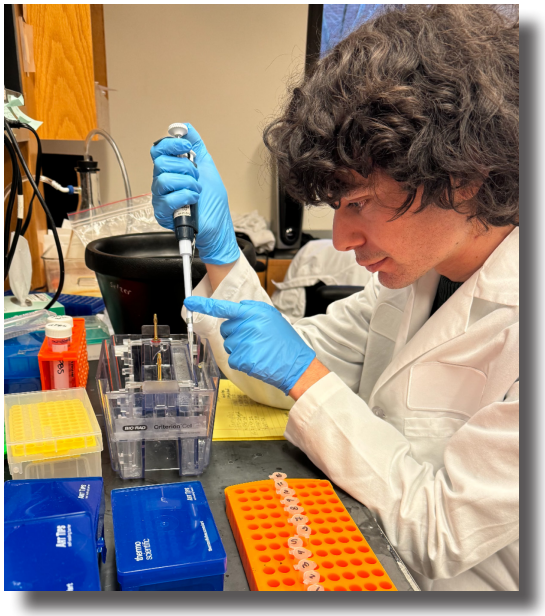
A Scientist's Experience with the Target ALS Data Engine

Cooper Penner is an MD-PhD candidate in the University of Pennsylvania's Department of Neuroscience currently studying the pathogenesis of ALS under the guidance of Dr. Alice Chen-Plotkin. **Cooper also has a personal connection to the disease.** He acted as his mother's primary caregiver for the three years she lived with ALS, and is himself a carrier of a pathological expansion of the C9orf72 repeat sequence, the most common single genetic cause of ALS, responsible for approximately 10% of all ALS cases.

Cooper has found the Target ALS Data Engine to be an incredibly valuable tool for accelerating his ALS research. He has used the bulk RNA-Seq data to generate new hypotheses about disease biology and explore potential targets for ALS treatments. He says, "The way I've used the resource thus far has really helped me with hypothesis generation," noting that it was the first step in discovering a new target with significant promise. By integrating data from Target ALS with his own research and other datasets, Cooper has been able to test biological hypotheses quickly and efficiently. He adds, **"Target ALS runs a very tight ship, so I have trusted this resource implicitly."**

For Cooper, one of the major benefits of the Target ALS Data Engine is its well-curated and easily accessible data, which has made a tangible difference in how fast he can move his research forward. "It's a really big deal, because that stuff just takes so much time," he explains. While he has not yet dived into some of the platform's cloud computing-based tools, he explains that the workbench might soon become necessary for certain types of analysis, especially as he dives deeper into more complicated datasets like single-cell data.

While Cooper recognizes the platform's utility, he also notes the unique opportunity that Target ALS provides in fostering collaboration and sharing high-quality data. **He believes that the Target ALS Data Engine is not just a valuable resource for his own work but for the broader research community** as well, providing researchers with a solid foundation to build upon and collaborate more effectively.



Cooper Penner, an MD-PhD Candidate studying ALS at the University of Pennsylvania, working in the laboratory.

Research we

CONDUCT

Our **ALS Global Research Initiative (AGRI)** encompasses two clinical research studies aimed to identify causes of the ALS and novel biomarkers to diagnose, predict, and monitor disease progression:

1. **Global Natural History Study (GNHS)**: A longitudinal collection of biofluid samples and health information from people living with ALS and healthy controls
2. **Community-based Pop-up Clinics:** One point in time studies exploring genetic and environmental determinants of ALS in underrepresented racial and ethnic groups

By conducting our own research, Target ALS fills gaps that are often overlooked or underfunded. ALS is a heterogenous disease, meaning it has several different root causes. Currently, there's a major gap in our understanding of ALS due to the lack of ethnic, genetic, and geographic diversity among research study participants. We're tackling this gap by prioritizing enrolling participants from diverse and underrepresented communities in our studies. AGRI is broadening our understanding of how ALS manifests and progresses in different populations, ensuring that treatments will be developed for everyone with ALS.

