EVERY ONE LIVES

TARGET ALS 2025
YEAR IN REVIEW

TARGET ALS

Dear Friend,

The past year served as a turning point for Target ALS, shaped by global outreach, deeper community engagement, and a research ecosystem moving with unprecedented urgency and purpose. Across continents, disciplines, and communities, we witnessed a powerful momentum take hold: researchers collaborating across borders, people living with ALS contributing to studies in new and meaningful ways, and data flowing more freely, openly, and rapidly than ever before. Together, these efforts signal a rising inflection point in ALS research.

At the center of this shift is our Fund, Enable, Conduct model, a radical, yet deliberate strategic approach that continues to set Target ALS apart. This model isn't just a framework but an engine propelling the field forward.

We fund the most ambitious ideas and rising scientific leaders across ALS biology, drug discovery, and biomarker development. These investments are generating tangible progress. A striking example is the advancement of Trace Neuroscience's drug discovery program. With Target ALS support, the idea of pursuing Unc13a as a therapeutic target for ALS moved from the lab toward a clinical trial in only two years. This progress demonstrates yet again that our collaborative model, which brings pharma/biotech and academics together, accelerates ideas from the lab toward the clinic.

We enable discovery by eliminating traditional barriers that slow science. Through our Research Cores, we provide unrestricted access to biospecimens, multi-omic datasets, stem cell lines, antibodies, animal models, and more—resources that are difficult or cost-prohibitive to obtain elsewhere. This "no strings attached" access continues to democratize innovation worldwide and expand what researchers can do, how fast they can do it, and who can participate.

We conduct foundational research ourselves through the ALS Global Research Initiative (AGRI), including the Global Natural History Study and our expanding network of community-based pop-up clinics. This year, we expanded our global footprint to Puerto Rico, Colombia, Israel, South Korea, and beyond, ensuring ALS research reflects the full diversity of the people it impacts, with 36% of AGRI participants coming from diverse backgrounds, compared to just 5% in other ALS studies. Our investment in long-read whole genome sequencing, large-scale proteomics, digital biomarkers, and epidemiological questionnaires has generated one of the most comprehensive ALS datasets in existence.

> "None of this happened by chance. It is the result of a deliberate, coordinated strategy to standardize what has long been fragmented, breaking down barriers that once slowed progress, and aligning the field toward shared goals."

This integrated approach - Funding, Enabling, and Conducting - creates a powerful positive feedback loop that accelerates discovery at every stage, compressing timelines that once took decades into years or even months.

Nowhere is this more visible than in the momentum behind the Target ALS Data Engine. What began as

a bold vision is now a rapidly expanding platform at the center of ALS research. Researchers across the world are using it to connect molecular, genetic, and clinical insights in real time, to test hypotheses faster, and to identify the next generation of drug targets and biomarkers. The impact is immediate and measurable: Data Engine usage has exploded since it was launched in 2024, now exceeding 500 users. Our first large proteomics upload this past summer triggered a notable spike in access and query activity, underscoring the desire for integrated, high-quality ALS datasets. A major breakthrough is also underway with a 200-case single-cell RNA sequencing effort newly launched at Mount Sinai under the leadership of Dr. Panos Roussos. These datasets will offer unprecedented insight into cell-type–specific drivers of ALS across the motor system.

The excitement around this resource is palpable and reflects not just technological progress but also a global community ready to accelerate impact together.

None of this happened by chance. It is the result of a deliberate, coordinated strategy to standardize what has long been fragmented, breaking down barriers that once slowed progress, and aligning the field toward shared goals.

As you read this report, you will see progress that is real, measurable, and deeply human. Progress shaped by scientists, clinicians, caregivers, donors, and people living with ALS, with each contributing to our shared mission. The advances captured here reflect an ALS research landscape moving faster, more openly, and more collaboratively than ever before.

There is still much to do. But we have never been closer to changing what an ALS diagnosis means. With urgency, partnership, and unwavering determination, we are shaping a future where ALS can be treated and ultimately, a world where Everyone Lives.

Thank you for your partnership, your belief in this mission, and your commitment to accelerating progress.

With gratitude and determination,

Dan Doctoroff
Founder and Chair,
Target ALS

Manish Raisinghani, M.B.B.S., Ph.D
Chief Executive Officer,
Target ALS

RESEARCH WE

FUND

DRIVING BREAKTHROUGHS: TARGET ALS GRANTS EMPOWER THE NEXT WAVE OF ALS RESEARCH

Target ALS is the largest and most impactful private funder of ALS research worldwide. Thanks to the generous trust placed in us by our donors, we can direct resources to the most promising ideas and emerging scientific leaders across the globe. Our funded projects have a high success rate, delivering meaningful results to advance ideas from early to late stage research.

In 2025, we continued to expand funding opportunities, driving nearly $12M into innovation across 151 grants in three critical areas:

- **Understanding ALS Biology:** Advancing insights into the root causes of disease to identify new drug targets.
- **Accelerating Drug Discovery:** Supporting proof-of-concept studies that pave the way toward clinical trials.
- **Developing Biomarkers:** Enabling earlier diagnosis, identifying ALS subtypes, and monitoring disease progression with precision.

Every grant that Target ALS funds is tied to a deliberate strategy and a long-range vision for the field, ensuring that promising ideas move through the full research pathway: uncovering disease biology, identifying and refining new therapeutic targets or biomarkers, validating them in rigorous models, generating translational data, and preparing the strongest candidates for clinical development. Our funding allocation reflects where the strongest ideas emerge. The distribution of our funding isn't set by quotas or percentages. It's shaped by where the most compelling science is happening. Each year, we invest in the proposals with the clearest biological rationale, the strongest evidence, and the greatest potential to advance the field.

The Innovation Ecosystem Approach

By encouraging unpublished observations from grantees to be shared with the broader ecosystem at our Target ALS Annual Meeting, these funding opportunities create a pipeline of therapeutic targets and biomarkers that the entire ALS landscape is informed about. This ensures breakthroughs don't stay trapped in individual labs but rapidly move toward therapies for people living with ALS.

We also bring a strategic, agile lens to deciding which funding calls to launch each year. Rather than repeating the same calls year after year, Target ALS scans the field, identifies the most critical bottlenecks, and tailors each funding call to deliver the greatest impact across the research ecosystem. We fund research through two mechanisms, collaborative consortia and individual investigator grants:

Collaborative Grants

Target ALS funds focused, multi-disciplinary consortia that cut through silos and speed the path from discovery toward clinical trials. These collaborations unite leading academic scientists with industry partners to focus on the same research problem together, including deciphering disease mechanisms, validating therapeutic targets, and discovering biomarkers. This mix matters. Academia brings novel ideas and foundational biology that push the field forward, while industry contributes by providing translational and drug development expertise, resources, infrastructure, and regulatory know-how that speed translation.

Rita Sattler, Ph.D. and Yuna Ayala, Ph.D. answer questions about their research at the 2025 Target ALS Annual Meeting.

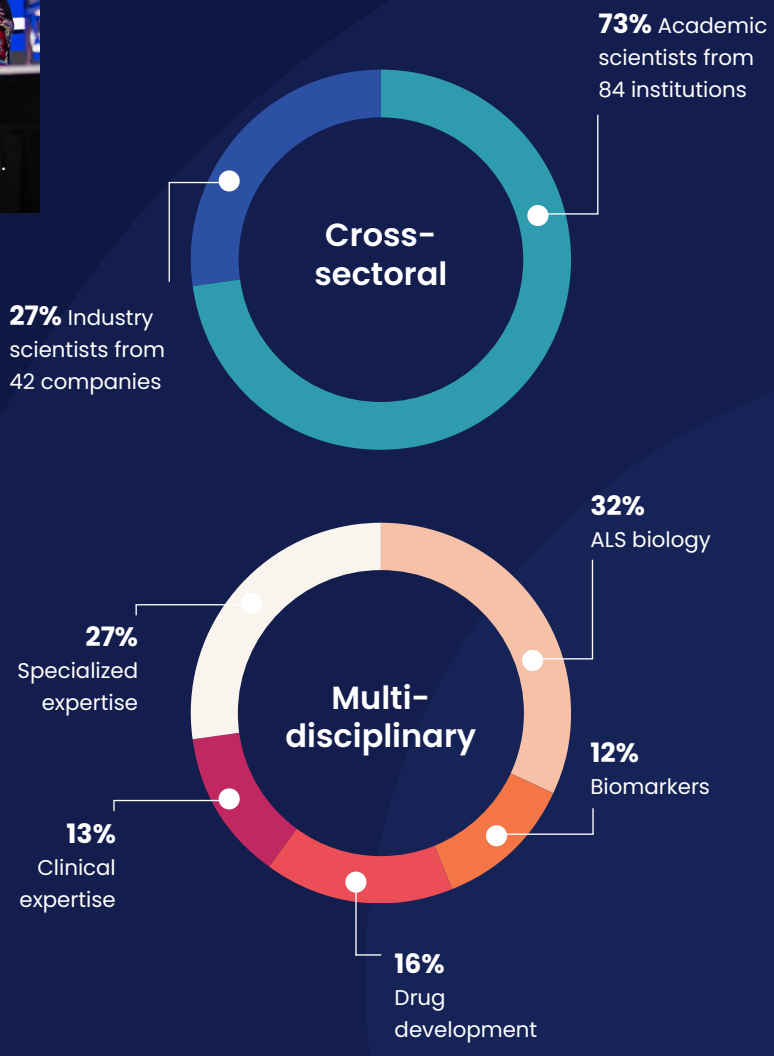
Individual Investigator Grants

Complementing our collaborative consortia, Target ALS invests in emerging scientific talent through individual investigator programs. These grants support early-career researchers with bold ideas, helping bring new ideas, cutting-edge expertise, technologies and fresh perspectives into the ALS field. This strategy strengthens the scientific pipeline, cultivates future leaders, and expands the community of innovators working toward effective treatments. Many of these scientists go on to become part of collaborative projects after being introduced to our network of global scientists, cementing their continued research in the ALS field. Programs include Springboard Fellowships, Early Stage ALS Clinicians, Neurology Residents, and New Academic Investigators.

Since our founding in 2013, Target ALS has granted over **$59 million to 78 consortia.**

Our collaborative consortia are **cross-sectoral**, including scientists from both academia and industry, and **multi-disciplinary**, including researchers with expertise in various scientific disciplines.

- Consortia include 219 scientists
- 58% of consortia are led by industry
- Four to six scientific disciplines or organizations are represented in each consortium



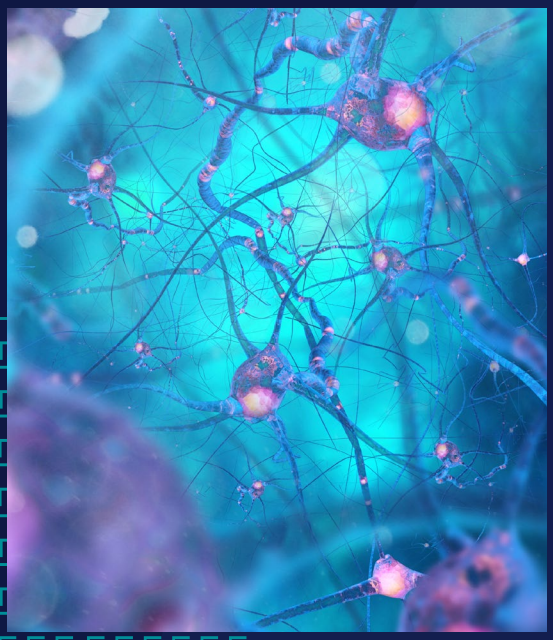
A Robust Preclinical Pipeline

At Target ALS, we build and support a robust preclinical pipeline with purpose. Each project we fund is anchored to a clear scientific rationale and a strategic vision for advancing therapies through the full drug discovery and development pathway, from basic biology and target discovery to screening, lead optimization, and preclinical validation.

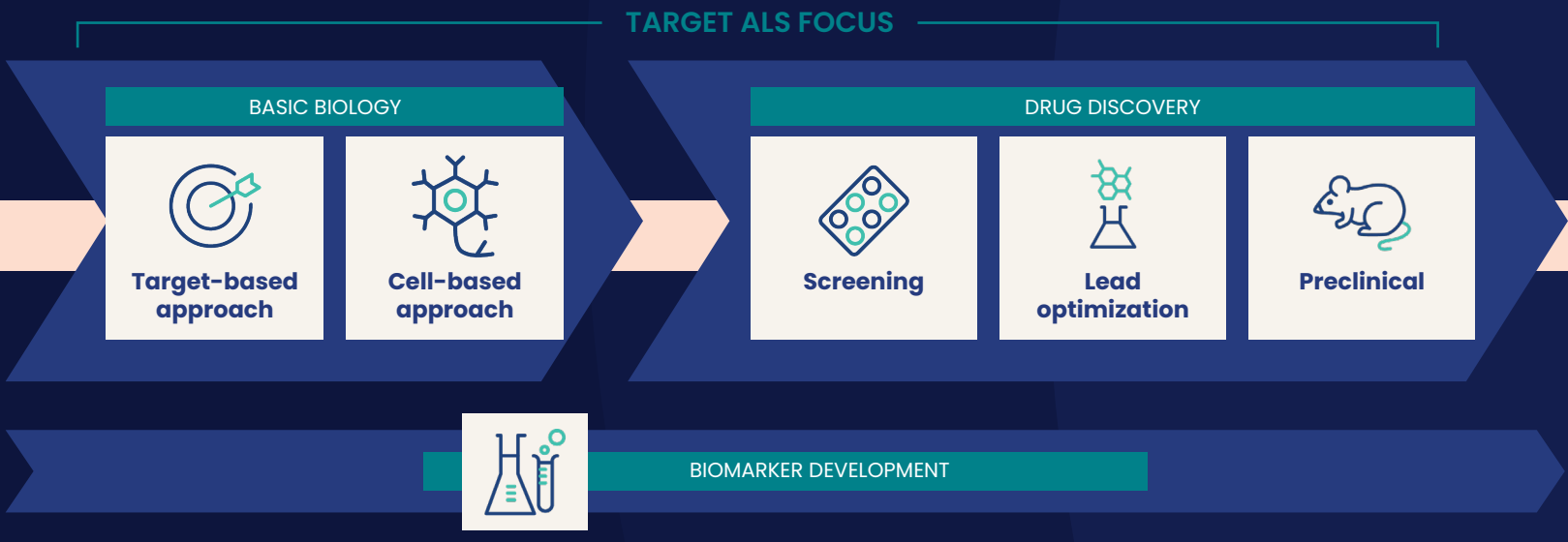
At every stage, the goal is to learn quickly and decisively. Sometimes that means recognizing which approaches should move forward. Just as often, it means identifying which ones should not. Both outcomes are successes, because each refines the path toward therapies that truly have the potential to benefit people living with ALS.

Our key focus areas and biological targets and pathways reflect this discipline: areas where the science is strongest and where new therapeutic opportunities are most likely to emerge and there is a meaningful path to clinical impact.

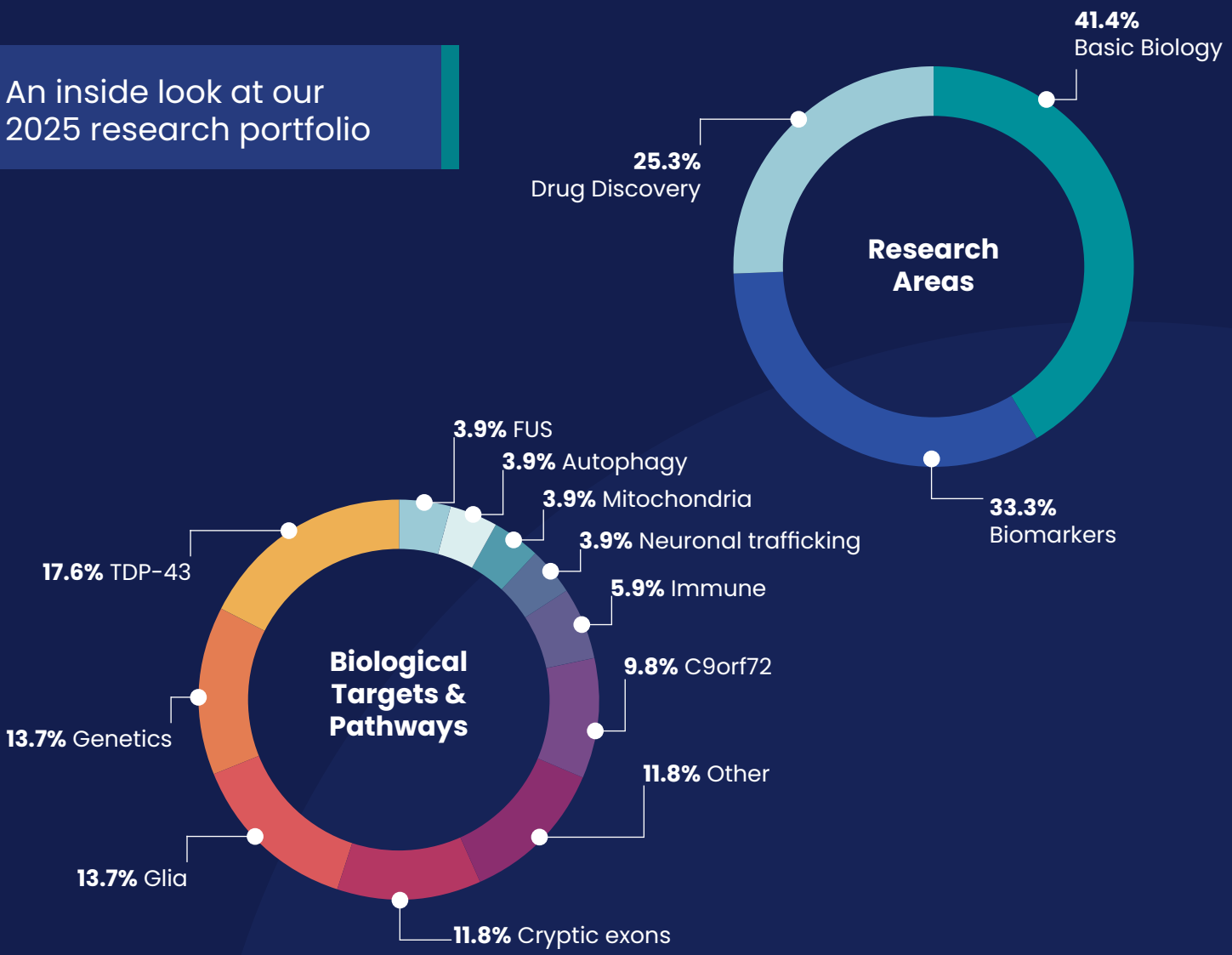
Strong targets drive strong therapies. That's why Target ALS backs research across the full biological landscape to find and validate the targets that matter.