Global Natural History Study (GNHS)

Our GNHS aims to enroll at least 800 symptomatic ALS participants and 200 healthy controls to create the most comprehensive collection of biofluids for ALS. The study involves longitudinal collection (samples collected over the course of the disease) of blood, urine, and CSF as well as clinical and digital measures of motor, cognitive, speech, and respiratory function.

In 2024, total enrollment doubled, reaching 182 participants, including 104 with ALS and 78 healthy controls. The study currently **spans 14 domestic and international sites**, with continued expansion into Latin America, Africa, and Asia planned in 2025. The biorepository now includes **17,000+ biofluid samples**. Researchers can request these samples to be shipped to their labs or analyze associated datasets via our Data Engine to identify novel targets for treatments and critical biomarkers.

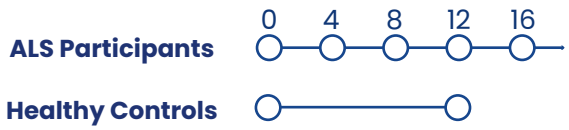
The Global Natural History Study is set to provide valuable insights into the heterogeneous nature of ALS, paving the way for innovative biomarkers that can predict and track disease progression. Engaging populations outside the U.S. will significantly enrich our understanding of ALS.

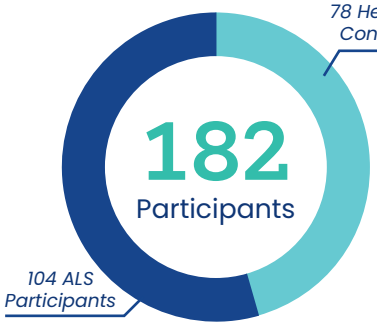
Biomarkers can be used to rapidly diagnose ALS and monitor disease progression as well as to demonstrate activity of test therapeutics and track treatment response. Limited availability of well-characterized patient biofluid samples is a common barrier to biomarker development.

GNHS by the Numbers

17,957
Vials of biofluid samples collected

Visit schedule
in months





Study Activities

Every 3-4 months	Biofluids collection and clinical assessments	In Clinic
Every 2 weeks	Digital collection of speech, respiratory, and cognitive assessments	At Home

Target ALS Global Natural History Study - Current Active Sites

1. Barrow Neurological Institute, AZ, USA
2. Columbia University, NY, USA
3. Georgetown University, DC, USA
4. Mayo Clinic Jacksonville, FL, USA
5. Massachusetts General Hospital, MA, USA
6. Northwestern University, IL, USA
7. University of California, San Diego, CA, USA
8. University of Washington, Seattle, WA, USA
9. Washington University in St. Louis, MO, USA
10. Baylor College of Medicine, TX, USA
11. University of Puerto Rico, PR, USA
12. Instituto Roosevelt, Colombia
13. Hebrew University of Jerusalem, Israel
14. Seoul National University Hospital, South Korea

Community-Based Pop-Up Clinics

By studying how genetic and environmental factors affect ALS in diverse populations, we can develop treatments that are safe and effective for everyone with ALS. However, many people living with ALS, especially those from underserved communities, face many challenges when it comes to participating in research. Barriers including financial difficulties, lack of insurance and access to healthcare, lack of educational materials, and limited ability to travel to ALS clinics may hinder participation. **To address these barriers, Target ALS has launched a series of one-time blood collection events in partnership with local ALS clinics and organizations.** The study aims to enroll approximately 5,000 symptomatic individuals living with ALS and 1,000 healthy control participants to provide a one-time blood sample and answer an environmental questionnaire, providing a less daunting opportunity to participate in ALS research.