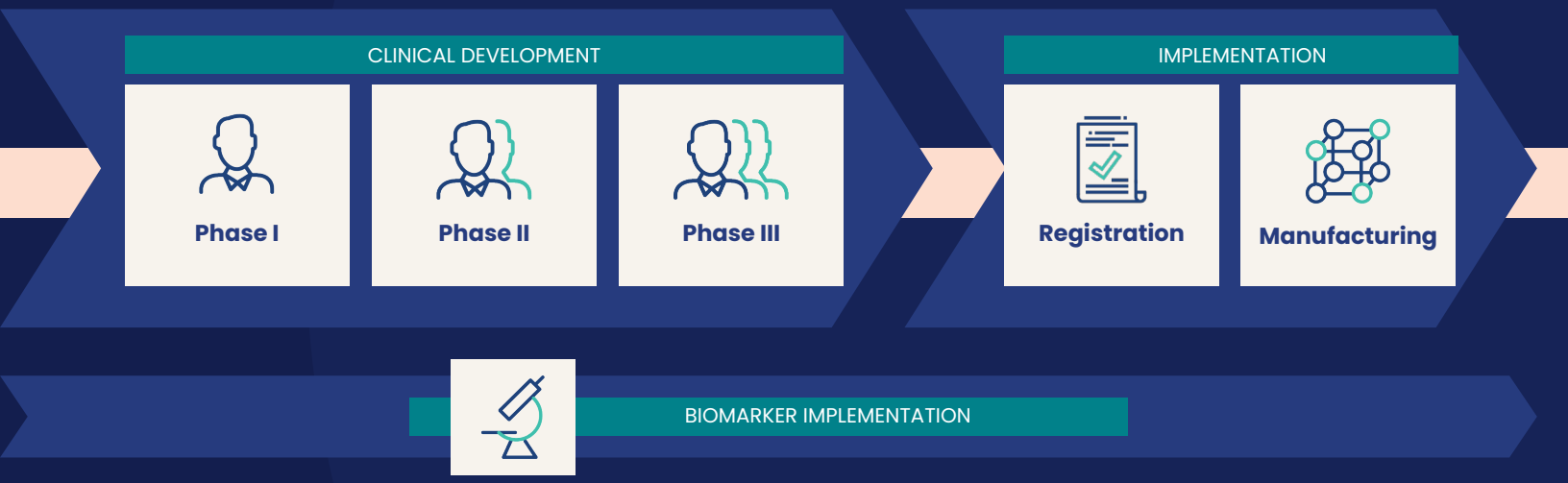


THE DRUG DISCOVERY PROCESS



An inside look at our 2025 research portfolio





FEATURED PROJECTS

Basic Biology Spotlight

Inside the Mystery of Sporadic ALS

A new Target ALS–funded consortium led by Clotilde Lagier-Tourenne is uncovering how innate immune pathways in neurons may drive sporadic ALS, the most common and least understood form of the disease. Partnering with Isaac Chiu, Brian Wainger, and Mark Albers, the team is revealing neurons as immune-active cells and identifying promising therapeutic targets already showing results in early studies.

KEY TAKEAWAY

By uniting experts across disciplines, Target ALS is advancing bold, collaborative science to unravel the mechanisms of sporadic ALS and bring new treatments closer to people with ALS.

Biomarker Development Spotlights

Tracking ALS at the Genetic Frontier

A Target ALS–funded collaboration between NeuroDex, Twilight Neuro, BrainEver Pharma, and NINDS is developing a blood-based biomarker to track transposable element (TE) activity: genetic elements that become overactive when TDP-43 loses function in ALS. By capturing neuron-derived extracellular vesicles and measuring TE levels, the team aims to monitor disease progression and treatment response across three therapeutic strategies: vaccine, protein replacement, and antiviral therapy.

KEY TAKEAWAY

This project could transform ALS care by turning a complex genetic signal into a simple blood test to guide and measure treatment effectiveness.

ALS 101

Familial vs Sporadic ALS
Most people with ALS have sporadic ALS (+90%), meaning it appears with no family history. A small portion have familial ALS, caused by inherited gene mutations. Both forms are devastating, and both urgently need better treatments.

Transposable Element
A small piece of DNA that can "jump" around the genome. Most of the time these elements stay quiet, but in ALS and other neurodegenerative diseases, they can become unusually active, which may contribute to cell stress and damage.

Clotilde Lagier-Tourenne, M.D., Ph.D.
Massachusetts General Hospital

Cracking the Code of ALS: Cryptic Exons as Early Biomarkers

The Leonard Petrucelli (Mayo Clinic, US), Michael Ward (NINDS, US) and Pietro Fratta (UCL Queen Square Institute of Neurology, UK) consortium, in partnership with BioMarin, is advancing a powerful new class of biomarkers based on cryptic peptides: molecular signatures that emerge when TDP-43, a key RNA regulator, malfunctions in ALS. Their discovery of the HDGFL2 cryptic peptide in blood and CSF could enable earlier diagnosis and better tracking of disease progression, even before symptoms appear.

VOICES OF ALS

"I think the women of Her ALS Story exemplify what it means to LIVE with ALS."

Leah Stavenhagen
Founder, Her ALS Story
Living with ALS

Diagnosed with ALS at just 26 years old, Leah Stavenhagen set out to shatter the misconception that ALS is an older white man's disease. In 2021, she established Her ALS Story, a global network of women diagnosed with ALS before the age of 35.

KEY TAKEAWAY

By transforming TDP-43 dysfunction into a measurable biomarker, this collaboration is opening the door to earlier diagnosis, faster clinical trials, and a future where ALS is a treatable condition.

Drug Discovery Spotlights

Unlocking ALS: How Cell Biology and Genetics Are Shaping New Treatments

A global team including Johnathan Cooper-Knock (Sheffield, UK), Michael Snyder (Stanford, US), Ophir Shalem (UPENN, US) and Eran Hornstein (Weizmann, Israel), is uncovering how ALS begins at the cellular level and how to intervene. Using advanced tools like AI and high-resolution imaging, they're mapping the early molecular changes that drive the disease.

A key finding centers on CCDC146, a gene that becomes overactive in ALS and affects tiny sensing structures on cells. When researchers lowered this gene using an antisense oligonucleotide (ASO) treatment, motor neurons survived longer, highlighting a promising new therapeutic target.

The team is also studying how different structures inside cells behave in ALS, revealing common patterns of damage across genetic and non-genetic forms of the disease. These insights suggest that targeting what happens inside cells may be just as important as targeting genes themselves.

KEY TAKEAWAY

By illuminating how genes and cells break down, especially around the emerging target CCDC146, scientists are identifying new, more tailored pathways for ALS treatments.

Johnathan Cooper-Knock, Ph.D.
University of Sheffield

Splice Correction of UNC13A: A New Frontier in ALS Treatment

A multi-institutional team including Ryan Morrie and Shila Mekhoubad (Trace Neuroscience), Aaron Gitler (Stanford), Sami Barmada (University of Michigan), and Noa Lipstein (FMP Berlin) is developing a promising and exciting new therapy that corrects RNA splicing errors in the UNC13A gene: a mistake seen in most ALS cases and linked to faster disease progression. By using ASOs, researchers have successfully restored normal UNC13A function in lab-grown neurons and genetically engineered mice. These corrections improved nerve cell communication, brain circuitry, and key survival markers. The team is now testing this approach in a mouse model that closely mimics human disease, laying the foundation for future clinical trials.

KEY TAKEAWAY

With early data showing restoration of neuron function and synaptic health, this work is a promising example of how understanding the genetic and mechanistic underpinnings of ALS can unlock transformative new treatments.

A New Modality in Motion: From Early Proof-of-Concept to Biotech Translation

At UCSF, Claire Clelland is pioneering a personalized CRISPR-based therapy for people with C9orf72-linked ALS and FTD. Her team has demonstrated that custom gene-editing tools can remove the toxic mutation from patient-derived neurons. Now, in partnership with Denali Therapeutics, they are developing a non-viral, IV-based delivery system to bring this treatment safely to the brain.

Target ALS first funded the early-stage, proof-of-concept work behind this ambitious CRISPR strategy, supporting Clelland's team as they showed, for the first time, that a personalized gene-editing approach could remove the toxic C9orf72 mutation in patient-derived neurons. With those foundational results in place, we have now helped transition this effort into the biotech arena, where Denali Therapeutics is advancing the next phase of development using its innovative delivery platform.

KEY TAKEAWAY

With support from Target ALS, Clelland is advancing one of the first personalized CRISPR strategies for ALS, combining proven gene-editing success with Denali's innovative delivery platform to move this bold science closer to people living with ALS.

> Every day I think about the patients who are waiting on us. **There's not a second to waste."**
>
> **Claire Clelland, Ph.D.**
> University of California, San Francisco

ALS 101

Antisense Oligonucleotide (ASO) Treatment
A small, lab-designed piece of genetic material that can turn down, turn off, or correct harmful gene activity. In ALS, ASO treatments are being developed to target specific gene mutations, helping cells reduce the toxic proteins that drive disease.

Splicing
The cell's editing process for turning raw genetic code into instructions a cell can use. It cuts out the parts of a gene that aren't needed and stitches together the parts that are. When splicing goes wrong in ALS, those "editing errors" can lead to faulty proteins that harm motor neurons.

CRISPR-based Therapy
When precise gene-editing tools are used to fix or silence the genetic mistakes that contribute to disease. In ALS, CRISPR approaches aim to directly correct harmful mutations or shut down toxic gene activity at the source, offering the possibility of truly disease-modifying treatment.

Frontotemporal Dementia (FTD)
A related neurodegenerative disease that affects behavior and language, and it shares key genetic and biological pathways with ALS.

BUILDING THE BLUEPRINT: THE GENETIC ARCHITECTURE OF ALS

Understanding the genetic architecture of ALS is essential to unlocking its underlying mechanisms and developing therapies that can slow or stop the disease at its source. From studying large multigenerational families to expanding global genomic datasets, Target ALS–funded researchers are leading groundbreaking work to uncover the variants, modifiers, and molecular pathways that drive ALS and related diseases. Together, these projects reflect our commitment to diversity, data sharing, and discovery, ensuring that the genetics of ALS is understood in every population.

Unlocking Answers in ALS and FTD: Juliana Acosta-Uribe's Groundbreaking Work in Colombia

In Colombia, where founder effects have revealed some of the world's most important genetic insights into Alzheimer's disease, Juliana Acosta-Uribe and collaborators are applying that legacy to ALS and Frontotemporal Dementia (FTD). Her team has identified several large Colombian families carrying the TARDBP Ile383Val mutation, which disrupts the TDP-43 protein, one of the key hallmarks of ALS pathology. Remarkably, some carriers develop ALS, others FTD, and others remain unaffected into old age. By combining genomic sequencing, organoid modeling, and longitudinal clinical studies, her work seeks to uncover the genetic and molecular modifiers that explain this variability.

Juliana Acosta-Uribe, M.D., Ph.D.
University of California, Santa Barbara

Key Takeaway

By studying these unique multigenerational families, Acosta-Uribe is uncovering how ancestral diversity shapes disease expression, revealing protective factors and therapeutic clues that could inform treatments for ALS and FTD worldwide.

ALS/FTD experts come together to study C9orf72 disease drivers: from genetic modifiers to toxic mechanisms

A new precompetitive consortium led by geneticist Rosa Rademakers (VIB), who first identified C9orf72 repeat expansions as the most common genetic cause of ALS and FTD, is uniting experts across both fields to unravel the drivers of C9 disease. Joined by Marka van Blitterswijk (Mayo Clinic), Adrian Isaac (University College London), and Renzo Mancuso (VIB), this team is working side by side to probe why symptoms vary so widely among people and families with the same mutation, from genetic modifiers to toxic mechanisms. This three-year initiative is designed to grow with science, with the potential to bring in industry partners or new collaborators to ensure that discoveries made in the lab translate into meaningful therapeutic development.

KEY TAKEAWAY

By uniting experts across disciplines, Target ALS is advancing bold, collaborative science to unravel the mechanisms of sporadic ALS and bring new treatments closer to people with ALS.

Unlocking ALS Risk in South Asian Populations: Inside a Groundbreaking Genetic Study Led by India and the UK

Led by Henry Houlden (University College London), Atchayaram Nalini (NIMHANS, Bengaluru), and Vishnu Venugopalan (AIIMS, New Delhi), this first-of-its-kind Genome-Wide Association Study (GWAS) is mapping ALS genetics across India, where an estimated 100,000 people live with the disease but remain largely unrepresented in global studies. The study aims to enroll 2,000 people with ALS and 2,000 controls, integrating deep clinical phenotyping, longitudinal biofluid collection, and genomic sequencing to uncover both risk and protective variants.

KEY TAKEAWAY

By bringing South Asian populations into the genetic landscape of ALS, this landmark study is closing critical gaps in representation, paving the way for precision medicine, equitable trial design, and globally relevant therapeutics.

Amy Easton, Ph.D.
Vice President, Scientific Programs, Target ALS

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Target ALS is excited to support the first GWAS study on Indian patients, led by a fantastic team of scientists. Disease genetics are not uniform across populations and historically have focused on white, European populations.

We believe that a global mindset, breaking down geographical barriers, is the path to groundbreaking research and more effective treatments for everyone.

RESEARCH WE

ENABLE

TARGET ALS RESEARCH CORES: EMPOWERING GLOBAL ALS DISCOVERY

Target ALS continues to break down barriers to progress by offering no-strings-attached access to critical tools and resources through our Research Cores. These shared resources address long-standing challenges in ALS research that have historically slowed discovery: limited access, high costs, and lack of standardization.

The Research Cores accelerate drug discovery and biomarker development while fostering collaboration across the global ALS community. In 2025, Target ALS invested over $8M to empower scientists with the materials, data, and infrastructure they need to drive progress from the bench to the clinic.

From our Postmortem Tissue Core to the Longitudinal Biofluids Core powered by our Global Natural History Study (GNHS) and open-access Data Engine, Target ALS provides researchers worldwide with state-of-the-art biosamples, datasets, antibodies, and more, with no reach-through on intellectual property (IP). These tools are available to both academia and industry, ensuring that scientific breakthroughs can move swiftly and collaboratively toward therapies for people living with ALS.

To date, more than 1,750 projects have relied on these resources, spanning basic biology, target validation, biomarker discovery, and therapeutic

TARGET ALS RESEARCH CORES

- Postmortem Tissue Core
- Longitudinal Biofluids Core
- Genomics Core
- Reagents Core
- Stem Cell Core
- Animal Models Core

development. And the momentum is only growing: over 500 researchers have accessed our Data Engine, while global consortia of preeminent scientists are working together with Target ALS funds to share data, replicate findings, and amplify impact.

At the 2025 Annual Meeting, dozens of scientists presented posters and abstracts showcasing research made possible through Target ALS's Biofluids, Postmortem Tissue, and Data Engine core resources. These projects reflect our vision to democratize ideation and innovation in ALS worldwide, empowering every qualified researcher, regardless of location or affiliation, to access the same foundational tools needed to make discoveries.

Why It's Different

The Target ALS Research Core model is unique. Unlike traditional grant-restricted or proprietary systems, our infrastructure is built on open science principles: shared access, standardized protocols, and unrestricted use.

By removing logistical and financial barriers, we've created a platform where ideas can move freely, where collaboration replaces competition, and every researcher can contribute to accelerating the development of effective ALS treatments.

Matthew Harms, M.D.
Genomics Core Advisor,
Target ALS
Associate Professor of Neurology,
Columbia University

The Target ALS Genomics Core is newly advised by Matthew Harms, an international leader in neuromuscular genetics and Associate Professor of Neurology at Columbia University. His work has identified multiple novel disease genes and advanced precision medicine approaches in ALS. The Target ALS Genomics Core represents one of the most significant investments in ALS and FTD data resources to date, bringing together the most comprehensive genomic, transcriptomic, and proteomic data from across all Target ALS collections into a single, accessible platform: the Target ALS Data Engine.

VOICES OF ALS

"It's not about what I've lost...

It's about what I still have."

Venky Krishnaswamy
Living with ALS

After his ALS diagnosis in 2024, tech entrepreneur Venky Krishnaswamy brought the same strategic mindset that defined his career to reimagining how ALS research and drug development could move faster and smarter. Grounded in what he calls "the magic of now," Venky has become a powerful advocate for open data, global representation, and AI-driven approaches that can transform the economics of therapy development. By bridging technology, patient experience, and collaboration, he is helping push the ALS field toward a more connected and effective future.