As with all data generated by Target ALS, the data from this study will be made available to scientists via the Target ALS Data Engine to advance research as rapidly as possible. The data will include long-read sequencing, a technique that can read much longer stretches of DNA than traditional short-read sequencing, allowing researchers to more easily see the complete structure of genes and the genetic information they contain without needing to rely on piecing together small fragments. **Both the inclusion of this type of data and the speed at which we're able to provide it to researchers worldwide through the Data Engine is unprecedented in the field.**

Target ALS Inaugural Pop-Up Clinic at Kaiser Permanente in Los Angeles in December 2024

In addition to blood collection, we are conducting a substudy to collect saliva samples and responses to a specialized questionnaire from approximately 40 people with ALS and 40 healthy controls. The samples will undergo microbial sequencing, a technique to study the genetic material of microbes, like bacteria that live in the digestive tract, providing insights into the gut microbiome in ALS.

At our inaugural pop up clinic at Kaiser Permanente in Los Angeles this December, we enrolled 13 participants in the study. Seven participants also contributed to a substudy collecting saliva to investigate potential links between diet and ALS. We were thrilled to see such **rich diversity among participants**, with nine identifying as Hispanic/Latino, one as Asian, two as Caucasian, and one as Indian. Target ALS' strategic decision to partner with Kaiser Permanente enables us to collect samples for a full year past the pop-up event. From this one site, we anticipate collecting blood samples from at least 60 participants overall. **A second, larger pop-up event is scheduled for February 28, 2025 in Phoenix, Arizona in collaboration with ALS Arizona,** a local ALS organization.

Putting together the puzzle of ALS

To truly understand ALS, we recognize the need to explore every piece of the puzzle—healthcare access and quality, social and community inequities, education, neighborhood environments, and genetics, all of which play a critical role in shaping outcomes. By bringing research directly to communities, we are reducing barriers to participation and ensuring the voices and experiences of underrepresented groups are included in the fight against ALS.

> **"The racial and ethnic diversity of ALS genetic datasets will be paramount for advancing our understanding of disease pathophysiology and driving therapeutic discovery, and increasing the number of diverse participants in clinical trials is critical."**

Ramita Karra, MD
Neurology Resident, UCLA

Dr. Ramita Karra on Addressing Inequities in ALS Healthcare

ALS affects individuals across all backgrounds, yet representation in ALS research has long been skewed. **Data reveals that approximately 95% of participants in previous ALS clinical trial studies were Caucasian, leaving other populations, particularly Black and Latino communities, significantly underrepresented**. This lack of diversity in research critically impacts diagnosis, treatment, and outcomes for underserved groups.

The Impact of Barriers to Care

"Disparities in accessing healthcare for people with ALS can be due to a multitude of factors, including but not limited to race and ethnicity, age, socioeconomic status, immigration status and availability of health insurance, religion and cultural differences," explains Dr. Ramita Karra, a neurology resident at UCLA.

Barriers to care contribute to delayed diagnosis, limited access to multidisciplinary care, and missed opportunities for patients to participate in life-extending clinical trials. Dr. Karra notes, "Black ALS patients have an increased diagnostic delay as compared to non-Hispanic Caucasian patients, with a lower ALSFRS-R score and vital capacity at the initial clinic visit." Language differences are a considerable barrier for Hispanic or Latino patients in Dr. Karra's California clinic. "Several of these patients followed up in the ALS clinic but were still unaware or unable to navigate the websites to connect with local ALS organizations and sign up for equipment through loan lockers," she shares. For those unable to access resources or fully comprehend available options, the path to ALS care is riddled with challenges. This often leads to reduced participation in clinical studies and a limited understanding of experimental therapies that could impact their quality of life.

Addressing the Health Equity Gap Through Innovative Solutions

Dr. Karra has observed that "genetic testing is less frequent in low-resource settings, and there is similarly decreased access to multidisciplinary ALS clinics for these patient populations, a factor that has been previously shown to affect overall disease prognosis." The lack of resources, from genetic testing to transportation for clinic visits, coupled with low health literacy and cultural barriers, often prevents patients from pursuing essential treatments. Dr. Karra points out that "the financial burden of arranging transportation and coming to the clinic during work hours can be an additional prohibitive factor," illustrating the impact of social determinants of health on ALS care accessibility.

With the urgency of these inequities in mind, Target ALS's community-based pop-up clinics are designed to provide convenient, one-time blood collections in underserved communities nationwide. Through this initiative, **Target ALS aims to address the scarcity of data on those living with ALS from diverse racial and ethnic backgrounds and enable more inclusive research on the genetic and environmental factors affecting ALS progression**. As Dr. Karra highlights, "The racial and ethnic diversity of ALS genetic datasets will be paramount for advancing our understanding of disease pathophysiology and driving therapeutic discovery, and increasing the number of diverse participants in clinical trials is critical."

The Target ALS Annual Meeting:

Inspiring Radical Collaboration

Each spring, the Target ALS Annual Meeting brings members of our Innovation Ecosystem together over three days to share the latest breakthroughs and forge new collaborations, driving progress toward effective treatments for ALS. Our 2024 meeting had the largest attendance in history, with over 850 attendees present from academic institutions, pharmaceutical and biotech companies, venture capital firms and nonprofit organizations - both in-person and virtually - reflecting the growth of both our funded portfolio of scientists and the impact our work has had on expanding ALS research.

The Target ALS Annual Meeting is hailed as the premier ALS conference globally. What makes it so unique?

Members of our Innovation Ecosystem present confidential information about their ongoing research – unpublished work that is truly on the cutting-edge – and receive real-time feedback from other experts in the field.

The presence of every stakeholder in a single room creates an atmosphere ripe for collaboration between groups that typically do not have an avenue to interact in one place. The collaborations that have formed at previous Annual Meetings have had a storied impact on the research landscape. By connecting academic researchers with pharmaceutical and biotech representatives and venture capitalists, research is able to move rapidly from the laboratory to the clinic.

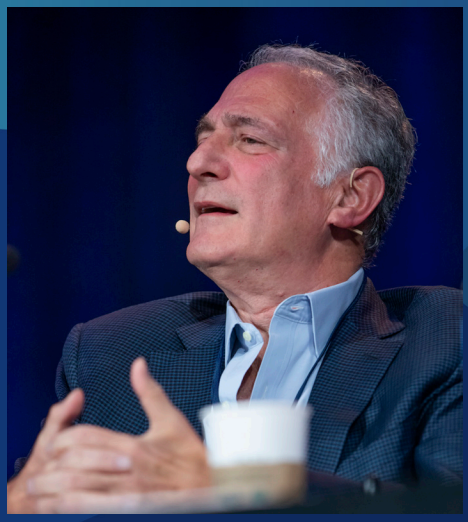
As the Innovation Ecosystem grows, each year's Annual Meeting brings a new sense of excitement and a renewed hope that a future where Everyone Lives is even closer on the horizon. We're looking forward to forging new collaborations and sharing the latest breakthroughs at our next Annual Meeting in May 2025.

Scientists listening to presentations at the 2024 Target ALS Annual Meeting.

Alisa Doctoroff giving a moving speech to open the second day of the meeting.

Networking breaks are built into the schedule, aiming to build new connections and foster collaboration.

Dan Doctoroff addressing the room during his opening remarks.



Dr. Fanny Elahi, Mount Sinai, member of the Target ALS IRC, moderating a Q&A session.

Drs. Caroline Ingre, Karolinska Institutet, (center) and Mai Yamakawa, UCLA, (right), receipients of Target ALS Early Stage ALS Clinician grants, taking questions after their presentation, moderated by Dr. Michela Deleidi, DZNE, (left).

2024 in Review: Transforming ALS Research

A timeline of progress, innovation, and collaboration

January

Target ALS Stem Cell Consortium assembles with a goal of providing scientists with advanced stem cell models. *Read more on p12.*

Dr. Clelland speaking at the Target ALS Annual Meeting.