Core Spotlights

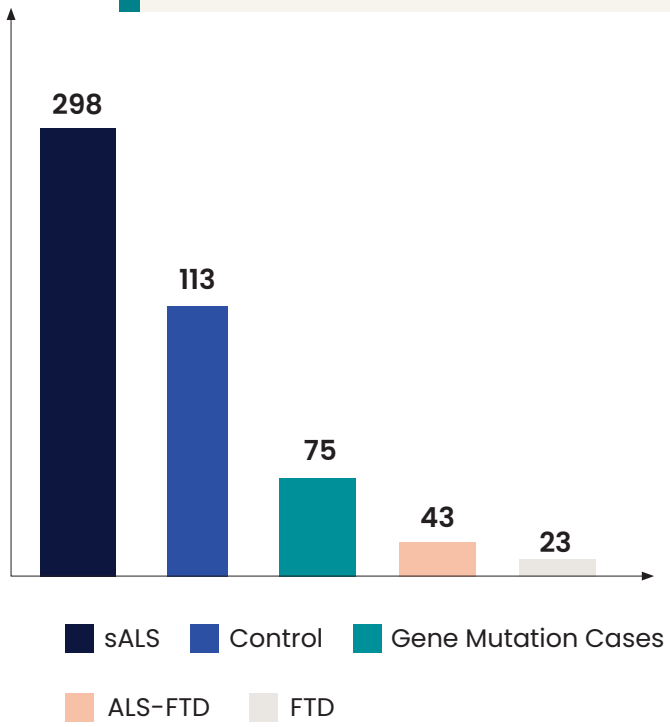
Postmortem Tissue Core: The Gold Standard for ALS Research

The Target ALS Postmortem Tissue Core has been a cornerstone resource since 2014 for ALS research, providing brain and spinal cord tissues that are uniquely valuable for studying the disease at the cellular and molecular level. These samples allow scientists to track disease progression, understand genetic influences, and identify therapeutic targets – insights that cannot be gained from other models.

Built through contributions from six leading ALS research institutions and expert neuropathologists, the Core has now grown to 534 cases, including 75 gene mutation cases, making it the largest ALS tissue repository in existence. Since its launch in 2014, the Core has steadily expanded its reach and capabilities. In 2025, it filled 50 requests, nearly one every week, supporting researchers around the world in their search for new answers.

One of the most exciting recent examples of how this resource accelerates progress is its role in the development of [18F]ACI-19626, a first-in-class PET tracer designed to visualize TDP-43, the protein that misbehaves in most ALS cases. Target ALS scientists provided guidance on the tissue needed to validate this tool. For people with ALS and their clinicians, this tracer could eventually make it easier to identify TDP-43-driven disease in living patients and match them to future therapies aimed at preventing this protein from clumping, moving to the wrong place, or malfunctioning.

The Target ALS Postmortem Tissue Core Case Collection



Scan the QR code to read the full paper on the PET tracer that Target ALS postmortem tissue helped validate:

Target ALS Research Core Team at the 2025 Annual Meeting

Unlocking Hidden Signals: The Next Frontier in ALS Biomarkers

With support from Target ALS and powered directly by tools and materials from the Target ALS Reagents Core, Leonard Petrucelli (Mayo Clinic Jacksonville) and Nicholas Ashton (Banner Health Foundation) are advancing research on cryptic peptides, the abnormal proteins that appear when TDP-43 malfunctions, a defining feature of ALS. Using these high-quality reagents, the team is able to sensitively detect and measure cryptic peptides, accelerating efforts to evaluate them as early, non-invasive biomarkers that could help diagnose ALS sooner, track disease in real time, and monitor whether treatments are working. By pursuing cryptic peptides as a new class of biomarkers, this research has the potential to change how ALS is detected and managed, opening the door to earlier intervention and more personalized care.

Leonard Petrucelli, Ph.D.
Mayo Clinic Jacksonville

VOICES OF ALS

"Life is always worth living, despite all you're facing. Even in the hardest moments, there is still space for gratitude, love, and hope."

Raquel Pozzani
ALS Caregiver and Family Member

When Raquel Pozzani's father, Valdir, was diagnosed with ALS, her family's life changed almost overnight as his health declined rapidly from an active cyclist to being bedridden. Amid profound grief, they found resilience in small moments, leaning on faith, family, and a community that showed up when it mattered most. Inspired by the urgency and dedication of Target ALS–supported scientists, Raquel is now working to help expand ALS research and clinical trials in Brazil, so more families can hold onto hope.

Sadly, Valdir passed away in December 2025 from ALS. Following his passing, Raquel shared "The love will never change – it will only change form. I am deeply sad, but also deeply thankful. What a wonderful soul I was blessed to have as a father. His legacy will continue."

VOICES OF ALS

"It's easy to lose hope when you have ALS, but knowing that people are doubling down on meaningful research makes me hopeful."

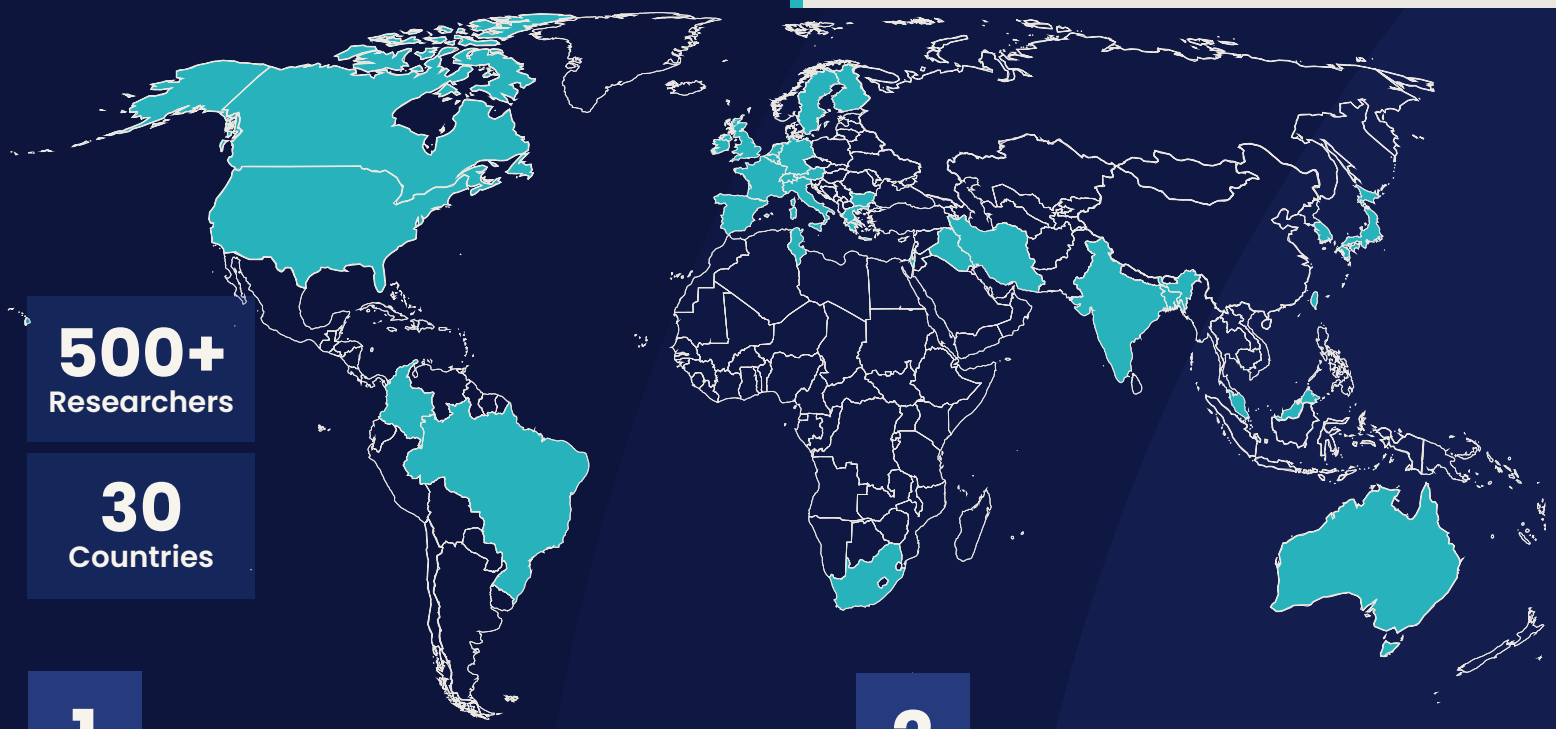
Brooke Eby
Living with ALS

Diagnosed with ALS at 33, Brooke Eby turned a life-altering moment into a powerful platform for change, using humor and radical honesty to make ALS impossible to ignore. Through viral storytelling and a rapidly growing community, she has helped humanize the disease, challenge outdated perceptions, and mobilize action at scale. To date, Brooke has raised more than $1 million for ALS research, including an ALS Awareness Month campaign in support of Target ALS in May.

POWERING PROGRESS:
THE TARGET ALS DATA ENGINE

The Target ALS Data Engine, now used by more than 500 researchers worldwide, continues to expand as the leading open-access hub for ALS research, delivering transformative datasets that accelerate discovery. **In 2025, three landmark initiatives pushed its impact even further.**

Geographic Representation of Data Engine Users



500+
Researchers

30
Countries

1

Proteomics Data Available in the Data Engine

The first batch of proteomics data from the GNHS is now complete and available on the Target ALS Data Engine. Generated by Johan Gobom and Henrik Zetterberg's team at the University of Gothenburg using the advanced TMTpro 35-plex method, the dataset includes about 2,000 proteins and 12,000 peptides from spinal fluid and plasma of ALS patients and healthy controls. Linked with longitudinal cognitive, motor, and clinical data, this powerful resource will accelerate biomarker discovery, validate emerging findings, and spark new research directions through global collaboration.

2

Launching the Largest Single-Cell Dataset for ALS

In partnership with Panos Roussos and his team at the Icahn School of Medicine at Mount Sinai, we are preparing to release the largest single-cell dataset ever generated for ALS research. This pioneering resource, RNA sequencing from tens of thousands of individual cells across brain and spinal cord regions in ALS, FTD, and control cases, will allow scientists to explore the disease at unprecedented resolution. Public release is planned for the first half of 2026.

Radical Data Collaborations

With HiFi Solves

Target ALS is also a member of HiFi Solves, a global consortium designed to maximize the power of long-read sequencing. Unlike short-read methods, which provide only fragmented views of the genome, long-read sequencing offers a complete, high-resolution picture, revealing repeat expansions and complex regions that are often where ALS hides.

By harmonizing our HiFi data with DNAstack and connecting it to 15 other research groups across the U.S., researchers can now "mine" all datasets simultaneously. This means they can quickly test hypotheses, rule out false signals, and identify genetic patterns that would be invisible in smaller, siloed datasets. What once took decades can now be compressed to just a few years.

Across Neurodegenerative Diseases

Target ALS is privileged to work alongside Michael J. Fox Foundation, ASAP, 10,000 Brains, the AD Data Initiative, and the Ontario Brain Institute to tackle the key barriers to effective sharing of large datasets across traditionally siloed research domains. The 2025 Private Funders' Parkinson's Disease and Related Disorders (PDRD) Data Interoperability Summit brought together technical leaders from North American-based private funders and research organizations engaged in large-scale neurodegenerative data efforts to address these challenges through the lens of FAIR (Findability, Accessibility, Interoperability, and Reusability) principles. Continued work in this area promises to accelerate discovery and innovation, with the potential to drive significant breakthroughs in the understanding, diagnosis, and treatment of neurodegenerative diseases.

3

Genomic Breakthroughs Begin Here

Target ALS has joined forces with PacBio to launch the largest ALS long-read whole-genome sequencing study to date. More than 6,000 genomes will be sequenced using PacBio HiFi technology, uncovering structural variants and hidden mutations that standard methods cannot detect. As part of our ALS Global Research Initiative (AGRI), all data will be openly shared via the Data Engine, removing barriers and enabling discovery worldwide.

In 2025, the Target ALS Data Engine provided researchers the tools to uncover and act on new insights faster than ever before. By removing logistical and financial barriers, we've created a platform where ideas can move freely, where collaboration replaces competition, and every researcher can contribute to accelerating the development of effective ALS treatments.

RESEARCH WE

CONDUCT

THE ALS GLOBAL RESEARCH INITIATIVE: PIONEERING ALS RESEARCH ACROSS THE GLOBE

ALS is a disease that affects people of every race and ethnicity around the world. However, clinical trials enroll primarily people of white, European descent resulting in a biased, incomplete view of disease biology across the ALS global population. The ALS Global Research Initiative (AGRI) is the only comprehensive, global research effort that brings together two complementary clinical studies designed to uncover the causes of ALS and identify new biomarkers that can diagnose the disease earlier, track its progression, and predict outcomes.

These studies provide researchers unprecedented access to patient data and biosamples worldwide, rapidly accelerating new discoveries and driving progress toward more effective therapies. Ultimately, inclusive research strengthens scientific validity, improves patient outcomes, and helps ensure that breakthroughs benefit everyone, not just a subset of the population.

Throughout the year, we invested over $1.5M, which fueled AGRI's bold goal: bring the world together to tackle ALS from every angle. Through our Global Natural History Study (GNHS) and Community-Based Pop-Up Clinics, we're making ALS research more inclusive, more immediate, and more collaborative than ever before.

In 2025, we launched the AGRI webpage, a central resource showcasing our groundbreaking efforts to diversify and expand ALS research globally.

A participant providing a blood sample at the Target ALS Community-Based Pop-Up Clinic in partnership with ALS Arizona in Phoenix.

Reflections on the Research We Conduct

Amy Easton, Ph.D., Vice President, Scientific Programs, Target ALS

AGRI is removing geographical, language, and financial barriers to participating in ALS research. In 2025, we were thrilled to see the AGRI deliver data that is truly driving the field forward. True to our mission, 36% of study participants identify as non-white and of non-European descent, representing a big improvement over the average 5% often reported. Multi-omic datasets have already been accessed by more than 500 researchers around the world. Our partnership with renowned biomarker experts has delivered the first high-quality proteomic datasets from the study, resulting in identification of new disease biomarkers and independent replication of previously identified candidates. Biofluids distributed from the study have been used to identify new biomarkers to facilitate early diagnosis and more effective clinical trials. These findings were presented at the PanAsian Consortium for Research and Treatment conference, the International ALS/MND Symposium in San Diego, and the International Alliance of ALS/MND Associations in Toronto, deepening our ties to the global research community.

THE GLOBAL NATURAL HISTORY STUDY

The Target ALS Global Natural History Study (GNHS) continues to grow as a cornerstone of global ALS research. Across 14 active sites worldwide, the study has now collected more than 30,000 blood, urine, and spinal fluid samples, with whole-genome sequencing performed on every patient's blood sample. In 2025, we introduced long-read sequencing, a powerful new technology that can detect genetic risks missed by older methods. All data generated is freely shared through the Target ALS Data Engine.

To strengthen our global reach, new collection sites launched in Puerto Rico, Colombia, Israel, and South Korea, with Malaysia anticipated next. Importantly, samples representing non-Caucasian ancestry increased from 10% in 2023 to 36% in 2025, expanding the diversity of the repository.

With broader global participation and cutting-edge sequencing, the GNHS is building one of the most diverse and powerful ALS data resources in the world, bringing us closer to unlocking the underpinnings of the disease for all people.

COMMUNITY-BASED POP-UP CLINICS

Many people living with ALS, especially those from underserved communities, face barriers that make it difficult to take part in research, including financial challenges, limited access to care, lack of information, and the burden of traveling to specialized clinics. To help bridge this gap, Target ALS launched a series of community-based pop-up clinics in partnership with local ALS centers and organizations.

Through these one-time blood collection events, the study aims to enroll about 5,000 individuals living with ALS and 1,000 healthy controls. Each participant provides a single blood sample and completes an environmental questionnaire, offering a simpler, more accessible way to contribute to research. By expanding who can participate, these clinics are helping ensure that future ALS treatments are safe and effective for everyone.

In 2025, we saw progress through two community-based pop-up clinics in Arizona. Earlier in the year, our second pop-up clinic in Phoenix took place on Rare Disease Day, February 28, drawing both people with ALS and healthy volunteers to contribute to the study. By the end of the day, 23 participants had joined, underscoring the appetite for accessible research opportunities within local communities.

In September, Target ALS hosted its third AGRI Pop-Up Clinic in partnership with ALS Arizona, bringing an opportunity to participate in research directly to the Tucson community. The event invited both people living with ALS and healthy controls to contribute blood and saliva samples, which are then analyzed.

A participant providing a blood sample at the Target ALS Community-Based Pop-Up Clinic in partnership with ALS Arizona in Tucson.

VOICES OF ALS

"Give every day the chance to become the best of your life."

Peter Ambühl
Living with ALS

After an unexpected fall while skiing led to an ALS diagnosis in 2019, Peter Ambühl chose action over fear, pursuing genetic testing that opened the door to a targeted clinical trial in Utrecht. Together with his wife, Bettina, he reframed research participation as an act of hope, believing that every study, even those with negative results, moves the field closer to effective treatments. Seven years on, Peter continues to champion community, collaboration, and the conviction that research is the way forward.

Target ALS is proud to be leading the first ever in-community outreach events to accelerate our understanding of genetic and environmental risk factors for disease.

If we want effective treatments for everyone with ALS, we need research that includes everyone. Community outreach events like this are making that possible — one blood sample at a time."

Laura Dugom, MPH
Associate Director of Clinical Research,
Target ALS

All data become immediately available to scientists in our effort to accelerate discovery through globally diverse datasets and our bold use of long-read sequencing to identify novel genetic risk factors of ALS.

What made the Tucson event stand out was the community's engagement; participants not only donated samples but shared ideas and questions that will help shape future research. As CEO Manish Raisinghani noted, "The voices of people living with ALS, alongside their families and healthy volunteers, guide us in shaping research that is not only scientifically rigorous but also deeply human."

By lowering barriers to participation, AGRI Pop-Up Clinics are helping build a faster, more inclusive research ecosystem: one that reflects the diversity of those impacted by ALS and ensures future treatments are safe and effective for everyone.