Dr. Claire Clelland publishes rigorous methods and standards for measuring C9orf72 ALS pathology, the most common genetic cause of ALS and FTD, using resources from the Target ALS Postmortem Tissue and Reagent Cores. This work addresses long-standing challenges in the field, laying the groundwork for advancing discovery and clinical trials targeting C9orf72-related ALS.

The University of Edinburgh joins the Target ALS Postmortem Core, enhancing our capacity to distribute ALS and FTD tissue globally. *Read more on p10.*

February

Biofluid samples from our Global Natural History Study become available for global distribution, offering researchers an unparalleled resource to advance ALS research. *Read more on p11.*

- 29 requests received
- 9 approved
- 14 shipments sent
- 2,122 biofluids vials distributed
- 17,957+ vials collected

March

Target ALS Data Engine launches, providing researchers with a centralized platform to access critical ALS research data. *Read more on p10.*

- 224 users from 161 unique organizations have applied for access (45% from Academia, 35% from Pharma/biotech)
- 24 new users per month
- Most users (19%) list biomarker discovery and validation as their main purpose for access

New funding call with Biospective announced as part of our Animal Models Core, expanding opportunities for *in vivo* target validation in ALS research. *Read more on p10.*

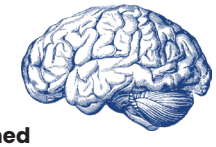
April

Dr. Johnathan Cooper-Knock's Basic Biology Consortium **publishes work establishing CCDC146 as a new potential therapeutic target for ALS.** *Read more on p7.*

Scan the QR code to watch Dr. Cooper-Knock discuss his research.

May

Capital campaign goal achieved. Spearheaded by our founder, Dan Doctoroff, the campaign raised more than $259M, bringing his total raised for ALS research to over $350M.



June

Dr. Moses Leavens published groundbreaking research utilizing the Target ALS Human Postmortem Tissue Core. *Read more on p12.*

July

Duke Health publishes an article featuring the role of Target ALS's genomic datasets in a groundbreaking discovery by researchers at Duke Health and St. Jude's Research Hospital. Scientists identified a genetic variant linked to a rare phenomenon where a subset of people with ALS experience reversal or normalization of symptoms, emphasizing the pathway as a key target for new treatments.

September

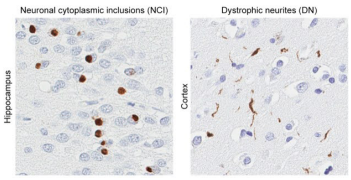
First spatial transcriptomic dataset uploaded to the Target ALS Data Engine, a groundbreaking collaboration with Dr. Hemali Phatnani's lab at the New York Genome Center. This advanced dataset provides detailed insights into gene activity within specific regions of tissue, enabling researchers to study ALS with unprecedented precision.

Two Target ALS-funded consortia uncover a promising potential diagnostic biomarker. The HDGFL2 cryptic peptide emerges in the absence of functional TDP-43, a protein implicated in 97% of ALS cases. Supported by leading researchers and industry partners, this discovery could transform early diagnosis and therapeutic intervention. *Read more on p8.*

Target ALS partners with Modality.AI to monitor ALS symptoms remotely using their innovative technology. A subset of participants in our GNHS will complete self-directed assessments from home, capturing speech, facial activity, respiratory function, and cognitive and motor function, testing whether the platform is sufficiently sensitive to detect early signs of disease and even small changes in disease progression.

November

New validated pTDP-43 antibody becomes available through the Target ALS Reagents Core, developed by Dr. Len Petrucelli's lab in collaboration with DSHB. This antibody targets pTDP-43, a protein whose aggregation is a hallmark of 97% of ALS cases. 99 vials have already been shipped, addressing a longstanding challenge in sourcing robustly validated tools for ALS research. *Read more on p13.*



Representative images of human postmortem tissue slices stained using the pTDP-43 antibody, generously provided by Petrucelli lab.