VOICES OF ALS

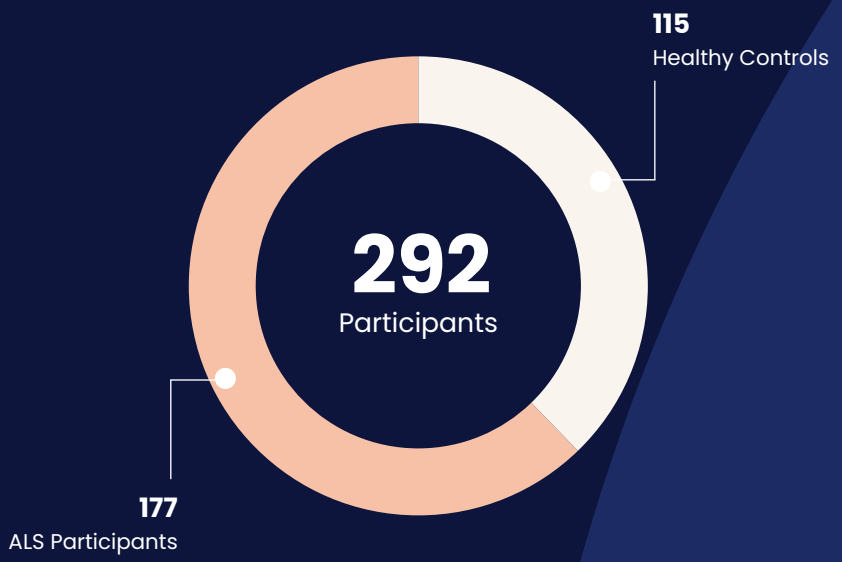
"Our voices matter in shaping global ALS science."

Premana Wardayanti Premadi

Founder, Indonesian ALS Foundation
Living with ALS

After being diagnosed with ALS in 2010, Indonesian astronomer Professor Premana W. Premadi confronted a startling reality: in her country, ALS was almost entirely invisible. What began as a personal blog translating medical information into Indonesian grew into the Indonesian ALS Foundation, now a critical lifeline connecting patients, families, doctors, and researchers across the country. Through science-driven advocacy, Premana has helped bring ALS into the national conversation while calling for global research that reflects genetic, geographic, and environmental diversity.

GLOBAL NATURAL HISTORY STUDY
BY THE NUMBERS



30,000+
Vials of biofluid samples collected

3,200+
Vials of biofluid samples distributed

24
Biofluids requests approved

14 sites worldwide

COMMUNITY-BASED POP-UP CLINICS
BY THE NUMBERS

3 partner events/ locations

1.
Standing Clinic
Los Angeles, CA
Kaiser Permanente

2.
One Day Event
February 2025
Phoenix, AZ
ALS Arizona

3.
One Day Event
September 2025
Tucson, AZ
ALS Arizona

97
Participants enrolled to date

66
Whole genomes have undergone long-read sequencing

100%
of data immediately available for research

DIVERSITY IN AGRI

36%

of participants are from diverse backgrounds

compared to just 5% in other ALS studies

"If we can do the research, hopefully we will find treatments for this disease.

It may not help me, but it may help someone else."

Regina Dahl
Living with ALS
Community Pop-Up Clinic Participant

TARGET ALS ANNUAL MEETING

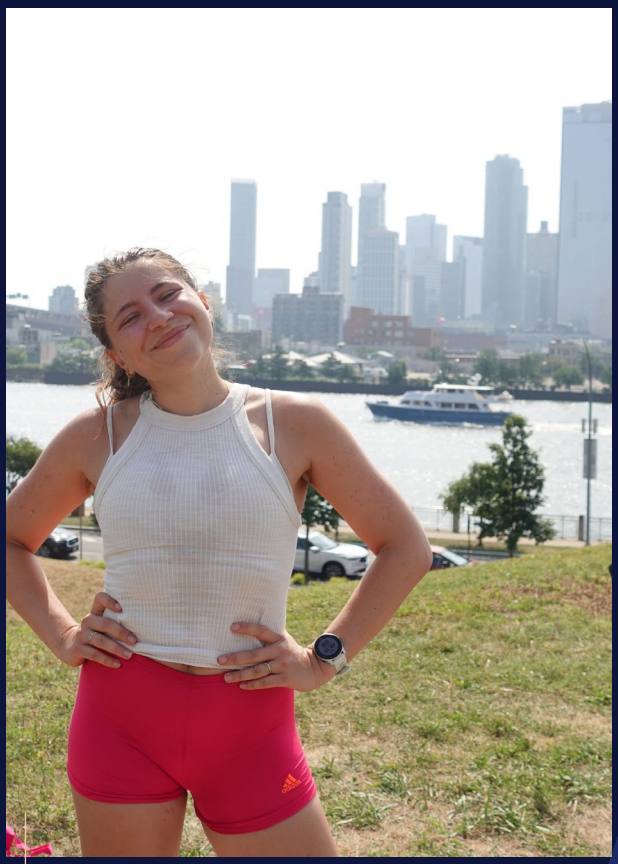
FORGING COLLABORATIONS
TO ADVANCE ALS RESEARCH

The 2025 Target ALS Annual Meeting demonstrated unprecedented momentum across ALS research, uniting more than 960 attendees from academia, industry, and the ALS community to showcase breakthrough science driven by Target ALS's unique model of funding, enabling, and conducting research. Over three days, researchers presented encouraging progress in drug discovery, biomarker development, and basic disease biology, with many projects funded within the past year already advancing toward clinical translation. Key themes included the rise of genetically informed therapies, emerging non-invasive biomarkers to accelerate trials, increased global diversity in the Target ALS research infrastructure, and collaborative consortia dismantling barriers that once slowed progress in ALS. The meeting reinforced Target ALS as the central hub of innovation in the field and highlighted a growing sense of urgency, optimism, and shared purpose toward the vision that Everyone with ALS Lives.

The Annual Meeting Impact Report highlights key advancements, such as new efforts to identify early biomarkers for diagnosis, real-time data sharing across our 14 international GNHS sites, and cutting-edge technologies being used to track disease progression and uncover new treatment targets. It's worth a read to understand where the field is headed next and how Target ALS is continuing to break down barriers to speed up discovery.

Scientists listening to a presentation at the 2025 Target ALS Annual Meeting.

Scan the QR code to download the full Annual Meeting Impact Report



Neuroscientist and ultramarathoner Sophie Imhof runs every mile for those who can't.

Pictured here with his wife Beth, Geoff Greulich aims to raise an incredible $1 million for ALS research.

The Mighty Mapes, a devoted group of high school classmates of Target ALS founder Dan Doctoroff, have rallied together to raise $100,000 for ALS research in Dan's honor.

Team Target ALS runner Alex Shapos celebrating with his medal after completing the 2025 TCS New York City Marathon.

FUNDRAISING FOR TARGET ALS: COMMUNITY ACTION

This year, individuals across the Target ALS community turned compassion into action, running marathons, sharing their stories, and rallying their networks to fuel the search for effective ALS treatments. Their creativity, courage, and commitment remind us that every voice, every mile, and every dollar raised brings us closer to a world where everyone lives.

Brooke Eby: Hope in Action

Diagnosed with ALS at 33, Brooke Eby turned her story, and unmistakable humor, into a movement. With 330k+ Instagram followers and national media attention, she's humanized ALS for a new generation and inspired record giving. In May, she rallied her community for Target ALS, raising her cumulative impact on ALS to over $1 million. As Brooke says, "In Dan we trust," pointing to founder Dan Doctoroff's vision and the momentum Target ALS is building toward effective treatments.

Geoff Greulich: Going for the Goal

When Geoff Greulich was diagnosed with ALS in 2023, he refused to step back. A former executive and college athlete, Geoff launched an ambitious campaign to raise $1 million for Target ALS, inspired by Dan Doctoroff and our bold approach to accelerating discovery. "ALS has taken a lot from me, but it hasn't taken my determination," Geoff shared. With his wife Beth leading alongside him, Geoff is once again "going for the goal", channeling perseverance, grit, and strength into a legacy that will advance ALS research for years to come.

Sophie Imhof: Running for Those Who Can't

Neuroscientist and endurance athlete Sophie Imhof brings the grit of the lab to the trail, raising funds and awareness with every mile. After a decade working in ALS research, from Vienna to Stanford to New York, she believes it's no longer "if," but "when" we'll find effective treatments. Sophie's next challenge is the 55 km Arizona Canyon Ultra on March 6, 2026, running in honor of people who can't. Her message is simple: every step, and every donation, moves ALS research forward.

2025 TCS New York City Marathon: Team Target ALS

Target ALS was named an Official Charity Partner for the 2025 TCS New York City Marathon held on November 2, 2025. Our charity bibs and independent runners raised critical funds and visibility for a future where Everyone Lives. Meet a few of our 2025 runners: Lori Berko, Alison Crawford, Alexander Shapos, Susan Griffin, and Andrew Beck, who turned every mile this year into momentum for ALS research.

Mighty Mapes

The Mighty Mapes are a devoted group of high school classmates of Target ALS founder Dan Doctoroff from the Class of 1976. United by decades of friendship, they rallied around Dan to raise $100,000 in support of Target ALS, both to advance the mission and to honor the bond they share with him.