New Therapeutic Modalities funding opportunity announced to support the development and optimization of next-generation therapies that target DNA and RNA. *Read more on p5.*

December

GNHS expands to East Asia with a new site at Seoul National University Hospital in South Korea, increasing geographic and demographic diversity in the study. *Read more on p7.*

First Community-Based Pop-Up Clinic hosted at Kaiser Permanente in Los Angeles, lowering barriers for diverse and underrepresented populations to participate in research and unlocking new insights. *Read more on p16.*

October

Dr. Pietro Fratta's lab publishes groundbreaking research on a novel precision medicine approach, leveraging genomic datasets to address the complexity of neurodegenerative diseases like ALS. This work emphasizes the importance of stratifying patients based on genetics, lifestyle, disease presentation, and ethnicity to better understand disease mechanisms and improve therapeutic efficacy. By utilizing humanized genetic and cellular models, this research paves the way for more personalized, effective treatments and brings us closer to translating laboratory findings into clinical breakthroughs.

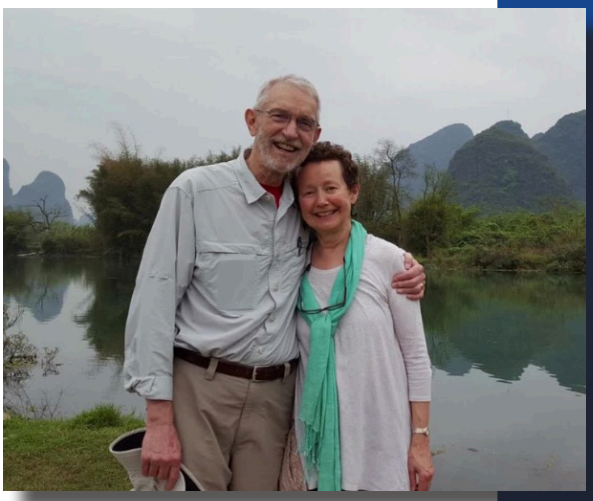
Dr. Fratta speaking at the Target ALS Annual Meeting.

8th clinical trial emerges from our funded work, a significant step toward effective treatments for ALS. QurAlis completed the first cohort of a Phase 1 trial for QRL-101, a groundbreaking precision therapy targeting hyperexcitability in ALS—a condition affecting nearly 50% of all cases and contributing to motor neuron degeneration.

Data from our partnership with ZEPHYRx becomes available in the Target ALS Data Engine, including real-time, lab-quality respiratory data from ZEPHYRx's at-home spirometry solutions, alongside daily activity tracking, from 68 participants in our GNHS.

Honoring ALS Caregivers

Recently, we had the privilege of sharing the inspiring stories of ALS caregivers — individuals whose strength, compassion, and resilience shine brightly in the face of unimaginable challenges. Their courage and willingness to share their journeys remind us why we remain steadfast in our mission. Their voices show us what's possible when love and determination meet and inspire us to push forward, together, toward a world where Everyone Lives.



Zach Hall, a neuroscientist and scientific co-founder of Target ALS, lost his wife, Julie Giacobassi, to ALS in 2022, a disease that robbed them of precious time together. As a renowned English horn player and compassionate volunteer, Julie's vibrant life was a testament to her generosity and resilience, even as ALS took away her ability to create and connect through her art. Zach's journey underscores the urgent need for ALS research and the invaluable role caregivers play in supporting their loved ones through the disease's devastating progression.

"If I regret anything, it's that I didn't take enough time just to sit with her and reminisce... We never had time to say, 'Haven't we had a nice life together?'"

Zach Hall

Charlie Kautz, a chiropractic physician from Nashville and experienced marathoner, brought his passion and personal connection to ALS by fundraising for Target ALS in the 2024 NYC Marathon. Inspired by his close friend Ben Sturgell, who is living with ALS, Charlie dedicated his run to supporting ALS research and raising awareness of the profound impact the disease has on individuals and their loved ones. As part of Ben's caregiving team alongside his wife, Amanda, Charlie embodies the spirit of resilience, community, and action that drives our mission forward.

"When I was looking at charities, this charity stood out, and there was no doubt in my mind that I wanted to help the cause."

Charlie Kautz

"We need to raise awareness of this awful disease and find effective methods and therapies that we can put in our bodies that will make a real difference. And we're going after it."

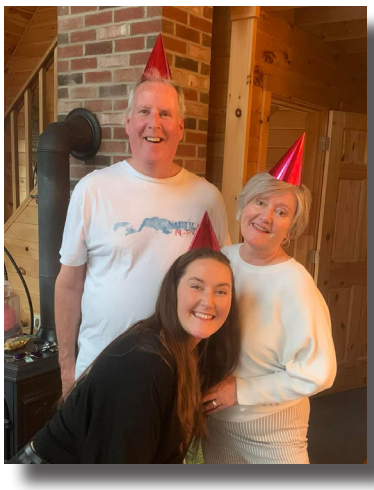
Ben Sturgell

At the 2024 Target ALS Annual Meeting, we had the privilege of sitting down with Emily Cox to capture her powerful story. Emily has faced the devastating impact of ALS across generations, losing her grandmother, great aunt, and father, Peter, to the disease. Now carrying the same genetic mutation, Emily lives with the uncertainty of her own future but channels her fear into hope and action by participating in ALS research. Her story highlights the urgent need for greater understanding, funding, and support, as she passionately advocates for a future where ALS no longer devastates families.

“If people knew how devastating this disease is—not just for the person, but for their family and caregivers—there would be more support, funding, and urgency for treatments. People don’t realize that this is something that continuously gets worse and takes everything. It’s almost like a nightmare that’s constantly unfolding, and you never know what’s going to be taken next.”

Emily Cox

Scan the QR code to hear Emily Cox share her deeply personal journey with ALS and why she’s driven to make a difference through research and advocacy.



Emily pictured with her parents. Her father, Peter, unfortunately passed from ALS in June 2024.

Scan the QR code to hear Alisa’s inspiring words from the 2024 Annual Meeting, reflecting on the impact of ALS and the importance of accelerating research to create a brighter future.

Alisa Doctoroff, Target ALS Board Member, founding donor, and wife of founder Dan Doctoroff, embodies the strength and resilience of caregivers as she supports her husband in his battle with ALS. Reflecting on her journey, she reminds us of the daily challenges caregivers face and calls on all of us to join the relentless pursuit of effective treatments. As Alisa says, we must “go to infinity and beyond” to change the future of ALS—for those living with it today and for generations to come.

“In the Jewish daily morning service, there’s a series of blessings thanking God for the little things we take for granted—opening our eyes, standing up. They don’t seem so small now.”

Alisa Doctoroff

As we reflect on 2024, we remain deeply grateful for the continued support of our community, researchers, donors, and partners. Together, we have made significant strides in advancing ALS research and bringing us closer to transformative discoveries. The success of our capital campaign — raising over $259 million — has allowed us to expand our research investment by 3.5 times over the past two years. But we're not stopping here. We remain relentless in our efforts to raise the resources needed to grow our research program and fund groundbreaking ideas worldwide.

The challenges ahead are complex, but our resolve is stronger than ever. With your continued partnership, we will pursue bold strategies, embrace innovative science, and accelerate the pace of discovery. Every step we take brings us closer to a future where everyone with ALS lives.

Thank you for being an essential part of this mission. Your trust, generosity, and belief in our vision empower us to make an impact every day. We look forward to building on this momentum in the year ahead and making 2025 a year of unprecedented progress — together.


TARGET
ALS