For the Mighty Mapes, Dan is the heart and soul of their group. Their gift is a powerful expression of their love, admiration, and gratitude for a truly remarkable lifelong friend. With steadfast commitment, they will continue to do all they can and will hold on to hope and prayer for a future where Everyone Lives.

FUNDRAISING FOR TARGET ALS: AMPLIFYING OUR MISSION

Short Film Premiere: Everyone Lives: Turning Vision into Reality

What happens when one man refuses to accept that ALS is unbeatable? "Everyone Lives: Turning Vision Into Reality" tells the story of how Target ALS Founder Dan Doctoroff turned personal loss into a global movement to transform ALS research. The short film, which premiered on October 29, revealed for the first time how Dan's vision, to build a world where everyone with ALS lives, sparked a new era of collaboration and discovery at Target ALS.

Scan the QR code to watch the premiere:

2025 Year-End Campaign: Ending ALS Starts With You

In 2025, Target ALS executed its most ambitious and integrated year-end fundraising campaign to date, built around a unifying theme: Ending ALS Starts with You. Throughout November and December, we shared powerful stories of hope, progress, and the breakthroughs you make possible. Because of you, we're one step closer to a world where everyone with ALS can live, a reminder that meaningful progress begins when we all come together.
A highlight of this year's campaign was the involvement of Eric Dane, acclaimed actor and person living with ALS, who served as our year-end spokesperson. His authenticity and personal connection to this disease brought tremendous visibility and heart to the campaign, inspiring many to engage, give, and amplify our mission. During the campaign, Eric joined the Target ALS Board of Directors to further his dedication to our mission.

We set an ambitious goal to raise $500,000 to advance our mission priorities and position us for a strong start in 2026. Thanks to your generosity, we surpassed that goal and we're now looking ahead with renewed momentum and optimism for the year to come.

"This is not the end of my story. **This is not the end of me.**"

IN CASE YOU MISSED IT

Target ALS thought leaders and experts participated in several panel discussions and webinars throughout the year. You can catch all of the recordings on demand.

CASE STUDY

Dan Doctoroff and the Power of Collaboration: Target ALS Accelerates the Race Against a Deadly Disease

The Harvard Kennedy School has released a new teaching case spotlighting how one man's vision and a culture of radical collaboration transformed ALS research. Now part of the Harvard Kennedy and Business School curricula, the case presents Target ALS as a blueprint for how strategic philanthropy and systems thinking can drive lasting change in science and beyond.

WEBINAR

Targeting ALS: Inside the Mission

Featuring Manish Raisinghani, M.B.B.S., Ph.D., & Amy Easton, Ph.D., Target ALS

WEBINAR

Introduction to the ALS Global Research Initiative

Featuring Laura Dugom, MPH, Target ALS, & Bjorn Oskarsson, M.D., Mayo Clinic

PODCAST

Nothing Left Unsaid Featuring Dan Doctoroff

Featuring Tim and Troy Green, Nothing Left Unsaid, & Dan Doctoroff, Target ALS

WEBINAR

Target ALS: Advancing ALS Research with Modality.AI

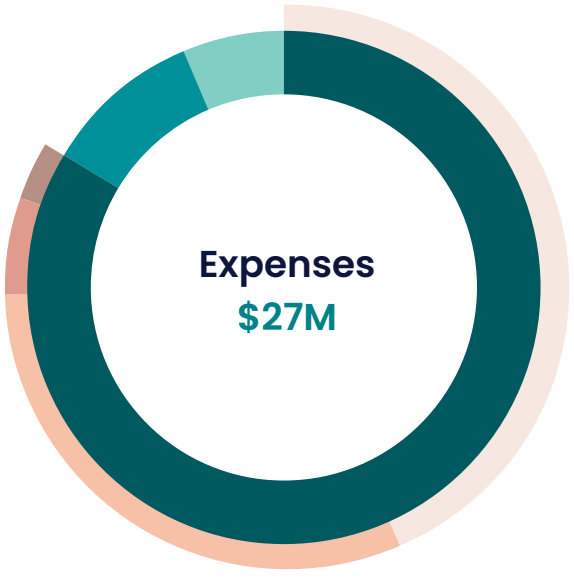
Featuring David "DSO" Suendermann-Oeft, Ph.D., Modality.AI,
& Amy Easton, Ph.D., Target ALS

PROJECTED 2025 FINANCIALS

At Target ALS, we are committed to the highest level of financial responsibility and transparency. Your donations propel our mission to break down barriers to ALS research and find effective treatments.

The summary below represents projected financials for 2025. Audited financial reports will become available on our website in early 2026.

- **Contributions and Grants** $29,120,345
- **Investment Earnings** $5,241,085
- **Other** $892,016



- **Research** $22,594,807
  - **Fund** $11,761,726
  - **Enable** $8,355,054
  - **Conduct** $1,564,957
  - **Science Operations** $913,070
- **Administrative** $2,718,484
- **Fundraising** $1,659,016

TARGET ALS TEAM

Board of Directors

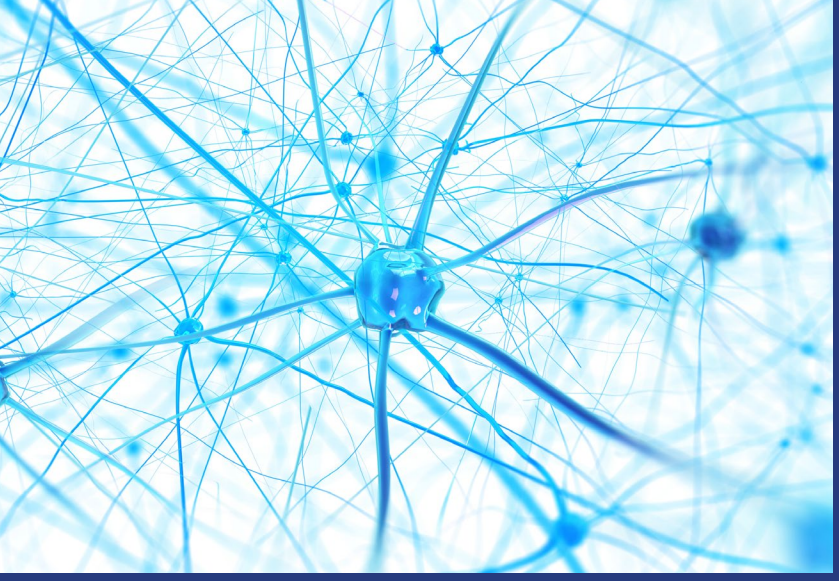
Dan Doctoroff, Founder and Chair
Andy Berndt
Eric Dane
Alisa Doctoroff
John Dunlop, Ph.D.
Steven Gruber
Zach Hall, Ph.D.
Richard Hargreaves, Ph.D.
Chris Henderson, Ph.D.
Carole Ho, M.D.
Allison Jaffin
Brad Karp
Story Landis, Ph.D.
Sarah Sheikh, BM BCh, MSc, MRCP
Stacie Weninger, Ph.D.

Staff

Jessica Chapman, MBA, CAP
Courtney Christa
Michael R. DeChellis-Marks, Ph.D.
Kenneth Devaney
Laura Dugom, MPH
Amy Easton, Ph.D.
Aiden Hipwell, MBA
Ruby Hoglund
Stephanie Ishoo
Ariella Leicht
Christine Aranyos Prouty
Manish Raisinghani, M.B.B.S., Ph.D.
Clint Ramnarine
Yuliya Rzad, MPA
Burhan Siddiqui
Tammy Sutherns, MPH
Daniel Weatherill, Ph.D.

Target ALS Board at the 2025 Annual Meeting

Target ALS Staff at the 2025 Annual Meeting



BUILDING A WORLD WHERE EVERYONE LIVES

As 2025 comes to a close, we extend our heartfelt thanks to you for standing beside Target ALS and helping us make meaningful strides in ALS research. This progress is only possible because of the collective strength of the ALS community, researchers, donors, and partners, united in a shared mission. Together, moving in the same direction, we are turning what once felt impossible into real progress toward a future where ALS is no longer a terminal diagnosis, but a disease people can live long, quality lives with.

Looking ahead to 2026, our belief has never been stronger that effective treatments for everyone with ALS are within reach. We will continue to fund the most promising ideas and empower the next generation of scientific leaders worldwide. Our commitment to innovation endures, and we will advance discovery in three critical areas: deepening our understanding of ALS biology, accelerating drug discovery, and developing biomarkers that enable earlier diagnosis and more precise care.

We will also expand investment in our Research Cores, shared resources that remove barriers of access, cost, and standardization, ensuring that every scientist has the tools needed to spark breakthrough discoveries. And through our ALS Global Research Initiative (AGRI), we will continue to pioneer research worldwide, uniting the international ALS and scientific communities through clinical studies to uncover the causes of ALS and identify biomarkers that can change the trajectory of this disease.

ALS is devastating, and at times it can feel unyielding. But at Target ALS, we are relentless. We are determined to stop this disease from devastating families and taking away those we love. We are building a future where an ALS diagnosis is no longer fatal. Thank you for joining us on this journey. Together, we will achieve our vision: Everyone Lives.


TARGET
ALS